Original Article

Etiological profile of short stature in rural Rajasthan

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ABSTRACT

Background: Short stature is one of the most common referrals to pediatric endocrinology clinics. Approximately 3% of children in any population are found to be short. **Aim:** This study aims to determine the etiology of short stature and their frequency of occurrence in 2–18 years old rural pediatric population and to classify the patients with short stature using anthropometric measurements. **Materials and Methods:** A total of 400 patients (age: 2–18 years) were diagnosed with short stature and admitted in pediatric ward. After meticulous history collection and complete physical examination, relevant investigations were performed in all the study subjects. Appropriate statistical analysis was carried out with the collected data. **Results:** Out of 400 study subjects, 70.50% were boys (male: female=2.33:1). Majority (n=241, 60.5%) of the affected children were in the age group of 2–<6 years and 7–<10 years. Of the 400 study subjects, 95% of cases (n=380) were classified as having proportionate short stature and the rest (n=20, 5%) had disproportionate short stature. Undernutrition (n=117, 29.25%) and familial short stature (n=90, 22.50%) were the leading causes of short stature. **Conclusion:** The current study helped to determine the etiological profile of short stature in children of adjoining rural population and in devising appropriate strategies for management and prevention.

Key words: Etiology, Children, Rural, Short stature

Short stature is defined as height below the third centile or less than 2 standard deviations (SD) below the median height for that age and sex according to the population standards. It is one of the most common conditions that are referred to the pediatric endocrinology clinics [1]. Approximately 3% of children in any population are found to be short [2]. There are no clear data for the prevalence of short stature in developing countries. Factors implicated in the pathogenesis of short stature in developing countries are different from developed countries because of the differences in race and lifestyle along with nutritional, cultural, and socioeconomic factors [3]. Most studies on children with short stature in India are from tertiary level centers [2-4]. The etiological profile and prevalence of short stature at community level hospitals in rural areas may differ from those reported from tertiary centers, and likewise, studies documenting the same, from these areas, are very rare in India [4]. This study was performed to enlist the etiology of short stature in children belonging to rural population and to carry out appropriate interventions to decrease its prevalence.

MATERIALS AND METHODS

This observational, prospective, cross-sectional study was conducted during January 2019–June 2020 in 400 patients (age: 2–18 years) admitted in the pediatric wards of a tertiary care teaching hospital, located 50 km from Jaipur city, amidst rural environment. Informed consent was obtained from their parents or guardians. The sample size (n) was calculated using the formula "$n=N/(1+Ne^2)$, where N=10000 (pediatric population assumed in adjoining rural area) and error e=0.05. Subsequently, patients were collected using purposive sampling technique.

The inclusion criteria for this study were children of either sex with age: 2–18 years, height: <3rd centile for age and sex as per age appropriate growth chart and those who provided consent for participation in the study. The exclusion criteria of this study were children of age <2 years, parents refusing to provide consent or refusing to perform laboratory investigations for etiological evaluation or failing to bring their children for follow-up. Following admission of study subjects in pediatric ward, a meticulous history was taken from their parents and physical examination of all study subjects was performed. Sexual maturity rating was performed in all adolescent patients. All bulky clothing and shoes that may interfere with anthropometric measurements were removed. Height of all study subjects was measured using a stadiometer (Prestige© portable stadiometer). All the study subjects were made to stand with feet flat together and against the scale of the stadiometer making sure that the legs were straight, arms were by the sides, and shoulders were at level. They were asked to look straight ahead in Frankfurt plane and that the line of sight was

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parallel with the floor. Their head, shoulders, buttocks, and heels touched the scale of the stadiometer. A flat headpiece with an inbuilt pointer and attached to the scale of stadiometer was lowered until it firmly touched the crown of the head. The inbuilt pointer indicated the reading of height in centimeter (cm). It was ensured that the eyes of the nursing staff measuring the height were at the same level on the headpiece and the study subject cooperated in this position during the procedure. In <5 years old study subjects, height, weight, midarm circumference, upper segment to lower segment ratio (US: LS), and head circumference were measured. In >5 years old, study subjects including adolescents, height, weight, and US: LS ratio were measured. The US: LS ratio was derived after independently determining each one of them. The lower segment was measured from the symphysis pubis to heel using a non-stretchable steel tape and two card boards pieces placed at both levels, respectively, in supine position. Upper segment was derived by deducting lower segment value from total height.

Mid-parental height or target height calculation for either sex was performed using height data for both parents as follows: Boys: (Father's Height + Mother's Height + 13)/2 in cm and girls: (Father's Height + Mother's Height -13)/2 in cm. The mid-parental height was plotted simultaneously to compare the growth potential of the study subjects with his/her parents. Subjects with height <3rd centile for age and sex were diagnosed as short stature, after plotting the patient's height on the age appropriate growth charts [5-8].

Height age was determined by drawing a horizontal line from the current height marking on the Y-axis of the growth chart up to the 50th centile curve and then dropping a perpendicular line to mark the corresponding age on the X-axis. Bone age was calculated using the radiograph of the left hand and wrist and Greulich Pyle method of estimation with the help of an in-house consultant radiologist. Chronological age was calculated according to the date of birth as provided by attendant and recorded in study pro forma. For the purpose of this study, the following working definitions of common clinical conditions associated with short stature were formulated: (a) Constitutional delay of growth and puberty (CDGP): Bone age equal to height age, both less than chronological age with a history of short stature in either parent during their childhood followed by pubertal spurt. (b) Familial short stature (FSS): Bone age equal to chronological age and both more than height age. Two growth curves indicating 3rd centile and 97th centile were drawn after plotting the midparental height ±8 cms for boys and ±6 cms for girls. If the present height of the study subjects was lying within the two growth curves, that patient was labelled as familial short stature. (c) Severe acute malnutrition: Diagnostic criteria as defined by the World Health Organization (WHO) and United Nations Children's Fund in children aged 2–5 years were weight for height <3 SD on the WHO growth standard, mid- upper arm circumference <11.5 cm, and presence of bipedal edema. In these patients, all other relevant investigations were within normal limits and no other obvious cause of short stature was evident except for significant under nutrition. In children >5 years age, crossing of two major percentile lines downward on weight or height chart with no obvious cause except poor dietary intake with respect to age, was considered as diagnostic criteria for under nutrition. On nutritional rehabilitation and regular follow-up, a significant improvement in height, weight, and other anthropometric measurements was observed.

Endocrinal disorders such as diabetes mellitus, hypothyroidism, and growth hormone (GH) deficiency were diagnosed using the standard clinical and laboratory criteria and with the help of in-house consultant endocrinologist. Genetic syndromes such as Down syndrome, Turner's syndrome, Noonan's syndrome, and Russell-Silver syndrome were diagnosed on basis of their typical clinical presentation. Chronic systemic diseases such as bronchial asthma and celiac disease were diagnosed as per standard guidelines [9,10]. Pulmonary tuberculosis was diagnosed and investigated as per latest Revised National Tuberculosis Control Programme guidelines [11].

Level 1 investigations include complete blood count with ESR, blood urea, creatinine, bicarbonate, pH, calcium, phosphate, alkaline phosphatase, fasting glucose, albumin, and transaminases, urinalysis including microscopy, osmolality, and pH, stool examination for parasites, steatorrhea and occult blood, bone age estimation using X-ray left hand, and wrist/complete skeletal survey. Level 2 investigations include serum free thyroxine (FT4), thyroid-stimulating hormone, and karyotyping. Level 3 investigations include tissue transglutaminase antibody and endomysial antibody levels, GH follicle-stimulating hormone, luteinizing hormone, and adrenocorticotrophic hormone levels using provocative tests. Serum levels of insulin-like growth factor-1, insulin-like growth factor binding protein-3 (IGFBP-3), cortisol and parathyroid hormone were measured, wherever indicated. Magnetic resonance imaging of the brain was performed in those with low peak GH levels.

An algorithmic approach (Fig. 1) was utilized for clinical evaluation and classification in all study subjects of short stature [12].

All relevant details of the study subjects including the probable diagnosis were entered in a pre-tested study pro forma. After discharge from pediatric ward, appropriate treatment and plan for follow-up was suggested. All study subjects were advised to follow-up once in 6 months to note their growth velocity, clinical progress and to institute changes in treatment accordingly. All relevant statistical analyses were performed using SPSS-20 software. Continuous variables were represented as mean±SD and categorical variables were expressed as frequencies and percentages. The study was approved by the ethics committee of our institution.

RESULTS

Out of the 400 study subjects, 70.50% were boys (male: female–2.33:1). Majority (n=241, 60.5%) of the subjects were in the age group of 2–<6 years and 7–<10 years (mean age±SD: 10.44±2.00 years). Sixty-two (15.5%) had weight for height < - 3SD, 55 (13.75%) having weight for height < - 2SD - > - 3 SD. About 95% of cases had proportionate short stature and the rest (5%) had disproportionate short stature.

The etiology of short stature as observed in male and female study subjects is mentioned in Table 1.

The various chronic systemic disorders associated with short stature in the study subjects are mentioned in Table 2.

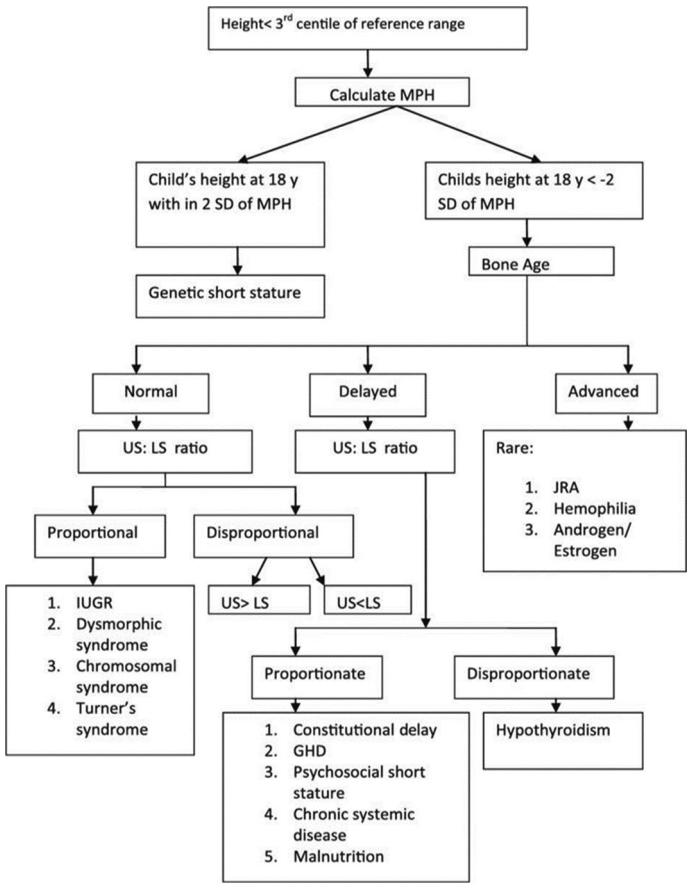

Figure 1: Algorithm for the evaluation of short stature in study subjects

The various endocrinal disorders associated with short stature in the study subjects are mentioned in Table 3.

DISCUSSION

This hospital-based study was performed to outline the etiology of short stature and their frequency of occurrence in 2–18-year-old rural pediatric population, where gender discrimination is rampant resulting in a skewed ratio with male predominance. The M: F ratio in other studies varied from 0.9:1 to 1.8:1 [3,13-16]. Majority of the affected children were in the age group of 2–<10 years, which may be due to the fact that parents are very worried and curious about the growth of their children during this early childhood period. This is also the time when children start going to school and various growth parameters are being regularly monitored by the school or Anganwadi staff members. In the study conducted by Lashari *et al*. [15], mean age of the study subjects was 9.9±3.4 years and most of the children (72.60%) were between 6 and 15 years of age. Similar observations were recorded by Hussein *et al*. [1].

In our study, the observation of undernutrition as a prominent etiology of short stature may be due to fact that majority of the study subjects belonged to lower socioeconomic class. Maternal illiteracy and ignorance regarding dietary requirements compounded by partial immunization status and recurrent infections,probably, resulted in their stunted growth. The prevalence of undernutrition as a cause of short stature was observed in the range of 6.9–20% in other studies [2,13]. This may be due to the reason that these studies were performed in urban area where the participants belonged from families of middle socioeconomic class bearing relatively significant level of maternal education and nutritional status.

Familial short stature was observed in 23.68% of the study subjects, which was similar to the observation of Rabbani *et al*. [14]. However, Velayutham *et al*. [2] reported familial and constitutional short stature in 66.67% of their study subjects where the study was performed at community level, and thus, had higher probability of detection of every

Table 1: Etiology of short stature in the study subjects

Etiology of short stature	Total		Male		Female	
	n	%	n	%	n	%
Undernutrition	117	29.25	96	24.00	21	5.25
FSS	90	22.5	73	18.25	17	4.25
Prematurity/IUGR	84	21	43	10.75	41	10.25
Chronic systemic disease	37	9.25	25	6.25	12	3.00
CDGP	30	7.5	18	4.50	12	3.00
Endocrinal disorders	19	4.75	11	2.75	8	2.00
Idiopathic	8	2	5	1.25	3	0.75
Chromosomal	5	1.25	3	0.75	2	0.50
Rickets	5	1.25	4	1.00	1	0.25
MPS	4	1	3	0.75	1	0.25
Skeletal dysplasia	1	0.25	1	0.25	0	0
Total	400	100	282	70.50	118	29.50

n: Numbers, %: Percentage, MPS = Mucopolysaccharidosis

Table 2: Chronic systemic disorders associated with short stature in study subjects

Chronic systemic disorders	Total		Male		Female	
	n	%	n	%	n	%
Celiac disease	15	40.60	11	29.72	4	10.81
Progressive pulmonary TB	8	21.60	6	16.21	2	5.40
Congenital heart disease	5	13.50	3	8.10	2	5.40
Chronic renal failure	3	8.10	2	5.40	1	2.70
Thalassemia	2	5.40	1	2.70	1	2.70
Bronchial asthma	2	5.40	1	2.70	1	2.70
Renal tubular acidosis	1	2.70	1	2.70	0	0
Inflammatory bowel disease	1	2.70	0	0	1	2.70
Total	37	100	25	67.56	12	32.44

Table 3: Endocrine causes of short stature in study subjects

Endocrinal disorders	Total		Male		Female	
	No.	%	No.	%	No.	%
Hypothyroidism	9	47.36	4	21.05	5	26.31
Diabetes mellitus	6	31.57	4	21.05	2	10.52
GH deficiency	2	10.52	1	5.26	1	5.26
Addison disease	1	5.26	0	0	1	5.26
Hypopituitarism	1	5.26	1	5.26	0	0
Total	19	100	10	52.65	9	47.35

GH: Growth hormone

asymptomatic normal variant of short stature. On the contrary, in our hospital-based study, the patients appeared in the outpatient department with symptoms of other disease or had severe degrees of short stature.

Chronic systemic diseases as a cause of short stature were observed in 9.25% of cases which were similar to the observation of Gutch *et al.* [3]. However, Ramagopal *et al.* [13] and Rabbani *et al.* [14] reported chronic systemic disease in 20.6% and 21.30% of cases, respectively. This relatively higher rate may be due to overcrowding, environmental pollution, and unhygienic conditions prevailing in the residential areas of their study subjects. Celiac disease was observed in 3.7% of cases in this study which was similar to the observation of Rabbani *et al.* [14]. This is due to the consumption of wheat and wheat-based products by the study subjects. Studies from South India [2,13] did not report celiac disease in their etiological profile due to intake of rice-based diet and consequently no gluten exposure.

Endocrinal causes were observed in 2.63% of the study subjects. However, other studies [3,14,16] have observed in the range of 15.9–37.2%. This may be due to the reason that many cases of hypothyroidism in rural areas are not reaching the tertiary care center, where endocrinology clinics are available. Further, such cases remain either underdiagnosed or are treated at level of primary care practitioners in the community. Thus, when studies are performed at community level, their reporting is higher than in hospital-based studies. GH deficiency, as a cause of short stature, was observed in only 0.5% of study subjects. However, other studies have reported its prevalence in the range of 2.4–69% [1,3,17]. Most of these studies were conducted in dedicated endocrine clinics. Some of them were having smaller sample size which may not reflect the actual occurrence of GH deficiency in their study community. Further, results of stimulation tests done to detect GH deficiency must be interpreted with caution. These tests must be carried out only when supported by suggestive clinical features of GH deficiency.

Idiopathic short stature was diagnosed in 2% of cases which was similar to other studies [1,3]. As this was a time-bound study, some cases could not be followed up further. They may actually be the cases of constitutional short stature as their investigations were all within normal limits and other obvious causes were ruled out. Hence, such patients were placed in idiopathic category. Disproportionate short stature was observed in 5% of cases. However, community- based study by Velauyutham *et al*. [2] has reported higher detection in 14.9% of their study subjects. Chromosomal disorders were observed in 1.2% of cases which was in consonance with Sultan *et al*. [16]. However, no other genetic syndromes were observed in our study.

The strength of this study was that a proper sample size was calculated keeping in reference the total population of children in adjoining rural area, thus, resulting in an adequately powered study. As it was carried out in rural children, this study addressed the paucity of studies related to short stature in rural children in India to some extent. The limitations of this study were that due to resource constraints, laboratory investigations such as karyotyping and genetic studies could not be performed in study subjects in which they were indicated. This was a hospital-based study, hence, the etiological profile as observed may not be completely representative of the varied causes of short stature in adjoining community under study.

In this study, it was further observed that 70% of study participants had correctable cause of short stature. Hence, timely detection and diagnosis by growth charts becomes mandatory for community pediatricians. This may be reinforced by organizing periodical training programs. Further, paramedical staff at rural health centers, school teachers, and parents share a responsibility in timely detection of short stature in children at primary level.

CONCLUSION

The findings of the present study help in determining the etiological profile of short stature and for devising strategies for its management and prevention in children of adjoining rural population.

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