SAT0520

DEFINING OUTCOME MEASURES IN JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS BY A SYSTEMATIC REVIEW ANALYSIS. DO WE NEED A CONSENSUS?

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Background: Juvenile Idiopathic Arthritis associated Uveitis (JIA-U) represents its most frequent extra-articular manifestation and the main cause of childhood uveitis in developed countries. The broad variety of outcome measures utilized makes the comparison of the disease course, risk for complications, impairment in visual function, and responses to treatment quite difficult.

Objectives: Our aim was to define related and unified outcome measures in JIA-U.

Methods: A systematic review between January 2000 and December 2018 was performed to identify studies investigating outcome measures used in JIA-U.

Results: The initial search identified 8252 articles of which 29 were potentially eligible. Eighteen eligible articles remained in the analysis. A total of 27 studies, including 2 RCTs, were included. Among these studies 12 outcome measures for JIA-U use have been identified (grade of cells in the AC, grade of flare in the AC, VA, amblyopia, structural complications, use and sparing of oral corticosteroids and immunosuppressive drugs, surgery requirement, biomarkers, bilateral disease, JIA persistence, quality of life assessments, uveitis subtype). As regards primary outcome measures, 44% among studies included one or more variables related to disease activity (i.e. grade of flare, grade of cells); 56% included visual function performance (i.e. visual acuity); 68% (17/25) included one or more variables of disease-associated tissue damage or complications (i.e. cataract, amblyopia); 24% included disease features (i.e. bilateral disease; uveitis subtype); 44% included laboratory features (i.e. biomarkers); 8% included JIA features (i.e. persistence of disease); 12% included quality of life (i.e. EYE-Q); 44% included management (i.e. use and sparing of oral corticosteroids and other immunosuppressive drugs; surgery requirement).

Conclusion: Our systematic review surveys the heterogeneity around outcome measures related to JIA-U in children, even in RCTs. It does not provide the solution to overcome the heterogeneity in uveitis studies, but it does provide an estimate of the scale of the problems and provides data to inform this important debate; highlighting the requirement to obtain a new consensus regarding a common approach to identify suitable and efficient outcome measures in JIA-U.

Figure 1. Study selection process flow diagram of literature research.

Legend. N= number of identified studies.

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SAT0521

RISK FACTORS FOR THE OCCURRENCE OF UVEITIS IN THE PATIENTS WITH OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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Background: Oligoarticular (oligo) onset juvenile idiopathic arthritis (JIA) is defined as 4 or fewer affected joints within 6 mo of disease onset. This JIA subtype typically involves large joints. Patients who develop arthritis in 4 joints after the first 6 mo are considered to have extended oligo JIA, and have a worse prognosis. Chronic uveitis is a common and serious comorbid condition of juvenile idiopathic arthritis, with insidious presentation and potential to cause blindness. Knowledge of clinical associations will improve risk stratification.

Objectives: We aim to analyzed identification of the incidence of oligo articular JIA-associated uveitis and its risk factors is essential to optimize early detection.

Methods: We enrolled 185 patients who were diagnosed with oligo JIA and seen at our clinic. Visual acuity was recorded in logMAR. LogMAR is the logarithmic representation of visual acuity. Visual impairment was stratified by severity as logMAR >0.3 (worse than 6/12) or ≥ 1.0 (6/60 or worse).

Results: A total of 185 oligo JIA patients were included in this study (61.6% female, 65.9% ANA positive). 32 of all patients (72.2%) developed uveitis within follow-up. The median age (IQR) at diagnosis was 89 (42-131.5) months, median follow-up of 24.5 (10-29) months. At disease onset, 12% of all patients were examined small joint arthritis (defined as involvement of any of the metatarsophalangeal or proximal or distal interphalangeal joints of the foot, or metacarpophalangeal or proximal or distal interphalangeal joints of the hand). 7 out of 35 (20%) patients with oligo onset JIA involving only small joints developed extended arthritis (>4 joints), compared to 15 out of 150 (10%) of patients with only large joint oligo onset JIA [p<0.01]. 10 of 32 patients with uveitis had small joints involvement (p<0.01)

Of these, 18 (56%) patients developed uveitis after enrollment while 14 (44%) patients had uveitis before first JIA symptoms. 58.8% of patients (n=8) developed uveitis with in first two years of JIA while 41.2 patients had uveitis developed up to 2 years. Uveitis was associated with positive ANA (p<0.001) and small joint involvement. In contrast, young age (< 7 years) at oligo JIA diagnosis, female sex, extended oligo JIA and used systemic steroid were not finding associated with uveitis. Of the 57 affected eyes, posterior synechiae (n=20) was the predominant complication on presentation. During the follow-up period new complications were seen in 11 eyes (13%). Posterior synechia (6 eyes, 7.5%) was the most frequent complication observed followed by cataract (3 eyes, 3%) and glaucoma (2 eyes, 2.5%). At the presentation, 8 patients (25%) had visual acuity loss to > 0.3 LogMAR (6/12) and to ≥1.0 LogMAR (6/60). However, 3 (0.09%) patients had visual acuity loss end of the follow up time. Biologically were used in 75% of JIA patients while 8 (25%) children with JIA did not require any biologic treatment. Systemic and topical steroids treatment were gradually tapered and discontinued in all patients after initiation of biologics. In JIA associated uveitis patients, biologic therapy was used in 24/32 (75%) at the follow up time (infliximab in 9, adalimumab in eleven, and tocilizumab in one patient) and 9 children (37.5%) required ≥2 biologics over the follow up period.

Conclusion: The patients with oligo JIA who had present antinuclear antibodies, and small joint involvement should be particularly close observation.

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SAT0522

COMPARISON OF CHILDREN CARRYING E148Q VARIANT WITH CHILDREN CARRYING HOMOZYGOUS PATHOGENIC VARIANTS

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Background: Familial Mediterranean fever (FMF) is the most frequent autoinflammatory disease. Nearly 300 *MEFV* variants had been reported and recorded in INFEVERS database. The most common disease-associated variants are mapped on exon 2 and 10 of chromosome 16. Although *E148Q* variant is the most common one among carriers, its role as a disease causing mutation is still debate (1).

Objectives: The aim of our study was to evaluate and compare the demographic data, clinical features and severity scores of patients carrying only *E148Q* variant with the patients homozygous for pathogenic *MEFV* mutations (*M694V*, *M694I*, *M680I*, *V726A*). One of our objective was to test and compare these two groups for the diagnostic utility of 2 adults and 1 pediatric FMF diagnostic criteria (Tel Hashomer, Livneh and Pediatric) (2-4).

Methods: The medical records of 1685 children diagnosed and followed up as FMF were reviewed retrospectively. The demographic, clinical and genetic data of children carrying only *E148Q* variant (either heterozygous or homozygous carriers) (group 1) and children with pathogenic homozygous mutations (*M694V*, *M694I*, *M680I*, *V726A*) (group 2) were collected. All patients were evaluated for three diagnostic criteria.

Results: Children with *E148Q* variant were 128 and children with pathogenic homozygous variants were 429. Male to female ratio was 1.13 in group 1 and 1.15 in group 2 ($p>0.05$). The mean age of patients in group 1 was 12.1 ± 4.7 , in group was $2\ 14\pm5.9$ ($p<0.001$). The mean age of symptom onset was 5.4 ± 4.1 in group 1, 4.3 ± 3.6 in group 2 ($p=0.01$). Consanguinity was significantly higher in group 2 (29% vs 53%, $p<0.01$). In group 1 17.9% had a sibling with FMF, while in group 2 27% had a sibling with FMF ($p=0.03$). Clinical features like pleuritis, synovitis, recurrent fever, erysipelas-like erythema and monoarthritis were significantly more common in group 2 than group 1 (31.7% vs 9.3%; $p<0.001$, 55.9% vs 32%; $p<0.001$, 86.9% vs 78.9%; $p<0.03$, 31.2% vs 7%; $p<0.001$, 51.7% vs 28.1%; $p<0.001$, respectively). Incomplete attacks were significantly more common in group 1 than group 2 (16.4% vs 7.4%; $p<0.005$). Moderate and severe PRAS scores were significantly higher in group 2 (93.9% vs 71.9%; $p<0.001$). Laboratory values like C-reactive protein, erythrocyte sedimentation rate, serum amyloid A were found significantly higher in group 2 than group 1. (3.6 ± 6.3 vs 0.8 ± 1.2 ; $p<0.001$, 13 ± 10 vs 7.3 ± 6 ; $p<0.001$, 6.9 ± 22.5 vs 2.9 ± 2.2 ; $p=0.007$, respectively). The percentage of children diagnosed according two Tel Hashomer and pediatric criteria was significantly higher in group 2 than group 1 (88.5% vs 77.3%; $p=0.002$, 95.3% vs 84.3%; $p<0.001$, respectively). But both groups show similar diagnostic utility according to Livneh criteria.

Conclusion: Although children carrying *E148Q* variants meet the three validated diagnostic criteria of FMF. They had milder course of disease than children homozygous for pathogenic *MEFV* variants both clinically and in laboratory means.

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SAT0523

EVALUATION OF COEXISTING DISEASES IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is most common periodic fever syndrome in childhood. It is characterized by fever attacks, abdominal pain lasting between 6 - 72 hours, serositis and erysipelas like erythema. Since FMF is inherited in autosomal recessive manner, it has higher frequency in populations that have higher rate of consanguineous marriages. As it is a lifelong chronic disorder, it is important to understand its clinical course for preventive medicine. Despite the higher incidence of variety of disorders shown studies among adult FMF patient, there is not enough data from pediatric populations.

Objectives: The objective of the study is to evaluate the comorbid disorders in a large pediatric familial Mediterranean fever cohort.

Methods: Six hundred and eighty-six children with FMF were interviewed by the same investigator between October 2018 and January 2019 in our pediatric rheumatology department. Demographic features and *MEFV* gene mutations were recorded from patients' charts. Patients and/or their parents were asked about characteristics of their fever episodes, presence of arthralgia, arthritis, abdominal pain, chest pain in the course of fever attack and coexistence of any other disease confirmed by a physician.

Results: Female-male ratio of our cohort was 0,85. Mean age of the patients was $12,8 \pm 7,4$ years. Mean age of patients at disease onset and at the time of diagnosis was $4,38 \pm 3,46$ years and $6,55 \pm 3,67$ years, respectively. Sixty-five and a half percent of patients had family history of FMF. Consanguineous marriage rate was 29,8%. Most common *MEFV* mutations were: *M694V* homozygotes (18,8%), *M694V* heterozygotes (17,7%), *R202Q* heterozygotes (13,1%), *R202Q* homozygotes (5,5%) and *V726A* heterozygotes (4,9%), respectively. Resistance to colchicine treatment was present in 43 (6,2%) patients. Number of patients that underwent tonsillectomy were 9 (1,3%) and number of patients that had appendectomy was 11 (1,6%). Detected coexisting diseases are listed in Table 1.

. Detected coexisting diseases in patients group.

	n(%)
Juvenile Idiopathic Arthritis	40(5,8)
• Systemic	4 (0,5)
• Oligoarticular	17(2,4)
• Polyarticular	5(0,7)
• Enthesitis Related Arthritis	1(0,1)
• Juvenile Spondylitis	13(1,8)
Asthma/Reactive Airway Disease	26(3,7)
Henoch Schonlein Purpura	18(2,6)
Uveitis	10(1,4)
Inflammatory bowel disease	9(1,3)
Periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis (PFAPA)	7(1)
Acute Rheumatic Fever	7(1)
Migraine	7(1)
Allergic Rhinitis	6(0,8)

Conclusion: In this study, we have reported increased frequency of juvenile idiopathic arthritis, asthma- reactive airway disease, Henoch Schonlein purpura, uveitis, inflammatory bowel disease, PFAPA syndrome and acute rheumatic fever in a large pediatric FMF cohort. Those findings consistent with data from literature. It is important to be alert about these diseases that may develop in patients with FMF for preventing them from the potential morbidities.

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