The Characteristics of Laboratory Parameters and Magnetic Resonance Imaging in Different Juvenile Idiopathic Arthritis Subtypes

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Abstract

Objectives: To explore the characteristics of laboratory parameters, magnetic resonance imaging (MRI) and their relationship in different juvenile idiopathic arthritis (JIA) subtypes.

Methods: One hundred and sixty-five patients with JIA identified by diagnostic criteria were involved in the study. Clinical inflammatory biomarkers, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), procalcitonin, IL-2, IL-4, IL-6, IL-10, tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ), C3, C4, and anti-nucleosome antibodies (ANA) was retrospectively reviewed. Semi-quantitative MRI score was calculated from symptomatic or suspected arthritis for each subject.

Results: The median age of onset, median disease duration, ESR, CRP, PLT, IL-6, IL-10, C3, and C4 values were statistically significantly different among different JIA subtypes. The accumulative score of synovitis for different subtype JIA patients has a significant difference ($P < 0.001$). A significant positive relationship between ESR, CRP, RF and C3 values with synovitis score for JIA patients ($r = 0.234$ and $P = 0.003$, $r = 0.251$ and $P = 0.001$, $r = 0.208$ and $P = 0.007$, $r = 0.241$ and $P = 0.002$ respectively), and a negative relationship between gender and onset age with total synovitis score ($r = -0.176$ $P = 0.014$ and $r = -0.194$ $P = 0.013$ respectively) was found by the spearman correlation analyses. Young age at onset, elevated CRP and C3, the long duration of disease were risk factors for synovitis ($P \leq 0.05$).

Conclusion: Although several risk factors were found for synovitis, the laboratory parameters could not fully explain the severity on MRI, timely baseline and follow-up MRI was still necessary for observing the involvement of symptomatic joints, synovitis especially.

Rheumatology Key Messages

Abnormal clinical laboratory variables were most frequent in those with systemic JIA.

Several risk factors have been found for synovitis with limited explanation.

MRI was still necessary for observing the involvement of symptomatic joints, synovitis especially.

Introduction

Juvenile idiopathic arthritis (JIA) represents seven heterogeneity basic subgroups with an exclusion diagnosis that applies to all forms of inflammatory arthropathies¹, which polyarticular-onset rheumatoid factor positive (RF⁺) and negative (RF⁻), oligoarticular-onset, enthesitis-related arthritis and systemic-onset are the most common types. Unknown origin, various clinical signs, hereditary and serological aspects of JIA contribute to different subgroups of the disease. Some clinical and immunological factors have been found as determinants for JIA outcome. Meanwhile, the basic parameters of humoral immunity as complement C3-C4 and clinical inflammatory biomarkers as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), represent very useful laboratory tool for monitoring disease activity². The crucial role of cytokines interleukin in the pathogenesis of JIA disease has also been widely demonstrated³. Despite the heterogeneity, the different JIA subtypes are characterized by prolonged synovial inflammation, which, if not adequately controlled, may ultimately cause the whole joint destruction. Structural damage of bone and cartilage of JIA could lead to serious impairment of physical functional ability, which is an important cause of acquired disability in childhood. Of note, modern imaging techniques^{4, 5}

have become a main domain of clinical and research investigation in paediatric rheumatology, musculoskeletal magnetic resonance imaging (MRI) scanning is capable of imaging joint tissues tomographically and for defining pathological changes, which is an ideal tool for informed clinical decision making.

In fact, even though numerous reports described MRI findings on affected joints in JIA and there were a few studies that described laboratory characteristics among different JIA subgroups, little investigation has been done on the MR imaging to clinical correlation in JIA. Identification of clinical and imaging characteristic of high-risk patient subgroups may lead to more aggressive therapeutic approaches.

Methods

The study was approved by the Institutional Review Board of Wuhan Children's Hospital and Tongji Hospital (No.2021R106-E01), and informed consent was waived because of the nature of retrospectively study. We retrospectively reviewed the 165 identified JIA patients first admitted to the Departments of Pediatric Rheumatology at two institutions between 9 June 2018 and 25 January 2021. All included confirmed JIA patients was followed up for at least 6 months, and met eligibility criteria of the revised International league of Associations for Rheumatology criteria⁶. Participants who received any treatment before clinical data collection or had a recent injury or associated with any chronic diseases in addition to arthritis were excluded.

Joints with symptomatic pain or with suspected arthritis (active, inactive or unsure) were performed by MRI scans during, which predominately involved knees, hips, ankles, wrists and sacroiliac joints in our study. MR images of the above-mentioned respectively susceptible joints were scanned in one of the 5 units, a 3.0T GE Discovery MR750 system, a 3.0T PHILIPS Ingenia CX Systems, a 3.0T GE Signa Excite HD GE system, a 3.0T Siemens Magnetom Skyra system, and a 1.5T GE Signa HD system, with particularly joint coil. The conventional MRI protocol of above-mentioned joints included fast spin-echo T2-weighted with short tau inversion recovery (STIR) images in three orthogonal planes, axial T1-weighted spin-echo with and without fat suppressed images and axial contrast-enhanced T1-weighted with fat suppressed STIR images. The field of view and slice thickness were adjusted relative to the patient's joint size so as to fully include the whole joint. The MRI presentation for affected joints was separately recorded and evaluated with synovial effusion, cartilage damage, bone edema and erosion (Figure 1). Thickened inflamed synovial membrane within the joints and investing tendon sheaths were analyzed and recorded according to contrast-enhanced T1-weighted sequence and T2-weighted with STIR sequence. Regional heterogeneity is the bug-bear of attempting to quantify synovitis, bone marrow edema and bone erosion score from different affected joints as a whole, one point was respectively given for one abnormality of each affected joints according to other studies^{7,8}. The total score of each affected joints was the accumulation score of synovial effusion, cartilage damage, bone edema and erosion for JIA subject. Two experienced paediatric radiologists were assigned to evaluate every examination by consensus, who were blinded to patient identification, clinical and laboratory data.

Demographic data were recorded in detail including clinical inflammatory biomarkers such as ESR, CRP, and procalcitonin (PCT), inflammatory cytokines as IL-2, IL-4, IL-6, IL-10, tumor necrosis factor- α (TNF- α) and interferon- γ (IFN- γ), autoantibodies as anti-nucleosome antibodies (ANA), and complement as C3 and C4. Elevated ESR value was defined as > 20 mm/h, abnormal CRP value was defined as > 3 mg/L, and PCT as > 0.046 ng/ml. Positive IgG RF was defined as titers ≥ 15.9 IU/ml, tested with the latex agglutination method. The normal range of IL-2 value was $0\sim 11.4$ pg/ml, IL-4 was $0\sim 12.9$ pg/ml, IL-6 was $0\sim 20$ pg/ml, IL-10 was $0\sim 5.9$ pg/ml, TNF- α was $0\sim 5.5$ pg/ml, and IFN- γ was $0\sim 17.3$ pg/ml. The normal range of C3 value was $0.8\sim 1.26$ g/L, and C4 was $0.1\sim 0.4$ g/L, the

abnormal elevated markers were recorded to be positive in our study. Antinuclear antibody (ANA) titer $\geq 1:100$ according to the standard of the laboratory, was considered positive. Positive human leukocyte antigen (HLA)-B₂₇ was defined as > 149 by serologic testing.

Statistics

The data were analyzed using a commercial statistics software package (SPSS 26.0, Armonk, NY, USA) and graphics creation was performed using GraphPad Prism (GraphPad Software). Variables were either quantitative or qualitative, quantitative values were presented as mean $\pm$ standard deviation ($M \pm Sd$), and qualitative values as medians and a range of percentiles from 25 ~75% ($Md, P_{25} \sim P_{75}$). Differences among subtype JIA groups were tested with Nonparametric test, Fisher's exact test for categorical variables, with Bonferroni's correction for multiple comparisons when appropriate, and the Kruskal-Wallis tests were performed on the candidate factors separately including ESR, CRP, PCT, IL-2, IL-4, IL-6, IL-10, TNF- α , IFN- γ , ANA, C3, and C4 parameters.

To identify risk factors for an unfavorable image outcome in JIA, Spearman correlation analyse was respectively performed between bone edema and synovitis score outcome with patient characteristics (sex, age at disease onset, and disease duration before admission), laboratory parameters (ESR, CRP, PCT, IL-2, IL-4, IL-6, IL-10, TNF- α , IFN- γ , ANA, C3, and C4). Subsequent multivariate analyses were used to identify a set of statistically significant predictors, including onset age, gender, and factors that were statistically significantly associated with unfavorable outcome of synovitis. Multiple logistic analyses were performed with backward deletion of possible risk factors, based on the likelihood ratio test (removal P value < 0.10). Hosmer-Lemeshow good-ness-of-fit statistics were used to assess how well the logistic regression models fitted the data ($P > 0.05$ were considered fit). Data on the strength of the associations were expressed as odds ratios (OR) per unit change of the independent variable and 95% confidence intervals (CI). P values less than 0.05 were considered significant.

Results

According to the revised classification criteria, 49 patients (29.70%) had oligoarthritis (25 females and 24 males, median age, 85.69 months, range, 12-176 months), 47 patients (28.50%) had RF⁻ polyarticular (27 females and 20 males, median age, 94.22 months, range, 34-156 months), 18 patients (10.91%) had RF⁺ polyarticular (13 females and 5 males, median age, 125.14 months, range, 30-182 months), 35 patients (21.21%) had enthesitis-related arthritis (6 females and 29 males, median age, 90.00 months, range, 21-190 months) and 16 patients (9.70%) had systemic JIA (8 females and 8 males, median age, 97.3 months, range, 18-183 months). There were statistically significant differences on age ($P=0.03$) and gender ($P=0.001$) among the 165 JIA subjects. The median disease duration prior to first admission was 7.01 months (range 0.5-48 months) for oligoarthritis patients, 12.01 months (range 0.5-72 months) for RF⁻ polyarticular, 8.0 months (range 1.5-24 months) for RF⁺ polyarticular, 7.27 months (range 0.25-48 months) for enthesitis-related arthritis and 2.04 months (range 0.083-13 months) for systemic JIA patients. Account for a few subjects in clinical, both of Psoriatic arthritis (PsA) and undifferentiated arthritis subtype subjects were not enrolled and recorded in our study. All JIA patient characteristics and disease variables were retrospectively recorded of information about the disease onset within the first 6 months from the charts of their pediatrician and/or rheumatologist. Characteristics of the overall joint involvement and the laboratory parameters when first hospitalized are also depicted in Table1.

Table 1

Demographic, clinical, and laboratory characteristics of different subtypes with JIA patients (n=165) at disease onset.

Characteristic	oligoarthritis (n=49)	polyarticular with RF- (n=47)	polyarticular with RF+ (n=18)	enthesitis- related arthritis (n=35)	Systemic JIA (n=16)	<i>P</i> value
females	25	27	13	6	8	0.001
males	24	20	5	29	8	
disease onset, median months	85.69 (12-176)	94.22 (34-156)	125.14 (30-182)	90 (21-190)	97.3 (18-183)	0.03
median disease duration prior to admission,months	7.01 (0.5-48)	12.01 (0.5-72)	8 (1.5-24)	7.27 (0.25-48)	2.04 (0.083-13)	<0.001
ESR, mm/H	7.00 (4.00, 23.0)	19.00 (7.00,57.0)	24 (12.50,34.5)	21.00 (13.00,49.00)	84.50 (55.00, 91.50)	<0.001
CRP,	0.85 (0.61, 5.14)	8.94 (0.56, 34.0)	2.18 (0.89, 5.49)	4.39 (1.08,13.78)	68.65 (21.55, 91.70)	<0.001
PLT	0.04 (0.03, 0.06)	0.05 (0.03, 0.09)	0.03 (0.02, 0.05)	0.04 (0.03, 0.09)	0.28 (0.15, 1.40)	<0.001
IL-2	2.27 (1.65, 3.70)	2.60 (1.63, 4.52)	2.67 (1.98, 3.48)	2.01 (1.64, 3.66)	2.39 (1.97, 4.06)	0.885
IL-4	2.6 (2.06, 3.56)	2.93 (1.95, 3.78)	2.68 (2.49, 3.55)	2.82 (2.33, 3.67)	4.13 (2.43, 6.04)	0.18
IL-6	7.61 (4.98, 21.52)	12.18 (6.47, 41.5)	18.63 (7.02, 42.2)	23.31 (8.35,51.69)	65.17 (35.81,112.51)	<0.001
IL-10	3.85 (3.08, 6.85)	3.69 (3.00, 4.49)	4.23 (3.65, 6.18)	3.75 (3.02, 5.98)	23.02 (8.84, 37.27)	<0.001
TNF- α	4.32 (2.01, 13.10)	5.29 (2.92, 39.8)	14.13 (3.70, 30.00)	4.07 (2.18, 21.25)	13.32 (2.98, 34.89)	0.201
IFN- γ	3.43 (2.10, 5.43)	3.73 (2.5, 5.00)	3.42 (2.76, 4.67)	3.24 (2.58, 4.35)	3.58 (2.3, 6.07)	0.946
ANA	9(18.40%)	14(29.79%)	3(16.70%)	13(37.10%)	1(6.30%)	0.057
C3	1.16 (1.02, 1.43)	1.32 (1.10, 1.55)	1.27 (1.14, 1.44)	1.35 (1.15, 1.58)	1.58 (1.42, 1.73)	0.001

Characteristic	oligoarthritis (n=49)	polyarticular with RF- (n=47)	polyarticular with RF+ (n=18)	enthesitis- related arthritis (n=35)	Systemic JIA (n=16)	<i>P</i> value
C4	0.23 (0.17, 0.30)	0.26 (0.20, 0.32)	0.25 (0.20, 0.32)	0.26 (0.21, 0.37)	0.33 (0.26, 0.37)	0.012

In Kruskal-Wallis tests, the median age of onset, the median disease duration, ESR, CRP, PLT, IL-6, IL-10, C3, and C4 values were significantly different among JIA subtypes ($P=0.003$, <0.001 , <0.001 , <0.001 , <0.001 , <0.001 , <0.001 , 0.001 and 0.012 respectively). For systemic JIA patients, the median disease duration was significantly shorter than that of other groups ($P < 0.001$), and the respective mean values of ESR, CRP and PLT were higher than those of other groups ($P < 0.001$). For systemic JIA group, both of IL-6 ($P < 0.01$) and IL-10 ($P < 0.01$) are significantly higher than those of other subtypes, while without significant difference of IL-2, IL-4, TNF- α , and IFN- γ among JIA subtype ($P = 0.885$, 0.18 , 0.201 and 0.946 respectively). For C3 and C4 parameters, there are respectively statistically significantly different between oligoarthritis and systemic JIA patient ($P=0.01$ and $P= 0.012$ respectively). There are 9 of 49 (18.4%) oligoarthritis patients presented with positive ANA, 14 of 47 (29.79%) seronegative RF polyarticular patients presented with positive ANA, 3 of 18 (16.7%) seropositive RF cases demonstrated positive ANA, 13 of 35 (37.1%) enthesitis-related arthritis patients demonstrated positive ANA and only one (6.3%) systemic JIA presented with positive ANA. The positive rate of ANA was not significant difference among JIA subtypes ($P = 0.057$).

The percentage of suspected arthritis in JIA patients undergoing MRI examination in Figure2. The percentage of MRI affected joints in patients of each JIA subtype in Figure 3.

One of enthesitis-related arthritis JIA patients was found to be ankle damage presented with cartilage and bone erosion, and another one was recorded sacroiliitis presented with unilateral ilium cartilage and bone erosion and damage. The accumulative score of synovitis for different subtype JIA patients has a significant difference ($P < 0.001$), while the accumulative score of bone edema for affected joints was not statistically different ($P=0.101$).

The respective relationships between disease synovium score and bone edema score with patient's clinical characteristics and laboratory parameters were assessed by the spearman correlation analyses. Subsequently, we found that there was a significant positive relationship between ESR, CRP, RF and C3 values with synovitis score for JIA patients ($r= 0.234$ and $P=0.003$, $r=0.251$ and $P=0.001$, $r=0.208$ and $P=0.007$, $r=0.241$ and $P=0.002$ respectively), and a negative relationship between gender and onset age with total synovitis score ($r=-0.176$ $P=0.014$ and $r=-0.194$ $P=0.013$ respectively). Considering that the time duration of disease has been demonstrated to be a closely relation with severity of disease in other studies⁹, it has been involved in our multiple linear regression model. The relationship between age at onset, gender, the time duration of disease, ESR, CRP, RF and C3 with the accumulative synovitis score was evaluated by multiple linear regression. Young age at onset, elevated CRP and C3, the long duration of disease were risk factors for the high score of synovitis ($P<0.05$) (Table 2). The proportion of variation explained by the final model was 40.7%.

Table 2

Multiple linear regression model of the accumulative synovitis score in relation to several prognostic factors.

Prognostic factor	Regression coefficient	Standardized regression coefficient	Pvalue
age at onset	-0.007	-0.143	0.012
gender	-0.467	-0.189	0.069
the time duration of disease	0.028	0.196	0.01
ESR	-0.133	-0.096	0.404
CRP	0.193	0.219	0.04
RF	0.159	0.075	0.32
C3	1.212	0.209	0.026
ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PCT: procalcitonin; IL: cytokines Interleukin; TNF- α : tumor necrosis factor- α ; IFN- γ : interferon- γ ; ANA: anti-nucleosome antibodies; RF: rheumatoid factor; C3: complement-3 and C4: complement-4.			

Discussion

A better knowledge of the different subtype diseases by the search of homogeneity for each diagnostic category is necessary for conducting research. Assessing inflammatory changes is crucial for developing a better control of inflammation and evaluating the effectiveness of therapeutic interventions for JIA children. To our knowledge, this study is first evaluating the laboratory parameters involvement among different JIA subtype, in particularly analyzing the relationship between laboratory inflammatory and immunological parameters with semi-quantitative MR imaging score.

In our study, oligoarthritis onset JIA was a major proportion, which was the most frequent chronic inflammatory rheumatic condition in childhood with approximately 27-60%¹⁰. The sex distribution varied with disease subtype, with a striking female predominance in the oligoarthritis and polyarticular onset groups, and male predominance in enthesitis related arthritis, which was similar with other studies^{11,12}. The age of onset also differed, with a median 10 years of age in RF⁺ polyarticular arthritis, slightly older than in systemic and seronegative polyarticular arthritis, and even higher in enthesitis related arthritis. The median age of onset may be slight difference with other studies, in general, two major peaks in JIA onset were observed at 1-2 years and between the ages of 9 and 15 years¹³.

Markedly distinct pathogenesis of JIA subtypes implies that there are different presentations on laboratory characteristics, which may represent useful tools to distinguish systemic JIA from other JIA subtypes. Our study illustrated the differences in clinical laboratory variables among JIA onset subtypes, and abnormalities were most frequent in those with systemic JIA. Laboratory investigations showed high levels of inflammatory markers including ESR, CRP and PCT, which were present at very higher circulating levels in systemic JIA and at lower levels in oligoarthritis than in other JIA subtypes, these conventional parameters of inflammation could be useful in monitoring of JIA activity. The time of disease duration prior to first admission may be responsible for these adverse findings, each subtype differs with respect to presentation and anticipated disease course for first admission. Another reason may be that the uncomfortable symptom of affected joints may be difficult to assess in

young children, particularly toddlers with limited expressive skills. In fact, swelling is a complaint specific, and as a major characteristic for active arthritis, which is often not correctly identified by families. Oligoarthritis has long been considered as a benign disease¹⁴, and oligo/polyarticular JIA is an antigen-driven lymphocyte-mediated autoimmune disease with abnormality in the adaptive immune system, while systemic JIA is demonstrated to be an autoinflammatory disease with abnormality in the innate immune system, and the classic form of systemic JIA is characterized by fevers accompanied associated lymphadenopathy, serositis, and markedly increased acute phase reactants, these symptom is easily assess by families. The values of IL-6 and IL-10 were significantly higher than those of other of JIA subtypes. Aberrant activation of phagocytes leads to the release of pro-inflammatory cytokines including IL-6 in both peripheral blood and synovial fluid, which contribute to the multisystem inflammation of systemic JIA. IL-6 as a cytokine with many biological activities have been implicated in most inflammatory diseases¹⁵, and regulated immune responses and acute-phase reactions, which is correlated with spikes of fever, thrombocytosis, and joint involvement. while decreased anti-inflammatory cytokine IL-10 leads to the failure of T cell tolerance to self-antigens, which contributes to the synovial inflammation of oligo/polyarticular JIA. There appear to be complex interactions between disease subtypes and other incompletely defined factors. The most important findings of this work were the clear differences in pattern of complement activation among oligoarthritis JIA, systemic JIA and polyarticular JIA. Circulating immune complexes are elevated in JIA. In work using a qualitative test for C3 and C4 values, higher concentrations of C3 and C4 values have been described in systemic JIA than in oligoarthritis JIA. Immune complexes containing RF were detectable in synovial fluid of patients with polyarticular RF⁺ JIA. The reason may be that complement-mediated tissue damage was induced by the classical complement activation pathway in JIA. The precise pathogenesis still remained unknown, however, the occurrence of autoantibodies in a significant proportion of patients suggested involvement of autoimmune mechanisms. In population-based studies, ANA were not specific and present in 16-44% of patients¹⁶, but the positivity has been reported to be an independent risk factor for a longer duration of active disease, which itself was a risk factor for increased disability. In this study, only rare patients had positive antinuclear antibody test, we found that the positive rates in patients with whole JIA (24.24%), oligoarticular JIA (18.36%), and polyarticular JIA (26.15%) were lower than those reported by previous literatures¹⁷. False positivity and transient positivity of the ANA were common occurrences. Furthermore, the criterion for defining ANA positivity differently should be also considered when comparing results.

Among the whole cohort of the patients, the limb joints of ankle and wrist were also preferentially involved in our study, particularly the ankle. The ankle was also the second most frequently affected joint after the large joint of knee in children with JIA^{18,19}, which has been relatively ignored. The ankle examination is difficult in small children because of anatomically and mechanically complex. The wrist joint was less commonly affected but was one of the most vulnerable site of structural damage and was associated with a more severe progressive disease course^{20,21}. Synovial thickening, joint effusions, and bone marrow edema were the most prevalent disease features²². The importance of synovial hypertrophy as the hallmark of arthritis was again underscored by our imaging study because it was the most frequent MRI abnormality in the affected joints for all JIA subtypes. Synovial proliferation and infiltration by inflammatory cells could result in increased secretion of synovial fluid and synovial hypertrophy. Persistent synovitis may eventually lead to articular cartilage lesions and bone erosions that are responsible for disability and reduced quality of life in JIA. According to the prevalence and predominant of synovitis in all kinds of JIA, enhanced MRI was essential, while whole body MRI was not sufficient because of unachievable enhancement²³. In our study, there were two patients respectively presented with ankle articular cartilage damage and iliac erosion. Erosive changes in affected joints are rare among patients with JIA nowadays and are seen only

in very advanced cases as a late complication. Owing to the incompleteness of ossification, the articular cartilage is thicker in growing children than in adults. Importantly, articular cartilage of growing children has a distinctive regenerative capacity. This attribute might explain the rare presentation of joint cartilage damage on conventional MR imaging in those with JIA.

We identified several predictive factors of severity in synovitis-onset JIA that could help to select high-risk subgroups of children who might possibly benefit from earlier and more aggressive therapeutic strategies. The number of joints involved with synovitis was correlated with the ESR and CRP, higher CRP value was a predictive factor according to the multivariate analyses, but without the inflamed parameter of ESR in our study. In contrast, higher ESR values on first MRI examination predicted the development of joint erosions on oligoarthritis JIA by Guillaume, et al ²⁴. Furthermore, young age of onset and gender were risk factors for a poor prognosis in our study. While, gender, as well as age at disease onset, were not identified as predictive factors of poor joint outcome in other studies. The overall seroprevalence of RF in patients with JIA was found very low, and the multivariate analyses showed that it may be not related to the severity of synovitis. Patients² with RF⁺ polyarticular JIA were at higher risk of a more aggressive disease course and bone erosion than JIA patients without RF⁺. In fact, RF was a non-specifically positive indicator for JIA severity, because it can also be abnormal in other autoimmune disorders such as acute rheumatic fever and SLE, as well as in otherwise healthy individuals. The variation in results may have been influenced by differences in patient selection, methods for assessing outcome, and criteria for remission. The positive results of the multivariate analyses were limited because some of the predictive factors had an OR close to one per unit change or a wide CI. The variance explained by the models was low, indicated that there were still other factors than those identified here were important determinants for outcome in JIA. Furthermore, as the laboratory parameters could not fully explain and predict the severity on MRI, timely baseline and follow-up MRI should be carried out for observing the involvement of symptomatic joints, synovitis especially. Interpretation of thus-far-published prognostic studies of JIA patients was difficult because of the heterogeneity of the populations studied, which have been constituted not only of oligoarthritis-onset JIA patients, but also of polyarticular-and systemic onset JIA patients. Prospective testing of these predictors is needed to establish a set of reliable criteria for the early recognition of children with severe JIA who need aggressive management.

We acknowledged that our research had some limitations. This study was limited by its retrospective nature, which led to incomplete data collection for some items such as HLA-B₂₇ level retrieved from medical record. Second, though ANAs were directed against a variety of components of the cell nucleus, we only performed the overall ANA positivity or negativity, and did not pursue fine specificities of ANA for subgroups of autoantibodies in present study. In addition to these, a limited sample size and a bias on selection of clinically suspected affected joints for imaging, especially in oligoarthritis patients, may underestimate the severity of JIA imaging, as it was known that some authors had found a high prevalence of subclinical synovitis.

Conclusion

In summary, we have shown divergent laboratory parameters patterns within different JIA subgroups, and the relationship between clinical laboratory and MR imaging presentations. Dissecting the laboratory parameters network and MR imaging could evolve suitable monitoring technology. However, further studies are needed to investigate whether these methods can monitor disease course.

Abbreviations

JIA
Juvenile idiopathic arthritis
RF
rheumatoid factor
CRP
C-reactive protein
ESR
erythrocyte sedimentation rate
MRI
magnetic resonance imaging
STIR
T2-weighted with short tau inversion recovery
TNF- α
tumor necrosis factor- α
IFN- γ
interferon- γ
ANA
autoantibodies as anti-nucleosome antibodies
PCT
procalcitonin
HLA
human leukocyte antigen
OR
odds ratios
CI
confidence intervals
PsA
Psoriatic arthritis

Declarations

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Authors' contributions

WX- ethics approval, and manuscript revision; YZ, YG and CL- data collection and preparation; JR-project concept and manuscript draft; YH- figures; XP- manuscript revision; JS- statistical analysis and project concept. All authors read and approved the final manuscript as submitted.

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Data availability statement

The data underlying this article cannot be shared publicly due for the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Wuhan Children's Hospital and Tongji Hospital (No.2021R106-E01)

Consent for publication

Not applicable

Competing interests

The authors have declared no conflicts of interest.

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Figures

Figure 1

MR imaging of affected knee of a ten-year old boy with oligoarthritis JIA.

Figure 2

The percentage of suspected arthritis in JIA patients undergoing MRI examination.

Figure 3

The percentage of MRI affected joints in patients of each JIA subtype.