Original Article

Impact of genetic diseases on anthropometric parameters – A case–control study

Suvarna Magar[1], Anjali Kale[2], Shrushti Agarwal[3], Pranoti Toshniwal[3]

From [1]Assistant Professor, [2]Professor, [3]Resident, Department of Pediatrics, MGM Medical College, Aurangabad, Maharashtra, India

ABSTRACT

Background: It is observed that anthropometric parameters are lower in children suffering from genetic diseases as compared to other children. The WHO growth charts help us to get information if the anthropometric parameters are below or above 3 standard deviations (SD) but getting exact SD, can diagnose different etiologies and mechanisms of underlying growth faltering much precisely. **Objectives:** The objectives of the study were to calculate the exact SD of anthropometric parameters in cases with genetic diseases and to compare the SDs with the age- and sex-matched controls to find the impact of same on genetic diagnoses. **Materials and Methods:** This study was done in tertiary care center of Maharashtra. Cases (n=47) were defined as children with global developmental delay (GDD) (age 3 months–5 years) referred to the genetic clinic. Controls (n=47) were children with normal developmental milestones admitted in pediatric ward for community-acquired infections or illnesses. **Results:** There was a statistically significant lower mean weight ([8.3 vs. 10.4 kg]; $p<0.05$) and length ([74.7 vs. 82.5 cm]; $p<0.001$) and head circumference (HC) ([43.2 vs. 46.07 cm]; $p<0.05$), among children with developmental delay. The exact SD was calculated based on the "anthropometric calculator" digital mobile app based on the WHO growth charts. It revealed that means of SD for weight, height, and HC in both GDD and normal development of children were –2.9, –3.2, and –2.6 and –1.01, –0.84, and –0.64, respectively. **Conclusion:** Measuring the anthropometric parameters and interpreting growth and development are an important step in evaluation of a patient but identifying exact SDs of anthropometric measurements are a vital step for getting the genetic clues.

Key words: Anthropometric parameters, Genetic diseases, Global developmental delay

Anthropometry is the measurement of physical characteristics of the human body at different ages [1]. It includes taking accurate, highly standardized measurements to objectively depict size and form of body. Anthropometric measurement is an integral part of pediatric examination which includes weight, height or length, head circumference (HC), mid-arm circumference, and body mass index. The data on anthropometric measurements of children reflect general health status, and growth and development overtime [2]. Anthropometry has become an important tool in the study of genetic conditions, particularly as a diagnostic aid for the clinical geneticist [3]. As the best pediatric practice, anthropometric measurements have always played a role as one of the first and best screening tools for growth, nutrition, and development of child.

Widely used WHO growth charts are available in the form of digital apps and software for easy access, uploading, and data recovery for pediatricians. Most of the apps will mention only if the parameters are <–3 or more than +3 standard deviations (SD) and not beyond that. The exact SD is important in identifying the severity of growth failure and microcephaly and also they give clues to the genetic mechanisms and diagnostic clues responsible for the reduced somatic growth. We planned this study to calculate the exact SD of the weight, height, and HC in children with global developmental delay (GDD) using "anthropometry calculator" a digital app, based on the WHO growth charts.

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MATERIALS AND METHODS

This case–control study was done in the Department of Paediatrics of a Medical College of Maharashtra by retrospectively analyzing the data of children admitted between March 2018 and May 2019. Ethical clearance was obtained for the study from the Institutional Ethics Committee. Cases were children of age group 3 months–5 years presenting with GDD to the pediatric genetic clinic during the study period. Diagnostic criteria for GDD included a delay in two or more developmental domains: Gross and fine motor; speech and language; cognition; and personal and social developmental [4]. Those children with intrapartum asphyxia, postnatal central nervous infections, or birth trauma were excluded from the study.

Correspondence to: Dr. Suvarna Magar, Department of Pediatrics, MGM Medical College, Aurangabad, Maharashtra, India. E-mail: drsuvarnamagar@gmail.com

Consecutive cases were selected for the study and concurrent controls were selected from the records of patient data included developmentally normal children of 3 months–5 years who were admitted for acute febrile infections. Sample size was calculated using Epi Info program based on the assumptions that alpha error 5%, beta error 20%, that is, power of study 80%, odds ratio 2, and prevalence of GDD of 2% (obtained from the previous studies) provided a value of 47 children in each group.

Cases and controls were selected in 1:1 ratio after age and sex matching. We retrospectively retrieved data of anthropometric measurements of 47 cases and 47 controls including HC, weight, and length or height of the enrolled children along with final genetic, MRI brain or biochemical investigation-based diagnosis. The anthropometric parameters were entered in "anthropometry calculator" digital app in mobile after uploading age and sex of the children; exact SD was noted for each of the parameters for each patient. Data were entered into MS Excel, cleaned, and completeness checked. Analysis was done using SPSS Version 25. Student's *t*-test was applied for this normally distributed data.

RESULTS

A total of 47 cases and 47 controls were included in the study. The mean weight, height, and HC values in GDD group were 8.3 kg, 74.7 cm, and 43.2 cm as compared to 10.4 kg, 82.5 cm, and 46.07 cm, respectively, in the normal development group. Height, weight, and HC differences were statistically significant in all the anthropometric parameters with all parameters smaller in GDD group (Table 1). The mean SD for weight, height, and HC in both GDD and normal development groups was –2.9, –3.2, and –2.6 and –1.01, –0.84, and –0.64, respectively. The difference in the SD was statistically significant in the GDD group (Table 2).

We also made subclasses of anthropometric parameters based on SD (Table 3). The number of children, who had normal (+2—2 SD of the WHO growth charts) weight, height, and HC in developmentally normal children, was 38 (80%), 34 (72%), and 45 (96%), respectively. This indicated that children in control group may have been admitted for various acquired reasons in pediatric ward, majority of them had normal HC and weight and height had been impacted by various reasons. GDD group had weight, height, and HC not just below –2 SD but between –2—4 SD, between –4—6 SD, and also below –6 SD. Growth faltering in acquired diseases lied between –2 and –4 SD for few and less than –4 occasionally. For acquired diseases and developmentally normal children, we would label these children as moderate or severe acute malnutrition based on exact SD. We wanted to analyze various reasons or genetic mechanisms responsible for so much reduced somatic growth in GDD group.

We analyzed SD of anthropometric parameters in cases who had received diagnosis so that we could correlate growth failure with etiology. Out of 47 children, 13 children had confirmed diagnosis. Out of 13 diagnosed cases, 6 were inborn errors of metabolism, 2 children with skeletal dysplasia, 1 with growth failure syndrome, 2 with abnormal MRI brain, and 2 with Down's syndrome (Table 4).

Table 1: Mean of anthropometric parameters and statistical analysis

Group	n	Mean	SD	p-value
Weight (kg)				
Case	47	8.35	3.64	0.006
Control	47	10.44	3.57	
Height (cm)				
Case	47	74.76	13.5	0.008
Control	47	82.51	14.2	
Head circumference (cm)				
Case	47	43.28	4.18	0.0001
Control	47	46.08	2.86	

Table 2: Means of standard deviations of anthropometric parameters and analysis

Group	n	Mean	SD	p-value
Weight SD				
Case	47	–2.92	2.00	<0.0001
Control	47	–1.08	1.11	
Height SD				
Case	47	–3.2	2.91	<0.0001
Control	47	–0.84	1.65	
Head circumference SD				
Case	47	–2.63	2.08	<0.0001
Control	47	–0.64	1.04	

SD: Standard deviation

DISCUSSION

Our study highlights that identifying exact SD of anthropometric parameters helps us in reaching to diagnostic clues of genetic diseases and also helps understand the etiologies responsible for reduced somatic growth in a child. First, we searched literature that if the WHO growth charts can be used in the assessment of growth of developmentally delayed children. We could not get any reference but developmental assessment and correlation to anthropometry were studied at Agra, with positive correlation between developmental delay and malnutrition [5].

In developmentally normal child, HC was the parameter which lied in normal SD for 96% children and only few had head size less than –2 SD, indicating head sparing even if weight and height were less than normal. Those with HC smaller than –2 SD may be normal variants. Second, few children in control group had reduced height and weight. The cause could be mostly attributed to sickness or faulty feeding practices in otherwise developmentally normal children and genetic potential based on small parental stature needs to be considered too.

Among the GDD group, many children had dysmorphism, abnormal MRI brain but definitive diagnosis needed further genetic testing based on clinical picture. We had confirmed diagnosis in 13 children. Our six diagnosed patients of inborn errors of metabolism had significant failure to thrive, though significant microcephaly and reduced length were seen in mucolipidosis type II. A study by Spranger *et al*. revealed that there is reduced skeletal growth in mucolipidosis because of

Table 3: Stratification of anthropometric parameters in cases and controls

Standard deviations	Weight (%)		Height (%)		Head circumference (%)	
	Cases	Controls	Cases	Controls	Cases	Controls
+2—2 SD	21 (44)	38 (80)	19 (40)	34 (72)	20 (47)	45 (96)
–2—4 SD	13 (28)	8 (18)	13 (28)	11 (24)	15 (32)	2 (4)
–4—6 SD	9 (19)	1 (2)	11 (24)	2 (4)	9 (19	0
<–6 SD	4 (8)	0	4 (8)	0	3	0

Table 4: Anthropometric parameters in cases with final diagnosis

No.	Diagnosis	Weight SD	Height SD	HC SD
1.	Inborn errors of metabolisms			
	Arginosuccinase	–3.5	–0.7	–1.9
	Mucolipidosis type II	–5.8	–8	–5.3
	Succinic semialdehyde deficiency	–3.2	–0.7	–1.6
	Hyperphenylalaninemia	–4.7	–4.3	–3.8
	Mucopolysaccharidosis III	–0.4	0.4	0.8
	Mucopolysaccharidosis III	–2.4	–2.5	–1.4
2.	Skeletal dysplasia			
	Cranioectodermal dysplasia	–3.7	–5.4	+0.2
	Camurati-Engelman syndrome	–2.2	–3.6	1.5
3.	Growth failure syndromes			
	Cockayne syndrome	–7.4	–8.9	–6.5
4.	MRI brain diagnosis			
	Cystic leukoencephalopathy	0.1	1.2	–2.2
	Alobar holoprosencephaly	–2.6	–3.1	–4.5
5.	Down's syndrome (2 patients)	–4.3	0.05	–4.7
		–1.4	–3.1	–1.8

dysostosis multiplex changes [4]. Failure to thrive with other manifestations of metabolic diseases such as recurrent vomiting, encephalopathy, cholestasis, developmental delay, and dysostosis multiplex changes helps us to identify the inborn errors of metabolism [6].

Among the skeletal dysplasia group, we had one patient with cranioectodermal dysplasia and another with Camurati-Engelmann syndrome. Cranioectodermal dysplasia is part of a spectrum of disorders caused by disruption of the cilium, an organelle of the cell that appears and functions as an antenna [7]. These disorders, collectively referred to as ciliopathies, display marked phenotypic overlap. Typical clinical features of ciliopathies are renal cystic disease, retinal dystrophy, shortening of ribs, phalanges and long bones, polydactyly, hepatic fibrosis, and developmental delay. Camurati-Engelmann syndrome is an increased bone density syndrome also named as progressive diaphyseal dysplasia. It usually has macrocephaly and hyperostosis of long bones in X-ray [8]. Both patients of skeletal dysplasia had relative macrocephaly, that is, significantly reduced weights and heights in comparison to head size, making head appear bigger, though SD for HC lied in normal range.

Growth failure syndrome like Cockayne syndrome was diagnosed in one patient with severely reduced weight height and HC. CS type II (severe) is suspected in infants with growth failure at birth and little postnatal increase in height, weight, or HC and little or no postnatal neurologic development. They have a characteristic physical appearance of "cachectic dwarfism" with sunken eyes which is recognized based on anthropometry [9,10]. Children with Down's syndrome (DS) have lower birth weights and grow more slowly than children without DS. There are already existing growth charts for children with DS [11]. Hypothyroidism, celiac disease, and congenital heart disease are known to interfere with growth in DS children.

There are certain limitations of this study. Considering so much variation in growth parameters in developmentally delayed children, the WHO standard growth charts may not be applicable to these children. Hence, we need specialized growth charts which will help in diagnosis and growth surveillance of these groups of children. Larger studies are needed with proven genetic diagnosis so that findings of anthropometry can help develop guidelines for general pediatricians also.

CONCLUSION

The WHO growth charts are widely used to monitor growth and development in children and SD below –2 suggests growth failure in children. Calculating exact SDs of anthropometric parameters in children with GDD may help in the clinical diagnosis of various genetic syndromes and give insight into mechanisms of reduced somatic growth in these children.

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