

# Etiology of short stature in children and adolescents: experience at a tertiary care hospital in Bangladesh

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## ABSTRACT

**Background:** Short stature can cause psychosocial problems both in parents and children. It can be a normal variant or secondary to an underlying pathological condition. It is necessary to evaluate cause of short stature and thus to decide whether further management needed. This study aimed to determine the causes of short stature in children and adolescents.

**Methods:** This cross-sectional study was done at the paediatric endocrine out patient department, BIRDEM General Hospital 2, Dhaka from January to December 2019. A total 175 patient with short stature who fulfilled the inclusion criteria were recruited. Detailed history, physical examinations including anthropometric measurements and relevant investigations were recorded.

**Results:** The mean age of the children was  $9 \pm 4$  years, with female preponderance (female: male 1.27:1). Majority of the children had normal variation of growth (29%). Systemic illness and non-endocrine causes were found in 27.4%, endocrine cause in 26.85%, 13.7% cases had dysmorphic features and idiopathic short stature was found in 2.85% cases. Familial short stature (FSS) was the most common cause (20.57%) followed by hypothyroidism (13.14%), familial short stature co-existing with nutritional problem (8.6%), growth hormone deficiency (7.4%), Turner syndrome (6.28%). Other causes that contributed for short stature in our study included constitutional delay of growth and puberty (CDGP) (2.85%), FSS coexisting with CDGP (5.7%) and systemic diseases and chromosomal abnormalities.

**Conclusions:** The majority of short stature in children had normal variations of growth. Potentially treatable causes such as hypothyroidism, growth hormone deficiency, nutritional problem, Turner syndrome etc. accounted for a considerable percentage of short stature in our study.

**Key words:** Bangladesh, short stature, familial short stature, constitutional delay of growth and puberty, hypothyroidism.

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## INTRODUCTION

Growth is a continuous biologic process subjected to genetic, environmental, nutritional and hormonal influences. Altered growth potential may result from disturbance of any of these factors.<sup>1</sup> Short stature, a common problem in paediatric population of developing countries,<sup>2</sup> is defined as height or length below 3rd centile or less than 2 standard deviations for that specific age and sex.<sup>3</sup>

Short stature is commonly related to a normal variant of growth, including familial short stature and constitutional growth delay.<sup>4-6</sup> However, it may be the first manifestation of an underlying pathological condition requiring early adequate treatment, such as hormonal disorders or chronic diseases. Thus, careful evaluation and identification of the underlying etiologies is crucial for early prevention and treatment.<sup>7</sup>

The final adult height in human is controlled by multiple genes. In familial short stature, the final adult height is short but within the target range of height for the family.<sup>8</sup>

Constitutional delay of growth and maturation (CDGM) having subtle defects in growth hormone-insulin like growth factor (GH-IGF) axis, obligates higher rates of overall energy expenditure compared with age and size matched controls, this increased metabolism may result in impaired tempo of growth.<sup>9</sup> Puberty is delayed and there is a delayed and reduced pubertal growth spurt but the final adult height is usually not affected and remains in the lower parental target height zone.<sup>10</sup>

Endocrine causes are classically associated with being overweight for height. In appropriately treated children with growth hormone deficiency or congenital hypothyroidism, puberty and final adult height are within the normal range in treated cases.<sup>11</sup>

Severe malnutrition (3rd degree) is one of the common causes of short stature in third world countries. Specific nutritional deficiencies can have an effect on child growth.<sup>12</sup>

Chronic childhood diseases, if sufficiently severe can lead to growth failure and short stature. Important examples include renal, pulmonary, cardiac

disease, malignancy, cystic fibrosis and celiac disease.<sup>12-14</sup> Celiac disease is a prime example of a remediable cause of short stature especially in younger children.<sup>15,16</sup>

Short stature may also be seen with severe intrauterine growth retardation (IUGR)<sup>17</sup> and in large number of dysmorphic syndromes.<sup>18</sup> Emotional deprivation is an important cause of retardation of growth.<sup>19</sup> Idiopathic short stature (ISS) is considered when no causative disorder can be identified.<sup>20</sup>

In Bangladesh, there are very few pediatric studies focusing on short stature.<sup>21,22</sup> The aim of our study was to describe the characteristics and determine the etiological profile of children referred to our pediatric endocrinology clinic for short stature.

## METHODS

This cross-sectional study was conducted at the paediatric endocrine out patient department at BIRDEM General Hospital 2, a tertiary care hospital, Dhaka, the capital city of Bangladesh from January to December 2019. Children below 18 years attending at paediatric endocrine OPD with height below 3rd centile were included in the study and children with gross bony deformity or cerebral palsy were excluded. Patient who did not have adequate information regarding history and investigation reports were also excluded.

### Working definitions

Familial short stature (FSS): Height is below 3rd centile but corresponds with their MPH. bone age and chronological age similar.

Constitutional delay of growth and puberty (CDGP): Positive family history of delayed growth and puberty. Bone age=height age

Nutritional problem: BMI is below 5th centile and bone age delayed. May be accompanied with micronutrient deficiency.

Malnutrition: Weight less than 60% of the expected weight for age and sex according to NCHS (National Child Health Services) standard and nutritional history of decreased caloric intake.

A structured questionnaire gathered the data regarding the patients' medical history including sex, age at diagnosis, birth weight, past medical history, nutritional history, parental height and puberty.

All children were carefully examined for any abnormal findings such as pallor, dysmorphism, disproportion, hypertension, goiter, coarse skin, central obesity, striae, cardiac murmur, mental retardation, midline defects etc.

Patient's physical findings including anthropometric measurements at diagnosis (weight, height, body mass index, occipito-frontal circumference in case of below 3 year of age) and pubertal status were recorded.

Occipito-frontal circumference was measured by non-stretchable tape.

Height was measured in centimeters by standard technique using a stadiometer and weight in kilograms using a digital scale.

Target height was calculated by the method of MPH, the average of the mother's and father's height  $\pm 6.5$  cm (addition in boys or subtraction in girls). Height was plotted on CDC growth chart.

Lower segment (LS) was measured from symphysis pubis to floor and upper segment (US) was calculated by subtracting LS from total height. US/LS was calculated from these measurements.

Puberty was assessed in by rating the breast development in girls, genital developments in boys, pubic and axillary hair development in both sexes, according to Tanner2 s staging.<sup>23,24</sup>

Parents were asked for any available previous record.

Initial investigations performed in all our patients included complete blood count, S. ALT, S. creatinine, free T4, thyroid stimulating hormone (TSH) and bone age.

Other investigations such as blood gas, serum electrolyte, calcium, phosphate, alkaline phosphatase, Vitamin D level, tTGlgA etc. were done if indicated.

Karyotype was performed in patients with dysmorphism and in girls in whom other causes of short stature were excluded.

Skeletal survey was performed when dysplasia was suspected.

IGF-1 and growth hormone stimulation tests were performed (with L-Dopa stimulation) in patients with suspected growth hormone deficiency.

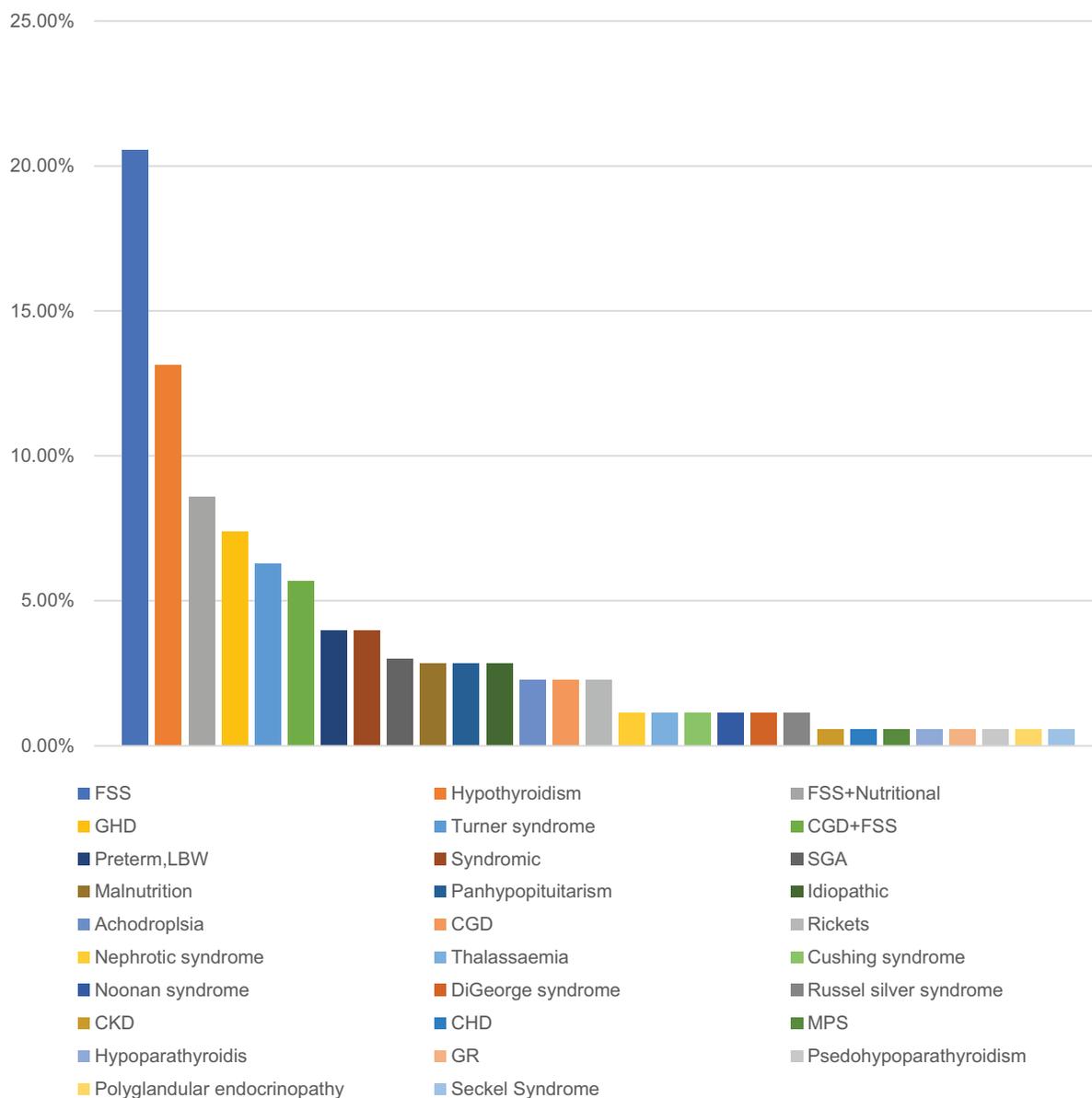
Data was entered in SPSS version (19.0). Descriptive statistics were applied. Mean and standard deviation for age were computed. Frequency of various causes of short stature was calculated. Confounding variables like age and gender was controlled by stratification. All p value  $<0.05$  was considered as statistically significant.

## RESULTS

During 2019, a total of 40971 children visited paediatric endocrine out patient department of BIRDEM General Hospital 2, among them 1022 were new cases. Total 218 children presented with the complaints of not growing well. Hundred and ninety children had height below 2SD. Fifteen children had inadequate information. Finally, 175 children were recruited in our study. Among them 98 were female (56%) and 77 were male (44%) with a ratio of 1.27:1. The age ranged from 4 months to 17.5 years, mean age was  $9 \pm 4.18$  years and median age was 9.4 years.

The frequencies of various causes of short stature in this study are shown in (Figure 1). The predominant causes of short stature were familial short stature (20.57%), followed by hypothyroidism (13.14%), familial short stature coexisting with nutritional problem (8.57%), growth hormone deficiency (7.45%), Turner syndrome (6.28%). The other causes that contributed for short stature in our study included constitutional delay of growth and puberty, small for gestational age, preterm low birth weight, idiopathic short stature and other systemic diseases.

Among the 175 children with short stature, majority (29%) of the children had normal variant of short stature. FSS was the most common cause found in 36 of the children (20.57%), CDGP was found only in 5 children (2.85%). Coexisting FSS and CDGP were found in 10 children (5.7%). Table I shows distribution of normal variant of short stature among the total 175 children.



**Figure 1** Distribution of frequency of various causes (%) of short stature

**Table I** Distribution of normal variant of short stature(n=175)

Diagnosis	Number	Percentage
Familial short stature (FSS) only	36	20.57
Coexisting FSS and CDGP	10	5.7
Constitutional growth delay (CGD) only	5	2.85

Forty seven patients (26.86%) of the 175 children presented with endocrine problem. Hypothyroidism was the most common cause, found in 23 children (13.14%). Growth hormone deficiency found in 13 children (7.42%) and 5 children had panhypopituitarism (2.85%), one patient was found to have growth hormone resistance. Two children had Cushing syndrome. Hypoparathyroidism, pseudohypoparathyroidism, polyglandular endocrinopathy was found in one patient in each group. Table II shows distribution of endocrine causes of short stature among the total 175 children.

**Table II** Distribution of Endocrine causes of short stature (n=175)

Disease	Number	Percentage
Hypothyroidism	23	13.14
Growth hormone deficiency	13	7.4
Panhypopituitarism	5	2.85
Cushing syndrome	2	2.28
Growth hormone resistance	1	0.57
Hypoparathyroidism	1	0.57
Polyglandular endocrinopathy	1	0.57
Pseudo hypoparathyroidism	1	0.57

Familial short stature with coexisting nutritional problem was found in 15 children (8.57%). Seven children had history of preterm, low birth weight (4.0%) and 6 children (3.43%) were born small for gestational age (SGA). Malnutrition was present in 5 children (2.85%). Achondroplasia was found in four patient (2.28%), Rickets was also found in 4 patient (2.28%). Mucopolysaccharidosis was found in one patient (1.14%). Two patients presented with thalassemia and two with nephrotic syndrome. Congenital heart disease (CHD), chronic kidney disease (CKD) and renal tubular acidosis (RTA) was found in one patient in each group. Five children (2.85%) were diagnosed as idiopathic short stature. (Table III).

**Table III** Distribution of systemic or non-endocrine causes short stature(n=175)

Diagnosis	Number	Percentage
Nutritional with FSS	15	8.57
Preterm low birth weight	7	4.0
SGA	6	3.43
Malnutrition	5	2.85
Idiopathic	5	2.85
Achondroplasia	4	2.28
Rickets	4	2.2
Nephrotic syndrome	2	1.14
Thalassemia	2	1.14
CKD	1	0.57
CHD	1	0.57
MPS-IV	1	0.57

Among the total 175 children, twenty-four children with short stature had dysmorphic features (13.71%). Turner syndrome which was found in 11 girls (6.28%). Two patients were diagnosed as DiGeorge syndrome, 2 as Russel silver syndrome, 2 as Noonan syndrome. One patient had Seckel syndrome. In six children, exact diagnosis couldn't be done who were labeled as Syndromic.

**Table IV** Distribution of dysmorphic patients(n=175)

Diagnosis	Number	Percentage
Turner syndrome	11	6.28%
Syndromic	6	3.43%
Noonan syndrome	2	1.14%
Russel silver syndrome	2	1.14%
DiGeorge syndrome	2	1.14%
Seckel syndrome	1	0.57%

There was no significant difference in sex among the common causes of short stature except in case of combined familial short stature with CDGP, which was more common in male (p=0.04). (Table V)

**Table V** Gender distribution among the common causes of short stature

Diagnosis	Male	Female	P-value
FSS	15	21	0.89
FSS+CDGP	8	2	0.042
FSS+ nutritional	9	6	0.30
CDGP	4	1	0.23
Hypothyroidism	9	14	0.77
GHD	4	9	0.47
Preterm	2	5	0.65
SGA	2	4	0.90

## DISCUSSION

This cross-sectional study was conducted to find out the etiology of short stature in children, who attended the pediatric endocrinology OPD in BIRDEM General Hospital in the year 2019.

In our study there were 175 children. Among them 98 were female (56%) and male were 77 (44%) with a ratio of 1.27:1, FSS with coexisting nutritional problem was more common in boys than girls but no significant difference in sex were found in other conditions.

It is not similar with most of the studies done in different countries where males outnumbered the females,<sup>25,26</sup> but similar result was found another study in Bangladesh.<sup>21</sup>

Female preponderance of short stature in this study may be due to the fact that, there is increasing awareness among people about health seeking in most of the families.

Mean age of the patients was 9±4.18 years and median age was 9.4 years. Most of the study shown most common age group was 6-11 year which are similar to our study.<sup>21,27</sup>

Familial short stature (FSS) was the leading cause of SS in the children (20.57%) as found in other studies.<sup>21,27</sup> Another study done in Bangladesh found CDGP leading cause<sup>22</sup> where some studies found endocrine problems more.<sup>5,28</sup>

Forty-seven children (26.86%) had endocrine problem. Most common cause was hypothyroidism found in 23 children (13.14%) followed by growth hormone deficiency in 13 children (7.42%). One study done in Pakistan found hypothyroidism as the leading endocrine cause for short stature which was 17.2% and the next common cause was GHD (10.7%)<sup>5</sup>. Another study done in India found hypothyroidism and GHD in 14.2% and 7.4% of short children respectively<sup>15</sup>. These findings are similar to the results of our study.

In the present study, FSS with coexisting nutritional problem were found in 9.7% of the children. Malnutrition was present in 6 children (3.43%) which is similar with other studies ranging from 4.7-9.8%.<sup>5,21</sup>

Dysmorphism was found in 23 children (13.14%). Turner syndrome was found in 6.28% of children. Another study done in Bangladesh found chromosomal abnormality in 5% of children.<sup>21</sup> Another study done in Tunisia found chromosomal abnormality in 15% children among them 8% were turner.<sup>28</sup>

The limitations of this study include, this was a hospital based cross-sectional study done with a small sample size.

A large scale, community-based, longitudinal study is needed to better delineate the cause short stature in general population. In Bangladesh there are very few data regarding the etiology of short stature. This study will provide a baseline data which will help the future studies.

## Conclusion

Familial short stature was the most common cause (20.57%), followed by hypothyroidism (13.14%), familial short stature with coexisting nutritional problem (8.57%), GHD (7.4%), Turner syndrome (6.28%) etc. Potentially treatable causes accounted for a considerable percentage of short stature. It is very important for physician to monitor height and weight of children routinely so that timely diagnosis and referral can be made, as early initiation of appropriate treatment in case of short stature can improve final adult height.

**Authors' contribution:** SJ: Concept and designed the study, analyzed data and drafted the manuscript. FM: Helped in data collection, data analysis and review of the whole process. All authors read and approved the final manuscript.

**Conflict of interest:** Nothing to declare.

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