Musculoskeletal Complications of Juvenile Idiopathic Arthritis in a Tertiary Care Hospital Peshawar

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Abstract

Objective: The objective of this retrospective cross-sectional research was to examine the musculoskeletal problems associated with Juvenile Idiopathic Arthritis (JIA) at a tertiary care hospital located in Peshawar, Pakistan, during the period spanning from March 2022 to March 2023.

Methods: The study included the collection and analysis of data from patients with Juvenile Idiopathic Arthritis (JIA) who were undergoing treatment at the hospital. Descriptive statistics, subgroup analyses, and Fisher's Exact test were used to investigate potential connections between JIA and musculoskeletal problems.

Results: The analysis revealed a range of demographic features, with a significant proportion of patients (52.9%) falling between the age range of 11-15 years. The most common subtype of JIA was Polyarticular RF Negative, accounting for 44.1% of cases. This subtype was characterized by high levels of Erythrocyte Sedimentation Rate (ESR) (64.7%) and C-reactive protein (CRP) (47.1%), which are indicative of inflammation. The study revealed statistically significant correlations between substantial joint involvement, swelling, and discomfort in individuals with musculoskeletal conditions ($p < 0.05$). Nevertheless, the health evaluations conducted by patients and parents did not reveal any significant association with musculoskeletal issues. Significant correlations were seen between a positive family history of JIA or other RMDS and musculoskeletal disorders ($p < 0.05$).

Conclusion: The present research emphasizes the need to conduct a thorough medical history and physical tests for diagnosing Juvenile Idiopathic Arthritis (JIA), with a special focus on children who have distinct symptoms. Providing healthcare personnel with knowledge about musculoskeletal complaints may assist in promptly identifying and treating them, therefore enhancing patient results.

Keywords: Juvenile idiopathic arthritis, musculoskeletal complications, fisher's exact test, joint stiffness, Peshawar, Pakistan.

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Introduction

Juvenile Idiopathic Arthritis (JIA) encompasses a wide range of idiopathic inflammatory arthritis that mostly affects individuals under the age of 16, lasting for six weeks or more. The 2001 consensus conference of the International League of Associations for Rheumatology (ILAR) defined seven categories for Juvenile Idiopathic Arthritis (JIA). a) Oligoarthritic; b) Polyarthritis with positive rheumatoid factor (RF); c) Polyarthritis without RF; d) Systemic arthritis; e) Psoriatic arthritis; f) Arthritis associated with enthesitis; g) Joint arthritis without differentiation[1]. The precise etiology and precipitating factors of chronic arthritis in JIA remain elusive. The speculative nature of abnormal immune responses in genetically vulnerable individuals is attributed to the interplay between environmental variables. Environmental variables such as exposure to antibiotics and deliveries by C-section provide significant dan-

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gers. However, breastfeeding and having siblings in the family may serve as preventative measures[2]. The precise functions of microorganisms, including Parvovirus B19, Epstein-Barr virus, enteric bacteria, Chlamydophila pneumonia, and streptococcal infections, remain uncertain[3].

The prevalence estimates of various subtypes are as follows: oligoarthritic occurs in 50% to 60% of cases, RF negative polyarthritis in 11% to 28% of cases, RF positive polyarthritis in 2% to 7% of cases, systemic arthritis in 10% to 20% of cases, psoriatic arthritis in 2% to 15% of cases, and enthesitis-related arthritis in 1% to 7% of cases[4]. Certain subtypes have a higher prevalence in certain geographic locations. Radiofrequency (RF)-negative polyarthritis has a higher prevalence in North America, whereas oligoarthritic is more prevalent in southern Europe[5]. The prevalence of systemic arthritis and enthesitis-related arthritis is higher in the Southeast Asian region. The prevalence of uveitis is most pronounced in northern Europe and southern Europe, whereas it is somewhat lower in Latin America, Africa, the Middle East, and Southeast Asia[6-8]. Most JIA subtypes are mostly seen in females, except for enthesitis-related arthritis, which primarily affects men. Systemic JIA has an equal prevalence in both males and females[9].

Prior studies have consistently shown that pain is a prevalent and medically relevant symptom in children with JI[10]. A comprehensive analysis of research conducted from 1991 to 2009 revealed significant variations in prevalence rates among children and adolescents. The prevalence of musculoskeletal pain ranged from 4% to 40%, with a greater incidence seen in females and an upward trend with advancing age[11]. The distinction between the general population and children diagnosed with Juvenile Idiopathic Arthritis (JIA) lies in the fact that the pain experienced by children with JIA is associated with a condition characterized by recurrent bouts of acute inflammation. The management of these crises has improved compared to previous times due to the introduction of a novel class of pharmaceuticals known as biologic disease-modifying anti-rheumatic therapies[12].

Pain significantly affects the lives of children with JIA, diminishing their ability to engage in regular physical activities and participate in social or school-related events. The effect on activities and involvement is influenced by the type of JIA, disease activity, and illness severity[12,13]. The findings revealed that the primary elements that received the highest level of agreement among participants were the number of active joints, pain levels, and the quality of life as described by the participants[14]. Several research have shown correlations between pain and restrictions in physical activity. The presence of pain, stiffness, and exhaustion symptoms was shown to be a strong indicator of limited engagement in educational and social pursuits[15,16]. The children's engagement in school and physical education was minimal at first diagnosis but subsequently rose during the progression of the condition. There was a correlation between school absenteeism and illness activity and discomfort[15]. The literature is deficient regarding the musculoskeletal complications of JIA in Pakistan and therefore this study was conducted to fill the gaps. The objective of this retrospective cross-sectional research was to examine the musculoskeletal problems associated with Juvenile Idiopathic Arthritis (JIA).

Methodology

This retrospective cross-sectional study was carried out at Khyber Teaching Hospital Peshawar Pakistan from March 24, 2022, to March 24, 2023. This study included 102 participants diagnosed with JIA and receiving special treatment at Khyber Teaching Hospital Peshawar, Pakistan. Moreover, all the participants were included in this study according to the guidelines of the International League of Associations for Rheumatology (ILAR). Furthermore, patients with all types of JIA and with any duration of illness who have had musculoskeletal complications or other associated clinical conditions. This study was conducted according to the research ethical guidelines and was approved by the Institutional Review Board/Ethical Committee of Khyber Teaching Hospital, Peshawar, Pakistan. Additionally, being a retrospective cross-section study there was no need for informed consent from the

patients. Besides the confidentiality of the patient was kept secure.

The previous records from the database of the hospital were extracted that included the patient's registration, treatment, laboratory, and radiology examinations, demographic details, and discharge records. The demographic of the patient included age, gender, residence, socioeconomic status, etc while the laboratory test comprised of erythrocyte sedimentation rate and C reactive protein. Moreover, the X-ray report and ultrasound record were also elaborated.

Data was analyzed using IBM SPSS version 25. Descriptive statistics provide information on the demographic and clinical parameters, whereas subgroup analysis investigates variances within different subtypes of JIA. Moreover, to find out the association between JIA and musculoskeletal complications Fisher's Exact test was used. A p-value less the 0.05 was statistically significant.

Results

The age distribution of the patients indicates that the largest proportion (52.9%) belongs to the 11-15 years age group. A lesser proportion of patients between the age brackets of <5 years (6.9%) and 26-30 years (2%). The analysis of gender distribution reveals that 61.8% of the patients in this cohort are male. The examination of diagnostic subtypes reveals that Polyarticular RF-negative JIA is the predominant subtype, impacting 44.1% of individuals. In addition, a significant proportion of patients have elevated levels of Erythrocyte Sedimentation Rate (ESR) (64.7%) and C-reactive protein (CRP) (47.1%) (Table 1).

Table 1. Demographic detail of the participants

Parameter	Detail	Frequency (n) %
Age	<5 Years	7 (6.9)
	6-10 Years	17.6 (18)
	11-15 Years	52.9 (54)
	16-20 Years	20.6 (21)
	26-30 Years	2 (2)
Gender	Male	61.8 (63)
	Female	38.2 (39)
Diagnosis	Polyarticular RF Negative JIA	44.1 (45)
	Polyarticular RF Positive JIA	25.5 (26)
	Oligoarticular JIA Persistent	9.8 (10)
	Oligoarticular JIA	3.9 (4)
	Enthesitis-Related arthritis JIA	9.8 (10)
	Systemic JIA	5.9 (6)
	Extended	1 (1)
Erythrocyte Sedimentation Rate (ESR)	High	64.7 (66)
	Normal	35.3 (36)
C-reactive protein (CRP)	High	47.1 (48)
	Normal	52.9 (54)

A proportion of patients demonstrate engagement in 6-10 joints (27.5%). (The most prevalent range seen is 9-10 small joints, accounting for 23.5% of cases). Similarly, a significant proportion of individuals exhibit involvement in 1-6 major joints, with the highest prevalence seen in 2 joints (24.5%). The prevalence of swollen joints among patients exhibits variety, with the most frequent occurrence being 2 swollen joints (34.3%). Similarly, the distribution of sensitive joint counts demonstrates the range, with 2 tender joints being the most often seen (25.4%) (Table 2).

Table 2. Shows the involvement of joints being affected by JIA.

Parameter	Detail	Frequency (n) %
Number of Joint Involved	1-5	20.6 (21)
	6-10	27.5 (28)
	11-15	23.5 (24)
	16-20	18.6 (19)
	21-25	2.9 (3)
	26-30	6.9 (7)
Number of Small Joints Involved	0-1	17.6 (18)
	2	11.8 (12)
	3-4	8.8 (9)
	5-6	9.8 (10)
	7-8	14.7 (15)
	9-10	23.5 (24)
	11-12	4.9 (5)
	16	1 (1)
	18	2 (2)
	20	2.9 (3)
	30	2.9 (3)
Number of Large Joints Involved	0-1	6.9 (7)
	2	24.5 (25)
	3-4	19.6 (20)
	5-6	19.6 (20)
	7-8	15.7 (16)
	9-10	10.8 (11)
	11-12	2.9 (3)

Number of Swollen Joints	0-1	29.4 (30)
	2	34.3 (35)
	3-4	8.8 (9)
	5-6	7.8 (8)
	7-8	7.8 (8)
	9-10	6.9 (7)
	11-12	2.9 (3)
	22	1 (1)
	26	1 (1)
Tender Joint Count	0-1	11.7 (12)
	2	25.4 (26)
	3-4	13.7 (14)
	5-6	17.7 (18)
	7-8	11.7 (12)
	9-10	4.9 (5)
	11-12	2.9 (3)
	16	8.8 (9)
	22	1 (1)
	26	1 (1)
	28	1 (1)

The majority fall within the moderate range (1-4). Specifically, 31.4% of patients reported scores between 2, while 25.5% reported scores between 3-4. The evaluations made by parents reflect this pattern, as 21.6% rate their child's health as 2, while 38.2% rate it as 3-4. Significantly, the distribution demonstrates a cautious evaluation in contrast to the self-reports provided by patients. The prevalence of JIA in families is quite low, as shown by a positive history reported by only 7.8% of patients, in stark contrast to the negative history reported by 92.2% of patients. In the same vein, it is shown that 4.9% of patients exhibit a positive family history of other Rheumatic Musculoskeletal Diseases (RMDS), while a significant majority of 95.1% report a negative family history of other RMDS. It is worth mentioning that a significant proportion of the patients (47.1%) exhibit musculoskeletal difficulties (Table 3).

Table 3. Show the health assessment and history of the JIA patients.

Parameter	Detail	Frequency%(n)
Physical Global Health Assessment	0-1	14.7 (15)
	2	31.4 (32)
	3-4	25.5 (26)
	5-6	13.7 (14)
	7-8	10.8 (11)
	9-10	1 (1)
	28	2 (2)
Parents Global Health Assessment	0-1	8.8 (9)
	2	21.6 (22)
	3-4	38.2 (39)
	5-6	13.7 (14)
	7-8	13.7 (14)
	9-10	2 (2)
	11-12	2 (2)
Family History JIA	Positive	7.8 (8)
	Negative	92.2 (94)
Family History of Other RMDS	Positive	4.9 (5)
	Negative	95.1 (97)
Musculoskeletal Complications	Yes	47.1 (48)
	No	52.9 (54)

There was a significant correlation between the involvement of big joints (p = 0.006) and swollen joints (p = 0.007) and musculoskeletal issues. Likewise, there was a statistically significant association seen between painful joints and musculoskeletal problems (p = 0.006). There was no statistically significant correlation seen between physical global health assessment scores and musculoskeletal issues (p = 0.131). Nevertheless, there was a significant correlation between a family history of JIA and musculoskeletal problems (p = 0.020). The incidence of musculoskeletal problems was found to be considerably higher in patients who had a positive family history of Juvenile Idiopathic Arthritis (JIA) in comparison to those who did not have such a history. Likewise, a significant correlation was seen between a positive family history of other RMDS and musculoskeletal issues (p = 0.021), suggesting an increased susceptibility to difficulties in those with familial predispositions to RMDS (Table 4).

Table 4. Shows the association of JIA and health assessment and history with musculoskeletal complications.

Parameter	Detail	Musculoskeletal Complication	P-Value
		Yes	
Age	<5 Years	5	0.129
	6-10 Years	8	
	11-15 Years	20	
	16-20 Years	14	
	26-30 Years	1	
Gender Male	26	0.099	
Female	22		
Diagnosis of JIA	Polyarticular RF	23	0.293
	RF Negative JIA		
	Polyarticular RF	15	
	Positive JIA		

	Oligoarticular JIA Persistent	4	
	Oligoarticular JIA Enthesitis-Related arthritis JIA	0 3	
	Systemic JIA	3	
	Extended	0	
ESR	High	31	0.572
	Low	17	
CRP	High	26	0.124
	Low	22	
Number of Joint Involved	1-5	8	0.388
	6-10	10	
	11-15	12	
	16-20	11	
	21-25	2	
	26-30	5	
Small Joints	0-1	7	0.337
	2	4	
	3-4	3	
	5-6	5	
	7-8	7	
	9-10	11	
	11-12	4	
	16	1	
	18	2	
	20	1	
	30	3	
Large Joints	0-1	2	0.006
	2	11	
	3-4	10	
	5-6	7	
	7-8	9	
	9-10	7	
	11-12	2	
Swollen Joints	0-1	7	0.007
	2	17	
	3-4	5	
	5-6	6	
	7-8	5	
	9-10	5	

Discussion

This study included participants diagnosed with JIA and receiving special treatment at Khyber Teaching Hospital Peshawar, Pakistan. The demographic and clinical characteristics of individuals who have juvenile arthritis indicate that the largest proportion (52.9%) belongs to the 11-15 years age group, followed by the 6-10 years age group (17.6%) and the 16-20 years age group (20.6%). Furthermore, it is worth mentioning that there exists a lesser proportion of patients between the age brackets of <5 years (6.9%) and 26-30 years (2%), therefore highlighting the diverse age cohorts impacted by JIA. Previous research shows that pain is a prevalent and medically relevant symptom in children with JIA [17]. Whereas chronic pain is prevalent among children and adolescents. Prevalence rates among children and adolescents that ranged from 4% to 40% [12].

Genetic variables of the patients indicate that most of them fall within the moderate range of[3]. Specifically, 31.4% of patients reported scores between 2, while 25.5% reported scores between 3-4. Several previous investigations have specifically examined the factors that might predict the development of JIA [4,18]. In retrospective research conducted by McGhee et al., it was observed that children afflicted with chronic arthritis who were admitted to a rheumatology unit often reported symptoms of joint swelling or gait abnormalities. Additionally, scholars observed that children with chronic arthritis were less prone to reporting isolated MSK discomfort as their first symptom. Cattalini *et al.*, conducted recent research that revealed a significant association between a pattern of joint swelling, aggravating factors of pain, the incidence of pain, and the length of morning stiffness with a final diagnosis of chronic arthritis in patients with complaints of musculoskeletal (MSK) conditions[10,19].

A correlation between morning stiffness and the occurrence of JIA. Indicators of inflammatory arthritis include morning stiffness and the sensation of stiffness after periods of rest, sometimes referred to as the gelling phenomenon[20]. However, there is a lack of evidence specifically addressing the precise length of morning stiffness in children[21]. According to Cattalini et al., it was observed that almost 33% of children diagnosed with chronic arthritis had morning stiffness lasting less than one hour. The preliminary criteria established by the American College of Rheumatology include morning stiffness lasting 15 minutes as one of the criteria used to describe a clinically inactive illness in juvenile idiopathic arthritis (JIA)[20]. Our research is the first to establish a correlation between morning stiffness and JIA in children. Therefore, it might potentially serve as a predictor of juvenile idiopathic arthritis (JIA). In addition to systemic JIA, other systemic

inflammatory illnesses, such as SLE, JDM, and autoinflammatory syndromes, may cause MSK symptoms along with fever and rashes[4]. Patients with systemic lupus erythematosus (SLE) often have symmetrical severe arthralgia and non-erosive polyarthritis[3]. Childhood systemic lupus erythematosus (SLE) has a low incidence of chronic polyarthritis [31]. Patients with Juvenile Diabetes Mellitus (JDM) may have joint discomfort as an early clinical manifestation[14]. Nevertheless, it seems that morning stiffness is not often reported as an MSK symptom in children with JDM. Conversely, morning difficulty has been seen in 70% of instances of systemic-onset juvenile rheumatoid arthritis [19]. Hence, morning stiffness may serve as a clinical characteristic that differentiates systemic Juvenile Idiopathic Arthritis (JIA) from other systemic inflammatory illnesses.

Out of the 111 patients who had isolated MSK discomfort, 90% (n=91) were diagnosed with mechanical joint disease[22]. According to Cattalini et al., a significant proportion of final diagnoses were non-inflammatory illnesses, accounting for around 64% of the diagnoses. The prevalent subtype of joint inflammatory arthritis (JIA) identified in their study was oligoarthritic. According to recent research, the most prevalent causes of MSK pain in children and adolescents were non-inflammatory disorders (42.2%), followed by rheumatic diseases (31%), and infection-related problems (21.6%). It is worth mentioning that the percentage of JIA was only 8.3% in the group with rheumatic disease[22]. According to statistics from Southeast Asian nations, rheumatic disorders were the most common in the population of pediatric rheumatology clinics [22]. Due to the scarcity of pediatric rheumatologists in Thailand, probably, orthopedic surgeons would partially handle the management of children with MSK symptoms.

A study revealed that oligoarthritic was not the predominant subtype[14]. Two studies indicated a higher prevalence of individuals with systemic JIA in Thailand[20]. Hence, variations in the prevalence of JIA subtypes might potentially be ascribed to ethnic factors. Furthermore, it is plausible that a referral bias may serve as an alternative explanation for this outcome.

The current investigation corroborated the observation that MSK complaints differ among the various subtypes of JIA. Patients with systemic Juvenile Idiopathic Arthritis (JIA) may have a predominance of systemic symptoms rather than articular symptoms during the early stages of the illness. Morning stiffness was mostly seen in individuals with polyarticular joint arthroplasty (JIA) and arthritis associated with enthesitis.

This research has several constraints. Due to the use of a retrospective design, the study encountered several instances of missing data and memory bias originating from both patients and parents. Consequently, orthopedic surgeons, general pediatricians, or general practitioners may provide partial treatment for children with MSK symptoms. On the other hand, patients who are likely to have rheumatologic illnesses, such as JIA, are specifically recommended for a consultation with a pediatric rheumatologist. Finally, JIA exhibits heterogeneity in its clinical manifestations among its many subgroups. The lack of arthritic characteristics, in the beginning, does not rule out the possibility of systemic JIA[22].

Conclusion:

This study concluded that the factors being identified as predictors of JIA may not exclusively forecast JIA in cases with mild arthritis but children who have morning stiffness for a minimum duration of 15 minutes, accompanied by swollen joints during a musculoskeletal examination, may be considered as potential candidates for Juvenile Idiopathic Arthritis (JIA). An extensive medical history and thorough physical examination are often the fundamental basis for accurately diagnosing children with MSK symptoms. Improving the education of general practitioners and general pediatricians in MSK would be very advantageous.

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Disclaimer: None

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