RESEARCH PAPER

Growth of Children with Juvenile Idiopathic Arthritis

RAKESH MONDAL, SUMANTRA SARKAR, NILOY KUMAR DAS, SWATI CHAKRAVORTI, *AVIJIT HAZRA, TAPAS SABUI, MADHUMITA NANDI, #BIMAN RAY, ANJAN DAS AND SUSHAS GANGULI

*From Division of Pediatric Rheumatology, Department of Pediatric Medicine, *Department of Pharmacology and #Department of Physiology, IPGMER Kolkata.*

Correspondence to: *Dr Rakesh Mondal, Balarampur, Mahestala (PO), Kolkata 700 141, India. ivanrakesh2001@gmail.com.*

Received: June 03, 2013; Initial review: July 19, 2013; Accepted: January 09, 2014.

Objective: To evaluate the growth pattern in children with juvenile idiopathic arthritis and its subtypes in comparison with age, sex and temporally matched controls.

Study design: Prospective study.

Setting: Pediatric rheumatology clinic of a tertiary care hospital in Eastern part of India.

Participants: Seventy-five children (2-12 years) diagnosed as juvenile idiopathic erthritis by International League of Associations for Rheumatology criteria and 75 age- and sex-matched controls.

Intervention: Weight, height and body mass index were recorded at six monthly interval in both groups over a period of 3 years.

Main outcome measures: weight, height and body mass index.

Results: Subtype distribution of juvenile idiopathic arthritis was: oligoarthritis (49%, *n*=37), rheumatoid factor *negative* polyarthritis (27%, *n*=20), rheumatoid factor positive polyarthritis (8%, *n*=6), systemic onset (15%, *n*=11) and enthesitis related arthritis (1.3%, *n*=1). Anthropometric parameters in children with juvenile idiopathic arthritis were not significant different from controls. Comparison between the subtypes showed significant differences in height (*P*=0.011), weight (*P*=0.005), and growth velocity (*P*=0.005), but not in body mass index. Systemic onset disease led to significant restriction in height (*P*=0.018; 95% CI 2.13-33.77) and weight (*P*=0.008; 95% CI 1.47-14.43) compared to controls. Growth velocity was significantly affected in rheumatoid factor positive polyarthritis (*P*=0.003; 95% CIO. 46-3.14).

Conclusions: Children with juvenile idiopathic arthritis do not have significantly lower values of anthropometric parameters compared to controls. Significant restriction in height and weight is seen in systemic onset disease, and growth velocity is significantly reduced in rheumatoid factor positive subjects.

Keywords: *Anthropometry, Growth, Rheumatoid arthritis.*

Juvenile idiopathic arthritis (JIA) is frequently associated with growth retardation [1-3] varying from generalized growth impairment to local deceleration of growth of affected limb or spinal column [3-5]. Chronic inflammation mediated by several pro-inflammatory cytokines might be responsible for growth retardation. Other factors that might negatively contribute include the degree, extent and duration of disease activity, age at onset, suboptimal nutrition, reduced physical activity, hormonal influence, stress related to the long term illness, and corticosteroid therapy [3,6,7].

Several studies relate growth retardation and JIA but longitudinal comparative anthropometric data in different subsets of JIA population in a developing country are scarce. The objective of the present study was to evaluate the growth pattern in patients with JIA and its different subtypes in comparison to age, sex and temporally matched controls.

METHODS

This prospective study was carried out at pediatric rheumatology clinic of Institute of Post Graduate Medical Education and Research (IPGMER), Kolkata from January 2009 to December 2011. Ethical clearance was taken from the institutional ethics committee. A written consent was taken from the parents of all the participants.

Children between the ages of 2 and 12 years with symptoms of JIA, evaluated and diagnosed by International League of Associations for Rheumatology (ILAR) criteria [8] were included as study population. The categorization and the subtyping were also done as per ILAR guidelines. Children with similar age and sex attending the outpatient department at the same time for upper respiratory tract infections were taken as temporally matched controls. Children with chronic co-morbid endocrinal, renal, hematological or other diseases which cause growth retardation were not included in the study.

Children with JIA and control children were measured for body weight and standing height using the same equipment and the same observer. The weight was measured by digital weighing machine (Nova, India), with minimum clothing, to the nearest of 0.1 kg. Height was measured by a stadiometer (Hardik medi-tech, India) to the nearest 0.1 cm. The weight and height were recorded in triplicate and the average values were analyzed. Anthropometry was repeated at six-monthly intervals in both the cases and controls. Growth velocity (cm/y) was measured from the differential values of linear growth divided by the time under evaluation. The patients who missed the date were contacted over telephone to ensure attendance within 7 days. Those who did not return after two intimations were considered drop-outs and not included in the analysis.

Statistical Analysis: Descriptive analyses were done for most variables. Numerical variables were compared between JIA patients and controls by Student's unpaired t test when normally distributed, and by Mann Whitney U test when skewed. Multiple group analysis was done by One way analysis of variance (ANOVA) and Tukey's test as post hoc test for comparison between two individual subgroups. Chi-square test was used to compare categorical variables between groups. All analyses were 2 tailed and $P<0.05$ was considered statistically significant. Analysis were done using Statistica version 6 (Tulsa, Oklahoma: StatSoft Inc, 2001) and SPSS version 17 (Illinois, Chicago; SPSS Inc, 2008).

RESULTS

Out of 87 patients of JIA presenting during study period, 75 completed the study; 37 (49%) had oligoarthritis, 26 (35%) had polyarthritis [Rheumatoid factor (RF) negative 20 (27%), RF positive 6 (8%)], systemic JIA 11 (15%), and enthesitis related arthritis (ERA) 1(1.3%). The mean (SD) age of the study population (41 males and 34 females) was 8.48 (3.0) years. The mean (SD) age of onset of symptoms was 7.01 (3) years. The mean (SD) age of onset in different subtypes were 5.15 (3.0) years, 7.09 (3.0) years and 7.95 (3.0) years in systemic JIA, oligoarthritis and polyarthritis, respectively.

Anthropometry of JIA patients and controls are compared in ***Table* I**. Comparison between the different subtypes showed statistically significant difference in terms of height, weight and growth velocity but not in body mass index (BMI) (***Table* II**). Height and weight were more restricted in patients with systemic JIA; growth velocity was lowest in RF positive polyarthritis.

Multiple comparison analysis by Tukey's test showed significant difference in systemic JIA patients with respect to height (P=0.018; 95% CI 2.13-33.77) and weight (P=0.008; 95% CI 1.47-14.43) when compared with controls. Growth velocity was significantly affected in RF positive polyarthritis (P=0.003; 95% CI 0.46-3.14). Comparison between oligoarthritis and seronegetive polyarthritis did not reveal any significant difference in anthropometry (***Table* III**).

DISCUSSION

In the present prospective study, the JIA patients had lower (but statistically insignificant) weight, height, BMI and growth velocity as compared to age- and sex-matched controls. The patients with systemic JIA had signifiant impairment of weight and height whereas growth velocity was significantly lower in polyarticular RF positive subjects.

Limitations of the present study include small and unequal sample size in various subtypes of JIA. Moreover, the controls were not selected separately for each subtype as disease categorization was not complete at the time of entry of patients into the study. The degree of growth retardation or the etiology and influencing factors in each subject or category were not evaluated in the present study. The peak height velocity of adolescents was also not evaluated.

JIA, a chronic inflammatory disease, is frequently associated with growth retardation. [1-3,9,10]. The overall degree of such retardation is variable depending upon the study population, method of study, etiologic factors and disease subtypes. In a retrospective review by Padeh, *et al*. [2], growth retardation was found in 35.8% of patients

TABLE I ANTHROPOMETRIC DATA OF JIA PATIENTS (N=75) AND CONTROL (N=75) AT THE END OF THE STUDY

	JIA Patients		*Control*		
Parameter	*Mean ± SD*	*Median (IQR)*	*Mean ± SD*	*Median (IQR)*	*P value*
Weight (kg)	21.0 ± 7.8	20.2 (15.4-26.0)	22.7 ± 7.1	23.4 (16.1-28)	0.160
Height (cm)	120.6± 17.5	124.0 (108-133)	124.1 ± 18.8	130.0 (111-138)	0.254
BMI (kg/m^2)	13.9 ± 2.5	13.5 (12.3-15.2)	14.4 ± 1.4	14.4 (13.6-15.4)	0.162
Growth velocity (cm/y)	4.9 ± 1.2	4.8 (4.2-5.7)	5.3 ± 1.2	5.0 (4.5-6.0)	0.113

TABLE II COMPARISON BETWEEN DIFFERENT SUB-TYPES OF JIA PATIENTS AND MATCHED CONTROLS

Parameter	*Oligoarthritis (n=37)* *Mean ± SD*	*Polyarthritis RF(-) (n=20)* *Mean ± SD*	*Polyarthritis RF(+) (n=6)* *Mean ± SD*	*Systemic (n=11)* *Mean ± SD*	*Control (n=75)* *Mean ± SD*	*P value*
Weight (kg)	23.6±8.2	20.3 ± 8.2	19.3 ±3.4	14.8 ± 3.7	22.7±7.1	0.005
Height (cm)	126.5±15.9	118.9 ± 20.4	116.3 ±10.1	106.1± 12.0	124.1±18.	0.011
BMI (kg/M^2)	14.3 ± 2.7	13.7 ± 2.3	14.4 ± 3.0	13.1 ± 2.4	14.4 ± 1.4	0.290
Growth velocity (cm/year)	5.2±1.0	5.2 ± 1.4	3.5 ± 0.5	4.7 ± 1.0	5.3 ± 1.2	0.005

TABLE III SUMMARY OF STATISTICAL SIGNIFICANCE (*P* VALUE) OF COMPARISON BETWEEN SUBTYPES AND CONTROL

Dependent Variable	*Oligoarthritis with control*	*RF - polyarthritis with control*	*RF+ polyarthritis with control*	*Systemic JIA with control*	*Oligoarthritis with RF- polyarthritis*
Weight	0.977	0.649	0.796	0.008	0.458
Height	0.956	0.773	0.844	0.018	0.524
Growth Velocity	0.993	0.999	0.003	0.565	1.000

while another study [11] demonstrated short stature in only 4.3%. Significant retardation of growth was not demonstrated in JIA in the present study, which is consistent with an earlier report from United Kingdom [12]. The subtype-specific growth impairment, which showed systemic JIA and polyarthritis groups being most affected is also reported by other researchers [13-15]. A long-term study over 5 years by Okumus, *et al.* [16] found statistically significant difference in height standard deviation score in polyarticular and systemic JIA. Data from developing countries are still scarce. One recent study from India demonstrated a significant growth impairment in adolescent boys, with delay in peak height velocity [18]. Most affected subjects had polyarthritis and systemic JIA. They found 66% patients with JIA from Kolkata to be below the 3rd percentile of height when compared with CDC 2000 standards [18].

Meticulous evaluation of physical development and simultaneous monitoring of disease activity are essential components in the management of JIA. Growth monitoring in terms of weight, height, BMI essential for early detection of growth faltering.

We conclude that significant growth retardation occurs in systemic JIA and RF positive polyarthritis.

Contributors: RM, SS, NKD, SC, AD, BR, SG, MN: diagnosis and management of the patients; RM, NKD, SS, AH and TKS: drafted the manuscript; SS: critical review. All authors approved the final version; RM and SS shall act as guarantors.

F*unding*: None; *Competing interests*: None stated.

REFERENCES

1. Umawska W, Prusek-Dudkiewicz A. Growth retardation and delayed puberty in children and adolescents with juvenile idiopathic arthritis. Arch Med Sci. 2010;6:19-23.
2. Padeh S, Pinhas-Hamiel O, Zimmermann-Sloutskis D, Berkun Y. Children with oligoarticular juvenile idiopathic arthritis are at considerable risk for growth retardation. J Pediatr. 2011;159:832-7.
3. Gaspari S, Marcovecchio ML, Breda L, Chiarelli F. Growth in juvenile idiopathic arthritis: the role of inflammation. Clin Exp Rheumatol. 2011;29:104-10.
4. Vostrejs M, Hollister JR. Muscle atrophy and leg length discrepancies in pauciarticular juvenile rheumatoid arthritis. Am J Dis Child. 1988;142:343-5.
5. Minden K. Adult outcomes of patients with juvenile idiopathic arthritis. Horm Res. 2009; 1:20-5.
6. Cleary AG, Lancaster GA, Annan F, Sills JA, Davidson JE. Nutritional impairment in juvenile chronic arthritis. Rheumatology. 2004;43:1569-73.
7. Davies UM, Jones J, Reeve J, Camacho-Hubner C, Charlett A, Ansell BM, *et al.* Juvenile rheumatoid arthritis. Effects of disease activity and recombinant human growth hormone on insulin- likegrowth factor 1, insulin-like growth factor binding proteins 1 and 3, and osteocalcin. Arthritis Rheum. 1997.40: 332-40.
8. 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;31:390-2.
9. MacRae VE, Farquharson C, Ahmed SF. The restricted potential for recovery of growth plate chondrogenesis and longitudinal bone growth following exposure to pro-

inflammatory cytokines. J Endocrinol. 2006;189:319–28.
10. Bechtold S, Roth J. Natural history of growth and body composition in juvenile idiopathic arthritis. Horm Res. 2009;72: Suppl 1:13-9.
11. Umlawska W, Krzyzanowska M. Growth and menarche during remission in children with juvenile idiopathic arthritis. Med Wieku Rozwoj. 2009 ;13:194-200.
12. Lofthouse CM, Azad F, Baildam EM, Akobeng AK. Measuring the nutritional status of children with juvenile idiopathic arthritis using the bioelectrical impedance method. Rheumatology (Oxford). 2002; 41:1172-7.
13. Zak M, Müller J, Karup Pedersen F. Final height, armspan, subischial leg length and body proportions in juvenile chronic arthritis. A long-term follow-up study. Horm Res. 1999;52:80-5.
14. Saha MT, Verronen P, Laipalla P, Lenko HL. Growth of prepubertal children with juvenile chronic arthritis. Acta Paediatr. 1999;88:724-8.
15. García-Consuegra Molina J, Merino Muñoz R, Lama More R, Coya Viña J, Gracia Bouthelier R. Growth in children with juvenile idiopathic arthritis. Ann Pediatr (Barc). 2003;58:529-37.
16. Okumus O, Erguven M, Deveci M, Yilmaz O, Okumus M. Growth and bone mineralization in patients with juvenile idiopathic arthritis. Indian J Pediatr. 2008;75:239-43.
17. Aggarwal B, Bhalla AK, Singh S. Longitudinal growth attainments of Indian boys with juvenile rheumatoid arthritis. Rheumatol Int. 2011;31:635-40.
18. Sircar D, Ghosh B, Ghosh A, Halder S. Juvenile idiopathic arthritis. Indian Pediatr. 2006;43:429-33.