World Journal of Pediatrics
https://doi.org/10.1007/s12519-018-0212-0

ORIGINAL ARTICLE

Features distinguishing juvenile idiopathic arthritis among children with musculoskeletal complaints

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Received: 16 March 2018 / Accepted: 13 November 2018

Abstract

Background Musculoskeletal (MSK) complaints in children vary, ranging from benign, self-limited conditions to serious disorders. Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease, initially presenting with MSK complaints. Delayed diagnosis and appropriate treatment have an enormous impact on the long-term outcomes and the level of disability. This study aimed to identify the features distinguishing JIA among children presenting with MSK complaints and to describe the spectrum of diseases at a large, single, tertiary center.

Methods A retrospective chart review was performed of patients evaluated by pediatric rheumatology consultation at the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, from July 2011 to June 2015.

Results Of 531 patients, 285 (53.6%) had at least one MSK complaint. The mean age of the patients was 9.1 ± 4.1 years. Joint pain was the most common MSK complaint (86.3%), followed by limping (33%) and refusal to walk (19.6%). Joint swelling and limited range of motion were found in 146 (51.2%) and 115 (40.4%) patients, respectively. Seventy-three (25.6%) patients were diagnosed as JIA. The other common diagnoses included Henoch–Schönlein purpura (16.1%), reactive arthritis (14.2%), and systemic lupus erythematosus (13.7%). Morning stiffness ≥ 15 minutes [odds ratio (OR) 8.217 (3.404–19.833)]; joint swelling on MSK examination [OR 3.505 (1.754–7.004)]; a duration of MSK complaints of more than 6 weeks [OR 2.071 (1.120–3.829)]; and limping [OR 1.973 (1.048–3.712)] were significantly associated with the ultimate diagnosis of JIA.

Conclusions Morning stiffness ≥ 15 minutes is a strong predictor of JIA. Comprehensive history taking and an MSK examination will provide clues for making the ultimate diagnosis for children with MSK complaints.

Keywords Joint pain · Juvenile idiopathic arthritis · Limping · Morning stiffness · Musculoskeletal

Introduction

Musculoskeletal (MSK) diseases comprise multiple disorders affecting the joints, bones, muscles, and soft tissues. Children with MSK diseases may present with joint pain, limb pain, morning stiffness, refusal to walk, and/or limping with or without other systemic features. The overall prevalence of MSK complaints during childhood has been reported at up to 36% [1, 2]. A recent systematic review showed that MSK complaints occur more frequently in the lower extremities than the upper extremities [3]. Evaluating children with MSK complaints is complicated by the broad differential diagnoses, ranging from benign, self-limited conditions to serious disorders such as septic arthritis and malignancy-related arthritis [4–7]. Importantly, certain conditions require timely and appropriate treatment to prevent complications and disability.

Juvenile idiopathic arthritis (JIA), a heterogeneous group of disorders characterized by joint inflammation, is the most common rheumatic disease in children [8–11]. The prevalence of JIA has been reported to be approximately 16–150 cases per 100,000 children [9]. A delayed diagnosis has an enormous impact on the long-term outcomes and the quality of life of the children [12, 13]. Determining the features distinguishing JIA from other conditions may assist general practitioners and general pediatricians in making a diagnosis and result in prompt patient referral to a pediatric rheumatologist. However, only a limited number of reports have

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Published online: 29 November 2018

focused on the predictive factors of JIA among children presenting with MSK complaints [14, 15]. MSK complaints vary among the JIA subtypes. The differences could be due to the heterogeneity of JIA. Some recent evidence has suggested that the HLA genotype and the levels of proinflammatory cytokines might be different in each JIA subtype [16, 17].

Our primary objective was to identify the features distinguishing JIA among children presenting with MSK complaints. The secondary objective was to describe the spectrum of diseases presenting with MSK complaints at a large, single, tertiary center.

Methods

This was a retrospective study of hospital charts of all children aged ≤18 years who were evaluated by pediatric rheumatology service at the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, between July 2011 and June 2015. The data collected included demographic information (namely, age, gender and region of residence) and clinical data (such as the referral source, MSK complaints, duration of the MSK complaints, and ultimate diagnosis). MSK complaints were defined as complaints relating to the skeleton, including the joints, bones, tendons, and muscles. The clinical presentations of the MSK complaints at the time of the pediatric rheumatology evaluation were recorded; they included the symptoms of joint pain (at least 1 joint), limping, refusal to walk, morning stiffness, awakening pain, and other systemic manifestations. Morning stiffness was defined as a feeling of joint stiffness lasting for at least 15 minutes. The physical and MSK examinations were documented. The laboratory findings were also collected; they comprised a complete blood count, erythrocyte sedimentation rate, c-reactive protein, antinuclear antigen (ANA), and rheumatoid factor (RF). The ultimate diagnoses of JIA [8], systemic lupus erythematosus (SLE) [18, 19], juvenile dermatomyositis (JDM) [20], vasculitis [21], and benign joint hypermobility syndrome [22] were made based on each conditions' classification criteria.

All statistics analyses were performed using SPSS Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $P<0.05$, with a confidence interval (CI) of 95%. Descriptive statistics were reported as number and percentage (%), mean and standard deviation (SD), or median and interquartile range (IQR), as appropriate. Either a one-way analysis of variance or the Kruskal–Wallis test was applied for comparisons. The associations between the predicting parameters were analyzed and compared using the Chi-square test, Fisher's exact test, or the Mann–Whitney test, where appropriate. The Chi-square test, followed by a post hoc analysis by Bonferroni correction, was performed to determine where the differences occurred between 2 or more groups. A multivariate logistic regression analysis was conducted to identify independent predicting factors.

This study was approved by the Siriraj Institutional Review Board, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand (Si 325/2016).

Results

Data relating to the 531 patients seen by the pediatric rheumatology service between July 2011 and June 2015 were reviewed. Of those, 246 without MSK complaints were excluded, leaving 285 patients with MSK complaints. The proportion of females (57.9%) was slightly greater than

Table 1 Demographic and clinical characteristics of patients with musculoskeletal complaints ($n=285$)

Characteristics	Values
Age (y), mean ± SD	9.1 ± 4.1
Male/female, *n* (%)	120 (42.1)/165 (57.9)
Duration of symptom (wk), median (IQR)	6.6 (2–26.1)
Referral by, *n* (%)	
None	138 (48.4)
General pediatrician	95 (33.3)
General practitioner	30 (10.5)
Orthopedic surgeon	21 (7.4)
Adult rheumatologist	1 (0.4)
Region, *n* (%)	
Central	221 (77.5)
West	28 (9.8)
Northeastern	18 (6.3)
East	9 (3.2)
South	8 (2.8)
Other	1 (4)
Musculoskeletal complaints, *n* (%)	
Joint pain	246 (86.3)
Limping	94 (33.0)
Refusal to walk	56 (19.6)
Morning stiffness	33 (11.6)
Awakening pain	15 (5.3)
Other manifestations, *n* (%)	
Fever	114 (40.0)
Rash	96 (33.7)
Weight loss	19 (6.7)
Family history of rheumatic disease	7 (2.5)
Physical examination, *n* (%)	
Joint swelling	146 (51.2)
Limitation of range of motion	115 (40.4)
Generalized lymphadenopathy	6 (2.1)
Hepatosplenomegaly	6 (2.1)

that of males (42.1%). The mean age of the patients was 9.1 ± 4.1 years. The median duration of the MSK complaints was 6.6 (IQR 2–26.1) weeks. A plurality of patients (48.4%) was directly evaluated by our pediatric rheumatology service. One-third of patients had been referred to our service by general pediatricians.

Of the 285 patients in the study cohort, 246 (86.3%) reported joint pain as their MSK complaint. Limping was the second most common complaint (33%), followed by refusal to walk (19.6%); morning stiffness was reported by 33 (11.6%) patients. Regarding the non-MSK clinical manifestations, fever and rash were documented in 114 (40%) and 96 (33.7%) patients, respectively. A family history of rheumatic disease was found in only 7 patients (2.5%). The demographic and clinical characteristics of the patients with MSK complaints are shown at Table 1.

Of the patients with MSK complaints, 73 (25.6%) were diagnosed as JIA. Thirty-four (11.9%) had Henoch–Schönlein purpura. Reactive arthritis and SLE were diagnosed in 31 (10.9%) and 28 (9.8%) patients, respectively, while benign joint hypermobility syndrome was found in 22 (7.7%) patients. Amplified MSK pain syndrome and infection-related arthritis were each diagnosed in 10 (3.5%) patients. A flow chart outlining the study enrollment and the categories of diagnosis is at Fig. 1, and the spectrum of ultimate diseases of the patients with MSK complaints are illustrated at Fig. 2.

Among the JIA patients, systemic JIA was the most common subtype, being found in 26 out of 73 (35.6%) patients. Enthesitis-related arthritis was the second common (23.3%), while oligoarthritis ranked third, with 15 (20.5%) patients; in contrast, polyarthritis and undifferentiated arthritis were the least frequent subtypes. No patient in the present study was diagnosed with psoriatic arthritis. The distribution of the JIA subtypes is demonstrated at Fig. 3.

Significantly more JIA than non-JIA patients had morning stiffness ($P < 0.001$), joint swelling on MSK examination ($P < 0.001$), limping ($P = 0.021$), a limited joint range of motion on MSK examination ($P = 0.039$), and a duration of MSK complaints of more than 6 weeks ($P = 0.030$). Platelet counts were also significantly higher in JIA than non-JIA patients, with a median of 411,000 (IQR 323,500–514,000) and 320,000 (IQR 237,500–408,500) cells/mm^3, respectively. Moreover, JIA patients had a significantly elevated erythrocyte sedimentation rate (> 20 mm/hour) than patients without JIA ($P = 0.003$). A comparison of the clinical

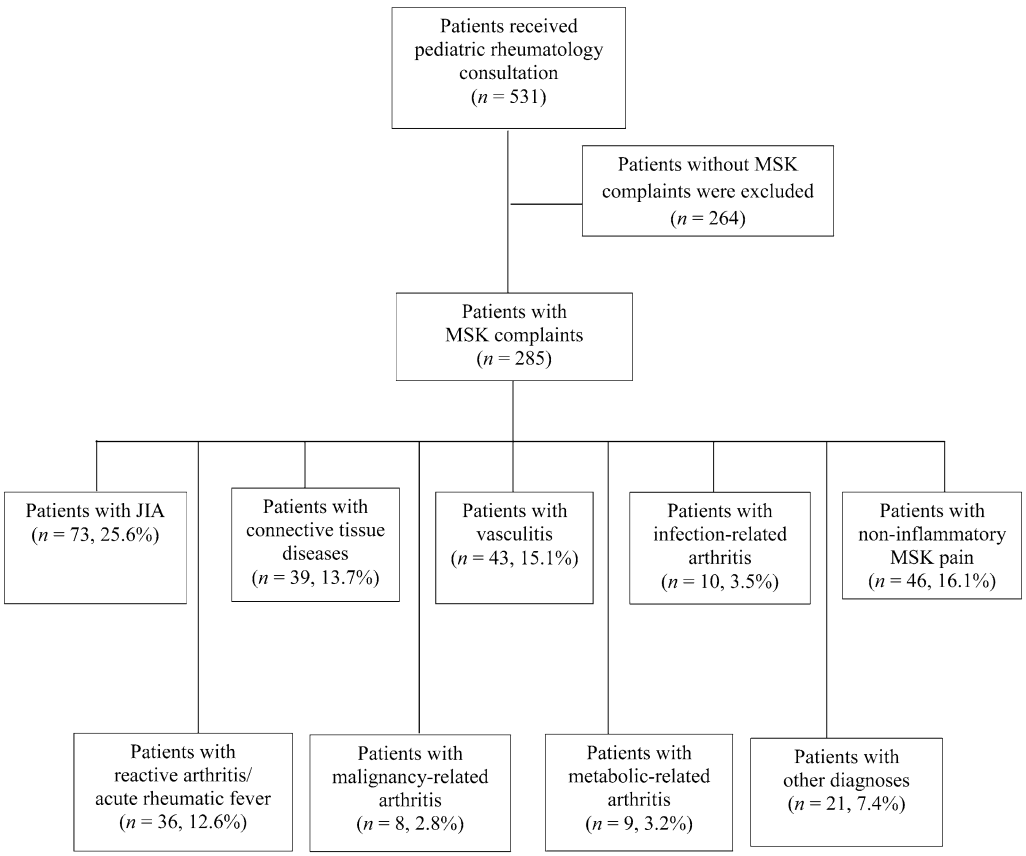

Fig. 1 Flow chart outlining the study enrollment and the categories of diagnosis. Metabolic-related arthritis was defined as arthritis in metabolic diseases, metabolic bone diseases and vitamin deficiency. *MSK* musculoskeletal, *JIA* juvenile idiopathic arthritis

characteristics and laboratory findings of JIA and non-JIA patients is shown at Table 2.

To identify the predictors of JIA, the significant factors were analyzed using multivariate logistic regression models. Morning stiffness was strongly associated with JIA (odds ratio 8.217, 95% CI 3.404–19.833). In addition, joint swelling on MSK examination (odds ratio 3.505, 95% CI 1.754–7.004); duration of MSK complaints of more than 6 weeks duration (odds ratio 2.071, 95% CI 1.120–3.829); and limping (odds ratio 1.973, 95% CI 1.048–3.712) were significantly associated with JIA (Table 3).

The clinical characteristics of each JIA subtype are shown at Table 4. Fever and rash were predominant in the systemic JIA patients. Of the 26 systemic JIA patients, fever was present in 24 patients (92.3%) at the time of their pediatric rheumatology consultation. Rash was documented in 19 JIA patients, 16 of whom were systemic JIA patients. Of the 3 non-systemic JIA patients, enthesitis-related arthritis ($n=1$), RF negative polyarticular JIA ($n=1$), and unclassified JIA ($n=1$) had rash attributed to dermatitis. Joint pain was common in all JIA subtypes, ranging from 83.3 to 100% of patients in the subtypes. Morning stiffness was found in 60% of patients with RF positive polyarticular JIA, 52.9% of patients with enthesitis-related arthritis, and 50% of patients with RF negative polyarticular JIA. Limping was more prevalent with enthesitis-related arthritis than in systemic JIA patients ($P=0.040$).

Discussion

This study suggests that the predictors of JIA to be the following: duration of morning stiffness lasting at least 15 minutes, limping, joint swelling on MSK examination, and duration of MSK complaints exceeding 6 weeks. Joint pain was the most common MSK complaint (86.3%). JIA was the predominant condition among children with MSK complaints in our series.

A few studies have previously focused on the predictors of developing JIA [14, 15]. In a retrospective study, McGhee et al., found that the complaints of joint swelling or gait abnormality were common among children diagnosed with chronic arthritis in children who were referred to a rheumatology unit [14]. The researchers also found that isolated MSK pain was less likely to be a presenting complaint of children with chronic arthritis. A recent study by Cattalini et al. showed that a pattern of joint swelling, exacerbating factors of pain, the occurrence of pain, and the duration of morning stiffness were significantly associated with a final diagnosis of chronic arthritis in their patients with MSK complaints [15]. The present study found similar predicting features to the aforementioned studies (namely, morning stiffness, limping, and joint swelling). Additionally, joint pain was not found to be associated with JIA.

Our study also demonstrated that at least 15 minutes of morning stiffness was associated with JIA. Morning stiffness and feeling stiff after periods of rest (the gel phenomenon) are well known as indicators of inflammatory arthritis [23]. However, data focusing on the exact significant duration of morning stiffness in the child population are scarce [4, 15, 24]. Cattalini et al. pointed out that approximately one-third of children with chronic arthritis had morning stiffness of less than 1 hour [15]. The American College of Rheumatology provisional criteria specified morning stiffness of $\leq$15 minutes as one of the criteria for describing a clinically inactive disease in JIA [24]. To our knowledge, our study is the first to document that morning stiffness lasting for at least 15 minutes is significantly related to inflammatory arthritis in children and hence could be a predictor of JIA.

Apart from systemic JIA, other systemic inflammatory diseases, such as SLE, JDM, and autoinflammatory syndromes, may present with MSK complaints accompanied by fever and rashes [25–28]. Symmetric painful arthralgia and non-erosive polyarthritis are usually found in patients with SLE [27, 29, 30]. Chronic polyarthritis has rarely been reported in childhood SLE [31]. JDM patients may have

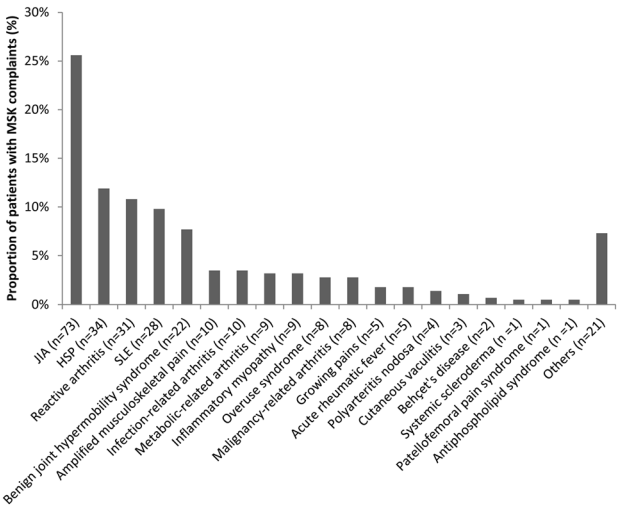

Fig. 2 Diseases of patients with musculoskeletal complaints ($n=285$). Infection-related arthritis ($n=10$): septic arthritis ($n=5$), disseminated gonococcal infection ($n=1$), viral arthritis ($n=2$), psoas abscess ($n=1$), osteomyelitis ($n=1$); metabolic-related arthritis ($n=9$): scurvy ($n=4$), gouty arthritis ($n=4$), hyperostosis hyperphosphatemia ($n=1$); malignancy-related arthritis ($n=8$): acute lymphoblastic leukemia ($n=6$), acute myeloid leukemia ($n=1$), osteosarcoma ($n=1$); other diseases ($n=21$): avascular necrosis ($n=2$), chronic recurrent multifocal osteomyelitis ($n=1$), chronic urticaria ($n=1$), cellulitis ($n=2$), congenital trigger finger ($n=1$), tendinitis ($n=2$), erythema nodosum ($n=2$), hemophilic arthritis ($n=1$), Perthes disease ($n=2$), primary immune deficiency ($n=1$), panniculitis ($n=1$), pustular psoriasis ($n=1$), heart failure ($n=1$), vascular anomaly ($n=1$), serum sickness ($n=1$), deferiprone induced arthropathy ($n=1$). *JIA* juvenile idiopathic arthritis, *HSP* Henoch-SchÖnlein Purpura, *SLE* systemic lupus erythematosus

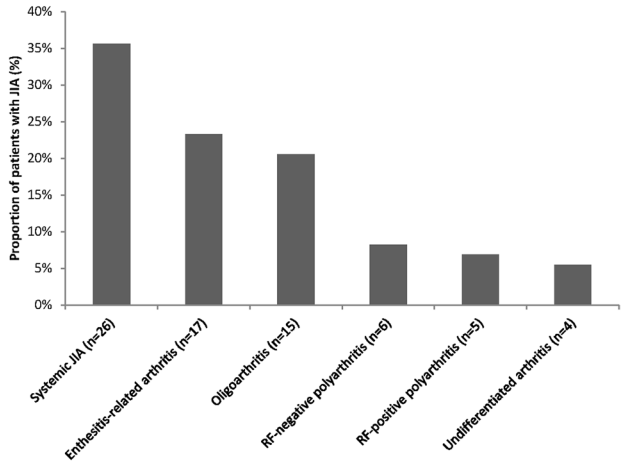

Fig. 3 Subtype of juvenile idiopathic arthritis ($n=73$). *RF* rheumatoid factor

joint pain as one of the initial clinical presentations [28, 32, 33]. However, morning stiffness does not seem to be a common MSK complaint among children with JDM. In contrast, morning stiffness has been found in 70% of cases of systemic-onset JRA [34]. Therefore, morning stiffness could be a clinical feature distinguishing systemic JIA from other systemic inflammatory diseases.

Our results demonstrate that the presence of ANA or RF is not indicative of JIA. The presence of ANA does not seem to be useful for the diagnosis of chronic arthritis [14, 35, 36]. Our finding was unlike prior studies which reported an association between ANA positivity and chronic arthritis [15]. This may be due to the fact that oligoarthritis, a subtype in which ANA is often positive, was not commonly seen in our JIA patient cohorts. Furthermore, since SLE was the second most common diagnosis in the non-JIA group in the current study, the presence of ANA would not be helpful in distinguishing the JIA and non-JIA groups. RF-positive polyarthritis was found in only 5 patients in our cohort; this is similar to the findings of earlier studies that demonstrated a low prevalence of this subtype in Thailand [37, 38]. The clinical utility of RF is to classify the JIA subtype and to provide prognosis [8, 39]. Thus, the clinical diagnosis of JIA should not be based solely on the presence of RF and ANA.

Of the 285 patients with MSK complaints in our series, rheumatic diseases constituted the main clinical conditions. JIA was the most common ultimate diagnosis (25.6%), followed by Henoch–Schönlein purpura (11.9%), reactive arthritis (10.8%), and SLE (13.7%). Mechanical pain (including benign joint hypermobility syndrome, overuse syndrome, growing pains, and patellofemoral pain

Table 2 Comparison of clinical characteristics and laboratory findings of JIA and non-JIA patients

Clinical characteristics and laboratory findings	JIA ($n=73$)	Non-JIA ($n=212$)	Odds ratio (95% CI)	*P* value
Age (y), mean ± SD	8.2 ± 4.1	8.8 ± 4.2	–	0.277
Joint pain, *n* (%)	67 (91.8)	179 (84.4)	2.059 (0.825–5.135)	0.166
Fever, *n* (%)	30 (41.1)	84 (39.6)	1.063 (0.619–1.827)	0.890
Rash, *n* (%)	19 (26.0)	77 (36.3)	0.617 (0.341–1.116)	0.116
Limping, *n* (%)	37 (50.7)	75 (35.4)	1.877 (1.096–3.216)	0.021*
Refusal to walk, *n* (%)	15 (20.5)	41 (19.3)	1.079 (0.556-2.092)	0.865
Weight loss, *n* (%)	6 (6.2)	13 (6.1)	1.371 (0.501–3.749)	0.588
Morning stiffness, *n* (%)	24 (32.9)	9 (4.2)	11.048 (4.831–25.264)	<0.001*
Awakening pain, *n* (%)	3 (4.1)	12 (5.7)	0.714 (0.196–2.606)	0.767
Family history of rheumatic disease, *n* (%)	2 (2.7)	5 (2.4)	1.166 (0.221–6.145)	1.000
Joint swelling, *n* (%)	54 (72.0)	92 (43.4)	3.707 (2.057–6.682)	<0.001*
Limitation of range of motion, *n* (%)	37 (50.7)	78 (36.8)	1.766 (1.032–3.021)	0.039*
Generalized lymphadenopathy, *n* (%)	3 (4.1)	3 (1.4)	2.986 (0.589–15.133)	0.344
Duration of symptoms > 6 wk, *n* (%)	45 (61.6)	99 (46.7)	1.834 (1.065–3.159)	0.030*
Hemoglobin (g/dL), mean ± SD	11.2 ± 1.5	11.3 ± 1.5	–	0.631
WBC count (/μL), median (IQR)	9760 (7425–13,805)	9490 (6170–12,930)	–	0.125
Platelet count (/μL), median (IQR)	411,000 (323,500–514,000)	322,000 (237,500–408,500)	–	<0.001*
ESR > 20 mm/h, *n* (%)	60 (84.5)	102 (65.0)	2.941 (1.429–6.052)	0.003*
CRP > 5 mg/dL, *n* (%)	38 (67.9)	63 (59.4)	1.441 (0.729–2.849)	0.608
Positive ANA, *n* (%)	15 (25.0)	32 (34.0)	0.646 (0.313−1.331)	0.283
Positive RF, *n* (%)	5 (9.6)	3 (7.3)	1.348 (0.303–6.002)	0.731

JIA juvenile idiopathic arthritis, *WBC* white blood cell, *IQR* interquartile range, *ESR* erythrocyte sedimentation rate, *CRP* c-reactive protein, *ANA* anti-nuclear antibody, *RF* rheumatoid factor, *CI* confidence interval, *SD* standard deviation. *Statistically significant result at $P<0.05$

Table 3 Multivariate logistic analysis demonstrating predictors of juvenile idiopathic arthritis

Clinical characteristics and laboratory findings	Odds ratio (95% CI)	*P* value
Morning stiffness	8.217 (3.404–19.833)	<0.001*
Joint swelling	3.505 (1.754–7.004)	<0.001*
Duration of symptoms > 6 wk	2.071 (1.120–3.829)	0.020*
Limping	1.973 (1.048–3.712)	0.035*
Limitation of range of motion	1.113 (0.567–2.183)	0.756

*Statistically significant result at $P < 0.05$

syndrome) was seen in a lower proportion. Our findings differed from studies from developed countries which reported that non-rheumatic conditions were more dominant [1, 14, 15, 40]. According to one study of 482 children evaluated by a pediatric rheumatology service, mechanical MSK pain was the most common final diagnosis (36.9%), whereas juvenile chronic arthritis was found much less frequently (17.5%). Ninety (81%) of 111 patients with isolated MSK pain had mechanical joint disease [14]. Cattalini et al. demonstrated that the majority of final diagnoses were non-inflammatory disorders, which represented up to 64% of the diagnoses, and the predominant JIA subtype was oligoarthritis [15]. A recent study found that non-inflammatory conditions (42.2%) were the most common etiologies of children and adolescents with MSK pain, followed by rheumatic diseases (31%) and infection-related conditions (21.6%); of note, the proportion of JIA was only 8.3% in the rheumatic disease group [40]. Interestingly, data from Southeast Asian countries indicated that rheumatic diseases predominated in the pediatric rheumatology clinic population [37]. Since pediatric rheumatologists are still rare in Thailand, children with MSK complaints are likely to be partly managed by orthopedic surgeons.

The most common JIA subtype in the current study was systemic JIA. This observation is different from the findings of epidemiological studies in Western countries, in which oligoarthritis was the most common subtype [11, 41]. Studies of Asian children demonstrated that oligoarthritis was not the most common subtype [37, 42, 43]. Two reports revealed a predominance of systemic JIA patients in Thailand [37, 38]. Therefore, differences in JIA subtype predominance may possibly be attributed to ethnicity. Additionally, a referral bias could be another explanation for this result. Since our hospital is one of the largest tertiary care centers in Thailand, patients with an unexplained etiology of prolonged fever are often referred to the hospital, and many are finally diagnosed as systemic JIA.

The present study supported the finding that MSK complaints vary among the JIA subtypes. Systemic JIA patients may have predominantly systemic symptoms rather than articular symptoms at the initial onset of the disease. By contrast, oligoarthritis and enthesitis-related arthritis patients are more likely to present with arthritis in the lower extremities, resulting in limping [9–11]. Limping was predominant in our enthesitis-related arthritis and oligoarthritis patients. Morning stiffness was mainly reported in polyarticular JIA and enthesitis-related arthritis patients.

Table 4 Clinical characteristics of each JIA subtype

Clinical characteristics	Systemic JIA ($n=26$)	Enthesitis-related arthritis ($n=17$)	Oligoarthritis ($n=15$)	RF-negative polyarthritis ($n=6$)	RF-positive polyarthritis ($n=5$)	Undifferentiated arthritis ($n=4$)	*P* value
Age (y), mean ± SD	7.5 ± 3.3	11.4 ± 2.9	6.6 ± 4.5	8.8 ± 4.3	11.6 ± 5.3	7.1 ± 5.3	0.008*
Joint pain, *n* (%)	23 (88.5)	16 (94.1)	14 (93.3)	5 (83.3)	5 (100)	4 (100)	0.977
Limping, *n* (%)	8 (30.8)	14 (82.4)	8 (53.3)	3 (50)	2 (40)	2 (50)	0.040*
Refusal to walk, *n* (%)	3 (11.5)	5 (29.4)	5 (33.3)	1 (16.7)	0 (0)	1 (25)	0.423
Morning stiffness, *n* (%)	4 (15.4)	9 (52.9)	5 (33.3)	3 (50)	3 (60)	0 (0)	0.044*
Awakening pain, *n* (%)	0 (0)	1 (5.9)	1 (6.7)	0 (0)	1 (20)	0 (0)	0.390
Fever, *n* (%)	24 (92.3)	3 (17.6)	0 (0)	1 (16.7)	1 (20)	1 (25)	<0.001*
Rash, *n* (%)	16 (61.5)	1 (5.9)	0 (0)	1 (16.7)	0 (0)	1 (25)	<0.001*
Weight loss, *n* (%)	0 (0)	3 (17.6)	0 (0)	1 (16.7)	2 (40)	0 (0)	0.024*
Joint swelling, *n* (%)	14 (53.8)	14 (82.4)	13 (86.7)	5 (83.3)	4 (50)	4 (100)	0.098
Limitation of range of motion, *n* (%)	10 (38.5)	9 (52.9)	10 (66.7)	3 (50)	3 (60)	2 (50)	0.675
Generalized lymphadenopathy, *n* (%)	2 (7.7)	0 (0)	1 (6.7)	0 (0)	0 (0)	0 (0)	0.805
Hepatosplenomegaly, *n* (%)	2 (7.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.586

JIA juvenile idiopathic arthritis, *RF* rheumatoid factor. *Statistically significant result at $P < 0.05$

There were limitations of this study. As it utilized a retrospective design, there were some missing data as well as a recall bias from patient and parents. In addition, pediatric rheumatology is a relatively new discipline at our tertiary care hospital and in Thailand. Therefore, children with MSK complaints may be partly treated by orthopedic surgeons, general pediatricians, or general practitioners. In contrast, patients with a likelihood of rheumatologic diseases, including JIA, are specifically referred for a pediatric rheumatology consultation. Lastly, JIA is a heterogenous disease with clinical variations among its subtypes. The absence of arthritic features at onset cannot exclude systemic JIA [44]. Therefore, the predictors of JIA from our study may not solely predict systemic JIA with minimal arthritis.

In summary, the main goal of this study was to provide some clinical clues of the presence of JIA in children with MSK complaints. Children with morning stiffness lasting for at least 15 minutes or limping for more than 6 weeks with swollen joints on MSK examination should be suspected of having JIA. A comprehensive history and physical examination are almost always the cornerstone for making correct diagnoses in children with MSK complaints. An enhancement of MSK education for general practitioners and general pediatricians would be highly beneficial.

Author contributions SJ contributed to concept and design, acquisition of data, analysis and drafting the manuscript. SC contributed to concept and design, acquisition of data, analysis, interpretation of data, drafting and revising the manuscript and corresponding author. Both authors approved the final version of the manuscript.

Funding None.

Compliance with ethical standards

Ethical approval Research procedures were performed in accordance with the *Declaration of Helsinki*. Ethical approval for the study was obtained from Siriraj Institutional Review Board (Si 325/2016), Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Conflict of interest No financial or nonfinancial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

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