

# Comparative analysis of pediatric rheumatic patient growth patterns against norms: A cross-sectional study conducted in an eastern indian hospital

*By Kaushik Sur*

## Comparative analysis of pediatric rheumatic patient growth patterns against norms: A cross-sectional study conducted in an eastern indian hospital

Kaushik Sur, Suparna Guha, Debabrata Manna, Ajitesh Roy, Tabasume Khatun

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Department of Pediatrics, Vivekananda Institute of Medical Sciences, Kolkata, West Bengal, India

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### ABSTRACT

**Background.** Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease, an autoimmune disorder that affects bones, skin, and muscles. Rheumatic diseases are a major cause of chronic illness in children around the world. SLE is a further prevalent inflammatory illness.

**Aims and objectives.** To study different growth parameters of Pediatric patients with inflammatory arthritis attending Pediatric Rheumatology clinic, to compare the growth parameters with age and sex matched Controls and to compare growth among different types of Pediatric patients with inflammatory arthritis.

Method – Different growth parameters (weight, Height, BMI) and SMI (for children above 9 years) were recorded. Consecutive Patients with inflammatory arthritis attending Pediatric Rheumatology OPD having disease duration more than one year and willing to be a part of the study were included.

**Results.** Among 121 patients, JIA (71.9%) was most common followed by SLE (14.8%). Among Different types of JIA, SOJIA (37.9%) is most common, followed by Polyarticular variety (20.6%). Among JIA subtypes, mean age of presentation was earlier in SOJIA variety (Mean 5 years 7 months) and late in JoAS (Mean 12 years 6 months). SLE patients had larger Duration of illness (Mean 4.39 years) prior to diagnosis than JIA patients (Mean 3.43 years). In JIA patients, mean height was significantly less than controls ( $p=0.02$ ). Mean weight and BMI was not significantly different from controls. SOJIA and Polyarticular variety had significantly less weight and height compared to controls. SLE patients had significantly less weight and height compared to control. Mean Weight, Height and BMI was significantly more in SLE patients compared to JIA cohort. There was significantly more delayed puberty both in JIA and SLE patients compared to controls.

**Conclusion.** Among patients with inflammatory arthritis attending Pediatric Rheumatic Clinic, JIA was most common, followed by SLE. Among JIA patients, SOJIA variety was most common, JIA patients had significantly lower height than age and sex matched Controls. SLE patients had significantly lower weight and height than age and sex matched Controls. Delayed Puberty was significantly more in both JIA and SLE patients compared to controls.

## INTRODUCTION

A large number of children around the world suffer from rheumatic diseases, the most prevalent of which is juvenile idiopathic arthritis (JIA), which are autoimmune disorders that impact the musculoskeletal system.<sup>1</sup> In some children, symptoms start early and last until they reach their full developmental potential<sup>1</sup>. Increased disease burden, joint injury, deformity, and delayed growth and development are some of the long-term effects that might result from a delayed diagnosis.

There is a great deal of clinical variability in the course of systemic lupus erythematosus (SLE), a chronic autoimmune illness affecting multiple systems. Despite the prevalence of SLE in adults, around 10% to 20% of cases occur in youngsters. There are some shared characteristics of SLE across age groups, but there have also been some notable distinctions. Compared to SLE that begins in adults, cSLE manifests more severely, progresses more aggressively clinically, and causes damage more quickly<sup>2</sup>.

Chronic disease, pharmaceutical side effects, and other comorbidities cause SLE in children and adolescents to progress to adulthood with significant morbidity<sup>2</sup>. Out of all the known morbidities, growth failure is specific to cSLE. It can impact people's quality of life and make it hard for them to adapt physically and mentally to living with a chronic illness. A number of issues can arise from juvenile idiopathic arthritis, including growth and pubertal disorders, which can lead to handicap both in the short and long term, as well as a decrease in quality of life. Symptoms of growth failure, which can range from a slowing of the rate of height gain to a complete absence of height altogether, are common in patients with chronic inflammatory diseases. In juvenile inflammatory arthritis (JIA), the frequency of low height ranges from 10.4% in children with polyarticular disease to 41% in patients with the systemic type. In contrast, oligoarthritis is most commonly linked to asymmetrical limb growth in affected areas. Chronic inflammation, long-term corticosteroid usage, malnutrition, changed body composition, delayed pubertal onset, or sluggish pubertal advancement are all factors in the pathophysiology of growth disorders. These factors can have an impact on the growth plate homeostasis and function on a local level, or they can have an effect on the GH/IGF-1 and GnRH/gonadotropin-gonadic axes systemically. Even though there are novel ways to manage inflammation, 10–20% of those with severe types of the condition still experience stunted growth that ultimately leads to a low stature<sup>4</sup>. Delays in puberty are linked to a lower peak bone mass and an increased risk of bone fragility both now and in the future. For a comprehensive evaluation of adolescents with JIA<sup>4</sup>, it is crucial to track their bone health and puberty progress. Starting at age 9, it is advised that these patients undergo a pubertal stage assessment every six months. It is essential to always take the patient's bone age into account while evaluating linear growth. While the exact effects of rhGH (recombinant human Growth Hormone) treatment on JIA children are yet unknown, research has demonstrated that, when administered at high doses in an anti-inflammatory environment, following steroids and biologic therapy, it can promote a rapid acceleration of growth in the prepubescent years, similar to the catch-up growth response seen in patients lacking GH. This article aims to assist pediatricians in making accurate and early diagnoses of growth and pubertal problems in children with JIA by providing a thorough overview of the mechanisms that contribute to these conditions.

## 13 MATERIALS AND METHODS

**Study Design and Population-** This study was conducted at Pediatric Rheumatology OPD ( Out Patient Department) of a tertiary hospital in eastern Indian metro city Kolkata with indoor bed strength of 680.

Pediatric patients with inflammatory arthritis attending the once weekly clinic from 1<sup>st</sup> January 2023 to 31<sup>st</sup> December 2023 were selected for the study.

The approval of the Institutional Ethics Committee was sought and granted. Parents or legal guardians of children under the age of thirteen were asked to provide written consent. For patients aged 13 years to 16 years, consent was taken with help of Assent form.

For Children with symptoms of JIA, diagnosis was done by ILAR (International League of Associations for Rheumatology) classification criteria. For SLE, diagnosis was done by SLICC (Systemic Lupus International Collaborating Clinics) classification criteria.

**Inclusion Criteria –** Consecutive Patients with inflammatory arthritis attending Pediatric Rheumatology OPD with upper age limit of 16 completed years (No lower age limit) having disease duration more than one year and willing to be a part of the study.

**Exclusion Criteria –** other causes of joint pain like those with growth pain, Hypermobility, Pain amplification Syndrome, blood dyscrasias, Chronic Kidney, endocrine or Metabolic Diseases.

**Procedure -**

This was a Cross sectional study of children diagnosed with Pediatric Rheumatic Diseases.

Following growth parameters was recorded

1. Height
2. weight
3. Body Mass Index
4. Sexual Maturity Ratings of children above 9 years of age

Disease activity was assessed using SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) and JADAS 10 (Juvenile Arthritis Disease Activity Score) for SLE and JIA respectively.

The weight was recorded to the closest 0.1 kg using an electronic weighing scale. A wall-mounted stanometer was used to measure height to the closest 0.1 cm. Weight in kilograms divided by height in meters ( $\text{Kg/m}^2$ ) is the method used to determine body mass index (BMI). For Puberty assessment, staging was carried out according to Tanner criteria.

Then, these parameters were compared with controls. Controls were selected from age and sex matched healthy children without any chronic disease attending general paediatric OPD.

Lastly, the parameters of Different Rheumatic Diseases Like JRA, SLE, Scleroderma was compared with controls.

Statistical Analysis – For most variables, descriptive analysis was done. Mean with standard deviation (SD) or median with range (where outliers were present) were used to summarise continuous variables. We used Student's t-test to examine the quantitative variables. For this, the Android app ‘Statistics Calculator’ was used. Numerical variables were related between

1. Controls and JIA patients
2. SLE patients and controls
3. Different types of JIA patients with controls
4. SLE and JIA patients by Student unpaired t test.

It was regarded as statistically important if the p-value was less than 0.05.

## RESULTS

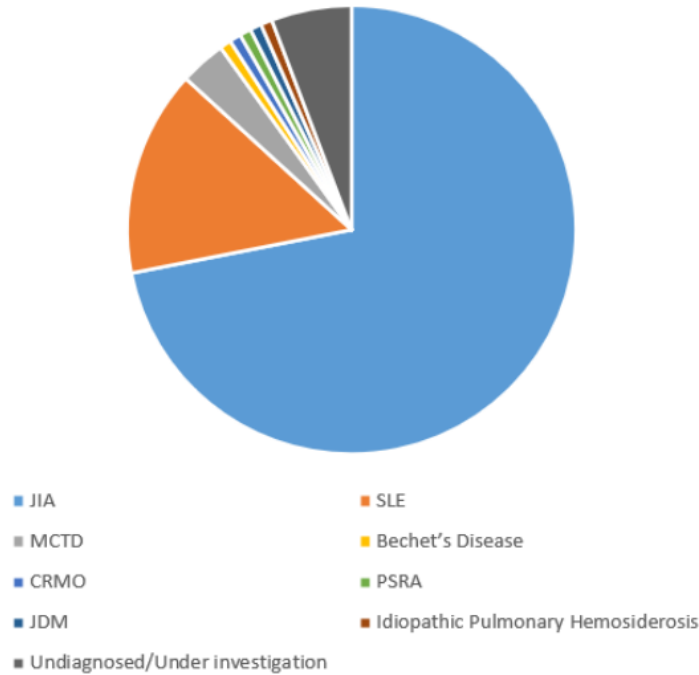
**Table 1**

Incidence of different types of Pediatric Rheumatic diseases identified

Disease	Number of patients in our cohort	Percentage of total
JIA	87	71.9
SLE	18	14.8
MCTD	4	3.3
Bechet’s Disease	1	0.82
CRMO	1	0.82
PSRA	1	0.82
JDM	1	0.82
Idiopathic Pulmonary Hemosiderosis	1	0.82
Undiagnosed/Under investigation	7	5.78

**Figure 1**

Incidence of different types of Pediatric Rheumatic diseases identified



MCTD – Mixed Connective Tissue Disease, CRMO – Chronic Recurrent Multifocal Osteomyelitis, PSRA – Post Streptococcal Reactive Arthritis, JDM – Juvenile Dermatomyositis.

Among 121 Pediatric Rheumatic patients attending our clinic, JIA was most common 87 patients (71.9%) followed by SLE 18 patients (14.8%).

**TABLE 2**  
Different types of JIA

	Number of patients	Percentage
SOJIA	33	37.9 %
POLY	18	20.6%
ERA	16	18.3%
JoAS	6	6.8%
Undifferentiated arthritis	6	6.8%
Psoriatic Arthritis	4	4.5%
Oligoarthritis	4	4.5%

Among different types of JIA patients, SOJIA variety was most common (37.9%), followed by Polyarticular variety (20.6%)

JIA and SLE were found to be predominant in number in our cohort, other Rheumatic diseases were minimal. So, for ease of statistical analysis they were not taken into

consideration. For this reason, we considered only JIA and SLE to compare with controls and among themselves.

Table 3  
Age and Sex of the patients

Disease	Male	Female	Mean age of Presentation
JIA	46	41	9 years 1 month
SLE	2	16	13 years 10 month

Table 3 showing Female sex predominance in SLE, Male sex predominance is JIA. Mean age of presentation in JIA is earlier than SLE. The reason is we had a significant number of SOJIA which has early presentation.

Table 4  
Different types of JIA and mean age of Presentation

Type of JIA	Mean age of Presentation
SOJIA	5 years 7 months
Psoriatic Arthritis	6 years
Oligoarticular	9 years
unclassified	10 years
ERA	12 years
Polyarticular	12 years 3 months
JOAS	12 Years 6 months

Among JIA subtypes, mean age of presentation was earlier in SOJIA variety (Mean 5 years 7 months) and late in JoAS (Mean 12 years 6 months).

Table 5  
Duration of illness prior to diagnosis in Paediatric Rheumatic Patients

Disease	Mean (In years)	SD (In years)
JIA	3.43	2.21
SLE	4.39	2.25

JIA patients had comparatively shorter period of illness previous to diagnosis than SLE. Among JIA patients, polyarticular JIA had longest duration of illness previous to diagnosis (Mean  $4.95 \pm 2.94$  years) and Psoriatic Arthritis had shortest duration (Mean  $2.5 \pm 1.2$  years).

Table 6A  
Anthropometric Data of JIA Patients (n = 87) and Control (n = 87)

Parameters	JIA Mean	Control Mean	p Value
Weight (Kg)	27.14 ± 11.9	29.59 ± 12.97	0.8
Height (Cm)	125.43± 19.84	130.46 ±20.83	0.02
BMI (Kg/m2)	16.02±2.84	16.34±2.01	0.39

Table 6A showing JIA patients, had significantly less height than age and sex matched controls. Though mean weight was less than controls, it was not statistically significant. BMI was not significantly altered with control.

In our cohort of JIA patients, Short Stature (height less 2 SD) was found in 11 patients (12.46 %).

**Table 6B**  
Mean Z – score of JIA patients

Parameters	Mean Z score
Weight	-0.67 ±1.02
Height	-0.8 ±0.98
BMI	-0.3 ±1.09

**Table 6C**  
Anthropometric data of common 3 types of JIA patients in our study

Parameters	SOJIA (n=33) – cases and control		Polyarticular (n=18) - cases and control		ERA (n=16)- cases and control		Significant p value in
Weight	16.93±4.28	19.18±3.85	29.8±7.84	38.21±12.69	38.73±13.69	38.93±12.51	SOJIA, Polyarticular
Height	108.06±9.88	112.72±10.11	132.89±12.9	143.36±15.95	145.56±16.89	145.93±19.33	SOJIA, polyarticular
BMI	14.20±1.31	14.91±0.46	16.56±2.09	17.94±2.19	17.8±3.84	17.61±1.73	SOJIA, Polyarticular

Table 6C showing among 3 common types of JIA in our cohort, SOJIA and Polyarticular variety had significantly less Weight, Height and BMI than age and sex matched controls

**Table 7A**  
Anthropometric Data of SLE Patients (n = 18) and Control (n = 18)

Parameters	Mean ± SD (SLE patients)	Mean ± SD (Control)	p Value
Weight (Kg)	36.28 ± 11.52	44.33 ± 8.2	0.01
Height (Cm)	140.3 ± 13.57	151.16±8.77	0.007
BMI (Kg/m2)	17.98 ± 3.62	19.1 ± 1.67	0.24



Table 4 showing SLE patients had significantly less weight and height compared to control. BMI value was not significantly different.

In our cohort of SLE patients, Shoer Stature (Height less 2 SD) was found in 7 patients (38.8%). Among them, 1 patient was male rest females. So, the percentage among males are 100% and females (35.2%).

Table 7B

Mean Z – score of SLE patients

Parameters	Mean Z score
Weight	-1.2 ±1.3
Height	-1.63 ±1.1
BMI	-0.53 ±1.15

Table 8

Comparison between Anthropometric parameters of JIA Patients (n = 87) and SLE patients (n = 18)

Parameters	Mean ± SD (JIA patients)	Mean ± SD (SLE patients)	p Value
Weight (Kg)	27.14 ± 11.9	36.28 ± 11.52	0.0036
Height (Cm)	125.43± 19.84	140.3 ± 13.57	0.0031
BMI (Kg/m2)	16.02±2.84	17.98± 3.62	<0.001

Table 5 showing though mean Weight, Height and BMI was significantly more in SLE patients than JIA patients.

Among JIA patients, 30 were active on presentation with much higher JADAS 10 score than 57 non active JIA present in the study.

Among SLE patients, 10 were active on presentation with much higher SLEDAI score than 8 non active SLE present in the study.

Table 9

Delayed Puberty among JIA and controls

Diagnosis	Total Patients	Delayed puberty
JIA	87	25

Controls	87	3
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The p value was found to be  $< 0.0001$ . so, delayed puberty was significantly more than JIA cohort than controls.

Among JIA patients, Delayed Puberty was common among Polyarticular and SOJIA Variety.

**Table 10**  
Delayed Puberty among SLE and controls

Diagnosis	Total Patients	Delayed puberty
SLE	18	6
Controls	18	0

p value was found to be 0.01, so Delayed puberty was more common in SLE cohorts than controls.

**Table 11**  
Delayed Puberty among JIA and SLE patients

Diagnosis	Total Patients	Delayed puberty
JIA	87	25
Controls	18	6

p value was found to be 0.7, so incidence of delayed puberty was not significantly different between JIA and SLE cohort.

## DISCUSSION

In our cross-sectional study mean age and duration of illness prior to diagnosis of JIA (71.9% of total cohort) patients were 9 years 1 month and  $3.43 \pm 2.41$  years respectively. There was mild male (52.8%) predominance.

In other Indian studies, mean age was 8.49 years<sup>5</sup> (Kolkata) and 12 years<sup>6</sup> (Pune). International studies revealed mean age to be  $5.33 \pm 3.4$  years<sup>7</sup> (Jordan), 9.5 years (Canada, ReA<sup>7</sup>Ch-out cohort)<sup>8</sup>. According to Childhood Arthritis Prospective Study (CAPS)<sup>9</sup> from UK, the Median age was 7.4 years (IQR 3.6,11.2).

Our study revealed mean height of JIA patients were less than age and sex matched controls. The difference was not significant for weight and BMI.

Another Indian study from same city (Kolkata)<sup>5</sup> didn't find any significant difference of weight, height and BMI among JIA patients and controls.

Growth retardation is a common symptom of juvenile inflammatory arthritis (JIA), a chronic inflammatory illness. Study population, research methodology, etiologic factors, and illness subtypes all play a role in determining the overall severity of such retardation<sup>5</sup>. However, similar to our study, another study from same city (Kolkata) revealed 66% of patients with JIA were below 3<sup>rd</sup> percentile of height for age (CDC 2000 standard).

Table 12

p value of JIA patients and controls in different growth parameters – comparison among different studies

	Our Study	Kolkata <sup>5</sup>	UK <sup>11</sup>
Weight	0.8	0.160	0.075
Height	0.02	0.254	0.096
BMI	0.38	0.162	Not considered

We compared p value of difference between cohort of JIA patients and controls among three studies. Other than our study, one was from same city (Kolkata) and another one from UK. We found p value was not significant in all 3 growth parameters from Kolkata study and 2 growth parameters from UK study (didn't compare BMI).

In our cross-sectional study mean age was 13 years 10 month and time period of illness prior to diagnosis of SLE (14.8% of total cohort) patients was  $4.39 \pm 2.25$  years. There was high female (88.8%) predominance.

But study from another Indian study Bangalore<sup>12</sup> revealed mean age to be 13.2 years and duration of illness prior to diagnosis 1 year.

Among international studies, mean age at diagnosis from Thailand study<sup>13</sup> ( $11.3 \pm 2.4$  years) was nearer to us. Whereas, study from Oman<sup>2</sup> ( $6.4 \pm 3.1$  years) and Italy<sup>14</sup> ( $14.6 \pm 1.6$  years) was different from our study.

Period of illness prior to diagnosis was  $4.2 \pm 3.2$  years from Omanian<sup>2</sup> study was nearer to us. Whereas value from study from Thailand<sup>13</sup> (6 months) was much lower.

Our study showed SLE patients had significantly less weight and height compared to age and sex match controls control. Even after through literature search, we couldn't find any study comparing SLE patients with sex and age matched controls.

In our cohort of SLE patients, Short Stature (height less 2 SD) was found in 38.8% patients. Study from Bangkok<sup>15</sup> by Ponin et al revealed nearly 25% of children with SLE develop growth impairment.

Research has shown inconsistent results about the severity of growth impairment due to factors such as different definitions of the term, different ages at diagnosis, and different ethnicities of the participants.

<sup>21</sup> comparison to other research, we discovered that our results were comparable to those of the Pediatric Rheumatology International Trials Organization (PRINTO)<sup>16</sup> longitudinal study. Among boys, 24.5% had growth impairment, while among girls, 14.7% did.

The reason why SLE patients had significantly decreased weight compared to controls is but not JIA patients compared to controls are probably due to following

1. SLE has multisystem involvement
2. JIA patients have early detection and treatment
3. Our SLE patients had delayed treatment compared to JIA, whose mean duration of illness was lesser.

<sup>19</sup> In our study, there was no significant difference in weight, height and BMI parameters among JIA and SLE patients. We didn't find any other study comparing Growth parameters of JIA and SLE.

The reason can be

- Both diseases being chronic inflammatory disease
- Both requires Steroid and immunosuppressive agents
- All SLE and SOJIA variety (29% of all JIA cohort in our study) have systemic symptoms

In our study, among SLE patients (n = 18), 55.5% patients were with active SLE on diagnosis, rest 44.4 were not active. Among active patients mean SLEDAI score was 9.4, among non-active patients, mean SLEDAI score was 1. Overall mean SLEDAI Score was 5.6.

Study from Italy<sup>14</sup> revealed mean score of 8 at diagnosis for all SLE patients.

In our study, among JIA patients (n = 87), 34.4% patients were with active JIA on diagnosis, rest 65.5% were not active. Among active patients mean JADAS 10 score was 4.2, among non-active patients, mean JADAS 10 score was 0.5.

In one study from Finland<sup>1</sup> inactive JIA patients had median score of 0.5, Low disease activity had Median score 1.6 and Moderate disease activity had median score 6.2.

In our study, incidence of delayed puberty among 2 main Rheumatic Diseases (Covering 86.7 % of our cohort of Pediatric rheumatic patients) SLE and JIA were 33.3% and 28.7%.

The incidence of delayed puberty in general population in different studies varies from 2% to 5 %. That means Patients with Pediatric Rheumatic problems are much more prone to develop Delayed Puberty.

In our study, delayed puberty was significantly more in JIA and SLE patients compared to controls.

A person's physical development into a sexually mature adult is the consequence of puberty, a crucial life transition characterized by a complicated sequence of hormonal and neurological changes. Researchers have only scratched the surface of the mysteries surrounding the processes that determine when adolescence begins. It is evident, however, that numerous internal and external variables (such as diet, genes, inflammatory condition, endocrine-disruptor drugs, and social changes) can impact the neuroendocrine events that occur during puberty. Adaptive changes, which are both a constraint and an opportunity for healthy growth and development during adolescence, are made possible by the clear plasticity of the timing of puberty and the significance of environmental influences. In children suffering from long-term health conditions, the onset and development of puberty are clear indicators of their emotional and physical well-being. Actually, similar to other inflammatory diseases, pubertal problems are common in children with JIA. This is particularly true in cases when the disease begins before puberty and the chronic inflammatory course is severe and long-lasting (sJIA). The maximum common pubertal abnormality in these patients is delayed puberty, which means that the breasts do not develop or the testicles do not enlarge until a 2-2.5 SD later than the average age of the population. In Western countries, this corresponds to a B2 stage in girls after 13 years of age and a Tanner stage G2 in boys after 14 years. Additionally, there have been reports of sluggish clinical advancement of puberty, isolated delayed menarche in women, and decreased period and intensity of puberty growth<sup>18</sup>.

At last, we have noticed that other studies involving growth of pediatric inflammatory arthritis had observed different growth parameters over at diagnosis and follow up or compared the patients with controls. The novelty of our study is that we have compared growth parameters of two common pediatric inflammatory arthritis – JIA and SLE.

### Limitations of this study

1. This is a cross sectional study, for a proper evaluation of Growth and development, we need to study growth velocity. For this, recording at different stages of the disease is required.
2. A larger population of Pediatric Rheumatic patients are needed. For this, we will need a longer duration of study.
3. This was a single centered study, a multi centered study is needed to include a large population and cover population of different areas.
4. No evaluation was made regarding the severity of growth retardation or its causes or factors affecting any subject or group.

### CONCLUSIONS

Among patients with inflammatory arthritis attending Paediatric Rheumatic Clinic, JIA was most common, followed by SLE. Among JIA patients SOJIA variety was most common, JIA patients had significantly lower height than age and sex matched Controls. SOJIA a Polyarticular variety had significantly less weight and height than controls. SLE patients had significantly lower weight and height than age and sex matched Controls. Delayed Puberty was significantly more in both JIA and SLE patients compared to controls.

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