The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 4, 2025

JUVENILE IDIOPATHIC ARTHRITIS IN FOCUS: A HOLISTIC EXAMINATION OF CLINICAL PROFILES, DIAGNOSTICS, AND INDIVIDUALIZED TREATMENT APPROACHES IN SOUTHERN PAKISTAN

Syeda Rida E Zehra[*1], Syed Muhammad Aqeel Abidi[2], Lubna Nazir[3], Tahira Perveen[4], Syeda Namayah Fatima Hussain[5], Samar Abbas Jaffri[6], Misal Jawed[7], Saad Naviwala[8], Hammad Ali Khan[9], Khawaja Moiz Ullah Ghouri[10]

[*1,3,4,5,6,9]*Liaquat National Hospital & Medical College, Karachi*
[2,7,8]*Aga Khan University Hospital, Karachi*
[10]*Department of Statistics, University of Karachi*

[*1]s.rida.e.zehra@gmail.com, [2]syed.abidi2@scholar.edu, [3]seedling7602@gmail.com, [4]tp.umer@gmail.com, [5]namayah.hussain@gmail.com, [6]abbasraza569@hotmail.com, [7]misal.jawed@gmail.com, [8]saadsimnaviwala@gmail.com, [9]drhammadalikhan@gmail.com, [10]moizghouri689@gmail.com

DOI: https://doi.org/10.5281/zenodo.15221384

Keywords
Biomarkers, Disease Management, Individualized Treatment, Juvenile Idiopathic Arthritis, Therapeutic Approaches

Article History
Received on 08 March 2025
Accepted on 08 April 2025
Published on 15 April 2025

Corresponding Author: *

Abstract

OBJECTIVE

To investigate clinical features, diagnostic methods, and personalized treatment strategies of Juvenile Idiopathic Arthritis (JIA) in Southern Pakistan

METHODOLOGY

A retrospective cohort investigation was executed at Liaquat National Hospital, Karachi, spanning from January 2015 to December 2021, comprising 134 patients aged under 16 years who were diagnosed with Juvenile Idiopathic Arthritis (JIA) in accordance with ILAR classification. The study examined disease presentation patterns, accuracy of diagnostic studies, and tailored treatment plans. Based on this time period, patients who visited the outpatient department were part of this analysis. All the collected data were analyzed by using SPSS version 26, and $p \leq 0.05$ indicates the criteria of statistical significant.

RESULTS

Among a cohort of 134 patients identified with Juvenile Idiopathic Arthritis (JIA), the average age was calculated to be 11.22 ± 3.91 years, with a male proportion of 53.7%. The common subtypes were polyarticular (44%) and oligoarticular (35.8%). The most prevalent extra-articular manifestations were fever (20.9% of the cases). ANA, anti-CCP and RA factors were all positive in 18.7%, 20.1% and 27.6% of the cases, respectively. Methotrexate represented the most frequently prescribed DMARD (69.3%), highlighting the specifics of individual management relative to a patient's clinical profile.

CONCLUSION

This study highlights the clinical diversity, diagnostic markers, and treatment patterns of Juvenile Idiopathic Arthritis in Southern Pakistan. Polyarticular and

oligoarticular subtypes were most common, with methotrexate as the primary treatment. Although serological markers aided diagnosis, clinical evaluation remained essential. These findings emphasize the need for individualized care and provide valuable regional data to inform future diagnostic and management strategies.

INTRODUCTION

Juvenile Idiopathic Arthritis (JIA), however, is an autoimmune chronic inflammatory joint disease which can cause permanent damage to a developing child and define a persistent arthritis in a child or adolescent. The chronic, persistent inflammation restricts activities of daily living and productivity, greatly diminishing the quality of life of affected patients. Juvenile idiopathic arthritis (JIA) is the most prevalent chronic rheumatic pediatric condition [1] but its cause is unknown. JIA is categorized into certain types based on its heterogeneity in terms of clinical manifestations, pathophysiology, genetic predisposition or serological laboratory results, disease progression, and prognosis. JIA can be classified into one of seven subtypes according to the International League of Associations for Rheumatology (ILAR) [2]: (1) oligoarthritis; (2) rheumatoid factor (RF) positive polyarthritis; (3) RF negative polyarthritis; (4) systemic arthritis; (5) psoriatic arthritis;(6) enthesitis-related arthritis; and (7) undifferentiated arthritis.

The International League of Associations for Rheumatology (ILAR) defines seven JIA subtypes: oligoarthritis, rheumatoid factor (RF) positive polyarthritis, RF negative polyarthritis, systemic arthritis, psoriatic arthritis, enthesitis-related arthritis, and undifferentiated arthritis (2). This subtype categorization governs therapeutic decision-making and prognostication, making proper diagnosis via serologic markers and imaging examination of the subtype imperative.

The pathogenesis of the illness involves both endogenous and exogenous antigens with a raised inflammatory response have been proven to have a significant role [1]. JIA, being a clinically heterogeneous group of arthritides, manifests as chronic or recurring pain, restricted physical activity, and limited use of upper limbs or hands in afflicted children. The diagnosis of JIA is a diagnosis of exclusion, with the criteria defined as lasting at least 6 weeks and onset before the age of 16 and with no known etiology [3].

In 2020, JIA was estimated to have an incidence of 1.6 to 23/100,000 and a prevalence of 3.8 to 400/100,000 [4]. Worldwide, JIA influences an estimated three million children and youth [5]. In Pakistan or in the region, there is no data on the incidence and prevalence of JIA. JIA is associated highly heterogeneous regarding frequency and subtype distribution worldwide, suggesting contributory by diverse risk factors including ethnicity, environment and the genetic background. The disease can result in temporary disability, but it may also become chronically disabling and significantly alter the overall health status of affected children.

Juvenile Idiopathic Arthritis represents a complex and impactful health challenge in pediatric rheumatology, demanding a meticulous understanding of its clinical manifestations and varied subtypes for timely and personalized interventions. We combine our retrospective analysis and synthesis of existing literature to offer not only a holistic view of the clinical landscape of JIA but also a call to action. This includes clinical manifestations, subtypes, and diagnostic approaches. Early recognition is paramount given the absence of a discernable etiological cause, we will discuss various serologic markers and imaging studies available. Personalized and timely management strategies have been seen to improve outcomes in JIA patients.

METHODOLOGY

A retrospective cohort study carried out at the Department of Rheumatology, Liaquat National Hospital, Karachi, Jan 2015-Dec 2021. The primary aim of this investigation was to elucidate patterns in disease presentation, assess the effectiveness of prevailing diagnostic techniques, and evaluate individualized therapeutic approaches designed to

improve patient outcomes within the specified region. The study sample included 134 patients aged <16 years with JIA according to ILAR criteria who attended the outpatient department during the study period.

Individuals exceeding the age of 16 years, those exhibiting active infections, comorbid diabetes, or chronic pain syndromes not associated with Juvenile Idiopathic Arthritis (JIA) were systematically excluded to promote a concentrated examination of JIA-specific clinical attributes and therapeutic outcomes. The research protocol received endorsement from the Ethical Review Board (ERB) of Liaquat National Hospital, thus ensuring adherence to ethical guidelines applicable to retrospective studies. A structured proforma was employed to retrieve pertinent clinical data from electronic medical records (EMRs). The collected variables characterized patient demographics (age, gender), disease classification and subtype, serological marker outcomes (Antinuclear Antibodies [ANA], Anti-Cyclic Citrullinated Peptide [Anti-CCP], and Rheumatoid Factor [RA Factor]), medication history, and extra-articular manifestations. The data were entered into and analyzed using SPSS version 26.0. Continuous variables were described using descriptive statistics. Counts and percentages were used to describe categorical variables. The Chi-Square test was used to evaluate the statistical significance of associations at two sides ($P \leq 0.05$).

RESULTS

The investigation encompassed a cohort of 134 individuals with a mean chronological age of 11.22 ± 3.91 years. Within this cohort, 66 participants (49.3%) were within the age range of 3 to 12 years, while 68 participants (50.7%) were above the age of 12 years. Regarding the gender composition, 72 participants (53.7%) were identified as male, and 62 participants (46.3%) were identified as female.

The categorization of arthritis types among the study participants indicates that a predominant proportion presented with polyarticular arthritis, representing 59 individuals (44%). This was succeeded by oligoarticular arthritis, which was detected in 48 individuals (35.8%). Enthesitis-related arthritis was diagnosed in 10 individuals (7.5%). Systemic and psoriatic arthritis were each diagnosed in 6 individuals (4.5%). It is noteworthy that 5 individuals (3.7%) did not manifest any form of arthritis, as depicted in FIGURE I.

Among the 134 individuals diagnosed with juvenile idiopathic arthritis (JIA), 93 individuals (69.4%) did not demonstrate any extra-articular manifestations.

The most frequently observed extra-articular manifestation was fever, which was recorded in 28 subjects (20.9%), succeeded by the simultaneous presentation of weight loss and fever in 8 subjects (6%). Uveitis was detected in 2 subjects (1.5%), whereas solitary instances of weight loss, lymphadenopathy, and a composite manifestation of visceromegaly (encompassing the liver and spleen), fever, and rash were each documented in 1 subject (0.7%), as delineated in TABLE I.

The analysis of serological and inflammatory markers indicated a mean erythrocyte sedimentation rate (ESR) of 49.88 ± 38.20 mm/hr and a mean C-reactive protein (CRP) concentration of 35.34 ± 49.47 mg/dL. Among the serological parameters, antinuclear antibodies (ANA) were positive in 25 individuals (18.7%), anti-cyclic citrullinated peptide (Anti-CCP) antibodies were present in 27 individuals (20.1%), and rheumatoid factor (RA Factor) was detected in 37 individuals (27.6%), as delineated in TABLE II.

The therapeutic overview of the patients indicates that disease-modifying antirheumatic drugs (DMARDs) represented the most frequently prescribed therapeutic agents. Methotrexate (MTX) emerged as the most prevalently administered DMARD, utilized by 61 individuals (69.32%) either as monotherapy or in conjunction with other agents. Combination therapies exhibited methotrexate (MTX) in conjunction with hydroxychloroquine (HCQ) in a cohort of 7 subjects (7.95%), MTX in combination with leflunomide in another group of 7 subjects (7.95%), and MTX combined with sulfasalazine in 2 subjects (2.27%). Additional therapeutic combinations encompassed HCQ paired with MTX in 7 subjects (7.95%), HCQ in conjunction with leflunomide in 1 subject (1.14%), HCQ combined with both leflunomide and MTX in 1 subject (1.14%), and a triad combination of MTX, sulfasalazine, and HCQ administered to 1 subject (1.14%). Biological therapies encompassed tumor necrosis factor (TNF) antagonists, including etanercept, which was administered to a cohort of 14 participants (10.4%), whereas adalimumab and infliximab were each

employed in a singular participant (0.7%). Furthermore, the interleukin-6 (IL-6) antagonist tocilizumab was administered to a total of 8 participants (6%).

With respect to immunosuppressants, corticosteroids represented the principal agents, being administered intra-articularly to 46 subjects (77.9%) and systemically to 6 subjects (10.2%). Cyclosporine was also administered to 6 subjects (10.2%), while systemic corticosteroids alone were delivered to 1 subject (1.7%), as illustrated in TABLE III.

The examination of the correlation between the various classifications of Juvenile Idiopathic Arthritis (JIA) and serological indicators unveiled multiple consequential findings. The distribution of gender among males and females exhibited no statistically significant disparity across the JIA classifications (p=0.445). The incidence of antinuclear antibodies (ANA) was markedly elevated in cases of polyarticular JIA (20.3%) when juxtaposed with alternative classifications, yielding a significant p-value of 0.053. In relation to anti-cyclic citrullinated peptide (CCP) antibodies, a significant correlation was identified, characterized by heightened positivity in systemic JIA (66.7%) and oligoarticular JIA (20.8%), in comparison to other classifications (p=0.033). The rheumatoid factor (RA Factor) did not demonstrate a statistically significant variation among the JIA classifications (p = 0.158), as delineated in TABLE IV. The correlation between extra-articular manifestations and serological indicators disclosed noteworthy findings. The presence of uveitis, fever, and weight loss did not exhibit a statistically significant correlation with the initial status of ANA (p = 0.958). Nevertheless, a significant relationship was noted between anti-CCP positivity and fever, with 14.3% of individuals experiencing fever displaying positive anti-CCP antibodies (p = 0.039*). The positivity of rheumatoid factor (RA Factor) was not significantly correlated with any of the extra-articular manifestations (p=0.391), as illustrated in TABLE VI.

DISCUSSION

Studies have indicated that JIA is a heterogeneous autoimmune disease clinically and pathophysiologically [6]. Globally, its management differs from one region to another, while its diagnostic and therapeutic challenges are pronounced in resource-limited settings [7]. Pediatric rheumatic disease care seen through the lens of genetic diversity and disparities in healthcare access underscores a need for tailored approaches [8]. Serological markers such as the antinuclear antibodies (ANA) are used extensively in the framework of systemic rheumatic diseases [9]. Moreover, different genes polymorphisms and additional factors including biomarker such as Insulin-like Growth Factor-1 (IGF-1) also contribute in disease mechanisms and progression [10].

However, this study also highlighted clinical features, diagnostic markers, and treatment features, of JIA in southern Pakistan that can aid in better management of the disease in the regions concerned. There is scarce data available in literature regarding Juvenile Idiopathic Arthritis (JIA) in Pakistani setting [11]. However, there are no studies in Pakistan that assess the incidence, prevalence of this disease. This review summarizes an overview of JIA including clinical features, subtypes, diagnosis and management.

Our study corroborates with previously identified patterns of higher prevalence for polyarticular (44.0%) and for oligoarticular (35.8%) subtypes. This finding is also supported with Naz et al., study in which 11% of patients had JIA and 71.9% and 22.7% were polyarticular JIA and oligoarticular JIA respectively in the sample population [12].

These results were similar to those published by Gowa et al., who categorized JIA into polyarticular (53.7%) and pauciarticular (46.3%) [13]. However, a study conducted in the United Arab Emirates found oligoarticular (55%) to be the most common followed by polyarticular (23%) [14].

There are no studies from Pakistan that report extra-articular manifestations in the patients. The literature describes certain extra-articular manifestations to be more prevalent with certain subtypes of JIA [15]. Our study found that most patients (69.4%) didn't report any extra-articular manifestation at all.

A systematic review reported anti-CCP to be positive in around a quarter of JIA patients, this is similar to the 20.1% positivity seen in our patients [16]. Anti-CCP has a high specificity for JIA, however, it has low sensitivity hence a negative result doesn't mean absence of the disease. In a study from Pakistan, Ahmed et al. reported ANA positivity to be 16%, which is similar to the 18.7% finding in our study [11]. Meanwhile, Naz et al. reported RA factor

positivity in 10.27% of the patients, this is less than the 27.6% positivity seen in our study [12]. While serological markers are used often in the cases of juvenile idiopathic arthritis, our study findings show that there is no significant association between any of these serological markers. This finding reemphasizes that the diagnosis of JIA is a clinical diagnosis rather than a serological diagnosis, there is no single test that can be used to diagnose JIA [15].

While the treatment options vary throughout the world, there are some uniformities seen in the regimen being prescribed. The findings of our study showed that DMARDs were the most popular treatment option followed by immunosuppressants, while biologics were the least preferred treatment. This same finding was seen in the settings of Canada and Germany [17]. However, the study conducted in Lahore by Naz et al. showed that the doctors preferred combination of Methotrexate and Steroid over either of them alone, however, they didn't account for the use of biologics [12]. Our study also found a significant association between the subtype of JIA and the usage of immunosuppressants. Literature search revealed that in most cases of JIA, the patients were prescribed an immunosuppressant during the treatment course [18]. In immunosuppressants, corticosteroids were the most commonly used modality and most of it was either administered orally or intraarticularly, this finding was seen in most studies worldwide [17,18].

The findings from this study hold significant implications in the clinical approach to JIA. This is one of the only studies in Pakistan that investigate JIA holistically, taking into account everything from diagnosis to manifestations to treatment. The study reiterates the need for clinicians to rely on comprehensive clinical assessments rather than solely on serological markers for diagnosis. The study also reinforces the call for holistic and personalized approach to patient care as the disease holds different details for each patient hence there can't be any generalized protocols. This personalized approach can enhance the efficacy of interventions, improve patient outcomes, and ultimately lead to better management of JIA. The study calls for continued research and the development of refined diagnostic criteria and therapeutic strategies, aiming to provide optimized care for all children affected by this complex rheumatic disease.

There were several limitations that we encountered in this study. Firstly, as this was a retrospective study and relied on pre-existing data from EMRs, there were certain biases in the data which might have potentially skewed the findings. One of the bias seen in the study is regarding the selection of patients, as patients seeking care can differ systematically from those who didn't visit hospitals. As this was a study from only one center, the results received might not be applied to broader populations, especially in the study above we have discussed how JIA presentations vary due to geographics and demographics.

The study does possess multiple strengths, as the cohort of 134 patients is a substantial dataset and one of the biggest datasets taken in Pakistan, hence it holds importance in analyzing trends and associations. This study takes into account details of serologic markers and extra-articular manifestations along with management, something that offers valuable insights of JIA in Pakistan not examined before. By controlling for effect modifiers and employing robust statistical analyses, the study enhances the reliability of its findings.

Despite significant advancements in our understanding and management of JIA, there are a lot of unknowns regarding JIA, hence there is a need for further research into the components of JIA. Figuring out the intricate interplay between genetic, environmental, and immunological factors that contribute to JIA could lead to the identification of new therapeutic targets. Furthermore, as discussed above there aren't any biomarkers present that can aid in early diagnosis, predict disease progression, and monitor treatment response, hence development of such a biomarker might be of great help in preventing irreversible damage and disability. Research for more effective and targeted therapies could reduce disease morbidity, improve patient outcomes, and improve quality of life.

CONCLUSION

This study highlights the clinical diversity, diagnostic markers, and treatment patterns of Juvenile Idiopathic Arthritis in Southern Pakistan. Polyarticular and oligoarticular subtypes were most common, with methotrexate as the primary

treatment. Although serological markers aided diagnosis, clinical evaluation remained essential. These findings emphasize the need for individualized care and provide valuable regional data to inform future diagnostic and management strategies.

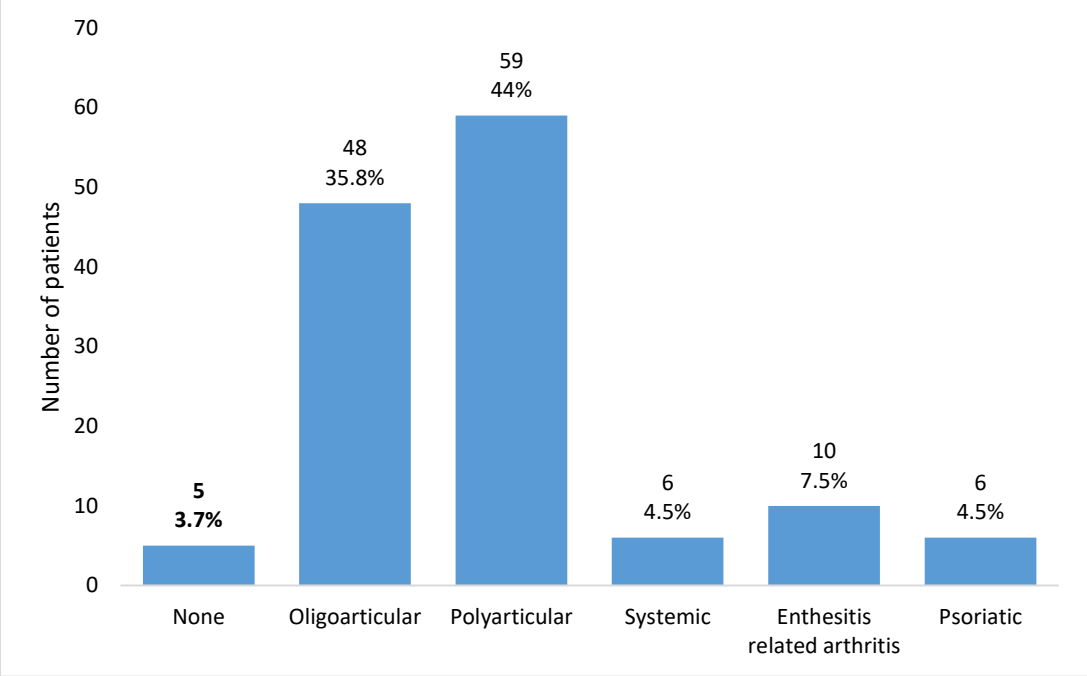

Figure-1: Distribution of patients according to types of JIA

Table I: Extra-articular Manifestations in Patients with JIA (n=134)	
Variables, n (%)	
None	93 (69.4)
Uveitis	2 (1.5)
Fever	28 (20.9)
Weight Loss	1 (0.7)
Lymphadenopathy	1 (0.7)
Visceromegaly (liver, spleen) + Fever + Rash	1 (0.7)
Weight Loss + Fever	8 (6)

Table II: Serology and Inflammatory Markers	
ESR, mm/hr (Mean ± SD)	49.88±38.20
CRP, mg/dL (Mean ± SD)	35.34±49.47
ANA, n (%)	25 (18.7)
Anti CCP, n (%)	27 (20.1)
RA Factor, n (%)	37 (27.6)

Table III: Overview of Treatment			
DMARDS, n (%)	HCQ		3 (3.41)
	MTX		61 (69.32)
	Leflunomid		2 (2.27)
	Sulfasalazine		3 (3.41)
	HCQ + MTX		7 (7.95)
	HCQ + Leflunomid		1 (1.14)
	HCQ + Leflunomid + MTX		1 (1.14)
	MTX + Leflunomid		7 (7.95)
	MTX + Sulfasalazine		2 (2.27)
	MTX + Sulfasalazine + HCQ		1 (1.14)
Biologics, n (%)	TNF1 - Etanercept		14 (10.4)
	TNF1 - Adalimumab		1 (0.7)
	TNF1-Infliximab		1 (0.7)
	IL61 - Toclizumab		8(6)
Immuno Suppressants, n (%)	Corticosteroid	Intra-articular	46 (77.9)
		Systemic	06 (10.2)
	Cyclosporin		6 (10.2)
	Corticosteroids		1(1.7)

Table IV: Association of Type of JIA with Serologies								
Variables		Types of JIA, n (%)						P-Values
		Oligoarticular	Polyarticular	Systemic	ERA	Psoriatic	None	
Gender	Male	26 (54.2)	30 (50.8)	2 (33.3)	8 (80)	4 (66.7)	2 (40)	0.445
	Female	22 (45.8)	29 (49.2)	4 (66.7)	2 (20)	2 (33.3)	3 (60)	
ANA Initial	Positive	6 (12.5)	12 (20.3)	1 (16.7)	1 (10)	4 (66.7)	1 (20)	0.053*
	Negative	42 (87.5)	47 (79.7)	5 (83.3)	9 (90)	2 (33.3)	4 (80)	
Anti CCP	Positive	10 (20.8)	12 (20.3)	4 (66.7)	0 (0)	0 (0)	1 (20)	0.033*
	Negative	38 (79.2)	47 (79.7)	2 (33.3)	10 (100)	6 (100)	4 (80)	
RA Factor	Positive	12 (25)	21 (35.6)	2 (33.3)	0 (0)	2 (33.3)	0 (0)	0.158
	Negative	36 (75)	38 (64.4)	4 (66.7)	10 (100)	4 (66.7)	5 (100)	

Table 6: Association of Extra-articular Manifestation with Serologies

Variables		Extra-articular Manifestation, n (%)							P-values
		Uveitis	Fever	Weight Loss	Lymphadenopathy	Visceromegaly + Fever + Rash	Weight Loss + Fever	None	
ANA Initial	Positive	0 (0.0)	6 (21.4)	0 (0.0)	0 (0)	0 (0.0)	1 (12.5)	18 (19.4)	0.958
	Negative	2 (100)	22 (78.6)	1 (100)	1 (100)	1 (100)	7 (87.5)	75 (80.6)	
Anti CCP	Positive	2 (100)	4 (14.3)	0 (0)	0 (0)	1 (100)	1 (12.5)	19 (20.4)	0.039*
	Negative	0 (0)	24 (85.7)	1 (100)	1 (100)	0 (0)	7 (87.5)	74 (79.6)	
RA Factor	Positive	1 (50)	8 (28.6)	1 (100)	0 (0)	0 (0)	4 (50)	23 (24.7)	0.391
	Negative	1 (50)	20 (71.4)	0 (0)	1 (100)	1 (100)	4 (50)	70 (75.3)	

REFERENCES

1. Barut K, Adrovic A, Şahin S, Kasapçopur Ö. Juvenile idiopathic arthritis. Balkan Med J. 2017; 34(2):90-101.
2. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390-2.
3. Giancane G, Consolaro A, Lanni S, Davì S, Schiappapietra B, Ravelli A. Juvenile idiopathic arthritis: diagnosis and treatment. Rheumatol Ther. 2016;3(2):187-207.
4. Thierry S, Fautrel B, Lemelle I, Guillemin F. Prevalence and incidence of juvenile idiopathic arthritis: a systematic review. Joint Bone Spine. 2014;81(2):112-7.
5. Dave M, Rankin J, Pearce M, Foster HE. Global prevalence estimates of three chronic musculoskeletal conditions: club foot, juvenile idiopathic arthritis and juvenile systemic lupus erythematosus. Pediatr Rheumatol Online J. 2020;18(1):49.
6. Huang HY, Wireko AA, Miteu GD, Khan A, Roy S, Ferreira T, et al. Advancements and progress in juvenile idiopathic arthritis: a review of pathophysiology and treatment. Medicine. 2024;103(13):e37567.
7. Scott C, Chan M, Slamang W, Okong'o L, Petty R, Laxer RM, et al. Juvenile arthritis management in less resourced countries (JAMLess): consensus recommendations from the Cradle of Humankind. Clin Rheumatol. 2019;38:563-75.
8. Scott C, Sawhney S, Lewandowski LB. Pediatric rheumatic disease in lower to middle-income countries: impact of global disparities, ancestral diversity, and the path forward. Rheum Dis Clin. 2022;48(1):199-215.
9. Tipu HN, Bashir MM, Iqbal W. Determination of specificity and pattern of antinuclear antibodies (ANA) in systemic rheumatic disease patients positive for ANA testing. J Coll Physicians Surg Pak. 2018;28(1):40-3.
10. Fayyaz I, Khaliq S, Bano F, Kaul H. Genetic Polymorphism and serum levels of Insulin like Growth Factor-1 (Igf-1) in patients of rheumatoid arthritis. Pak J Med Sci. 2023;39(3):764.
11. Ahmed S, Ali SR, Ishaque S, Sami N. Clinical and biochemical characteristics of children with juvenile idiopathic arthritis. J Coll Physicians Surg Pak. 2014;24(7):498-502.
12. Naz S, Mushtaq A, Rehman S, Bari A, Maqsud A, Khan MZ, et al. Juvenile rheumatoid arthritis. J Coll Physicians Surg Pak. 2013;23(6):409-12.
13. Gowa MA, Ibrahim MN, Memon BN, Raza SJ. A cross sectional study on juvenile idiopathic arthritis in paediatric population. J Pak Med Assoc. 2015;65(4):370-3.

14. Khawaja K, Kalas R, Almasri N. Subtype frequency, demographic features, treatment and outcome of juvenile arthritis in one Centre in Abu Dhabi in the United Arab Emirates. Pediatr Rheumatol Online J. 2023;21(1):14.
15. Garner AJ, Saatchi R, Ward O, Hawley DP. Juvenile idiopathic arthritis: a review of novel diagnostic and monitoring technologies. Healthcare (Basel, Switzerland). 2021;9(12).
16. Braschi E, Shojania K, Allan GM. Anti-CCP: a truly helpful rheumatoid arthritis test? Can Fam Physician. 2016;62(3):234.
17. Hugle B, Haas JP, Benseler SM. Treatment preferences in juvenile idiopathic arthritis - a comparative analysis in two health care systems. Pediatr Rheumatol Online J. 2013;11(1): 3.
18. Kip MMA, de Roock S, Currie G, Marshall DA, Grazziotin LR, Twilt M, et al. Pharmacological treatment patterns in patients with juvenile idiopathic arthritis in the Netherlands: a real-world data analysis. Rheumatology. 2022;62(SI2):SI170-80.