

Clinical and Laboratory Profile of Patients with Newly Diagnosed Juvenile Idiopathic Arthritis: An Observational Study from a Tertiary Care Centre, Karnataka, India

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ABSTRACT

Introduction: Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic condition of childhood. It represents a heterogeneous group of childhood arthritis.

Aim: To study the clinical profile and laboratory characteristics of all newly diagnosed JIA patients.

Materials and Methods: This hospital-based prospective observational study was conducted in the Department of Paediatric Rheumatology at Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India between December 2017 to May 2019. All children who fulfilled International League of Associations for Rheumatology (ILAR) criteria for the diagnosis of JIA were enrolled in the study, and their clinical and laboratory parameters were evaluated. The analysis between matched-pairs data like the comparison between age of onset and age of presentation in males and females were done by paired t-test.

Results: The mean age of the study participants was 9.67±3.96 years. A total of 51 children were included in the study with

Male:Female (M:F) of 1:1.12. Mean age at onset was 8.71±4.02 years and median duration of disease was 13 months (2-96 months). The most common subgroup was polyarticular JIA 18 (35.3%) followed by Systemic Onset Juvenile Idiopathic Arthritis (SOJIA) 14 (27.5%), enthesitis-related arthritis 13 (25.5%) and oligoarticular JIA 4 (7.8%). Knee (94%) was the most common joint involved followed by the ankle (70.5%). Fever was the most common extra-articular feature present in 73% of cases. Hepatomegaly, splenomegaly and lymphadenopathy was present in 33.3%, 9.8% and 21.6% children, respectively. Anaemia, leukocytosis, thrombocytosis and elevated Erythrocyte Sedimentation Rate (ESR) were more common in SOJIA. Macrophage Activation Syndrome (MAS) was diagnosed in two cases of SOJIA (14.3%) with no mortality.

Conclusion: Polyarticular JIA was the common subtype in the study, followed by SOJIA. Most common joint involved was knee, followed by ankle and fever is the most common extraarticular manifestation.

Keywords: Enthesitis related arthritis, Polyarticular juvenile idiopathic arthritis, Splenomegaly

INTRODUCTION

The JIA is the most common rheumatological condition seen in the paediatric rheumatology clinic. It is a heterogeneous group of diseases with arthritis as the common denominator. The data on JIA is sparse from Indian subcontinent [1]. It is also necessary to consider that paediatric age groups share about 10-20% of the total burden of rheumatological disorders, which on delayed intervention leads to significant disability, disability adjusted life years and loss of economic productivity [2]. JIA is defined as arthritis that persists for more than six weeks with an onset before the age of 16 years [3]. The overall prevalence of JIA is estimated to range from 3.8 to 400 cases per 100000 children, with an incidence of 1.6 to 23 cases per lac children [4].

Epidemiologic studies have noted wide differences in occurrence of JIA with accordance to environmental exposure and immunogenetic susceptibility among different populations. Potential protective factors for development of JIA were breast feeding, hygiene hypothesis, where as potential harmful factors include infections, antibiotics and cesarean section delivery. Uncertain association were found in seasonality, second hand smoking, air pollutants, dietary factors and low vitamin D levels [5]. Hence, a study to establish clinicoepidemiological statistics is warranted to increase awareness in the medical community along with strengthening of paediatric rheumatological services to cater to these patients [6].

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the Department of Paediatric Rheumatology at

Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India between December 2017 to May 2019. The study was approved by the Institutional Ethical Committee (IGICH/ACA/IEC/19/2017-18). Informed written consent was obtained from the parents of each patient before enrollment.

Inclusion criteria: Patients fulfilling ILAR criteria for the diagnosis of JIA and presenting to the Department of Paediatric Rheumatology for the very first visit during the study period [7] were included in the study.

Exclusion criteria: All the follow-up cases of JIA which were diagnosed before the study period were excluded from the study.

Sample size calculation: Based on the hospital records during 2015 to 2017, an overall estimate of 40-50 incident cases were found in the Department of Paediatric Rheumatology. Hence, it was decided to study the children attending the Out Patient Department (OPD) from December 2017 to May 2019 with approximate study sample size of 50.

Study Procedure

Detailed clinical history was taken and physical examination was done for each study subject as per predesigned and prestructured proforma. Baseline laboratory parameters like Haemoglobin (Hb), Total Leukocyte Count (TLC), Differential Leukocyte Count (DLC), ESR, Platelet Count (PLT), C-Reactive Protein (CRP), liver function tests were documented. Besides these routine investigations, serum ferritin levels, serum Rheumatoid Factor (RF), Anti-nuclear Antibody Assay (ANA) by immunofluorescence method and Human Leukocyte

Antigen B-27 (HLA-B27) assessment by polymerase chain reaction, were done only in a few selected cases due to financial constraints. Serum ferritin levels were done in SOJIA cases when Macrophage Activation Syndrome (MAS) was suspected. Test for Rheumatoid Factor (RF) was done in polyarticular JIA patients. HLA-B27 was tested for all cases with clinical features suggestive of Enthesitis-related Arthritis (ERA).

STATISTICAL ANALYSIS

The data was entered in Microsoft Excel and analysed using the Statistical Package for Social Science (SPSS), version 25.0. The averages (mean±standard deviation) were done for continuous data and percentages for discrete categorical data. The analysis between matched-pairs data like the comparison between age of onset and age of presentation in males and females were done by paired t-test. The probability value (p-value <0.005) was considered significant.

RESULTS

A total of 51 children were diagnosed with JIA according to ILAR criteria were included in the study. A total of 24 (47.1%) were male with a M:F ratio of 1:1.12. The mean age at presentation was 9.67±3.96 years. The mean age at onset was 8.71±4.02 years, the youngest being a patient with SOJIA. There was a mean delay in the diagnosis of 0.96 years (11 months). The age at onset for males and females were 9.1±3.46 years and 8.36±4.49 years, respectively. The age of presentation for males and females were 10.07±3.29 years and 9.54±4.5 years, respectively. The age at onset and age at presentation was early for females compared to males. The most common subgroup of JIA in the study was poly JIA 18 (35.3%), of which four were RF positive (7.8%) and 14 were RF negative (27.5%) followed by SOJIA 14 (27.5%). The third major category was ERA 13 (25.5%). Only 4 cases were oligoarticular arthritis (7.8%). There were two cases of undifferentiated arthritis and no cases of psoriatic arthritis [Table/Fig-1].

JIA subtypes	Male n (%)	Female n (%)	Age of onset (years) Mean±SD	Median duration of the disease (months)	n (%)
SOJIA (n=14)	5 (35.7)	9 (64.3)	7.29±4.80	5	14 (27.5)
Poly JIA (n=18)	6 (33)	12(67)	8.36±4.30	6.16	18 (35.3)
Oligo JIA (n=4)	2	2	8.85±3.25	28.5	4 (7.8)
ERA (n=13)	10	3	10.29±2.56	12	13 (25.5)
Undifferentiated (n=2)	1	1	11.15±0.21	29	2 (4)
Total (N=51)	24 (47.1)	27 (52.9)	8.71±4.02	7	51

[Table/Fig-1]: Characteristics of the study population.

The onset of disease was most common in the age group >10 to ≤16 years 25 (49%) closely followed by those between >5 to ≤10 years 17 (33.3%) [Table/Fig-2].

Age of onset (years)	SOJIA (n=14)	Poly JIA (n=18)	Oligo JIA (n=4)	ERA (n=13)	Undifferentiated (n=2)	Total cases n (%)
0-5	4	5	0	0	0	9 (17.6)
>5-10 Years	4	5	2	6	0	17 (33.3)
>10-16 Years	6	8	2	7	2	25 (49)

[Table/Fig-2]: Age-based distribution in various subgroups of JIA. N=51

The onset of disease was most common in the age group >10 to ≤16 years 25 (49%) closely followed by those between >5 to ≤10 years 17 (33.3%).

The most common joint involved at presentation was the knee 47 (92%) in SOJIA (100%), oligo JIA (100%), poly JIA (100%)

and ERA (84.6%) followed by ankle in poly JIA (83.3%) and ERA (76.9%), wrist joint in case of SOJIA (71.4%). Majority of poly JIA cases had involvement of small joints of hands (77.7%) and foot (66.6%). Cervical spine involvement was seen in 12 cases and sacroiliac joint involvement in one child [Table/Fig-3]. Children with oligo JIA did not have axial involvement at presentation.

Joints	SOJIA (%)	Poly JIA (%)	Oligo JIA (%)	ERA (%)	Total
Knee	14 (100)	18 (100)	4 (100)	11 (84.6)	47
Ankle	9 (64.3)	15 (83.3)	1 (25)	10 (76.9)	35
Elbow	7 (50)	15 (83.3)	-	5 (38.5)	27
Shoulder	5 (35.7)	10 (55.5)	-	3 (23.1)	18
Wrist	10 (71.4)	9 (50)	-	8 (61.5)	27
Hip	6 (42.9)	9 (50)	1 (25)	4 (30.7)	20
Small joints hand	8 (57.1)	14 (77.7)	1 (25)	6 (46.2)	29
Small joints foot	10 (71.4)	12 (66.6)	-	7 (53.8)	29
Cervical	4 (28.5)	5 (35.7)	-	3 (23.1)	12
Sacroiliac	-	-	-	1 (7.6)	1
TMJ	3 (21.4)	3 (16.6)	-	1 (7.6)	7

[Table/Fig-3]: Pattern of joint involvement-major joints, minor joints and axial joints.

The most common extra articular feature was fever which was present at the onset of illness in 73% of cases (n=37). Rash was present in 8 cases (15.7%) out of which six cases belonged to SOJIA. Hepatomegaly was seen in 17 (33.3%) cases, among them 11 were SOJIA. Splenomegaly was seen in five cases. Lymphadenopathy was seen in 11 cases among them six were SOJIA [Table/Fig-4]. None of the cases had uveitis at first presentation. When plotted on the Indian Academy of Paediatrics (IAP) growth charts for weight and height, 29.4% (n=15) had a weight <3rd centile and 33% (n=17) had a height <3rd centile. Height was most restricted in children with SOJIA, while weight was most restricted in ERA (38.5%) subgroup followed by SOJIA (35.7%) [Table/Fig-4].

Subtypes	SOJIA (n=14)	Poly JIA (n=18)	Oligo JIA (n=4)	ERA (n=13)	Undifferentiated arthritis (n=2)	Total
Joint pain and swelling	14 (100%)	18 (100%)	4 (100%)	13 (100%)	2 (100%)	51
Early morning stiffness	12 (85.7%)	10 (55.5%)	4 (100%)	12 (92.3%)	2 (100%)	40
Fever	14 (100%)	13 (72%)	1 (25%)	7 (53.8%)	2 (100%)	37
Rash	6 (42.9%)	-	-	1 (7.6%)	1 (50%)	8
Hepatomegaly	11 (78.6%)	4 (22.2%)	1 (25%)	-	1 (50%)	17
Splenomegaly	2 (14.3%)	2 (11.1%)	1 (25%)	-	-	5
Lymphadenopathy	6 (43%)	4 (22.2%)	1 (25%)	-	-	11
Uveitis	-	-	-	-	-	-
Serositis	1 (7%)	-	-	-	-	1
MAS	2 (3.9%)	-	-	-	-	2
Weight		3 (21.4%)	1 (25%)	5 (38.5%)	1 (50%)	
<3 rd centile	5 (35.7%)	11 (78.5%)	-	2 (15.4%)	1 (50%)	15
3 rd to 10 th centile	5 (35.7%)					19
Height		6 (33.3%)	1 (25%)	2 (15.4%)	2 (100%)	17
<3 rd centile	6 (42.9%)	5 (27.7%)	1 (25%)	4 (30.7%)	-	13
3 rd to 10 th centile	3 (21.4%)					
Limb length discrepancy	2 (3.9%)	-	-	-	-	2

[Table/Fig-4]: Clinical features of JIA subtypes.

Anaemia, leukocytosis, thrombocytosis and elevated ESR were significantly more common in SOJIA with 64%, 78.5%, 42.8% and 92.8%, respectively. Elevated CRP was present in all the cases of RF positive polyarticular JIA subgroup [Table/Fig-5]. ANA was positive in 2 (22.2%) cases among nine cases of Poly JIA for whom it was tested, while five patients were tested for ANA in ERA subgroup and one patient was found to be positive. HLA-B27 was done in all the cases having clinical suspicion fitting to ERA. Five (38.4%) out of 13 cases with ERA were HLA-B27 positive. MAS was the initial presentation in 2 (3.9%) patients of SOJIA. There was no mortality in the study population.

Subtypes	Anaemia <100 g/L (%)	Leuko-cytosis >10×10 ⁹ /L (%)	Elevated PLT >500×10 ⁹ /L (%)	Elevated ESR >20 mm/hour (%)	Elevated CRP >mg/L (%)
Systemic (n=14)	9 (64)	11 (78.5)	6 (42.8)	13 (92.8)	8 (57)
Poly JIA (RF positive) (n=4)	2 (50)	2 (50)	1 (25)	3 (75)	4 (100)
Poly JIA (RF negative) (n=14)	5 (35.7)	9 (64)	6 (42.8)	13 (92.8)	10 (68.8)
Oligo JIA (n=4)	2 (50)	1 (25)	1 (25)	4 (100)	2 (50)
ERA (n=13)	1 (7.6)	5 (38.4)	1 (7.6)	12 (92.3)	5 (38.5)
Undifferentiated (n=2)	1 (50)	1 (50)	0	2 (100)	1 (50)
Total N=51	20 (39.2)	28 (54.9)	15 (29.4)	47 (92.2)	30 (58.8)

[Table/Fig-5]: Laboratory investigations.

Subtypes	Seth V et al., [1]	Menon NV et al., [10]	Viswanatha Kumar HM and Kumar GV [11]	Al-Hemairi MH et al., [12]	Chandrasekaran AN et al., [9]	Present study
Place of study	India (Delhi)	India (Kerala)	India (Karnataka)	Saudi Arabia	India (Madras)	Bengaluru (Karnataka)
Study period	1986-1995	2011-2012	2009-2013	2007-2015	1991-1995	2017-2019
Systemic onset (%)	24	32.3	8.93	36.5	13.3	27.5
Poly JIA (%)	46	42	55.36	29.26	51.7	35.3
Oligo JIA (%)	30	24.2	35.7	28.04	35.1	7.8
ERA (%)	0	1.6	0	1.21	-	25.5
Psoriatic arthritis (%)	-	0	0	4.87	-	0
Total patients	361	62	112	82	331	51

[Table/Fig-6]: Comparison of JIA subtypes in various studies [1,9-11,13].

Clinical features	Seth V et al., [1]	Menon NV et al., [10]	Viswanatha Kumar HM et al., [11]	Chandrasekaran AN et al., [9]	Present study
Fever (%)	100	71	100	31.1	72.5
Rash (%)	57	25.8	10	5.7	15.7
Hepatomegaly (%)	51	30.6	60	10.6	33.3
Lymphadenopathy (%)	25	19.4	40	17.8	21.6
Splenomegaly (%)	7.7	21	70	7.3	9.8
Uveitis (%)	3.3	1.6	-	3.0	-
MAS (%)	-	10	-	-	3.9
Height <3 rd centile (%)	-	19.3	-	-	33.3
Weight <3 rd centile (%)	-	25.8	-	-	29.4
Subcutaneous nodules (%)	0.8	-	-	2.4	-

[Table/Fig-7]: Clinical features in various study population [1,9-11].

Study	JIA subtypes	Anaemia	Elevated ESR	Elevated WBC	RF	ANA	HLA-B27
Seth V et al., [1]	Systemic	52.3	100	67.8	9.5	-	
	Polyarticular	36.8	95.9	57.6	14.8	6.5	
	Pauciarticular	35.4	91.1	67.9	3.0	4.5	
Menon NV et al., [10]	Systemic	95	95	85	-	-	-
	Poly JIA	58	84.6	46	7.7	3.8	-
	Oligo JIA	40	47.7	26	-	-	-
	ERA	100	100	-	-	-	100

DISCUSSION

The study was conducted to evaluate the epidemiological, clinical and biochemical characteristics of all patients who were diagnosed with JIA. JIA is a disease of exclusion which is difficult to diagnose and treat which may lead to high rates of deformity and affects the standard of living. The present study helps in early recognition and prevents morbidity. The study includes 51 children done over a period of one and half years, indicating a high prevalence of the condition. The study shows female predilection. This is in contrast to the other studies from India [1,8,9] which show a male preponderance. The most common subtype was poly JIA (35.3%), similar to a few other studies from India and Pakistan [Table/Fig-6] [1,9-11,12].

The most common joint involved in the study population was the knee followed by ankle joint, similar to other studies from India [1,13]. The most common extra articular feature was fever, similar to most of the other studies [1,10-12]. Uveitis wasn't noted in any of the patients. The incidence of uveitis is low in Indian studies [9,13-15], as compared to Western data, however Seth V et al., reported 3.3% (12 cases) of uveitis [1]. Of the children in the study, 29.4% and 33.3% had weight and height <3rd centile, respectively. Menon NV et al., reported majority of growth delay was noted in SOJIA subtype [Table/Fig-7] [1,9-11].

Anaemia, leukocytosis, thrombocytosis and elevated ESR were significantly more common in SOJIA with 64%, 78.5%, 42.8% and 92.8% respectively. ANA was tested in six children with SOJIA among which, three were positive, while 22.2% of polyarticular JIA subgroup were also found to be ANA positive. ANA positivity rate was low in

Present study	Systemic	64	92.8	78.5	-	50	-
	Poly JIA	38.8	88.8	61.1	28.6	22.2	-
	Oligo JIA	50	100	25	-	-	-
	ERA	7.6	92.3	38.4	-	25	38.4

[Table/Fig-8]: Comparison of laboratory parameters in various studies [1,10].
*WBC-White blood cells. The values presented in percentages

various other studies, from India and South Africa [1,15,16]. The comparison of various laboratory parameters of previous studies with the present study has been shown in [Table/Fig-8] [1,10].

Limitation(s)

The study was conducted at a tertiary care hospital, hence, it may not represent the population in the community. The data was collected at the time of diagnosis, hence long-term follow-up and progression of the disease could not be assessed.

CONCLUSION(S)

The JIA is not an infrequent condition encountered in this setting. Polyarticular JIA was the most common subtype in this hospital-based study, followed by systemic onset JIA. The diagnosis and long-term management of these patients will be assisted by the recognition of these different subtypes. It can be concluded that, the clinical and epidemiological profile of children with JIA from this region is different from the western world, in terms of frequency of the different subtypes, early presentation of females compared to males, less incidence of ANA positivity and rare presentation of uveitis. There is still a need of further exploration on JIA, for a better knowledge about the trends of JIA and also, to measure the long-term outcome with reference to impact on chronic health of the children.

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