

Plotting the Articular Disease Impact of Juvenile Idiopathic Arthritis: Discernments into Clinical Phenotypes and Demographic Tide in a Pakistani Cohort

Annam Javed, Amer Fakhr, Sadia Ali*, Amina Khurshid, Usama Zahid

Department of Medicine, Pak Emirates Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan, *Department of Pathology, Armed Forces Institute of Transfusion, Rawalpindi /National University of Medical Sciences (NUMS) Pakistan,

ABSTRACT

Objective: To investigate into the pattern of joint engagement along with the laboratory markers in Juvenile Idiopathic Arthritis (JIA) amongst the Pakistani cohort.

Study Design: Cross-sectional study.

Place and Duration of Study: Pak-Emirates Military Hospital, Rawalpindi Pakistan from Dec 2023 to Dec 2025.

Methodology: Demographic profile, clinical, and serological statistics were collected focusing on joint distributions, autoimmune biomarkers, inflammatory parameters and treatment strategies. Statistical tests were performed to equate these variables among patient subgroups.

Results: A total of 151 pediatric patients with Juvenile Idiopathic Arthritis (JIA) were included in the study. Polyarticular disease was the most common pattern of joint involvement (64.2%), followed by oligoarticular (33.8%) and monoarticular (2.0%). Antinuclear Antibodies (ANA) were the most frequently detected serological marker (13.2%), followed by Anti-Cyclic Citrullinated Peptide (Anti-CCP, 12.6%), Human leukocyte Antigen B27 (HLA-B27, 4.0%), and Rheumatoid Factor (2.6%). Growth retardation was observed in 26.5% of patients, while uveitis was seen in 2.6%. Methotrexate was the predominant treatment modality (69.5%). Significant differences were observed in Erythrocyte Sedimentation Rate (ESR, $p=0.025$), C-Reactive Protein (CRP, $p=0.006$), and Anti-CCP antibody positivity ($p<0.001$) across joint patterns, while other serological markers showed no significant association.

Conclusion: Polyarticular disease was the most common pattern of joint involvement, followed by oligoarticular and monoarticular. Antinuclear Antibodies were the most frequently detected serological marker, followed by Anti-Cyclic Citrullinated Peptide, Human leukocyte Antigen B27, and Rheumatoid Factor.

Keywords: Autoimmune Profile, Joint Involvement, Juvenile Idiopathic Arthritis.

How to Cite This Article: Javed A, Fakhr A, Ali S, Khurshid A, Zahid U. Plotting the Articular Disease Impact of Juvenile Idiopathic Arthritis: Discernments into Clinical Phenotypes and Demographic Tide in a Pakistani Cohort. *Pak Armed Forces Med J* 2026; 76(Suppl-9): S1511-S1515.

DOI: <https://doi.org/10.51253/pafmj.v76iSUPPL-9.14480>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a chronic rheumatologic disease in children, characterized by persistent inflammation of joints.¹ The reported incidence worldwide ranges between 1.6 and 23 per 100,000 children. Depending on the geography, inheritance pattern and methodological variables, the prevalence varies from 3.8 to 400 per 100,000 children.^{2,3} Almost 10–20% of JIA cases globally are complicated by uveitis, which contributes to be a leading cause of visual morbidity among this population.⁴

Regional data highlights significant phenotypic variation across South Asia. In Pakistan, polyarticular JIA was the most frequent subtype (54%), with a mean onset of 6.45 years and low ANA positivity (16%).⁵ Conversely, other studies identify Enthesitis-Related

Arthritis (ERA) as the leading subtype (33.7%), with multicentric data showing 80% knee involvement predominantly in males.⁶⁻⁸ There is a vital gap in comprehensive local data elucidating specific patterns of disease manifestation, especially pertaining to joint involvement, ocular complications like uveitis, and exclusive autoimmune profiles. Without this regional data health care provider struggle to deliver precise and personalized therapeutic plans for their patients. Therefore, there is a crucial requirement to comprehensively analyze as well as map the articular burden and laboratory findings within this zone to effectively tailor interventions and augment the patients overall quality of life.⁹

This study aimed to enhance understanding the interrelationship of different factors to unfold disease behavior in our population of this age group which can ultimately contribute local evidence to the international database creating a more holistic knowledge. Therefore, it is designed to demarcate the

Correspondence: Dr Annam Javed, Department of Medicine, Pak Emirates Military Hospital, Rawalpindi Pakistan
Received: 27 Apr 2026; revision received: 11 Jun 2026; accepted: 12 Jun 2026

frequency, clinical characteristics, autoimmune biomarkers and correlation of uveitis among Pakistani children with JIA.

METHODOLOGY

This cross-sectional study was conducted at Pak-Emirates Military Hospital Rawalpindi, Pakistan spanning a period from Dec 2023 to Dec 2025. The study adhered to ethical guidelines and obtained institutional approval (vide letter A/28/EC/2/24 dated Nov 2023).

Inclusion Criteria: Juvenile patients of either gender, up to 16 years of age, diagnosed with JIA, encompassing various disease subtypes (polyarticular, oligoarticular, and monoarticular etc.), and having accessible clinical, serological, and treatment details for data scrutiny were included.

Exclusion Criteria: Patients with JIA mimickers (leukemia/ malignancy or autoinflammatory diseases or hereditary conditions), and those with prior treatment were excluded.

Sample size was calculated using WHO sample taking a reported prevalence of JIA of 20/100,000.¹⁰

In-depth baseline demographic data, comprising of age, gender identity, and geographical distribution, was documented for each participant. Clinical parameters like age at disease onset, joint involvement pattern (polyarticular, oligoarticular, monoarticular), and concomitant disease related complications such as growth retardation and refractory disease were also documented.

Serum samples were collected from all participants for laboratory scrutiny, to evaluate and validate disease specific autoimmune biomarkers, including Rheumatoid Arthritis Factor (RA-F), Antinuclear Antibodies (ANA), Human Leukocyte Antigen B27 (HLA-B27), and Anti-Cyclic Citrullinated Peptide (Anti-CCP) antibody. These parameters were detected by employing standardized assays. The frequencies of positive and negative outcomes were duly archived.

Inflammatory markers comprising of Erythrocyte Sedimentation Rate (ESR) in first hour, and Quantitative C-Reactive Protein levels were quantified to gauge the magnitude of systemic inflammation. Detailed information regarding the treatment regimens dispensed was compiled, including methotrexate (MTX), sulphasalazine, leflunomide, hydroxychloroquine, and corticosteroid use,

administered either as monotherapy or in combination.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 22. Normality of data was checked by using Kolmogorov-Smirnov test. Age, age at disease onset, CRP, ESR were non-normally distributed, and represented by median (IQR). Qualitative data (gender, province, serological markers, disease complication and treatment) was presented using percentage and frequency. Chi-square test (for qualitative variables) and Mann Whitney U test (for normally distributed quantitative data) were applied. A *p*-value of ≤ 0.05 was considered statistically significant

RESULTS

A total of 151 pediatric patients with Juvenile Idiopathic Arthritis were included. Median age was 10.0 (13.0 – 7.0) years, with 74(49.0%) females and 77(51.0%) males. Median age at disease onset was 7.00 (10.0–4.0) years, and majority of patients (n=91, 60.3%) belonged to Punjab shown in Table-I. Polyarticular joint involvement was the most common pattern observed in 97 patients (64.2%) followed by oligoarticular involvement (n=51, 33.8%) and monoarticular was seen only in 3 patients (2.0%), as shown in Figure-1. Median Erythrocyte Sedimentation Rate (ESR) was 40.0 (60.0 – 23.0) mm at 1st hour, while median C reactive protein levels were 18.0 (39.0 – 4.0) mg/L. However, Rheumatoid Arthritis Factor Positivity was observed in 4 (2.6%) patients, Anti-Nuclear Antibodies were positive in 20(13.2%) patients, Human Leukocyte Antigen B27 (HLA-B27) positivity was detected in 6 (4.0%) patients, and Anti-Cyclic Citrullinated Protein (Anti-CCP) antibody positivity was found in 19 (12.6%) patients. Regarding disease-related complications, growth retardation was present in 40 (26.5%) patients, while uveitis was identified in 4 (2.6%) patients (Table-II). Furthermore, methotrexate was the most commonly prescribed treatment modality, administered to 105(69.5%) patients. Combination therapy with methotrexate and leflunomide was used in 15(9.9%) patients followed by hydroxychloroquine in 12(7.9%) patients. Sulphasalazine monotherapy was received by 8(5.4%) patients, while steroids were used in 7(4.7%) patients. The combination of methotrexate and sulphasalazine was the least frequently prescribed regimen, utilized in 4(2.6%) patients, as shown in Table-III.

There was no significant difference in age of disease onset ($p=0.195$), Rheumatoid Arthritis Factor positivity ($p=0.319$), Anti-Nuclear Antibody positivity ($p=0.719$), or HLA-B27 positivity ($p=0.176$) among the joint patterns. In contrast, ESR ($p=0.025$), CRP ($p=0.006$), and Anti-CCP antibody positivity ($p<0.001$) showed statistically significant differences across the joint involvement groups, as shown in Table-IV.

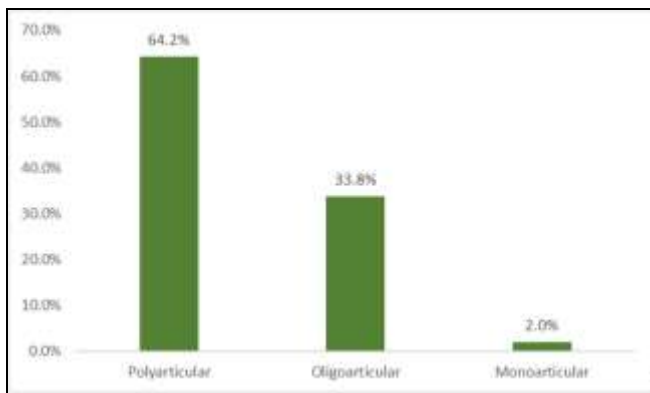


Figure-1: Percentage of Joint Involvement (n=151)

Table-I: Demographic Characteristics of Study Participants (n=151)

Variables	Categories	Values
Age (years)	Median (IQR)	10.0(13.0 – 7.0)
Gender	Male	77(51.0%)
	Female	74(49.0%)
Age at disease onset	Median (IQR)	7.0(10.0 – 4.0)
Province	Punjab	91(60.3%)
	Khyber Pakhtunkhwa	39(25.8%)
	Azad Jammu and Kashmir	9(6.0%)
	Sindh	6(4.0%)
	Gilgit Baltistan	6(4.0%)

Table-II: Inflammatory Markers, Serological Profile, and Disease-Related Complications among Pediatric Patients with Juvenile Idiopathic Arthritis (n = 151)

Variables	Categories	Values
Inflammatory Markers		
ESR (mm)	Median (IQR)	40.0(60.0 – 23.0)
CRP mg/L	Median (IQR)	18.0(39.0 – 4.0)
Serological Markers		
Rheumatoid Arthritis Factor	Positive	4(2.6%)
	Negative	147(97.4%)
Anti-Nuclear Antibodies	Positive	20(13.2%)
	Negative	131(86.8%)
Human Leucocyte Antigen B27	Positive	6(4.0%)
	Negative	145(96.0%)
Anti- Cyclic Citrullinated Protein antibody	Positive	19(12.6%)
	Negative	132(87.4%)
Anti-Nuclear Antibodies	Positive	20(13.2%)
	Negative	131(86.8%)
Disease Complication		
Growth retardation	Positive	40(26.5%)
	Negative	111(73.5%)
Uveitis	Positive	4(2.6%)
	Negative	147(97.4%)

Table-III: Treatment Modalities used among Patients with Juvenile Idiopathic Arthritis (n=151)

Treatment Modality	n (%)
Methotrexate	105(69.5%)
Methotrexate + Sulphasalazine	4(2.6%)
Methotrexate + Leflunomide	15(9.9%)
Hydroxychloroquine	12(7.9%)
Sulphasalazine	8(5.4%)
Steroids	7(4.7%)

Table-IV: Comparison of Age and Inflammatory Markers Among Different Joint Distributions (n=151)

Parameter	Joint Pattern n(%)			p value
	Oligoarticular (n=51)	Polyarticular (n=97)	Monoarticular (n=3)	
Age of disease onset in years, Median (IQR)	7.0 (11.0–4.0)	6.5 (9.0–3.0)	10.0 (10.0–10.0)	0.195
Inflammatory Markers				
ESR (mm), Median (IQR)	40.0 (60.0 – 20.0)	44.0 (60.0–27.0)	80.0 (80.0–80.0)	0.025
CRP (Q) mg/L, Median (IQR)	15.0 (25.0 – 4.0)	20.0 (56.0–11.0)	45.0 (45.0– 45.0)	0.006
Serological Markers				
Rheumatoid Arthritis Factor	0(0.0%)	4(4.1%)	0(0.0%)	0.319
Anti-Nuclear Antibodies	7(13.7%)	13(13.4%)	0(0.0%)	0.719
Human Leucocyte Antigen B27	0(0.0%)	6(6.2%)	0(0.0%)	0.176
Anti- Cyclic Citrullinated Protein antibody	3 (5.9%)	13(13.4%)	3(100.0%)	<0.001

*ESR: Erythrocyte Sedimentation Rate, CRP (Q): C-Reactive Protein (Quantitative)

DISCUSSION

The results from this study provide a detailed layout of the clinico-demographic variables of Juvenile Idiopathic Arthritis (JIA) within a Pakistani cohort, illuminating predominantly polyarticular joint involvement in 64.2% of the 151 participants which is in contrasts with results from the Middle East and Africa, where Al-Mayouf *et al.* reported the oligoarticular pattern to be the most frequent.⁷ The median age of onset in our population was 7.0 years, which is earlier than the one reported in English studies by Costello *et al.* at 9 years.⁸ Furthermore, our data showed a higher prevalence in males at 51.0% compared to females at 49.0%, diverging from the female-heavy demographics typically reported in Western cohorts.

In our study, median age was also found to be 10.0 years, whereas most of the patients belonged to Punjab region. Shiff *et al.* found an overall decrease in prevalence and incidence of JIA among Canadian population.⁹

Lovell *et al.* from Cincinnati reported an increased incidence of autoimmune diseases in

patients with JIA Click or tap here to enter text.¹¹ Consolaro *et al.* reported systemic arthritis as the most widespread presentation in Southeast Asians, while oligoarticular involvement was common in Northern Europeans.¹² Our study suggests a significantly higher articular burden in the Pakistani pediatric population.

Serological analysis depicted that 13.9% of patients were positive for ANA and 14.6% for Anti-CCP. This data is notably lower than the one reported by Khodra *et al.* in Alaska, where 56% were ANA positive. Similarly, uveitis and use of biological therapy was more prevalent in northern Europe whereas both were uncommon in Asia. These findings are in accordance with the findings of our study,¹³ in which uveitis was found only in one patient and most of the patients were on methotrexate. Khodra *et al.* also found oligoarticular pattern to be more common, with a high prevalence of enthesitis-related arthritis.¹³ Over 97% of patients in our study were negative for Rheumatoid Factor (RF), which is in accordance with Bansal *et al.*, who concluded that rheumatoid factor usually lacks in this cohort.¹⁴ Studies by Ramanan *et al.*, suggest biological therapies like tocilizumab or baricitinib for refractory cases, our cohort relied primarily on conventional synthetic DMARDs, with only 9.9% of patients using a Methotrexate and Leflunomide combination,^{15,16} Meerwijk *et al.* in their mini-review also suggested an early screening and early intervention in patients with uveitis and JIA, to prevent vision loss.¹⁷

Treatment in our cohort was subjugated by methotrexate monotherapy at 69.5%, which is in concordance with the 2019 American College of Rheumatology guidelines, recommending methotrexate due to its time-tested evidence base. Furthermore, these guidelines suggested moderate evidence of leflunomide and adalimumab in patients with juvenile idiopathic arthritis. They also recommended conditional use of methotrexate over leflunomide due to more prevalent use of methotrexate and more studies done on it.¹⁸ These findings highlight the need for tailored interventions in the Pakistani population, though the study's scope is limited by a short duration and the absence of long-term follow-up.

Apropos of inflammatory markers, our cohort had a median ESR of 36.6 mm/hour with polyarticular patients exhibiting a higher median ESR of 44.0 mm/hour compared to 40.0 mm/hour in oligoarticular ones which was statistically significant

($p=0.025$). This finding is contradictory to Kavachandha *et al.*, who associated higher ESR levels with HLA-B27 positivity, while in our study, the mean ESR was interestingly higher in HLA-B27 negative patients.¹⁹ Mitra *et al.* recommended ultrasonography as a useful tool in patients of JIA.²⁰

We recommend larger, multicentric studies along with longer duration and follow up. Future long-term and large-scale studies focusing on better understanding of treatment responses and genetic predispositions within various JIA subgroups in Pakistani juvenile cohort are indispensable for optimizing understanding and designing personalized management protocols for this deforming condition.

LIMITATIONS OF STUDY

Limitations of our study include comparatively shorter study period and unavailability of long-term follow-up.

CONCLUSION

This study highlights the essential insights into the diverse clinical presentations, autoantibody phenotype and treatment algorithms observed in Pakistani JIA cohort. Decoding these multidimensional facets is instrumental in tailoring targeted management tactics as well as optimizing patient outcomes with the aim of mitigating disease-associated sequelae such as uveitis and stunted growth.

Conflict of Interest: None.

Disclosure:

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AJ & AF: Data acquisition, data analysis, critical review, approval of the final version to be published.

SA & AK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

UZ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Hinze CH, Foell D, Kessel C. Treatment of systemic juvenile idiopathic arthritis. *Nat Rev Rheumatol* 2023; 19(12): 778-789. <https://doi.org/10.1038/s41584-023-01034-9>
2. Martini A, Lovell DJ, Albani S, Brunner HI, Hyrich KL, Thompson SD, et al. Juvenile idiopathic arthritis. *Nat Rev Dis Primers* 2022; 8(1):5. <https://doi.org/10.1038/s41572-021-00332-2>
3. Agarwal M, Freychet C, Jain S, Shivpuri A, Singh A, Dinand V, et al. Factors impacting referral of JIA patients to a tertiary level pediatric rheumatology center in North India: A retrospective cohort study. *Pediatr Rheumatol* 2020; 18(1): 1-11. <https://doi.org/10.1186/s12969-020-0408-4>

Impact of Juvenile Idiopathic Arthritis

4. Onel KB, Horton DB, Lovell DJ, Shenoi S, Cuello CA, Angeles-Han ST, et al. 2021 American College of Rheumatology guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for oligoarthritis, temporomandibular joint arthritis, and systemic juvenile idiopathic arthritis. *Arthritis Rheumatol* 2022; 74(4): 553-569.
<https://doi.org/10.1002/art.42037>
5. Hameed K, Amanullah F, Ullah S, Abbas S. Clinical and Biochemical Characteristics of Children with Juvenile Idiopathic Arthritis. *J Coll Physicians Surg Pak* 2014; 24(7): 487-491.
<https://doi.org/10.2014/jcsp.48749>
6. Abrawan S, Sultana R, Akhter S, Islam M. Comparison of juvenile idiopathic arthritis subtype distribution among different countries. *Bangl J Child Health* 2020; 44(1): 34-39.
<https://doi.org/10.3329/bjch.v44i1.48450>
7. Al-Mayouf SM, Al Mutairi M, Bouayed K, Habjoka S, Hadeef D, Lotfy HM, et al. Epidemiology and demographics of juvenile idiopathic arthritis in Africa and Middle East. *Pediatric Rheumatology*. 2021; 19(1): 1-30.
<https://doi.org/10.1186/s12969-021-00650-x>
8. Costello R, McDonagh J, Hyrich KL, Humphreys JH. Incidence and prevalence of juvenile idiopathic arthritis in the United Kingdom, 2000–2018: results from the Clinical Practice Research Datalink. *Rheumatology* 2022; 61(6): 2548–2554.
<https://doi.org/10.1093/rheumatology/keab714>
9. Shiff NJ, Oen K, Kroeker K, Lix LM. Trends in Population-Based Incidence and Prevalence of Juvenile Idiopathic Arthritis in Manitoba, Canada. *Arthritis Care Res* 2019; 71(3): 413–418.
<https://doi.org/10.1002/acr.23606>
10. Abdwani R, Abdalla E, Al Abrawi S, Al-Zakwani I. Epidemiology of juvenile idiopathic arthritis in Oman. *Pediatr Rheumatol Online J* 2015; 13(1): 33.
<https://doi.org/10.1186/s12969-015-0030-z>
11. Lovell DJ, Huang B, Chen C, Angeles-Han ST, Simon TA, Brunner HI et al. Prevalence of autoimmune diseases and other associated conditions in children and young adults with juvenile idiopathic arthritis. *RMD Open* 2021; 7(1): e001558.
<https://doi.org/10.1136/rmdopen-2020-001558>
12. Consolaro A, Giancane G, Alongi A, van Dijkhuizen EHP, Aggarwal A, Al-Mayouf SM, et al. Phenotypic variability and disparities in treatment and outcomes of childhood arthritis throughout the world: an observational cohort study. *Lancet Child Adolesc Health* 2019; 3(4): 255–263.
[https://doi.org/10.1016/S2352-4642\(19\)30027-6](https://doi.org/10.1016/S2352-4642(19)30027-6)
13. Khodra B, Stevens A, Ferucci ED. Prevalence of Juvenile Idiopathic Arthritis in the Alaska Native Population. *Arthritis Care Res* 2020; 72(8): 1152–1158.
<https://doi.org/10.1002/acr.23997>
14. Bansal N, Pasricha C, Kumari P, Jangra S, Kaur R, Singh R. A comprehensive overview of juvenile idiopathic arthritis: From pathophysiology to management. *Autoimmun Rev* 2023; 22(7): 103337.
<https://doi.org/10.1016/j.autrev.2023.103337>
15. Ramanan AV, Dick AD, Jones AP, McKay A, Williamson PR, Compeyrot-Lacassagne S, et al. Adalimumab plus Methotrexate for Uveitis in Juvenile Idiopathic Arthritis. *N Engl J Med* 2017; 376(17): 1637–1646.
<https://doi.org/10.1056/NEJMoa1614161>
16. Ramanan AV, Quartier P, Okamoto N, Foeldvari I, Spindler A, Fingerhutová S, et al. Baricitinib in juvenile idiopathic arthritis: an international, phase 3, randomised, double-blind, placebo-controlled, withdrawal, efficacy, and safety trial. *Lancet* 2023; 402(10401): 555–570.
[https://doi.org/10.1016/S0140-6736\(23\)00921-2](https://doi.org/10.1016/S0140-6736(23)00921-2)
17. Meerwijk C, Kuiper J, Straalen J, Ayuso VK, Wennink R, Haasnoot AM, et al. Uveitis Associated with Juvenile Idiopathic Arthritis. *Ocul Immunol Inflamm* 2023; 31(9): 1848–1853.
<https://doi.org/10.1080/09273948.2023.2278060>
18. Angeles-Han ST, Ringold S, Beukelman T, Lovell D, Cuello CA, Becker ML, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis–Associated Uveitis. *Arthritis Care Res* 2019; 71(6): 703–716. <https://doi.org/10.1002/acr.23871>
19. Kavadiachanda CG, Seth G, Kumar G, Gulati R, Negi VS. Clinical correlates of HLA-B*27 and its subtypes in enthesitis-related arthritis variant of juvenile idiopathic arthritis in south Indian Tamil patients. *Int J Rheum Dis* 2019; 22(7): 1289–1296.
<https://doi.org/10.1111/1756-185X.13551>
20. Mitra S, Samui PP, Samanta M, Mondal RK, Hazra A, Mandal K, et al. Ultrasound detected changes in joint cartilage thickness in juvenile idiopathic arthritis. *Int J Rheum Dis* 2019; 22(7): 1263–1270. <https://doi.org/10.1111/1756-185X.13584>
21. García-Rodríguez F, Gamboa-Alonso A, Jiménez-Hernández S, Ochoa-Alderete L, Barrientos-Martínez VA, Alvarez-Villalobos NA, et al. Economic impact of Juvenile Idiopathic Arthritis: a systematic review. *Pediatr Rheumatol* 2021; 19(1): 1–10.
<https://doi.org/10.1186/s12969-021-00641-y>