YOUNG INVESTIGATORS MEETING

YIM2024

ABSTRACT BOOK

EMERGE

10-11th September 2024 - VGR Campus Konferens
Nya varvet - Gothenburg
Sweden

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Oral Communications

13:30-14:50---SESSION I- (JIA, SJIA, Macrophage activation syndrome)

13:30-13:40 - Jelleke B. De Jonge (Netherlands)

HARNESSING THE WINDOW OF OPPORTUNITY IN CHILDHOOD ARTHRITIS: RESULTS FROM THE UCAN CANDU STUDY

J. B. De Jonge [1 2,*], S. de Roock [1], S. J. Vastert [1 2], R. S.M. Yeung [3], D. Marshall [4], J. F. Swart [1], S. M. Benseler [5 6] on behalf of on behalf of the UCAN CAN-DU consortia.

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Introduction: Childhood arthritis (Juvenile Idiopathic Arthritis, JIA) is the most common chronic rheumatic disease carrying a dramatic individual and societal burden. Biologic therapies can effectively target inflammatory pathways, control joint inflammation, and prevent disability. Recent studies suggested a window of opportunity, in which early precision treatment start may result in rapid and sustained remission.

Objectives: To determine the timing of starting biologic therapies for childhood arthritis across two countries, compare practice patterns, and analyse their impact on achieving a state of inactive disease.

Methods: The international UCAN CAN-DU study prospective enrols children with arthritis across Canada (CAN) and the Netherlands (DU) since 2018. This nested cohort study included consecutive, biologic-naïve non-systemic patients at start of biologics and observed for six months. Baseline characteristics including demographics, ILAR JIA subtype, active joint counts and extraarticular features were captured, as well as biologic pathway and selected biologic therapies. Time to biologic treatment was defined as time from symptom onset to the start date of the first biologic. Outcome: Inactive disease at six months defined as evidence of no active joints while maintaining in the initial biologic treatment. Analysis: descriptive statistics, comparative analyses.

Results: A total of 188 children from 13 centres were included; 75% were Dutch patients. Overall, these were 119 girls (63%), median age was 9.6 years (4.1,12.6). JIA subtype per country: CAN - 45% poly, 32% ERA, 22% oligo/psoriatic versus DU - 43% poly, 19% ERA, 37% oligo/psoriatic. The predominantly targeted biological pathway was TNFα in both countries (96%). Significant differences were found for generic medication versus biosimilar between countries, with higher biosimilar use in CA (p10 patients

included) started at 34 weeks (IQR: 22-93) late centres at 131 weeks (IQR: 59-259). Window of opportunity: The rate of inactive disease was the highest in children receiving biologics early (<6 months, 78%) compared to intermediate (6-12 months, 63%) and late biologics starters (12-24 months, 56%).

Conclusion: Childhood arthritis has a window of opportunity. Early start of targeted biologic therapies controls joint inflammation in 4 out of 5 children with arthritis at six months. Potential individual and treatment associated risk factors and biologic signatures need to be determined to further advance the effectiveness of precision therapies.

13:40-13:50 - Ana Isabel Rebollo-Gimenez (Spain)

SEEKING FOR PREDICTORS OF INACTIVE DISEASE IN JUVENILE IDIOPATHIC ARTHRITIS WITH ARTIFICIAL INTELLIGENCE

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Introduction: The achievement of inactive disease (ID) is the goal of contemporary treatment strategies in all patients with juvenile idiopathic arthritis (JIA). Complete disease quiescence is regarded as the ideal therapeutic goal as its attainment helps to minimize pain and disability associated with active disease, prevent articular and extraarticular damage, and improve the quality of life of children and their families. Artificial intelligence is a powerful tool that is well suited to identify the variables that are of foremost relevance to predict a desired outcome. Objectives: The aim of our study is to seek for the disease parameters that have the best ability to predict the achievement of the state of ID at 24 months using artificial intelligence methods.

Methods: The clinical charts of all consecutive patients with JIA by ILAR criteria who were first seen at study centre within 6 months after disease onset between 2007 and 2019 and had follow-up visits at 6, 12, 18, and 24 months after initial evaluation were reviewed retrospectively. Demographic parameters, clinical features (including physician-centred and parent-reported outcomes), laboratory tests and prescribed therapy were collected at all visits and entered into an excel dataset. ID was defined by 2004 Wallace criteria. The Last Observation Carried Forward (LOCF) and posteriorly Baseline Observation Carried Forward (BOCF) methods were used to impute missing values. Patients in whom imputation could not be performed with these computational techniques were excluded. Data recorded at baseline and at 0-, 6- and 12- month follow-up visits were included in the analysis of prediction of achievement of ID at 24 months. The study cohort was divided into two subsets:a training set (50%) and a test set (50%). Multivariate time series forecasting was applied to the longitudinal data

through the Light Gradient Boosting Machine (LightGBM) method using the Scikit-learn with mlforecast to train and test the predictive model. Features were ranked by importance to determine their relative impact on achievement of ID. Hyperparameter tuning was carried out using the optuna package. Matthews correlation coefficient (MCC) was used as a metric to assess model performance. The entire analysis procedure was implemented in Python.

Results: Of the 449 patients who had their initial evaluation within 6 months after disease onset at study centre in the study period, 294 had longitudinal assessments available. 147 patients were randomly allocated to the training set and 147 to the test set. For each follow up visit 74 features were collected. By applying the mlforecast method coupled with LightGBM algorithm, we obtained 71% of MCC in the training set and 69% in the test set, which indicated a strong ability of our artificial intelligence model to predict the state of ID from the identified clinical variables at 0, 6 and 12 months. The best predictor of ID was the physician's global assessment of disease activity (PhGA), followed by the age at onset and count of active joints. Other relevant features were acute phase reactants (erythrocyte sedimentation rate and C-reactive protein).

Conclusion: The PhGA over time was the strongest predictor of achievement of ID at 24 months, which highlights the importance of its regular scoring and its key role in guiding treatment decisions. The prominent importance of physiciancentred outcome measures (PhGA and active joint count) and acute phase reactants in ID prediction supports the use of the Juvenile Arthritis Disease Activity Score (JADAS), which includes all these variables, in deciding treatment adaptations within treat-to-target strategies aimed to attain complete disease control.

13:50-14:00 - Giusyda Tarantino (Italy)

ADALIMUMAB AND ANTI-DRUG ANTIBODIES IN A COHORT OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

G. Tarantino [1,*], R. Simeoli [2] , E. Marasco [1] , R. Nicolai [1] , A. Aquilani [1] , B. M. Goffredo [2] , S. Magni Manzoni [1] , F. De Benedetti [1]

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Introduction: Adalimumab (ADA), a fully humanized antibody against tumor necrosis factor (TNF)-α, has revolutionized treatment of patients with juvenile idiopathic arthritis (JIA). Although most of these respond within the first weeks, a minority may show loss of response (LOR) after continued exposure. Many studies demonstrate the influence of antiadalimumab antibodies (AAA) on serum drug concentrations and clinical outcome in adults. However, little information about AAA and LOR is available for children with JIA.

Objectives: Firstly, to describe demographic and clinical features in a single-center cohort of JIA patients treated with ADA, grouped according to frequency (1W vs 2W), to dosage of drug administration (20 vs 40 mg) and to disease activity (from inactive ID to high HDA). Also to assess ADA levels versus AAA titer and, finally, to investigate possible correlation between LOR and AAA.

Methods: Records of JIA patients on ADA treatment were retrospectively reviewed with focus on medical history and ELISA (enzyme-linked immunosorbent assay) ADA/AAA levels in a 3-years-period. Children with idiopathic uveitis and systemic JIA were excluded.

Results: From June 2019 to January 2024 we collected 446 ADA/AAA samples in 128 JIA patients treated with ADA (a median of 3.3/pt). Of them (65% females), 62 had ANA-positive oligoarthritis, 40 RF-negative polyarthritis, 13 HLA-B27 positive enthesitis-related arthritis and 10 psoriatic. The median age at disease onset was about 3.9 years. Half of study cohort was b-DMARDS naive at ADA start, while all children were on concomitant c-DMARDs (98% on Methotrexate). Chronic recurrent uveitis was the main reason for ADA starting, followed-by tenosynovitis, bowel inflammation and spine or hip active arthritis. The median disease duration at first sampling was 3.1 (IQ 1.3-6.4). About pharmacinetics, in the study group there was an inverse correlation, previously described for adults, between ADA and AAA. Among AAA positive (>50 AU/ml) patients, higher levels of body mass (BMI) and basal protein C reactivity (CRP) were detected. About pharmacodinamics, the concentration of ADA, at the same dosing time, resulted lower in children with moderate (MDA) and high (HDA) disease activity, stratified into oligo (c-JADAS10 >4) and polyarticular forms (cJADAS10 >8.5). Finally, in 65% of these last we collected very high AAA titer (105-1230 AU/mL).

Conclusion: Our preliminary "real life" data showed association between occurrence of AAA and lower ADA levels. The clinical response expressed as c-JADAS10 depends firstly on certain drug exposure. A targeted risk analysis about high AAA titers and LOR incidence is still pending at our center. Monitoring of drug immunogenicity should be implemented in daily practice and become subject of future modelling studies.

References: A. Marino. Anti-adalimumab antibodies in a cohort of patients with juvenile idiopathic arthritis: incidence and clinical correlations. Clin Rheumatol. 2018 May;37:1407-1411. J. B. Brunelli. Anti-adalimumab antibodies kinetics: an early guide for juvenile idiopathic arthritis (JIA) switching. Clin Rheumatol 2020 Feb;39:515-521.

14:00-14:10 - Remco Erkens (Netherlands)

BIOMARKER-GUIDED TREATMENT-AND-STOP-STRATEGY FOR RECOMBINANT IL-1RECEPTOR ANTAGONIST (ANAKINRA) IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

R. Erkens [1 2,*], G. Den Engelsman [1], S. De Roock [1 2], D. Hamann [2], D. Schonenberg-Meinema [3], M. Van den Berg [3], M. Gruppen [3], W. Armbrust [4], E. Legger [4], S. Kamphuis [5], M. Verkaaik [5], E. Schatorjé [6], E. Hoppenreijs [6], T. Vogl [7], J. Roth [7], P. Hissink Muller [8], J. Swart [1], M. Jansen [1], J. Van Loosdregt [2], B. Vastert [1 2]

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Introduction: Early initiation of treatment with the recombinant Interleukin 1 receptor antagonist (IL-1Ra), anakinra, in new-onset steroid naïve systemic Juvenile Idiopathic Arthritis (sJIA) patients is safe and results in quick resolution of fever and systemic inflammation and remarkably high response rates

in the majority of patients[1-2]. Although anakinra is very effective and safe it is relatively expensive, not without side effects and the daily burden of injections can be high. Therefore, we previously investigated a taper-and-stop strategy for anakinra treatment in sJIA where patients with clinically inactive disease (CID) at time point ~3 months after the start of anakinra were tapered to alternate day administration and subsequently stopped. This resulted in around 50% of patients in remission without medication after 1 year[1,2]. Retrospectively, the patients that relapsed in that cohort showed significantly higher levels of IL-18 at time point 3 months than the patients with a successful taper and stop attempt. Consequently biomarker guidance has the potential to improve the taper and stop strategy.

Objectives: Here we describe the first results of the Dutch multi-center, prospective, intervention study aiming to develop a safe and personalized 'taper and stop strategy' for sJIA patients with a complete response with 1st line use of rIL-1RA after 3 months of treatment.

Methods: The study consisted of an open-label lead-in part, in which patients with new-onset, biological and steroid naïve sJIA, from 6 centers in the Netherlands were included. SJIA diagnosis was in accordance with the criteria proposed by Martini et al [3]. Serum levels of IL-18 were measured by Luminex technology in the diagnostic laboratory of the UMC Utrecht, using standard operating protocols for processing and shipment of samples[1]. All patients received anakinra as first-line therapy in accordance with the Dutch national protocol with frequent follow-up and sampling. Only patients that had a good initial clinical response and achievement of CID at T=3 months after start on rIL-1RA mono-therapy were allowed to enter the intervention part of the study: these patients were then assessed every month for both clinical response and measurement of IL-18. Patients with IL-18 <1200pg/mL were switched to an alternate day regimen and the rIL-1RA was subsequently stopped 1 month later. If the IL-18 remained above the threshold of 1200 pg/mL, rIL-1RA was continued in a daily dose. Patients with CID at t=9 months after start of treatment were tapered (1 month alternate day) and stopped regardless of IL-18 levels. Patients were followed up to 2 years after start of treatment.

Results: In total, 67 patients were enrolled in the study of which 44 showed CID on rIL-1RA monotherapy at t=3 months, allowing entry in the intervention phase of the trial. The median age at the start of treatment was 9 years (range 0.8-16.5) and 56% were female. The 23 patients that were not enrolled in the intervention phase, due to active disease while on rIL1RA, due to the start of concomitant steroids or to a switch of therapy, were prospectively followed up for 2 years. In total, 6 patients developed MAS before the taper and stop phase, 9 had continued or relapsing disease, 5 experienced adverse events of the therapy and 3 were unable to continue on anakinra due to the burden of injections. There was no significant difference in the clinical and laboratory characteristics between the intervention (CID) and the non-intervention (more refractory course up to 3 months) group at t=0 except for the percentage of females, 43% and 79% respectively (p=0.004). In the intervention group, 75% (33/44) of sJIA patient were successfully tapered and stopped, with a sustained clinical response at t=12 months. This is significantly (p=0,043) better than the percentage of successful taper and stop in our historic cohort (47%, 7/15)[1].

Conclusion: Our prospective, multicenter intervention trial shows that IL-18 with a cut-of value of 1200 pg/mL is helpful in successful tapering and stop of rIL-1RA in well-responding patients.

References: 1. PMID: 247571542. PMID: 30848528 3. PMID: 30275259

14:10-14:20 Andrea Ippoliti (Italy)

EFFICACY OF MAS825, A BISPECIFIC IL-1 AND IL-18 NEUTRALIZING ANTIBODY, IN REFRACTORY STILL´S DISEASE WITH RECURRENT MACROPHAGE ACTIVATION SYNDROME AND LUNG INVOLVEMENT

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Introduction: Still´s disease (SD) represents a clinical challenge due to the multifaceted systemic inflammation and to the predisposition to severe complications including macrophage activation syndrome (MAS) and lung disease (LD). Patients with refractory SD frequently require long-term immunosuppressive treatment with potential side effects. MAS825, a bispecific monoclonal antibody targeting IL-1b and IL-18, is a potential therapeutic option for refractory SD, particularly with recurrent MAS and LD, as these patients have very high levels of IL-18.

Objectives: To describe 4 patients with refractory SD complicated by MAS and LD treated with MAS825 in the context of a compassionate use program.

Methods: IL-18 levels were measured by ELISA.

Results: 3 out of 4 patients were female, the mean age at disease onset was 2,4 yrs (range 0,5-6,4 yrs) and at the start of MAS825 was 5 yrs (range 1,9-8,7 yrs). The mean follow-up was 14,5 months (range 9,2-23,1 months). MAS825 was administered intravenously at the dose of 10 mg/kg every 2 weeks in addition to glucocorticoid (GC) at the dose ranging from 0.3-1 mg/kg/day in 3 patients, to mycophenolate mofetil (MMF) in 3 and cyclosporine-A (CYA) in 1. All four patients showed a good response to MAS825 with rapid improvement of clinical systemic features and normalization of inflammatory parameters. IL-18 levels at baseline (10965, 37500,199015, 60568 pg/ml respectively), decreased after 6 months (2483, 23858, 11639, 26516 pg/ml respectively) and normalized in two patients after 7 months (< 4800 pg/ml). GC treatment was tapered in 2 patients to 0,2 mg/kg/day and was stopped in 1 patient after 3 months. MMF and CYA were maintained during MAS825 therapy. None of the patients experienced further MAS episodes. All the patients presented interstitial lung disease (ILD) diagnosed by high resolution chest computed tomography (HRCT) and characterized by septal thickening in all of them, peribronchovascular thickening in 2, ground glass opacities in 2 and peripheral consolidations in 1. HRCT, repeated after 6 months, showed a significant improvement of ILD, with reduction of the consolidation areas, and of the fibrotic changes. None of the patients experienced adverse events during treatment with MAS825. One patient discontinued MAS825 after 1 year of treatment for inadequate control of joint symptoms that required repetitive intra-articular glucocorticoid injections. Despite she experience optimal control of systemic symptoms, ILD and no MAS recurrences.

Conclusion: Our case series suggest that simultaneous neutralization of IL-1β and IL-18 may represent a promising therapeutic approach in refractory SD with recurrent MAS and ILD.

14:20-14:30 Greta Rogani (Netherlands)

A POTENTIAL ROLE OF LONG-LASTING IL-18 STIMULATION IN THE SUSCEPTIBILITY FOR MACROPHAGE ACTIVATION SYNDROME IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Macrophage Activation Syndrome (MAS) is a pathologic condition of immune hyperactivation, which occurs in 10-30% of cases of systemic Juvenile Idiopathic Arthritis (sJIA) and represents one of its major cause of mortality. Although targeted biological treatment such as interleukin (IL)-1 or IL-6 blockade is highly effective in inducing clinical inactive disease in most sJIA patients, long term follow-up studies show no reduction in the incidence of MAS1 . The immunological connection between these two disorders is still incompletely understood. Recently, a population of highly proliferative CD8+ T cells, characterized by the surface activation markers CD38 and HLA-DR, has been identified to be expanded and to act as the main source of interferon-gamma in MAS patients2 . Although these cells have been thoroughly characterized in MAS, only limited data are available in the disease course of sJIA in general, and the mechanism which leads to their expansion has not yet been elucidated.

Objectives: The aim of this research was to evaluate this subset of CD8+ T cells longitudinally in patients with sJIA at different stages of disease. In addition, we sought to identify factors which drive the increase of these cells in vitro.

Methods: We quantified the percentage of CD38+ HLA-DR+ CD8+ T cells in peripheral blood mononuclear cells (PBMC) in paired samples of patients with active sJIA (n=7), inactive sJIA (n=6), MAS (n=3) and healthy donors (HD) (n=5), using flowcytometry. Then, we cultured PBMC and MACS-isolated CD8+ T cells of HD with different stimulants (IL-6, IL-18, IL6+IL-18, IFNα+IL15, TLR 7-3-9 agonists). The percentage of CD38+ HLA-DR+ CD8+ induction was evaluated over a duration of 7 days.

Results: In patients with active sJIA the percentage of CD38+ HLA-DR+ CD8+ cells was significantly increased compared to both HD and patients in remission. Similarly to what was previously reported, the percentage of these CD38+ HLA-DR+ CD8+ cells was even more increased in patients with MAS. Our in vitro data confirmed a previous observation that stimulation with IFNα+IL15 induces these activated CD8+ cells after a short-term stimulation of 48 hours. However, at day 7 (representing long term stimulation), IL18 was also able to induce high percentage of CD38+ HLA-DR+ CD8+ cells. The induction of CD38+ HLA-DR+ CD8+ T cells by INFα+IL15 and IL18 over time was comparable between PBMCs and isolated CD8, suggesting a possible direct role of IL-18 stimulation on CD8+ cells.

Conclusion: We observed that CD38+ HLA-DR+ CD8+ cells, which have specifically been linked to MAS patients, are also increased in sJIA patients with active disease, representing a potential biological connection between the two disorders. Moreover, the in vitro effect of longer lasting IL18 stimulation, known to be high in the plasma of sJIA patients and even higher in MAS patients, induced significantly high percentages of these CD8+ cells. Therefore IL18 might contribute in the expansion of this cell population and, therefore, in the susceptibility for this potentially fatal complication.

References: 1. Erkens R et Al. Arthritis Rheumatol. 2024 Jan;76(1):119-129 2. Huang Z et Al. J Clin Invest. 2023 Nov 15;133(22):e165616

14:30-14:40 - Vincent Jallot (France)

PREDICTIVE FACTORS OF RELAPSES AFTER WITHDRAWING BIOTHERAPIES IN CHILDREN WITH INACTIVE JIA: A RETROSPECTIVE COHORT STUDY

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Introduction: The modalities of stopping biological treatments in JIA-patients after remission period under treatment, are still exploratory. To date, there are only a few articles about the best way to stop the b-DMARDS treatment and in most of them s-DMARDS and b-DMARDS are included and analysed together, whereas in practice, s-DMARDS may be stopped before biological drugs. We would like to identify one or more predictors of relapse after b-DMARDS cessation that would guide adaptation of the withdrawal strategy.

Objectives: We aimed to identify one or more predictors of relapse after b-DMARDS discontinuation in JIA patients.

Methods: We performed a retrospective chart review of JIA patients who fulfilled the ILAR criteria and stopped their bDMARDS between 2000 and 2023 in French hospitals. We used data from the JIR cohort, a multicentre international registry created in 2013 to collect data on patients with juvenile inflammatory rheumatic diseases. The definition of remission was based on the Wallace criteria. The primary outcome was defined as either the absence or the presence of a relapse within one year following the b-DMARD treatment cessation due to remission status. A relapse was defined as no longer fulfilling remission criteria within one year after b-DMARD withdrawal.

Results: In two main centers, CHU Bicêtre and CH Versailles, 690 patients were treated for JIA during the study period. 120 of them (17.3%) met the inclusion criteria in whom (26 % oligo-JIA, 23% poly-JIA, 12% pso-JIA, 23% ERA, and 16% s-JIA). To date, we analyzed more than 110 patients, two-thirds were girls, with a median age of 5.3 years at diagnosis. Patients received Anakinra, Canakinumab, Tocilizumab, Etanercept, Adalimumab, Infliximab or Baricitinib. All discontinued treatments after a median duration of 2.5 years under b-DMARDS. Around 51% of them flared within one year after treatment discontinuation (the highest relapse rate was in the psoriasis group with a rate of 84%, the lowest in the systemic group with a rate of 29.5%). Positive anti-nuclear antibodies at diagnosis appeared associated with a higher flare probability ($p < 0.05$); on the contrary, a high CRP at diagnosis was associated with fewer flare-ups within one year after b-DMARD withdrawal ($p < 0.05$). We will supplement our results during the meeting with subgroup analyses after processing data from all the centers.

Conclusion: Data from our large cohort of JIA patients showed as a whole 50% of flares after b-Dmards discontinuation. So-JIA appeared at the lowest risk of relapse after stopping biologic treatment, as previously reported. Other original data will be added after the end of the statistical analyses

14:40-14:50 - Federica Lucioni (Italy)

PERFORMANCE OF THE 2016 CRITERIA IN RECOGNIZING MACROPHAGE ACTIVATION SYNDROME IN MULTISISTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C): DATA FROM THE HYPER-PED-COVID REGISTRY

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Introduction: Macrophage activation syndrome (MAS) has been reported as a complication of Multisystem Inflammatory Syndrome in Children (MIS-C) in up to 20-50% of cases. As clinical and laboratory features of MIS-C partially overlap with MAS, diagnosis may be challenging. The 2016 classification criteria for MAS in systemic juvenile idiopathic arthritis (sJIA) have been largely used to diagnose MAS in MIS-C; however, their performance has never been evaluated in MIS-C and no specific diagnostic criteria for MAS in MIS-C exist.

Objectives: To evaluate the performance of 2016 classification criteria in recognizing MAS in patients with MIS-C.

Methods: The HyperPED-COVID is the largest international registry of patients with MIS-C. In the case reported form, clinicians were asked to specify if MIS-C patients developed MAS and to provide clinical and laboratory data at MIS-C and MAS onset. Chi-square, Fisher and Mann-Whitney test were used, as appropriate, to compare patients with and without MAS. Sensitivity (SE), specificity (SP) and area under the curve (AUC) were calculated to test the performance of the 2016 criteria at MAS onset and a multivariate analysis was performed to evaluate strength of association between variables and the diagnosis of MAS.

Results: Currently, data regarding 1019 patients with MIS-C were collected in the HyperPED-COVID registry; in 82 cases (8.0%) a diagnosis of MAS was made by the caring physician. Patients with MAS were older (9.0 vs 7.9 years, p 0.022), with a longer disease duration (9 vs 5 days, p <.001) and a higher rate of myocardial dysfunction (40% vs 19%, p<.001) and a higher rate of myocardial dysfunction (40% vs 19%, p<.0001) at MIS-C onset. Lymphadenopathy, hepatomegaly and splenomegaly were more frequently reported in MAS than in nonMAS patients, albeit in low percentages (16%, 28% and 18%, respectively). At MAS onset, patients presented higher levels of ferritin (1446 vs 403 ng/ml, p<.0001,

triglycerides (235 vs 186 mg/dl, p <.0001), liver enzymes (AST 60 vs 35 U/l, p <.0001) and lower platelet counts (133 vs 193 x 10^9/l, p <.0001) and fibrinogen (463 vs 543 mg/dl, p 0.004) compared to acute MIS-C. The 2016 criteria had a SE of 0.80, a SP of 0.83 and an AUC of 0.81 (p<.0001) in recognizing MAS from acute MIS-C. Ferritin and triglycerides resulted the strongest variables associated with the diagnosis of MAS in multivariate analysis. Despite a more aggressive treatment, especially with steroids (99% vs 80%, p <.0001) and anakinra (40% vs 9%, p <.0001), patients with MAS required more frequently a circulatory support (40 % vs 25%, p 0.005), with higher mortality (3.7% vs 0.6%, p 0.003).

Conclusion: MAS is associated with older age, longer disease duration and a more severe MIS-C phenotype and can further complicate the course of MIS-C, increasing morbidity and mortality. MAS prompt recognition is crucial and the 2016 criteria could represent a valid aid in clinical practice.

15:50-17:10---SESSION III (SLE, JDM, Sjögren)

15:50-16:00 - Chandni Sarker (United Kingdom)

COMPARATIVE EFFICACY OF PAEDIATRIC AND ADULT SLE TREAT-TO-TARGET GOALS IN PREVENTING SEVERE FLARES AND DAMAGE ACCRUAL

C. Sarker [1,*], A. L. Jorgensen [2] , M. W. Beresford [1 3], E. M. D. Smith [1 3] on behalf of on behalf of the UK JSLE Cohort Study

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Introduction: The Paediatric Rheumatology European Society (PReS) has endorsed Childhood Lupus (cSLE) treat-totarget (T2T) definitions include childhood Lupus Low Disease Activity State (cLLDAS), cSLE clinical remission on (cCR) and off-corticosteroids (cCR-0). These targets feature weight-based corticosteroid dosing to avoid inappropriately high corticosteroid doses in children. Additionally, the stricter second remission target, cCR-0, aims for steroid discontinuation.

Objectives: To compare cSLE targets (cLLDAS, cCR, cCR-0) with adult-onset SLE (aSLE) targets (LLDAS, DORIS 2021 Remission) for attainability and protection against severe flares and new damage.

Methods: Analysis included UK JSLE Cohort Study patients (n=430), <18 years at diagnosis, with ≥4 ACR criteria for SLE. Attainability and time to targets were described, with Wilcoxon signed-rank tests used to test for differences in time to target attainment between cSLE and aSLE targets. Association between attainment of cSLE- and aSLE-specific targets and both new damage and severe flare was explored using Prentice-Williams-Peterson (PWP) gap-time models. Severe flare was defined by a BILAG score A or B in any organ domain. New damage was defined by an increase of SDI score by ≥1 unit. Student's t-tests for dependent samples were conducted to compare the hazard ratios (HRs) obtained from the PWP gap-time models for cSLE versus aSLE targets.

Results: A comparable number of patients were found to attain cLLDAS (n=290, 67%) and LLDAS (n=293, 68%), cCR (n=249, 58%) and DORIS 2021 Remission (n=261, 61%). Median time-to-target

(months) was significantly faster for aSLE-specific targets (LLDAS: 17.4, DORIS 2021 Remission: 19.3) compared to cSLE-specific targets (cLLDAS: 18.4, cCR: 20.4, cCR-0: 23.4, all p<0.001). Childhood SLE targets were less attainable than aSLE targets: cCR 796 visits vs DORIS remission 848 visits, with corticosteroid dosage representing the main barrier to paediatric-specific target attainment. All cSLE and aSLE target attainment led to a comparable reduction in the hazards of severe flare and new damage. For example, the hazards of severe flare when either cLLDAS and LLDAS were attained reduced by around 82% (cLLDAS: HR 0.18, CI 0.14, 0.23; LLDAS: HR 0.18, CI 0.14, 0.24, p>0.05). The hazards of new damage was comparable with cLLDAS (HR 0.22, CI 0.11, 0.44), and LLDAS attainment (HR 0.24, CI 0.13, 0.46, p>0.05). Similarly, the hazards of severe flare and new damage was comparable when cCR and DORIS 2021 Remission were attained (all p>0.05).

Conclusion: The study highlighted that cSLE and aSLE targets performed comparably in reducing severe flare and new damage, with cSLE targets preventing inappropriate target attainment.

16:00-16:10 - Katherine Nay Yaung (Singapore)

DECIPHERING THE INTRICACIES OF CHILDHOOD-ONSET SLE (CSLE) THROUGH HIGH-DIMENSIONAL DATA ANALYSIS: AUGMENTING THERAGNOSIS WITH AN IMMUNOLOGICAL-BASED DIAGNOSTIC MODEL THAT UNVEILS MECHANISTIC INSIGHTS

K. Nay Yaung [1 2,*], J. G. Yeo [1 2 3], M. Wasser [1], S. L. Poh [1], K. L. Teh [3], L. Das [3], Y. X. Book [3], N. K. H. Khoo [1], Z. M. Y. Tay [1], R. Cheong [1 3], J. J. M. Wong [1 3], T. Arkachaisri [2 3], S. Albani [1 2 3]

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Introduction: Childhood-onset systemic lupus erythematosus (cSLE) presents diagnostic challenges due to its heterogeneous nature, representing an unmet need. To capture this inherent heterogeneity, a diagnostic model which uncovers underlying mechanistic immune perturbations can provide valuable theragnostic insights for SLE.

Objectives: We aim to resolve this immunopathogenic complexity with high-dimensional mass cytometry (CyTOF) to study the lupus immunome. Using machine learning, we developed a diagnostic model which utilized mechanistically relevant cell clusters distinguishing patients from controls and was validated with an independent cSLE cohort.

Methods: The discovery cohort examined peripheral blood mononuclear cells (PBMCs) from 26 cSLE patients (53 timepoints, median age: 14 years) and 17 age-matched healthy controls using a 43-marker CyTOF panel. Quality check, cell clustering and phenotypic annotation were done using our unsupervised Extended Poly-dimensional Immunome Characterisation (EPIC) pipeline.1 Machine learning algorithms [linear SVM, PLS-DA, random forest (RF) using MetaboAnalyst 6.0] identified predictive cell clusters for cSLE to ensure model robustness. Cell frequencies are shown as percentages of total CD45+ PBMCs with median and interquartile range (IQR), with statistical significance set at p<0.05 (Mann-Whitney U). Validation was conducted on a new cohort of 18 cSLE patients (median age: 11.5) and 23 agematched controls using the same CyTOF panel.

Results: Multiple immune cell derangements were noted between cSLE and healthy in the discovery

cohort. 67 unique cell clusters were derived, of which 26 were significantly different. All 67 cell clusters were used to map the validation cohort. Mapping was automated based on previous expert annotation of the derived cell clusters from unsupervised analysis of discovery data. Validation cohort clusters mirrored accurately the phenotypes of the discovery cohort cell populations. Interestingly, there were increased memory Tregs in cSLE (cSLE vs. healthy: 1.16 [0.79-1.92]% vs. 0.48 [0.32- 0.80]%, p<0.0001) but no changes in naive Tregs. Memory Treg-like populations (such as CD3+CD4+CD45RO+CD25-Foxp3+CTLA+) were also higher in cSLE than healthy (2.75 [1.90-4.36] vs. 1.28 [0.83-1.78], p<0.0001). Concurrently, CD8+CD45RA+BAFF+ T cells were raised in cSLE (8.91 [6.78-11.4] vs. 3.22 [2.79-4.86], p<0.0001). These populations, in addition to other unique cell clusters, were used to build a cSLE classification model. Ten immunological features were selected through collective ranking of the most important features generated by machine learning algorithms on discovery cohort data. The average accuracy of discriminating cSLE and healthy based on 100 cross validations (with linear SVM, PLS-DA and RF algorithms) in the discovery cohort is 85.4% (median), (IQR 83.3-85.6%). Sensitivity for the validation cohort is 88.9% (83.3-100%). Further studies will quantitate autoantibody titers (anti-c1q/-nucleosome/-dsDNA/-Smith) for comparison.

Conclusion: High-dimensional and machine learning methods were used to craft an immunological classifier for discriminating cSLE from healthy. The ten selected features reflect broad changes in the lupus immunome: perturbed immunoregulation, cytokine production and reduced immune activation threshold. This aids our understanding of SLE immunopathogenesis and can reinforce current diagnostic criteria.

References: 1Yeo JG et al. The EPIC web-based reference and discovery tool for cytometry data. Nature Biotechnology. 2020 Jun 1;38(6):679-84.

16:10-16:20 - Maria Hanif (United Kingdom)

CONTRIBUTORS TO DAMAGE ACCRUAL IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (CSLE): INFLUENCE OF CORTICOSTEROIDS AND DISEASE ACTIVITY

M. Hanif [1,*], C. Sarker [1] , M. W. Beresford [1 2], E. M. D. Smith [1 2] on behalf of on behalf of the UK JSLE Cohort Study

[1]Institute of Life Course and Medical Sciences, [2]Alder Hey Children's NHS Foundation Trust Hospital, Liverpool, United Kingdom

Objectives: To identify independent predictors of damage in patients stratified by levels of disease activity and treatment.

Methods: Analysis included UK JSLE Cohort Study participants diagnosed ≤18 years and meeting ≥4 ACR 1997 SLE classification criteria. New damage was defined as an increase in ≥1 unit in the SLICC SDI score. Univariable and multivariable Prentice-Williams-Peterson gap-time models investigated how demographics, time-adjusted mean prednisolone dose, methylprednisolone exposure, time-adjusted mean Physicians Global Assessment (PGA) score, baseline organ damage and average disease activity (time-adjusted average SLEDAI-2K score, AMS) influenced the hazards of new damage. Analyses were performed across the entire cohort and four subgroups: (1) minimal activity (AMS≤2), (2) low activity (AMS≤4), (3) moderate-high activity (AMS>4), and (4) those with no corticosteroids during follow-up.

Results: 430 patients were included with a median of 10 visits/patient, with 66/410 patients displaying organ damage at first visit and 99/430 accruing further damage. Baseline organ damage predicted further damage in patients with no corticosteroids (HR 3.64 CI 1.83-7.24, p<0.001) and in those with minimal disease activity (HR 1.33 CI 1.78-8.08, p=0.001) during follow-up. For those in low disease activity during follow-up, methylprednisolone exposure and timeadjusted mean PGA score were associated with damage accrual (HR 2.61 CI 1.04-6.53 and HR 3.41 CI 1.52-7.67 respectively, both p<0.05). Methylprednisolone exposure, time-adjusted mean PGA score and AMS score were all significant predictors of damage in the whole cohort (HR 2.20 CI 1.33-3.62, HR 2.87 CI 1.48-5.56 and HR 1.13 CI 1.03-1.24 respectively, all p<0.05) and the moderate-high disease activity subgroup (HR 2.29 CI 1.31-4.00, HR 2.66 CI 1.20-5.87 and HR 1.15 CI 1.03-1.29 respectively, all p<0.05).

Conclusion: Methylprednisolone exposure is a significant, modifiable risk factor for damage in cSLE, warranting further research to optimise paediatric dosage regimens. Baseline organ damage predicts occurrence of further damage, underscoring the need for early specialist referral and optimising initial treatment. In patients with an AMS>4, a 1 unit increase in SLEDAI raises damage risk by 15%. This correlation was absent in the AMS≤4 subgroup, indicating maintenance of low disease activity through T2T strategies could mitigate damage accrual.

16:20-16:30 - Meredyth Grace Llewellyn Wilkinson (United Kingdom)

A MITOCHONDRIAL GENE SIGNATURE TO STRATIFY JUVENILE DERMATOMYOSITIS PATIENT GROUPS FOR MORE TARGETED TREATMENTS

M. G. L. Wilkinson [1 2 3,*], A. E. Syntakas [1 2], R. Restuadi [1 2 3], H. D. Nguyen [1 2], M. M. Kartawinata [1 2], D. Cancemi [1 2], V. Alexiou [1 2], L. R. Marshall [1 2], B. R. Jebson [1 2], E. Ralph [1 2], H. Peckham [2], A. Radziszewska [2], W.-Y. Lin [4], G. W. Otto [3 5], G. Hall [3 5], D. Kelberman [3 5], S. Castellano [3 5], C. Cuirtin [2], S. Eaton [3 6], C. T. Deakin [1 2 3 7], E. C. Rosser [2 8], C. Wallace [4 9], L. R. Wedderburn [1 2 3]

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Introduction: Juvenile dermatomyositis (JDM) is a rare childhood autoimmune myositis, typically presents with proximal muscle weakness and skin manifestations. JDM is characterised by abnormal interferon (IFN) type I signalling and mitochondrial abnormalities contributing to the disease pathogenesis. There is a need for better treatments, with novel therapeutics targeting IFN and mitochondria pathways, being the clear candidates.

Objectives: This study aimed to define and validate a JDM mitochondrial gene signature and investigate how this signature correlates with disease activity. Establish the signature as a tool to

improve the understanding of what drives JDM inflammation, support individualised selection of treatments and new target discovery. Methods: Peripheral blood mononuclear cell (PBMC) samples were obtained from treatment-naïve, early-treatment and on-treatment JDM and age/sex-matched child healthy controls (controls). RNA-sequencing (RNAseq) was performed from total PBMC and sorted CD14+ monocytes. The dataset comprised JDM pre-treatment (n=33), early-treatment (n=5), ontreatment (n=10) and controls (n=19). Differentially expressed genes (DEG) between conditions were analysed using EdgeR. Factor analysis was used to model interrelationships across genes to identify common and unique genes.

Results: Validation of our previously published RNAseq results in a new, larger cohort of JDM patients identified an overlapping gene signature which encapsulated 37 genes from the mitochondrial gene ontology term. By using unsupervised, hierarchical clustering, a clear separation was observed in the normalised gene counts for the defined 37 mitochondrial gene set (MGS) between the four different groups, JDM treatment naïve (n=26), early-treatment (n=4, <2 months on treatment), on-treatment (n=8, average time on treatment = 14 months (range=4.3-32 months)) and controls (n=19). Factor analysis was performed on the 37-gene MGS to model interrelationships among individual genes. While certain groups of genes were found to have shared variance, we identified a set of 18 genes with unique contributions to the overall MGS. Calculating a factor score for each sample, we showed that mitochondrial dysfunction is significantly abnormal in JDM treatment naïve patients and it is still abnormal at early/later on-treatment timepoints even, relative to controls. This demonstrated that current treatment does not resolve this pathological mitochondrial signature even in those patients that have improved disease. This finding was observed in the PBMC RNAseq data as well. We found significant positive correlation between the MGS factor score derived from JDM treatment naïve monocytes with the Manual Muscle Test (MMT8) score (p=0.0007, R2=0.4841). These data suggest that the signature could have strong clinical utility for biomarker development in blood.

Conclusion: This study identified and validated a dysregulated mitochondrial signature in treatment naïve JDM CD14+ monocytes, further validated in PBMCs, which positively correlated with muscle weakness by MMT8 score tool. This signature could have clinical implications as a biomarker of mitochondrial health in JDM, potentially useful for patient treatment optimisation.

16:30-16:40 - Helena Codes-Méndez (Spain)

EXPLORING THE INTERFERON SIGNATURE AS A BIOMARKER FOR DISEASE ACTIVITY AND ORGAN DAMAGE IN JUVENILE DERMATOMYOSITIS

H. Codes-Méndez [1,*], S. Cuyx [2], A. Barmpakou [2], E. Moraitis [2], S. Compeyrot-Lacassagne [2], M. Al-Obaidi [2], C. Papadopoulou [2]

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Introduction: Juvenile dermatomyositis (JDM) is a systemic autoimmune disease with a prominent up-regulation of interferon (IFN) signaling system. To date, no validated markers for assessing disease activity have been identified.

Objectives: To analyze the IFN signature in patients with JDM and evaluate its potential as biomarkers

for disease activity and organ damage, including manifestations in the skin, muscle, joints, lung, and gastrointestinal (GI) tract.

Methods: Retrospective study on a cohort of 69 JDM patients from the largest paediatric rheumatology department in the UK between 03/2020 and 05/2024. IFN type I/II pathways were assessed by RT-PCR quantitation1. Disease activity assessment included the evaluation of muscle strength (CMAS/MMT8), skin (modified DAS), and the physician's global assessment. Statistical analysis included Mann-Whitney tests and Spearman's correlations to explore associations between disease activity, organ involvement, and expression levels of each IFN gene. Statistical significance was set at $p<0.05$.

Results: A total of 150 blood samples were obtained from 69 patients (48 females), with a median age at diagnosis of 7(1-13) years. All presented muscle and skin involvement at disease onset. GI involvement (dysphagia) was observed in 18 patients, while 13 presented interstitial lung disease (ILD). Longitudinal follow-up data were available for 41 patients. The most prevalent myositis-specific autoantibodies were TIFγ(18.3%), NXP2(12.6%), MDA5(12.6%), and Mi2(8.4%). Patients with active muscle involvement presented higher expressions of IFI27 ($p<0.001$), IFI44L ($p<0.001$), IFIT1 ($p<0.001$), IFNB1 ($p=0.02$), RSAD2 ($p<0.001$), SIGLEC1 ($p<0.001$), CXCL10 ($p=0.04$), and IL-18 ($p=0.004$). Arthritis was associated with elevated IFI27 ($p=0.004$), IFI44L ($p=0.01$), SIGLEC1 ($p=0.03$), and CXCL9 ($p=0.04$). Patients with active skin disease presented higher expressions of IFI27 ($p<0.001$), IFI44L ($p<0.001$), IFIT1 ($p<0.001$), RSAD2 ($p<0.001$), SIGLEC1 ($p<0.001$), and CXCL10 ($p=0.02$). Calcinosis reached statistical significance for IFIT1 ($p=0.03$), RSAD2 ($p=0.02$) and IL-18 ($p=0.02$); whereas patients with V-sign, mucous membrane lesions and subcutaneous oedema had higher expressions of CXCL9 ($p=0.005$, 0.03, 0.03; respectively). No significant association was found with skin ulcerations. Patients with ILD presented higher expressions of IFI27 ($p=0.04$) and CXCL9 ($p=0.01$), while those with dysphagia had elevated IFI27 ($p=0.02$), IFIT1 ($p=0.02$), SIGLEC1 ($p=0.01$). Baricitinib was initiated in 11 patients due to refractory disease activity. Among them, 4 experienced normalization of IFN levels and achieved clinical remission. The remaining patients have shown promising initial responses, though it is premature to fully evaluate outcomes due to the recent treatment initiation.

Conclusion: Our study demonstrates hyperactivation of the IFN signaling systems in JDM patients. Both IFN I/II regulated transcripts were associated with muscle and skin disease activity. Our findings indicate that calcinosis is associated with RSAD2 and IFIT1, as well as IL-18, whereas skin ulceration did not show any association. Notably, ILD was associated with IFI27 and CXCL9. Patients with dysphagia exclusively exhibited hyperactivation of IFN-I signaling system. The serum IFN gene signature shows promise as a biomarker in JDM. Further studies are needed to confirm these results.

References: 1 Papadopoulou C, et al. Janus kinase 1/2 inhibition with baricitinib in the treatment of JDM. Brain. 2019 Mar.

16:40-16:50 - Silvia Rosina (Italy)

TOWARD A TREAT-TO-TARGET STRATEGY IN JUVENILE DERMATOMYOSITIS: SEEKING FOR SUITABLE TARGETS AND OPTIMAL TIMING OF THEIR ACHIEVEMENT

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Introduction: The management of juvenile dermatomyositis (JDM) is not standardized and no widely embraced therapeutic protocols are available. Furthermore, the optimal therapeutic targets as well as the ideal timing of their achievement are not established. Defining these aspects of the therapeutic approach would be fundamental to implement the treat-to-target (T2T) strategy.

Objectives: To investigate the longitudinal trends of indicators of treatment effectiveness in a cohort of JDM patients, with the aim of identifying suitable targets and optimal timing of their achievement.

Methods: We reviewed retrospectively the charts of 44 patients diagnosed with JDM, seen at our center within 6 months after disease diagnosis and followed for ≥ 6 months. The disease course was assessed at the following time points: baseline (diagnosis) and after 1.5, 3, 6, 12, 18 and 24 months. Collected data included demographic features, muscle enzymes, and the main physician- and parent-centered JDM outcome measures. Time to skin and muscle remission, normalization of muscle enzymes, inactive disease (ID) by PRINTO modified criteria, complete clinical response (CCR), ID by JDMAI1 and JDMAI2, reduction of prednisone (PDN) dose < 0.3 mg/kg/day and < 0.1 mg/kg/day, and glucocorticoid (GC) discontinuation was calculated. Treatment response by IMACS and PRINTO criteria, as well as longitudinal changes in JDMAI1 and JDMAI2 were also evaluated.

Results: A total of 44 patients (median age at diagnosis 7.5 years; median time from onset to diagnosis 4.2 months) were included. All but 4 patients received high-dose GC at diagnosis, associated with methotrexate and IVIG in 64% and 20.5%, respectively. The frequency of and median time to achievement of established targets were: 82.9% and 12.0 months for skin remission; 94.7% and 5.6 months for muscle remission; 94.1% and 3.0 months for normalization of muscle enzymes; 79.5% and 13.0 months for ID by PRINTO modified criteria; 68.2% and 18.6 months for CCR; 60% and 13.0 months for ID by JDMAI1; 64% and 12.9 months for ID by JDMAI2; 100% and 11.2 months for PDN dose reduction to < 0.3 mg/kg/day; and 56.1% and 24.7 months for PDN dose reduction to < 0.1 mg/kg/day. GC were discontinued in 34.1% patients (median time not reached). IMACS minimal/moderate/major improvement was reached in 36.4%/56.8%/40.9% of patients, whereas PRINTO minimal/moderate/major improvement in 32%/76%/52%, respectively. JDMAI1 and JDMAI2 scores declined over time, especially at 12 months (mean absolute/percentage change from baseline: -14.1/-90.0% for JDMAI1, -14.7/-84.4% for JDMAI2).

Conclusion: Our findings provide preliminary figures derived from the real world of clinical practice that may help to define suitable targets and optimal timing of their achievement for the future introduction of the T2T strategy in JDM.

References: Rosina S, et al. Development and validation of a composite disease activity score for measurement of muscle and skin involvement in juvenile dermatomyositis. Rheumatology (Oxford) 2019;58(7):1196-1205. Rosina S, et al.; Paediatric Rheumatology International Trials Organisation (PRINTO). Defining criteria for disease activity states in juvenile dermatomyositis based on the Juvenile Dermatomyositis Activity Index. RMD Open 2024;10(1):e003093.

16:50-17:00 - Letizia Tarantola (Italy)

DEVELOPMENT AND VALIDATION OF A COMPOSITE PARENT-CENTERED DISEASE ACTIVITY SCORE FOR JUVENILE DERMATOMYOSITIS

L. Tarantola [1,*], A. I. Rebollo-Giménez [2] , R. Naddei [3] , A. Consolaro [2] , A. Pistorio [4] , A. Ravelli [4] , S. Rosina[2]

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Introduction: Increasing attention has been recently paid to the development of parent-centered composite disease activity scores for the assessment of health status of children with rheumatic diseases.

Objectives: The aim of the present study was to develop and validate an entirely parent-centered composite disease activity score for JDM, named parent Juvenile DermatoMyositis Activity Index (parJDMAI).

Methods: The parJDMAI includes the following items: 1) parent assessment of skin disease activity (Parent Skin Scale) on a 0-5 Likert scale, by giving 1 point to each of: i) rash on eyelids, ii) rash on nose/cheeks, iii) rash on knuckles, iv) rash on trunk/arms, v) skin ulceration; 2) parent assessment of muscle disease activity (Parent Muscle Scale) on a 0-5 Likert scale, by giving 1 point to each of: i) fatigue/discomfort, ii) muscle weakness, iii) muscle pain, iv) voice change, v) difficulty swallowing; 3) parent assessment of child's fatigue on a 0-10 VAS (0 =no fatigue; 10 = maximum fatigue); 4) parent global assessment of disease activity on a 0-10 VAS (0 = no activity; 10 = maximum activity). To give the 4 components the same weight, the scores of the Parent Skin and Muscle Scales were converted to a 0-10 scale. Thus, the total ParJDMAI score ranges from 0 to 40. Initial validation was conducted on a multicentric prospective sample of 263 patients followed in standard clinical care assessed at baseline and at a second follow-up visit. Construct validity was assessed by calculating the correlations between parJDMAI and: i) physician-centered JDM outcome measures; ii) JDMAI1 and JDMAI2 with or without the Parent's global assessment of overall wellbeing. Validation procedures included: responsiveness to change, internal consistency, discriminant ability and factor analysis.

Results: Spearman's correlations between parJDMAI and physician-centered JDM outcome measures were moderate (0.4-0.59), whereas those with JDMAI1 and JDMAI2 were strong (0.6-0.79); correlations between parJDMAI and 3itemJDMAI1 and 3item-JDMAI2 were moderate but lower than those with original (4item-) JDMAI1 and JDMAI2, as expected. Responsiveness to change was good and internal consistency was substantial (Crombach alpha>0.8). Discriminant ability was satisfactory. Factor analysis and principal component analysis confirmed the unidimensionality and internal consistency of the scale.

Conclusion: The parJDMAI revealed satisfactory measurement properties and is, therefore, suitable for use in clinical practice and research. The new tool should be further tested in different clinical and cultural environments.

References: Rosina S, Consolaro A, van Dijkhuizen P, Pistorio A, Varnier GC, Bovis F, Nistala K, Maillard S, Civino A, Tsitsami E, de Inocencio J, Jelusic M, Vojinovic J, Espada G, Makay B, Katsicas MM,

Pratsidou-Gertsi P, Lazarevic D, Rao AP, Pires Marafon D, Martini A, Pilkington C, Ruperto N, Ravelli A. Development and validation of a composite disease activity score for measurement of muscle and skin involvement in juvenile dermatomyositis. Rheumatology (Oxford). 2019 Jul 1;58(7):1196-1205. doi: 10.1093/rheumatology/key421. PMID: 30690571.

17:00-17:10 - Flavia Riccio (Italy)

A LARGE COHORT COMPARISON OF PAEDIATRIC SJOGREN'S DISEASE WITH ADULT-ONSET

F. Riccio [1,*], S. Gandolfo [2], S. Ancona [3], R. Irace [1], A. Marino [4], S. Campus [5], G. Simonini [6], F. Baldo [4], E. Marrani [6], A. Mauro [7], S. D'Elios [8], A. Civino [9], C. Covizzi [10], V. Manfrè [11], R. Naddei [12], R. Loconte [13], V. Ibba [5], F. Alessi [3], M. Gattorno [3], F. Ciccia [1], C. Malattia [3 14]

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Introduction: Paediatric Sjögren's Disease (SjD) is a rare, poorly defined and probably under-recognized condition. A limited number of studies have highlighted some clinical and immunologic differences with adult patients diagnosed with SjD. However, no comparative studies have been published to date.

Objectives: To compare the clinical features, immunologic profile and management in children and adults with SjD. Methods: We recruited 76 patients diagnosed with paediatric SjD from 12 paediatric rheumatology centres and 115 adult SjD patients from a single rheumatology centre. All patients met the ACR/EULAR 2016 classification criteria for SjD. We collected demographic, clinical and laboratory data at the time of diagnosis and at 1-year follow-up.

Results: The paediatric cohort consisted of 76 patients (69 female (90.8%)) with a median age at onset of 10.83 years (0.42-16.75) and a mean time from onset to diagnosis of 18 months. The adult cohort consisted of 115 patients (107 female (93%)), with a median age at diagnosis of 55.33 years (21.58-77.58) and a mean time from onset to diagnosis of 23 months. At baseline, we observed significant differences between paediatric and adult SjD patients in xerophthalmia (43.24% vs. 93.9%, p<0.00001), xerostomia (31.08% vs. 86.2%, p<0.00001), myalgia (17.56% vs. 70.69%, p<0.00001), and fatigue (28.37% vs. 66.38%, p<0.00001), which were the predominant symptoms in the adult cohort. Consistent with these findings, Schirmer's test (29.31% vs. 94.44%, p<0.00001) and unstimulated salivary flow rates (56.25% vs. 86.48%,

p=0.005) were more frequently pathologic in adult patients. Recurrent parotid swelling was more common in children (43.2% vs. 16.37%, p=0.00005) who also had a higher incidence of arthritis (p<0.00001), purpura (p=0.01), and other skin manifestations such as erythema multiforme (p=0.005). Serum IgG levels (p<0.0001) and rheumatoid factor values (p=0.001) were significantly higher in children than in adults. A higher frequency of ANA positivity (p=0.001) and anti-SSA (p< 0.00001) and

anti-SSB (p=0.0004) antibodies was observed in the adult cohort. No significant differences in treatment were found, except for saliva and tear substitutes, which were used more frequently in adults (p=0.0002 and p=0.035, respectively). ESSDAI values were significantly higher in the paediatric group (p<0.00001), while ESSPRI values were significantly lower (p<0.00001). At 1 year follow-up, although both scores improved in the two groups, ESSDAI scores remained significantly elevated in children compared to adults (p<0.00001).

Conclusion: Adults and children with SjD have different clinical and serological phenotypes. Pediatric SjD patients had higher disease activity as confirmed by ESSDAI despite lower ESSPRI. Overall, our results support the need to develop specific recommendations and outcome measures for the management of paediatric SjD.

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08:25-: 09:45 SESSION IV- (Vasculitides, autoinflammatory diseases, and miscellaneous)

08:25-08:35 - Ummusen Kaya Akca (Türkiye)

A RARE DISEASE WITH MANY FACES: A MULTICENTER REGISTRY OF IGG4-RELATED DISEASE IN CHILDREN

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Introduction: IgG4-related disease (IgG4-RD) is a fibroinflammatory disease, affecting almost any organ. Given its rarity and the paucity of pediatric clinical trials, our knowledge of the diagnosis and management is mainly based on adult experience and reports of case series in children.

Objectives: We aimed to report the characteristics of pediatric IgG4-RD through a multicenter registry, to assess disease clusters, and to evaluate the performances of the 2019 American College of Rheumatology and European League Against Rheumatism (ACR/EULAR) classification criteria and the 2020 revised comprehensive diagnostic (RCD) criteria in this cohort.

Methods: Data of IgG4-RD patients in 13 pediatric rheumatology centers were recorded to a web-based registration system. The diagnosis of IgG4-RD was made according to the 2011 comprehensive diagnostic criteria. The clinical phenotypes, disease subsets, and sensitivities of the criteria sets were also investigated.

Results: Thirty-five children (19 females and 16 males) with IgG4-RD were enrolled. The median age at diagnosis and median follow-up time were 13.3 (25p-75p; 9.9-15.2) years and 1.8 (25p-75p; 0.6-3.4) years, respectively. The most common organ involvement was ocular findings in 21 (60%) patients, followed by lymph nodes in 12 (34.3%), musculoskeletal system in 12 (34.3%), neurological system in 9 (25.7%), pancreatic and biliary tract in 8 (22.9%) and lacrimal and major salivary glands in 8 (22.9%) patients. Sixteen patients (45.7%) were classified as having proliferative subtype whereas 19 (54.3%) had fibrotic subtype. We identified three clusters in our study cohort: those with eye involvement (n=11, 31.4%), those with eye involvement and neurological findings (n=15, 42.9%), and those with pancreato-hepatobiliary disease and lymph node involvement (n=9, 25.7%). Serum IgG4 levels were high in 19 out of 28 patients (67.8%). Biopsy was performed in 31 patients (88.6%) in diagnostic process and 27 of them (87.0%) had findings associated with IgG4-RD. Dense lymphocytic infiltrate and storiform fibrosis were the most prominent histopathological findings. The sensitivities of the 2019 ACR/EULAR classification criteria and the 2020 RCD criteria were 5.7% and 88.5%, respectively. All patients except one received corticosteroid treatment, and azathioprine was the most preferred drug as a steroid sparing agent. Complete response was observed in 33.3% of the patients, partial response in 23.3%, and stable disease in 6.6%. Relapse occurred in 11 patients (31.4%).

Conclusion: IgG4-RD has a wide variety of clinical manifestations, however in children the most common presentation was orbital involvement. The 2020 RCD criteria had a better performance whereas the 2019 ACR/EULAR classification criteria performed poorly in pediatric patients.

08:35-08:45 - Jade Cognard (France)

HAPLOINSUFFICIENCY OF PTPN2 AND EARLY SYSTEMIC AUTOIMMUNITY: FROM EVANS SYNDROME TO SYSTEMIC LUPUS

M. Jean-Pierre [1] , **J. Cognard** [2,*], M. Tusseau [2] , Q. Riller [1] , L.-C. Bui [3] , J. Berthelet [3] , A. Laurent [4] , E. Crickx [5] , M. Parlato [6] , M.-C. Stolzenberg [6] , F. Suarez [5] , G. Leverger [5] , N. Aladjidi [7] , S. Collardeau-Frachon [4] , C. Pietrement [8] , F. Rodrigues-Lima [3] , M. Malphettes [5] , T. Walzer [2] , F. Rieux-Laucat [9] , A. Belot [2 4], A.-L. Mathieu [2]

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Introduction: The immune system is tasked with deploying effective defenses against infections while simultaneously maintaining tolerance towards self-components. This delicate balance is maintained by a set of mechanisms that negatively regulate immune cell activation pathways. Among these, the

phosphatase PTPN2, which modulates the JAK/STAT pathway pivotal in the signaling of various cytokines, has been implicated in the onset of autoimmunity (1–3).

Objectives: We sought to understand the impact of PTPN2 variants on the clinical phenotype and immune responses, thereby gaining a better understanding of the role of this key phosphatase in pathophysiology.

Methods: Whole exome analysis of patients with pediatric-onset systemic lupus erythematosus or Evans syndrome has led to the identification of six new mutations in PTPN2. In vitro analyses including cytokine reporter, phosphatase assays and flow cytometry have enabled to characterize how these mutations affect cellular functions and signaling pathways.

Results: All identified heterozygous mutations resulted in the loss of regulatory function of PTPN2. This occurred either through loss of expression or changes in its phosphatase activity, leading to hyperactivation of the JAK/STAT pathway and hyperproliferation of patient T cells upon cytokine's stimulation. Furthermore, patients exhibited high serum levels of various inflammatory cytokines, mimicking the profile observed in individuals with gain-of-function mutations in various STAT factors. Flow cytometry analysis of patient cells revealed typical alterations associated with autoimmunity, such as expansion of CD11c+ B lymphocytes, also known as "age-associated B cells", follicular helper T lymphocytes and classical monocytes. The clinical phenotype observed varied depending on the mutation's localization, with incomplete penetrance among relatives, but all patients had positive antinuclear autoantibodies, antiplatelet antibodies, and a positive Coombs test.

Conclusion: We report six new monoallelic variants of PTPN2 in six unrelated families. They were variably associated with the development of systemic lupus in one family and Evans syndrome in five families, thus extending the spectrum of clinical manifestations associated with PTPN2 deficiency. All six variants lead to functional defects in PTPN2, either through loss of expression or alterations in its activity resulting in hyperactivation of JAK/STAT pathways. These findings support the notion that loss of function of negative regulators of cytokine pathways can lead to a wide range of autoimmune manifestations and that PTPN2 is playing a pivotal role as a regulator of the immune system. Haploinsufficiency of PTPN2 may constitute a new subset of autoimmune diseases, with clinical expression potentially influenced by other modifying or epigenetic factors, many of which are yet to be discovered. Identifying and understanding the mechanisms of action of these variants allows for the proposition of targeted therapies to affected individuals.

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08:45-08:55 - Shuya Kaneko (Japan)

PATHOGENIC ROLE OF INFLAMMASOME ACTIVATION AND INTERLEUKIN-1B OVERPRODUCTION IN KAWASAKI DISEASE

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Introduction: Kawasaki disease (KD) is an acute self-limited systemic vasculitis with a predilection for coronary arteries that occurs in young children. Although activation of innate immune cells and excessive production of inflammatory cytokines are thought to be relevant to the pathogenesis of KD, the pathological mechanisms of vasculitis in KD are obscure.

Objectives: To investigate the activation profile of inflammatory molecules in innate immune cells and vascular endothelial cells from the view of inflammation-immune cells-vascular crosstalk.

Methods: Thirty-eight patients with KD were enrolled in this study. Transcription levels of whole blood RNA were comprehensively analyzed using the RT-qPCR array kit regarding inflammasome-associated molecules. Serum cytokine levels were quantified with the Luminex assay. In addition, we developed a new in vitro cell stimulation assay that serves as a vasculitis model by co-culturing monocytes differentiated from iPS cells derived from healthy individuals (iPSCMonocytes), human coronary artery endothelial cells (HCAEC), and serum from KD patients or healthy controls (HCs). The changes in RNA signatures in iPSC-Monocytes and HCAEC were analyzed with RT-qPCR.

Results: Transcription levels of 10 inflammasome-associated molecules including IL1B, NLRC4, AIM2, CASP1, CASP5, CARD6, MYD88, NLRP12, NAIP, and TNFSF14 in whole blood RNA were increased in the acute phase of KD patients compared to those of HCs. The transcription levels of these gene expressions decreased in the convalescent phase. No differences in gene expressions were revealed between the good-responsive group and the poor-responsive group to initial treatments for KD. Serum IL-1β levels were increased in patients with KD, especially in patients complicated with coronary artery lesions. With the in vitro vasculitis model, transcriptions of IL1B and TNF in monocytes and IL1B, VEGF, and ANGPT2, which reflect vasculitis/angiogenesis, in HACEC were increased in the KD groups rather than those in the HC groups. On the other hand, the transcription level of ANGPT1 was decreased in the KD groups.

Conclusion: Inflammasome activation and excessive production of IL-1β might play an important role in the pathogenesis of vasculitis in KD.

08:55-09:05 - Maria Vincenza Mastrolia (Italy)

THE KIWI REGISTRY: CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF CHILDREN WITH KAWASAKI DISEASE

M. V. Mastrolia [1 2,*], V. Pandiarajan [3], M. Cattalini [4], A. Taddio [5], S. Vergnano [6], J. Anton [7], W. Sontichai [8], B. Sozeri [9], S. Ozen [10], S. Rosina [11], J. Sánchez-Manubens [12], R. Haviv [13], P. Pal [14], A. Rodrigues Fonseca [15], A. Gagro [16], A. Bagga [17], L. Verdoni [18], D. Montin [19], M. C. Maggio [20], M. Garrone [21], E. Patrone [21], N. Ruperto [21], G. Simonini [1 2] on behalf of for the Pediatric Rheumatology European Society (PReS) and the Paediatric Rheumatology International Trial Organization (PRINTO)

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Introduction: 10-20% of Kawasaki disease (KD) patients are resistant to intravenous immunoglobulins (IVIg). Previous studies on different scoring scales developed by Kobayashi, Egami and Sano had shown a godd sensitivity (77–86%) and specificity (67–86%) in predicting IVIg unresponsiveness in Japanese KD populations1 . Their predictive value was not confirmed in European, American and other Asian populations. The Kawanet group have proposed a score providing good sensitivity (77%) and acceptable specificity (60%) in a not-Asian KD population2.

Objectives: The Comparison and performance of Kobayashi and Kawanet IVIg resistance scores in a multi-centric European and North Indian cohort of KaWasaki dIsease, the KIWI study, has the aim to analyze demographic, clinical, biological and echocardiographic variables associated with IVIg resistance and to assess differences in clinical and treatment outcomes in Caucasian and Asian cohorts of KD children. Methods: This is a retrospective-prospective, observational, international and multicenter study of patients with KD according to the American Heart Association (AHA) criteria. The KIWI study was awarded the 2020 PRINTO/PReS grant, enrollment span from April 2022 to January 2024. Data deriving from KD patients diagnosed from January 1st, 2015, were collected retrospectively by revising medical charts, new KD diagnosis were collected prospectively during the study period.

Results: 612 patients were enrolled with complete data as of January 31st, 2024, from 19 pediatric Rheumatology Units. 372 were male (60.7%), with a median age of 2.4 years. 419 patients (66.0%) were Caucasian, 103 (16.8%) Asian, 19 (3.1%) African and 15 (2.5%) Latin-American. 348 patients (56.9%) presented with complete KD, 234 (38.2%) with incomplete KD, and 19 (3.1%) children reported atypical features. Coronary abnormalities (ectasia) were observed in 90 patients (14.7%), aneurysms in 120 (19.6%) during the disease course. 10 patients (1.6%) developed macrophage activation syndrome (MAS), while 11 (1.8%) presented with Kawasaki disease shock syndrome (KDSS). Mucocutaneous signs were reported in 600 children (98.0%), musculoskeletal signs in 77 (12.6%), lymphadenopathy was observed in 367(60.0%). Gastrointestinal system involvement was recorded in 275 patients (44.9%), and neurological manifestations in 43 cases (7.0%). 595 patients (97.2%) received an IVIg dose at onset,154 (25.2%) received glucocorticoid therapy as first-line treatment. The rate of IVIg resistance in the study population was 21.9% (134). Second-line therapy was administered to 56 patients (41.8%) with glucocorticoids, 15 (11.2%) with anakinra, 11 (8.2%) with infliximab, 4 (3.0%)

with cyclosporine, and 1 (0.8%) with tocilizumab. A full recovery was observed in 568 patients (92.8%), while 44 children (7.2%) experienced sequelae. No deaths were reported.

Conclusion: Our preliminary results confirm an IVIG resistance rate of 20%. Almost 3% of patients experienced MAS or KDSS. Glucocorticoids were the most commonly used second-line therapy, anakinra represented the most frequently administered biologic drug.

Trial registration identifying number: NCT06305611

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09:05-09:15 - Busra Seniz Demir (Türkiye)

INVESTIGATION OF CD4+ T AND INNATE LYMPHOID CELL SUBTYPES IN PATIENTS WITH MEVALONATE KINASE DEFICIENCY

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Introduction: Mevalonate kinase deficiency (MKD) is an autoinflammatory disease with an autosomal recessive inheritance caused by a mutation in the mevalonate kinase enzyme gene. Mevalonate Kinase enzyme contributes to the conversion of Mevalonate-5-Phosphate, an intermediate metabolite, which is essential for synthesis of main proteins involved in cholesterol biosynthesis, ubiquinones production, and protein prenylation. Existing research supports the idea that mevalonate metabolism, in particular, negatively influences the frequency of regulatory T cells (Treg) and T-helper 2 cells (Th2). Furthermore, mevalonate metabolism also has an impact on cell size and proliferation. Changes caused by MVK deficiency in macrophages/ antigen-presenting cells have been questioned in MKD patients until now. Despite the significant role of T cells in metabolism, the changes caused by MVK deficiency in T cells in MKD patients and their contribution to attacks and immunological disorders have not yet been studied.

Objectives: Our study aims to investigate the changes in CD4+ T and Innate Lymphoid Cells (ILCs) which are counterparts of T lymphocytes, immunobiology resulting from mutations that lead to MVK deficiency in MKD patients. We hypothesized that individuals with MVK deficiency may induce certain changes, particularly in the development of Th17 and Treg cells.

Methods: We categorised the patients as HIDS MKD patients in attack and HIDS patients in remission, paediatric patients using statins that simultaneously inhibit mevalonate metabolism and cholesterol biosynthesis, and healthy controls. We collected peripheral blood samples and isolated peripheric

mononuclear blood cells (PBMC) from these patients and healthy volunteers. We collected serum samples from blood and quantified them using a LEGENDplex™ HU Th Cytokine Panel (12-plex) w/ VbP V02 panel. 1x106 PBMC were investigated for CD4+ T cells phenotypes; Th1, Th2, Th17 and Treg cells. We stained the cell surfaces directly with ILC-specific antibodies.

Results: There was no change in total ILCs, Th1 and Th17 cells, a significant decrease in Th2 cells and a significant increase in Treg cells in MVK patients. TCR-mediated T cell proliferation and activation were impaired in MVK patients.

Conclusion: In patients with MVK deficiency, alterations in T cell phenotypes and T cell responses were observed, in particular a reduced type 2 immune response. These results support that MVK deficiency leads to defects in CD4+ T cell subtypes and T cell activation and proliferation in general, and shed light on the broad spectrum of immunodeficiency defects in the adaptive immune system of HIDS patients.

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09:50-11:00 ---*SESSION V*--- Innovations from the Perspective of Health Professionals

10:10-10:20 - Asena Yekdaneh (Türkiye)

EMPOWERING PEDIATRIC RHEUMATIC YOUNGSTERS: A JOURNEY THROUGH PAIN AWARENESS INSIGHTS FROM AN ONLINE WEBINAR

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Introduction: Pediatric rheumatic diseases (PRDs) encompass conditions with unpredictable prognoses, leading to impairments and negatively impacting functioning and quality of life (QoL) (1). Chronic pain, common in PRDs, can significantly limit physical activity and QoL. Biopsychosocial models in pediatrics recognize that chronic pain perception and associated limitations are influenced by physiological and psychological processes (2). Comprehensive assessments are emphasized to identify factors affecting pain, fear of pain, participation, and to provide chronic pain awareness education for children and adolescents (3). Despite the recognized importance of pain awareness, self-management,

and education in adults and PRDs, there's a lack of interactive educational programs specifically targeting pain awareness in PRDs.

Objectives: The aim of this study was to question the effects of a webinar on pain in patients with PRD on pain awareness.

Methods: Twenty-two children and adolescents aged 12-18 years with PRDs were included, consisting of 18 girls and 4 boys. Among them, 4 had Familial Mediterranean Fever, 17 had Juvenile Idiopathic Arthritis, and 1 had Juvenile Fibromyalgia. An interactive webinar via Zoom, comprising a single 30-minute session spread over 2 days within a week, was organized based on participants' preferred timings. Pain awareness levels were assessed using Google Forms with 11 questions before and after the webinar. The webinar provided informative presentations on pain awareness and coping methods. Following the webinar, the same questions were presented as a game-competition using the "Quizizz platform". Participants were also verbally asked about their satisfaction levels during and after the webinar.

Results: The mean age of participants with PRDs were 13.8 years. Before the webinar, 21 of them perceived pain as a negative sensation, and 8 of them believed they couldn't cope with pain in the long term. After the webinar, these numbers changed to 14 and 5, respectively. Additionally, the number of participants preferring physical activity as a coping method for pain increased from 14 to 21. Awareness of stress levels affecting pain increased from 16 participant to 21. Furthermore, 18 participants expressed a desire for the educational webinar to be organized again. Lastly, while only 17 participants considered pain to be a shareable emotion before the webinar, all children held this view after the webinar.

Conclusion: The preliminary findings of this study indicate that a single educational webinar session can influence pain awareness levels in PRDs. After the webinar, children and adolescents show an enhanced understanding of managing their chronic pain and acquiring coping mechanisms. Moreover, we propose that interactive webinars designed for this purpose can effectively address barriers to participation and provide motivational reinforcement for PRD patients. Encouraged by the positive reception from the participants, we advocate for the integration of physiotherapists and other healthcare professionals working with this patient group in comprehensive educational programs aimed at mitigating the long-term symptoms of PRDs.

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10:20-10:30 - Klaudia Kupiec (United Kingdom)

"I HAVE NEVER SPOKEN TO ANYONE ABOUT THIS BEFORE" : GIVING FATHERS AN OPPORTUNITY TO SHARE THEIR EXPERIENCES

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Introduction: Fathers of children and young people with Juvenile Idiopathic Arthritis have been shown to experience different thoughts and emotions compared to mothers. These different perspectives are important when considering the completion of patient reported outcomes in clinical appointments and as part of research protocols. However, our work has also shown that providing an opportunity for fathers to share their perspective of raising a child or young person with a rheumatological condition is cathartic and provides a release for fathers to talk openly without worry about sharing how they feel. Health Care Professionals can consider these differences and aide parents with strategies to strengthen their partnership in their child's healthcare. This is the first known piece of work to involve fathers of a range of paediatric rheumatological conditions.

Objectives: The IMPACT study is a large four phased UK wide study to design, develop and test a technology intervention to support parents of children and young people with rheumatological conditions. The study follows Experience Based Co-Design Methodology where the patients and their families help shape the study from design through to dissemination. Understanding their viewpoints is critical to ensure the technology we create is useful and usable by parents.

Methods: As part of the first phase of this study we invited children, young people, young adults, parents and healthcare professionals to share with us their experiences and perspectives in focus groups. We wanted to understand their particular barriers and facilitators to good care for all paediatric rheumatological diseases, at all ages. The child and young person groups talked through a vignette to save each child needing to feel they needed to share their own experiences. The other groups had minimal structure and were led by both the research team and in most instances a member of the wide Steering Group, made up of children, young people, parents and health care professionals. Reflexive thematic analysis by Braun and Clark was used to code the data.

Results: We conducted 24 focus groups with 158 participants between 19th Dec 2023 and 18th April 2024. By chance some of the parent groups ended up with just mother participation, we therefore purposefully encouraged the participation of fathers to form a father only group. We ended up running two of these groups with a total of 14 fathers involved and included a range of rheumatological conditions (JIA = 6, JDM=3, CRMO=1, PFAPA=1). Themes arising from the fathers included: Wanting control, Being the bad parent, Their role in the healthcare system, Communication difficulties and Loneliness.

Conclusion: Fathers felt that they often have a different role to play to the child's mother and that when this works well, the roles can contemplate each other. However, fathers also felt that their responsibilities were often challenging, such as for example when they are expected to cause weekly pain through injection administration as the other parent wants to be the comforter. They also talked about a loss of control from not knowing as much as their partner and the worry that this could have on their child's care for example by recalling incorrect medications – some described this as feeling this was a 'test'. This work highlights the need to consider the fathers perspectives and provide strategies for families to consider how to improve communication and work together for the best interests of their child. Fathers also commented that they had never shared their reflections with anyone before and how beneficial they found sharing this within the safety of the fathers group.

10:30-10:40 - Naima Hangström (Sweden)

FOOD AND NUTRIENT INTAKE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: EXPLORING NUTRITIONAL RISKS OF THE SPECIFIC CARBOHYDRATE DIET

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Introduction: The James Lind Alliance has recognized diet as a key research priority for juvenile idiopathic arthritis (JIA)(1). Despite this, and considerable interest from families affected by JIA, studies focusing on dietary interventions are scarce. The Specific Carbohydrate Diet (SCD), known for its potential in managing inflammatory bowel disease, has also shown promise for JIA(2). Nonetheless, there is a lack of knowledge regarding its nutritional impact and associated risks.

Objectives: To comprehensively describe and evaluate food and nutrient intakes in children with JIA following the SCD and contextualize the results relative to general recommendations and intakes in the general population.

Methods: Using three-day dietary records at the end of a 4-week SCD intervention, food and nutrient intakes were evaluated in relation to the Nordic Nutrition Recommendations 2023 and data from a large Swedish dietary survey, Riksmaten Adolescents 2016-17 (RMA) (n=1282).

Results: Out of the 21 children who completed the one-month SCD intervention, ten submitted complete food records. All ten reported a high fruit and vegetable intake, meeting the recommended minimum intake of 500g/day, compared to only 6% in RMA. Median dietary fiber intake was 26g/d, (IQR 21-33) in SCD compared to 16g/d (IQR 12-22) in RMA. Both groups showed elevated saturated fat intake; however, the SCD group also had a high red meat intake compared to recommendations. While the SCD provided high intakes of most micronutrients, four out of ten children had a low Vitamin D intake. Calcium was the only nutrient for which a standard diet offered a higher intake than the SCD, with nine out of ten in the SCD group having inadequate intake.

Conclusion: The high consumption of fruits and vegetables likely contributed to a lower likelihood of nutrient inadequacy among children on the SCD compared to the general population. It also provided beneficial fiber and anti-inflammatory phytonutrients. However, inadequate calcium intake, and low vitamin D levels are concerns relevant for children with JIA who may be prone to low bone mineral density. For further dietary optimization, particular attention should be given to reducing saturated fat and red meat intake, considering the increased risk of cardiovascular disease that children with JIA may face in adulthood. These findings underline the necessity of tailored dietary guidance, specific to the disease, for optimal patient and parent support, regardless of adherence to a specialized diet. Further research is imperative to establish specific nutrient recommendations for children with chronic inflammatory conditions, paving the way for improved disease management.

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10:40-10:50 - Asya Albayrak (Türkiye)

ASSESSMENT OF GRIP STRENGTH, BODY COMPOSITION AND PHYSICAL PERFORMANCE OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: COULD SARCOPENIA BE POSSIBLE?

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Introduction: Sarcopenia is described by the loss of skeletal muscle mass and reduced muscle strength or physical performance (1). Historically, sarcopenia was primarily linked with older adults; however, a decrease in muscle mass, strength, and function associated with chronic diseases has also been observed in pediatric populations (2). Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood, which can cause a decrease in muscle strength and physical performance and may be associated with sarcopenia (3).

Objectives: The aim of this study was to evaluate grip strength, body composition, and physical performance in adolescents with JIA to identify possible sarcopenia and to compare them with healthy controls.

Methods: Twenty-one adolescents with JIA and 16 healthy controls aged between 12 to 17 years old were included in the study. The grip strength of the patients was assessed with the hand-held dynamometer (Kinvent Physio K-Grip), in terms of peak force (PF), mean force (MF), mean RFD, time to peak force (TPF), and fatigue parameters. Grip measurements were repeated three times for both hands. The body composition was analyzed using the Bioelectrical Impedance Analysis Device (Tanita SC240MA), and for each participant, appendicular skeletal muscle mass (ASM)/weight and muscle-to-fat ratio (MTF) were calculated. The physical performance was evaluated through the 6 Minute Walk Test (6MWT) and walking speed.

Results: The mean age of the children and adolescents diagnosed with JIA and healty controls included in the study was 14.71±1.79 and 15.43±0.96 years, respectively. When compared with healthy controls, grip strength measured for three repetitions for both hands in adolescents with JIA was significantly lower in terms of PF, MF, and mean RFD ($p<0.05$), while there was no difference in terms of TPF and fatigue ($p>0.05$). When body composition and physical performance results were compared, ASM/weight and MTF ratios, 6MWT and walking speed of adolescents with JIA were significantly lower compared to healthy peers ($p<0.05$).

Conclusion: The results of this study indicate that grip strength, muscle mass, and physical performance are significantly affected in adolescents with JIA compared to their healthy peers. We believe that the observed decrease in grip strength, muscle mass, and physical performance in children with JIA may suggest the potential development of sarcopenia. Therefore, we recommend a detailed evaluation of these parameters in adolescents with JIA before planning physical activity and exercise programs. Given these findings, we believe that sarcopenia in adolescents with Juvenile Idiopathic Arthritis emerges not merely as a possibility but as a critical condition that necessitates proactive, targeted interventions to mitigate its progression and optimize health outcomes. This study was supported by TÜBİTAK 1001- Scientific and Technological Research Projects Support Program with project number 121E690.

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10:50-11:00 - Nilay Arman (Türkiye)

THE EFFECT OF AN IMMERSIVE VIRTUAL REALITY EXERCISE PROGRAM (JIAFIT-XR) ON PHYSICAL FITNESS AND FUNCTIONAL CAPACITY IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: PRELIMINARY RESULTS OF A RANDOMIZED CONTROL TRIAL

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Introduction: Juvenile Idiopathic Arthritis (JIA), the most common pediatric inflammatory disease characterized by chronic joint pain, swelling, and limited range of motion, highlights the importance of prescribing physical activity and exercise in this population (1). The combination of exercise training and video games, termed "Exergaming," merges the competitive aspects and enjoyment of video games with physical activity, potentially reducing perceived exertion while maintaining high energy expenditure and increasing motivation (2). In recent years, exergaming has begun to incorporate immersive virtual reality (IVR) elements to further enhance the user experience (3).

Objectives: The aim of the present study was to investigate the effect of a personalized home-based exercise program (HBEP) versus an IVR exergame (JiaFIT-XR) program on physical fitness (PF) and functional capacity in adolescents with JIA.

Methods: Seventeen patients with JIA were randomly assigned to an IVR exergame program (n=10) called JiaFIT-XR and the HBEP (n=7). For the JiaFIT-XR program, utilizing the Oculus Quest 3 headset, a virtual reality experience for PF was provided through Fit-XR games including "Boxing", "HIIT", "Combat", "Sculpt" and "Dance" tailored to the individual's level of PF, thus creating an individualized multicomponent (balance, strength, agility, endurance) IVR exergame program. The exercise program was limited to 25-30 min per day and implemented under physiotherapist supervision in the clinic twice a week for 8 weeks. In the HBEP, a personalized multicomponent exercises were implemented based on the participants' level of PF. The participants' PF was assessed using the FitnessGram test battery, which included the Curlup Test, Push-up Test, Trunk Lift Test (TLT) and Back Saver Sit and Reach Test (BSSRT). Functional capacity was evaluated through the 6-minute walk test (6MWT), the 10-step stair climbing (10-SSC) test and 1-minute sit-to-stand test (1-STS), along with isometric muscle strength of upper and lower extremities using a dynamometer. Additionally, in the JiaFit-XR group, participants' scores after each game, as well as the estimated calorie expenditure (ECX) recorded and perceived rate of exertion (PRE) were assessed using the Borg Scale.

Results: Intragroup analysis showed significant improvements in the JiaFIT-XR group for the scores of the TLT, 6MWT, 10- SSC, and 1-STS, while the HBEP group demonstrated significant improvements in the scores of TLT, BSSRT, and 1-STS ($p<0.05$). In intergroup analysis, however, test results were similar in both groups ($p>0.05$). Additionally, a significant change was observed in hamstring strength at 30 degrees of flexion and isometric muscle

strength in the clubbing position of the upper extremity in JiaFIT-XR group. Furthermore, while there was a statistically significant increase in ECX for the JiaFIT-XR group over 16 sessions ($p<0.05$), no significant change was found in the PRE ($p>0.05$).

Conclusion: The preliminary results of this study indicate that the JiaFIT-XR program, applied for the first time for exercise purposes, is suitable for improving PF and functional capacity in JIA. It was found to be similarly effective as a HBEP in terms of trunk endurance and flexibility. Furthermore, as a significant outcome, while the ECX increased significantly as the difficulty level of the games increased, there was no significant change in the PRE. This suggests that despite the increasing challenge of the games and the consequent increase in physical activity, the perceived exertion level remaining unchanged indicates that children are benefiting optimally from the exercises, possibly due to the motivation and enjoyment provided by the games.

Trial registration identifying number: ClinicalTrials ID: NCT06176846

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e-Poster Tours DAY 1

e-Poster Tour 1 – Autoinflammatory Diseases

ePoster short communications-1 Autoinflammatory Diseases	
LONG-TERM FOLLOW-UP AND OUTCOMES OF COLCHICINE DISCONTINUATION IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER	Selen Duygu Arık
FAMILIAL MEDITERRANEAN FEVER: WITHOUT FEVER?	Hatice Dilara Karakas
CROSS-NATIONAL BIOLOGIC TREATMENT GUIDELINES FOR FAMILIAL MEDITERRANEAN FEVER: A COMPARATIVE ANALYSIS	Tanja Hinze
TRANSCRIPTOMIC LANDSCAPE OF FAMILIAL MEDITERRANEAN FEVER; A TRANSLATIONAL STUDY	Erdal Sag
THE DIAGNOSTIC AND THERAPEUTIC CHALLENGES OF CHRONIC ARTHRITIS IN FAMILIAL MEDITERRANEAN FEVER	Eray Tunce
VALIDATION OF HUMAN PHENOTYPE ONTOLOGY (HPO) TERMS USING THE EUROFEVER REGISTRY: THE ODINO PROJECT	Caterina Matucci-Cerinic
"OBSERVATIONAL FRENCH COHORT STUDY ON PATIENTS WITH H SYNDROME (SLC29A3-RELATED DISORDERS): EXPLORING INFLAMMATORY AND AUTOIMMUNE MANIFESTATIONS"	Maurine Jouret

LONG-TERM FOLLOW-UP AND OUTCOMES OF COLCHICINE DISCONTINUATION IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Introduction: Familial Mediterranean Fever (FMF) is a monogenic autoinflammatory disease with frequent attacks in Turkey. Colchicine is the main drug to prevent attacks in FMF patients and the main goal is to reduce clinical and subclinical inflammation to prevent long-term complications.

Objectives: The aim of this study is to present the characteristics and follow-up results of children diagnosed with FMF, with at least one genetic mutation in the MEFV gene, who were treated with colchicine for a period of time during the course of the disease and who were discontinued colchicine during follow-up Methods: The medical files of all children with FMF who were followed up regularly every 3-6 months at one Pediatric Rheumatology Clinic center were retrospectively analyzed. Colchicine was discontinued by pediatric rheumatologists if there was no family history of amyloidosis, no attacks during 6 months of colchicine treatment, no homozygous or compound heterozygous exon 10 MEFV mutations, and no proteinuria. Patients who did not need colchicine after colchicine discontinuation were classified as Group 1 and patients who restarted colchicine treatment were classified as group 2. Both groups 1 and 2 were compared in terms of demographic characteristics, clinical findings, and MEFV mutations.

Results: In a cohort of 2300 FMF patients, 100 patients who discontinued colchicine treatment were included. Of the entire cohort, 64% were male. Median age at symptom onset and median age at diagnosis were 5.4 (min-max: 0.2-13.7) and 6.7 (min-max: 1.2-16.1) years, respectively. The median disease duration was 9.1 (min-max: 1.6-18.7) years. The median follow-up period after colchicine discontinuation was 5.1 (min-max: 0.2-18.4) years. Colchicine treatment was discontinued by physician's decision in 63 patients and voluntarily in 37 patients. During follow-up, 78 patients continued to follow-up without medication, while 22 patients restarted colchicine treatment due to clinical attacks and/or elevated acute phase reactants and proteinuria. There was no significant difference between the two groups in terms of baseline clinical characteristics and the appropriateness of colchicine initiation and discontinuation dose according to age. Also there was no significant difference between the two groups in terms of age at symptom onset, age at diagnosis, duration of colchicine treatment and duration of disease follow-up. The duration of the attack-free period before discontinuation of colchicine treatment was analyzed in groups 1 and 2 and no significant difference was found (p:0.77). When the clinical findings of 20 patients who restarted colchicine treatment were evaluated, it was observed that 55% of the patients had abdominal pain and arthralgia, 50% had fever and 5% had chest pain before restarting. However, no patient had arthritis or erysipelas-like erythema. When the two groups were compared for the presence of MEFV mutations, no significant difference was found between the two groups in terms of carrying exon 10 mutations. The MEFV mutation carriage observed in the total cohort consisted of heterozygous mutations of M694V (40%), E148Q (30%) and V726A (16%) alleles in order of frequency.

Conclusion: This study is one of the few long-term studies evaluating the discontinuation of colchicine treatment in childhood AAA patients. It is known that there are no proven data and/or guidelines on the discontinuation of colchicine treatment in childhood. Long-term and large studies on this subject are needed in the following years.

FAMILIAL MEDITERRANEAN FEVER: WITHOUT FEVER?

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Introduction: Familial Mediterranean fever (FMF), one of the most common periodic fever syndromes of childhood, is an autosomal recessive autoinflammatory disease characterized by manifestations of polyserositis, arthritis, or erysipelas-like erythema accompanying recurrent fever. Its pathophysiology is based on the uncontrolled release of proinflammatory and pyrogen cytokines, primarily IL-1β, by MEFV gene mutations encoding the pyrin protein.

Objectives: The aim of this study was to investigate the demographic, clinical, and laboratory findings of patients diagnosed with FMF without fever. In addition, their differences with other patients without fever in the study group were evaluated. Methods: Patients who were followed up for at least 6 months with the diagnosis of FMF in the last 10 years (2011-2021) in the Department of Pediatric Rheumatology of Ankara University Faculty of Medicine were included in the study. The diagnosis of familial Mediterranean fever was made according to the "Ankara" pediatric diagnostic criteria. The data were taken from electronic patient files and analyzed retrospectively.

Results: In the last 10 years, 576 patients (52.3% female) were followed up with FMF in our clinic. In 7.1% (n=41) of these patients, fever was not a sign of FMF attacks. There was no difference in gender distribution between the groups with and without fever ($p>0.05$). Patients without fever were compared to patients with fever; it was found that the age of onset and diagnosis was statistically significantly later ($p<0.001$), but recurrent acute arthritis was more common ($p=0.020$). FMF-related diseases were found to be more common in these patients ($p<0.001$), and FMF was less common in the family ($p=0.040$). It was determined that this group did not require any anti-IL-1 treatment.

Conclusion: Fever may not accompany attacks as a clinical complaint in a very small proportion of FMF patients. In patients with recurrent short-term abdominal pain, chest pain, inflammatory complaints such as arthritis, and family history, FMF should also be considered in the differential diagnosis in the absence of fever.

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CROSS-NATIONAL BIOLOGIC TREATMENT GUIDELINES FOR FAMILIAL MEDITERRANEAN FEVER: A COMPARATIVE ANALYSIS

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Introduction: Familial Mediterranean fever (FMF), the most common genetic autoinflammatory disease (AID), exhibits a distinct geographic distribution predominantly in populations of the eastern Mediterranean.(1) While colchicine stands as the cornerstone therapy for FMF, 5-10% of patients exhibits colchicine resistance or intolerance, necessitating alternative treatments such as biological disease-modifying anti-rheumatic drugs (bDMARDs), particularly interleukin-1 (IL-1) inhibitors.(2)

Objectives: This study explores the accessibility and reimbursement policies concerning IL-1 inhibitors for the treatment of FMF across various countries. Additionally, it aims to compare the official national guidelines utilized in different regions globally.

Methods: This study is a part of the Clinical Practice Strategies (CLiPS) project that aims to collect real life clinical practice strategies from worldwide physicians dealing different medical topics with the Juvenile Inflammatory Rheumatism - Clinical Practice Strategies (JIR-CliPS) Action falling under its umbrella. The JIR-CliPS is a project that aims to collect real life clinical practice strategies from worldwide physicians dealing with five different medical topics. One of the five topics is the use of bDMARDs for treatment of AID. We initially collected data on access to bDMARDs and reimbursement policies by country through a questionnaire distributed to adults and pediatric rheumatologists, as well as experts who completed the CLiPS questionnaire. Subsequently, we contacted experts from countries that did not respond to the questionnaire, asking the same questions via email. In addition, we conducted a comprehensive search for national recommendations on FMF treatment using the PubMed/MEDLINE database and Google search, without language restrictions. Finally, we conducted an analysis of standardized recommendations, focusing on variations between countries in defining colchicine resistance, colchicine intolerance, colchicine-related adverse events, indications for biologic use, and the availability of IL-1 inhibitors.

Results: We examined 31 countries and obtained national guidelines for 11 of them. Among these, articles were published in PubMed for five countries (Brazil, Egypt, Iran, Germany, France). Two guidelines (from The Netherlands and Turkey) were received via email from experts who completed the CLiPS questionnaire. For the remaining four countries (England, Israel, Belgium, Spain), we accessed the guidelines in the respective national language using Google search. Furthermore, representatives from five countries (Italy, Portugal, Slovenia, Switzerland, Armenia) indicated the utilization of the EULAR 2016 guideline (3). Anakinra treatment was available for colchicine- resistant FMF treatment in 21 countries, with 14 of them covered by National Health Insurance reimbursement. Canakinumab treatment was accessible in 17 countries, with reimbursement coverage in 14 of them. Reimbursement conditions varied across many countries, with seven countries (Belgium, England, Spain, Lithuania, Romania, Brazil, Turkey) having additional indications for restricted prescription of biological drugs in FMF patients.

Conclusion: This study underscores the heterogeneous landscape of prescribing IL-1 inhibitors for FMF globally, reflecting variations in national guidelines, medication availability, and reimbursement policies. Standardized guidelines incorporating clear definitions of treatment indications and harmonized access to therapeutic options are warranted to optimize patient care and outcomes.

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TRANSCRIPTOMIC LANDSCAPE OF FAMILIAL MEDITERRANEAN FEVER; A TRANSLATIONAL STUDY

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Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease, characterized by recurrent attacks of inflammation. Although it is an autosomal recessive disease, some patients develop disease phenotype even with only 1 MEFV mutations. Furthermore, about 3-5% of the patients do not respond adequately to colchicine treatment.

Objectives: We investigated the transcriptomic profile of FMF patients with different phenotypes and genotypes to figure out the possible differential signatures and diagnostic pathways.

Methods: RNAs derived from peripheral blood mononuclear cells (PBMCs) of 20 FMF patients, all meeting Eurofever criteria and on colchicine treatment (colchicine resistant with homozygous exon 10 mutations n=5; colchicine responsive with homozygous exon 10 mutations n=5; compound heterozygous with VOUS n=5; heterozygous exon 10 mutations n=5) were studied. Samples from 10 healthy controls (heterozygous MEFV carriers without clinical features n=5; healthy none MEFV mutation carriers n=5) were included as the healthy group. RNA-sequencing was performed on Illumina NextSeq550 with Qiaseq library kits. CLC software was used for data analysis. We first compared the transcriptomic profiles between patients expressing the FMF phenotype and healthy individuals. Later on, we analyzed the differences between FMF patients with heterozygous mutations and the ones without FMF phenotype but are heterozygous carriers.

Results: When we compared FMF patients with healthy individuals, we encountered 157 differently expressed genes overall. Among those genes, 104 of them were down-regulated in FMF patients while 53 of them were upregulated. We then analyzed the pathways. Interestingly, genes related with inflammatory response, IFN type 2 pathway, adaptive immune system pathway, IL-10 and IL-6 were downregulated. On the other hand, genes related with ubiquitination, apoptosis, heat shock proteins, IL-23, tubulin proteins, FOS-B and LAT pathway were upregulated. We than compared the differences between FMF carriers with the FMF phenotype to those without any features (healthy). We have seen a gradual difference with a similar signature showing these proteins might be useful for differentiating patients from healthy carriers. Among those genes SPP1 (Osteopontin) has been the most powerful one to help to discriminate the FMF patients.

Conclusion: The immune system pathways seem exhausted in FMF patients, which might explain the downregulation of these pathways and upregulation of LAT, involved in exhaustion. Another important gene discriminating colchicine resistant group was FOS-B (together with Rho-GTPase) which is also an important proinflammatory transcription factor. Osteopontin (SPP1) and FOS-B might be an important biomarker to discriminate the FMF phenotype requiring treatment. We are continuing further analysis and confirmation studies.

References: Acknowledgement: First two authors contributed equally. This study was supported by Scientific and Technological Research Council of Turkey (TUBITAK) under the Grant Number 120C127 as part of 2247-A National Outstanding Researchers Program. The authors thank to TUBITAK for their supports.

THE DIAGNOSTIC AND THERAPEUTIC CHALLENGES OF CHRONIC ARTHRITIS IN FAMILIAL MEDITERRANEAN FEVER

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Introduction: Familial Mediterranean Fever (FMF) and Juvenile Idiopathic Arthritis (JIA) are two significant rheumatological diseases commonly seen in childhood. FMF is an autosomal recessive disorder typically observed in populations of Mediterranean origin, characterized by recurrent episodes of fever, peritonitis, pleuritis, and arthralgia/arthritis. FMF is an autoinflammatory disease, while JIA is an autoimmune disease. It is not yet fully understood whether chronic arthritis in FMF patients is related to FMF itself or occurs independently of FMF

Objectives: We aimed the diagnostic and therapeutic challenges of chronic arthritis in patients with FMF.

Methods: This study was a retrospective analysis of pediatric FMF patients followed at our pediatric rheumatology clinic between 2016 and 2023. A total of 472 pediatric patients diagnosed with FMF and having a homozygous genotype in exon 10 were included in the study, and out of these patients, 32 who developed chronic arthritis during follow-up were evaluated. We tried to include the 32 patients with FMF diagnosis who developed chronic arthritis during follow-up in the JIA subgroup. The 2019 Eurofever/PRINTO criteria were used to diagnose AAA and the 2001 ILAR criteria were used to diagnose JIA. Demographic and clinical data were recorded from the patients' medical charts.

Results: A total of 472 children (251 (53,2%) female and 221 male) were included in the study. The median (IQR; 25 - 75) of age disease onset and age at diagnose was 3.5 (1.8-6) years and 5 (3-8) years, respectively. Parental consanguinity was present in 36.2% of patients and 58% had a family history of FMF. The median of following time was 32 (18-43) months. Genotypes of patients: 402 (85,2%) M694V/M694V, 38 (8,1%) M680I/M680I, 23 (4,9%) V726A/V726A, 8 (1,7%) R761H/R761H, 1 (0,2%) I641F/I641F. Chronic arthritis was observed in 32 out of 472 patients (6.8%) during follow-ups. 17 (53,1%) were female. The median (IQR; 25 - 75) of age disease onset and age at diagnose was 5 (3-8) years and 7 (5-15) years, respectively. Parental consanguinity was present in 25% of patients and 50% had a family history of FMF. Genotypes of patients: 30 (94%) M694V/M694V, 1 (3%) M680I/M680I, 1 (3%) V726A/V726A. JIA subgroups were as follows: 16 (50%) oligoarticular JIA, 10 (31,3%) juvenile spondyloarthritis (SpA), 2 (6,3%) polyarticular JIA, 1 (3,1%) psoriatic arthritis (PsA), 2 (6,3%) systemic JIA and 1 (3,1%) unclassified arthritis. In patients, ANA positivity rate was 25% and HLA B27 positivity rate was 18,6% (The HLA-B27 test was able to be performed in 27 patients.). RF and CCP values were negative in 2 patients with polyarticular JIA. Only 1 patient was found to have uveitis, and that patient had SpA. Complete response to diseasemodifying antirheumatic drugs (methotrexate, salazoprine, leflunomide) was achieved in 34,4% of patients, while 65,6% needed biological agents (mainly etanercept, adalimumab, anakinra, kanakinumab, infliximab). Biological treatment was required in 62,5% of oligoarticular JIA, 60% of SpA, 100% of polyarticular JIA, 100% of PsA, 50% of systemic JIA and 100% of unclassified arthritis.

Conclusion: Chronic arthritis was observed in 32 out of 472 patients (6.8%) during follow-ups in FMF patients. In the group with chronic arthritis, the age at onset of attacks and diagnosis was higher. The need for biological therapy in this group was 65.6%, significantly higher than in JIA studies in the literature.

VALIDATION OF HUMAN PHENOTYPE ONTOLOGY (HPO) TERMS USING THE EUROFEVER REGISTRY: THE ODINO PROJECT

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Introduction: The HPO project (Human Phenotype Ontology) represents the creation of a terminology database for phenotypical, clinical and laboratory characteristics of genetic diseases. In 2022 the AutoInflammatory diseases section has been revised and updated (1), but the accuracy of the new terms has not yet been validated in real patients

Objectives: to validate the HPO terms in a cohort of real patients, in order to evaluate their diagnostic accuracy and to implement the database with missing terms

Methods: the clinical variables have been extracted from the Eurofever registry and codified with their HPO matching terms. Every patient in Eurofever with an autoinflammatory disease has been recoded with the HPO corresponding to his phenotype. To evaluate the phenotypical similarity between the HPO terms assigned to every patient in Eurofever and the HPO already linked to that disease, computerized tools of graph-aware distance were used.

Results: 224 variables from EF were considered and codified into one or more HPO codes (as appropriate): 215 clinical, 5 laboratory and 4 demographic terms. The variables without any HPO corresponding term were retained. Specifically, a full correspondence Eurofever-HPO was found for 195 terms, a partial one for 12 and no correspondence for 17. Of these, the time lenght of the fever and the ethnicity of the patients were the most important missing variables. The clinical variables of 3650 patients present in the Eurofever registry were then reconverted using HPO codes. The phenotypic similarity between the HPO terms assigned to each patient in EF and all the HPO annotated diseases was then calculated using graph-aware distances (R ontology Similarity) to estimate the discriminative power of HPO in assigning a patient phenotype to the correct diagnosis. Using the frequencies of clinical manifestations observed in the Eurofever dataset, we applied four clustering algorithms: Multiclass elastic net penalized regression, K nearest neighbors, Random forest, and

Gradient Boosting (XG-Boost). Preliminary findings reveal that Multiclass elastic net penalized regression outperform other clustering algorithms with an average accuracy higher than 0.70. Our preliminary findings suggest that clustering patients using HPO terms differ significantly from cluster analysis based on the actual frequency of clinical manifestations observed in the Eurofever registry. This discrepancy arises from differences in the frequencies of clinical variables reported by HPO and based on the literature, compared to their frequency in a real-life dataset provided by Eurofever.

Conclusion: additional analyses are needed to improve classification accuracy and identification of the most relevant symptoms for each disease. Moreover, the HPO terminology needs an implementation with the missing terms, and a revision of the codes associated to each disease.

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OBSERVATIONAL FRENCH COHORT STUDY ON PATIENTS WITH H SYNDROME (SLC29A3-RELATED DISORDERS): EXPLORING INFLAMMATORY AND AUTOIMMUNE MANIFESTATIONS

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Introduction: The H syndrome is an autoinflammatory disorder associated with mutations in the SLC29A3 gene, classified within the R group of histiocytosis. Recent studies have suggested that Toll-like receptor (TLR7/8) activation is due to impaired nucleoside trafficking, resulting in persistent activation of ERK and histiocytosis proliferation.

Objectives: This cohort study aims to investigate the long-term evolution over several years and evaluate the efficacy of novel therapeutic interventions for individuals with H Syndrome.

Methods: In November 2023, an observational call was distributed through various nationwide rare disease networks and French adult and pediatric scientific societies. Inclusion criteria involved

individuals, whether children or adults, diagnosed with H syndrome. Demographic, clinical, and biological data were collected using an electronic database called "Histiobase."

Results: In May 2024, thirty patients from France were enrolled. The gender distribution was balanced, with a median age at inclusion of 23 years (ranging from 0.5 to 58 years). Patients exhibited diverse inflammatory phenotypes including skin hyperpigmentation or induration (n=19), adenopathy enlargement (n=15), articular deformities (n=16), arthritis (n=8), kidney involvement (tubular (n=3) and glomerular lesions (n=4)), pericarditis (n=5), aortic inflammation (n=2), pachymeningitis (n=2), and macrophagic activation syndrome (n=1). A few patients also showed signs of autoimmunity, such as autoimmune cytopenia (n=1), ANCA-vasculitis with MPO antibodies (n=1), type 1 diabetes with specific autoantibodies (n=2), and antinuclear antibodies (n=2). Two patients experienced infectious complications associated with lymphocyte B deficiency. Twenty patients were found to have deafness. Some severe complications could be attributed to histiocyte infiltrations, such as ureteral compression (n=3), cardiac mass (n=1), and peridural infiltration (n=2). Thirteen patients received treatment with Tocilizumab, 5 with Cobimetinib (MEK inhibitor), and 2 with anti-TNF biotherapies, resulting in complete or partial responses to inflammatory and proliferative manifestations. H syndrome can mimick various rheumatologic diseases. Prior to genetic analysis, diagnoses retained included idiopathic juvenile arthritis, IgG4- related syndrome, systemic scleroderma, Erdheim-Chester disease, periarteritis nodosa, unclassified auto-inflammatory disease and immune deficiency.
Conclusion: H syndrome presents as a rare condition with a wide spectrum of systemic clinical features, encompassing proliferative, autoinflammatory, autoimmune manifestations, and immune deficiency. Although promising therapeutics show efficacy, their long-term effectiveness needs assessment. An international cohort study could offer more insights to enhance patient management.

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LONG-TERM FOLLOW-UP PATIENTS WITH IGA VASCULITIS NEPHRITIS - THE EXPERIENCE OF THE CROATIAN NATIONAL CENTER

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Introduction: The discussion surrounding the duration of follow-up for IgA vasculitis (IgAV) patients at risk of developing nephritis (IgAVN) remains unresolved. Moreover, there's still no consensus on the appropriate follow-up period for patients who develop IgAVN.

Objectives: Hence, our research sought to delineate the clinical and laboratory traits of individuals with IgAVN, alongside probing factors linked to both short and long-term prognoses in these patients.

Methods: We extracted patients diagnosed with IgAVN from the national cohort of individuals with IgAV diagnosed between 2010 and 2024, utilizing the EULAR/PRES/PRINTO criteria. Specifically, we focused on patients who received follow-up care for a minimum of six months at the largest tertiary center.

Results: During the specified timeframe, 739 patients received an IgAV diagnosis, with 155 subsequently developing IgAVN. Among these, 93 were monitored for more than six months, of whom 43 (46%) were male. The median age at IgAVN diagnosis was 7.62 (5.62, 11.635) years, with nephritis typically appearing 4 (0, 20) days after initial symptoms, though onset could occur as late as 559 days afterward. Nephritic syndrome manifested in 14 patients (15%), nephrotic syndrome in 6 (6.5%), and the remainder exhibited abnormal urine findings, primarily erythrocyturia and proteinuria (43%), or isolated erythrocyturia (40.9%). Hypertension was recorded in 22.5% of patients. Median follow-up was 15 (9.5, 43.5) months. Treatment predominantly consisted of systemic glucocorticoids (50.5%), followed by NSAIDs (33.3%) and immunosuppressants (17.2%). At the six-month mark post-diagnosis, abnormalities in urine persisted in 34 patients (36.6%), decreasing to 14 patients (15%) after 12 months, signifying a noteworthy enhancement in laboratory results ($p < 0.01$). However, after 6 and 12 months, patient outcomes did not significantly differ ($p = 1.0$), with 78 patients (83.9%) experiencing a good outcome, 13 (14%) achieving a good but suboptimal outcome, and 1% encountering renal function failure.There was no significant outcome difference between patients with isolated erythrocyturia and those with proteinuria after six or twelve months ($p = 0.74$). Among patients followed-up for over six months (44% of the cohort), there were significantly more males ($p = 0.02$) and individuals treated with immunosuppressive agents ($p = 0.08$).

Conclusion: Our findings indicate that IgAVN typically arises within the initial 4 days of IgAV onset, with most patients experiencing a positive outcome. We considered outcomes most favorable after more than 12 months post-diagnosis, aligning with simultaneous improvements in our patients' laboratory findings. However, there's no notable contrast in outcomes between individuals with isolated erythrocyturia and those with proteinuria. While the outcome doesn't significantly differ between patients at six and twelve months of follow-up, our study highlights that 4% of patients developed IgAVN after surpassing six months but less than twelve months of monitoring. This underscores the importance of extending follow-up to at least twelve months for individuals with IgAV.
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INVOLVEMENT OF GD-IGA1, HMGB1, RAGE, AND PCDH1 IN CHILDHOOD IGA VASCULITIS (IGAV)

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Introduction: IgA vasculitis (IgAV) is the most common systemic vasculitis of childhood. The pathogenesis of IgAV is more complex than it appears with many intertwined factors, including various molecules that may play the role of biomarkers. Regarding the latter, biomarkers are some of the current research topics related to IgAV since identification of a useful surrogate biomarker that could indicate an active disease and predict possible damage, particularly IgA vasculitis nephritis (IgAVN), remains a challenge.

Objectives: We aimed to investigate potential role of four molecules in the pathogenesis of IgAV: high mobility group box 1 (HMGB1), receptor for advanced glycation end products (RAGE), galactose-deficient immunoglobulin A1 (Gd-IgA1) and protocadherin 1 (PCDH1).

Methods: A prospective study enrolled 86 children with IgAV and 70 children from the control group. HMGB1, RAGE, GdIgA1 and PCDH1 in serum and urine were determined by the enzyme-linked immunosorbent assay (ELISA) method at the onset of the disease and after six months interval and once in the control group.

Results: Concentrations of HMGB1, RAGE and PCDH1 in sera and concentrations of HMGB1, RAGE, Gd-IgA1 and PCDH1 in urine were statistically significantly higher in children with IgAV than in the control group ($p<0.001$). A statistically significant difference was observed in concentrations of HMGB1 (5573 pg/mL vs. 3477 pg/mL vs. 1088 pg/mL, $p<0.001$) and RAGE (309 pg/mL vs. 302.4 pg/mL vs. 201.3 pg/mL, $p=0.012$) in sera of children with IgAV at the onset of the disease compared to six months interval and between the control group. Logistic regression distinguished serum GdIgA1 (CI 0.943-0.982, $p=0.028$), RAGE (CI 0.983-0.998, $p=0.026$) and PCDH1 (CI 1.021-1.137, $p=0.012$) and urinary HMGB1 (CI 1.000-1.002, $p=0.026$) as predictors of arthritis. Cox regression analysis didn't reveal any of investigated biomarkers as a predictor of IgAVN. However, concentration of HMGB1 in urine after six month follow-up was higher in children with IgAVN compared to IgAV without nephritis (270.9 (146.7-542.7) ng/mmol vs. 133.2 (85.9-318.6) ng/mmol, $p=0.049$) and significantly positively correlated with urine albumine to creatinine ratio ($\tau=0.184$, $p<0.05$), the number of erythrocytes in urine samples ($\tau=0.193$, $p<0.05$) and with outcome of nephritis ($\tau=0.287$, $p<0.05$).

Conclusion: Our results suggest that Gd-IgA1, HMGB1, RAGE and PCDH1 interplay in the complex pathogenesis of IgAV, with HMGB1 and RAGE showing elevated values during the disease follow-up interval and thus may indicate residual low inflammatory activity or tissue damage. Although none of the assessed molecules revealed as a predictor of IgAVN, urinary HMGB1 highlighted as a potential tool in the follow up of children who developed IgAVN.
SUPPORT: Croatian Science Foundation Project IP-2019-04-8822.

FACTORS ASSOCIATED WITH THE NEED FOR IMMUNOSUPPRESSIVE THERAPY IN PEDIATRIC BEHCET'S DISEASE

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Introduction: In the treatment of Behcet's Disease, early management is essential to relieve symptoms, control inflammation, and prevent relapses, damage and complications.

Objectives: Our study aimed to determine the predictors for the need for immunosuppressive therapy in pediatric Behcet's Disease at the time of diagnosis.

Methods: This retrospective observational study was conducted in patients diagnosed with Behcet's Disease in our center between 2010 and 2023. The diagnosis of Behcet's Disease was confirmed with the Pediatric Behcet's Disease criteria. Patients were divided into two groups: those treated with only colchicine and those with immunosuppressives.

Results: 107 (100%) patients diagnosed with Behcet's Disease were included in the study. 59 (55.1%) of the patients were female and 48 (44.9%) were male. The median age at symptom onset was 11 (8-13) years, and the median age at diagnosis was 14 (11-15) years. The median duration of symptoms until diagnosis was 1 (1-2) year. There was a family history of Behcet's Disease in 40 (37.4%) patients. 107 (100%) patients had oral ulcer, 62 (57.9%) had genital ulcer, 46 (43%) had cutaneous involvement, 22 (20.6%) had vascular involvement, 16 (15%) had neurological involvement, 22 (20.6%) had ocular involvement, 37 (34.6%) had musculoskeletal involvement and 8 (5.7%) had epididymitis. 34 (31.8%) patients had a positive pathergy test and 54 (50.5%) patients had a positive human leucocyte antigen (HLA) B5/51 gene test. The median follow-up period was 2 (1-5) years. While 70 (65.4%) patients were treated with only colchicine, 37 (34.6%) patients were treated with immunosuppressive. 27 (25.2%) patients treated with immunosuppressive at the time of diagnosis and 10 (9.3%) patients with during follow-up. 27 (25.2%) patients were treated with azathioprine, 10 (9.3%) with cyclophosphamide, 8 (7.5%) with infliximab, 3 (2.8%) with adalimumab, 23 (21.5%) with steroid and 4 (3.8%) with methotrexate. 13 (12.1%) patients were treated with 1, 13 (12.1%) with 2, 8 (7.5%) with 3, and 3 (2.8%) with 4 different immunosuppressive. The most frequently used biologic immunosuppressive was infliximab. Median leukocyte count, neutrophil count and erythrocyte sedimentation rate values at the time of diagnosis were higher in immunosuppressive treated patients (p=0.001, p=0.004, p=0.001). Fever was more common in immunosuppressive-treated patients and genital ulcers were more common in patients treated with only colchicine (p=0.0001, p=0.004).

Conclusion: It is important to predict patients who may need immunosuppressive therapy at the time of diagnosis in Behcet's disease. Patients presenting with fever and elevated leukocyte count, neutrophil count and erythrocyte sedimentation rate values should be considered to have higher immunosuppressive needs in treatment management.

A GENETIC INSIGHT TO THE ETIOPATHOGENESIS OF KAWASAKI DISEASE- A REAL TIME PCR BASED STUDY OF 15 GENES IN NORTH INDIAN CHILDREN

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Introduction: The pathogenesis of KD is still an enigma even after 5 decades. In an in-silico analysis from our institute, we found that 15 genes (IL1B, S100A12, MMP9, ITGAM, TLR2, PRF1, CD44, TLR8, TREM1, UBB, IL7R, FCER1G, CXCL8, SPI1and FCGR1A) were associated with pathogenies of KD. In this study, we analysed gene expression of these 15 genes by real-time- polymerase chain reaction (RT-PCR) method.

Objectives: To study the expression of genes IL1B, S100A12, MMP9, ITGAM, TLR2, PRF1, CD44, TLR8, TREM1, UBB, IL7R, FCER1G, CXCL8, SPI1and FCGR1Ain children with KD To analyse the genetic expressions of these 15 genes in children with KD versus controls. Gene expression of the 15 genes was compared pre and post-IVIG treatment, the gene expressions were compared with disease controls (systemic lupus erythematosus) and in KD patients with and without coronary artery aneurysms (CAA)

Methods: The study was conducted from July 2022-December 2023. We enrolled 34 patients with KD, (samples were taken before and after treatment with IVIG), 9 healthy controls and 4 disease controls. We used TaqMann assay for doing RT-PCR in Step-one plus system. Relative gene expression was calculated as 2-ΔΔCT (Livak method).

Results: Mean age at diagnosis was 32.5 months. Male to female ratio was 2.4:1. Of the 34 patients, 59% had incomplete KD. Twelve genes were up regulated (IL1B, ITGAM, TLR2, CXCL8, SPI1, S100A12, MMP9, PRF1, TLR8, CD44, FCER1G,and FCGR1A), while 3 genes (UBB, IL7R, and TREM1) were down regulated. IL1B and MMP9 showed 6-fold increased expression, and S100A12 showed 4-fold increased expression. ILIB showed statistically significant upregulation in patients with KD compared to controls (P=0.049). SPI-1 (p=0.0425) and TREM1 (p=0.0180) showed a significant downregulation compared to healthy controls. On comparing pre- vs post-IVIG group in KD, genes that were downregulated during pre-IVIg phase has shown increased expression post-IVIg [PRF1 (p=0.0313), UBB (p=<0.0001), IL7R (p=0.0022) and TREM1 (p=0.0187)]. On comparing with the disease controls, expression of CD44 (p=0.0400) and TLR2 (p=0.0184) was significantly low in patients with KD. IL1B expression is increased in the CAA group compared to controls (p=0.025) The relative gene expression of CD44 (p=0.023), ITGAM (p=0.026), TLR2 (p=0.008) and FCGR1A(p=0.017) were found to be significantly downregulated in CAA group compared to KD without CAA.

Conclusion: Among the 15 genes, IL1B and MMP9 had a 6-fold increase in expression, and IL1B expressions were reduced after treatment with IVIG. Decreased expression of UBB and PRF1 gene in pre IVIG group suggests an involvement of interferon pathways and NK cells in the pathogenesis of KD. In KD patients with CAA, IL1B is found to be upregulated and FCGR1A, TLR2, ITGAM, and CD44 are expressed lower compared to KD patients without CAA.

INFANTILE KAWASAKI DISEASE-AN EXPERIENCE FROM A TERTIARY CARE HOSPITAL IN BRISTOL

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Introduction: Kawasaki disease (KD) is a small to medium vessel vasculitis affecting young children. KD in infants can be a diagnostic challenge due to incomplete/atypical presentations. Upto two thirds of infants with KD develop coronary artery aneurysms (CAA)1.

Objectives: To describe the clinical profile, echocardiography and outcomes in infants diagnosed with KD.

Methods: A retrospective observational study was conducted at Bristol Royal Hospital for Children to include children

Results: Among a total of 156 children diagnosed with KD, 28 were aged under 1 and included in this study(17.95%). Mean age was 5. 8 months [2-11] with more boys affected (Male: Female= 2.1:1). Only 8 infants fulfilled criteria for complete KD; with the remaining 20 diagnosed as incomplete KD. The presenting symptoms were rash (78.57%), mucosal changes (67.86%), bilateral non-purulent conjunctivitis (64.29%), extremity changes (42.86%) and lymphadenopathy (17.86%). 1 had reactivation of Bacillus-Calmette-Guerin scar. 21/28 (75%) developed CAA. Left main coronary artery (LMCA) was the most common, followed by right coronary artery (RCA). Giant coronary aneurysms (Z score >+10) were seen in 6/28 (21.42%). Maximum coronary artery Z score was +50. Other cardiac findings included pericardial effusion-6/28 (21.42%), severe LV dysfunction (1/28) and distal RCA thrombus (1/28). All children received intravenous immunoglobulin (IVIG) and aspirin as per protocol. Additional treatment included 2nd dose IVIG in 11/28 (39.29%), methylprednisolone in 11/28 (39.29%), infliximab in 3/28 (10.71%) and anakinra in 1/28.1 infant succumbed secondary to rupture of giant aneurysm. A 1 year follow up showed resolution in 12/21 (57.14%) whereas 7/21 (33.33%) had persistent CAA and 1 had recurrence. 1 child had extensive myocardial damage and underwent heart transplant with good outcome.

Conclusion: Infantile KD is a diagnostic challenge with incomplete presentations being more common which may result in delayed diagnosis. Infants with KD have a higher risk of developing CAA. Infantile KD should be considered in any infant with persistent fever early to avoid long term morbidity or mortality.

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GENE EXPRESSION, CLINICAL AND DEMOGRAPHIC DATA DISTINGUISH KAWASAKI DISEASE FROM OTHER INFLAMMATORY CONDITIONS IN SOUTH AFRICAN CHILDREN

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Introduction: Diagnosis of Kawasaki Disease (KD) remains a challenge due to difficulty in distinguishing it from similar paediatric inflammatory disorders. Studies in patients of European ancestry have shown the clinical utility of polygenic scores in identifying KD, but no such study has been conducted in children with KD from Africa.

Objectives: To determine the discriminatory capacity of gene expression, demographic and clinical data for KD, compared to other presenting inflammatory conditions in Cape Town, South Africa.

Methods: RNA was collected from 13 pre-treatment children with KD, 42 children with multisystem inflammatory syndrome in children (MIS-C), 44 controls with other inflammatory conditions, and 74 healthy non-inflammatory paediatric controls. Expression of 80 genes with broad relevance to inflammation, immunopathology, immune regulation, and type I interferon response, was determined by real-time quantitative PCR. Differentially expressed genes (DEGs) were identified through nonparametric pairwise comparisons between experimental groups, adjusted by Holms correction. Receiver operating curve analysis was used to assess the discriminatory capacity of each gene for KD or MIS-C compared to controls. Discriminatory capacity of polygenic scores (the mean normalised expression values for each transcript of interest), clinical and demographic factors were similarly assessed.

Results: Children with KD were younger than those with MIS-C ($p = 0.0061$) and the inflammatory controls ($p = 0.0049$). Both KD and MIS-C were characterised by the presence of conjunctivitis, rash and tachycardia at baseline. A total of 32 DEGs were identified in KD compared to healthy children, but only two transcripts were up-regulated in KD compared to the inflammatory controls. A multi-factor score consisting of CASP5 and TREM1 expression, presence of conjunctivitis, and age could reliably differentiate KD from inflammatory controls (AUC 95.4%; 95% CI: 89.8-100%). This score did not perform as well in distinguishing KD from MIS-C (AUC 69.1%; 95% CI: 51.2-87.1%); however, a two-gene score of IL27 and SOCS1 expression could distinguish these disease groups (AUC 89.5%; 95% CI: 76.6-100%).

Conclusion: These data suggest that patient demographic and clinical data can be incorporated into a diagnostic algorithm for KD and MIS-C that includes gene expression of four key genes. This has the potential to greatly improve diagnosis of KD in African children. Notably, our results do not replicate recently described gene signatures of KD and MIS-C in children of European ethnicity, partly due to the use of a limited 80 gene panel in this study. Nevertheless, this highlights the importance of conducting work of this nature in underrepresented patient populations.

CLINICAL PHENOTYPE AND LABORATORY MARKERS IN PATIENTS AFFECTED BY A20 HAPLOINSUFFICIENCY (HA20): A CASE SERIES FROM 2 ITALIAN CENTERS

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Introduction: HA20 is a monogenic disease caused by heterozygous mutations in TNFAIP3 which encodes A20, a negative regulator of inflammation. A20 reduced expression is associated with a wide range of clinical phenotypes including autoinflammatory and autoimmune manifestations. Despite the increasing number of patients described, no clear genotype-phenotype correlation has been found thus far1 .Central nervous system(CNS) involvement has been reported in murine models carrying TNFAIP3 variants but its prevalence in vivo is unknown2. We previously described high circulating levels of IFNγ-inducible chemokines(CXCL9/10) in a family with HA203.

Objectives: To describe a cohort of patients with HA20 from 2 centers evaluating the different clinical features and their variability with patients' age; to assess the prevalence of CNS manifestations; to examine possible associations between the clinical phenotype, ongoing therapy and the inflammatory profile including CXCL9/10 and/or Interferon Score(IS) values.

Methods: Clinical and laboratory data of 25 subjects from 11 families with TNFAIP3 variants were collected. We measured the circulating levels of CXCL9/10 and/or IS. Categorical variables were expressed as medians and IQR, median ages of symptoms onset were compared through Kruskal-Wallis test and groups were compared using R function Wilcoxon test.

Results: 6 out of 11 families carry mutations resulting in stop codon(AGMC class4-5) while 5 had missense variants(AGMC class3).Patients' clinical features were as follows: 76% oral aphtosis; 60% gastrointestinal inflammation; 44% recurrent fever;44% autoimmunity (celiac disease or type 1 diabetes or thyroiditis); 44% CNS involvement; 40% genital ulcers; 24% skin inflammation; 24% arthritis/tenosynovitis.15 patients had clinical onset 2) and CNS symptoms was found (r=0.53).

Conclusion: A marked clinical heterogeneity was observed among patients, even within the same variants. Children with early onset(<6 yrs) presented more often oral aphtosis and gastrointestinal disease. Different symptoms seem to be more prevalent in specific age ranges. Neuropsychiatric involvement has been found in several patients and might further expand the clinical phenotype. No correlation between CXCL9/10 values and clinical features, disease activity or response to treatment have been found, suggesting they cannnot be used as reliable markers of disease activity or response to treatment.

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DEFICIENCY OF ADENOSINE DEAMINASE 2: A LARGE NATIONAL MULTICENTER COHORT

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Introduction: The deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessively inherited autoinflammatory disease. Disease manifestations could be separated into three major phenotypes: inflammatory/vascular, immune dysregulation, and hematologic, however, most patients present with significant overlap between these three phenotype groups. Treatment responses may vary between groups.

Objectives: This study aimed to evaluate the clinical findings, treatments and treatment responses of DADA2 patients in a large national multicenter cohort.

Methods: Until 2024, the patients diagnosed with DADA2 who were followed up in 11 different centers in Turkey were included in the study. The patients' demographics, clinical findings, treatments and treatment responses were assessed.

Results: A total of 89 patients (46 female, 43 male) were included in the study. The median age at symptom onset was 6.5 years, diagnosis was 10.3 years. The median duration from symptom onset to diagnosis was 3.0 years. Sixty-one (68.5%) patients had a history of parental consanguinity and 38 (42.7%) patients had a family history of DADA2. Two (2.2%) patients were asymptomatic, they were diagnosed after screening for DADA2 in their siblings. The most common clinical findings were skin(n=71, 79.8%), constitutional (n=69,77.5%) and musculoskeletal (n=61, 68.5%) findings, respectively. Hematologic abnormalities were found in 43 (48.3%) patients while immunologic abnormalities were found in 38 (42.7%) patients. Eighteen patients (20.2%) had systemic vasculitis. Forty-eight (53.9%) patients were initially diagnosed with other rheumatological diseases, and the most common diagnoses were polyarteritis nodosa and familial Mediterranean fever. The median PVAS at the diagnosis was 4. The most commonly used treatments before diagnosis were steroids (47.2%), colchicine (33.7%), methotrexate (12.4%) and azathioprine (12.4%) while after diagnosis almost all received anti-tumor necrosis factor (anti-TNF), and some were also on steroids (30.3%) and colchicine (13.5%). By antiTNF therapy were constitutional and gastrointestinal symptoms improved. Hematopoietic stem cell transplantation was performed in one patient with the diagnosis of Diamand Blackfan anemia before the diagnosis of DADA2, two patients due to severe hematological involvement and one patient with severe neutropenia. At the last follow-up, 63 (71.6%) patients were

in complete remission while 17 (19.3%) patients were in partial remission. Five (5.6%) patients died due to resistant disease.

Conclusion: The clinical findings of DADA2 are very variable and delay in diagnosis is very common. Childhood polyarteritis nodosa patients should also be evaluated for DADA2 in this respect. Early diagnosis and effective treatment may improve disease course.

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e-Poster Tour 3 – MAS, MISC and COVID-19

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SERUM LEVELS OF INTERLEUKIN-18, CXCL9, AND INTERFERON GAMMA IN STILL'S DISEASE COMPLICATED BY MACROPHAGE ACTIVATION SYNDROME

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Introduction: Macrophage activation syndrome (MAS) is classified as a form of secondary haemophagocytic lymphohistiocytosis (HLH) is a life-threatening complication of various rheumatic diseases such as Still's disease affecting up to 46% of all paediatric Still's patients (1,2). The immunological mechanisms involve the self-perpetuating activation of T cells and macrophages with sustained production of key pro-inflammatory mediators including IL-18, Interferon-gamma (IFNg) and CXCL9, a marker of IFNg activity (2,3). Limited data exist on the serum cytokine levels potentially guiding the implementation of tailored therapeutic strategies for MAS.

Objectives: To document the serum levels of IL-18, CXCL9, and IFNg in patients with active Still's-MAS; inactive Still'sMAS, healthy controls, and disease controls (pHLH or other connective tissue diseases [CTDs] without MAS) and explore their diagnostic utility to differentiate Still's-MAS from pHLH.

Methods: The analysis included 72 serum samples collected before the COVID pandemic and stored at the Immunology laboratory at Great Ormond Street Hospital. The samples included: 13 with active Still's-MAS; 3 with inactive Still's-MAS; 18 with pHLH; 15 with CTDs without MAS and 23 non-matched healthy controls. Serum samples were analysed using Multiplex immunoassay (Meso Scale Diagnostics, (MSDâ) LLC, Rockville, Maryland, USA) for IFNg, CXCL9 and IL-18. Statistical analyses employed GraphPad-Prism10.

Results: IL-18 levels were highest in active Still's-MAS, followed by pHLH and inactive Still's-MAS patients ($p<0.0001$). Although not significant ($p=0.06$), IL-18 was higher in active Still's-MAS compared to pHLH, while IL-18 was higher in active Still's-MAS versus inactive Still's-MAS group ($p=0.014$). CXCL9 level was overall higher in active and inactive Still's-MAS or pHLH versus CTDs without MAS and healthy controls ($p<0.0001$). There was no statistical difference in CXCL9 between patients with MAS and pHLH ($p=0.77$). IFNg concentrations did not significantly differ among all groups ($p=0.122$). ROC-analyses were performed to explore the diagnostic utility of IL-18 to differentiate active Still's-MAS from pHLH: at an optimal cut-off level of 30,764 pg/ml IL-18 demonstrated only modest diagnostic utility (sensitivity 0.615, specificity 0.778, AUC 0.705, J index 0.393, $p=0.055$).

Conclusion: IL-18 could emerge as a crucial therapeutic target for Still's-MAS, warranting trials in children and adults. However, IL-18 levels may not reliably distinguish Still's-MAS from pHLH.

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DEVELOPMENT AND INITIAL VALIDATION OF PRELIMINARY CRITERIA OF MACROPHAGE ACTIVATION SYNDROME IN MULTISYSTEM INFLAMMATORY SYNDROME ASSOCIATED WITH COVID-19 IN CHILDREN

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Introduction: Multisystem inflammatory syndrome associated with COVID-19 in children (MIS-C) is a rare, serious disease which affects almost all organs and systems. Macrophage activation syndrome (MAS) seems to be to be one of the most important factors determining the severity of the course of MIS-C, and often requires hospitalization to intensive care unit (ICU), due to its association with unfavorable prognosis for patients. There are no specific validated criteria for MAS in MIS-C patients, and the existing criteria for hemophagocytic syndromes, such as HLH-2004, MAS-2005, and MAS-2016 (Ravelli et. al.) are not optimal for evaluating hemophagocytosis in MIS-C.

Objectives: The aim of the study was to develop the MIS-C-specific criteria for early diagnosis of MAS.

Methods: The retrospective multicenter cohort study included 166 patients with MIS-C. Two of the most experienced independent experts in the field selected MAS cases based on their expertise . The patients were divided into 3 groups: MAS group (n=19), without MAS (n=78), and probable MAS (n=67), which was identified if there was no consensus among the experts. The third group was excluded from the analysis. Variables which allowed to differentiate MAS were used to develop and validate the diagnostic score.

Results: Patients with MAS were significantly older (9 years 8 months vs. 6 years 4 months, p<0.0008), and had higher prevalence of such clinical signs as edematous syndrome (86.7 vs. 31.6%, p<0.0006), hypotension and/or shock (68.4 vs. 23.1% p<0.0001), splenomegaly (94.1 vs. 26.9% p<0.000003), CNS involvement (83.3 vs. 40.8%, p<0.005). Among laboratory parameters thrombocytopenia (94.7 vs. 18%, p<0.000001), hypoalbuminemia (25.0 vs. 30.2 g/l, p<0. 0000001), hypertriglyceridemia (3.6 vs. 2.0 mmol/L, p<0.003) were more often observed in MAS-MIS-C patients. They also had higher levels of inflammatory biomarkers such as ferritin (100 vs. 63.4%, p<0.0000001), CRP (23.2 vs. 9.9 mg/dL, p<0.00007), troponin (117.7 vs. 2.0 pg/mL, p<0.001), as well as AST (68.7 vs. 38.0 IU/l, p<0.0000001), and ALT (62.0 vs. 30.1 IU/l, p<0.0003). There were signs of coagulation abnormalities: fibrinogen (2.7 vs. 5.5 g/L, p<0.000002), and D-dimer (3460 vs. 944 ng/mL, p<0.000008) in the MAS-MIS-C group. We selected continuous and categorical variables with statistical significance, and analysis of sensitivity and specificity with OR calculation was done to find the 21 main predictor of MAS in MIS-C. Two of them were used to develop the criteria: ferritin > 469 ng/L (65 points), platelets < 114 x 109/L (35 points), were included in the diagnostic score (p=5x10-31).

Conclusion: The obtained diagnostic criteria allow differentiation of MAS in MIS-C patients with a sensitivity of 100% and specificity of 94.9% and can be used, along with other diagnostic tests and procedures.

EVALUATION OF LONG-TERM COMORBIDITIES AND PROGNOSES OF CHILDREN WITH COVID-19-ASSOCIATED MULTISYSTEM INFLAMMATORY SYNDROME

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Introduction: Multisystem inflammatory syndrome in children (MIS-C) is a life-threatening condition characterized by persistent fever, multi-organ involvement, and significant elevation of inflammatory markers following a SARS-CoV-2 infection (1).

Objectives: The objective of this study is to evaluate the follow-up and outcome of patients with MIS-C.

Methods: This is a single-center retrospective cohort study evaluating MIS-C patients (0-18yr) diagnosed between 2020 and 2023. At the time of diagnosis, at 6 weeks, and at 1 year follow-up, the following data of the patients were recorded: demographic characteristics, clinical and laboratory findings (including autoantibodies), echocardiography and other imaging results, treatments received, development of autoimmune disease and neurological sequelae and prognoses. In addition the follow-up was compared to that of 13 patients who experienced severe COVID pneumonia between 2020 and 2023.

Results: Of the 132 patients, 65,9% were male and 34,1% were female. The median age at diagnosis was 8.2 years (0,2- 17,6). Prior to December 2021, 98 children were diagnosed with MIS-C (mostly associated with the delta variant), whereas following the emergence of the omicron variant (after December 2021), MIS-C was observed in a total of 34 patients. The most commonly observed symptoms at the time of diagnosis were fever (100%).At the time of diagnosis, almost all had lymphopenia (0.2-1.58), platelets were 180 x 10^3/µL (27-649), and almost all had high C-reactive protein (CRP) levels with a mean of 18.5 mg/dL (0.5-144.7). Abnormal liver function tests were detected in 57 patients (43.2%). Abnormal echocardiography findings were observed in 88 patients (67.2%) with an average ejection fraction was 65% (22-85). During treatment, all patients received IV antibiotics, intravenous immunoglobulin (IVIG) and steroids, with 123 patients (93.2%) also receiving enoxaparin sodium, and 100 patients (75.8%) receiving aspirin. Anakinra therapy was administered to 82 patients (62.1%). The average duration of steroid therapy was 5 days (2-60), and the duration of anakinra therapy was also 5 days (2-21). Inotropic support was required by 44 patients (33.3%). Additionally, Therapeutic Plasma Exchange was performed in 30 patients (22.7%), and 4 patients (3%) underwent extracorporeal membrane oxygenation (ECMO). Clinical remission was achieved in 127 patients (96.2%), and 3 patients (2.3%) died (all before December 2021). After discharge, sequelae were observed in 78 patients (82.1%). Decreased school performance (32.5%) and neurological symptoms were among the significant sequelae. Neurological symptoms ranging from headache to ocular myasthenia were detected in 15.8% of the patients. 60 patients had autoantibodies (ANA, anti-ds DNA, ENA, APS) (63.2%), and thyroid autoantibodies were positive in 29 patients (30.5%).

Conclusion: We were able to reach a high remission rate in our MIS-C patients. However at follow-up neurological symptoms were present in 15% and 2/3 had autoantibodies. This data suggests that MIS-C is a distinct immunopathogenic disease.

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GENES INVOLVED INTO INTERLEUKIN OR INTERFERON SIGNALLING PATHWAYS ARE DIFFERENTIALLY EXPRESSED IN COVID19 ASSOCIATED MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN AT SINGLE CELL LEVEL

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Introduction: Children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) usually present minimal symptoms or are asymptomatic. Nevertheless, a subset of children 2-6 weeks after the initial SARS-CoV-2 infection develops a postinfectious SARS-CoV-2-related multisystem inflammatory syndrome in (MIS-C).

Objectives: The purpose of our project is to characterize the complexity of cell populations and capture cellular heterogeneity to uncover the regulatory networks that are disrupted during MIS-C flare with simultaneous profiling of gene expression and open chromatin regions. Moreover, we are exploring gene regulatory interactions driving inflammation in MIS-C.

Methods: Samples of peripheral blood mononuclear cells from patients with MIS-C diagnosed at the University Children's Hospital, University Medical Center Ljubljana, were collected during the initial presentation before any treatment and at 6- 12 months in remission. To enable simultaneous profiling of epigenomic landscape and gene expression from the same nuclei, we are using Chromium Next GEM Single Cell Multiome ATAC + Gene Expression kit from 10X Genomics.

Results: We included 20 MIS-C patients with MIS-C from whom we collected paired blood samples during the initial presentation before treatment and at 6-12 months in remission. Samples in two time points from 10 patients, with the most viable cell count prior cryopreservation were included into single cell multiomic experiment. After low cells quality filtering and doublets removal, we had 89154 cells, where 51312 were at the time point of 6-12 months in remission and 37842 at initial disease presentation before any treatment. On average 5131 cells (SD=1626,2) per patient remained in analyses at the time of remission state and 3784,2 per patient at initial disease presentation time point. Genes that were differentially expressed (DE) in at least 6 patients per cell type were selected for gene set enrichment analysis. The higest number of DE genes was found in CD4 Naive cells (n=70), while CD4 TCM and CD8 Naive had 33 DE genes, B naive 15, NK cells 12, and finally CD8 TEM 4 and B intermediate 3. Interferon Alpha/Beta Signaling, Interferon Gamma Signaling, nterleukin6 Family Signaling and Interleukin-4 And Interleukin-13 Signaling were significantelly enriched most cell types with DE signature. Interferon Alpha/Beta Signaling and Interferon Gamma Signaling were significantelly enriched in B naive ($p.adjust=0.001$), CD4 naive ($p.adjust<0.001$), CD4 TCM ($p.adjust=0.005$) as well as in NK cells ($p.adjust=0.03$), while Interleukin-6 Family Signaling and Interleukin-4 And Interleukin-13 Signaling were significantly enriched in CD8 Naive ($p.adjust<0.05$), CD4 TCM ($p.adjust<0.001$) and in CD4 Naive ($p.adjust<0.001$) cells.

Conclusion: The results of this project are expected to enlighten the underlying pathophysiology of MIS-C flare and thus support clinical decision on more targeted treatment. The identified disrupted networks during MIS-C flare could lead the way to establish an early diagnosis and improve long-term outcome, including prevention of myocardial and neuropsychological impairment.

FERROPTOSIS IN SJIA AND MIS-C: STRIKE WHILE THE IRON IS HOT

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Introduction: Systemic Juvenile Idiopathic Arthritis (sJIA) and Multisystem inflammatory syndrome in children (MIS-C) are both hyperinflammatory syndromes of childhood that share clinical features and immunobiology. For both entities inflammasome activation is involved, highlighted by expression of IL-1β and IL-18. Ferroptosis has been described to be a very immunogenic form of cell death, which is distinct from conventional cell death modes as it uniquely hinges on dysregulated iron metabolism and is characterized by unrestricted lipid peroxidation of phospholipids, resulting in plasma membrane rupture and release of damage-associated molecular pattern signals (DAMPs). There is growing evidence that ferroptosis is involved in the activation of several inflammatory pathways, including the inflammasome and STING. Correspondingly, ferroptosis has been implicated in the pathogenesis of COVID-19 and inflammatory arthritis.

Objectives: To determine whether the ferroptosis pathway is activated in patients with sJIA and MIS-C and is involved in the pathogenesis of these hyperinflammatory syndromes.

Methods: We measured lipid peroxidation and assessed the expression of ferroptosis-associated genes in patient samples. Malondialdehyde (MDA) was used as a readout of ferroptosis as it is the final product of lipid peroxidation. MDA levels were measured in plasma of 52 MIS-C patients. Moreover, RNA sequencing was performed on neutrophils, monocytes, CD4 and CD8 T cells from patients with active sJIA (n=3-7) and healthy controls (n=3-9).

Results: MDA levels were highly elevated in our pre-treatment MIS-C cohort (n=35, median 177.9 nmol/ml) and were undetectable in 14 out of 19 (74%) post-treatment samples. Moreover, MDA levels were significantly higher in MIS-C patients with aneurysm formation, compared to patients with no aneurysms (median 248.81 versus 159.84; p = 0.0080) and correlated positively with coronary artery Z-scores (Spearman r 0.40, p=0.0180). Furthermore, gene set enrichment analysis showed that the expression of genes associated with the ferroptosis pathway is significantly enriched in neutrophils, monocytes, CD4 and CD8 cells of active sJIA patients compared to healthy controls.

Conclusion: Our findings provide new insights into the pathobiology of sJIA and MIS-C and indicate the involvement of the ferroptosis pathway. Obtaining a better understanding of the interplay between ferroptosis, inflammatory pathways, and other types of cell death is important as this could provide novel avenues for clinical treatment strategies of hyperinflammatory syndromes in children.

PEDIATRIC RHEUMATIC DISEASES IN THE LIGHT OF COVID-19 PANDEMIC, A RETROSPECTIVE OBSERVATIONAL BIG DATA STUDY

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Introduction: Viral infections like SARS-CoV-2 have been implicated in triggering autoimmune diseases potentially through mechanisms such as molecular mimicry and bystander activation. COVID-19 patients exhibited autoantibodies and viral peptide similarities to human proteins, which could provoke autoimmune responses.

Objectives: To compare the incidence rate (IR) of different pediatric autoimmune rheumatic diseases over the last five years before, through, and after the COVID-19 pandemic.

Methods: An anonymous big data cohort analysis between 2019 and 2023 spanned nearly 1.5 million pediatric patients aged 0 to 18 years. The study focused on newly diagnosed cases of Juvenile Idiopathic Arthritis (JIA), Systemic Lupus Erythematosus (SLE), or Henoch-Schönlein Purpura (HSP).

Results: No statistical significance in IR change was noted over the years for JIA or SLE when comparing each year to the following year or the pre-pandemic year 2019. However, a statistically significant increase was observed for HSP when comparing 2021 to 2022 (P=0.01), while a trend was noted when comparing 2021 to 2019 (P=0.078).

Conclusion: The IR of these pediatric autoimmune diseases showed some fluctuations over the years, with no statistically significant changes except for HSP, which showed a significant increase in IR when comparing 2022 to 2021. Overall, the IR increased in the latter years of the study period. These findings suggest a potential association between the occurrence of these autoimmune diseases and factors or events that may have influenced their incidence rates, particularly in recent years, but further research is needed to establish a causal relationship

Trial registration identifying number: Helsinki Comitte Protocil Number : 0017-23-CMC

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e-Poster Tour 4 – JDM I

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UNDERSTANDING THE MECHANISMS OF B CELL AND INTERFERON PATHWAY DYSREGULATION IN JUVENILE DERMATOMYOSITIS

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Introduction: Juvenile Dermatomyositis (JDM) is a rare childhood autoimmune disease, characterized by muscle inflammation and skin rash. Recent investigations have implicated dysregulation of the interferon (IFN) pathways and B cell involvement.

Objectives: This study aims to elucidate alterations in B cell populations, their association with disease severity, and their correlation with IFN pathway dysregulation in JDM patients.

Methods: Transcriptomic, flow cytometry, and clinical data were generated and collected from 52 JDM patients recruited from the UK Juvenile Dermatomyositis Cohort and Biomarker Study (JDCBS). Flow cytometry was used to assess B cell populations in treatment-naïve (pre-treatment, n=42) and treated (on-treatment, n=24) JDM patients, alongside agematched healthy donors (n=35). Differential gene expression (DGE) analysis was conducted on CD19+ B cells. Genes with $|LogFC| > 0.58$ and adjusted p-value < 0.05 were considered differentially expressed. Pathway over-representation and gene set enrichment analysis were performed using the Enrichr and fgsea tools. An IFN score was calculated relative to the healthy controls by summing the z-scores of the differentially expressed IFN genes per patient.

Results: Flow cytometry analysis revealed a significant expansion of total B cells (CD19+, $p < 0.0001$, ANOVA) and immature B cells (CD19+ CD24hi CD38hi, $p = 0.0055$, Kruskal-Wallis) in pre-treatment JDM patients compared to healthy controls, which were normalized by treatment. Additionally, memory B cells were decreased (CD19+ CD24hi CD38lo, $p < 0.0001$, Kruskal-Wallis). A negative correlation between total B cells and the Childhood Myositis Assessment Scale (CMAS) was observed in pre-treatment JDM patients ($p = 0.0034$, R-squared = 0.2517), suggesting a link between B cell expansion and increased muscle weakness. DGE analysis revealed 210 DE genes in pre-treatment JDM patients, 48 of which were IFN-related. Distinct clustering of pre-treatment patients was observed based on the expression of the IFN genes. Pathway analysis of CD19+ B cells confirmed significant enrichment of IFN pathways in pre-treatment JDM patients. The IFN score positively correlated ($p = 0.0352$, R-squared = 0.2132) with the immature B cell population in pre-treatment patients.

Conclusion: This study validates our previous findings1, indicating a significant role of B cells in JDM pathogenesis. An expansion of the total and immature B cell populations was observed in pre-treatment JDM patients, which correlated with disease activity and was normalized with treatment.

IFN gene expression was able to cluster pre-treatment JDM patients and the IFN score positively correlated with the immature B cell population, suggesting increased involvement of this specific cell subset in JDM pathogenesis. Overall, these findings offer insights into the complex nature of JDM, potentially leading to the future identification of novel biomarkers.

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LUNG INVOLVEMENT IN JUVENILE DERMATOMYOSITIS: A FRENCH RETROSPECTIVE STUDY

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Introduction: Juvenile dermatomyositis (JDM) is a rare juvenile idiopathic inflammatory myopathy. Lung involvement may be associated with JDM, and may be life threatening(1). However, little is known about its prevalence, characteristics and course during JDM.

Objectives: To describe the characteristics and course of lung involvement in a cohort of children with JDM.

Methods: Retrospective analysis of clinical, radiological and pulmonary function tests (PFTs) data of patients with JDM and lung involvement followed in the Paris referral center for Rare Paediatric Rheumatism and Systemic Autoimmune diseases (RAISE) from January 2009 to December 2022. Inclusion criteria were: i) diagnosis of JDM according to conventional clinico-pathological criteria, ii) lung involvement assessed by evaluation of pulmonary function test (PFT) and/or chest CT scan at diagnosis and iii) follow-up of at least six months after the diagnosis. The diagnosis of interstitial lung disease (ILD) was based on CT chest scan abnormalities. All CT scans were reviewed by the same paediatric radiologist (LB). Patient's characteristics were compared using Chi-square or Fisher's exact test.

Results: Among the 148 patients followed during the considered period, 87 underwent pulmonary investigations. Sixteen patients (18%) had a diagnosis of ILD. The median age at diagnosis of JDM was 10.6 years old (8,6- 12,3). Fifteen (94%) patients had MSA: 12 anti-MDA5 (75%), 4 anti-NXP2 and 1 anti-TIF1gamma antibodies respectively. At diagnosis 9/16 (56%) had respiratory symptoms (dry cough (17%) or dyspnoea on exertion (47%)). Nine patients (56%) had abnormal PFT, including 4 patients without pulmonary symptoms: 3 had both restrictive syndrome and low DLCO, 2 had isolated low DLCO and 3 had isolated restrictive syndrome. Chest scan at diagnosis showed: ground glass lesions (82%), nodules or micronodules (47%) and condensations (41%). Pulmonary lesions were always present at

diagnosis of JDM except for one patient with anti-TIF1-gamma antibodies who developed ILD two years later. Among patients with ILD there was a higher prevalence of respiratory symptoms (56% vs 13,6%, p=0.00103), a higher prevalence of MDA5 Ab (75% vs 13%, p=1.454e-05) and a higher prevalence of hospitalization in an intensive care unit (25% vs 7,6%, p =0.04948) compared to the patients with no lung involvement. Patients with ILD were treated more often with plasma exchange (37,5% vs 12%, p=0.06247) than the other patients. Other treatments were similar in the two groups : oral corticosteroids (100%), corticosteroid pulses (n=7, 43%), methotrexate (n=12, 75%), intravenous immunoglobulins (n=7, 43%) , plaquenil (n=7), jak inhibitors (n=7), rituximab (n=8, 50%), cellcept (n=6, 37,5%) and endoxan (n=2, 12,5%). At last evaluation (median follow up: 3.1 years), 3 patients still had dyspnoea resulting from JDM. CT chest scan improved in 9 patients (56%) and remitted in two patients. All PFTs were normal at last evaluation except for 2 patients who had low DLCO (50-73%), without clinical or radiological abnormalities. One patient with anti-TIF1-gamma antibody-positive JDM died from multivisceral failure including a severe ILD.

Conclusion: In our cohort of patients with JDM we observe a relatively high prevalence of ILD, which occurred mainly in patients with anti-MDA5 positive JDM. Pulmonary involvement was moderate, without case of rapidly progressive interstitial lung disease. It was present at diagnosis of JDM and improved with time in most of the patients.

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FIBROBLAST GROWTH FACTOR 21 (FGF21) AND GROWTH DIFFERENTIATION FACTOR 15 (GDF15) PLASMATIC LEVELS ARE INCREASED IN TREATMENT-NAIVE JUVENILE DERMATOMYOSITIS (JDM) PATIENTS AND DIFFER AMONG MSA SUBGROUPS

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Introduction: Recently published evidence suggests a role for mitochondrial dysfunction in idiopathic inflammatory myopathies (IIM). The mitokines GDF15 and FGF21 are induced in situations of muscle stress, particularly mitochondrial myopathies. Previous studies demonstrated that GDF15 is increased in serum and muscle of adult patients with IIM and in plasma of JDM patients.

Objectives: To investigate serum levels of GDF15 and FGF21 in JDM patients at diagnosis, before start of treatment, and evaluate possible correlations with clinical and laboratory findings, as well as with IFN-related biomarkers in blood (type I IFN score, CXCL10, CXCL9 and neopterin) and muscle (type I and II IFN score on muscle biopsies).

Methods: We collected muscle biopsy and blood samples of 24 treatment naïve JDM patients enrolled at time of diagnosis. Serum levels of FGF21, GDF15, CXCL10, CXCL9 and neopterin were analyzed by ELISA (normal values: 0- 200 pg/ml, 200-1000 pg/ml, <300 pg/ml, <150 pg/ml, <1.59 ng/ml); expression of 6 IFN-induced genes (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1) was measured by real-time PCR and used to calculate a type I IFN score in blood and a type I score in muscle (measuring the expression

of the genes cited previously). A muscle type II IFN score, based on expression levels of CIITA, IFNγ and CXCL9 was also calculated. For each patient, physician's global assessment (PGA) of disease activity VAS (Visual Analogue Scale), Childhood Myositis Assessment Score (CMAS), serum levels of creatine phosphokinase (CK, IU/l), MSA (Myositis Specific Autoantibodies) status were recorded. Correlations were determined by the Spearman's rank correlation coefficient. Non-parametric tests were used for comparisons between 2 groups.

Results: 18 out of 24 patients were female (75%). Median age at disease onset was 5.6 years [IQR 4.27, 12.03] and median disease duration at diagnosis 2.4 months [IQR 1.65, 6.95]. 17 patients were positive for at least one MSA. Median FGF21 levels were increased [261 pg/ml (IQR 43.75-617.25)], as well as median GDF15 levels [1521 pg/ml (IQR 1022- 2350)]. Median GDF15 levels tended to be higher in anti-NXP2pos patients (n=4) [3675 pg/ml, (IQR 2535,4645)] when compared to the anti-NXP2neg patients (n=20), [1430 pg/ml, IQR 883-1888) (p=0.053), whereas they tended to be lower in anti-MDA5 positive patients (n=3) [896 pg/ml, IQR 817-1011)] when compared to anti-MDA5 neg patients (n=21), [1704 pg/ml, IQR 1181-2562)] (p=0.08). FGF21 levels showed significant correlation with CMAS (p=0.01, rs=-0.46) and a tendency to correlate with higher muscle type I IFN score (p=0.057, rs=0.33). GDF15 levels showed significant correlation with CK levels (p=0.002, rs=0.57), PGA-VAS (p=0.02, rs=0.4), CMAS (p=0.002, rs=-0.56) and IFN score (p=0.04, rs=0.36). GDF15 also correlated with muscle type I IFN score (p=0.05, rs=0.34).

Conclusion: In our cohort, a significant number of JDM patients showed increased levels of FGF21 and GDF15. GDF15 levels were highest in anti-NXP2+ patients and lowest in anti-MDA5 patients. FGF21 levels correlated with CMAS and tended to correlate with muscular type I IFN score. GDF15 levels were correlated to global and muscular disease activity. Our data support the use of GDF15, and potentially of FGF21, as biomarker for IMM.

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SPECTRUM OF CLINICAL PHENOTYPES ASSOCIATED WITH MYOSITIS-SPECIFIC ANTIBODIES IN JUVENILE IDIOPATHIC INFLAMMATORY MYOSITIS: AN UPDATE FROM NORTH INDIA

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Introduction: Idiopathic Inflammatory Myositis (IIM) are a heterogenous group of disorders with distinct clinical phenotypes associated with specific myositis-specific antibodies (MSA).

Objectives: To evaluate the frequency, pattern, and associations of MSA in a large Indian cohort of juvenile IIM (JIIM).

Methods: A review of medical records of all patients diagnosed to have JIIM during the period January 1992 - April 2024 in Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute

of Medical Education and Research, Chandigarh, India, was done. Case records of children with JIIM who had significant positivity for MSA by myositis immunoblot were analyzed in detail.

Results: Of the 166 children with JIIM, MSA immunoblot was carried out in 95 patients. Myositis antibody was positive in 71/95 (74.7%) cases, and 17 of them were positive for multiple antibodies. The most common MSA was anti-NXP2 24 (25.3%) followed by anti-MDA5 15 (15.8%) and anti-TIF-gamma 12 (12.6%). Anti-Mi2, anti-Ro52, and anti-PM-Scl positivity were found in 9 (9.5%), 10 (10.5%), and 9 (9.5%) cases, respectively. We observed 4 (4.2%) cases of anti-SAE antibody, all of them having cutaneous disease predating muscle disease, and the myositis responded briskly to immunosuppressants. Calcinosis-predominant presentation with no clinical muscle involvement at presentation was seen in 4/24 (16.6%) cases with the anti-NXP2 antibody group. While the severe and relapsing cutaneous disease is more commonly noted in the anti-TIF-gamma group, cutaneous ulcers, arthritis and interstitial lung disease (ILD) were noted at higher rates in the anti-MDA5 group. However, we have not noted an amyopathic form in anti-MDA5 JDM in our cohort. Conclusion: The spectrum of MSAs and clinical phenotypes within the particular category of MSAs in our cohort varies from other reported cohorts from the Eastern and Western world. Anti-NXP2 is the most common MSA in our cohort, with 16.6% of them presenting as calcinosis-predominant clinically amyopathic form. The anti-MDA5 subgroup had high rates of arthritis presentation, and no amyopathic form was noted in this group.

SWALLOW ASSESSMENT IN NEWLY DIAGNOSED JUVENILE DERMATOMYOSITIS: BEDSIDE OR VIDEOFLUOROSCOPY?

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Introduction: Juvenile Dermatomyositis (JDM) is characterised by small vessel inflammation leading to myopathy, including pharyngeal weakness with dysphagia. Literature suggests that dysphagia and silent aspiration are inaccurately predicted by muscle weakness(1). International recommendations advise bedside swallow assessment (BSA) or instrumental swallow assessment at JDM diagnosis(2).

Objectives: To explore if BSA is as effective as videofluroscopy swallow study (VFSS) in diagnosing oropharyngeal dysphagia and aspiration risk in newly diagnosed JDM patients.

Methods: This service evaluation was registered with the Great Ormond Street Hospital clinical audit and service evaluation department: Registration 3758. All information was anonymised. Using the electronic patient record, SlicerDicer identified all patients with a diagnosis of juvenile myositis/ juvenile dermatomyositis between April 2019 - June 2023. 23 patients were identified with new diagnoses of JDM in this period. 2 were excluded for not receiving dual swallow assessments. Retrospective case note review collated data from BSA and VFSS tests. Swallow assessments were done by speech and language therapists (SLT). The childhood eating and drinking activity scale (CEDAS) was used to compare BSA and VFSS assessments using Spearman's Correlation. VFSS was positioned

as the gold standard test for sensitivity and specificity comparing BSA to VFSS CEDAS and BSA CEDAS to VFSS penetration aspirations scale (PAS). CEDAS scores of 6 were considered normal and ≤ 5 abnormal, PAS 1-2 were considered normal and ≥ 3 abnormal.

Results: BSA and VFSS CEDAS had a positive correlation with a coefficient of 0.675, $p<0.001$ using two-tailed analysis. 7/21 patients (33%) had worse VFSS CEDAS scores compared to BSA. For 14 patients (66%), CEDAS scores were either the same in both assessments (57%) or the CEDAS score was better in VFSS (9%). Normal BSA CEDAS compared to normal VFSS CEDAS sensitivity was 45%, with a specificity of 100%. BSA CEDAS compared to PAS sensitivity was 33% with a specificity of 80%. PAS scores were made for each food/fluid consistency tested and termed using the IDDSI framework 0-7. For IDDSI 0 and 1, 5 participants scored 6 or 5 with BSA CEDAS but had abnormal PAS. 15 of the remaining patients had normal PAS scores, despite one of these being given an abnormal score of 1 with BSA CEDAS. For IDDSI 3-4, there were no abnormal results. For IDDSI 6-8, there was one abnormal result in a participant who scored 1 on the BSA CEDAS.

Conclusion: These patients underwent dual swallow assessments comparing BSA and VFSS in the role of diagnosing dysphagia and aspiration risk. This service evaluation shows a correlation between the assessments indicating value in both. Dysphagia and aspiration risk are difficult to quantify from general muscle strength assessments alone. VFSS provides a more detailed assessment of swallow physiology and therefore is likelier to expose aspiration and difficulties with oropharyngeal residue in patients with pharyngeal weakness. Many of the patients with worse VFSS scores had abnormalities with thin fluids that had not been apparent from BSA alone. No data was gathered on rates of aspiration pneumonia, which could have further qualified these findings. However, this sample may have been biased as abnormal assessments receive SLT guidance to manage aspiration risk.

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SHOULD CAPILLAROSCOPY BE TRUSTED IN THE MANAGEMENT OF PATIENTS WITH JUVENILE DERMATOMYOSITIS?

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Introduction: Considering the often early disability of patients with juvenile dermatomyositis (jDM), a search is being carried out, among other things, for instrumental diagnostic methods that make it possible to early suspect the disease and predict the response to therapy. Nailfold videocapillaroscopy (NVC), an accessible and non-invasive method for assessing microangiopathy, has shown promise, but should it be trusted?

Objectives: To determine the role of NVC in the management of patients with jDM.

Methods: The study included 30 children with a definite diagnosis of jDM according to the EULAR/ACR 2017 criteria. All patients had typical skin changes, weakness of the muscles of the shoulder and pelvic girdle of varying degrees of severity, increased serum levels of CPK, and a primary muscle pattern according to needle electromyography. All patients underwent NVC using a stereomicroscope with 200x magnification and displaying images on a widescreen monitor. The study was performed on 2-5 fingers of both hands, assessing the density, size, shape of capillaries and the presence of hemorrhages. NVC was performed at the time of diagnosis of dermatomyositis and after 6, 12, 18, 24 months against the background of pathogenetic therapy.

Results: Of the 30 examined patients with jDM, pronounced changes in the vessels of the microvasculature were detected, often visualized with the naked eye. In the vast majority of patients they were similar to systemic sclerosis (SSc). In children, a relationship was identified between the severity of the skin process and the pathology of the capillaries, while the correlation between myopathy and changes in the periungual bed was not established. Mixed vascular disorders (abnormally shaped capillaries, giant capillaries, formation of avascular areas, hemorrhages) were observed in patients with a disease duration of more than 6 months and no therapy. Against the background of active treatment, after 6, 12, 18 and 24 months, all children achieved a decrease in disease activity and/or remission, which affected the condition of the periungual bed in the form of transformation into nonspecific changes in the capillaries.

Conclusion: NVC is a useful tool to complement the diagnosis of jDM. But the method cannot be considered as a reliable assistant, since the type of changes in the capillaries is similar to SSc or is of a nonspecific nature, disguised as other nosologies, reflects the severity of an already easily distinguishable skin process, and changes against the background of active therapy for dermatomyositis.

CAPILLAROSCOPIC FINDINGS AND DISEASE ACTIVITY IN JUVENILE DERMATOMYOSITIS: A YEAR-LONG PROSPECTIVE STUDY

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Introduction: Capillaroscopy is a non-invasive imaging technique used for the evaluation and follow-up of juvenile dermatomyositis (JDM) patients. It provides valuable insights into the microcirculation of the nailfold capillaries, aiding in the diagnosis and monitoring of disease activity. Serial capillaroscopy examinations can track changes in capillary morphology, indicating disease flares or remission. Data on the use of capillaroscopy in children and adolescents with JDM are limited.

Objectives: This study aims to prospectively assess the relationship between capillaroscopic changes and disease activity in juvenile dermatomyositis patients.

Methods: Capillaroscopy images of 19 JDM patients followed in two tertiary paediatric rheumatology centres were assessed in a total of 72 visits at 3-month intervals. Thirty-two images were captured with 200x magnification, four images from each of the eight fingers of each patient. The area of one

mm was evaluated for each image. Visits in which eight clear images could not be obtained due to technical reasons were excluded from the study.

Results: Fifteen (78%) of the 19 patients were female. The mean age at diagnosis for the patients was 7.2 (±3.3) years. 2304 images were analyzed. Major abnormalities were found on capillaroscopic images in 76% of visits. The mean capillary density was calculated to be 4.89 (±1.9) and the mean apical loop width was calculated to be 30 (±21) µm in all images obtained. The results indicate a moderate positive correlation between CMAS and capillary density mean (p=0.05, 95% CI (-0.0002, 0.4805)). Correlations between CMAS and capillary, arterial part, venous part, and apical loop widths were generally low or very weak, and no strong correlations were observed. Capillary density showed a moderate negative correlation with both the physician VAS and the patient/parent VAS (p=0.012, p=0.021). The CMAS scores were found to be significantly lower in the presence of dilated capillaries, bushy capillaries, neoangiogenesis and avascular areas. (p=0.013, p=0.001, p=0,002, p=0.005). In the follow-up visits, a significant increase in capillary density was found between the first and last visit (p=0.005).

Conclusion: The study highlights the value of capillaroscopy as a non-invasive tool for monitoring disease activity in JDM. The observed correlations between capillary density and disease activity scores indicate that capillaroscopic findings can provide valuable insights into disease progression and response to therapy. The significant increase in capillary density over the follow-up period provides further support for the utility of capillaroscopy in evaluating therapeutic outcomes in JDM patients.

e-Poster Tour 5 – SLE I

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ALTERNATIVE ALLELE COUNTS ASSOCIATE WITH ANCESTRY, AGE AT DISEASE ONSET, ORGAN INVOLVEMENT AND DISEASE SEVERITY IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS	Valentina Natoli
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ALTERNATIVE ALLELE COUNTS ASSOCIATE WITH ANCESTRY, AGE AT DISEASE ONSET, ORGAN INVOLVEMENT AND DISEASE SEVERITY IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Systemic Lupus Erythematosus (SLE) is a systemic autoimmune/inflammatory condition characterized by extremely variable clinical presentations. While across age groups, genetic determinants play a key pathomechanistic role, they are likely to have a more pronounced role in juvenile-onset (jSLE) when compared to adult-onset SLE patients, contributing to earlier disease-onset, more severe phenotypes and less favorable outcomes.

Objectives: This study investigated the relationship between alternative allele counts (AAC), and age at disease onset, sex, ancestry, organ involvement and clinical severity in a multi-ethnic jSLE cohort from the UK. It furthermore explored associations between gene-level alternative allele scores (GAAS), organ involvement and disease severity.

Methods: 315 jSLE patients from the UK JSLE Cohort Study were studied using a panel sequencing approach covering 62 genes/genomic regions. Demographic and clinical features, along with disease activity (pBILAG-2004 and SLEDAI) and damage index (SLICC-SDI) scores were recorded. AAC were generated by counting the number of alternative alleles within a SNP and multiplying the AAC by their in silico predicted functional impact of that SNP on gene function (low or modifier=1, moderate=2, high=3) and then summed across all SNPs to give a patient level AAC. GAAS was calculated, similarly to the AAC, by counting the number of alternative alleles and multiplying by functional impact, and then summed across SNPs within a gene, to give a GAAS for each gene and patient. A generalised linear model, adjusted for ethnicity, sex and family history, was used to assess their relationship with organ involvement and severity.

Results: A (weak) inverse correlation between age at diagnosis and AAC was observed (R=-0.15, p=0.01), when ethnicity was not considered. Notably, the inverse correlation between age at disease-onset and AAC across ethnicities was primarily influenced by South-Asian patients (R=-0.28, p<0.001). Across the whole cohort, constitutional (p<0.001), renal (p=0.001), haematological (p=0.001) and neuropsychiatric (p=0.03) involvement were significantly associated with AAC. When examining cumulative GAAS across ethnicities, higher scores were recorded in patients of Black African/Caribbean ancestry when compared to White Caucasians, and East and South Asian participants (p<0.001). GAAS associated significantly with some clinical variables, including severity of neuropsychiatric (ACP5, TYK2 and RNASEH2A, p<0.001; RASGRP3, p=0.04) and renal (ACP5, ITGAM, and LYN, p<0.001; TNFAIP3, p=0.007) involvement.

Conclusion: Genetic variability contributes to early disease expression, especially in South-Asian jSLE patients. Some GAAS associate with specific organ involvement and severity across ethnicities.

Observations from this study may allow for future genetic risk assessment and patient stratification towards individualized treatment and care.

IDENTIFYING CROSS-REGISTRY COMMONALITIES TO FACILITATE INTERNATIONAL PEDIATRIC ANTIPHOSPHOLIPID SYNDROME RESEARCH

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Introduction: Antiphospholipid syndrome (APS) is a systemic autoimmune disease defined as the development of venous and/or arterial thromboses with persistently positive antiphospholipid antibodies. Although pediatric APS is rare, it is associated with significant morbidity and mortality and evidence-based data regarding its diagnosis and management are limited. Much of the current knowledge on pediatric APS is from a 2009 review of 121 cases through the Ped-APS Registry which was initiated as a joint project of the European aPL Forum and the Juvenile SLE Working Group of PReS. In North America, CARRA hosts the largest ongoing observational registry of children with SLE and APS, though limited data have been published on the subset with APS. The recently introduced 2023 ACR-EULAR APS classification criteria, developed for adult patients, have significantly higher specificity compared to the revised Sapporo criteria and provide a new basis for future APS research. However, there is still a lack of pediatric-specific APS criteria and current classification criteria were only validated for adult population studies.

Objectives: To develope an international data set to facilitate international registry based pediatric APS research.

Methods: We initiated by comparing data fields from existing European and North American registries, including the Ped-APS Registry and the CARRA Lupus-APS Subgroup Registry. This comparative analysis aimed to identify commonalities and discrepancies in data collection practices across registries. Additionally, we conducted a systematic literature review on Pubmed to identify relevant studies focusing on pediatric APS between 2003-2024. In the second phase of our study, we plan to utilize the Delphi methodology and convene a consensus meeting among experts to define core clinical and laboratory data fields that should be collected and harmonized between international registries for pediatric APS.

Results: A comprehensive literature search was conducted and yielded 2,105 articles. Of these,1607 articles were excluded for the following reasons (reasons determined a priori): 25 articles because we were not able to retrieve them, 123 articles because they were not in English, 453 articles that were about pregnancy/obstetric APS, 519 articles that included adults without sufficient data on pediatric patients and 487 articles that were not relevant. We included 498 articles, out of which 311 were case reports/case series with a maximum of 10 patients included. Resulting from this, we have identified 325 candidate items for the registry. Of them, 102 from Pediatric APS Registry and CARRA registry review, 99 from the recently published adult classification criteria, and 124 from the systematic

literature review. We prepared a list of candidate items for Delphi questionnaire for the following areas: demographics, comorbidities, family history, laboratory testing, involved systems, anticoagulation, antiaggregant and immunosuppressive treatment.

Conclusion: Through systematic evaluation of existing data sources, literature review, and preparation for Delphi and expert consensus, we are laying a solid foundation for the development of a robust and collaborative registry for pediatric APS. This global dataset will facilitate international collaboration and research efforts to improve outcomes for children with APS worldwide.

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EVALUATION OF NEONATAL LUPUS SYNDROME AND BABIES BORN TO MOTHERS WITH LUPUS: A MULTICENTRE STUDY

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Introduction: Neonatal lupus erythematosus (NLE) is a rare and acquired autoimmune disease caused by maternal autoantibodies crossing the placenta. Autoantibodies related to NLE are anti-SSA/Ro, anti-SSB/La and anti-RNP antibodies.

Objectives: The aim is to evaluate the national data of NLE.To compare neonatal lupus syndrome and babies born to mothers with lupus who do not fulfil the diagnostic criteria for neonatal lupus syndrome.

Methods: In our study, we collected data on infants diagnosed with neonatal lupus syndrome and infants born to mothers diagnosed with SLE or SS who did not meet the diagnostic criteria for NLE.Neonatal lupus syndrome was defined as infants who were positive for at least one of the maternally transmitted anti-SSA, anti-SSB and anti-RNP antibodies and had systemic findings. Infants with negative antibodies and no systemic involvement were defined as baby born to a mother with lupus who did not develop neonatal lupus syndrome. Clinical and laboratory characteristics of the mothers and infants and the treatments they received were analysed.

Results: A total of 38 patients from 9 centres were included in the study.Of these, 18 had a diagnosis of NLE and 20 babies born to a mother with lupus. There were 37 patients whose mothers had a diagnosis of rheumatic disease at birth.In one patient, fetal hydrops was detected during pregnancy and the mother was diagnosed with Sjögren's syndrome.The infants with neonatal lupus syndrome had mean gestational age of 37+2 (± 2.1) weeks and mean birth weight of 2899.71(± 476.237) grams.Anti-SSA was positive in 11(61.1%), anti-SSB in 5(27.8%) and anti-RNP in 2(11.1%) of the babies

with neonatal lupus syndrome. System involvement in patients with NLE was cardiac in 9(50%), skin in 7(38.9%), haematological in 8(44.4%), hepatobiliary in 4(22.2%) and neurological in 2(11.1%).Treatment (medical/surgical) was required in 9 patients.Fetal bradycardia was noted in 6 of 9 patients with cardiac involvement in the prenatal period.In 4 of these patients, a pacemaker was implanted in the postnatal period because of complete AV block.The babies born to mothers with lupus who did not fulfil the diagnostic criteria for neonatal lupus syndrome had mean gestational age of 38(29-39) weeks and mean birth weight of 3150 (900-3700) grams.Five mothers were positive for anti-SSA antibodies.Anatomical abnormalities were observed on routine echocardiography in 9 asymptomatic babies born to mothers with lupus. Patent foramen ovale was observed in 7 patients and the anatomical defects resolved during follow-up. One baby born to a mother with lupus underwent PDA closure surgery. There were 2 patients with transient transaminase elevation. One patient had thrombocytopenia and neurological findings (intracranial haemorrhage) were observed in this patient. No baby born to a mother with lupus had cutaneous findings. In logistic regression analysis, maternal anti-SSA positivity [OR: 36.000 (95% CI: 3.692-351.002), p=0.002] and maternal anti-SSB positivity [OR: 18.286 (95% CI: 1.907-175.347, p=0.012] increased the development of neonatal lupus syndrome.

Conclusion: In our study, cardiac involvement was most common in patients with NLE, followed by haematological, skin, hepatobiliary and neurological involvement. Maternal anti-SSA or anti-SSB positivity was found to increase the risk of developing NLE.

RARE TURNER SYNDROME AND LUPUS COEXISTENCE WITH INSIGHTS FROM DNA METHYLATION PATTERNS

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Introduction: Systemic lupus erythematosus (SLE or lupus) is a complex autoimmune disease affecting multiple organs. Although the etiology and pathogenesis have not been fully elucidated, the influence of X chromosome dosage has been suggested. Besides the higher prevalence of lupus in women, individuals with Klinefelter syndrome (47, XXY) exhibit a heightened susceptibility compared to other men. Additionally, the occurrence of SLE alongside Turner syndrome is exceedingly rare.

Objectives: In this study, we aim to present a rare case of a patient diagnosed with mosaic Turner syndrome and subsequently presenting with juvenile-onset SLE, analyze DNA methylation patterns in this patient and compare with age- matched female SLE controls.

Methods: The study included the patient diagnosed with juvenile-onset SLE and Turner syndrome, as well as four juvenile-onset SLE patients matched for age, sex, ethnicity, and treatment. All patients

fulfilled the 1997 revised ACR classification criteria for SLE. DNA was isolated from peripheral blood mononuclear cells and genome-wide DNA methylation patterns were determined using the Illumina Infinium MethylationEPIC v2.0 BeadChip array. Beta values were adjusted by cell type composition differences, and adjusted beta values were used to assess differences of DNA methylation levels of the SLE patient with Turner syndrome and control SLE patients.

Results: Case: A 9-year-old female patient presented to the pediatric clinic due to short stature. Upon examination, short neck, short 4th metacarpals, cubitus valgus, and widely spaced nipples were observed. Karyotype analysis revealed a chromosomal pattern of 45,X/46,X,i(X)(q10), leading to the diagnosis of mosaic Turner syndrome. The patient presented to the pediatric rheumatology clinic at the age of 11 with joint pain, malar and discoid rash, photosensitivity, oral ulcers, and a positive ANA test with a titer of 1:160, and diagnosed with juvenile-onset SLE. Methylation analysis: DNA methylation patterns were analyzed in this patient and compared with age-matched female SLE controls, revealing higher methylation levels in interferon-regulated genes previously shown to be hypomethylated in SLE (p-value = 0.018). Four hundred CpG regions showing the greatest differences in methylation levels between SLE patients with and without Turner syndrome were investigated. Enrichment analysis of the genes annotated with these regions revealed significant enrichment in neurological pathways.

Conclusion: These data provide a mechanistic link between a gene-dose effect from the X-chromosome and the lupus- defining epigenotype. We hypothesize that the attenuated demethylation in interferon-regulated genes might provide a protective effect explaining the rarity of SLE in Turner syndrome. Further research is needed to determine whether MECP2 or other X chromosome genes are involved in this conclusion.

INVOLVEMENT OF TYPE 1 INTERFERON IN ANTI-NUCLEAR ANTIBODY-ASSOCIATED CHILDHOOD IMMUNE THROMBOCYTOPENIC PURPURA: A PRE-LUPUS CONDITION

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Introduction: Anti-nuclear antibody-associated immune thrombocytopenic purpura (ITP-ANA+) is a pre-lupus condition, called incomplete lupus erythematous (ILE), as 20% of children will develop systemic lupus erythematosus (SLE) (1). In adults with ILE, elevation of interferon score (IS), measuring the expression of a panel of type 1 interferon-stimulated genes, is associated with progression to SLE (2) and hydroxychloroquine could prevent progression to SLE by reducing type 1 interferon signaling (3).

Objectives: Description of the IS in childhood-onset ITP-ANA+.

Methods: Thirty-four children followed at the Bordeaux University Hospital had an IS evaluation in the Immunology Department of the Lyon University Hospital in 2022-2023. A score was positive if > 2.3.

Results: Eleven of the 34 children had ITP-ANA+, 9 were girls and median age at ITP diagnosis was 13 years (1.1-15.7). At IS evaluation, ITP was acute (n=2), persistent (n=3) or chronic (n=6). IS was positive

in 9/11 (82%) children with a median score of 18 (1.2-68). This median IS was higher than in 2 children with ITP-ANA- (2.4 (1.5-3.3)), and than in 11 children with juvenile arthritis (1.9 (0.9-6.5), p=0.004), but not different than in 10 children with SLE (35 (2.1-90), p=0.3). Among ITP-ANA+ children, IS was significantly higher in patients with ITP diagnosed after the age of 11 (n=7, p=0.02), within the first year after ITP diagnosis (n=5, p=0.02), in the presence of anti-SSA (n=5, p=0.02), and in the absence of a treatment by hydroxychloroquine (n=5, p=0.048). Finaly, hydroxychloroquine reduced the IS in 3/3 children with available pre- and post-treatment scores: from 30, 51, and 68, to 1.1, 20, and 34, respectively (p=0.002).

Conclusion: These results suggest the involvement of the type 1 interferon signaling in the pathophysiology of childhood ITP-ANA+. Further studies are needed to define the variables associated with this IS and progression from ILE to SLE, and to use it for early treatment by hydroxychloroquine.

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HOW DO THE CLINICAL, LABORATORY, TREATMENT FEATURES, AND OUTCOMES IN PEDIATRIC PATIENTS WITH LUPUS NEPHRITIS PROGRESS OVER THE LAST 30 YEARS?

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Introduction: Management of the systemic lupus erythematosus (SLE) through new treatment options has improved lupus nephritis (LN) prognosis (1,2).

Objectives: The aim of this study was to compare the changes in the demographic, laboratory and treatment characteristics, prognosis, and outcomes of pediatric LN patients over 30 years

Methods: We retrospectively reviewed the medical records of 103 pediatric-onset LN patients. Patients were divided into two subgroups according to the years of LN diagnosis. Group 1 consisted of patients diagnosed with LN between the years of 1993 to 2005, and group 2 consisted of patients diagnosed with LN between the years of 2006 to 2023.

Results: The mean age at diagnosis of SLE, age at diagnosis of LN, time to LN development, and mean delay time to diagnosis were significantly higher in group 1 ($p<0.001$, $p<0.001$, $p=0.049$, and $p=0.004$, respectively). Baseline SLEDAI scores and anti-phospholipid antibody positivity were found to be higher

in patients with group 1 (p= 0.040 and p=0.025, respectively). Azathiopurine in maintenance phase was given more frequently in group 1 (p=0.016), while rituximab was more frequently used in group 2 (p=0.042). In both groups, the majority of the patients had proliferative nephritis (class III and/or class IV) (53.5% in group 1 vs. 68% in group 2). Complete renal remission was significantly more common in group 2 (p=0.005), while end-stage kidney disease (ESKD) and death were significantly more common in group 1 (p=0.005 and p=0.001, respectively). Proteinuria and SLEDAI scores at the first visit were independent risk factors for progression to ESKD (p=0.034 and p=0.024).

Conclusion: High disease activity scores and proteinuria levels may be the signs of the development of ESKD. Over the last decades, new treatment options such as rituximab have provided better disease outcomes in patients with juvenile- onset LN.

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ATTAINMENT OF CHILDHOOD LUPUS LOW DISEASE ACTIVITY STATE IS ASSOCIATED WITH IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE

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Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is associated with poorer health-related quality of life (HRQoL)1. In adult-onset SLE, attainment of the treat-to-target (T2T) goal Lupus Low Disease Activity State (LLDAS) has been associated with a significant improvement in HRQoL2.

Objectives: To determine if attainment of the T2T goal of childhood Lupus Low Disease Activity State (cLLDAS)3 is associated with improvements in HRQoL.

Methods: The analysis included UK JSLE Cohort Study participants diagnosed with cSLE by age 18 years, meeting ≥4 ACR 1997 criteria, and assessed ≥2 times for HRQoL using the Short Form 36-Item (SF-36) survey. The SF-36 provides scores for eight health-related domains, including Emotional Wellbeing, Energy/Fatigue, General Health, Pain, Physical Functioning, Role Limitations due to Emotional Problems, Role Limitations due to Physical Health and Social Functioning. These scores are summarised and normalised against healthy population data producing Physical and Mental Component Scores respectively (PCS and MCS). Clinically derived, real world patient data was used to determine if the cLLDAS target was met at each visit. Markov multi-state modelling assessed the longitudinal impact of cLLDAS attainment on the eight SF-36 HRQoL domain scores, and the PCS and MCS scores.

Results: The analysis included 241 patients, median age 13 years (IQR 11.3-14.7), with 85.1% being female. Markov multi-state models indicated that maintenance of cLLDAS between visits was associated with a statistically significant improvement in General Health (HR 2.80, CI 1.16, 6.78) and MCS (HR 2.62, CI 1.04, 6.62). Persistent non-attainment of cLLDAS between visits was associated with poorer Emotional Wellbeing (HR 0.80, CI 0.65, 0.98), Role Limitations due to Emotional Problems [HR

0.71, CI 0.56, 0.91) and MCS scores (HR 0.78, CI 0.62, 0.97) (all $p<0.05$). Patients who were not in cLLDAS but subsequently attained cLLDAS demonstrated a statistically significant improvement in Emotional Wellbeing (HR 1.68, CI 1.10, 2.56), Physical Functioning (HR 1.68, CI 1.02, 2.77), Role Limitations due to Physical Health (HR 2.21, CI 1.23, 3.97) scores and PCS (HR 1.64, CI 1.07, 2.53). Notably, three SF-36 domains were not impacted by either cLLDAS attainment or cLLDAS non-attainment, including: Energy/Fatigue, Social Functioning, and Pain.

Conclusion: Attainment and maintenance of cLLDAS over time was shown to have a positive impact on key domains of HRQoL in patients with cSLE. These data support the implementation of cLLDAS as a target to help control disease activity and contribute to improvements in HRQoL. Clearly, however, not all aspects of HRQoL can be improved by attainment of cLLDAS alone; highlighting a need to collaborate with the multidisciplinary team to monitor and address broader goals like fatigue and pain.

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e-Poster Tour 6 - JIA

ePoster short communications -6 JIA	
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FLARES AFTER WITHDRAWAL OF ANTI-TUMOR NECROSIS FACTOR THERAPY IN PATIENTS WITH NON- SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease of childhood which is based on a chronic autoimmune inflammation. With modern treatment and especially biologic treatment, remission is now a realistic goal for patients. Prolonged treatment of patients with inactive disease may result in unnecessary exposure to adverse effects. Given these data our study has been focused on important question is whether anti-tumor necrosis factor (anti- TNF) therapy can be reduced or even stopped in patients with stable JIA.

Objectives: To determine the frequency and time to flare upon withdrawal of anti–tumor necrosis factor (anti-TNF) therapy in patients with non-systemic juvenile idiopathic arthritis

Methods: We enrolled 76 patients with clinically inactive JIA who were receiving anti-TNF therapy (59% of whom were also receiving methotrexate [MTX]) were prospectively followed up. If the disease remained clinically inactive for the initial 24 months of the study, anti-TNF was stopped and patients were assessed for flare at 3, 6, 9, 12 and 18 months. In 25 patients the withdrawal of drug was performed abruptly, and in 51 in a progressive way, either by reducing the dose (n=26) or by increasing the interval between doses (n=25). Remission time was evaluated according to the Kaplan-Meier survival curve.

Results: The mean duration of anti-TNF therapy was 54 (IQR 40; 74) months. The disease persisted at an inactive stage for a mean 46 (IQR 33; 67) months before anti-TNF therapy was interrupted. 58 cases (76%) relapsed at a mean 12,4 (IQR7,7; 12,9) months after drug discontinuation. The survival curve shows that 76% of the patients continued to have inactive disease at 3 months, 58% at 6 months, 47% at 9 months, 42% at 12 months and 24% at 18 months after drug discontinuation. No significant differences were observed in the time to relapse between the group in whom the drug was tapered in progressive way and the group in whom TNFi was discontinued abruptly (12,6 vs 10 vs 12,6 months, respectively; p>0,05). Similarly, no association was found between the duration of inactive disease prior to drug withdrawal and the time to relapse. The first case of flare was after 2 months, the peak of cases of flares of JIA occurred in the 3rd month after stopping anti-TNF therapy (up to half all cases of flares were noted in the period from the 3rd to the 6th month). Patients who relapsed were started again on anti-TNF therapy and 54/56 (96%) responded satisfactorily. In 2/56 (4%) patients due to the ineffectiveness of repeated prescription of etanercept, a “switch” was made to adalimumab.

Conclusion: In this real-practice JIA cohort, flares were frequent, the majority of patients (76%) relapsed after discontinuation of anti-TNF therapy, the probability of remaining symptom-free at 6 months was 58%, and the response to reintroduction of treatment was satisfactory. More research is needed to identify the most effective approaches to withdraw medications and predictors of outcomes.

FEASIBILITY AND VALIDITY OF A DECISION SUPPORT TOOL FOR WITHDRAWAL OF BIOLOGIC THERAPY IN NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Biologic disease-modifying anti-rheumatic drugs are highly effective in controlling disease activity in children with juvenile idiopathic arthritis (JIA). However, evidence on if and when to withdraw biologic therapy after a child has reached clinically inactive disease (CID) is urgently needed.

Objectives: To evaluate a judgement-based Decision Support Tool (DST) to support pediatric rheumatologists in making biologic therapy withdrawal decisions in children with non-systemic JIA.

Methods: The web-based DST model was based on multi-criteria decision analysis (MCDA). The DST content, including criteria and relative weightings, were based on interviews, focus groups and a clinical vignette study that were published previously (1-3). A combination of focus groups and surveys were used to elicit feedback about the design, face and content validity and feasibility in clinical practice of the prototype version of the DST among a sample of potential users from the Dutch-Canadian UCAN consortium.

Results: Eleven pediatric rheumatologists were included; eight (73%) were female and five (45%) were from Canada. Key themes that arose during the focus groups were: 1) The need to precisely define terminology, such as "clinically inactive disease", to ensure uniform interpretation among all users; 2) The need for concise instructions on how and when to adjust relative importance of criteria in the model; 3) The need to practice with the DST to increase trust in the DST; 4) Suggestions about different purposes for use of the DST in clinical practice, such as its potential to explain a decision to patients or to involve patients in the decision-making process; 5) Future improvements of the DST, such as the inclusion of predictive clinical data regarding successful withdrawal decisions. The survey results showed that user willingness to use the DST in practice was high. Two respondents were willing to spend 1-2 minutes per patient consult on using the DST, 6 respondents 3-5 minutes, and 2 respondents were willing to spend 5-10 minutes.

Conclusion: Overall, the DST was well received in terms of its value in supporting pediatric rheumatologists in their decision process. Minor modifications were needed to improve the design and instructions in the DST. The next development step will be to add predictive clinical data regarding successful withdrawal decisions. The DST offers a structured approach to decision making regarding the withdrawal of biologic therapy, which could increase patient and parent involvement in decision making, and result in more consistent decision making among pediatric rheumatologists. **Patient Consent:** Not applicable (there are no patient data)

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INTERFERON PATHWAYS ARE ASSOCIATED WITH THE RESPONSE TO METHOTREXATE TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common autoimmune rheumatic disease in children with methotrexate (MTX) as the first line treatment. However, about 50% of JIA patients will not respond well to MTX yet still experience drug side effects.

Objectives: To establish biomarkers that predict response to methotrexate treatment in patients with JIA.

Methods: Transcriptional analysis was performed on peripheral blood mononuclear cells (PBMC) from pre-MTX-treated JIA patients (n = 97) of all ILAR JIA subtypes but excluding systemic JIA. RNAseq was performed on total PBMC and sorted immune cell populations: CD4+ T cells, CD8+ T cells, CD19+ B cells, and CD14+ monocytes. Clinical data collected at the time of sampling (baseline) and at follow-up (between 3-12 months) were used to define outcomes, measured as change in active joint count (AJC) and change in Physician VAS (PhysVAS). After batch normalisation with ComBat-seq, differential gene expression (DGE) analysis was performed using limma-voom (R version) with age, sex, ethnicity, and steroid status included as covariates in each cell type. MTX outcome measures as continuous variables were used in the design matrix of DGE analysis. Gene set enrichment analysis (GSEA) was performed using gene-based permutation (fgsea[1]) and phenotype-based permutation (Broad Institute GSEA[2]) with MSigDb Hallmark pathways.

Results: DGE analysis showed minimal significant differentially expressed (DE) genes that passed 5% false discovery rate (FDR < 0.05) across different cell types. The greatest number of significant DE genes were observed in CD14+ monocytes, where baseline expression of 13 genes were significantly associated with change in PhysVAS. As alterations of gene expression for a heterogeneous disease such as JIA can be subtle and correlated between genes, GSEA was performed to investigate expression changes at pathway level. Both GSEA methods showed significant association of interferon-alpha and interferon gamma pathways with MTX response in all cell types including total PBMC (FDR < 0.05). Specifically in B cells, IL6-JAK/STAT3 signaling pathway also showed association to MTX response (FDR < 0.25). Pathway divergence between T cell and non-T cell lineages was also observed in the overall blood signature of pre-MTX JIA in association with their response outcomes.

Conclusion: Interferon pathways are associated with response to MTX and significantly enriched across all mononuclear cell lineages, suggesting genes in these pathways could be predictive biomarkers for response to MTX. Different directionality of pathways that might be relevant to JIA response to treatment with MTX is also observed in different cell lineages. This could potentially explain the difficulties of finding biomarkers which correlate with response to treatment from whole blood or PBMC.

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METHOTREXATE POLYGLUTAMATE CONCENTRATIONS IN PEDIATRIC PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND ASSOCIATION WITH CLINICAL RESPONSE

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Introduction: Methotrexate (MTX) is one of the first-line medications for the treatment of juvenile idiopathic arthritis (JIA). Unfortunately, about 35% of patients does not respond to MTX. To personalize MTX therapy it would be important to carry out therapeutic drug monitoring, quantifying the erythrocyte levels of MTX and its polyglutamate (MTX-PG1-7) active metabolites. It appears that levels of long-chain polyglutamates (MTX-PG3-5) correlates with lower disease activity.

Objectives: This study aims to determine the concentrations of MTX-PG1-7 and their association with clinical response in a cohort of pediatric JIA patients.

Methods: The study was conducted at IRCCS Burlo Garofolo (Trieste, Italy). Pediatric JIA patients, treated with MTX since more than 3 months, not suspected of poor compliance (total polyglutamate levels (MTX-PGTOT) > 2 nM), both in cotreatment with biological drug or not, were recruited. MTX-PG1-7 quantification was carried out by LC-MS/MS. Disease activity and remission were calculated using JADAS27 score and Wallace criteria, respectively. Association between MTX-PG levels and demographic/clinical variables was assessed by non-parametric tests (Kruskal-Wallis test for categorical variables and Spearman's test for continuous variables). For diseases remission, association was evaluated by generalized linear mixed effect models of the binomial family, with remission as dependent variable, MTX-PG levels as independent variables (fixed effect) and the patient as the random effect.

Results: Thirty-four patients, for a total of 85 samples (median age: 11 y, 24 female, median dose: 0.34 mg/kg, median therapy duration: 13 months, 51 on biological cotreatment (22 adalimumab, 11 infliximab and 18 other) were enrolled. MTX-PG3-5 levels were significantly higher in MTX monotherapy patients (kruskal-wallis test, p=0.0069) while a trend show that MTX-PG1 levels were higher in patients cotreated with biologic (kruskal-wallis test, p=0.061). Patients receiving subcutaneous MTX showed significantly higher MTX-PGTOT levels than patients taking it orally (Kruskal-wallis test, p=0.0015). No association was observed between MTX-PG levels and the JADAS27 score. A trend for an association between MTX-PG3-5 levels with clinical remission was seen (OR: 1.01, 95% CI: 1-1.02, p=0.090).

Conclusion: MTX-PG3-5 levels were significantly higher in MTX monotherapy patients while MTX-PG1 levels tended to be higher in patients cotreated with biologics: since it was previously shown that MTX-PG3-5 levels correlate with response, our hypothesis is that low MTX-PG3-5 levels require biologic therapy. Then, we found that MTX-PGTOT levels are significantly higher in patients taking subcutaneous MTX than oral. Finally, we found a trend for an association between MTX-PG3-5 levels with clinical remission, that must be further confirmed.

REGULATORY T CELL BLOOD SIGNATURES CAN MEASURE AND PREDICT DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: No reliable biomarker currently exists to predict the erratic disease course of Juvenile Idiopathic Arthritis (JIA), characterised by persistent inflammatory flares of the joint. Normally, regulatory T cells (Tregs) maintain immune tolerance, with altered Tregs associated with autoimmunity. Treg signatures have shown promise in monitoring other autoimmune conditions, therefore a Treg gene and/or protein signature could offer novel biomarker potential in JIA.

Objectives: Here, we aim to assess peripheral blood (PB) Treg mRNA signatures, and Treg subsets by protein expression, to distinguish active from inactive JIA. If PB Treg measurements correlate with disease activity and can predict the risk of imminent flares, a Treg-derived biomarker could inform clinical decisions and treatment outcomes.

Methods: A 48 gene nanoString Treg signature was analysed on sorted CD4+CD25highCD127low PB Tregs from healthy controls, and individuals with active (active joint count, AJC ≥1) and inactive (AJC=0) oligoarticular or polyarticular RF negative JIA. Additionally, JIA Tregs were assessed by spectral flow cytometry, with unbiased clustering on gated CD4+Foxp3+ cells across 20 markers for activation, proliferation, and co-receptor expression.

Results: Machine learning on our Treg gene signature on PB Tregs generated a model to distinguish active JIA Tregs from healthy controls (AUC=0.9875). Biomarker scores from this model successfully differentiated inactive from active JIA PB Tregs. Scores correlated with clinical disease activity (cJADAS), and identified subclinical disease (AJC=0, cJADAS≥0.5) from remission (AUC=0.8980, Sens=0.8571, Spec= 0.8571). Furthermore, spectral flow cytometry revealed three Treg clusters by protein expression increased in active JIA PB, while one Treg cluster predominated in inactive JIA PB (AJC=0). The ratio of these Treg clusters correlated to cJADAS, and higher ratios (>4.0) could predict inactive individuals that flared by 6-month follow-up. Methotrexate (MTX) had no effect on biomarker potential of these Treg measures, yet active individuals on MTX had lower Treg cluster ratios closer to those in remission, possibly suggesting Treg cluster ratios could be adapted as a treatment response biomarker to indicate when remission has been achieved.

Conclusion: We therefore demonstrate altered Treg signatures and subsets as an important factor, and useful biomarker, for maintained remission in JIA. Ultimately, PB Treg signatures could serve as routine biomarkers to guide disease and treatment management.

AGE AT ONSET OF DIAGNOSIS AS A PROGNOSTIC FACTOR IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Age at onset of a chronic disease may have a negative impact on wellbeing. There are only few studies concerning age at onset as a prognostic factor for juvenile idiopathic arthritis (JIA).

Objectives: The aim of this study was to clarify how age at onset of JIA affects the outcome of the disease. We focused on the primary outcome parameters such as remission and Health-Related Quality of Life (HRQoL). In addition, functional ability after 18 years of the diagnosis was evaluated.

Methods: This study is part of the population-based Nordic JIA cohort study (1). Newly diagnosed patients with JIA were recruited consecutively between 1997-2000 in specific regions in Finland, Sweden, Norway, and Denmark. Initially, 510 patients were recruited and 358 (70%) of them attended this study. Patients were divided into three age groups: <3 years, 3-5 years and ≥6 years. They were also categorized into three groups according to their International League of Associations for Rheumatology (ILAR) JIA subtypes (2) at six months after the onset of the disease: oligoarthritis, seronegative polyarthritis and others (enthesitis-related arthritis, psoriatic arthritis, and undifferentiated arthritis). Few seropositive and systemic onset patients were excluded. Clinical data were collected six months and 18 years after the disease onset.

Results: Mean age was 5.8 years (N=201, 72% female), 5.9 years (N=85, 74% female) and 8.7 years (N=72, 51% female) for oligoarthritis, seronegative polyarthritis and in the group of others, respectively. Remission rates off medication were 62% (95% CI: 54-68), 49% (95% CI: 38-60) and 51% (95% CI: 39-66), respectively, p=0.012. Related factors predicting remission at the time point of 18 years in the three JIA subgroups are shown in the Table 1. Related factors predicting remission in the oligoarthritis group included age of onset, male gender, JADAS71 score, and uveitis. In the seronegative polyarthritis group, onset age and JADAS71 score predicted remission. By using logistic regression models, estimated probability of achieving remission 18 years after the diagnosis shows that both genders achieve remission earlier when diagnosed at an earlier age in the oligoarthritis group. In seronegative polyarthritis group, achieving remission is the opposite compared to oligoarthritis group in females. In the group of others, patients in remission were similar (U-shaped) in both genders. Onset age had no significant effect on HRQoL and functional ability. ROC-analyses shows optimal different age cut-off points between JIA subgroups and gender.

Conclusion: The current study shows a relationship between continuous age at the diagnosis of the oligoarthritis and seronegative polyarthritis and remission outcome.

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e-Poster Tour 7 – sJIA and uveitis

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IL-18 LEVELS CAN DIFFERENTIATE BETWEEN SJIA AND CHILDHOOD MALIGNANCIES, AIDING IN THE DIAGNOSTIC WORKUP FOR SJIA

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Introduction: Systemic JIA (sJIA) exhibits a predominantly autoinflammatory signature and therefore differs markedly from the other JIA subtypes. It is characterized at onset by a quotidian spiking fever, a marked acute phase response, skin rash and enlargement of liver/spleen/lymph nodes. These key features unfortunately are not very specific, so the differential diagnosis of sJIA is broad. An additional challenge is the absence of arthritis during the first months of the disease in about 30% of patients. Therefore, the sJIA phenotype may initially overlap considerably with childhood malignancies, often resulting in a possible diagnostic delay or additional diagnostic procedures such as bone marrow aspiration or PET CT scans in order to rule out malignancy.

Objectives: To evaluate the potential of using inflammatory cytokines and chemokines as potential diagnostic biomarkers to differentiate between sJIA and malignancy at onset of disease.

Methods: In collaboration with the national pediatric oncology center (Princess Maxima Center) in the Netherlands, we assembled a cohort of patients (as part of prospective cohort studies / biobank studies) sampled at diagnosis before the start of treatment with the following diagnoses: sJIA (*n*=34, of which *n*=9 presenting without arthritis) and childhood malignancies (precursor B-ALL *n*=24, T-ALL *n*=14, AML *n*=12, Hodgkin's lymphoma *n*=20, non-Hodgkin lymphoma *n*=4, neuroblastoma *n*=15). Clinical and laboratory data were retrospectively extracted from patient files. In total, 17 inflammation associated cytokines and chemokines were measured in serum and plasma using a multiplex immunoassay based on Luminex technology and additionally the same serum/plasma samples were used for the measurement of 92 protein biomarkers using the OLINK high-multiplex immunoassay "immuno-oncology" panel.

Results: All sJIA patients exhibited (spiking) fever in the two weeks leading up to diagnosis, compared to *45%* of malignancy patients (ranging from *72%* in B-ALL to 25% in Hodgkin's lymphoma). Arthritis or arthralgia, defined as either joint pain or reduced range of motion, was present in 73.5% of sJIA patients compared to 27.5% of malignancy (ranging from 52% in B-ALL to 7.1% in T-ALL). Skin rash was most prevalent in sJIA (85.3% of patients at admittance, compared to 4.4% of malignancy patients). Mean IL-18 levels were significantly elevated in sJIA when compared to malignancy. We evaluated different cut-off values for IL-18 in ROC curves. A value of 1500pg/ml performed best, with a sensitivity of 0.94 and a specificity of 0.83. The OLINK panel (semi-quantitative analysis) suggested several other potential biomarkers, amongst others IL-8, CXCL10, MCP3 and TWEAK. The addition of IL-8 levels (Luminex) slightly improved the model's performance.

Conclusion: We hereby validate the value of IL-18 as a diagnostic biomarker in sJIA, differentiating between sJIA and childhood malignancy. A cut off value of 1500pg/ml in our lab showed the highest AUC in a ROC curve. Our data suggest that patients evaluated for sJIA in a diagnostic work up could reliably be diagnosed with sJIA when having IL-18 levels > 1500pg/ml. For patients with IL-18 levels

lower than 1500pg/mL, we suggest to consider a bone marrow aspiration and/or PET CT to rule out malignancy.

CLONALLY EXPANDED TPH CELLS FUEL MALADAPTIVE IMMUNE RESPONSES IN THE JOINTS OF SYSTEMIC JIA PATIENTS

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Introduction: Systemic juvenile idiopathic arthritis (sJIA) differs from other forms of JIA by systemic features of inflammation, often preceding the onset of arthritis. While presumed to ensue from an autoinflammatory pathogenesis, the 'biphasic hypothesis' suggests that the inflammatory milieu during early sJIA may skew pathogenic T cell responses, that perpetuate arthritis in the chronic phase. This hypothesis is supported by augmented polarization of circulating naïve CD4+ T cells towards peripheral T helper (TPH) cells in sJIA patients. TPH cell play pivotal roles in many autoimmune diseases, and their expansion has been documented in inflamed joints of antinuclear antibody positive oligo-/poly- JIA (ANA+ JIA)

Objectives: In this study, we aimed at unraveling the cellular phenotype and the clonal evolution of $CD4^+$ T cells in the inflamed joints of sJIA patients during the chronic phase. Specifically, we set out to investigate whether TPH cell expansion occurs in the joints of sJIA patients, and whether these TPH cells might differ from those found in ANA+ JIA on a molecular level.

Methods: Deep-phenotyping of synovial fluid (SF) $CD4^+$ T cells by flow cytometry and single cell RNA- and V(D)J- sequencing (10X Genomics) of SF CD4+ T cells from sJIA patients (n=5) and ANA+ JIA patients (n=4).

Results: Flow cytometric analysis revealed high frequencies of SF PD-1^{hi}HLA-$DR^+$$CD161^+$TPH cells in sJIA patients, similar to ANA+ oligo/poly-JIA patients but significantly higher than in other forms of childhood arthritis. These cells were characterized by IL-21 or CXCL13 expression together with intermediate levels of IFN-γ production. In scRNA-seq, sJIA SF CD4+ T cells revealed a higher abundance of cells assigned to TPH or Treg clusters and showed significantly upregulated transcriptomic features of a TPH phenotype compared to ANA+ JIA patients. Integrating T cell receptor (TCR) repertoire analysis revealed an unexpected high level of clonal expansion in sJIA $CD4^+$ T cells particularly among cells with a TPH phenotype. Comparing clonal connections between clusters identified a higher plasticity in sJIA compared to ANA+ JIA patients. Finally, tracking of clonotypes in two sJIA patients with follow-up samples available, uncovered persisting clones preferentially in TPH and Treg clusters. Application of cytokine signaling signatures to the transcriptomic scRNA-seq data revealed significant differences between ANA+ JIA and sJIA samples and correlations to differential treatment.

Conclusion: This comprehensive analysis, integrating cytokine expression, transcriptional profiling and TCR repertoire assessment of SF CD4+ T cells at the single cell level, uncovers mutually pronounced

involvement of sustained and dysregulated adaptive immune responses at the site of inflammation during the chronic phase of sJIA. Notably, TPH cells emerge as pivotal drivers of the 'maladaptive' T helper cell response observed in sJIA patients.

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STILL'S DISEASE-ASSOCIATED LUNG DISEASE ACROSS LIFESPAN: A MULTICENTRIC STUDY

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Introduction: Still's disease (SD) is understood as a life course entity encompassing systemic-onset juvenile idiopathic arthritis (SoJIA) and adult-onset Still's disease (AOSD). SD-associated lung disease (LD) is an emerging severe complication that is apparently increasing in frequency.

Objectives: To describe and compare SoJIA and AOSD in a multicentric population emphasizing pulmonary involvement.

Methods: Clinical records of patients classified as SoJIA or AOSD, from 18 Portuguese centers, were reviewed. Patients with clinical or chest imaging objective findings were considered to have LD, including interstitial lung disease, pulmonary alveolar proteinosis and pulmonary arterial hypertension. Previous/concomitant known LD related to other causes was excluded. Data on demographic variables and clinical features were presented as frequencies and mean ± standard deviation for categorical and continuous variables, respectively. Linear regression was performed to assess the independent association of relevant covariables.

Results: We collected data from 175 patients, 104 with SoJIA, 67 with AOSD, 4 unknown age of symptoms onset. The mean age of symptoms onset was 8.2 years for SoJIA and 38.5 years for AOSD patients. LD developed in 14 patients (8%), 7 with SoJIA (6.7% of the total), and 7 with AOSD. At SD onset 99% of the patients had fever, 89.1% arthritis, 81.3% rash, 43.5% odynophagia, 43% myalgia, 40.6% adenomegaly, 37.1% hepatomegaly/splenomegaly with no significant differences between SoJIA and AOSD except for lower reports of odynophagia and adenomegaly in SoJIA. Similar results

were obtained in the subgroup of paediatric and adult patients that developed LD. LD presented with tiredness in 57.1%, dyspnea in 42.9% and clubbed fingers in 15.4% of the cases. Low peripheral oxygen saturation was more frequent in AOSD than SoJIA (57.1% vs 14.3%). The average time between SD symptoms onset and diagnosis of LD was 6.1 years for SoJIA and 7.3 years for AOSD, with a mean age at LD diagnosis of 9.0 and 39.2 years for SoJIA and AOSD, respectively. At LD diagnosis, all patients with AOSD and 57.1% with SoJIA had active SD. The most common radiological findings were ground glass (42.9%), peripheral consolidation (35.7%) and septal thickening (21.4%), while pulmonary hypertension was found in 21.4% of the patients, with similar frequencies in both subgroups. Patients with LD had more pleuritis (42.9% vs 10.9%; p=0.024) and a higher frequency of macrophage activation syndrome (MAS) (35.7% vs 9.4%; p<0.001) independent of age of SD-onset. Half of the patients, all adults, had eosinophilia at LD diagnosis. After LD diagnosis, patients were treated with glucocorticoids (69.2%), tocilizumab (21.4%) and anakinra (7.1%), in similar proportions in both subgroups. After a mean of 1.8 years of follow-up after LD diagnosis, 6 patients (42.9%) needed intensive care (3 with SoJIA), 4 (28.6%) died (1 with SoJIA) and 9 (64.3%) had improvement or stabilization of the LD (5 with SoJIA and 4 with AOSD).

Conclusion: LD is a significant and severe complication in patients with SD, affecting both paediatric and adult populations. Despite similar symptoms at onset in SoJIA and AOSD patients, those with LD may face a more severe prognosis, including higher rates of pleuritis and MAS.

PREDICTORS OF REMISSION IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS / STILL'S DISEASE IN THE BIOLOGIC ERA - A REAL-LIFE EXPERIENCE CONSISTENT WITH THE "WINDOW OF OPPORTUNITY"

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Introduction: Among the various subtypes of juvenile idiopathic arthritis (JIA), systemic JIA (sJIA) / Still's disease, stands out as a distinct clinical entity because of its peculiar pathogenesis attributable to the spectrum of autoinflammatory disorders. The evidence about the role of epidemiological and clinical factors as predictors of different disease trajectories in sJIA patients remains limited, especially because most studies dated back to the pre-biological era [1].

Objectives: To investigate potential predictors of remission and relapse in sJIA, in a real-life clinical setting.

Methods: An observational bicentric cohort study was conducted including patients diagnosed with sJIA between January 2017 and December 2022 at Meyer Children's Hospital IRCCS (Florence, Italy), or at Hospices Civils de Lyon (France). Data on demographics, clinical and laboratory features, treatment approaches, and disease evolution were collected through retrospective chart reviews.

Results: Of the 64 sJIA patients included, 57.8% exhibited a monophasic course, and 42.2% had a non-monophasic course. 46.9% of patients (30/64) were females. The median age at diagnosis was 6.5 years (IQR 3-12), with a median time from symptom onset to the diagnosis of 23 days (IQR 14-32.5).

Patients were followed up for a median of 22 months (IQR 12-38.8) and 60/64 (93.7%) achieved remission on medication and 35/64 (54.7%) remission off medication. The time from first symptom to diagnosis (Hazard Ratio (HR): 0.991) and interleukin 1 (IL1) inhibitors treatment failure (HR: 0.236) resulted predictors of a longer time to achieve remission on therapy. Clinical inactive disease at month 3 (HR: 3.506) predicted a shorter interval of time to remission off medication while anti-IL1 failure (HR: 0.153) was found to be a predictor of longer time to achieve remission off medication. The presence of rash three months after onset (HR: 5.763) resulted significantly associated with a shorter time to relapse, while the male gender resulted a protective factor (HR: 0.247). IL1 inhibitors non-responder patients (15/42, 35.7%) presented a lower age (p=0.040) and a higher frequency of polyarthritis at onset (p=0.029), a non-monophasic disease course (p<0.001), a higher number of relapses (p=0.010), and a longer time to achieve remission on therapy (p<0.001). Non-responder patients reported a longer time interval in starting anti-IL1 treatment (median 56 days vs 27 days), although this result did not reach a statistically significant (p=0.098) value.

Conclusion: A diagnostic and therapeutic delay predicts a longer time to reach remission in sJIA patients, and seems to affect the response to IL1 inhibition, according to the "window of opportunity" hypothesis in sJIA treatment. A failure to IL1 inhibitors predicts a longer time to reach remission both on and off medications and is associated with an early polyarticular onset and non-monophasic disease course.

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CLINICAL CHARACTERISTICS AND RISK FACTORS OF SEVERE DISEASE IN PEDIATRIC NON-INFECTIOUS UVEITIS: A SINGLE CENTER STUDY

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Introduction: Pediatric non-infectious uveitis is a rare condition characterized by inflammation of the uveal components of the eye. Untreated, it may cause blindness and is sometimes linked to rheumatologic diseases like juvenile idiopathic arthritis (JIA).

Objectives: In our study, we aimed to present the demographic, clinical, laboratory and treatment data of patients with non-infectious uveitis. We also aimed to evaluate the effect of extraocular involvement on the clinic and prognosis, as well as to evaluate the risk factors for the development of complications and the need for biological treatment.

Methods: Patients diagnosed with non-infectious uveitis in childhood and followed up in our tertiary care center for at least 1 year were included in the study. Demographic data including age, gender, age at diagnosis, uveitis in first-degree relatives and rheumatologic diseases were obtained retrospectively from medical records. The presence of complications or the need for biologic therapy was considered as a composite outcome and patients with this composite outcome were considered to have severe disease.

Results: The study included 123 patients (Female: n=59 (40.7%)). The mean age at diagnosis was 14.89 ± 4.86years. Uveitis was symptomatic in 104 patients (71.7%). Approximately one quarter of the

patients had at least one rheumatic disease (n=35, 24.1%), the most common being JIA. Thirty-three patients (22.8%) were anti-nuclear antibody (ANA) positive. Biologic agents were needed in 60 (41.4%) patients. Complications developed in 9.7% (n=14) of patients. Early age (aOR, 0.875; 95% C.I.: 0.795-0.915, p=0.007)and female gender (aOR, 2.99; 95% C.I.: 1.439- 6.248, p=0.003 was found to be an independent risk factor for the need for biological treatment. Additionally, Behcet's disease was found to be a independent risk factor for uveitis-related complication (aOR, 0.071; 95% C.I.: 0.014- 0.362, p=0.001).

Conclusion: Patients with uveitis, particularly those with an early onset of the disease, female patients, and those with Behçet's disease, should be closely monitored for the necessity of biologic therapy and potential complications.

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LATE ONSET JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED UVEITIS: PRELIMINARY DATA FROM A SINGLE- CENTER STUDY

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Introduction: Uveitis is the most fearful extra-articular complication in juvenile idiopathic arthritis (JIA) and a significant cause of disability. In most cases, it occurs simultaneously or after the diagnosis of arthritis, usually in the first four years after the onset of the joint disease.

Objectives: The study aims to evaluate and describe cases of late-onset uveitis.

Methods: We retrospectively reviewed medical records of patients followed in our Center suffering from JIA-associated uveitis from 1985 to 2023.

Results: 114 patients suffering from JIA complicated by uveitis were included in the study (F 78%; n=89) with a mean follow-up time of 21 years (SD ± 10.9) from the joint or ocular disease onset. 99 patients (87%) were classified into the oligoarticular JIA subgroup, 12 (11%) in the polyarticular FR negative category, 2 (2%) in the psoriatic form, and 1 (1%) presented a form of acute anterior uveitis HLA B27 correlated with the diagnosis of enthesitis-arthritis. ANA antibodies were positive in 111 patients (97%). In 108 patients (95%) joint disease preceded ocular involvement, while in only 6 patients (5%) uveitis preceded arthritis.
In the majority of cases, uveitis manifested itself in the first 4 years from diagnosis of the joint disease with a median arthritis-uveitis time of 12 months (IQR 37); however, in 25 patients (25/108; 23%), uveitis appeared after the first 4 years of the disease. In the latter subgroup, all patients had disease onset before 5 years of life and were classified as oligoarticular JIA ANA positive, except for 4 patients diagnosed with polyarticular JIA FR negative, ANA positive. 19/25 patients (76%) were female. The

median time between the onset of arthritis and uveitis was 7 years (IQR 3.5; range 4.5-23), with a mean number of visits equal to 19 (SD ±7.9) before the detection of uveitis. At the time of uveitis onset, 10 patients were on methotrexate monotherapy and 2 on methotrexate in combination with etanercept. In patients with uveitis appearing in the first 5 years of life, the onset of ocular disease occurred within 4 years from the onset of arthritis, unlike patients with uveitis onset in the first 5 years of life in whom uveitis could manifest after many years from the onset of the joint disease (p= 0.011). Furthermore, a negative correlation was found between age at onset of arthritis and age at onset of uveitis (r= -0.2; p=0.036).

Conclusion: The greatest risk of uveitis occurs in the first years of the disease after the onset of the joint disease. However, a non-negligible portion of patients with risk factors for uveitis appear even after many years of disease; therefore, long-term follow-up seems to be the most prudent approach in this subgroup of patients.

PREDICTORS OF RECURRENCE IN PEDIATRIC PATIENTS WITH NON-INFECTIOUS UVEITIS UNDERGOING ADALIMUMAB TAPERING: AN INTERNATIONAL MULTICENTER STUDY

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Introduction: Adalimumab (ADA) is frequently administered to pediatric patients with non-infectious uveitis (NIU). Given safety considerations and cost implications, exploring the possibility of tapering/withdrawing ADA in patients experiencing a prolonged period of persistent remission has been suggested.

Objectives: To evaluate factors associated with the risk of NIU relapse in patients undergoing ADA tapering.

Methods: A multicenter retrospective cohort study was conducted. Patients diagnosed with NIU, with or without an associated systemic disease, before age 18 and treated with ADA were included. All patients underwent ADA tapering due to NIU inactivity. ADA tapering consisted of progressive injection spacing decided by the treating clinician.

Results: The cohort comprised 114 patients (57% female) with NIU treated with ADA. Demographic and clinical characteristics of the cohort are detailed in Table 1. Fifty-three patients (46%) experienced NIU recurrence after a median of 30 weeks (IQR 15-58 weeks) from the onset of ADA tapering. The interval between ADA injections was increased by 1 week every month (n =1), 1 week every 2 months (n =2), 1 week every 3 months (n = 50), 2 weeks every 4 months (n = 1), 1 week every 4 months (n=4),1week every 5 months(n=5), 4 weeks every 6 months(n=1), 2 weeks every 6 months(n=2),1 week every 6 months (n = 24), 1 week every 12 months (n = 24). Considering the heterogeneity in the distribution of patients across the speed of tapering, ADA tapering was classified into two main groups based on the rate of drug reduction: faster (fast_t, comprising tapering speeds from 1 week every

month to 2 weeks every 4 months, N = 54) and slower (slow_t, encompassing tapering speeds from 1 week every 4 months to 1 week every 12 months, N = 60). An association between the speed class and the incidence of uveitis relapse was observed, with 56% of recurrences in the fast_t group compared to 38% in the slow_t group (p = 0.06). A multivariate Cox regression analysis was conducted to identify independent predictors of the recurrence rate. In the multivariate model, being Caucasian was associated with more than a two-fold increase in the risk of developing uveitis relapse (HR 2.33; 95% CI 1.12-4.85; p = 0.02). Furthermore, the adjusted analysis showed that a slower ADA tapering is associated with a 50% lower risk of recurrence than a faster tapering (HR 0.49; 95% CI 0.26-0.95; p = 0.03).

Conclusion: About half of the cohort experienced a NIU relapse after the initiation of ADA tapering. Caucasian race and fast tapering were associated with a higher risk of recurrences. Therefore, a strict follow-up for these patients should be advisable, and a gradual ADA taper is recommended.

EFFICACY OF TOCILIZUMAB VERSUS ANTI-TNF SWITCHING IN REFRACTORY JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED UVEITIS

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Introduction: Juvenile idiopathic arthritis-associated uveitis (JIA-U) can often be refractory not only to methotrexate (MTX) but also to first-line biological disease modifying antirheumatic drug (bDMARD). The optimal choice of therapy following the failure of initial anti-TNF treatment remains uncertain.

Objectives: Assessing therapeutic strategies in a cohort of JIA-U patients resistant to methotrexate and first-line bDMARDs to determine the optimal treatment approach.

Methods: Clinical records of patients with JIA-U followed at our tertiary Pediatric Rheumatology centre were retrospectively reviewed, collecting data regarding clinical features, treatment and outcomes. Differences between patients managed with a single bDMARD and those requiring multiple biologic agents were evaluated using $\chi 2$ or unpaired T-tests, as appropriate.

Results: Data from 65 JIA-U patients treated with MTX (83.1% female) were analyzed, with a mean follow-up of 8.41 years and a mean age at uveitis onset of 5.28 years. Among these patients, 48 required at least one bDMARD for uveitis management, while 17 (26.2%) needed multiple bDMARDs (9 patients required two bDMARDs, while 8 patients necessitated 3 or more bDMARDs). Adalimumab and infliximab served as first-line agents in 41 and 7 patients, respectively. Following the failure of initial anti- TNF treatment, 11 patients transitioned to a new anti-TNFa (infliximab or adalimumab), while 6 switched to tocilizumab. Uveitis control was more frequently achieved by switching from adalimumab to tocilizumab compared to infliximab (p=0.044). Additionally, tocilizumab proved effective in other 4 patients unresponsive to anti-TNF switching. Golimumab and Abatacept were employed as third-line biologics in 3 and 4 patients, respectively. However, Golimumab did not lead to remission of uveitis in any patient, whereas only two patients receiving Abatacept achieved remission. Children requiring multiple bDMARDs for uveitis had a more frequent polyarticular course (p=0.03) and a higher prevalence of systemic steroid use (p<0.001) compared to those responsive to first-line

bDMARDs. Despite a similar frequency of ocular damage at onset, patients needing multiple bDMARSs exhibited a higher percentage of ocular damage at the last visit (58.8% vs 27.6%, p=0.02).

Conclusion: Managing refractory JIA-U can be challenging, particularly in patients failing first-line anti-TNF. Switching to tocilizumab may represent a relevant therapeutic option, although these results need to be confirmed in larger cohort studies.

e-Poster Tours DAY 2

e-Poster Tour 8: Innovation in Health Professional Assessment and Care

ePoster short communications 8- Innovation in Health Professional Assessment and Care	
IMPLEMENTATION AND OUTCOMES OF A PHYSIOTHERAPY-LED PAEDIATRIC RHEUMATOLOGY TRIAGE SERVICE IN THE NATIONAL CENTRE FOR PAEDIATRIC RHEUMATOLOGY, IRELAND	Edel Carberry (Ireland)
DEVELOPMENT AND CONTENT VALIDITY OF A PHYSICAL PERFORMANCE TEST BATTERY FOR CHILDREN DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS	Su-Ané Zwiegelaar (South Africa)
EXPLORING OCCUPATIONAL PARTICIPATION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A QUALITATIVE STUDY ON PARENTS & CARERS PERSPECTIVES	Amy Wescott (United Kingdom)
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IMPLEMENTATION AND OUTCOMES OF A PHYSIOTHERAPY-LED PAEDIATRIC RHEUMATOLOGY TRIAGE SERVICE IN THE NATIONAL CENTRE FOR PAEDIATRIC RHEUMATOLOGY, IRELAND

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Introduction: A novel physiotherapist-led paediatric rheumatology triage service was established at the Irish National Centre for Paediatric Rheumatology (NCPR), in Children's Health Ireland (CHI) at Crumlin in 2019. This was an initiative in response to waiting times which were in significant breach of access to care as per Standards of Care for children and young people with JIA (Davies et. al, 2010). This model of care has successfully and safely reduced waiting lists and provided intermediate care pathways for patients who do not necessarily require rheumatologist review in adult and paediatric services (Stanhope *et al.*, 2012).

Objectives: - Establish how many referrals are suitable for a physiotherapy-led paediatric rheumatology triage service
- Outline how many referrals are managed independently
- Outline the number and type of outcomes following assessment
- Identify the frequency of imaging and other investigations as a result of this model of care

Methods: Referrals were actively triaged by a Consultant Paediatric Rheumatologist and deemed appropriate for physiotherapy-led triage service if: i) pattern of signs and symptoms appear to be non-inflammatory in nature, and ii) cases were not indicative of connective tissue disorder, specific rheumatologic disorder, nor an unexplained and/or significant co-morbid medical condition or complex neuro-disability history. Appropriate patients were then assessed by the Clinical Specialist Physiotherapist in the physiotherapy-led triage clinic.

Results: Between September 2019 and March 2024, n=434 new patients were managed in the physiotherapy-led triage clinic. 70% (n=303) were managed independently, of those 74% (n=250) were discharged following the first visit. 30% (n=131) of total patients seen required review with a Rheumatologist. Investigations were required to augment the clinical exam for 52% (n=224) of patients, including x-ray (38%, n=163), MRI (5%, n=20) and blood tests (41%, n=178)). Of the total patients 43% (n=185) were identified with non-inflammatory musculoskeletal pain, and 15% (n=69) were suspected to have JIA.

Conclusion: Physiotherapy-led triage clinics effectively manage paediatric rheumatology patients. Under the governance of Consultant Paediatric Rheumatologists, this service can independently manage patients who do not require Consultant Rheumatologist review and can appropriately identify those patients who do require further assessment with a Consultant Paediatric Rheumatologist. Almost 40% of patients who attended this service required imaging following clinical assessment.

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DEVELOPMENT AND CONTENT VALIDITY OF A PHYSICAL PERFORMANCE TEST BATTERY FOR CHILDREN DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Movement specialists have a vital role in the treatment of children diagnosed with juvenile idiopathic arthritis (JIA) due to the long- and short-term musculoskeletal disabilities resulting from the disease, pharmacological intervention, and a resulting deconditioning cycle. Consequently, physical health assessment is critical to ensure the appropriate exercise prescription. Yet, within JIA exercise intervention research a high volume of outcome measures are being used, making it challenging to select appropriate physical performance outcome measures (PPOMs) in clinical practice and compare different interventions.

Objectives: The current research aimed to describe the development of a physical performance test battery, the Juvenile Arthritis Kinetic Health Index (JAKHI), and determine its content validity through expert opinion based on the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) guidelines.

Methods: The JAKHI was developed by selecting an appropriate conceptual framework, completing a systematic review, interviewing children with JIA, and surveying clinicians' opinions regarding PPOMs. Content validity was assessed by 15 experts, namely four pediatric rheumatologists and 11 pediatric movement specialists based on the COSMIN guidelines through REDCap® (Version 12.0.3, EDC Software by Vanderbilt University).

Results: The systematic review, semi-structured interviews, and clinician questionnaire support the six JAKHI domains' assessments. The JAKHI achieved satisfactory validity based on an 85% agreement. However, some experts did raise concerns, such as the lack of upper extremity activity inclusion, which the principal investigator addressed.

Conclusion: The JAKHI has satisfactory content validity and seems applicable as a low-cost, easy-to-use, individualized, instructor-administered assessment of holistic physical health in children aged six to 16, diagnosed with JIA.

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EXPLORING OCCUPATIONAL PARTICIPATION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A QUALITATIVE STUDY ON PARENTS & CARERS PERSPECTIVES

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Introduction: Juvenile Idiopathic Arthritis (JIA) is a condition diagnosed before 16 years of age & is the most common rheumatic condition in children. It is reported children with JIA have reduced health related quality of life and participate less in physical & social activities. Participation within leisure activities is critical to childhood development (Bult et al. 2011). Occupational participation is engaging in work, play & activities of daily living which are desired and/or necessary to well-being (Forsyth, 2021). Participation is complex but vital for development & families with a child with a disability experience changes in their occupational routines and family participation (Law, 2002). Little research has been completed into how JIA impacts the child and the family.

Objectives: To explore parents/caregiver's perspectives of their child & family's occupational participation and how JIA has an impact on this. Barriers & facilitators to participation were also investigated.

Methods: The project was approved by the University of Worcester's ethics committee following submission of relevant documents. A phenomenological approach was chosen as this encompasses an interpretive constructivist paradigm. The study aims to understand the lived experiences of parents/caregivers of a child with JIA & phenomenology recognises the depth of information that a person's lived experience can offer to research. Using a qualitative methodology, eight semi-structured interviews were conducted to gain the perspectives of parents/caregivers. Thematic Analysis was used to identify themes.

Results: Three themes were found with six subthemes. As occupational therapy aims to encompass holistic values (RCOT, 2021), it is important to acknowledge the relationship the themes have with each other & how families manage this when experiencing occupational participation. The themes found were "Just getting on with it" including adapting. Outside support including relationships and support groups. Finally, the impact on mental health including the child's mental health & parental stress. JIA impacts the whole family which influences occupational participation. The mental health aspect was significant when exploring the family's occupational participation.

Conclusion: Occupational therapists & allied health professionals can use knowledge from the study to ensure collaborated approaches with families are taken to address family occupational participation. Holistic approaches are necessary to understand the complexities of participation and the barriers and facilitators experienced by families. The research has highlighted barriers and facilitators of family occupational participation. The themes of "Just getting on with it", outside support and the impact on mental health were found to be barriers & facilitators to participation. With participation being an important area of childhood development, it is vital for participation to be addressed by health professionals to support the continuing care of children with JIA & their families.

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EMPOWERING COPING STRATEGIES FOR JSLE: THE ROLE OF CARE-PROFESSIONALS IN PROMOTING WELL-BEING

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Introduction: Systemic Lupus Erythematosus (SLE) is an autoimmune chronic inflammatory multisystemic disease. The main psychosocial symptoms are pain, anxiety, insecurity, fatigue and sleep disorders, which, in addition to other symptoms, can trigger further stress reactions.

Objectives: Promoting individual well-being and improving the quality of life are important for children and adolescents with jSLE, as this has impact on disease progression and thus on further development. Coping strategies can reduce or prevent stress reactions and improve self-efficacy.
Various therapeutic concepts in pediatric rheumatology (e.g. the "Garmischer Therapiekonzept") have proven multiprofessional collaboration to be fundamental for successful treatment.[i]
The aim was to identify disease management strategies specifically attributed to the nursing sector, to categorize them in order to specify issues for future development.

Methods: A structured and an integrative review was carried out including the PubMed and LIVIVO databases. The conducted data have been analyzed and stratified using a model defining five categories. In addition we screened for studies demonstrating positive effects of coping strategies provided by care-givers on the course of the disease.

Results: A total of 3280 hits were checked for relevance, quality and suitability.
Results of 19 implemented studies show a variety of coping strategies and prove the assumption that individual coping strategies tailored to the needs of the patient are crucial for success. 5 studies have defined the influence of different dimensions. Both the number of categories and the content varied, although overlaps could be identified. om these findings, an overarching structure was derived:
1. Cognitive
2. Emotional
3. Motor/sensory
4. Social
5. Self-esteem regulating

In each of these categories there are measures that can be implemented specifically by nursing staff. In this way, they can complement and support the therapies of the other professional groups.
In addition, 16 studies suggest that coping strategies are tailored to improve specific disease symptoms, with most strategies described for pain.

Conclusion: The results of the literature search make it clear that there are a number of possible influences on coping with the disease and that nurses must be aware of the dimensions that need to be taken into account.
Nurses should offer patients strategies from different categories. Increased knowledge of different strategies expands the individual range of coping options.

The classification of coping strategies into five categories also shows that collaboration in multi-professional teams is fundamental to ensure holistic therapy and to fully utilize the potential of coping strategies in jSLE.

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EXPANDING THE TOOLBOX: A COMPREHENSIVE REVIEW OF QUESTIONNAIRE UTILIZATION IN PEDIATRIC RHEUMATOLOGY

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Introduction: Pediatric rheumatologic diseases can be assessed using various methods, including questionnaires that measure parameters like fatigue, pain, quality of life, functional capacity, and joint damage. Among these, the Childhood Health Assessment Questionnaire (CHAQ) and the Child Health Questionnaire (CHQ) are commonly used. However, a wider range of questionnaires also exists (1,2).

Objectives: The aim of this review was to evaluate the use of less common questionnaires in pediatric rheumatologic diseases, beyond the frequently utilized CHAQ and CHQ.

Methods: The eligibility criteria for the studies included in this study were that they had to 1) be conducted on children and adolescents with a rheumatic disease (aged 0–18 years); 2) be randomized controlled trials (RCTs), a controlled study, or pre-post studies, or trial, or review, or clinical answers and 3) be published in the English language. An internet-based search of three databases- PubMed, PEDro, and CENTRAL-was conducted for studies. The following search terms were used Childhood Myositis Assessment Scale (CMAS), Juvenile Arthritis Damage Index (JADI), Juvenile Arthritis Functional Status Index (JAFSI), Juvenile Arthritis Functional Assessment Report (JAFAR), Pediatric Quality of Life Inventory- Multidimensional Fatigue Scale (PedsQL-MFS), Pediatric Quality-of-Life Inventory Arthritis Module (PedsQL) and Pediatric Gait Arms Legs and Spine (pGALS) for Juvenile Idiopathic Arthritis (JIA), Juvenile dermatomyositis/Juvenile systemic lupus/juvenile fibromyalgia/Juvenile scleroderma/Juvenile spondyloarthritis/inflammatory myopathy.

Results: Our search yielded numerous studies: 64 on CMAS, 139 on JADI, 89 on JAFSI, 565 on JAFAR, 40 on PedsQl-MFS, 15 on PedsQl, and 30 on pGALS. Notably, for CMAS, 21 studies were on patients with JIA and 5 with juvenile inflammatory myopathy. JADI was featured in 19 JIA studies, JAFSI and JAFAR each in 5 JIA studies, PedsQl-MFS in 4 studies (3 on JIA, 1 on juvenile dermatomyositis), and PedsQL in 8 studies (7 on JIA, 1 on juvenile fibromyalgia).

Conclusion: Questionnaires are extensively used in pediatric rheumatology, particularly among JIA patients. The review highlights the diverse array of questionnaires deployed and underscores the need for incorporating a broader spectrum of tools to enhance diagnostic and therapeutic strategies.

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CHATGPT VS. PEDIATRIC RHEUMATOLOGISTS: A QUEST FOR EXCELLENCE IN PEDIATRIC RHEUMATOLOGY

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Introduction: Importance Chat Generative Pre-Trained Transformer (ChatGPT) has shown promising performance in various fields, including medicine, but its accuracy on subject-specific medical questions, especially in pediatric rheumatology, is still uncertain.

Objectives: With this study, we aimed to investigate the ability of ChatGPT to correctly answer pediatric rheumatology questions asked in specialty exams in our country. This study, which focuses on how accurately and effectively the model can answer the exam questions set by experts, can help understand the role of artificial intelligence in pediatric rheumatology.

Methods: The examinations were scanned and questions on pediatric rheumatology that had been asked in specialist examinations over the last 10 years were collected. From the collected questions, 35 questions were randomly selected and forwarded to the ChatGPT 3.5 version. In the original exam version, we asked ChatGPT the questions with five options and explained that there was only one option. The answers were recorded and the performance of ChatGPT was evaluated. The incorrectly answered questions were classified according to their main themes and question formats, and frequently recurring themes were identified. The main topics were: inflammatory joint diseases, inflammatory connective tissue diseases, autoinflammatory diseases, vasculitides and rheumatic manifestations of non-rheumatic diseases.

Results: ChatGPT achieved 60% success by answering 21 out of 35 questions correctly. Success performance was 100% in inflammatory connective tissue diseases, 57% in autoinflammatory diseases, 55% in vasculitis, 50% in inflammatory joint diseases (JIA) and 50% in rheumatic manifestations of non-rheumatic diseases, respectively. While the success rate for questions based on clinical solutions was 29%, the success rate for questions based on general information was 89%.

Conclusion: With the knowledge base currently available, ChatGPT's performance in answering questions may unfortunately fall short of the success of pediatric rheumatologists who achieve very high exam scores. In particular, the low performance in solving patient questions in a clinical setting suggests that artificial intelligence models cannot replace clinicians over an extended period of time. Artificial intelligence models may perform better in collaboration with clinicians.

e-Poster Tour 9: Psychosocial well-being and rehabilitation, e-health and disease experience

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INVESTIGATION OF FUNCTIONALITY, PARTICIPATION, AND BIOPSYCHOSOCIAL STATUS OF INDIVIDUALS WITH JIA ACCORDING TO DISEASE ACTIVITY

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Introduction: The relationship between disease activity status in JIA and the functionality, participation, and psychosocial status of these individuals has been emphasized. However, upon reviewing the literature, the need for evaluation of disease activity status in JIA in these aspects is reported (1, 2).

Objectives: This study aimed to investigate the functionality, participation, and biopsychosocial status of individuals with JIA according to disease activity.

Methods: Our study included fifty individuals (31 girls, 19 boys) diagnosed with JIA, of whom 35 had oligoarticular and 15 had polyarticular JIA, and who were followed up with routine controls. Demographic information of the participants was documented, and disease activity status was assessed using the Juvenile Arthritis Disease Activity Score in 71 joints (JADAS-71). Functionality was measured using the Childhood Health Assessment Questionnaire (CHAQ), participation was evaluated using the Child and Adolescent Scale of Participation (CASP), and biopsychosocial status was examined using the Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Q). Disease activity was categorized based on the JADAS-71 score: ≤1 indicated inactive disease, while >10.5 indicated high disease activity (3). Group characteristics were compared using the Mann-Whitney U test.

Results: Demographic characteristics of inactive and high disease activity JIA patients were similar ($p>0.05$). CHAQ pain, general well-being, and total score, CASP home participation and total score, JAB-Q-child disease activity, joint, functionality, fatigue, and total scores were significantly better in favor of the inactive group; ESR value and number of affected active joints were higher in individuals with high disease activity ($p<0.05$).

Conclusion: This study showed that individuals with JIA exhibiting high disease activity were more affected in functionality, participation, and biopsychosocial status compared to those with inactive disease. The findings of this study suggest that these factors should be considered in the disease management of individuals with JIA starting from high disease activity.

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THE LONG-TERM EFFECTS OF A SHORT-TERM SPECIFIC CARBOHYDRATE DIET INTERVENTION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Diet is discussed for its potential to serve as an adjunctive treatment option for juvenile idiopathic arthritis (JIA). To date, research has focused on the specific carbohydrate diet (SCD), showing promising results albeit in a limited patient cohort (1). However, little is known regarding long-term sustainability and efficacy over time, factors critical to validate its role as an adjunctive, therapeutic approach for JIA.

Objectives: To examine long-term effects of the SCD in children with JIA as well as the change in use of disease-modifying antirheumatic drugs (DMARDs) before and after the intervention.

Methods: Influence of the one-month diet intervention and results from follow-up assessments at 3, 6, and 12 months were included. Disease activity was assessed using Juvenile Arthritis Disease Activity Score 27 (JADAS27), other measurements included Pain Visual Analog Scale (VAS) (0-10 cm), global assessment (GlobAss) patient/parent VAS (0-10 cm), duration of morning stiffness in minutes and the frequency of DMARDs usage both one year before and one year after the intervention.

Results: A total of 28 children were enrolled, with 21 completing the one-month intervention; 15 were followed for one year. The majority of patients adhered strictly to the diet for one to two months after the initial one-month intervention and then gradually returned to a standard diet. The levels of JADAS27, pain VAS (0-10 cm), Glob Ass patient/parent VAS (0-10 cm) and minutes of morning stiffness decreased significantly after one month of dietary intervention. The improvement observed in JADAS27 scores was sustained for the 15 patients who completed the one-year follow up ($p = 0.037$, Kruskal Wallis). Additionally, there was a noticeable decrease in the use of DMARDs the year following the dietary intervention compared to the previous year.

Conclusion: The significant clinical impact observed following a short trial of the SCD, and sustained improvement in JADAS27 scores throughout the year, highlight the potential for long-term benefits. However, the high dropout rate and brief adherence to the diet suggest it may be challenging to maintain long-term. Although, preliminary findings also point to a potential decrease in medical burden, further verification is necessary.
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EXPLORING THE HIDDEN WATERS: EVALUATING LOWER URINARY TRACT INVOLVEMENT IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND FAMILIAL MEDITERRANEAN FEVER

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Introduction: Juvenile Idiopathic Arthritis (JIA) and Familial Mediterranean Fever (FMF) are the most common autoimmune and autoinflammatory rheumatic diseases in childhood (1,2). The effects of these diseases, especially on the lower urinary tract (LUT), have not been sufficiently addressed in the literature. Uroflowmetry is a simple and practical method and has been accepted as the first-line screening tool for evaluating LUT symptoms in children (3). However, there are limited studies evaluating uroflowmetry in JIA and FMF.

Objectives: The aim of this study was to investigate the urological involvement in patients with JIA and FMF.

Methods: Thirty-eight children and adolescents (15 JIA, 13 FMF, 10 healthy peers) aged 6-17 years, participated in the study. The Childhood Bladder and Bowel Dysfunction Questionnaire (CBBDQ) and the Dysfunction Voiding Symptom Score (DVSS) were used to assess the LUT symptoms of the participants. 15 patients with JIA and FMF with the highest scores were assessed with simple uroflowmetry. Uroflowmetry parameters included maximum flow rate (Qmax), voided volume and time, average flow rate, time to Qmax, hesitancy, and post-void residual (PVR) values.

Results: The mean ages of JIA, FMF and healthy controls were 13.06±3.12, 11.53±2.14, and 9.22±2.77 years, respectively. The scores of CBBDQ and DVSS were similar in JIA and FMF ($p>0.05$). However, statistically higher scores were found in CBBDQ and DVSS in JIA and FMF compared to the healthy controls ($p<0.001$). Of the JIA-FMF patients, 35.7% reported urinary incontinence, 57.7% reported postponement, 49.4% reported urgency. According to the uroflowmetry results, differences were found in 12 out of 15 children with JIA and FMF. In these 12 children voided volume, average flow rate, time to Qmax, hesitancy and post-void residual were 321.00±315.11 ml, 11.67±8.26 ml/s, 10.25±7.23 s, 13.00±7.60 s and 54.42±50.24 ml, respectively. Voided volume and the average flow rate were found to be lower than the determined normative values, whereas other values were found to be higher.

Conclusion: It is seen that the lower urinary system is negatively affected in patients with JIA and FMF compared the their healty peers. We consider that the multisystemic nature of the diseases, chronic inflammation, changes in the musculaskeletal system and medications can alter urine biochemistry and can lead to structural changes in the LUT in patients with JIA and FMF. This study emphasizes the importance of evaluating urinary system involvement in patients with JIA and FMF, and we believe that pelvic floor rehabilitation should be considered as a potential treatment method in managing lower urinary system dysfunctions in children with JIA and FMF.

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POSTURAL BALANCE MAY BE MORE INFLUENTIAL THAN MUSCLE STRENGTH IN STAIR ASCENT-DESCENT PERFORMANCE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) stands as the most prevalent chronic, autoimmune, and inflammatory disease within the pediatric population. It's characterized by symptoms such as muscle weakness, joint involvement, pain and fatigue(1). The accompanying symptoms of the disease often impact the functional abilities of children(2). Studies have shown that individuals with JIA have lower muscle strength and walking speed, poorer postural balance and slower stair descent-ascent skills compared to their healthy peers(3). In children with JIA exhibiting lower physical proficiency compared to their healthy peers, it remains uncertain which condition should be prioritized in rehabilitation.

Objectives: The primary aim of this study was to investigate the relationship between lower extremity endurance, muscle strength and postural balance in patients with JIA and to determine which parameter is prioritized for enhancing endurance in the rehabilitation program.

Methods: A total of 45 individuals (21 girls-24 boys) diagnosed with JIA were included in the study. A 10-step stair ascent-descent test (10SCT) was applied to evaluate the participants' functional performance.Objective measurements were made using the newly developed K-Plates and K-Push (Kinvent Physio, France) devices for isometric muscle strength and postural balance assessment.For postural balance measurement, they were asked to stand on one leg for 15 seconds with their eyes closed and open, and the asymmetry between the two extremities was recorded using the application of the device.Isometric muscle strength was measured with the knee flexed at 60° for Quadriceps muscle and at 30° for Hamstring muscle. Participants were instructed to maintain isometric contraction for 5 seconds in each position with a 5-second rest interval between limb measurements.Extremity muscle strengths were recorded with the application of the device.SPSS Version 24.0 program was used for statistical analysis.

Results: The mean age, height and weight of children with JIA were 13.76±2.14 years, 158.38±11.79 cm and 52.73±16.19 kg respectively. The mean of the 10SCT performance was 8.31±2.618 seconds. A significant correlation was observed between the stair ascent-descent test and the isometric muscle strength results of the eyes-closed single-leg stance test, 60° quadriceps, and 30° hamstring muscles($p<0.005$). However, no correlation was found with eyes-open balance($p>0.005$). The regression analysis of the relevant parameters indicated that the asymmetry in the single-leg stance with eyes closed was the most influential factor on the 10SCT performance($p<0.001$).

Conclusion: The findings of our study indicate that postural alignment takes precedence in the stair ascent-descent performance in JIA. While the test conducted with eyes open did not yield statistical significance, a significant difference was observed in the measurement with eyes closed. This

difference underlines the importance of sensory input and proprioception in physical competence. Consequently, when planning exercise prescription for individuals with JIA, it's imperative to not only address muscle strength but also emphasize exercises aimed at improving balance and proprioception and to provide appropriate posture instructions during exercise.
This study was supported within the scope of TUBITAK 1001-Scientific and Technological Research Projects Support Program 121E690.

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RELATION BETWEEN FATIGUE A OTHER PARENT REPORTED OUTCOMES IN A CHORT OF CHILDREN WITH JIA

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Introduction: Although fatigue is considered to be common in children and young people with juvenile idiopathic arthritis (JIA), the relevance of this symptom within the burden of the disease was poorly studied.

Objectives: To assess correlation of fatigue with physician centered measures and other patient reported outcomes (PROs) in a cohort of JIA patients

Methods: We enrolled in the study all JIA patient attending the outpatient clinic at the Study Unit in April 2024. Patients were asked to complete the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) and the PROMIS® Item Bank v1.0 – Fatigue – Short Form 13a (FACIT-Fatigue), measuring the level of fatigue in 13 items with a 5-points Likert scales yielding a score of 0 to 52, with higher scores indicating more sever fatigue. Physician centered measures included the rheumatological examination form and the physician global assessment of disease activity (PhGA). We calculated Spearman rank correlation between fatigue score and quantitative measures included in the JAMAR, active joints count, and PhGA. Finally, we compared the levels of fatigue in patients considering themselves to be satisfied or not satisfied with current disease outcome.

Results: The questionnaires were proposed for completion before clinical examination to 51 JIA patients; 49 (87.2% females) completed both questionnaires and were included in the study. Patients had a median disease duration of 9.6 years (IQR 5.3-13.5) and were predominantly affected with oligoarticular JIA (72.3%). All JIA categories were represented. Median PhGA was 0 (0-2). Median fatigue score was 47 (38-51.5). Fatigue correlations were higher with JAMAR HRQoL tool (r = -0.67) and with JAMAR functional ability tool (r = -0.60). Correlation coefficients were between -0.4 and -0.6 with well-being VAS, patient disease activity VAS, pain VAS, morning stiffness duration, and cJADAS10. Correlations were poor (r < -0.4) with PhGA and active joint count. Correlations with HRQoL items in

the JAMAR that were suggested to explore the domain of fatigue were the highest (r = -0.70 between fatigue score and JAMAR HRQoL items 3 and 9). Fatigue score was 37 (35-44) in 21 patients who were not satisfied with current disease outcome and was 51 (47-52) in 26 patients who considered their disease status as satisfactory ($p < 0.001$).

Conclusion: Fatigue seems to have a relevant weigh in the disease perception of children with JIA in a cohort of children with a generally well controlled disease. It is strongly correlated with HRQoL score and functional ability score. Patients not satisfied with disease outcome had significantly higher level of fatigue.

SOCIAL MEDIA PLATFORMS AS NEW CLASSROOMS FOR PEDIATRIC RHEUMATOLOGY: A LARGE COMPARATIVE STUDY WITH REAL-DATA FROM OVER 14500 CONTENTS

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Introduction: Social media platforms are free and familiar tools used by patients, caregivers, influencers, and health professionals (HPs) for medical purposes, including Pediatric Rheumatology (1,2).

Objectives: The aim of this study was to investigate the characteristics, accuracy, and quality of social media content related to Pediatric Rheumatology.

Methods: The 150 most popular posts from 18 relevant hashtags/topics related to Pediatric Rheumatology were assessed on the social media platforms Facebook, Instagram, and TikTok.
Metrics, content creator types, sentiment, and misinformation were evaluated; for videos, the Journal of American Medical Association Benchmark Scale (JAMAS) was used for determining quality, while understandability and actionability were evaluated with the Patient Education Materials Assessment Tool (PEMAT).

Results: Of the 14551 posts evaluated, 6723 were included (pertinent content in English or Italian).
Videos obtained 520,8 million views and had a duration of more than 76,3 hours; videos and photos accounted for 34,6 million likes and 37,6 million interactions. 3165 posts regarded autoimmune diseases (47,1%), 1441 vasculitis (21,4%), 992 autoinflammatory diseases (14,8%), and 1125 other diseases/topics (16,7%).
Non-health professionals (NHPs) represented the majority of creators (5160, 76,8%), with 2700 patients (40,2%) and 1119 caregivers (17,8%). HPs were 1563 (23,2%), with 142 pediatric rheumatologists, 124 rheumatologists, and 68 pediatricians. Content was most often shared for reporting a patient or caregiver experience (3462, 51,5%), usually with neutral (1303, 34,8%) or positive sentiment (1296, 34,7%).
Educational content (2074/6723, 30,8%) consisted of 907/3593 videos and 1167/3130 photos. HPs provided longer (59 sec, IQR 85 sec vs 50 sec, IQR 77 sec; *p<0,001*) more understandable (PEMAT understandability 85,7, IQR 18,9 vs 75, IQR 25; *p<0,001*), more actionable (PEMAT actionability 66,7, IQR 33,3 vs 50, IQR 41,7; *p<0,001*), and higher-quality (JAMAS 3, IQR 0 vs 3, IQR 1; *p<0,001*) educational videos than NHPs. NHPs shared educational photos (3, IQR 11 vs 1, IQR 8; *p<0,001*) and videos (8, IQR

50 vs 4, IQR 27; *p<0,001*) with more comments, videos with more views (6181, IQR 23417 vs 2967,5, IQR 20943; *p=0,034*), likes (116, IQR 691 vs 61, IQR 488; *p=0,014*), and interactions (172, IQR 904 vs 93,5, IQR 656; *p=0,011*) than HPs, probably due to the major personal involvement and interest of other users with similar health issues. Educational videos without misinformation (827/907) were mostly provided by HPs (514 vs 313; *p<0,001*); in addition, quality was correlated with duration (rho 0,172, *p<0,*001), understandability (rho 0,150; *p<0,001*), actionability (rho 0,106; *p<0,001*), and being HPs (rho 0,206; *p<0,001*).

Conclusion: This is the largest study on Pediatric Rheumatology content on social media. While NHPs are actively participating in these discussions, there is a need for more high-quality, accurate information from HPs. The medical community should take a decisive step in this new field of education.

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SIGNIFICANT LEVELS OF PSYCHOLOGICAL STRESS, DEPRESSION AND ANXIETY SYMPTOMS IN CHILDREN WITH PEDIATRIC RHEUMATOLOGIC DISEASES

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Introduction: Mental health problems are common in children with pediatric rheumatologic diseases (PRDs) and are associated with worsened quality of life and poorer disease-related outcomes. Psychological distress results from exposure to stress, may be exacerbated in response to traumatic events (e.g., COVID-19 pandemic), and can lead to significant mental health problems.

Objectives: We aimed to determine the burden of psychological distress in children with PRDs as defined by psychological stress experiences and investigate associations between physical stress, perceived psychological distress, anxiety, depressive symptoms, and COVID-related distress.

Methods: Patients at participating centers with a diagnosis of JIA (juvenile idiopathic arthritis), jSLE (juvenile systemic lupus erythematosus), or JDM (juvenile dermatomyositis) registered in The Childhood Arthritis and Research Alliance (CARRA) Registry were approached for enrollment. Consented participants completed a one-time survey during a scheduled rheumatology visit, including Patient-Reported Outcomes Measurement Information System® (PROMIS) measures for psychological stress experiences, physical stress, and depressive symptoms, in addition to the NIH-Toolbox Perceived Stress survey, clinically validated measures of depression (PROMIS, PHQ-9) and anxiety (SCARED), and a visual analog scale for COVID-related distress. Scores on the PROMIS and NIH-Toolbox measures of one standard deviation above the mean of the reference population (T-score 50) indicated high levels of that measure; for these measures, high levels signify a positive screen. Elevated scores on the PHQ-9 and SCARED were determined by clinical cutoffs (5 and 30 respectively). Descriptive statistics were used for patient characteristics and patient-reported outcomes. The relationship between psychological stress and other measures was determined by Pearson Correlation Coefficient.

Results: The 150 patients who completed the survey had a mean age of 13.5 years (SD=2.7) and a diagnosis of JIA in 136 (91%) (Table 1). Psychological stress experiences were elevated in 34% and

physical stress experiences in 41% (Table 2). High levels of perceived stress were reported in 20% of patients aged 13-17 years and 16% of those aged 8-12 years. While increased depressive symptoms were seen in only 24% on the PROMIS measure, 51% of patients had a positive PHQ-9 depression screen; of those with a positive PHQ-9, only 6 (5%) had severe depression. Over a third of the cohort (38%) had SCARED scores concerning for anxiety disorder. Most patients endorsed mild distress from the COVID-19 pandemic (median 2, IQR 0,5); only 5 (3.5%) endorsed severe distress. Psychological stress was highly correlated with perceived stress, depressive symptoms (PROMIS and PHQ-9), and anxiety and COVID stress (Table 3); however, correlation with physical stress was not statistically significant.

Conclusion: Psychological distress is common in children with PRDs and associated with perceived stress, depressive symptoms, and anxiety, but not physical stress. Next steps include expanding this cohort to include a greater number of patients with JDM and jSLE, to ensure findings are representative of a broader general rheumatology clinical sample. Further study is needed to understand the relationship between psychological distress and disease factors, as well as the potential role of targeting psychological distress to mitigate risk of poor mental health and clinical outcomes.

PSYCHIATRIC DISORDERS IN PATIENTS WITH JUVENILE FIBROMYALGIA SYNDROME

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Introduction: Juvenile fibromyalgia syndrome (JFS) is a disabling condition characterized by musculoskeletal pain, fatigue, sleep disturbances, and cognitive impairment. Psychiatric disorders (PDs) are common in adults with fibromyalgia and are associated with greater physical impairment (1). Very little data are available on PDs in JFS.

Objectives: To investigate PDs in JFS and their impact on the global burden of the disease.

Methods: We included patients with JFS diagnosed according to the 2010 American College of Rheumatology (ACR) criteria who were visited at our center between June 2021 and June 2023. We collected clinical data, including psychiatric comorbidity, and ongoing treatment. Depressive symptoms were assessed using the Children Depression Inventory 2 (CDI-2) for patients aged 11 to 17 years and the Beck Depression Inventory (BDI-2) for patients older than 17 years. Anxiety symptoms were assessed using the Multidimensional Anxiety Scale for Children 2 (MASC-2). Suicidal ideation risk was assessed by responses to item 8 of the CDI-2 and item 9 of the BDI-2. Severity of symptoms, quality of life (QoL), and functional ability (FA) were assessed using the Juvenile Fibromyalgia Multidimensional Assessment Report.

Results: 58 patients (52 females) with a median age of 17.7 years (11.4-19.4) and a median age at onset of 13.6 years were included in this cross-sectional study. 31 of 58 patients (53.4%) had the following isolated or associated psychiatric comorbidities: depressive disorder (35.5%), social anxiety disorder (35.5%), feeding and eating disorder (25.8%), panic disorder (19.3%), generalized anxiety disorder (12.9%), bipolar disorder (0.06%), posttraumatic stress disorder (0.03%), schizophrenia (0.03%), and depersonalization-derealization disorder (0.03%). 17 of 58 JFS patients (29.3%) expressed

suicidal ideation. 15/31 (48.4%) patients received psychotherapeutic intervention and 21 patients (36.2%) received pharmacological therapy (10 gabapentinoids, 5 selective serotonin reuptake inhibitors, 4 amitriptyline, and 2 duloxetine). Psychiatric comorbidity in JFS was significantly associated with impaired physical functioning (p=0.031) and fatigue (p=0.027).

Conclusion: This study reveals that PDs are common in JFS and provides important insights into the impact of PDs on relevant clinical domains of the disease, such as fatigue and disability. Elucidation of the influence of PDs on disease severity could provide insights for the development of more comprehensive and targeted therapeutic approaches.

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DYSREGULATION OF THE TLR3/IFIH1 PATHWAY AT JUVENILE DERMATOMYOSITIS ONSET IMPLICATES VIRAL INFECTION AS A DISEASE TRIGGER

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Introduction: We previously reported elevated plasmatic interferon alpha levels concomitant with SARS-CoV-2 infection in juvenile dermatomyositis (JDM) at onset1.

Objectives: Here we tested the hypothesis that (i) dysregulation of specific nucleic acid sensor pathways may be implicated in JDM and (ii) specific pathogens sensed by these pathways may be associated with JDM onset.

Methods: We prospectively recruited 18 JDM patients at diagnosis and age-matched paediatric controls. Whole blood cellular phenotyping and single-cell phosphoproteomics were performed by mass cytometry. Responses of specific nucleic acid sensors were evaluated using standardized *ex-vivo* whole blood stimulation assays (TruCulture) with Toll-like receptor (TLR) agonists Poly(I:C), ODN 2216 and R848. Cytokine secretion was quantified using Luminex and digital ELISA (Simoa) and transcriptomic signatures by bulk-RNA-sequencing. IgG levels against 20 RNA viruses were quantified by Luminex at diagnosis.

Results: We observed increased proportions of transitional B cells and naïve CD8 T cells, and reduced memory B cells and effector memory CD8 T cells, in JDM patients at diagnosis compared to age-matched controls. Phosphoproteome profiles within JDM patients at diagnosis did not identify a shared inflammatory pattern between patients. In contrast, they revealed heterogeneous and globally elevated inflammatory responses. Median levels of type I interferon and specific interferon induced proteins were highly elevated in JDM patients at basal state compared to controls. Transcriptomic analysis confirmed an enrichment of the interferon pathway in JDM at diagnosis. Following TLR stimulation JDM patients showed a defective response to Poly(I:C) stimulation at both proteomic and transcriptomic levels compared to controls. In contrast, responses to R848 and ODN stimulation were not different. *IFIH1,* but not *TLR3,* was up-regulated in JDM compared to controls. Antibody analysis showed that JDM patients at diagnosis had a greater history of infections with SARS-CoV-2 and Enterovirus compared to controls.

Conclusion: We identified a defective response to Poly(I:C) stimulation in JDM patients implicating the IFIH1 pathway. JDM patients at diagnosis had elevated seropositivity to specific RNA viruses, suggesting their potential role in triggering *IFIH1* dysregulation and JDM onset. Validation of these viral signatures by current antibody analysis in an independent cohort may provide further confirmation. Additionally, ongoing single-cell studies will help to better understand the molecular and cellular specificities that drive RNA sensing dysregulation in JDM patients.

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JAK INHIBITOR USE IN PATIENTS WITH JUVENILE DERMATOMYOSITIS, TÜRKIYE EXPERIENCE

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Introduction: JDM, which can be classically treated with methotrexate and steroids, may require the use of DMARDs or biological drugs due to findings such as refractory muscle disease, skin ulcers, lung involvement, and calcinosis. The IFN pathway is upregulated in JDM. Therefore, the JAK-STAT pathway, which leads to the transcription of IFN-stimulated genes, is a potential target in the treatment of JDM. Clinical trials of specific JAK inhibitors in adult patients are ongoing.

Objectives: In this multicenter study, we aimed to share our JAK inhibitor experience in a JDM.

Methods: 13 JDM patients from 7 Pediatric Rheumatology centers who received JAKis between July 2015 and March 2023 were retrospectively reviewed. All patients fulfilled the Bohan-Peter classification criteria. Patients aged <18 years who started Jak inhibitor treatment and had at least 6 months follow-up data were included. Indications for treatment and response to that indication, physician VAS before and after treatment, reduction in steroid dose (6. Month if available, 12. Month), side effects, need for drug change due to treatment failure were assessed. Muscle strength, if previously recorded, was assessed with the Childhood Myositis Assessment Scale (CMAS, range 0-52) and the Manual Muscle Testing (MMT) scale (range 0-80). Organ involvement such as lung, cardiac and gastrointestinal system (GIS) was evaluated as remission-stable disesase-progression. Descriptive statistics were presented as median (IQR) for continuous variables and as number and percentage for nominal/categorical variables.

Results: Data from 13 patients were included. Main indications were muscle weakness (n=9), calcinosis (n=9), skin ulcers (n=3), dysphagia (n=1), interstitial lung disease (ILD) (n=1) and cardiac involvement (n=1).). Due to payment terms, all patients received Tofacitinib. All patients had a history of glucocorticoid use, 12 patients with hydroxychloroquine, 5 patients with MMF, 12 patients with Methotrexate, 11 patients with IVIG, 7 patients with anti-TNF, and 6 patients with rituximab. Along with tofacitinib, glucocorticoid was used in ten patients, IVIG in three patients, hydroxychloroquine in five patients, and mycophenolate mofetil in two patients. One patient used it as monotherapy. No significant adverse events were reported. Progressive disease in 5 of the patients remained stable after tofacitinib. Partial remission was observed in 5 patients. In the follow-up of these, treatment was discontinued due to relapse in four of them. In 3 patients, treatment was discontinued due to lack of response. Steroid dose reduced in seven patients.

Conclusion: Our findings suggest that Tofacitinib is a safe alternative in the treatment of JDM. However complete remission was achieved in half of the patients. Further studies should aim to define the group of patients who would benefit from Jak inhibitors.

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CALCINOSIS PREVALENCE AND TREATMENT RESPONSE IN JUVENILE DERMATOMYOSITIS: A RETROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Calcinosis is one of the most typical complications of Juvenile dermatomyositis (JDM), which is difficult to treat and may cause long-term morbidity. It is defined as the intracellular deposition of insoluble calcium salts in affected tissues. [1] Different types of antibodies are associated with specific phenotypes; in the literature, anti-NXP2 is reported to be more frequently associated with the development of calcinosis. [2]

Objectives: We aimed to investigate the prevalence of calcinosis, its association with MSA and MAA patterns, and the response to treatment in JDM patients.

Methods: Patients with JDM followed from 2015 to 2024 in our pediatric tertiary care center were enrolled in this retrospective observational study. Patients with no available data on MSA and MAA were excluded. Descriptive analyses were reported as median and IQR for continuous variables and absolute frequencies and percentages for categorical. The T-student test and Z-test were used to analyze the two groups.

Results: Twenty-four patients (75% female) were enrolled. The median age at disease presentation was 6.9 y (IQR 3.3-9.6), and the median diagnosis delay was 3.5 months (IQR 0.9–3.1 months). MSA was positive in 15 patients (62%) and MAA in 3 (12.5%). Anti-NXP2 was the most frequently reported antibody in our cohort (53%). 29.1% patients presented calcinosis during the follow-up; none had calcinosis at diagnosis. Four patients were NXP2+ (57%), 1 patient was anti-SAE+, and 1 anti-Ku+. Patients were divided into 2 groups based on its presence. The median time from diagnosis to the development of calcinosis was 4 y (IQR 2.5-3.3). There was no difference in the age at onset, the delay between onset and therapy, and the CPK levels at onset between the groups with and without calcinosis. The difference in the prevalence of NXP2+ patients between the two groups was not statistically significant. Seventy-one percent of patients in the calcinosis group had disease relapse versus 29% in the group without calcinosis; (P-value 0.04). Treatments used for patients with calcinosis included MTX and GCS and IVIg for all patients. Two patients underwent therapy with bisphosphonates. Three patients underwent anti-TNF, one of which halted progression and completely dissolved the calcinosis, one showed partial resolution (treatment ongoing), and one did not respond. One patient received Jak-inhibitor for one year, showing no further progression but no improvement in calcinosis.

Conclusion: Calcinosis is a significant complication in JDM, affecting 29.1% of our cohort. In our cohort patients with calcinosis exhibited a higher relapse rate. Furthermore, no significant association was found between anti-NXP2 antibodies and calcinosis. Treatment outcomes for calcinosis varied, indicating the need for further research to identify risk factors and develop standardized therapeutic approaches for this debilitating complication.

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DNA METHYLATION PROFILES IN IMMUNE CELL SUBSETS FROM JUVENILE SYSTEMIC SCLEROSIS PATIENTS IDENTIFY DISEASE-ASSOCIATED PATHWAYS

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Introduction: Juvenile systemic sclerosis (jSSc) is a rare and complex autoimmune/inflammatory disease that affects connective tissues resulting in organ sclerosis and failure. The pathophysiology of jSSc is multifactorial and, due to its rarity, poorly understood. Both innate and adaptive immune cells, particularly monocytes and T lymphocytes have been suggested to play an important role in jSSc.

Objectives: To investigate epigenetic and gene expression signatures in immune cell subsets from jSSc patients that may serve as future biomarkers and/or treatment targets.

Methods: This study is part of the PASTIES project: PAtient STratification and Individualised trEatment in Systemic sclerosis. Peripheral blood mononuclear cells from jSSc patients (N=14) and matched healthy controls (HC, N=17) were isolated from venous blood. Cells were stained for CD3, CD4, CD8, CD14, CD19, and CD86, and immune cell populations (CD3-CD19+, $CD3^+CD4^+$, $CD3^+CD8^+$, $CD14^+$, $CD14^+CD86^+$) were collected using flow cytometry sorting. $CD3^+CD4^+$ T lymphocytes, $CD14^+$ monocytes, and CD3-CD19+ B lymphocytes were collected and used for DNA methylation analysis via Illumina Infinium 930K MethylationEPIC Arrays (Diagenode). Flow cytometry data were analysed using FlowJo Software (v10.6.1, BD Life Sciences); DNA methylation data were analysed using the R environment (v4.4.0) and ChAMP, minfi, limma, and clusterProfiler packages.

Results: No statistically significant differences were seen in the proportions of monocytes, B or T lymphocytes between jSSc patients (N=14) and matched controls (N=17). More than 12,500 differentially methylated positions (DMPs) were detected when comparing CD4+ T lymphocytes from the two groups (N=4 each), more than 2,500 when comparing monocytes (N=5 each), and more than 1,300 when looking at B cells (N=4 jSSc and 6 HC). KEGG pathway analysis of genes with at least two differentially methylated positions (DMPs) in their promoter region delivered hypermethylation of genes involved in “cell cycle”, “longevity regulating pathway”, “AMPK signalling pathway”, “ubiquitin mediated proteolysis”, and “FoxO signalling pathway” in T cells, “longevity regulating pathway”, “fatty acid metabolism”, and “insulin resistance and signalling pathways” in monocytes, and “homologous recombination” in B cells.

Conclusion: Differentially methylated genes in immune cell subsets inform our understanding of jSSc pathophysiology. In a next step, RNA from collected immune cells will be used towards RNA sequencing to integrate gene expression patterns with DNA methylation signatures. Additional samples will be used for validation of findings (NanoString custom RNA expression panels; DNA bisulfite pyrosequencing). Differentially methylated and expressed genes and pathways may inform the development of biomarkers and future treatments of jSSc.

EFFICACY OF TOCILIZUMAB ON DISEASE ACTIVITY IN PATIENTS WITH JUVENILE LOCALIZED SCLERODERMA: A RETROSPECTIVE MONOCENTRIC STUDY

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Introduction: Biologic agents have been proposed as potential therapeutic options for juvenile localized scleroderma (JLS) refractory to prior therapy. Recently, some case series reported the effectiveness of tocilizumab (TCZ) in these patients.

Objectives: To evaluate the efficacy of tocilizumab in JLS patients resistant or intolerant to previous therapy (as second- or third-line therapy) and as first line in patients with severe disease.

Methods: We enrolled 10 patients with JLS (circumscribed, linear, pansclerotic and mixed scleroderma) followed at Bambino Gesù Children's Hospital, who received TCZ for at least 2 years. The modified Localized Scleroderma Activity Index (mLoSSI) and the Localized Scleroderma Skin Damage Index (LoSDI), PGA-disease activity and PGA-damage were retrieved from patients' charts and used to assess disease activity and damage, respectively.

Results: All patients were treated with methotrexate (MTX). Four patients with extensive skin involvement were started on a combination of TCZ + MTX as first line therapy. Six patients were started on TCZ as second-or third-line therapy (4 for refractory disease and 2 for MTX-related side effects), three of these patients had received rituximab (RTX) before TCZ. In the 6 patients who started TCZ as second or third-line therapy, we did not observe statistically significant differences for mLoSSI and PGA activity between baseline (pre-MTX) and pre-TCZ. Two patients showed a reduction in both mLoSSI and PGA activity while receiving MTX treatment but had to discontinue MTX due to side effects. The other 4 patients showed stable or worsening mLoSSI and PGA activity. One year after starting TCZ, all 10 patients showed a reduction in both mLoSSI and PGA activity. The improvement further progressed after 2 years of treatment and overall there was a statistically significant reduction in both mLoSSI (Friedman test p= 0.00013, Kendall W coefficient = 0.814) and PGA activity (Friedman test p= 0.00013, Kendall W coefficient = 0.814). No significant differences in LoSDI and PGA damage between baseline (pre-MTX) and pre-TCZ were observed in the 6 patients who started TCZ as second-or third-line therapy. After starting TCZ, patients did not show a significant reduction in neither LoSDI nor PGA damage after 1 or 2 years of therapy.

Conclusion: TCZ effectively reduced disease activity in JLS patients who were resistant or intolerant to prior therapies, but it did not reverse existing damage. Thus, TCZ may represent a possible therapeutic option for patients with severe or refractory JLS. We hypothesize that the irreversible damage associated with extensive tissue sclerosis is secondary to an ongoing skin inflammatory response and an earlier use of TCZ may be useful in promptly abating skin inflammation and preventing chronic outcomes and disability.

JUVENILE LOCALISED SCLERODERMA (JLS) PATIENTS EXPERIENCE DELAY IN DIAGNOSIS, DISEASE DAMAGE AND POOR PATIENT-RELATED OUTCOMES: INITIAL DATA FROM AN INTERNATIONAL, PROSPECTIVE COHORT STUDY

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Introduction: JLS is characterised by chronic inflammation of the skin leading to fibrosis and may be associated with local complications and extra-cutaneous manifestations. Patient-related outcome measures are not well-established for JLS research or widely used in clinical settings. The Localised Scleroderma Quality of Life Index (LoSQI) was developed following work showing that the Children's Dermatology Quality of Life Index (CDLQI) may not capture the full impact of JLS(1,2). The LoSQI study was developed to facilitate cross-cultural adaptation and validation of the LOSQI.

Objectives: To evaluate established outcome measures and delay in diagnosis in patients enrolled within the LoSQI study.

Methods: Patients aged 8-18 years with JLS were recruited via PRINTO centres participating in the LoSQI study. Demographic, disease data and clinician and patient-reported outcome measures were collected prospectively (where translation available) using the PRINTO web platform. Data from this interim analysis is described descriptively from patients with locked baseline data. Ethical approval was obtained in accordance with local/national requirements.

Results: To date 142 patients have been recruited from 25 sites in 17 countries. There were 83 patients with locked data at baseline visit included in this analysis. Patients were mostly Caucasian (64/83, 77%), female (59/83, 71%) with a median age at baseline visit of 9.5 years (interquartile range 7.4-11.8 years). The median age at diagnosis was 8.8 years (6.1-10.5) with a median delay in diagnosis of 1.0 years (0.4-2.0). Over a third (38%) of patients experienced a delay in diagnosis of >1 year. Most patients had inactive disease at baseline (mLoSSI 1 (0-5), physician activity VAS 0 (0-2.3)) but many patients had damage (LoSDI 6 (4-12.5), physician damage VAS 2 (1-4)). The median CHAQ score was 0 (0.0-0.1).
Patients and parents/carers completed VASs on a 0-10 scale and scored the impact of JLS on them/their child in the last month similarly with a median of 1 (IQR 0-3.5 and 0-3 respectively). Parents were also asked to score worry about long-term impact of JLS and worry about medications with median scores of 6.5 (3.5-8.0) and 5 (2.0-8.0) respectively.
Patient-Reported Outcomes Measurement Information System (PROMIS) outcomes were categorised as per Carle et al(3). Patients were categorised as moderate or severe for fatigue in 33%, pain in 31%, anxiety in 29%, and depression in 19%. Patients were categorised as fair or poor in mobility in 35%, global health in 23%, and upper extremity in 21%. Median CDLQI score was 2 (0-5) suggesting a small effect, but as above may not capture the full impact of JLS.

Conclusion: This large, international prospective study of patients with JLS demonstrates that patients experience significant delay in diagnosis and disease damage. Despite most patients achieving clinically inactive disease they continue to experience fatigue and anxiety with parents having high levels of worry regarding long-term outcomes and medication impact.

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e-Poster Tour 11: Spondylarthropahies and imaging

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RUSSIAN MULTICENTER STUDY OF CLINICAL FEATURES OF ENTESITIS-RELATED ARTHRITIS AND/OR JUVENILE ANKYLOSING SPONDYLITIS

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Introduction: Among all categories of juvenile idiopathic arthritis according to the classification ILAR there is a variant of arthritis associated with enthesitis (EAA), which may correspond to the prespondylitic stages of juvenile ankylosing spondylitis (JAS) and be a dominant part of the spectrum of juvenile spondyloarthropathies (JSpA), which unites a group of clinically and pathogenetically similar diseases. The need to meet the criteria of EAA, mutually exclusive with respect to the category of psoriatic arthritis, incomplete compliance with the diagnostic criteria of AS make it difficult to identify JSpA in children. The relevance of the study is due to the ambiguity of existing nomenclatures and definitions defining the group of diseases belonging to JSpA.

Objectives: In real clinical practice, analyze the clinical features of the course of JSpA diseases in children in the Russian Federation with assessment of formal compliance with existing classification and diagnostic criteria (modified New York criteria for JAS)

Methods: A multicentre, observational, observational cross-section study was conducted. Patients who, in the opinion of the physician, could be classified as JAS or EAA were included in the study. A 'historical' (over 18 years of age at the time of the study) and prospective cohort of patients were analyzed. Descriptive statistics of the study results for qualitative and ordinal characteristics are presented in the form of absolute values and percentages (%), quantitative - with the median (Me) (IQR).

Results: 402 patients were included, 76% were boys, Me age of onset was 11 (8;13) years, Me duration of diagnosis was 7 (3;15.5) months, Me duration of disease was 64 (39;95) months.The clinical picture of EAA/UAS in the patients in the study is represented by: spinal column symptoms in 238/402(59%) (predominant symptom is spinal stiffness in 114/238 (48%) cases), axial skeletal structures in 75/402 (19%), arthritis in 371/402 (92%), entheses in 110/402 (27%), eyes (uveitis) in 26/402 (6%), gastrointestinal tract (unspecified colitis, Crohn's Disease, ulcerative colitis) in 49/402 (12%), cardiovascular system in 4/402 (1%) patients respectively, psoriasis was detected in 37/402 (9.2%) patients. The most frequent combinations of clinical symptoms were: spinal column lesion and arthritis - in 90/402 (22%), axial lesion combined with arthritis and enthesitis - 45/402 (11%), arthritis and enthesitis - 21/402 (5%) patients, respectively. There were no symptoms of damage to the respiratory and urinary systems. Radiological diagnostic data were analyzed in 307/402(76%). The prevailing method of radial diagnosis was MRI of sacroiliac joints - the study was performed in 277/307 (90%) patients. Sacroiliitis was verified in 269/307 (88%) patients. There were no differences in clinical manifestation, frequency and spectrum of extraaxial manifestations between the EAA and JAS groups.

Conclusion: The peculiarities of clinical manifestations of patients referred to the JSpA group described in our study confirm the possibility of evaluating these diseases within a single nosological group, which

indicates the need to develop a unified nomenclature and diagnostic criteria for JAS/EAA with subsequent implementation in real clinical practice.

CLINICAL CHARACTERISTICS AND DISEASE OUTCOMES OF MUSCULOSKELETAL EXTRAINTESTINAL MANIFESTATION IN PEDIATRIC PATIENTS WITH IBD: A NATIONWIDE STUDY ON BEHALF OF THE ITALIAN SOCIETY OF GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

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Introduction: Musculoskeletal (MSK) Extraintestinal Manifestations (EIMs) are frequent in Inflammatory Bowel Diseases (IBD) and they can have a significant impact on morbidity of IBD patients [1]. Although knowledge and focus on EIM is increasing, data on prevalence, characterization, and clinical course of pediatric MSK EIM are limited [2].

Objectives: Aim of the study was to assess the prevalence and to characterize IBD-related MSK EIMs and to assess articular-related outcomes in a nationwide cohort of pediatric IBD patients.

Methods: We collected data of pediatric IBD patients experiencing articular EIMs from the Italian national IBD registry. We gathered baseline and one-year follow-up data from concomitant IBD and arthritis diagnosis.

Results: 150 patients [(99 Crohn's Disease (CD), 51 Ulcerative Colitis (UC) and Unclassified IBD (IBDU)] with MSK EIMs out of 3061 (1301 CD and 1760 UC) patients were identified, with an overall prevalence of 4.9%. Peripheral arthritis was present in 84% of patients, mainly oligoarticular, and affecting large joints. Axial arthritis was present by 42% of the cohort. MSK EIMs were more frequent in CD than in UC (7.6% vs 2.9%, $p<0.01$). Patients with CD had more frequently concomitant MSK EIM diagnosis than those affected by UC, where EIMs were more frequently observed after IBD diagnosis. Peripheral arthritis was more frequently diagnosed in patients with active IBD than in those with quiescent disease (94.6% vs 67.3%, $p < 0.01$). At one-year follow-up, articular remission was achieved more frequently in patients with peripheral arthritis than in those with axial involvement (69.9% vs 50.6%, $p<0.01$). Clinically active IBD was independently associated with lower peripheral arthritis remission and no impact on axial arthritis activity has been detected. The presence of additional EIMs was associated with lower IBD clinical remission rates.

Conclusion: We characterized MSK manifestations in the largest pediatric IBD cohort. MSK EIMs were more frequently observed in CD than UC and/or IBDU. Peripheral arthritis, particularly oligoarthritis, was the most frequent articular manifestation. Active intestinal inflammation had a negative impact on peripheral arthritis remission but apparently had no effect on axial arthritis-related outcomes. The coexistence of other EIM are associated with worse articular as well of poorer intestinal outcomes.

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OUTCOME OF SPONDYLOARTHRITIS/ ENTHESITIS RELATED ARTHRITIS TREATED WITH SULFASALAZINE: EXPERIENCE FROM A SINGLE CENTER

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Introduction: The 2019 American College of Rheumatology (ACR)/ Arthritis Foundation Guidelines for the management of Juvenile Idiopathic arthritis (JIA) strongly recommend the use of anti-tumor necrosis factor (TNF) agents in those patients with active sacroiliitis [1]. However, the use of these drugs in low and middle income countries is limited because of logistical issues involving availability, high costs and a high burden of tuberculosis [2]. This study was planned to assess the effectiveness of conventional drugs, namely sulfasalazine, in the treatment of spondyloarthritis/Enthesitis related arthritis (SSA/ERA).

Objectives: To evaluate the effectiveness of sulfasalazine in the primary treatment of newly diagnosed SSA/ERA patients.

Methods: This prospective cohort study was conducted over a period of four years from 2019 to 2023 with due approval from the institutional ethics committee. 112 patients diagnosed with SSA/ERA according to the ILAR criteria [3] were enrolled into the study after taking consent from the parent/guardians. Patients with chronic renal, hepatic and cardiac disease were excluded. Demographic parameters, HLA-B27, JADAS-27 scores [4] and radiological assessment of sacroiliitis were recorded at enrolment. Patients with MRI-proven active sacroiliitis (n=100) were started on sulfasalazine at a dose of 30-50 mg/kg/day. Over a follow up period of six months, they were assessed for disease activity scores and radiological improvement. Those with persistent moderate/high disease activity (JADAS-27 score>=6) were shifted to biological therapy.

Results: Of the 112 patients enrolled, 75 (66.96%) were males. The median age of the study population was 9 years [IQR: 7.8-16.9 years]. 79 patients (70.5%) were HLA-B27 positive. 100 patients had evidence of sacroiliitis on MRI, rest were excluded from the analysis. Out of this 85 patients had bilateral involvement while the remaining 15% had unilateral involvement at diagnosis. Median JADAS-27 scores at baseline were 14.00 [IQR: 6.00-20.25]**.** At 6 months of treatment, 51 patients had moderate/high disease activity scores and were shifted to etanercept (51%). The remaining 49 patients showed good response to sulfasalazine and were continued on the same regimen.

Conclusion: While biologicals based therapy is currently the recommended standard of care for SSA/ERA patients, conventional therapy with sulfasalazine must not be written off as ineffective. A good trial of sulfasalazine for up to six months is warranted, especially in settings where availability or costs are limiting factors, along with those situations where biological therapy is otherwise contraindicated.

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PREDICTIVE ABILITY OF THE JADAS10- AND CJADAS10-BASED DISEASE ACTIVITY STATES FOR PSORIATIC ARTHRITIS AND ENTHESITIS-RELATED ARTHRITIS

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Introduction: The measurement of disease activity level is of central importance in the evaluation of the patient with juvenile idiopathic arthritis (JIA) and the need to have cutoffs for all the arthritis categories is increasingly evident. The cutoff for Juvenile Arthritis Disease Activity Score (JADAS) and its clinical version excluding the acute phase reactant (cJADAS) in RF-polyarthritis and oligoarthritis were validated and are being used in clinical trials and routine practice. We have recently demonstrated on the large multinational dataset of patients enrolled in the Epidemiology, Treatment and Outcome of Childhood Arthritis (EPOCA) study that 2021 ACR JADAS10 and cJADAS10 cutoffs to define disease activity states showed good discriminative validity in juvenile psoriatic arthritis (PsA) and enthesitis-related arthritis (ERA) (oligoarthritis cutoffs) and in RF positive polyarthritis (polyarthritis cutoffs).

Objectives: Aim of this study is to assess the predictive ability of the JADAS10 and cJADAS10 disease state cutoffs to separate the states of inactive disease (ID), minimal disease activity (MiDA), moderate disease activity (MoDA), and high disease activity (HDA) in children with PsA and ERA.

Methods: 86 JIA children aged 2 to 18 years included in the clinical trial to assess efficacy and safety of secukinumab in ERA and PsA were considered. This phase 3 trial is a randomised, double-blind, placebo-controlled, treatment-withdrawal, in which biologic-naïve patients with active disease were treated with open-label subcutaneous secukinumab for up to 8 weeks and then switched to a randomised, double-blind, placebo-controlled, withdrawal period until week 104. We compared the frequency of patients in ACR clinically inactive disease (CID) and normal functional ability (i.e. with Childhood Health Assessment Questionnaire (CHAQ) = 0) at week 104 among those who achieved or did not achieve the states of ID and MiDA at week 12. We expected that patients who achieved ID or MiDA at week 12 had a higher probability of achieving ACR CID or normal physical function at week 104.

Results: Of the 74 patients with ERA and PsA at week 104, 28 (37.8%) met the definition of ACR CID and 42 (56.8%) had CHAQ = 0. Of the 28 patients in ACR CID at week 104, more than 60% of patients were in JADAS10 or cJADAS10 ID at week 12; whereas of the of the 46 patients who did not achieve ACR CID less than 22% were in JADAS10 or cJADAS10 ID at week 12 ($p < 0.001$ for both comparisons). Of the 42 patients with normal physical function at week 104, more than 47% of patients were in JADAS10 or cJADAS10 ID at week 12; whereas of the 32 patients who lacked normal physical function fewer than 19% were in JADAS 10 or cJADAS10 ID at week 12 ($p < 0.01$ for both comparisons). Among patients in ACR CID and with CHAQ = 0 at week 104, the 78,6% were in MiDA at week 12 according to both JADAS10 and cJADAS10 cutoffs; whereas of the patients who didn't achieve ACR CID and who had CHAQ > 0 less than 59% were in JADAS10 and cJADAS10 MiDA at week 12.

Conclusion: Both the JADAS10 and cJADAS10 cutoffs to define disease activity states validated for oligoarthritis showed also a good predictive ability in PsA and ERA. These results confirm our prior indication that the available cutoffs might be used for these categories of JIA.

IS IT WORTH INCLUDING THE POSTERIOR SCANNING APPROACH IN THE ULTRASOUND ASSESSMENT OF THE TIBIOTALAR JOINT IN JUVENILE IDIOPATHIC ARTHRITIS?

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Introduction: The ankle is a complex anatomical structure owing to the multiple joint recesses and surrounding tendons. The tibiotalar joint (TTJ) is one of the main articular compartments of the ankle region. Ultrasound (US) is a valuable tool to confirm the presence of synovitis in the TTJ in children with juvenile idiopathic arthritis (JIA). It has been suggested to evaluate the TTJ on US using both an anterior and a posterior scanning approach.

Objectives: The aims of the study were: 1) to assess the frequency of synovitis on US in the anterior and posterior recesses of the TTJ; 2) to determine the most informative scanning approach to assess the TTJ on US in patients with JIA.

Methods: Fifty ankles of 38 patients with JIA with clinical arthritis were included in the study. The TTJs were scanned by a physician (SL) with experience in the US assessment of children with JIA, using an anterior and a posterior scanning approach. For both the joint recesses of the TTJ the detection of joint effusion (JE), synovial hypertrophy (SH) and power Doppler (PD) signal inside the area of SH were recorded on US evaluation. For the purpose of scoring, JE and SH were combined into a grey-scale (GS) US-score, which was representative of the joint cavity widening. The GS-US score and PD-US score were graded on a 4-point semiquantitative scale. An overall US severity score was calculated as the sum of the GS and PD scores for the anterior and the posterior recess of the TTJ.

Results: US-detected synovitis in 31/50 (62.0%) TTJs. All 31 ankles with US-detected TTJ involvement showed US findings on the anterior scanning approach. Only eight (25.8%) of them also had synovitis on the posterior scanning approach to the TTJ. Overall, JE and PD signals were recorded more frequently in the anterior recess of the TTJ than in the posterior (96.8% and 35.5% *versus* 77.8% and 44.4%, respectively). The frequency of SH as detected on US was equal for the anterior and the posterior side of the joint (100%). In the 31 ankles with US-determined TTJ involvement, the overall US

severity score resulted as higher in the anterior aspect of the joint (median 3.0, IQR 2.0-4.0) compared to the posterior side (median 0.0, IQR 0.0-2.0).

Conclusion: Inflammation is frequently detected on US in the TTJ of patients with JIA and clinical ankle arthritis. The anterior scanning approach to the joint seems to be more appropriate for US evaluation of the TTJ. In this perspective, the possibility to scan only the more representative aspect of the TTJ may help to shorten the length of the US session, especially in the younger and poorly cooperative patients.

SPECTRUM OF IMAGING ASSESSEMENT IN PATIENTS WITH FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

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Introduction: Fibrodysplasia ossificans progressiva (FOP) is an orphan genetic condition characterized by progressive replacement of muscle and connective tissue with bone due to mutation in the ACVR1 gene. Uncontrolled heterotopic ossification (HO) leads to severe disability in patients. It is crucial to use different informative monitoring techniques for control of HO progression.

Objectives: To evaluate available imaging methods and their importance in FOP patients (pts)

Methods: From 1998 to 2024 we identified 54 pts with FOP. For routine examination and evaluation of different «flare-up» stages we used wide spectrum of imaging including X-Ray, MRI, CT and low-dose whole-body CT (WBCT).

Results: In our cohort X-Ray scan was performed to identify the structure of malformated thumbs and great toes. In all cases we observed clinodactyly with deformity of the 1st metatarsal bones with gradual ankylosis of the 1st interphalangeal joint during follow-up. In one-third pts we verified shortening of metacarpal bones. Also X-Ray scan revealed abnormalities of the cervical spine – ankylosis of facet joints and spinous processes. WBCT with 3D modelling allowed us to measure volume of HO and visualize non-visible ossification and peripheral osteochondromas in all pts. We performed WBCT in 25 pts and in 7 pts we did it twice in 1-year period. We compared HO volume: in 3 cases we identified low progression of HO, in 3 pts – stable status of HO, in 1 case we recognized decreasing of HO volume due to resolving of small ossificates in thoracic area. MRI was effective in visualizing diffuse soft tissue edema during the active phase of a "flare-up" especially in deep localizations such as piriform muscle. In 1 pt we detected subtotal stenosis of the spinal canal without any neurologic symptoms. Also we used MRI for identification of rheumatic signs such as synovitis in large joints and active sacroiliitis which observed in FOP pts very often. We could not perform MRI in some pts due to their inability and installed metallic constructions.

Conclusion: All of imaging methods are important for management of FOP patients. X-ray and CT are preferred methods when the enchondral pathway of ossification is complete and visualized. It seems that WBCT plays huge role for FOP patients and may be extrapolated in rheumatological practice while MRI as classical rheumatological imaging may be important method for FOP patients to detect inflammatory signs of FOP nodules, synovitis, sacroiliitis etc.

EVALUATION OF CHILDREN WITH SACROILIITIS WITH LOW-DOSE COMPUTED TOMOGRAPHY

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Introduction: Recent findings from adult studies suggest that low-dose computed tomography (ldCT) may offer a viable alternative for diagnosing sacroiliitis. ldCT examinations, administered at radiation rates comparable to those used in radiography, have been proven to be superior to radiography in detecting structural lesions.

Objectives: This study investigated the utility of low-dose computed tomography (ldCT) compared with magnetic resonance imaging (MRI) in diagnosing sacroiliitis in enthesitis-related arthritis (ERA) patients.

Methods: For each patient, we assessed the density changes on ldCT at corresponding locations, employing the signal intensity observed on MRI across each joint surface as a reference. The density of regions exhibiting bone marrow edema (heightened signal intensity) on MRI was lower on CT, whereas the density of regions devoid of signal (no bone marrow edema) on MRI was higher on CT.

Results: Thirty patients (11 girls/19 boys) diagnosed with ERA were enrolled. The median (IQR) age was 14.44 (6.08) years and the median (IQR) follow-up time was 1.47 (2.05) years. During radiologic evaluation, eighteen patients (60%) exhibited clinical sacroiliitis, and 10 (33.3%) experienced morning stiffness. The median JSpADA was 2.5 (1.3). MRI revealed bilateral bone marrow edema in 22 (73.3%) patients. We assessed the density changes on ldCT at the corresponding locations of the areas of bone marrow edema on MRI. On ldCT evaluation of the right iliac crest, lower density was found on ldCT in regions exhibiting heightened signal intensity in MRI for 20 (66.6%) patients. On the right sacral side, lower density was observed on ldCT in regions exhibiting heightened signal intensity in MRI for 22 (73.3%) patients. On the left iliac crest, lower density was observed in 18 (60%) patients. On the left sacral side, lower density was observed on ldCT in regions exhibiting heightened signal intensity in MRI for 22 (73.3%) patients. A correlation was found between the density measurement in ldCT and the signal intensity in MRI. Erosion was detected in 23 (76.6%) patients on ldCT while erosion was detected in only 11 (36.7%) patients on MRI.

Conclusion: This study suggests that ldCT is superior to MRI for early structural change detection. Pixel-based density evaluation in ldCT aligns with MRI findings for bone marrow edema.

e-Poster Tour 12: JIA-II

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THE DISCREPANCY BETWEEN PHYSICIAN GLOBAL ASSESSMENT AND THE PARENT/PATIENT WELL-BEING EVALUATION MAY HAVE TWO SOULS

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Introduction: Parent/child-reported outcomes (PCROs) are crucial for assessing the perception of rheumatic disease course and therapeutic effectiveness, particularly in Juvenile Idiopathic Arthritis (JIA). The parent/patient global evaluation or well-being visual analogue scale (WB-VAS) is widely used in JIA patients, yet discrepancies between physician and parent/patient evaluations have been described.

Objectives: The study aimed to evaluate which variables might determine the differences between physician assessment of inactive disease and the parent/patient perception of well-being.

Methods: We analyzed data from a large multinational sample of JIA patients from the Epidemiology Treatment and Outcome of Childhood Arthritis (EPOCA) study. Demographic factors, socioeconomic status, education level, JIA subtype, and various patient-reported outcomes (PROs) were examined. We only included patients with a Physician Global Assessment (PGA) score of 0 and we divided them in two groups, according to their answer to the WB-VAS score: group 1 reported WB-VAS ≤ 1 and group 2 reported WB-VAS >1. We then checked with factor analysis if items that were different between the two groups could be reduced into a smaller set of factors.

Results: Results from 3537 patients revealed two groups based on WB-VAS score: 2862 with WB-VAS ≤ 1 and 675 with WB-VAS > 1. Socioeconomic status and education did not significantly differ between the groups: lower socioeconomic status was noted in 17.6% and 18.1% of families, intermediate in 70.5% and 71%, and higher in 11.9% and 10.8%, respectively; education levels were similarly distributed. No significant difference was observed in JIA subtype distribution. Patients with higher WB-VAS scores were slightly older at disease onset (6.4 and 5.6 years); they reported more pain (VAS pain mean 2.4 vs 0.3 in group 1), morning stiffness (42.4% vs 8% of patients in group 1), joint inflammation (1.4 vs 0.2 number of proxy-assessed active joints in group 1), medication side effects (42.9% vs 21% of patients in group 1), and had greater functional impairment (3 vs 0.5 mean score in the JIA Assessment of Functionality Score) and lower health-related quality of life (6.4 vs1.6 mean score in the JIA Quality of Life Score). Exploratory factor analysis identified two key factors: "Joint symptoms" (factor 1) and "Disease burden" (factor 2). The variable with the strongest association to the underlying latent variable factor 1, is VAS pain. Factor 1 also correlated with joint inflammation signs, morning stiffness, and disease activity, while factor 2 correlated with functional ability, Health-Related Quality of Life (HRQoL), medication side effects, and school problems.

Conclusion: In conclusion, the study highlighted factors contributing to discrepancies between physician assessments and parent/patient perceptions of well-being in JIA. Our data suggests that the

disagreement can be due either to a different perception of the disease status, or to the fact that WB-VAS measures a broader domain than disease activity

FROM PAEDIATRIC TO ADULT CARE: VALIDATING JADAS FOR ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Many children with Juvenile Idiopathic Arthritis (JIA) continue to experience active disease into adulthood, yet no validated disease activity measure exists for adult use. While the Juvenile Arthritis Disease Activity Score (JADAS) is established for children, its relevance and validation for adults remain unexplored.

Objectives: Validate JADAS for JIA patients older than 18 years, focusing on criterion and construct validity.

Methods: This analysis used data from EPOCA (cross-sectional cohort) and two prospective cohorts: Rheumatic Diseases Portuguese Registry (Reuma.pt), and Spanish national registry for adults with JIA (JUVENSER). Included JIA patients were >18 years old, met ILAR criteria, and had data available for JADAS and other disease activity scores (DAS28, SDAI, CDAI). Demographic details, disease characteristics, and clinical assessments were collected. Patient's most recent visits, ranging from January-2001 to February-2024 (99% from 2010 onwards) were used. Construct validity was evaluated through Spearman's rank correlation between JADAS (10/27/71/cJADAS10), joint counts, physician, and patient global assessment with the adult constructs (DAS28/SDAI/CDAI). Criterion validity was assessed using Cohen's weighted kappa to assess accuracy of JADAS versus adult constructs, and sensitivity and specificity of detecting clinically inactive disease (CID).

Results: Analysis included 1315 adult JIA patients, from Reuma.pt (N=545), JUVENSER (N=392), and EPOCA (N=378) across 39 nationalities. Median age at disease onset was 9 years for Reuma.pt (IQR 4-13) and JUVENSER (IQR 3.7-13) patients, and 11 years (IQR 6.7-14) for EPOCA patients. The median age at the last study visit and disease duration varied: Reuma.pt patients were older (25 versus 19-21 years), with longer disease duration (18 versus 8-13 years). EPOCA patients had higher JADAS in the registered visits versus the other cohorts; median JADAS27 3.5 versus 2 (Reuma.pt) and 0 (JUVENSER). For construct validity, the Spearman's correlations between JADAS10 and cJADAS10 with SDAI (JADAS10:0.95; cJADAS10: 0.96) and CDAI (JADAS10: 0.96; cJADAS10:0.99) were high. Whilst correlation between JADAS10 and cJADAS10 with DAS28 was lower: 0.69 and 0.64 respectively. Similar correlations were seen for JADAS27 and JADAS71, and also when limited to only those patients with RF-negative polyarthritis, or persistent or extended oligoarthritis. All JADAS versions showed higher correlation with active joint count and patient and physician global assessment than DAS28.
For criterion validity, the Cohen's weighted kappa for JADAS10 with the adult indices were 0.51 (95% CI 0.48-0.54) for DAS28, 0.72 (0.70-0.74) for SDAI, and 0.72 (0.70-0.74) for CDAI. Results were similar when limited to patients with RF-negative polyarthritis, or persistent or extended oligoarthritis.

However, performance was poorer across the other JADAS versions. For those with CID, sensitivity ranged from 0.64-0.87, and specificity ranged from 0.96-0.97.

Conclusion: Preliminary findings suggest that JADAS is a valid tool for measuring disease activity in adults with JIA. Its strong performance in criterion and construct validity supports its potential for broader use in clinical practice, helping to bridge the gap in transition care from paediatric to adult rheumatology. Further studies are needed to explore other aspects of validity.

SYNOVIAL TISSUE BIOPSIES FOR THE PURPOSE OF RESEARCH IN THE UK TISSUE RESEARCH IN CHILDHOOD ARTHRITIS CONSORTIUM

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Introduction: Analysis of synovial tissue in adult-onset inflammatory arthritis has resulted in a shift-change in our understanding of the disease pathophysiology; biopsy-driven, pathology-led treatment stratification trials are ongoing. Despite this success in adults, progress of tissue research in children has been hindered by lack of access to tissue.

Objectives: To develop a national, multi-centre synovial tissue biopsy research program to build capacity to perform tissue-based research studies in children and young people with Juvenile Idiopathic Arthritis (JIA).

Methods: Minimally invasive ultrasound-guided synovial tissue biopsies were obtained from children during joint injection procedures. Records of adverse events were made along with patient demographic and disease-related data. Pre and post-procedure questionnaires were performed to explore tolerability of the procedure. Joint tissue was fixed and paraffin embedded for histological analysis.

Results: We have established a UK wide observational cohort study (MAP-JAG) which has recruited seventy-six children diagnosed with JIA. In this tolerability analysis, data from fifty-nine participants were analysed. The demographics of recruited patients aligned with previous observations of JIA, with a female preponderance (67.1%) and a majority white ethnic background (59.2%). Within those that underwent biopsy procedures, biopsies were well tolerated with no serious adverse events, and no additional hospital stays or re-presentations. Eight children went on to have repeat biopsy procedures later in their disease course. Seventy-one percent of families who completed post-procedure quesionnaires within thirty days stated that they would be "very likely" to allow their children to have a repeat procedure, whereas only three percent stated they would be "very unlikely" to do so. Histology showed synovial lining layer confirming the presence of synovium and analysis revealved key inflammatory features of the sub-lining synovium.

Conclusion: Synovial tissue sampling can be integrated into routine care during joint injection procedures. Minimally invasive, ultrasound-guided synovial biopsies in children are safe, well tolerated and acceptable to families.

JUVENILE IDIOPATHIC ARTHRITIS: WHAT PROMISE DO THE PRINTO CLASSIFICATION CRITERIA HOLD?

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Introduction: The currently generally accepted classification criteria for Juvenile Idiopathic Arthritis (JIA) are the ILAR criteria, and a new draft classification criteria set was proposed by the PRINTO group in 2018.

Objectives: This study aims to evaluate the efficacy of preliminary PRINTO criteria, particularly in categorizing patients who were previously under undifferentiated JIA group according to ILAR classification criteria, thereby assessing the improvement in diagnostic inclusivity and potentially enhancing patient management and treatment strategies.

Methods: In a study conducted at the Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa Cerrahpasa Medical School, in-person interviews were conducted with individuals diagnosed with JIA and attending the outpatient clinics. The study included patients who met the ILAR and/or PRINTO classification criteria, provided informed consent, and had a minimum six-month follow-up period. An experienced pediatric rheumatologist (MY) who was unaware of the patients' diagnoses used the ILAR and PRINTO systems to assign each patient to a specific JIA subtype based on their clinical, laboratory, and imaging data.

Results: The study included 364 patients (female: 200, male: 164). The mean age of the patients at the time of the study was 167.9 ± 59.5 months. In the patient group, the mean age at onset of symptoms, mean age at diagnosis and mean follow-up period were 78.7 ± 54.7 months, 88.3 ± 57.4 months and 71 ± 53.4 months, respectively. When ILAR diagnostic criteria were applied to the patient group, 155 (42.6%) patients could be classified as oligoarticular JIA, 78 (21.4%) as enthesitis-related arthritis, 33 (9.1%) as RF negative polyarticular JIA, 20 (5.5%) as systemic JIA, 15 (4.1%) as psoriatic arthritis, and 7 (1.9%) as RF positive polyarticular JIA. The number of patients in the undifferentiated JIA group was 56 (15.4%). According to the classification criteria proposed by PRINTO, 113 (31%) patients were classified as early-onset ANA-positive JIA, 112 (30.8%) as other JIA, 89 (24.5%) as enthesitis/spondylitis-related arthritis, 28 (7.7%) as systemic JIA, 16 (4.4%) as RF-positive JIA and 6 (1.6%) as unclassified JIA. Upon evaluating the 56 patients within the undifferentiated JIA group according to the ILAR classification using the PRINTO classification, it was observed that 14 (25%) were classified within the enthesitis/spondylitis-related arthritis group, 13 (23.2%) within the other JIA group, 11 (19.6%) within the early-onset ANA positive group, 9 (16.1%) within the RF positive JIA group, 8 (14.3%) within the systemic JIA group, and 1 (1.8%) within the unclassified JIA group.

Conclusion: This study suggests that the use of PRINTO criteria may be effective especially in the classification of patients who remain in the undifferentiated group in the ILAR classification criteria. Prospective studies are needed to make definitive conclusions.

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NEW EARLY INDICATORS OF POLYARTICULAR COURSE IN NEW-ONSET OLIGOARTHRITIS PATIENTS

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Introduction: Oligoarthritis represents the most common category of Juvenile Idiopathic Arthritis in Western countries. Disease course and prognosis within the first two years after diagnosis exhibit considerable variability. The majority of patients shows an oligoarticular course, more benign and with a higher likelihood of achieving remission. However, a substantial proportion of patients (30-40%) develops a polyarticular course (pcJIA), more severe and requiring more aggressive therapeutic interventions. New biomarkers are demanded for early discrimination of patients at risk of developing pcJIA.

Objectives: The aim of this study was to identify new early biomarkers of pcJIA by characterizing inflammatory cells both in plasma and synovial fluid of patients with Oligoarthritis at disease onset combined with the analysis of extracellular vesicles (EVs) released by these cells.

Methods: We employed a strategy that combines classical methodologies for investigating inflammatory cells in liquid biopsies with system biology-driven omics techniques (miRNomics/proteomics) for analyzing extracellular vesicles (EVs) released by these cells. Ninety-seven treatment-naïve Oligoarthritis patients were recruited at disease onset and followed up for 24 months after diagnosis. Expression profiling of EV-miRNA (EV-miR) and EV-protein (EV-Prot) was carried out in plasma and synovial fluid samples collected at disease onset. Plasma samples from 25 age-matched healthy children were utilized as controls. Phenotypic characterization of monocytes/macrophages and T cell subsets was performed in peripheral blood samples from 26 patients and compared across different clinical courses.

Results: By omics approaches, we identified a signature of 7 EV-miRNAs and 112 proteins expressed both systemically and locally, able to discriminate new-onset patients from controls with a high potential diagnostic value. Employing supervised machine learning techniques and WGCNA analysis, we demonstrated the ability of EV-miR 29a, EV-miR 223, and 16 protein clusters in stratifying patients undergoing different disease course. Cytofluorimetric analysis revealed different proportions of activated CD4/CD8, effector memory CD8, T regulatory cells, and M1/M2 monocyte/macrophages expressing the inflammatory hypoxic receptor TREM1 between outcome groups both in synovial fluid and peripheral blood samples.

Conclusion: Our findings provide novel early potential indicators of pcJIA in new-onset Oligoarthritis patients, encompassing EV-miRNAs, EV-proteins, and distinct inflammatory cell subsets.

EARLY SYSTEMIC TREATMENT MAY REDUCE THE FREQUENCY FOR TEMPOROMANDIBULAR JOINT INVOLVEMENT IN CHILDREN WITH JIA

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Introduction: In Juvenile Idiopathic Arthritis (JIA), temporomandibular joint (TMJ) involvement still represents a major source of long-term damage and reduced life quality health. No specific risk factors have been identified for this disease manifestation and it is not clear if an early aggressive intervention may prevent the TMJ disease in children with JIA.

Objectives: To study the frequency of TMJ involvement among patients affected with JIA, together with the investigation of clinical characteristics associated and the impact of early JIA treatment on TMJ involvement.

Methods: We included in the study the clinical charts of consecutive patients with oligoarthritis and RF negative polyarthritis, visited in our center in the first six months from disease onset between January 2018 and February 2020 with at least 4 years of follow-up. Only patients who received the first treatment for arthritis at the study Unit were included. TMJ involvement was assessed by magnetic resonance imaging (MRI). We compared baseline disease characteristics between children with or without TMJ involvement and the therapeutic intervention done before TMJ involvement.

Results: A total of 67 patients (71.6 % females, median age at JIA onset 3.5 years) with a median disease duration of 4.3 years were included in the study. The JIA category distribution was: 64.2% oligoarticular arthritis, 35.8% polyarticular arthritis. In the first six months of disease course, 91.0% of children received intraarticular corticosteroid injections (IACIs), 58.2% methotrexate, 13.4% biologic DMARDs. TMJ involvement was radiologically identified in 31/67 patients (46.3%). No significant difference was observed in the frequency of TMJ involvement based on gender, age at onset, disease duration at first intervention, JIA category, number of active joints, ANA positivity, baseline CRP and ESR. Twenty children received only IACIs until the last follow up visit or until TMJ disease was diagnosed. Of these, 16 (80%) had TMJ involvement. Of the remaining 47 patients who were treated with conventional or biological DMARDs until the last follow up visit or until TMJ disease was diagnosed, 15 (32%) had TMJ involvement (Chi-squared test $P < 0.001$).

Conclusion: TMJ involvement was common in in the first 5 years of disease course in this cohort of JIA children. No clinical risk factor for TMJ was observed at disease onset. Early treatment with systemic medication seems to protect JIA patients from these potentially severe complications.

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PROTEOMIC ANALYSIS TO IDENTIFY NOVEL BIOMARKERS IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Juvenile-onset systemic lupus erythematosus (jSLE) is an autoimmune disease characterized by its heterogeneity and unpredictable course, often marked by substantial damage and disability. Compared to individuals who develop the disease in adulthood, jSLE patients typically experience increased disease activity and damage, requiring more aggressive treatment approaches. While numerous autoantibodies are linked to disease expression, there is a lack of age-specific validation for these potential diagnostic biomarkers.

Objectives: This study aimed to identify novel biomarkers that may be used in disease activity in jSLE.

Methods: Proximity extension immunoassay (PEA, Olink) was used to assess the serum levels of 92 inflammation proteins in patients with jSLE (n = 19) and age-matched healthy controls (HCs; n = 9). SLE Disease Activity Index (SLEDAI) was assessed in SLE patients to characterize the disease status of all patients. To evaluate the contribution of molecular profiles to the course of disease, we also assessed the association of serum vitamin D levels with differentially expressed proteins.

Results: Several circulating proteins related to inflammation were altered in the serum of jSLE patients in relation to HCs. This analysis differentiated two clusters presenting low-inflammatory and high-inflammatory proteomic profiles. Eight upregulated, high-inflammatory proteins were identified in jSLE patients. CXCL6 și CST5 were expressed at significantly higher levels in jSLE group compared to HCs, whereas TNF, HGF, FGF-5, CD244, MMP-10, TNFRSF9 were upregulated, but did not reach statistical significance at $p<0.05$. Described abnormalities included changes in the expression of IFN-inducible chemokines, alterations in B cell receptor signaling, and shifts in the expression of cytokines associated with leukocyte, neutrophil, and macrophage trafficking. Patients with jSLE exhibited significantly elevated levels of disease activity (SLEDAI score), alongside with renal and hematologic manifestations both at diagnosis and during flares. However, no significant correlation was found with a specific protein profile. Pearson's correlation analysis between inflammatory proteins in the juvenile SLE cohort and vitamin D levels revealed a significant positive correlation between CX3CL1 and serum vitamin D levels.

Conclusion: Through this highly sensitive proteomic analysis, we discovered several new candidate proteins that reveal distinctive molecular patterns in jSLE patients with increased disease activity. This observed proteomic signature underscores the necessity for tailored, age-specific treatment approaches in SLE.

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SYSTEMIC INFLAMMATORY INDEX AND CLINICAL FEATURES IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS: A 10-YEAR RETROSPECTIVE STUDY

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Introduction: Pediatric systemic inflammatory diseases, such as systemic lupus erythematosus (SLE), present significant diagnostic and therapeutic challenges. Recent research has highlighted the potential of the Systemic Inflammatory Index (SII) as a valuable marker for assessing inflammation and disease activity. Studies have shown promise in reflecting the inflammatory burden in various conditions, including autoimmune diseases. However, its application and significance in pediatric SLE, especially in relation to specific organ involvement, remain underexplored.

Objectives: To evaluate the clinical features, organ involvement, laboratory and inflammatory markers, biopsy results, and treatment modalities in pediatric patients with SLE, providing a detailed correlation of inflammatory markers with clinical outcomes. This study is the first to compare the SII among different organ involvements in pediatric SLE patients.

Methods: This retrospective study was conducted at the Pediatric Rheumatology Department from 2013 to 2023. A total of 104 pediatric patients diagnosed with SLE were included, without discrimination based on gender. Data collected comprised demographic information, clinical features, laboratory markers, and inflammatory markers. Patients were divided into groups based on organ involvement, specifically skin, renal, and CNS involvement, and further categorized into renal involvement with joint involvement, renal involvement with skin, and renal involvement with CNS to compare inflammatory markers (NLR, PLR, and SII) across these groups.

Results: This study included 85 (81.7%) female patients and 19 (18.3%) male patients, with a mean age of 17.2 ± 4.7 years at diagnosis. Joint involvement was reported in 78 (75.0%) patients. Organ involvement included skin involvement in 60 (57.7%) patients, renal involvement in 44 (42.3%) patients, and CNS involvement in 9 (8.6%) patients. Inflammatory markers indicated a mean NLR of 2.70, a PLR of 181.25, and an SII of 806.00. Statistical comparisons of these markers across organ involvements indicated no significant differences in PLR values ($p > 0.14$). NLR analyses showed some variance but were generally non-significant ($p > 0.05$). Joint involvement had a mean NLR of 2.14 (CI 1.78 to 2.49) compared to 3.66 (CI 1.85 to 5.47) in those without, with a statistically significant difference ($p = 0.0370$). For SII, renal involvement had a mean of 1092.81 (CI 551.17 to 1634.45) compared to 601.13 (CI 458.51 to 743.76) in those without, with a statistically significant difference ($p = 0.0442$). Among the further categorized renal groups, none showed statistically significant differences in SII ($p > 0.05$).

Conclusion: This study underscores the significant inflammatory burden in pediatric systemic inflammatory diseases, evidenced by elevated NLR, PLR, and SII levels. The statistically significant higher SII in patients with renal involvement and lower NLR in patients with joint involvement highlight the potential of these markers in reflecting specific organ involvement. The detailed correlation between clinical features, biopsy results, and inflammatory markers provides valuable insights for diagnosis and management.

CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS LIVING IN EARTQUAKE AREA ARE AT RISK FOR HIGHER DISEASE ACTIVITY AND DEVELOPMENT OF MAJOR ORGAN INVOLVEMENT

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Introduction: A devastating earthquake with a magnitude of 7.8 on the Richter scale struck southeast region of Turkiye on February 6, 2023. Widespread damage occurred in 11 cities, covering an area of about 350,000 km2, approximately the size of a European country. Approximately 15% of the Turkish population was affected by this earthquake, making it the deadliest disaster in Turkiye in the last millennium. There are only two studies in the literature that evaluate the role of emotional trauma, stress, sun exposure and activity in triggering lupus flares following the earthquake. Additionally, these studies have been conducted on a very limited number of systemic lupus erythematosus (SLE) patients.

Objectives: We aimed to compare the frequency of clinical and serologic activity flares in childhood onset SLE (cSLE) patients living in the earthquake region and cSLE patients living away from the epicenter at two time points (T1: within 45 days after the earthquake; T2: from 45th day to the last visit) following the earthquake) in Turkiye.

Methods: cSLE patients who have been followed up in 12 pediatric rheumatology clinics and were living in the earthquake region (Gaziantep, Hatay, Adıyaman, Şanlıurfa, Adana, Osmaniye, Diyarbakır, Malatya, Elazığ) were included in our study. cSLE patients living outside the epicenter have been enrolled as control patients. The demographic, clinical, laboratory and treatment characteristics of cSLE patients before and after the earthquake were retrospectively recorded from patient files. Besides, all the patients living in the earthquake zone were interviewed regarding accommodation status and duration (prefabricated container, tent, house), post-earthquake medication supply, access to hospitals, hospitalizations, and changes in treatment.

Results: A total of 142 cSLE patients were included in this multicenter study from 12 pediatric rheumatology clinics: Sixty-one patients living in the earthquake zone (Group 1) and 81 patients living away from the earthquake's epicenter (Group 2). Within 45 days after the earthquake, higher rates of fever($p=0.012$), constitutional manifestations ($p=0.001$), malar rash ($p<0.001$) were observed in cSLE patients living in the earthquake region compared to those living away from epicenter.Dose escalation of corticosteroid ($p<0.001$) and change in immunosuppressive medication ($p=0.004$) were more frequently required in Group 1 compared to Group 2. From the 45th day of earthquake until the last visit, proteinuria ($p<0.001$), kidney involvement ($p<0.001$), class III/IV lupus nephritis ($p<0.001$), and hospitalization ($p<0.001$) were more frequently developed in Group 1 than in Group 2.

Conclusion: During the early period after the earthquake, children with SLE who lived in the affected area were at a higher risk of developing fever, constitutional manifestations, malar rash, and

hypocomplementemia. These patients also required more frequent increases in corticosteroid doses and changes in immunosuppressive therapies. Longer follow-ups of these patients revealed that major organ involvement and hospitalization were more frequently pronounced in the late post-earthquake period.However, more extensive studies are needed to explore the underlying reasons responsible for this unfavourable course of cSLE after the earthquake.

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EVALUATION OF HYDROXYCHLOROQUINE CARDIOTOXICITY IN PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Hydroxychloroquine, the mainstay of treatment, is recommended for all patients with systemic lupus erythematosus (SLE). Studies conducted in adults have suggested that hydroxychloroquine may have cardiotoxic effects, such as cardiac conduction disorders and myocardial hypertrophy.

Objectives: In this study, we aimed to evaluate the effects of hydroxychloroquine on cardiac functions and left ventricular mass in patients with childhood-onset SLE (cSLE).

Methods: Fifty cSLE patients treated with hydroxychloroquine were included in the study. These patients were evaluated by echocardiography (ECHO) during their routine outpatient controls. All patients had negative disease activity markers and were clinically in remission at the ECHO visit.

Results: The median (min-max) age at diagnosis and the current median age of the patients were 11.5 (3-16) and 17.5 (12-21) years, respectively (F/M=3.2). As comorbidities; six patients (12%) had hypertension, five (10%) had obesity, three (6%) had antiphospholipid antibody syndrome (AFAS), two (4%) had autoimmune hepatitis, and one (2%) had immunodeficiency. All patients were on hydroxychloroquine, %56 (n=28) and on low-dose corticosteroids (5-10 mg/day), and 52% (n=26) were on other disease modifying anti-rheumatic drugs (DMARDs). The median hydroxychloroquine exposure time of the patients was 7.1 (5.2-9.5) years, and the median cumulative hydroxychloroquine dose was 784.8 (509.5-3437.6) grams. No correlation was detected between the parameters of left ventricular ejection fraction, left ventricular mass index, geometry and the cumulative hydroxychloroquine dose (p=0.245, p=0.094, and p=0.146, respectively). In addition, no significant correlation was found between the cumulative dose of hydroxychloroquine and diastolic cardiac parameters (all p>0.005). When we compared the patients who received less than the median cumulative dose of hydroxychloroquine (low dose group) and patients who received more (high dose group), there were again no significant differences according to the ECHO parameters (all p>0.005).

Conclusion: Our findings revealed that chronic hydroxychloroquine use in cSLE patients did not adversely increase left ventricular mass or impair left ventricular systolic and diastolic functions. However, it is beneficial for patients using chronic hydroxychloroquine to be evaluated with ECHO at regular intervals to monitor cardiotoxicity.

ASSESSMENT AND VALIDATION OF PAEDIATRIC TREAT-TO-TARGET ENDPOINTS IN CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: The Paediatric Rheumatology European Society (PReS) have endorsed consensus derived Childhood Lupus (cSLE) treat-to-target (T2T) goals; including childhood Lupus Low Disease Activity State (cLLDAS) (1), clinical remission on (cCR) and off-corticosteroids (cCR-0) (2).

Objectives: To employ a data-driven approach to evaluate how effective the agreed-upon consensus criteria are in protecting against severe flares and new damage accrual in cSLE.

Methods: Data from UK JSLE Cohort Study patients, <18 years at diagnosis, with ≥4 ACR criteria for SLE were utilised. Individual criteria of the existing cSLE targets were either removed or varied (9, 6 and 5 variations of the cLLDAS, cCR and cCR-0 targets were assessed, respectively). The impact of these variations was explored by using Prentice-Williams-Peterson (PWP) gap-time models, assessing the hazard ratios (HRs) of severe flare and new damage in those attaining original vs varied target definitions. For a given target, where variations of >1 criterion significantly improved outcomes, we integrated these together into a modified target. Student's t-test for dependent samples compared the HRs between original consensus-derived cSLE targets and corresponding modified targets on the impact of severe flare and new damage.

Results: All consensus-derived cSLE targets significantly reduced the hazards of severe flare (cLLDAS: HR 0.18 [CI 0.14, 0.23], cCR: HR 0.18 [CI 0.13, 0.23], cCR-0: HR 0.17 [CI 0.13, 0.23]) and new damage (cLLDAS: HR 0.22 [CI 0.11, 0.44], cCR: HR 0.25 [CI 0.13, 0.49], cCR-0: HR 0.30 [CI 0.15, 0.60]) (all p<0.001). Of the 9 variations of cLLDAS, transformation of SLEDAI-2K cut-off to ≤3 (HR 0.13 [CI 0.09, 0.19]) and transformation of Physician Global Assessment (PGA) cut-off to ≤0.5 (HR 0.15 [CI 0.12, 0.21]) led to significant reduction in the hazards of severe flare compared to the original definition (all p<0.001). A modified version of cLLDAS was investigated, integrating both variations to cLLDAS criteria. This demonstrated a significant decrease in hazards of severe flare compared to the original cLLDAS target (HR 0.12 [CI 0.08, 0.17], p<0.001), but had no impact on the hazards of new damage. Regarding the cCR and cCR-0 definitions, no variations to the initial consensus-derived target criteria could improve protection from severe flare or new damage (all p>0.05).

Conclusion: Refinement of the cLLDAS criteria, specifically transforming SLEDAI-2K score cut-off to ≤3 and the PGA score cut-off to ≤0.5 could potentially enhance protection against severe flare. However, it does not appear to impact on protection from new damage. Further research is needed to evaluate how effective the agreed-upon consensus criteria are in protecting against severe flares and new damage accrual in international patient cohorts.

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COVID19-RELATED SYSTEMIC LUPUS ERYTHEMATOSUS IN CHILDREN: A SINGLE CENTER STUDY

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Introduction: It is well known that SARS-CoV-2 virus is a powerful inducer of autoimmune phenomena both during the disease and later on. Observations coming from our own clinical practice seem to highlight that Systemic Lupus Erythematosus that began during the SARS-CoV-2 pandemic (CR-SLE) is somehow different from those with onset in the pre-Covid period (pC-SLE).

Objectives: To compare the clinical characteristics of a cohort of patients with CR-SLE with a cohort of pC-SLE.

Methods: We performed a retrospective analysis of a prospective collection of data to compared demographic, clinical and laboratory features of pediatric patients with CR-SLE and pC-SLE at disease onset. Covid-19 correlation was defined as recent infection (< 8 weeks interval time), serology or significant recent family history for Covid.

Results: A total of 47 patients (10 CR-SLE, 37 pC-SLE) were included in the study. The mean age at presentation was 12.7 years in the CR-SLE group and 10.9 years in the cSLE group. At disease onset, the majority of patients in both groups presented with systemic and/or mucocutaneous symptoms. In the CR-SLE patients, musculoskeletal (30% vs 65%, $p=0.07$) and renal involvement (10% vs 59.5%, $p=0.010$) were significantly less common than pC-SLE. This different clinical picture correlates with the lower SLEDAI score in CR-SLE (mean 7.0 vs 17.5, $p<0.001$). Thrombocytopenia was significantly more frequent in the CR-SLE group (70% vs 21%, $p<0.05$), while low C3-C4 and high erythrocyte sedimentation rate (ESR) were rarer than in pC-SLE (20% vs 67-70%, $p<0.05$). Similarly, hematuria and proteinuria were present in only one CR-SLE patient (10%) as compared with 54-57% in the pC-SLE group ($p<0.05$). ANA antibodies (abs) were equally present in the vast majority of patients in both groups. Conversely, while anti-dsDNA abs were less frequent in CR-SLE (40% vs 67.6%), ACL abs and Lupus anticoagulant (LAC) were found with higher frequency in this group (70% vs 58.3 and 50% vs 30.4, respectively). In the CR-SLE cohort, hydroxychloroquine (HCQ) was more commonly used than in pC-SLE (70% vs 13.5%, $p<0.001$), whereas immunosuppressive (IS) drugs were more rarely used (20% vs 49%, $p<0.05$). At 12 month follow up, 6/10 CR-SLE patients were either on HCQ or off-therapy and only 2 on IS while 56.7% of the CR-SLE patients were still on IS treatment and only 2/30 off therapy.

Conclusion: CR-SLE represents a milder disease in childhood. The systemic symptoms with thrombocytopenia with autoantibodies typical of antiphospholipid syndrome and the rarity of renal involvement represent the peculiar clinical aspects. These, together with the need for less aggressive treatment and a better prognosis, represent distinguishing characteristics as compared to the classic pC-SLE. Very few pediatric SLE cases following COVID-19 have been reported so far. The possible role of SARS-COV-2 in triggering pediatric SLE in genetically susceptible individuals is conceivable as interferons are thought to play an important role in the development of autoimmune diseases after COVID-19 infection and an increased expression of IFN-α has been observed in many patients with SLE. Further studies are needed to confirm these preliminary results.

CHILDHOOD ONSET SJOGREN DISEASE AS AN IMMUNODISREGULATIVE PROCESS: HIGH FREQUENCY OF IMMUNODEFICIENCY IN A SINGLE COHORT

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Introduction: Childhood-onset Sjogren Disease (coSjD) is an underdiagnosed disease which present unique diagnostic and therapeutic challenges. Once considered an inflammatory disorder limited to salivary and lacrimal glands, recent evidence uggests that in children and young adults SjD lead to a systemic inflammatory state. Immunodisregulative processes are associated with higher disease burden and high risk of malignancies. In adults an overlap between Common Variable Immunodeficiency and Sjogren Disease is reported. However, no studies address the frequency of immunodeficiency within coSjD cohorts remain scarce.

Objectives: This study aimed to investigate the prevalence of immunodeficiency in a single cohort of pediatric patients with coSjD. Specifically, we sought to determine the frequency of immunodeficiency among patients diagnosed with coSjD and explore its implications for disease management and prognosis.

Methods: We conducted a retrospective analysis of medical records from a cohort of pediatric patients diagnosed with coSjD and in follow-up at our unit between 2022 and 2024. Demographic data, clinical presentations, laboratory findings, and immunological profiles were extracted and analyzed. Immunodeficiency was defined based on established criteria, including quantitative and qualitative abnormalities in immunoglobulin levels, lymphocyte subsets, functional assays or genetic confirmatory tests.

Results: Among the cohort of pediatric patients diagnosed with coSjD (n = 20), we identified a strikingly high frequency of immunodeficiency, with 20% (4 out of 20) of patients meeting criteria for immunodeficiency. One patient has a chromosomal disorder associated with immunodeficiency, one patient suffers of genetical confirmed Iper-IgE syndrome, one patient has a genetical confirmed APECED syndrome due to mutation of AIRE gene and the last patient suffers of a complex phenotype characterized by reduced IgG, T- and CD19 deficiency, chronic skin disorder, interstial lung disease suggestive of an *PI3K* deficiency (exome analysis ongoing). The diagnosis of SjD followed the diagnosis of immunodeficiency in 3 cases and relies on a combination of minor salivary glands biopsy and on ultrasounds of the salivary glands. Due to the limited sample size, no significant differences between immunodeficiency associated SjD and coSJD without immunodeficiency was found. Immunosuppressive treatment was required in three patients (mycophenolate mofetil in two, rituximab in combination with sirolimus in one patient) while the other patient received hydroxicloroquine without significant benefit (persistence of parotiditis).

Conclusion: Our study highlights the significant prevalence of immunodeficiency as a comorbidity in pediatric patients with coSjD, emphasizing the need for heightened awareness and proactive management strategies. Early identification of immunodeficiency in these patients is crucial for mitigating infectious risks and optimizing long-term outcomes. Clinicians should maintain a high index of suspicion for coSjD in immunodeficient patients presenting with recurrent parotitis, connective tissue disease symptoms, or unexplained elevations in inflammatory markers. Salivary gland ultrasound emerges as a promising screening tool in this context. Further studies in larger cohorts are warranted to elucidate the underlying mechanisms linking immunodisregulation and coSjD,

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PRELIMINARY REPORT ON THE PROSPECTIVE STUDY ON MMR VACCINE IN CHILDREN WITH RHEUMATIC DISEASES TREATED WITH DMARDS AND/OR BIOLOGICS

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Introduction: According to the EULAR/PReS recommendations, measles-mumps-rubella (MMR) booster vaccine can be considered in children with rheumatic diseases (RD) on specified biologic disease-modifying antirheumatic drugs (bDMARDs), but the level of evidence for this approach is low (1).

Objectives: To prospectively evaluate safety and long-term immunogenicity of the MMR vaccine in children with RD treated with immunosuppressive therapy.

Methods: This is an ongoing multinational, multicentre prospective study. Patients with RD on conventional synthetic (cs), biologic (b) or targeted synthetic (ts) DMARDs with stable disease were included if they were scheduled to receive the 2nd dose of MMR vaccine according to their National Immunisation Programme. In case of favourable safety profile of the 2nd dose of the vaccine in the first 50 included patients, the 1st dose would be considered in areas with measles outbreaks. Controls were patients without therapy and healthy children. Infections with vaccine or wild-type viruses and adverse events (AE) were monitored after vaccination and disease activity before and after vaccination. Protective antibodies were measured before and at predetermined time points after vaccination.

Results: By the end of April 2024, 4 patients received the 1st dose and 67 patients the 2nd dose of MMR vaccine while treated with csDMARDs and/or bDMARDs. Two patients who received the 1st dose were on bDMARDs and csDMARDs, one on bDMARD and one on csDMARD. Among patients who received the 2nd dose, 26 were on bDMARDs and csDMARDs, 20 each on bDMARDs/csDMARDs and 1 on tsDMARD. Majority (89%) had juvenile idiopathic arthritis. Median age at diagnosis was 2.8 yrs (range 0.6-12.3 yrs), at 1st dose of MMR vaccine 1.2 yrs (range 0.6-4.4 yrs) and at 2nd dose 8.3 yrs (range 2.5-15.8 yrs). There were no vaccine strain infections, serious AE or disease flares after vaccination. Twenty eight percent of patients reported mild AE (fever, fatigue, arthralgia, myalgia, headache, cough). Protective antibodies against measles and mumps were positive in 75% of patients before 2nd dose, in 95% at 2-3 months, in 94% for measles and 100% for mumps at 12-18 months after vaccination.

Conclusion: The 2nd dose of MMR vaccine was safe and mostly immunogenic in children with RD treated with immunosuppressive therapy. Our results strengthen the updated EULAR\PReS recommendations to give booster MMR vaccine to children with RD treated with bDMARDs. Furthermore, four patients received the 1st dose of MMR vaccine due to the epidemiological situation and it was safe in all of them.

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EXPLORING VACCINATION COVERAGE AND ATTITUDES AMONG CHILDREN AND ADULTS WITH RHEUMATIC DISEASES ON BIOLOGIC THERAPIES: UNDERSTANDING COCOONING STRATEGIES, UNDER-VACCINATION FACTORS AND PREDICTORS OF FAVORABLE ATTITUDES

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Introduction: In patients receiving therapy with biologic agents, infections pose a substantial risk of morbidity and mortality, which can be mitigated by vaccination of both the patients themselves and their close contacts. However, a notable gap exists in comprehending the adequacy of immunization among individuals receiving biologic agents, as published data on this matter are scarce, while no studies have been published regarding the vaccination status of their close contacts.

Objectives: To evaluate the vaccination coverage of children and adults with rheumatic diseases who are treated with biologics, as well as their household contacts, in a cohort of patients followed in different clinical settings in Heraklion, Crete. Second, to determine the reasons for inadequate vaccination, highlight possible correlations of demographic, clinical and behavioral parameters with vaccination status, as well as to identify factors related to the favorable attitude of patients toward vaccination.

Methods: A cross-sectional observational study was conducted in adult and pediatric patients treated with biologic agents and followed in different clinical settings in Heraklion, Crete, from October 2022 to January 2023. Face-to-face or telephone interviews were conducted using pre-structured questionnaires and further data were collected from medical files and the electronic prescription system. Analysis was performed considering the compliance of each individual to the age–appropriate recommended types and doses per vaccine examined, according to the National Immunization Program of Greece.

Results: Among 446 adult patients examined, vaccination rates were as follows: COVID-19 - 83%, influenza - 73.8%, PCV - 64.5% and PPSV - 29.6%, while Tdap vaccination stood at 4%. Among 26 pediatric patients, coverage rates with the vaccines of the basic schedule exceeded 96%, but rates for the vaccines administered usually at adolescence were lower (Tdap 47.8%, HPV 42.1%, MenACWY 66.7%). COVID-19 vaccination stood at 38.5%. Regarding the additional vaccines recommended due to treatment-induced immunosuppression, annual influenza vaccination was complete in 69.2% of pediatric patients, while only 19.2% had received the PPSV vaccine. Household contacts demonstrated low vaccination rates across most vaccines, except for COVID-19. Female gender ($p<0.007$) and increased age ($p<0.001$) were associated with favorable attitudes and higher vaccination coverage in adults, while in pediatric patients there were no statistically significant associations. Finally, the primary reason for not being vaccinated was the lack of recommendation from their treating physician.

Conclusion: The results of the present study indicate that receipt of a biologic agent may be underestimated and not always taken into account among indications for vaccination of the patients and their close contacts. Appropriate actions focusing on improving information about the indications and benefits of vaccines, strengthening the importance of treating physicians' recommendations and promoting knowledge among physicians, patients and their close contacts should be encouraged.

CHILDREN WITH TYPE 1 INTERFERONOPATHY: COMMONALITIES AND DIVERSITIES IN A LARGE PATIENT COHORT

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Introduction: Type I interferonopathies are a class of genetic autoinflammatory disorders that result from an imbalance in the interferon pathway. These diseases are related to the innate immune system's response to viral antigens, with a variety of genetic mutations leading to different clinical manifestations. Patients with these disorders may experience symptoms related to autoinflammation, autoimmunity, and immunodeficiency. Most of our understanding of these conditions has been derived from case reports.

Objectives: Owing to the lack of cohort studies, our main objective was to provide a comprehensive overview of the clinical features, laboratory and screening results, treatment options, and outcomes of patients with various subtypes of type 1 interferonopathy. We also sought to illustrate the relationship between genotype and phenotype based on the involvement of specific systems or organs and the varying degrees of autoinflammation, immunodeficiency, and autoimmunity. Our secondary objective was to determine the factors that predict long-term morbidities or fatalities, which are typically associated with poor outcomes.

Methods: We included children with genetically confirmed type 1 interferonopathies, with a follow-up duration of > 1 year. Data were obtained retrospectively from medical records.

Results: Of the 40 eligible patients for the study, 52.5% were female, with a median age of disease onset of 1.5 years (0.1-13.2). They were diagnosed at an average age of 6.85 ± 4.56 years. Aicardi-Goutières Syndrome was the most common diagnosis (n=15; 37.5%). The central nervous system was the most frequently affected system (n=27; 67.5%). Janus kinase inhibitors were administered to 17 (42.5%) patients. Twenty-five patients (62.5%) developed at least one permanent morbidity or died during follow-up; thus, they were included in the poor-outcome group. While younger age at disease onset, intracranial calcification (ICC), and lack of chilblains and elevated acute phase reactants (APRs) were significant in univariate logistic regression analysis, only ICC on MRI at admission (aOR, 19.691; 95% C.I.: 1.080-359.054, p=0.044) was found to be a significant predictor of poor outcomes in multivariate logistic regression analysis.

Conclusion: For the first time, we evaluated the predictors of poor outcomes in patients with type 1 interferonopathy with a broad spectrum of subtypes. Furthermore, our study's unique patient characteristics and phenoytpe-genotype correlation data can provide valuable insights into these extremely rare conditions.

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RETROSPECTIVE SINGLE-CENTRE STUDY OF THE CHARACTERISTICS, MANAGEMENT AND OUTCOMES OF PEDIATRIC COMPLEX REGIONAL PAIN SYNDROME

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Introduction: Complex regional pain syndrome (CRPS) is a severe pain condition that causes functional impairment and impacts greatly the patients' quality of life. Despite some progress in research, more studies are required to improve diagnosis, clarify the molecular mechanisms of the disease and identify predictors of outcome so that targeted treatments can be developed.

Objectives: To describe demographic, clinical features and management of a single-center cohort of patients with pediatric CRPS and identify potential predictors of disease course.

Methods: This is a retrospective cohort study of patients with pediatric CRPS seen at the study center over the past 10 years. Demographic, clinical, radiologic data and therapeutic strategies were compared between patients with a favorable outcome and those who experienced at least one flare during the course of the disease. Pearson $\chi 2$ test or Fisher exact test were used to compare continuous and categorical clinical data between groups. P values < 0.05 were considered statistically significant.

Results: Fifty-three patients were admitted to our institute with a diagnosis of CRPS. Twenty-nine of 53 patients (54.7%) fulfilled the Budapest criteria for the diagnosis of CRPS and were included in the present study. Twenty-three patients (79.3%) were females. The mean age at disease onset was 11.2 years (5.7-13.6 years), with a mean time from symptom onset to diagnosis of 78 days (30-275 days). Most cases (82.7%) had lower extremity involvement. Sixteen patients (55.1%) identified an inciting physical traumatic event. At disease onset, 26 patients (89,6%) received the following pharmacologic treatments: nonsteroidal anti-inflammatory drugs in 22 (84.6%), acetaminophen in 11 (42.3%), gabapentinoids in 10 (38.5%), neridronate in 6 (23%), and tricyclic antidepressants in 4 (15.3%). Prompt referral to physiotherapy was reported in 20 patients (68.9%). Follow-up data were available for 18 patients (mean follow-up 20 months), of which nine (50%) had a favorable course of the disease and the remaining 9 (50%) had a relapsing disease (5 had a single relapse, one had 2 episodes of relapses and the remaining 3 had >3 relapses). Psychiatric comorbidities including depression, generalized anxiety, eating disorders, bipolar disorders and suicidal ideation were diagnosed in seven patients (38.9%). Patients who relapsed had a mean time to diagnosis of 84.55 days compared to 57.77 days for patients with a favorable disease course. The percentage of patients treated with neridronate was significantly higher in patients experiencing complete and sustained resolution of symptoms compared to patients with relapsing disease (66.7% versus 22.3%). There were no differences between the groups in age, sex, duration of the first episode, pain intensity, radiological features and psychological symptoms.

Conclusion: Approximately half of the patients with suspected CRPS do not meet the Budapest criteria thus highlighting the need for diagnostic criteria appropriate for the pediatric age group. Shorter time to diagnosis and bisphosphonate therapy may predispose patients to more favorable outcomes. Longitudinal multicenter clinical trials are required to develop consensus guidelines for treatment, which should be based on an interdisciplinary approach due to the high frequency of psychiatric comorbidities.

CHALLENGES OF PEDIATRIC RHEUMATOLOGY AT THE RESOURCE-CONSTRAINED HIMALAYAN REGIONS– LONE AND UNSEEN EFFORTS

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Introduction: Pediatric rheumatological diseases (PRDs) including immune dysregulation disorders (IDDs) are increasingly being diagnosed with accuracy in resource-limited Himalayan regions due to the availability of a single subspecialist.

Objectives: To describe the profile of patients diagnosed with PRDs/IDDs in Nepal and the surrounding Himalayan regions during 2020-2024

Methods: Records of all patients diagnosed with PRDs/IDDs at a tertiary care center in Nepal (including children referred from surrounding Himalayan regions like Bhutan, and North-East India) from August 2020 to February 2024 were analyzed. The pediatric rheumatologist, [lead author (DB)] has examined and diagnosed all cases. Diseases were diagnosed based on internationally acclaimed criteria and genetic analyses.

Results: A total of 1175 children with PRDs (M: F = 1.4:1) and 114 children with IDDs were diagnosed during the study period. Genetic analysis was done on 69 patients with monogenic rheumatic/immune dysregulation disorders. Most patients had come after multiple admissions (1-94 times) before patient met the only pediatric rheumatologist in the country. Most children were misdiagnosed as tuberculosis, infections, septic arthritis, allergy, dermatitis, muscular dystrophy, malnutrition, or asthma. About 1/3rd of children were wrongly commenced on steroids without evidence. The diagnostic profile of the patients includes various common autoimmune and autoinflammatory disorders to rare IDDs (e.g., *ARPC1B* deficiency). Monogenic autoinflammatory disorders were diagnosed in 44 patients. Some patients succumbed before the scope of diagnosis. Stem cell transplantation is done in 4 children. Commonly diagnosed PRDs included chronic arthritis, connective tissue disorders, vasculitis, autoinflammatory diseases, and reactive diseases.

Conclusion: With a single subspecialist, our is the first report of proven PRDs in Nepal. Skepticism about the existence of PRDs and lack of referrals may lead to the missing of these serious illnesses. Logistic constraints coupled with a lack of awareness of IEIs accounted for missed diagnoses and poor outcomes in resource-limited settings.

IMMUNODEFICIENCY DUE TO A NOVEL VARIANT IN PIK3CD

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Introduction: Abstract Background Primary immunodeficiencies are immunological disorders caused by gene mutations involved in immune system development and activation. Recently, activated phosphoinositide 3-kinase delta syndrome (APDS) due to mutations in the phosphoinositide 3-kinase (PI3K), phosphatidylinositol-4, 5-bisphosphate 3-kinase, catalytic subunit delta gene (PIK3CD), and phosphoinositide 3-kinase regulatory subunit 1 (PIK3R1) genes have been reported to induce a combined immunodeficiency syndrome leading to senescent T cells, lymphadenopathy, and immunodeficiency. The exact diagnosis of these deficiencies is essential for treatment and prognosis. In recent years, targeted treatment with selective PI3Kd inhibitors has had a significant effect on controlling the symptoms of these patients

Objectives: whole blood sample. Variant interpretation of interested variants was accomplished through the American College of Medical Genetics and Genomics (ACMG). A novel heterozygous variant (c.1429 G>A; p.Glu477Lys) was found in the PIK3CD gene (Table 2). The variant was validated in the patient, and segregation analysis showed the mother is the carrier for the variant. According to the ACMG guideline, this variant can be classified as a Variant of Unknown Significance (VUS).

Methods: .

Results: In this report, we described a girl with a novel mutation in the PIK3CD gene. She had a recurrent fever, and erythema nodosum with the manifestations of combined immunodeficiency in immunological investigations. She experienced several episodes of viral and bacterial infections, autoimmune disorders (hypothyroidism and type 1 diabetes mellitus), and auto-inflammatory manifestations (left knee arthritis, pericardial effusion).

Conclusion: Conclusion The genetic analysis found a novel variant of PIK3CD (c.1429 G>A) in the patient. Following daily antibiotic prophylaxis and monthly IV therapy, the patient's frequent infections and fevers were controlled.

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Abstract book only

Autoinflammatory diseases

CLINICAL CHARACTERISTICS AND BIOMARKERS OF PATIENTS WITH NON-HEREDITARY PERIODIC FEVER SYNDROMES IN A CZECH SINGLE CENTRE COHORT

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Introduction: Non-hereditary periodic fevers encompass syndromes lacking a known causal gene. Although periodic fever-aphtae-pharyngitis-adenitis syndrome (PFAPA) is the most prevalent among Caucasian children, some individuals are categorized under the syndrome of undifferentiated recurrent fever (SURF). Nevertheless, proposed classification criteria for SURF are yet to be validated.

Objectives: To define clinical, biochemical, and immune profiles of children with PFAPA and SURF during febrile and afebrile phases, comparing them to control subjects.

Methods: Patients diagnosed with PFAPA and SURF were prospectively enrolled and their symptoms systematically recorded. Blood samples were collected at specific time points: during the febrile episode (within 24 hours of fever >38.0°C) and afebrile interval (at least 2 weeks after the last fever). Febrile controls (FC) were otherwise healthy children with acute infections, healthy controls (HC) had non-inflammatory conditions. Sera were analysed for standard parameters (CRP, SAA, procalcitonin (PCT), ferritin), S100A8/9 and S100A12 proteins and a 48-cytokine Bio-Plex panel.

Results: Total of 93 periodic fever patients and 35 controls were recruited: PFAPA (n=71), SURF (n=22), HC (n=28), FC (n=7). In 34 patients (15 PFAPA, 19 SURF) paired (febrile/afebrile) samples were available. While the most prevalent symptoms in PFAPA were pharyngitis (96%), adenitis (69%), fatigue (39%), and aphthae (26%), in SURF patients fatigue (55%), abdominalgia (46%), arthralgia (42%) and myalgia (36,%) prevailed. Following symptoms were significantly more frequent in SURF: skin rash and diarrhea ($p<0,001$), arthralgia ($p=0,002$), myalgia ($p=0,019$), abdominalgia ($p=0,031$). The mean duration of fever episodes was significantly longer in SURF than PFAPA (5.7 (SD 2.8) vs. 3.9 (SD 0.9) days, p= 0,0001). In all paired samples proinflammatory parameters differed significantly. There were no significant differences between febrile PFAPA and SURF patients, or between febrile periodic fever patients and FC. Despite normal CRP, SAA, PCT and S100 protein levels in afebrile samples in both periodic fever groups, serum cytokines were significantly higher in SURF at $p<0.01$ for IL-1ra, IL-4, IL-17, G-CSF, MIP-1a, IL12p40, IL-18, HGF, M-CSF, and SCF, and at $p<0.05$ for IL-8, IL-2ra, IL-16, IFN-a2, LIF, and MIG. Afebrile PFAPA and SURF patients had higher levels than HC at $p<0.001$ in IL-1b, IL-1ra, FGF basic, IL-1ra, IL-18, GROa, LIF, SCF, TNF-b and TRAIL, at $p<0,005$ in TNF-a, IL-1a, IL-12p40, IFNa2 and SDF-1a, at $p<0,05$ in G-CSF, IP-10, MIP-1b, IL-16, IFNa2, M-CSF and SCGFb.

Conclusion: We have shown significant clinical differences between SURF and PFAPA patients, but their proinflammatory mediators did not differ as they did not differ from FC. Higher FC number is needed to confirm this finding. Multiple serum cytokines differed significantly in afebrile samples between SURF and PFAPA as well as between periodic fevers and HC reflecting potential ongoing immune dysbalance. Changes in cytokines that have not been reported so far will have to be confirmed by single ELISA.

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DOES HAVING ADDITIONAL MUTATIONS OTHER THAN MEFV VARIANTS AFFECT FMF PHENOTYPE?

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Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease caused by mutations in the MEFV gene. Fever, serositis, and arthritis are the major clinical findings.

Objectives: We aimed to evaluate the impact of concomitant autoinflammatory disease mutations on the phenotype of patients diagnosed with FMF.

Methods: The files of 2035 patients diagnosed with FMF according to the Eurofever/PRINTO autoinflammatory recurrent fever classification criteria in three Pediatric Rheumatology centers were retrospectively examined. An autoinflammatory panel was submitted from patients diagnosed with FMF who were unresponsive to colchicine or had additional clinical features such as rash, diarrhea, conjunctivitis, or a family history of other autoinflammatory diseases.

Fifty-eight patients who were sent an autoinflammatory genetic panel were included in the study. Patients were divided into two as only MEFV mutation carriers (group 1) and MEFV and concomitant autoinflammatory disease mutation carriers (group 2). Demographic findings, genetic mutations, clinical features, AIDAI and PRAS scores, and treatments used were recorded and the two groups were compared.

Results: Twenty-nine patients (50%) were carrying only MEFV mutation (group 1) and 29 patients (50%) were MEFV and concomitant autoinflammatory disease mutation carriers (group 2).

In group 1, 26 patients (89.6%) had heterozygous MEFV mutations, and 3 patients (10.4%) had compound heterozygous MEFV mutations. In group 2, 22 patients (75.9%) had heterozygous MEFV mutations, 5 patients (17.2%) had compound heterozygous, 2 patients (6.9%) had homozygous MEFV mutations. Patients in group 2 exhibit mutations in genes associated with autoinflammatory diseases apart from MEFV, including NLRP3, NLRP12, MVK, TNFRSF1A, NOD2, IL10-RB, CARD14, LPIN2, ADA2, PSMB8, PSTPIP1 in addition to MEFV mutations.

Demographic characteristics, time between the onset of symptoms and the number of attacks, clinical characteristics, disease activity and severity scores, and the number of patients using biologic drugs were similar between groups.

Conclusion: The coexistence of gene variants of other autoinflammatory diseases along with MEFV gene variants implied no significant difference in demographics, clinical findings, outcome measures, and treatments of patients carrying only MEFV gene variants. However, the results need to be validated in larger groups of patients with FMF to clarify the role of concomitant variants in pathology and phenotype of the disease.

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MALNUTRITION IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Introduction: Familial Mediterranean fever (FMF) is a monogenically autosomal recessively inherited autoinflammatory disease characterized by recurrent, self-limiting episodes of fever and sterile serositis. Malnutrition is a set of pathological conditions in which structural and functional disorders occur in tissues and organs due to unbalanced, inadequate or excessive intake of macro and micronutrients necessary for growth and development. Malnutrition may be observed in patients with FMF, but this may be overlooked during routine follow-up. It is essential to identify malnutrition that may accompany these patients to maintain their normal growth and development.

Objectives: Our study aims to determine the frequency and types of malnutrition in FMF patients and evaluate malnutrition status after colchicine treatment.

Methods: The electronic medical records of the patients who were followed up between 2011 and 2023 with the diagnosis of FMF were retrospectively analyzed. The types of malnutrition of all patients before and after treatment were determined as mild, moderate, severe, overweight, and obesity.

Results: A total of 532 patients were included in the study. The median (IQR) age at diagnosis was 6.5 (16.5) years. The median (IQR) follow-up period was 6 (15.5) years. Among 532 patients with FMF, 173 patients (32.5%) had malnutrition at diagnosis. 123 of these patients were underweight; 92 patients had mild (53.2%), 26 patients had moderate (15%) and 5 patients had severe (2.9%) malnutrition. 34 patients were overweight (19.7%) and 16 patients were obese (9.2%). The frequency of malnutrition decreased to 110 patients (20.7%) after colchicine treatment. Especially the frequency of mild, moderate malnutrition and obese patients decreased.

Conclusion: Malnutrition is an important issue in children with FMF. According to the results of this study, while approximately one-third of the patients had malnutrition before colchicine treatment, both the frequency and severity of malnutrition decreased after treatment. The presence and type of malnutrition should be considered in the clinical follow-up of FMF patients.

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EXPLORING THE FACTORS FOR PREDICTING COLCHICINE RESPONSIVENESS IN CHILDREN WITH PFAPA

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Introduction: Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis syndrome (PFAPA) is the most common autoinflammatory syndrome in children. Since there are no typical laboratory findings specific to the disease, diagnosis is often delayed, and treatment approaches vary. In this study, we aimed to examine the response to colchicine in PFAPA disease and evaluate whether parameters predicting the response to colchicine based on first-line clinical and laboratory parameters.

Objectives: Nine referral centers from our country enrolled in the study. Parameters were documented from the patient's medical records, retrospectively. The diagnosis of PFAPA syndrome was made according to modified Marshall's criteria. Patients whose disease episodes ceased or became less frequent after colchicine treatment were classified as "colchicine responsive."

Results: A total of 806 patients enrolled in the study. Fever was the most common clinical finding, reported in all patients, followed by exudative tonsillitis in 697 (86.5%), pharyngitis in 652 (80.9%), aphthous stomatitis in 407 (50.5%), cervical lymphadenopathy in 340 (42.2%), abdominal pain in 253 (31.4%), arthralgia in 191 (23.7%), headache in 34 (4.12%) and arthritis in 8 (1%) patients. The median age of diagnosis and symptom onset were 44 (9-151) and 24 (3-120) months, respectively. The mean attack frequency was 13.5 ± 6.8 attacks per year lasting for a mean of 3.9 ± 1.1 days. Colchicine treatment was attempted in 519 (64.4%) patients, with 419 (80.7%) showing a favorable response and 12 (2.3%) showing a partial response. MEFV gene sequencing was performed on 571 (70.8%) patients, revealing no genetic mutation in 335 (58.1%) patients, while the most common variant was M694V heterozygote in 96 (16.8%) patients. Clinical and laboratory parameters of patients were compared

based on their responses to colchicine (Table 1). A multivariate regression analysis identified several factors associated with colchicine unresponsiveness, including the presence of pharyngitis (p=0.03, CI95% 0.885 to 0.994), the presence of arthralgia (p=0.04, CI95% 0.169 to 0.958), and more frequent attacks (p= 0.001, CI95% 0.028 to 0.748). Carrying the M694V variant (p= 0.001, CI95% 0.065 to 0.242) was the sole factor predicting colchicine responsiveness.

Conclusion: Our study identified significant predictors of colchicine unresponsiveness in PFAPA disease, including the presence of pharyngitis, arthralgia, and increased attack frequency. Conversely, the presence of the M694V variant carriage emerged as a significant predictor of colchicine responsiveness. These findings underscore the potential utility of predicting colchicine response at disease onset, thereby facilitating more effective management of PFAPA disease.

CHRONIC NONBACTERIAL OSTEOMYELITIS OF MANDIBLE IN CHILDREN: DESCRIPTIVE STUDY FROM A TERTIARY CENTRE IN BRISTOL

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a focal non-infectious autoinflammatory bone disorder of unknown aetiology in children with mandibular involvement at presentation being a rarity(1).

Objectives: To describe the clinical presentation, radiographic appearances and response to treatment in children with mandibular CNO.

Methods: The study was conducted at Bristol Royal Hospital for Children. Records of all children less than 18 years diagnosed with CNO of mandible between 2010 to 2023 were retrospectively reviewed. Demographic, clinical, laboratory, radio imaging and response to treatment were recorded.

Results: A total of 142 children were diagnosed with CNO. Among them 7 children (4.9%) had mandibular involvement at presentation. All were girls with median age of presentation at 11 years. The presenting symptoms included swelling (n=6; 85.71%), pain (n=2; 28.57%), trismus (n=1; 14.28%) and difficulty in chewing (n=1; 14.28%). 2 children had a family history of psoriasis. Children most often presented to maxillofacial surgeons (n=4) followed by otorhinolaryngologist, orthopaedician and dentist (n=1 each) before being referred to a paediatric rheumatologist. Mean lag time between onset of symptoms and diagnosis was 2.8 years. C-reactive protein and erythrocyte sedimentation rate were within normal range in all children. HLA B27 was positive in 1 (14.28%) child. 6(85.71%) children had diagnostic biopsy. All children underwent whole body magnetic resonance imaging (MRI) at presentation. Monofocal mandibular lesions were present in 5 (71.42%) children. All children received non-steroidal anti-inflammatory drugs (NSAIDs). 1(14.28%) child responded to NSAIDs with complete resolution and required no further treatment. 6(85.71%) children received pamidronate and showed good clinical response with resolution of symptoms on follow up. Following pamidronate, 4 had follow up MRI at the end of 1 year from start of treatment. On repeat MRI, 3 showed radiological response with reduction in signal intensity and 1 showed complete radiological resolution.

Conclusion: Although CNO of mandible is rare, awareness of this entity among other specialties is prudent for early referral and initiation of treatment thus resulting in better outcomes. Radiological

response may not necessarily correlate with clinical response.

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UPDATE ON UNDIFFERENTIATED RECURRENT FEVERS (SURF) GASLINI'S COHORT: CONSOLIDATING CLINICAL CHARACTERISTICS, EVALUATING PERSISTENCE OF COLCHICINE EFFICACY, AND EXPLORING THE ROLE OF ANTI-IL-1 TREATMENT

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Introduction: SURF syndrome, a recent described clinical entity, differs from other monogenic recurrent fevers and PFAPA syndrome. Although clinically similar to familial Mediterranean fever, they lack compatible genetics. Our recent study further delineates biological differences between SURF, FMF and PFAPA.(1,2)

Objectives: To describe, updating and supplementing the existing literature data, the follow-up of a homogeneous cohort of 90 patients with SURF, managed at a tertiary referral center.

Methods: Patients followed for SURF from 2008 to 2023 were retrospectively included. Exclusions criteria were: confirmed mutations for monogenic recurrent fever (extensive NGS panel) or meeting Eurofever criteria for PFAPA. Treatment response was categorized as:i) complete response (no symptoms and normal acute phase reactants), ii) partial response (symptoms persist with ≥50% reduction in fever episodes), iii) resistance (minimal or no improvement, or worsening).

Results: Initially, 92 patients were enrolled, with 2 patients later excluded for meeting PFAPA criteria within 6 months. Of the selected 90 patients (59 males, 31 females), median age at onset was 2.6 years (CI 2.0-3.2), median age at diagnosis 6.5 years (CI 5.2-7.5), and median diagnostic delay 2.6 years (CI 1.8-3.6). Median duration of inflammatory episodes was 4.0 days (CI 3.5-4.0), with a median of 12.0 episodes/year (CI 12.0-15.0). Arthralgia (67%) and abdominal pain (64%) were common symptoms, while only 6% patients presented with oligoarthritis or monoarthritis. Median follow-up was 2.75 years (CI 1.8-3.2, range 0-15.4). Tonsillectomy was ineffective in all 14 patients who underwent the procedure. Colchicine was prescribed in 80/90 patients. Among those with 1-year follow-up data (55/80), it showed 95% efficacy: 39/55 (71%) had complete response, 13/55 (24%) partial, and 3/55 (5%) were ineffective. Two-year follow-up data for 39 patients indicated 97% efficacy: 30/39 (77%) complete response, 8/39 (20%) partial, and 1/39 (3%) resistant. Four patients with complete 1-year response showed partial response by year 2, necessitating anti-IL1 anakinra in 3 cases. Anakinra was initiated in 7 patients: 3 due to colchicine-response decline, 3 for persistent partial response, and 1 for colchicine inefficacy. One patient switched to canakinumab post-allergic reaction to anakinra, reporting efficacy. At last follow-up, 2 patients had never been treated, 49 on colchicine (5 with anakinra, 1 with canakinumab), 13 discontinued colchicine, and 1 received only anakinra. Colchicine withdrawal reasons were: remission (7/13, 54%) and inefficacy (5/13, 38%).

Conclusion: This study provides data on an expanded SURF cohort at Gaslini Institute with extended follow-up. Abdominal pain, arthralgia, and minimal pharyngo-tonsillar involvement are confirmed as main clinical features. Colchicine efficacy is affirmed, but gradual loss of efficacy occurs in a small percentage of patients over time. Anti-IL-1 treatment, alone or with colchicine, benefits most non-responsive patients. Further research is needed to fully characterize this patient population, identify possible genetic determinants, and optimize treatment strategies for SURF.

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Bone in rheumatic diseases

ONE-YEAR POST-DIAGNOSIS OUTCOME IN A NATIONAL CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS / CHRONIC NON-BACTERIAL OSTEOMYELITIS (CRMO/CNO) COHORT

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Introduction: CRMO, also known as CNO, is an autoinflammatory condition affecting the bones of children. There is a wide spectrum of clinical presentations, ranging from singular lesions to relapsing, multifocal, or continuous disease. There is currently a lack of prospective study on the short to medium term disease outcome.

Objectives: The primary aim of this study was to understand the one-year post-diagnosis outcome in a prospectively identified national cohort of patients with CRMO/CNO in the United Kingdom and Republic of Ireland.

Methods: We conducted monthly surveys among all paediatric consultants and paediatric orthopaedic surgeons through British Paediatric Surveillance Unit and British Society for Children's Orthopaedic Surgery to identify children and young people (<16 years) newly diagnosed with CRMO/CNO between October 2020 and November 2022. Standardised questionnaires were sent to reporting clinicians to collect detailed clinical information about each case within a few months of diagnosis (baseline) and one-year post-diagnosis.

Results: Over the initial 25-month surveillance period, 185 children and young people with CRMO/CNO were identified. One-year follow-up questionnaires were received from 120/185 (65%) cases. Disease courses within the first year were categorised by the primary clinicians caring for the patients as continuous (23/113; 20%), recurrent (52/113; 46%) or a stand-alone episode (38/117; 34%). Disease

control compared to baseline was reported to have improved in 104/115 (90%) of cases, with 47/115 (41%) of patients in remission. Overall, at one-year, 38/107 (36%) were not on any medication (including analgesics), and 34/107 (32%) were on NSAID alone (with or without other analgesics). There was a trend towards improved mobility, though this was not statistically significant. Reported complications at one-year follow-up included pathological fractures (1/113; 0.88%) and bone deformity (4/113; 3.5%).

There was no difference in outcome between patients treated with pamidronate (n = 30) or zoledronate (n = 21). Multi-logistic regression analysis did not identify any presenting features that were significantly associated with better or worse one-year outcome.

Conclusion: The majority of children diagnosed with CRMO/CNO have disease relatively well controlled one-year post-diagnosis, as evidenced by clinician's perspective on disease control and the majority of patients treated only with NSAIDs, or no medication. A trend towards functional improvement was observed.

COVID-19 (Coronavirus)

IMMUNE RESPONSE TOWARDS SARS-COV-2 VACCINATION IN CHILDREN WITH PREVIOUS MULTI-SYSTEM INFLAMMATORY SYNDROME IN CHILDREN

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Introduction: Multi-system inflammatory syndrome in children (MIS-C) is a rare, severe hyperinflammatory condition triggered by SARS-CoV-2 infection. SARS-CoV-2 vaccination in children with previous MIS-C appears safe, and we have previously shown that there is no difference in SARS-CoV-2 antibody production or neutralisation ability; however, the immune response elicited towards SARS-CoV-2 vaccination in these children is not known.

Objectives: To investigate the cytokine and chemokine production, and whole blood RNA expression after SARS-CoV-2 vaccination in children with previous MIS-C.

Methods: Children older than 12 years, who were diagnosed with MIS-C between 2020 and 2021 and healthy children were offered 2 doses of Pfizer COMIRNATY vaccine, 3 weeks apart, as per international guidelines. Serum and whole blood RNA were collected prior to vaccination, 1 week after each vaccine and 6 weeks after the first vaccine dose. At every time point, Luminex for cytokine and chemokine production, and qPCR for immune gene expression were performed.

Results: Three out of the eleven eligible children with previous MIS-C agreed to receive vaccination (1 girl, 2 boys, all aged 12). Four healthy children volunteered for vaccination (3 boys, 1 girl, all aged 12). Throughout the vaccination schedule, there was no difference in serum IL-1β, IL-1RA, IL-6, IL-27, IP-10, MCP-1 or TNF-α between children with prior MIS-C or healthy children. However, at all sampling points children with prior MIS-C had a consistently raised serum IL-10 at baseline (p=0.011), 1 week after the first dose (p=0.002) and at 6 weeks follow-up (p=0.014). Immune gene expression analysis revealed no significant differences between the two groups at any timepoint, although several transcripts were

nominally differentially expressed (p = 0.057). *IL27* was upregulated in children with previous MIS-C after the first dose, while CXCR3 was downregulated at this timepoint and *TIMP2*, *TRMT2A*, *RAB33A* and *GZMB* were downregulated after the second dose. At 6 weeks after the first dose, *FCGR2A*, *IL1B*, *IFNAR1* and *GZMB* were all downregulated in children with prior MIS-C.

Conclusion: In this small group, the immune response to SARS-CoV-2 mRNA vaccination in children with previous MIS-C appears to be slightly altered compared to healthy controls. However, these differences do not appear to be clinically relevant, and vaccination of these children should continue.

Disease outcome and transition

THE TRANSITION FROM PEDIATRIC TO ADULT HEALTHCARE. CAREGIVER PARENTS POINT OF VIEW IN ITALY.

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Introduction: Rheumatological diseases affect over 5 and a half million people in Italy and are diversified into more than 180 pathologies. On average 10,000 adolescents in Italy are affected by rheumatological disease, the most common being juvenile idiopathic arthritis. The transition from pediatric to adult healthcare is a crucial moment in an adolescent's developmental direction. The research was carried out in Italy to investigate the barriers in the transition process, from the point of view parent caregivers.

Objectives: Gather data from Italian parents caregiver of patients (14-20 y.o.) affected from a rheumatological disease to understand the transition process in terms of: 1) touchpoints of information; 2) level of information.

Methods: A quantitative survey was carried out through a questionnaire administered throughout the Italian national territory to a sample of N=197 caregiver parents.

The total sample was divided into two targets.

Target 1: caregiver parents of rheumatological patients (14-20 y.o.) who made the transition (42,6%,N=84).

Target 2: caregiver parents of rheumatological patients (14-20 y.o.) who didn't make the transition (57,4%,N=113).

The questionnaire was made up of 26 questions, of which 23 were closed and 3 were open. For the administration of the questionnaires, the CAWI (Computer Aided Web Interview) methodology of on-line survey was used. The 197 interviews were carried out from September 1st to 30th 2023.

Results: 1) Touchpoints of information (multiple answers possible).

- Total sample (N=197): pediatric rheumatologist 55,8%, N=110; general practicioner 41,6%, N=82; adult rheumatologist 31,5%, N=62.

- Target 1: caregiver parents of rheumatological patients (14-20 y.o.) who made the transition (N=84): pediatric rheumatologist 48,8%, N=41; general practitioner 48,8%, N=41; adult rheumatologist 45,2%, N=38.

- Target 2: caregiver parents of rheumatological patients (14-20 y.o.) who didn't make the transition (N=113): pediatric rheumatologist 61,1%, N=69; general practitioner 36,3%, N=41; adult rheumatologist 21,2%, N=24).

2) Level of information (5 points Likert scale. 1: not complete at all, to 5: complete at all).

- Total sample: (N=197): 3 out of 10 parents caregiver (29,4%, N=58) declared that it has no complete information on the transition process.

- Target 1: (N=84) caregiver parents of rheumatological patients (14-20 y.o.) who made the transition: 20,2%,N=17, declared that it has no complete information on the transition process.

- Target 2: (N=113) caregiver parents of rheumatological patients (14-20 y.o.) who didn't make the transition: 36,3%, N=41, declared that it has no complete information on the transition process.

Conclusion: The main barrier that parents caregivers and patients face in the transition from pediatric to adult healthcare is the lack of clear information about this process. Also, the transition involves psychological and social challenges, such as adapting to new medical environments and increasing responsibility for your own health. The research highlights insufficient information as the main critical area that makes the transition a path that is not always easy in Italy. Future research will have to highlight the correlation between the level of information and a correct transition from pediatric to adult healthcare.

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Imaging

CAN ZERO ECHO TIME MAGNETIC RESONANCE IMAGING ENHANCE OUR ABILITY TO ASSESS EROSION IN SACROILIITIS MORE EFFECTIVELY?

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Introduction: Enthesitis-related arthritis (ERA), a subgroup of JIA, accounts for 18.9% of JIA cases in our region, with a higher prevalence of sacroiliac (SI) joint involvement. At the outset of the disease, approximately 30% of individuals with ERA exhibit symptomatic sacroiliitis, a rate that escalates to 70% over time. Although magnetic resonance imaging (MRI) is the most sensitive radiological method for detecting sacroiliitis, identifying early erosive changes remains still challenging. Conventional MRI pulse sequences have limitations in reliably depicting structures such as osseous and calcified tissues.

Objectives: Recently, novel MRI sequences, such as zero echo time (ZTE) MRI utilizing ultrashort echo times (UTEs), have emerged as a viable method to produce computed tomography (CT)-like images of ossified or calcified structures. This study aims to evaluate the utility of ZTE MRI to identify erosion.

Methods: All MRI scans were performed using a 1.5 T scanner. The MRI protocol included a fat-suppressed axial T2-weighted sequence, axial T1-weighted sequence, coronal STIR sequence, and axial T2-weighted sequence. Additionally, a ZTE sequence was conducted. The low-dose CT scan was performed using a 640-MSCT device, with patients exposed to an average effective dose of 0.615 mSv per sacroiliac CT. Structural lesions, including erosions, sclerosis, and joint space changes, were compared using ZTE and low-dose CT. Structural lesions, including erosions, sclerosis, and joint space changes were scored based on a previously described method.

Results: A total of 20 patients were evaluated (13 boys, 7 girls). Sixteen patients had a family history of rheumatic disease. The median age at diagnosis was 14.44 years, and the median follow-up time was 17 months. At the time of diagnosis, 18 (90%) patients experienced lower back pain, 18 (90%) had hip pain, 15 (75%) reported morning stiffness, 14 (70%) had peripheral arthritis, 8 (40%) experienced heel pain, 7 (35%) had enthesitis, and 5 (25%) had back pain. HLA-B27 was positive in 14 (70%) patients. The median JSpADA at diagnosis and at the time of MRI was 3.7 and 2.7, respectively. During radiologic evaluation, the median counts of active joint and enthesitis were 2 and 0, respectively. Fourteen patients (70%) exhibited clinical sacroiliitis, and 9 (45%) experienced morning stiffness. The mean erosion score on low-dose CT was 9.4, on ZTE-MRI was 8.8, and on MRI 4. The mean sclerosis score on low-dose CT was 9.15, on ZTE-MRI was 9.15, and on MRI 6.15. The mean joint space changes on low-dose CT was 5.1, on ZTE-MRI was 4.95, and on MRI 3.8. The kappa value for the detection of erosions on the quadrant level compared with low-dose CT was 0.514 ($p < 0.001$), for sclerosis it was 1 ($p < 0.001$), and for joint space changes, it was 0.814 ($p < 0.001$).

Conclusion: ZTE imaging may produce a visualization of the sacroiliac joints that closely resembles low-dose CT scans, thereby enhancing the detection of subtle erosions and sclerosis in the sacroiliac joints.

Immunoregulation and basic science

CHILDHOOD-ONSET SJÖGREN'S DISEASE HAS AN ACTIVATED PERIPHERAL BLOOD CD4+ MEMORY AND T-FOLLICULAR HELPER CELL PHENOTYPE WHICH COULD DRIVE B-CELL DYSREGULATION

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Introduction: Childhood-onset Sjögren Disease (cSjD) is a rare and poorly understood autoimmune rheumatic disease with onset before 18 years of age. Differences in clinical presentation compared to the adult phenotype, combined with a lack of evidence-based management strategies, warrants research into the pathogenesis of the disease.

Objectives: To investigate the in-depth peripheral blood immunological landscape of children and adolescents with cSjD using 30-marker spectral flow cytometry.

Methods: A pilot cross-sectional analysis was performed investigating the peripheral blood immune phenotype of children and adolescents with cSjD (N=10; mean age=18 years; age range=16-21 years; all females; mean disease duration=4 years; disease duration range=2-6 years; off steroids and biologic treatment naïve) compared to age and sex-matched healthy controls (cHCs; N=10; mean age=18 years; age range=15-25 years; all females). The identified phenotype was further explored using 30-feature spectral flow cytometry in a larger cohort of cSjD (mean age=21 years; age range=17-30 years; all females; mean disease duration=7 years; disease duration range=2-18 years) and cHCs (mean age=19 years; age range=15-27 years; all females) (N=19/group) using unsupervised dimensionality reduction (UMAP) and clustering analysis (FlowSOM in "Spectre" R package1). Serum cytokines assessed by Cytometric Bead Array and Luminex.

Results: CD4+ T-cell populations were significantly dysregulated in young people with cSjD compared with matched cHCs, characterised by elevated effector memory (EM, p=0.01) and terminally differentiated EMRA populations (p=0.0002) and reduced central memory T-cells (p=<0.0001). An unsupervised high-parameter analysis of T-cell phenotype using spectral flow cytometry identified twenty CD4+ T-cell clusters, of which four clusters were significantly elevated in young people with cSjD compared with cHCs (p<0.004) all characterised as CD45RA- memory T-cells. Two of these clusters expressed high levels of PD-1, CXCR3 and ICOS, suggesting an activated T-follicular helper-1 phenotype; one cluster expressed elevated PD-1 and ICOS and one cluster was characterised by elevated PD-1 only. This pro-inflammatory and activated T-cell phenotype was supported by increased production of IL-6 by CD4+ T-cells (p=0.04) and increased serum IL-6 levels (p=0.02) in young people with cSjD vs cHCs. Finally, cytokines associated with B-cell activation, IL-10 (p=0.01) and APRIL (p=0.0007), and immune cell trafficking, CCL8 (p=0.03), were also increased in cSjD supporting an ongoing systemic inflammatory environment.

Conclusion: While adult-onset SjD is characterised by peripheral CD4+ T-cell lymphopenia2, we detected an opposite trend towards significant expansion of CD4+ T-cell subset frequencies in cSjD. This could have significant therapeutic implications, suggesting that cSjD may recapitulate the early phase of the corresponding adult disease phenotype, when treatments with T-cell targeted (such as abatacept, low dose IL2) or broader (such as leflunomide or cyclosporine A) effects could be beneficial.

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SCREENING FOR COMORBID AUTOIMMUNE DISEASE SHOULD BE CONSIDERED IN CHILDREN WITH ANA POSITIVE JUVENILE IDIOPATHIC ARTHRITIS – RESULTS FROM THE SOUTH-SWEDISH JUVENILE IDIOPATHIC ARTHRITIS COHORT

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Introduction: There are no consensus or clinical guidelines for screening routines of autoimmune diseases in patients with juvenile idiopathic arthritis (JIA), since results are conflicting whether the risk for such conditions is increased (1-5).

Objectives: To investigate the occurrence- and the need for screening routines for comorbid autoimmune conditions in JIA by using a validated population-based JIA cohort from southern Sweden.

Methods: Autoimmune comorbidities were evaluated in a pre-existing population-based JIA cohort of 302 participants, constituting of individuals diagnosed with a validated JIA diagnosis 2000–2010 in southern Sweden. The comorbidities were determined through analysis of diagnosis codes registered after JIA diagnosis until 2019. Two registered diagnosis codes at separate outpatient healthcare visits or one registered inpatient diagnosis code was considered as a verified comorbidity. With the use of a reference population of 1510 age- and sex matched individuals, hazard ratios (HR) were calculated with Cox proportional models, and to further explore potential predictors for comorbid conditions, subgroup analyses of patient characteristics were performed.

Results: During the study period, 7.7% of the JIA cohort received an autoimmune diagnosis after their JIA diagnosis. JIA patients had an increased risk of autoimmune diseases in general (HR 2.01, 95% CI 1.16-3.51), as well as separately for celiac disease (HR 3.98, 95% CI 1.44-11.01) compared to the reference population. Antinuclear antibody (ANA) positivity as well as treatment with disease-modifying anti-rheumatic drugs (DMARD) was associated with a significantly increased risk of comorbid autoimmune disease in the JIA cohort.

Conclusion: JIA patients have a significantly increased risk of acquiring an autoimmune disease after receiving their JIA diagnosis compared to matched references. ANA positivity and treatment with DMARD are associated with a further increased risk. Our results emphasize awareness in physicians of additional autoimmune disorders in JIA patients and advocate serological screening of autoimmune conditions during follow-up, potentially preventing morbidity and the adverse effects of untreated, undiagnosed disease.

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EVALUATION OF ILAR AND PRINTO CLASSIFICATIONS FOR JUVENILE IDIOPATHIC ARTHRITIS: OLIGOARTICULAR JIA VS EARLY-ONSET ANA POSITIVE JIA

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Introduction: International League of Associations for Rheumatology (ILAR) juvenile idiopathic arthritis (JIA) classification revisited by Pediatric Rheumatology International Trials Organization (PRINTO) in 2018. Classifications should provide uniform groups to assist physicians to provide optimal care.

Objectives: We evaluated changes proposed by PRINTO to highlight their impact on forming consistent groups regarding uveitis and treatment responses, particularly focusing on early-onset anti-nuclear antibody (ANA) positive JIA.

Methods: Pediatric patients diagnosed with JIA according to ILAR and PRINTO classification, with a minimum one-year follow-up, were enrolled, excluding those meeting both oligoarticular JIA and early-onset ANA positive JIA groups' exclusion criteria.

Results: Among 139 enrolled patients, 110 (79.1%) had oligoarticular JIA, while 15 (10.8%) had early-onset ANA-positive JIA. Below age 5 criteria showed the strongest association with uveitis, while below age 7 provided similar associations without substantial exclusions (Odds ratio 8.62 [2.50-29.81] vs 7.45 [2.37-26.66]). Patients with single ANA positivity at a titer ≥ 1/160 and below age 7 had a notably higher risk of new-onset uveitis and biologic DMARDs requirement (Odds ratio 7.95 [2.37-26.66] and 3.6 [1.42-9.09], respectively).

Conclusion: Inclusion of age of disease onset and ANA positivity with a titer ≥ 1/160 has enhanced uniformity in uveitis risk and treatment response, including conventional synthetic DMARDs failure. A single ANA positivity at a ≥ 1/160 titer yields similar or better results, while the involved joint count criteria failed to form consistent groups. PRINTO's classification places a significant portion of patients into the "other JIA" group, necessitating further classification for improved clinical utility.

INCIDENCE OF JUVENILE IDIOPATHIC ARTHRITIS IN FINLAND, 2000–2020

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Introduction: The last epidemiological data of JIA in Finland are from the turn of the millennium, including restricted study periods and geographical coverage (1-4).

Objectives: The aim of this study was to assess the recent annual incidence of JIA in several consecutive years in Finland across different patient groups, subtypes and hospital districts.

Methods: All children <16 years of age who met the ILAR classification criteria for JIA were analyzed. Cases from 2000-2020 were identified from two national registers: the Care Register for Health Care of the Finnish Institute for Health and Welfare and the Reimbursement Register containing medication data from the Social Insurance Institution of Finland; cases from 2016-2020 were identified from the Finnish Rheumatology Quality Register. Joinpoint regression analysis on a logarithmic scale was used to detect increasing or decreasing trends in incidence over follow-up time segments. The annual percentage change (APC) was used to characterize trends in the incidence rate of JIA.

Results: The incidence of JIA was 31.7 per 100,000 (95% CI 30.2, 33.1), according to the Care Register in 2000-2020. Around the year 2012, the incidence peaked to 37.6 per 100,000 (95% CI 33.8, 41.7), but the annual incidence was similar at the end (28.7 per 100,000; 95% CI 25.3, 32.3) of the study period compared to the beginning (29.3 per 100,000; 95% CI 26.0, 32.8). No considerable differences in incidence rates were observed among registers. In all age groups, incidence in girls was predominant compared to boys. The incidence in girls peaked at the ages of 2 years (78.8 per 100,000; 95% CI 71.8, 86.3) and 14 years (50.7 per 100,000; 95% CI 45.4, 56.6). Decreasing incidence was observed among boys 0-3 years old during the entire study period (APC -2.5%; 95% CI -4.5%, -0.5%; p=0.016), whereas increasing incidence was observed in 2000-2013 among teenage girls (APC 5.7%; 95% CI 2.8%, 8.6%; p=0.001) and 4-7 years old boys (APC 3.8%; 95% CI 1.3%, 6.4%; p=0.006).

Conclusion: The incidence of JIA in Finland is globally high and higher than previously reported. Regional and annual variations in incidence of JIA were observed, yet the overall incidence remained stable at the end of the study period.

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GLUCOSE METABOLISM IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) represents a chronic inflammatory disease in childhood. From a pathophysiological point of view, the underlying immune dysregulation and inflammatory cytokines overproduction in JIA resembled those observed in adult rheumatoid arthritis (RA). As a consequence, chronic inflammation leads to insulin-resistance (IR), in turn resulting in glucose metabolism abnormalities. Although there is evidence in adults with RA for an increased risk of type 2 diabetes (T2D) and metabolic syndrome, similar data in children with JIA are still scarce.

Objectives: To investigate glucose metabolism in a cohort of children with JIA.

Methods: One-hundred thirty-nine children diagnosed with JIA classified according to the International League of Association for Rheumatology (ILAR) criteria attending our Rheumatology Clinic were retrospectively examined. Patients with acute conditions (e.g. severe infections, trauma, exacerbation of chronic disease) or diagnosed with type 1 diabetes or T2D prior to the study enrollment were excluded.

A detailed anthropometric and biochemical evaluation including homeostasis model assessment of insulin resistance (HOMA-IR) and *hemoglobin* A1c (HbA1c) assessment was performed in all the enrolled subjects. IR was defined according to HOMA-IR cut-offs for sex and pubertal stage. Disease activity was calculated by using the Juvenile Arthritis Disease Activity Score 10 (JADAS-10) joint reduced count, and cut-offs for disease states were applied. Based on JADAS-10 score, four categories of disease status such as “inactive disease”, “low disease activity”, “moderate disease activity”, and “high disease activity” were identified.

According to BMI-SDS quartiles, patients were divided into four groups. At the examination of the study population at the time of JIA diagnosis, none of patients received any pharmacological treatment.

Results: No differences for sex, age at disease onset, Tanner stage, and disease duration across the groups were found (all $p>0.05$). A trend for JADAS-10 score across BMI-SDS quartiles was observed ($p=0.06$), but disease activity did not significantly differ ($p=0.09$).

Compared to patients in the lower quartiles, those belonging to the highest quartile showed increased systolic and diastolic blood pressure, alanine transaminase (ALT), fasting insulin, and low-density lipoprotein (LDL) levels ($p=0.01$, $p=0.01$, $p=0.01$, $p=0.008$, and $p=0.04$, respectively). As inflammation markers, ferritin, C-reactive protein, and erythrocyte sedimentation rate levels did not significantly differ across BMI-SDS quartiles (all $p >0.05$).

Out of 139, 7 patients (5%) showed a HbA1c value between 5.7-6.5% and 3 (2.1%) had impaired fasting glucose as prediabetes phenotypes.

As cardiometabolic risk markers, they also presented with increased uric acid and tryglycerides (TG)/high-density lipoprotein (HDL) ratio values ($p=0.03$ and $p=0.04$, respectively). Both HOMA-IR, and HbA1c values significantly increased across BMI-SDS quartiles ($p=0.028$ and $p=0.026$, respectively). A higher percentage of subjects with IR was found in the highest quartile compared to others ($p=0.03$). Patients belonging to the highest quartile showed an adjusted odds ratio (OR) to show IR of 1.78 (95%

CI 1.07-2.94, p=0.025).

Conclusion: Overweight/obese children diagnosed with JIA showed an overall unfavorable cardiometabolic risk profile. These patients also presented with an increased risk of IR and prediabetes. Given the higher risk of developing T2D, cardiovascular disease, and metabolic syndrome overtime, a careful monitoring of glucose metabolism should be warranted in children with JIA. Further longitudinal studies in the field are required to confirm these important findings for pediatric cardiometabolic health in children with JIA.

CLINICAL INSIGHTS INTO HETEROGENEITY OF RHEUMATOID FACTOR NEGATIVE POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS ACROSS THE WORLD

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Introduction: Limited information is available about the differences in the characteristics of rheumatoid factor (RF)-negative polyarticular juvenile idiopathic arthritis (JIA) throughout the world.

Objectives: To compare the demographic and clinical features of patients with RF-negative polyarthritis across the world, in order to gain further insights into the geographic variability of this JIA subtype.

Methods: Data were extracted from a dataset of 9,081 subjects with JIA from 49 countries enrolled in the Epidemiology, treatment and Outcome of Childhood Arthritis study (1). All patients underwent a retrospective data collection and a cross-sectional assessment. Demographic and clinical data were compared across 8 geographic areas (northern Europe, western Europe, southern Europe, eastern Europe, North America, Latin America, Africa and Middle East, and southeast Asia). Dunn's test and Bonferroni correction were used for post-hoc analysis.

Results: 2,141 patients (23.6%) with RF-negative polyarthritis were included in the analysis. The prevalence of RF-negative polyarthritis was highest in North America (31.5%) and lowest in southeast Asia (12.7%). Age of onset showed a biphasic distribution in all areas. Northern and southern Europe presented the highest prevalence of patients with a disease onset before 6 years of age. Those two areas presented a significantly higher prevalence of uveitis (21.1% and 14.2%), as compared to western and eastern Europe (9.6% and 8%) and North America (9.1%), and to Southeast Asia (4.2%), Africa & Middle East (4.1%) and Latin America (1.8%). ANA positivity was more frequent in western and southern Europe (51% and 62.7%). The proportion of patients treated with conventional disease-modifying antirheumatic drugs (DMARDs) ranged from 75.8% (North America) to 93.8% (Southeast Asia). Biological DMARDs were used mostly in northern Europe and North America and less frequently

in southeast Asia. The prevalence of active joints at the cross-sectional visit resulted significantly lower in northern and southern Europe, and higher in eastern Europe. Subjects from southern Europe presented less frequently pain, morning stiffness and impairment of overall well-being, quality of life and function ability. The frequency of inactive disease resulted higher in patients from southern Europe. Subjects from Africa and Middle East and eastern Europe showed the highest scores of composite disease activity measures. Patients with early disease onset and ANA positivity, whose association resulted higher in southern Europe, presented a higher prevalence of uveitis but better outcomes in terms of joint count, physician and parent global assessments, physical function, quality of life, and disease activity.

Conclusion: Our results confirm the wide heterogeneity of the clinical presentation and outcome of children with RF-negative polyarticular JIA throughout the world. Patients with early disease onset and ANA positivity, predominant in southern Europe, showed a higher prevalence of uveitis but better outcomes in terms of joint disease. Further studies are needed to assess genetic and environmental factors underlying these findings.

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Juvenile dermatomyositis

THE USE OF ARTIFICIAL INTELLIGENCE SOFTWARE COMPARED WITH RECOMMENDED CLASSICAL SOFTWARE FOR THE QUANTITATIVE ASSESSMENT OF PATIENTS WITH JUVENILE DERMATOMYOSITIS

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Introduction: Introduction: Juvenile Dermatomyositis (JDM) is the most common of the pediatric inflammatory myopathies characterized by inflammatory microvasculopathy. Clasical software of Nailfold videocapillaroscopy (NVCP) is an in-vivo, rapid, and inexpensive imaging technique that allows quantitative assessment of microcirculation and storage of images for clinical and research. The SHARE guidelines for JDM recommends realization NVCP at diagnosis.(1) The resent uses of Artificial intelligence (AI) in software for analysis of capillaries was documented for adults(2) and demonstrates could differentiate between a healthy child and a JDM patient (3). But there is a lack of information regarding the reliability and concordance between the use of the validates software recommended by Microvasculatory Study Group of EULAR (Optipix) and Artificial Intelligence software (Capillary.iO

Objectives: Objectives: To compare the quantitative assessment of microvasculature of patients with JDM using the software Optipix by manual measure with the IA software to assess reliability between both systems

Methods: Methods: The present study was a cross-sectional observational NVCP was performed by the same examiner (AVT) Using the Software Optipix using an Optilia Videocapilaroscope at 200x optical prove, 4 (A-B-C-D) images were obtained from all fingers except thumbs of both hands using a

videocapillaroscope equipped with a 200x optical probe. The images were collected, coded, and stored using OptiPix software (version 1.7.16), 2015 Optilia Instruments. Same images at the same resolution were analyzed by de (AI) software. The statistical analysis were performed by SPSS 21.0, frecuecnces, percentages, mean and SD was made.

Results: A of 832 images were analyzed from 15 patients with JDM, 85% of patients were female and all have cutaneous activity during the assessment Mi2 was founded in 5.3%, and NXP2 8%. The qualitative assessment (Capillary Density, Apical Diameter, arterial and venous diameter) were performed by the two software, the analysis shows differences between the two softwares regarding the reliability in 96% of the images regarding the quantitative. Non statistical diference were found. Kappa 0.39 (p> 0.05).

Conclusion: Conclusion: NVCP is an useful tool to asses and diagnosis of the JDM patients, we didn't found correlation between the use of IA in patients with disease activity, and better correlation with active disease using the recommended software Optipix.

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SUCCESSFUL TREATMENT OF AN ANTI-MDA5 ANTIBODY-POSITIVE JUVENILE DERMATOMYOSITIS PATIENT WITH REFRACTORY INTERSTITIAL LUNG DISEASE USING TOFACITINIB

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Introduction: Juvenile dermatomyositis (JDM) is a rare systemic autoimmune disorder affecting children, mainly characterized by skin and muscle vasculopathy. Some patients also manifest life-threating complications of the disease, such as interstitial lung disease (ILD). Anti-MDA5 antibody-positive JDM represents a distinct phenotype of disease with a high risk of developing rapidly progressive or refractory ILD. A large body of evidence suggests the pivotal role of type I interferon (IFN) pathway in the pathogenesis of JDM.

Objectives: To report the efficacy and safety of tofacitinib, a Janus kinase (JAK) 1/3 inhibitor, in treating an anti-MDA5-positive JDM young girl with refractory ILD, highlighting the potential of JAK inhibitors

as targeted therapy in these patients.

Methods: A retrospective review of patient's clinical records, including laboratory and radiological findings, was performed. Laboratory evaluations focused on muscle enzymes, inflammatory markers, myositis-specific autoantibodies and type I IFN signature. Radiological assessments used chest HRCT to track ILD progression, and total body short tau inversion recovery (STIR) magnetic resonance imaging (MRI) to evaluate potential sub-clinical muscle involvement.

Results: A previously healthy 7-year-old female patient of Caucasian ethnicity, presenting with a 6-month history of fatigue, weight loss, skin lesions and mildly impaired muscle strength, was diagnosed with anti-MDA5 positive JDM. During the diagnostic work-up performed at disease diagnosis, JDM-associated ILD was also detected. Initial treatment with methylprednisolone pulses followed by high-dose intravenous glucocorticoids, oral cyclophosphamide and monthly intravenous immunoglobulin (IVIG) infusions led to skin and muscle disease remission (normal muscle strength and negative total body STIR MRI). Nevertheless, lung disease showed no significant signs of improvement, exhibiting both clinical and radiological deterioration over time. Supported by reports on adult-onset DM and the presence of the elevated type I-IFN signature in the patient, tofacitinib in combination with subcutaneous methotrexate and IVIG were initiated. This treatment led to a stable remission, near-complete resolution of the pulmonary involvement, and discontinuation of glucocorticoids. No adverse effects were observed during 2-year follow-up evaluations.

Conclusion: This case underscores the promising efficacy and safety of tofacitinib in managing anti-MDA5-positive JDM with ILD non-responsive to aggressive conventional immunosuppressive treatments. It also emphasizes the importance of early suppression of disease activity and the potential benefits of employing targeted therapies based on specific biomarkers, such as type I IFN signatures. Future research should focus on the design of international randomized controlled trials aimed to assess the efficacy and safety of JAK inhibitors in JDM, as to foster personalised treatment approaches and improve patient outcomes.

ANALYSIS OF TREATMENT APPROACHES IN JUVENILE DERMATOMYOSITIS PATIENTS IN THE JIR-COHORT DATABASE

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Introduction: Juvenile Dermatomyositis (JDM) is extremely rare, yet the most common idiopathic inflammatory myopathy in childhoodi, inflicting vasculopathic damage to muscle, skin and visceral organs. Treatment approaches vary widely globally, hindering standardisation and optimisationii. The JIR-Cohort, currently comprising data from aproximately 13,000 rheumatic disease patients across 10 countries, serves as an international network, a research tool and an electronic health recordiii

Objectives: We conducted an observational patient cohort study involving 250 JDM patients from 6 countries between January 2022 and June 2023, with retrospective data accepted from January 1990,

aiming to compare clinical care, treatment approaches and disease activity, while focusing on the use of immunosuppressive agents and IgG-formulations in this cohort.

Methods: Disease progression and activity were assessed up to 24-months post-diagnosis, with initial response categorised based upon steroid response. Disease activity was evaluated using established assesment tools (Visual Analogue Scale (VAS), childhood myositis assessment scale (CMAS) and physician assessment). We initially examined a smaller cohort of patients (n=57), hencefore referred to as 'test cohort', from four pediatric rheumatology centres with comprehensive datasets.

Results: The average age of the test cohort was 7.2 ± 3.6 years; upon diagnosis 87.7% presented with muscle involvement, 98.3% with skin involvement. 68.4% of patients tested positive for autoantibodies, with the most common being anti-nxp2 (15.8%), anti-mda5 (10.5%), anti-mi2 (7.0%) and anti-pmscl (7.0%). Additionally, 17.5% of the cohort received IgG-formulation (intravenous or subcutan) therapy.

Conclusion: Preliminary findings indicate demographic comparability with prior JDM cohortsiv. Statistical analysis of the test cohort is ongoing, with the goal of developing an algorithm that can be applied to the complete project cohort. Particularly the international nuances in steroid and IgG therapy are challenging to unravel, further underscoring the need for an international standardisation of treatment plans.

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Pain, fatigue, disease experience and quality of life

EFFICACY AND SAFETY OF ACUPUNCTURE IN JUVENILE FIBROMYALGIA SYNDROME: RESULTS OF A PILOT STUDY

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Introduction: Juvenile fibromyalgia syndrome (JFS) is a chronic disabling condition characterized by widespread non-inflammatory musculoskeletal pain, fatigue, sleep and mood disorders. Management of JFS requires a multidisciplinary approach with a combination of non-pharmacological and

pharmacological treatment modalities. Systematic reviews suggest that acupuncture may reduce pain and improve well-being in adults with fibromyalgia (1). No data are available for JFS.

Objectives: To investigate the efficacy and safety of acupuncture in patients with JFS.

Methods: We retrospectively analysed data of patients with JFS diagnosed according to the 2010 American College of Rheumatology (ACR) criteria, who underwent a course of six weekly sessions of acupuncture treatment in our institute during the past 2 years, due to significant refractoriness/intolerance to pharmacological therapy. Clinimetric assessment was based on multiple patient-reported outcomes (PROs), including: 1) 0-10 numeric rating scales (0=no symptoms, 10= great deal of symptoms) to measure the severity of musculoskeletal pain, fatigue, sleep quality, wake-up tiredness, headache, anxiety and depression, cognitive disturbances, abdominal pain and overall patient well-being); 2) Physical Function and Health-Related Quality of Life Questionnaire. Significant improvement, defined as a reduction of at least 30% in the PROs, was assessed at the end of the six-week treatment period.

Results: Ten female patients (median age 16.9 years, median disease duration 3.4 years) were included in this pilot study. Five patients were receiving pharmacological therapy (1 on pregabalin, 3 on amitriptyline, 1 on duloxetine) at stable doses for three months prior to treatment and during the study period. One patient discontinued treatment during the first session due to needle phobia. At the end of 6 weeks of acupuncture treatment, a significant reduction in the severity of musculoskeletal pain and headache was observed in 88.9% and 55.6% of patients, respectively. The median pain score was 8 (6-9) before treatment and significantly decreased to 2 (0-6.5), p=0.007, after treatment. Similarly, headache severity decreased from 6.5 (2-9.5) to 4 (0-7), p=0.01. Improvement in cognitive impairment was also seen in 33.3% of patients, with the median cognitive impairment score decreasing from 8 (7.5-9.5) to 6.5 (4-9), p=0.02. There was no significant improvement in other JFS-related symptoms, physical function, or health-related quality of life. Acupuncture was not associated with serious adverse events and had a reliable safety profile.

Conclusion: Acupuncture may be considered a potentially effective and safe therapeutic option for reducing musculoskeletal pain and headache in JFS. Our results suggest its use as part of a multimodal approach to the treatment of JFS. Further research is likely to provide data on effective regimens and combination therapies.

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Spondyloarthritis (SpA) and enthesitis related arthritis (ERA)

TEMPORAL TRENDS IN AND ASSOCIATIONS WITH NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID) PRESCRIPTION IN ADULT AND PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The role of nonsteroidal anti-inflammatory drugs (NSAIDs) in the management of patients with inflammatory bowel disease (IBD) and IBD-associated arthritis is unclear in light of mixed data on intestinal safety, and United States national prescribing patterns in patients with IBD are unknown.

Objectives: The objectives of this study are to determine real-world use of prescription NSAIDs in patients with IBD across the age spectrum, including factors associated with NSAID prescription and how NSAID prescribing patterns have changed over time.

Methods: This is a retrospective cohort study from 2000-2022 in Optum's de-identified Clinformatics® Data Mart Database. Children and adults with IBD and available pharmacy claims data were enrolled. NSAID and opioid prescriptions per calendar year were assessed. Descriptive statistics were used to assess differences in characteristics between adult vs. pediatric patients. Wilcoxon-Cruzick test of trend and generalized estimating equation models were used to evaluate trends in NSAID and opioid prescribing and assess characteristics associated with NSAID use.

Results: 361,025 patients met inclusion criteria of which 12,930 (3.6%) were <18 years old. 99,895 (27.7%) patients had at least one prescription NSAID during the study period. Adults were more likely than children to have 1 NSAID (28.1% vs. 14.9%, p<0.01) or opioid prescription (53.5% vs. 37.2%, p<0.01). They were also more likely to have ³1 diagnosis code for inflammatory arthritis, osteoarthritis, other joint pain not otherwise specified (NOS), or chronic pain (p<0.01 for all) irrespective of NSAID prescription. There was a significant decreasing trend in the proportion of patients prescribed NSAIDs over time (p<0.01). In the multivariable model, opioid prescription (OR 2.12, 95% CI 2.10-2.14), or a diagnostic code for inflammatory arthritis (OR 1.23, 95% CI 1.21-1.25), osteoarthritis (OR 1.56, 95% CI 1.54-1.58), or joint pain NOS (OR 1.59, 95% CI 1.57-1.61) had strong independent associations with NSAID prescription, while age <18 (OR 0.54, 95% CI 0.51-0.57) or 80 years (OR 0.69, 95% CI 0.67-0.71) at date of first IBD code were associated with significantly lower odds of NSAID prescription.

Conclusion: NSAID prescription in patients of all ages with IBD is common but fill patterns decreased over time. Pediatric patients were least likely to receive NSAIDs even though the comorbidity and side effect profile may be more favorable in this population.

EVALUATION OF DISEASE SEVERITY AND TREATMENT RESPONSES IN PATIENTS WITH ENTHESITIS-RELATED ARTHRITIS

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Introduction: Enthesitis-Related Arthritis (ERA) is a chronic inflammatory arthritis classified as a type of Juvenile Idiopathic Arthritis(JIA), constituting 15-20% of all cases(1). Sacroiliac joints are often involved (2).

Objectives: The objective of this study is to assess the disease severity and treatment responses in ERA patients.

Methods: This is a single-center retrospective cohort study evaluating ERA patients (aged 0-18 years) diagnosed between 2009-2023.The demographic and disease characteristics of patients, disease activity scores were recorded at the initiation of treatment, 12th weeks and current visits.

Results: Of the 118 patients, 72% were male and 28% were female. The median age at diagnosis was 13,3 (5,4-17,6) years. In the family history, 10,2% had ankylosing spondylitis and 2,5% had inflammatory bowel disease. As for comorbidities, 12,7% had Familial Mediterranean Fever (FMF), 4,2% had chronic recurrent nonbacterial osteomyelitis (CRMO), 3,4% had Crohn's disease and 1,7% had both FMF and Crohn's disease. HLA-B27 was positive in 51,7% of all cases, in 40% of FMF, in 40% of CRMO and in 25% of Crohn's patients.

At diagnosis, axial involvement and enthesitis were present in 55,9% and 49,2%, respectively. ESR was elevated in 44,1% and CRP in 83,1% of patients. At onset, median values for the Bath Ankylosing Spondylitis Dissease Activity Index (BASDAI) were 4 (0,8-8), for the Juvenile Arthritis Disease Activity Score (JADAS) were 14 (3,7-26,7) and for the Juvenile Spondyloarthritis Disease Activity Index (JSpADA) were 3 (1-7). The scores at diagnosis were found to be correlated in the repeated measures ANOVA analysis.

All patients were on Nonsteroidal Anti-Inflammatory Drugs(NSAIDs), while 46,6% sulfasalazine, 70,3% methotrexate, 64,4% anti-TNF agents, 39,8% (short-course) systemic steroids, 17,8% intra-articular steroids and 2 patients received secukinumab. The median values for BASDAI, JADAS, and JSpADA at the 3rd month were 1,6 (0-4,9), 5 (0-14,6), 1,5 (0-5) for patients taking NSAIDs (n=26); 1,4 (0-5,7), 4 (0-19), 1 (0-5) for those taking sulfasalazine (n=33); and 2 (0-6,4), 6 (0-24,1), 1,8 (0-7) for patients receiving methotrexate (n=79), respectively. For patients receiving anti-TNF agents, median activity scores at the 3rd month were all zero.

In current evaluations, ongoing treatments were as follows: NSAIDs 8,5%, sulfasalazine 4,2%, methotrexate 2,5% and anti-TNF agents in 68,4%.

Conclusion: The three acitivty scores had a good correlation. Although more patients achieved remission with anti-TNF agents, a group of patients responded to DMARDs.

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Systemic JIA

INTERSTITIAL LUNG DISEASE IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: A NATIONWIDE STUDY

D. Ünal [1,*], E. K. Könte [2], E. Çelikel [3], H. K. Zora [4], M. K. Gürgöze [5], V. Çam [1], Y. Bayındır [1], H. E. Emreol [1], Ö. Başaran [1], K. Barut [2], Y. Bilginer [1], Ö. Kasapçopur [2], S. Özen [1].

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Introduction: Interstitial lung disease (ILD) is becoming a major concern in systemic juvenile arthritis (sJIA). Several previous studies showed the severe course and fatal outcomes in these patients.

Objectives: To describe the features of sJIA patients with ILD from Turkey.

Methods: In the present retrospective cohort study, 18 patients younger than 18-years-old with sJIA and ILD were included. The diagnosis of sJIA was made according to the 2004 ILAR criteria. ILD was diagnosed with chest computed tomography with the exclusion of other possible reasons. Macrophage activation syndrome (MAS) was diagnosed with HLH-2004 and 2016 EULAR/ACR/PRINTO Classification Criteria.

Results: The onset age of sJIA ranged from 2 years to 16 years. Eight of the patients were female. The time interval between the diagnosis of sJIA and the development of ILD ranged from 2 months to 8 years. Ninety four percent (17/18) of the patients had a history of MAS, twelve of them had a MAS episode concomitantly with ILD diagnosis. Cough was the most common symptom in 94% (17/18), followed by dyspnea (83%) and clubbing (83%). Thirteen patients (72%) had been treated with anakinra and six out of these 13 patients were discontinued because of having diagnosed with sJIA-ILD and were switched to other drugs such as JAK-inhibitors. Three of the patients stopped treatment because they were in remission. Three of the ILD patients were positive for HLA DRB1*15. Adverse reactions to anti-IL-6 agent-had been observed in two patients. Only one patient (5,5%) had hyper-eosinophilia. Eight had ground-glass opacity on radiographic examination. Two patients (11%) developed pulmonary arterial hypertension. Six (33,3%) patients had sJIA-ILD remission clinically and radiologically. Mortality was seen in only one patient.

Conclusion: ILD is a severe life-threatening complication of sJIA that may affect children of different ages with different time intervals. Further studies are needed to define predictors, and treatment options, for preventing and treating ILD in sJIA.

WORLDWIDE EVALUATION OF CLINICAL PRACTICE STRATEGIES (CLIPS) FOR LUNG INVOLVEMENT IN STILL'S DISEASE WITHIN THE JIR-CLIPS NETWORK: A COST ACTION

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Introduction: Recent literature has documented a subset of patients with severe Still's Disease who are prone to develop lung disease (LD). This condition is described in both systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD). It may manifest as interstitial lung disease, pulmonary arterial hypertension, and/or alveolar proteinosis. The management of this complication remains challenging for physicians as it is often refractory to conventional treatment.

Objectives: This study aims to outline global clinical practices for Still's associated lung disease through the Clinical Practice Strategies (CliPS) network and compare them with existing recommendations.

Methods: This study is part of the CLiPS project, a work dedicated to capture clinical practice strategies worldwide by disseminating questionnaires to physicians about five diseases, including Still's disease. The project, funded as a COST (European Cooperation for Science and Technology) action, has been distributing the questionnaires since September 2022 through the JIRcohort network and national societies.

Results: On April 14, 2024, 337 physicians responded to the Still's disease questionnaire. Fifty-eight physicians (17%) from 5 continents reported following patients with lung involvement. Most respondents were pediatricians (86%) but adults rheumatologists (n=8/58) also reported encountering this condition. Acute digital clubbing, history of recurrent MAS and adverse events to cytokine-targeted biotherapies were identified as key clinical features to evoke LD. Radiography and thoracic computed tomography were performed by the majority of physicians (92% and 78% respectively). Bronchoalveolar lavage was carried out systematically by 40% of respondents. Cardiac echocardiography was performed either always (78%, 39 out of 50 respondents) or sometimes (22% of the respondents) to rule out pulmonary hypertension. Pulmonary biopsy was not deemed necessary to confirm lung disease. In fact, 71% of physicians performed biopsies occasionally, while the remainder never found the need for this invasive procedure. HLADRB1*15 was used by 65% of physicians to support LD diagnosis. Fifty percent of participants could use interferon signature to aid in the management of these patients while IL-18 cytokine assay is performed by a few clinicians (8/24 participants, 33%). Thirty-seven percent of the respondents chose to continue the same treatment with additional therapeutics, while 31% decided based on the effectiveness of biological treatment to control systemic activity, and 17% chose to stop biologics. JAK inhibitors were the medication most frequently chosen as additional treatment (n=25), followed by cyclosporine (n=18) and mycophenolate mofetil (n=14).

Conclusion: This study highlights variations in medical approaches regarding screening, follow-up and treatments for Still's Disease-LD. There is a need to define real-life clinical practice strategies that are tailored to the specific contexts of different regions worldwide to enhance the management of these

patients.

Systemic lupus erythematosus and antiphospholipid syndrome

THE RELATIONSHIP BETWEEN DISEASE PERCEPTION, DISEASE COURSE, AND QUALITY OF LIFE IN CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by recurrent flares affecting various organs such as skin, joints, and kidneys. One of the treatment goals for SLE is to preserve and improve patients' quality of life. Patients' perceptions of their disease and it's treatment can influence their quality of life.

Objectives: This study aims to evaluate disease perceptions in childhood SLE patients and their interaction with patient-parent quality of life.

Methods: Patients diagnosed with childhood SLE according to the SLICC 2012 classification were included between January 2023 and November 2023. Disease perception was assessed using the Brief Illness Perception Questionnaire, while quality of life was evaluated using PedsQL in patients and WHOQOL-BREF in parents.

Results: The study included 32 patients and 32 parents. Of the patients, 25 were female (78.1%), and 7 were male (21.9%), with a female-to-male ratio of 3.6. The mean age was 17.7±2.2 years, the median age at diagnosis was 13.9 years (range: 1.23 to 17.25 years), and the median disease duration was 4.2 years (range: 0.25 to 13.42 years). The most common organ involvement was musculoskeletal involvement in 21 patients (65.6%), followed by skin involvement in 19 patients (59.4%), and kidney and hematological involvement in 16 patients each (50%). No patient had neuropsychiatric involvement. The median SLEDAI score at the last visit was 2 (range: 0-18). The mean score of the Brief Illness Perception Questionnaire was 36±10.3. When categorized, 20 patients (62.5%) had low threat perception, 9 (28.1%) had moderate, and 3 (9.4%) had high threat perception. There was a significant negative correlation between patients' disease perception and quality of life (r=0.576, p=<0.001). However, there was no correlation between any subscale of parental quality of life and patients' disease perception (p=>0.05). The number of patients with a PedsQL total score below the cut-off value (<70) was 18 (56.3%), while 14 parents (43.8%) had a WHOQOL-BREF general health score below the cut-off value (<60).

Conclusion: Although disease perception in childhood SLE was not associated with disease activity, it was negatively correlated with patient quality of life. According to these results, approaches aimed at improving patients' perceptions of SLE and its treatment may be beneficial for enhancing their quality of life.

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (AHSCT) FOR TREATMENT-REFRACTORY AUTOIMMUNE DISEASES IN CHILDREN

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Introduction: Autoimmune diseases constitute a broad spectrum of conditions characterized by immune system dysfunction, leading to inflammation and affecting multiple organs. Despite advancements in treatments such as biologics and targeted synthetic drugs, certain patients continue to grapple with severe forms of autoimmune disease that resist conventional therapies. In such cases, autologous hematopoietic stem cell transplantation (AHSCT) has emerged as a viable alternative, having been employed for over two decades to address treatment-resistant autoimmune diseases.

Objectives: To evaluate the long-term effectiveness and safety of autologous hematopoietic stem cell transplantation (AHSCT) for severe, refractory autoimmune diseases in paediatric patients.

Methods: A single centre study of consecutive children and adolescents with refractory autoimmune diseases undergoing AHSCT was performed. Demographics, clinical, laboratory features, pre-AHSCT medications, disease activity and functional status were captured. The primary outcome was progression free survival, secondary outcomes included overall survival, disease-specific treatment responses, disease activity at the last follow-up and AHSCT safety.

Results: The study included seven patients: 2 systemic sclerosis, 1 pansclerotic morphea, 1 eosinophilic fasciitis, 1 JDM and 2 sJIA patients. These were 4 females, 3 males with a median age at AHSCT of 10 years (7-19), median follow-up post-AHSCT of 17 years. Median progression free survival and overall survival was 4.2 years (95% CI: 0.98-8.3) and 17 years (95% CI: 11.8-22.1), respectively. Progression free survival rates at 1 and 2 years post-AHSCT were 100% and 77%, respectively. All children survived. All patients are in clinical remission, of whom only 4 require ongoing immunotherapy. Safety: Three patients experienced infections most commonly HHV6; one developed a systemic inflammatory response syndrome (SIRS); two developed new onset secondary autoimmune diseases and one was found to have a breast fibroadenoma. Treatment toxicity: one cyclophosphamide-associated transient renal failure and one patient with amenorrhea/infertility.

Conclusion: AHSCT was an effective and safe approach for children and adolescents with treatment-refractory autoimmune diseases. The indication and timing of transplantation requires a careful consideration and a multidisciplinary approach.

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Uveitis

UVEITIS ONSET IN JUVENILE IDIOPATHIC ARTHRITIS: DO WE NEED TO RECONSIDER FACTORS DRIVING THE OPHTHALMOLOGY SCREENING?

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Introduction: Juvenile Idiopathic Arthritis (JIA) is the most common chronic rheumatic disease in childhood, and it is burdened by uveitis (U) in the 20-24% of cases. In most of the cases U have an onset within the first years from JIA onset, and only a minimal part later. Based on this, an ophthalmology screening was built.

Objectives: To describe a cohort of children with JIA associated U (JIA-U) and to report the factors associated with a later U onset.

Methods: In a retrospective cohort study, we enrolled all patients currently followed in our Rheumatology Unit, with a diagnosis of JIA according to ILAR criteria and U history. Demographics, clinical, laboratory and treatment data were collected. The main outcomes were U onset after 4 years of JIA and the time lapse between arthritis and U onset.

Results: We identified 82 children with JIA-U (68 female (82.9%), 75 ANA positive (91.5%)), with a median age at onset of arthritis of 28 months(m) (IQR 23-51) and U onset of 48 m (IQR 31-88), and a median follow-up of 88 m (IQR 46-128). 78 children had anterior-U (95.1%), 51 oligoarticular-JIA (62.2%), 23 polyarticular-JIA (28%), 6 psoriatic JIA (7.3%) and 2 ERA (2.4%). The median time between arthritis and U onset was 5.5 m (IQR 0-29), with 10 children with U onset before arthritis (12.2%), 16 after 3 years of JIA (19.5%) and 10 after 4 years (12.2%). JIA-U showed a median ESR at onset of 36 mm/h (IQR 26-60) and a CRP at onset of 1.41 mg/dl (IQR 0.38-3.45).

35 JIA received at least a systemic treatment (ST) any time before U onset (42.7%). At U onset 32 were on ST (24 methotrexate, 4 etanercept and 3 adalimumab) (39%), 54 had active arthritis (65.9%) and 7 developed U after drug withdrawal (8.5%). We observed significant differences in the time between arthritis and U onset, regarding the biologic sex (9 m (female) vs 0.5 m (male), p 0.024), to be on ST at U onset (18 m vs 1 m, p <0.001), to have active arthritis at U onset (29 m vs 3 m, p 0.001), to have stopped the ST (50 m vs 4 m, p<0.001), to have received a ST any time (21m m vs 1 m p<0.001 (e-7)). Furthemore, we observed significant differences regarding U onset before/after 4 years of JIA and to be on ST at U onset (χ_2 5.85 p0.016) regardless of the specific ST, the arthritis activity ($\chi_2$6.58 p 0.01), the withdral of ST ($\chi_2$15.66 p0.001 (e-105)), to have received a ST any time before U ($\chi_2$8.18 p0.004), the ESR value at onset (p0.033) and CRP value at onset (p 0.002).

Considering the significant variables identified, performing logistic regression, the only variables associated to U onset after 4 years of JIA were the arthritis status (OR 0.169, CI 0.029-0.985), the ST status at U onset (OR 8.71 CI 1.19-63.5) and the withdrawal of ST (OR 15.70 CI 2.02-121.59).

Conclusion: As evaluated in our retrospective study, we observed that timing of U onset in JIA may be influenced by the ST status, to have withdrawn a ST and the arthritis status. If these findings will be duplicated in a larger cohort, the ophthalmology screening in high-risk patients should be intensified after drug withdrawal, in case of active arthritis without ST. Conversely, receiving a ST seems to be protective for the development of U during the disease course.

Vasculitides

BCG SITE REACTIVATION IN KAWASAKI DISEASE - A CLUE TO CORONARY ARTERY ANEURYSMS: 30 YEARS OF EXPERIENCE FROM NORTH INDIA

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Introduction: BCG site reactivation is a pathognomic finding in KD but has not been included in the American Heart Association guidelines (AHA). In this study we have reported tour experience on reactivation of the BCG site in children with KD.

Objectives: To asses the incidents of BCG site reactivation in Kawasaki disease and it's relation with coronary artery aneurysm.

Methods: We reviewed the records of all children who were diagnosed with KD over the period January 1994 - June 2023. Diagnosis of KD was based on AHA guidelines. Patients with documented BCG site reactivation were analysed

Results: We have diagnosed 1245 patients with KD, Of these, 20 patients were found to have BCG site reactivation. Male to female ratio was 1.8 :1. Median age at diagnosis was 6 months. Median duration of fever was 10 days. The commonest presentations were bilateral conjunctival suffusion and redness of lips which were seen in 80% (n=16). Maculopapular rash was noticed in 12 (60%). Perianal or perineal rash was seen in 9 patients (45%), while periungual peeling was seen in 60% (n=12). Edema of hands and feet was seen in 6 (30%) patients. Unilateral cervical lymphadenopathy was seen in 2 (10 %) patients. Irritability at admission was seen in 9 patients (45%). ECHO revealed CAAs in 11 patients (55%; ectasia in 4; small and medium aneurysms in 3; and giant CAAs in 4). All patients received IVIG (2g/kg) and aspirin. IVIG resistance was seen in 4 patients they received additional therapy with infliximab (5-10mg/kg single dose). Primary Intensification was done in 3 patients who had risk factors for CAAs. All 3 patients received infliximab. Cyclosporine and prednisolone were used in 1 each. Nine patients received rescue therapy for CAAs at presentation. Cyclosporine was used in 2, infliximab in 8, and prednisolone (2mg/kg) in 3 patients (gradually tapering doses over 6 weeks). Three patients had persistent aneurysms on follow-up. In addition to CAAs, one patient had systemic artery aneurysms involving common iliac, internal iliac, subclavian, and axillary arteries, while another had a thrombus

in the left anterior descending coronary artery.

Conclusion: While BCG site reactivation is considered to be pathognomonic of KD, it was observed in only 1.6% of patients in our cohort. This phenomenon is primarily noted in infancy. More than half of the children with KD exhibiting BCG site reactivation developed CAAs despite timely diagnosis and management. It is our contention that children with KD who have BCG site reactivation may have a more severe disease course.

EVALUATION OF PEDIATRIC IMMUNOGLOBULIN A VASCULITIS WITH GASTROINTESTINAL TRACT INVOLVEMENT: NORMAL VS ABNORMAL ABDOMINAL ULTRASOUND

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Introduction: Gastrointestinal (GI) tract involvement is observed in 50-75% of patients with immunoglobulin A vasculitis (IgAV). Abdominal ultrasound (US) is the most commonly used diagnostic tool to assess the severity and complications of GI inflammation in symptomatic patients [1].

Objectives: The aim of this study was to compare the clinical, demographic and laboratory data of IgAV patients with GI symptoms with and without normal abdominal US.

Methods: A total of 187 IgAV patients with GI tract involvement who were followed up for at least 3 months were included in the study. Clinical, laboratory, and radiological data of the patients were analyzed from electronic file records. The pediatric vasculitis activity score (PVAS) was used to evaluate disease activity.

Results: Abdominal US was normal in 69 (36.9%) patients at the onset of symptoms. In the control US of these patients, which was performed a mean of 2.6±1.3 days after the first US, 26 (37.6%) patients had abnormal findings suggestive of GI involvement, such as intestinal wall thickening and edema. Patients were divided into 2 groups as those with a normal initial and control abdominal US (Group 1, n=43) and at least one pathological US (Group 2, n=144). Gender (p=1), age at diagnosis (p=0.9) and duration of GI symptom development (p=0.32) were similar in both groups. The duration of hospitalization was longer in group 2 (p=0.001). There was no difference between the symptoms on admission and GIS symptoms, articular, renal, and scrotal involvement during follow-up. Massive GI tract hemorrhage was observed in 7 (16.3%) patients in Group 1 and 27 (18.8%) patients in Group 2 (p=0.82) (Table 1). All patients in Group 1 and 97.9% in Group 2 received steroid treatment. Pulse steroid was more commonly prescribed in Group 2, whereas patients in Group 1 were treated with a 2 mg/kg/day steroid (p=0.001). The mean duration of steroid usage was 44.9±47.1 days in Group 1 and 55±52.8 days in Group 2 (p=0.002). Cyclophosphamide was initiated in one (2.3%) patient in Group 1 due to massive GI tract hemorrhage. In Group 2, 14 (9.7%) patients received cyclophosphamide, 10 (6.9%) received intravenous immunoglobulin, and 2 (1.4%) underwent plasmapheresis. At the time of diagnosis, the median PVAS was 3 (IQR:2-3) in both groups (p=0.58).

Conclusion: GI complications are one of the most important causes of morbidity and mortality in the early stages of the disease. In some patients with severe GI tract involvement, intestinal wall abnormalities may not be demonstrated on US [2,3]. Therefore, treatment should not be delayed in patients with GIS complaints, even if abdominal US is normal.

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