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An analysis of demographic and etiological factors of children and adolescents with short stature in the rural tertiary center- An observational study

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ABSTRACT

Objectives: (i) To determine pattern of and proportion of various etiology of short stature. (ii) To determine relationship of the Standard Deviation Score (SDS) with etiology.

Materials and Methods: This non-analytic observational study, assessed demographic parameters, anthropometry and etiology associate with short stature adolescents and children (6 months to 18 years). Short stature was defined as length/ height for age < 3^{rd} centile or < -2 SD as per age & gender specific growth charts.

Results: Out of 105 subjects, 22 were 6 months to < 5 years age, 33 were 5 to 10 years age and 50 were 10 to < 18 years age with M: F ratio of 1.28:1. Average value of chronological age, height age, and height SDS were 8.86 years, 5.62 years, and – 3.44 SD, respectively. 45.71% subjects were malnourished. Idiopathic short stature (24.7%), chronic renal diseases (12.3%) and endocrine disorders (12.3%) were found as etiology common in all three age groups. Chronic neurological diseases (9.5%) were more common in 6 months to < 5-year age group; while endocrine disorders (16%), respiratory diseases (12%), gastrointestinal diseases (8%), and renal diseases (8%) were common in adolescents. The maximum average height SDS (-2.3 ± 0.2) was observed with normal variants; while the lowest average SDS (-4.8 ± 2.0) was observed with syndromic short stature children.

Conclusion: Malnutrition was significant co-existing factor in pathological short stature. The common etiology of pathological short stature varied with different age groups. The SDS is important in deciding evaluation plan for particular short stature case.

1. Introduction

Growth monitoring is not only an essential part of preventive child health programs but is also pivotal for judging the children's well-being. The short stature is not a disease per se. It reflects growth faltering in an otherwise normal-child due to a variety of underlying diseases. The first step in approaching a child with short stature is to differentiate normal variants from pathological short stature as it needs a separate set of investigations.[1] The comparison of individual stunted child's height SDS (Standard Deviation Score) with his/her Mid-Parental-Height (MPH) SDS is an essential clinical step in identifying pathological short stature.[2] The aetiologies causing pathological short stature include chronic systemic diseases, endocrine disorders, genetic diseases, malnutrition, skeletal dysplasia, rickets, etc. The short stature can be subcategorized into proportionate and dis-proportionate short stature based on

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the US: LS ratio. Generally, long-bones and vertebral deformity e.g. rickets and skeletal dysplasia results in disproportionate short stature;[3] while rest aetiologies cause proportionate short stature. The individual self-esteem may be influenced by his/her physical height to some extent.[4] The short stature children experience impairments in the form of adverse impact on their academic performance and social life.[5,6] National Family Health Survey (NFHS)-4 data revealed 38.4% of under five-year children were stunted.[7] The Overall prevalence of short stature was 13.8% in Pankaj Garg et al study.[8] In a study of child growth, conducted at Bai Jerbai Wadia Hospital for Children in Bombay, India, 5.6% (140/2500) children were short stature.[9] However, studies reporting the burden and etiological profile of short stature in older children are very less from India. Hence, the early identification of pathological short stature and appropriate intervention before epiphyseal fusion is key for a good outcome. In this perspective, the present study was conducted to contribute demographic as well as etiological data to existing data and to demonstrate utility of height SDS in approach to short stature children. The objectives of the study were to determine the pattern and the proportion of various etiology of short stature as well as to demonstrate the relationship of SDS with various etiology.

2. Material and Methods

This is a prospective observational study; in which 105 children and adolescents between ages of completed 6 months - 18 years with short stature (length/ height for chronological age less than 3 percentile or minus 2 SD as per standard growth chart).[10] admitted in the pediatric ward of Dhiraj Hospital during December 2017 to July 2019, were included after approval from the institutional ethics committee. All children were enrolled after taking written informed consent from parents or guardians and also separate consent was taken from adolescent subjects. While children age less than 6 months and those whose parents or guardians did not give consent to participate were excluded.

The Sample size of 105 was obtained by using formula: $N = \frac{Z\,(1-\alpha/2)2\,pq}{d2}$. Where, N=Minimum sample size required, Z = Statistic for a level of confidence, p = Expected proportion (if the prevalence is 20%, p is 0.2), q= 1-p, and d = Precision (if the precision is 5%, then d is 0.05). Data was collected as per predesigned proforma.

Tools used in the study are

1. An infantometer for length measurement in children < 2 years age
2. A wall mount stadiometer for height measurement in children > 2 years age.
3. The gender-specific standard growth charts i.e., WHO length for age (for < 5-year age) and IAP height for age (for > 5-year age).

Length, height, and Mid-Parental Height (MPH) were calculated as per standard method and formula.[8] Furthermore SDS (Standard Deviation Score) for length/ height as well as for MPH was derived by using the following formula. Height SDS= (Observed height- Mean height) / 1SD and MPH SDS= (Observed TH- Mean TH) / 1SD, where 1 SD was calculated from length/ height for age growth charts.[11] The difference between Height SDS and MPH SDS of more 8.5 cm was considered significant to raise suspicion of pathological short stature. The physical findings like pallor, clubbing, lymphadenopathy, dysmorphism, typical features of particular chronic systemic disorder, skeletal deformity, Sexual-Maturating Rating were recorded. The findings of investigations, ordered as per standard protocol, were noted. Bone age was assessed by doing an age-appropriate skeletal x-ray and using Greulich and Pyle's Standards. Serum TSH and free-T4 were done by using the chemiluminescent immunoassay (CLIA) method. Epi Info Ver-7 software was used to analyse data statistically. Quantitative data are presented as frequency, proportion, ratio, and percentage.

3. Results

In the present study 105 children and adolescents with short stature were enrolled during the study period. 59 (56.2%) were boys and 46 (43.8%) girls. 22 (21%), 33 (31%), and 50 (48%) children were belonging to 6 months to < 5 years, 5 to < 10 years, and 10 to 18 years age group, respectively.

Amongst 22 children of < 5 years, 8 (36%) were wasted; of which 5 (62.5%) were girls and 3 (37.5%) were boys. The study incidence of thinness among children between 5 to 18 years of age was 48.2% (40/83); the same was more prevalent amongst boys (57.5%) than girls (42.5%). Average height SDS of girls, boys with overall were -3.62, -3.29, and -3.44, respectively.

In present study, distribution according to etiology in descending order was 26 (24.7%) Idiopathic short stature, 14 (13.3%) chronic renal disorders, 13 (12.4%) endocrine disorders, 9 (8.6%) chronic neurological disorders, 7 (6.8%) chronic respiratory diseases, 7 (6.8%) chronic hematologic disorders, 6 (5.7%) chronic gastrointestinal diseases, 6 (5.7%) constitutional short stature, 5 (4.7%) familial short stature, 4 (3.8%) metabolic diseases, 3 (2.8%) syndromic short stature, 2 (2%) systemic inflammatory diseases, and 2 (2%) skeletal deformity. Poor nutrition (Wasting+ Thinness) was found in 45.71% (48/ 105) children. Amongst noticed diseases, the commonest were hypothyroidism 11 (10.48%), chronic kidney disease 7 (6.67%) and Rickets 4 (3.80%).

The age group-wise distribution of various aetiologies shows Idiopathic short stature (8), chronic neurologic (5), and chronic kidney disorders (3) were common in 6 months to < 5 years aged children. Among 5 to < 10 years aged children, idiopathic short stature (8), chronic renal (6), chronic hematologic (4), and endocrine (4) disorders

were common. In the group of 50 adolescent children, idiopathic short stature (10), endocrine disorder (8), chronic respiratory diseases (6), gastrointestinal disease (6), and chronic renal disease (4) were common.

The relationship of SDS with different etiology shows that the mean SDS of more than 3 was observed with pathological short stature. The lowest mean SDS (about -2.3 with SD 0.2) was observed with constitutional and familial short stature while the highest mean SDS below - 4.00 was observed with syndromic and metabolic disorder. The observed mean SDS among idiopathic short stature was -3.5.

4. Discussion

In the present study, more than half of the subjects were boys with M: F ratio was 1.28:1. Similarly, in S.K. Bhadada et al study[12] and Gutch M et al[13] study the M: F was 1.25:1 and 1.64 respectively. Age distribution revealed predominantly affected age-group was adolescents followed by school-age and toddler-preschool-age. The study prevalence of wasting amongst toddler-preschool-age children was 36%, whereas the prevalence of same in India as well as in Gujarat is 7.3% and 25.1%, respectively.[14,15] The prevalence of thinness among children (5-10 years aged) and adolescents was 48.2%. While, the prevalence of thinness in India amongst adolescent was 26.1% in 2016.[16] The overall study prevalence of poor nutrition of was 48 (45.7%). In the present study, the mean chronologic-age and height were 8.86 (0.5-17) years and 109.87 (59-154) cms respectively; while Gutch M et al[13] mentioned the mean chronological-age: 11.6 + 3.2 years, and mean height: 119.3+12.6 cm. The average BMI of children more than 5 years of age was 14.83 Kgs/m2, which was similar to 15.9 Kgs/m2 average BMI found in EM Lee et al study.[17]

The proportion of normal variant short stature in this study was very low (11, 10.5%) and the same for pathological short stature was very high (94, 89.5%). In Phirke DS et al study 26.5% and 73.5% were the normal variant short stature and pathological short stature, respectively.[18] In the present study, common aetiologies in descending orders were idiopathic short stature, chronic renal disorders, endocrine disorders, chronic neurological disorders, chronic respiratory diseases, chronic hematologic disorders, chronic gastrointestinal diseases, etc. In Pankaj Garg et al study, the commonest cause of short stature was protein energy malnutrition (PEM) & chronic diseases occurring in 46 (53.5%) cases followed by normal variant short stature (24.4%), endocrine problems (4.7%) and miscellaneous (5.8%).[8] In contrast, S.K. Bhadada et al study[12] mentioned normal variant (36.1%) was most common etiology followed by endocrine (30.09%), IUGR and birth anoxia (8.52%), chronic systemic diseases (7.38%), metabolic bone diseases (5.68%) and malnutrition (5.1%). The reason behind this difference was the target population i.e., enrolment of hospitalized children with short stature. In a community-based study conducted by K Velayutham et al familial short stature was reported as the commonest etiology (66.6%).[19]

On exploring distribution of etiology among different age groups revealed that the proportion of Idiopathic short stature was highest in all age-groups. Among toddler-preschool-age group other predominant aetiologies were chronic neurologic diseases and chronic kidney disorders; while among school-age children chronic renal diseases, chronic hematologic diseases, and endocrine disorders were common. In the adolescent-group endocrine disorder, chronic respiratory diseases, chronic renal disease, and systemic inflammatory disease were commonly observed aetiologies apart from normal variant and idiopathic short stature. In present study, the commonest diseases were hypothyroidism (10.48%), chronic kidney disease (6.67%) and Rickets (3.80%). In Velayutham K et study, hypothyroidism (13.79%), growth hormone deficiency (9.20%), and malnutrition (6.9%) were commonest diseases causing pathological short stature.[19]

The current study showed that the average height SDS was -3.36 (± 1.0). The lowest mean SDS (about -2.3 ± 0.2) was observed with normal variant short stature while highest mean SDS was observed with syndromic disorders (-4.8 ± 2.0), metabolic disorder (-4.17 ± 1.3) and endocrine disorders (-3.8 ± 1.2). The observed mean SDS among idiopathic short stature was -3.5. Average Height SDS in a study conducted by S. Mohmmadian et al[20] was -4.16 ± 1.32. Maximum height SDS was observed in genetic disorder (-4.85 ± 1.26) followed by GH deficiency (-4.67 ± 1.35) constitutional short stature (-3.82 ± 1.22) and hypothyroidism (-3.63 ± 1.58).

The limitations of this study were: (i) Present study is hospital based only (ii) Karyotyping was not done in all idiopathic short stature girls. (iii) Some of the idiopathic short stature children did not evaluate after first-line investigations due to financial constraints and some of them left against medical advice.

5. Conclusion

Pathological short stature was more common among hospitalized children. Undernutrition was a predominant association found with short stature. Hypothyroidism was commonest endocrine disease-causing short stature. A good community-based survey is mandatory to know an exact aetiological profile as the majority of normal variant short stature children do not seek health-care. A list of commonest etiology varies with different age groups. A group of children having idiopathic short stature with height SDS significantly low on comparing with target height SDS needs separate attention and evaluation strategy as it may be sequelae of severe malnutrition that had occurred in early age or maybe result of an underlying undiagnosed condition.

Table 1: Various demographic factors analysis

Demographic factors	Female (n=46)	Male (n=59)	Total (n=105)
Average Chronologic Age (Range) years	8.7 (1.1 - 17)	8.98 (0.5- 17)	8.86 (0.5-17)
Average Weight (Range) Kgs	18.03 (5.7 - 50.58)	18.98 (4.2- 52.88)	18.57 (4.2-52.88)
Average Height age (Range) years	5.43 (0.7- 12)	5.77 (0.17- 13)	5.62 (0.17- 13)
WfL* Kgs (For < 5 years)	9.6	11.2	10.4
Wasted (WfL < -2SD)	5 (62.5%)	3 (37.5%)	8/22 (36%)
BMIĎ Kgs/m^2 (For 5 or more years)	15.18	14.57	14.83
Thinness (BMI < 5^{th} %le)	17 (42.5%)	23 (57.5%)	40/83 (48.2%)
Height SDS	-3.62	-3.29	-3.44

*WfL: Weight for length, ĎBMI: Body Mass Index

Table 2: Etiology wise distribution

Etiology	Diseases – number (percentage)
Idiopathic (26)	Idiopathic short stature - 26 (24.7%)
Normal variants (11)	Familial short stature - 5 (4.76%), Constitutional delay - 6 (5.71%)
Hematological diseases (7)	B thalassemia major - 1 (0.95%), Sickle cell disease - 4 (3.81%), Combined sickle- beta thalassemia - 2 (1.90%)
Neurological diseases (9)	Cerebral palsy - 4 (3.81%), Hydrocephalus - 2 (1.90%), Intellectual disability - 2 (1.90%), Epilepsy- 1 (0.95%)
Endocrine disorders (13)	Hypothyroidism - 11 (10.48%), Cushing syndrome with obesity - 1 (0.95%), Insulin dependent diabetes mellitus - 1 (0.95%)
Gastrointestinal diseases (6)	Ulcerative colitis - 2 (1.90%), Coeliac disease - 1 (0.95%), Functional abdominal pain - 1 (0.95%), Hirschprung's disease - 1 (0.95%), Juvenile polyposis syndrome - 1 (0.95%)
Metabolic disorders (4)	Calciopenic rickets - 2 (1.90%), Phosphopenic rickets - 1 (0.95%), Wilsons disease with rickets - 1 (0.95%)
Renal disorders (14)	Chronic kidney disease - 7 (6.67%), Distal renal tubular acidosis - 2 (1.90%), Frequent relapse nephrotic syndrome - 4 (3.81%), Infrequent relapse nephrotic syndrome - 1 (0.95%)
Respiratory diseases (7)	Asthma - 3 (2.86%), Tuberculosis - 4 (3.81%)
Skeletal deformity (2)	Spinal deformity with dorso-lumbar severe kyphosis - 1 (0.95%), Atlanto-axial subluxation with severe spinal cord stenosis - 1 (0.95%)
Genetic disorders (4)	Down syndrome - 1 (0.95%), Seckel syndrome -2 (1.90%)
Systemic inflammatory diseases (2)	Takayasu arteritis - 1 (0.95%), Rheumatoid arthritis - 1 (0.95%)

Table 3: Age group wise etiology distribution

Etiology	< 5 years (n=22)	5 to 10 years (n=33)	10 to 18 years (n=50)
Hematological disease	0	4 (12.1%)	3 (6%)
Constitutional Short stature	0	4 (12.1%)	2 (4%)
Neurological disease	5 (22.7%)	2 (6.1%)	3 (6%)
Endocrine disorder	1 (4.5%)	4 (12.1%)	8 (16%)
Familial short stature	0	2 (6.1%)	3 (6%)
Gastrointestinal disease	2 (9.1%)	0	4 (8%)
Idiopathic short stature	8 (36.5%)	8 (24.3%)	10 (20%)
Metabolic disorder	2 (9.1%)	1 (3%)	1 (2%)
Kidney disease	3 (13.6%)	6 (18.1%)	4 (8%)
Respiratory disease	1 (4.5%)	0	6 (12%)
Skeletal malformation	0	0	2 (4%)
Syndromic disease	0	2 (6.1%)	1 (2%)
Systemic inflammatory diseases	0	0	2 (4%)

Table 4: Average Height SDS in different etiology

Etology	Mean Height SDS	SD
Chronic hematologic disease	-2.57	0.65
Constitutional Short stature	-2.26	0.13
Chronic neurologic disease	-3.73	0.74
Endocrine disorder	-3.82	1.23
Familial short stature	-2.33	0.31
Chronic gastrointestinal disease	-3.79	1.07
Idiopathic short stature	-3.59	1.21
Metabolic disorder	-4.17	1.30
Chronic kidney disease	-3.56	1.29
Chronic respiratory disease	-3.44	1.31
Skeletal malformation	-2.56	0.21
Syndromic disease	-4.87	2.00
Systemic inflammatory diseases	-3.058	1.58

The calculation of height SDS is more useful than just labelling below -2SD, as more low height SDS the chances of having pathological short stature are high.

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8. Conflicts of Interest

No conflicts of interest.

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