**Original Research Article**

**Etiology of short stature in children attending pediatric endocrinology clinic of a tertiary care hospital in Bangladesh**

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**ABSTRACT**

**Background:** Short stature is a common problem to practicing pediatricians. It results from various etiologies, which are categorized as normal variants and pathological causes. Normal variant short stature consists of Familial Short Stature (FSS) and Constitutional Growth Delay (CGD), while pathological causes are subdivided into endocrine diseases, clinically defined syndromes, chronic diseases, metabolic diseases and others. There are not so much data available in Bangladesh in this respect. So, present study was conducted to know the common causes of short stature.

**Methods:** This cross-sectional study was done in pediatric endocrinology clinic of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from January 2017 to August 2018. One hundred children with short stature meeting inclusion criteria were recruited after taking an informed consent. The detailed history, physical examination including anthropometric measurements and relevant investigations were done. Data were recorded on a predesigned questionnaire for final analysis.

**Results:** The common causes of short stature identified were familial short stature (FSS) 51% cases, Constitutional Growth Delay (CGD) 14% cases and hypothyroidism 12% cases. Other less common causes of short stature were Growth Hormone Deficiency (GHD) 8% cases, malnutrition 6% cases and genetic syndrome 5% cases.

**Conclusions:** FSS and CGD were the leading cause of short stature in children. Endocrinological causes were the most common cause of short stature after normal variant while nonendocrine causes were the least.

**Keywords:** Etiology, Growth, Short stature

**INTRODUCTION**

Growth is an important objective parameter of general health of a child. Short stature is a common problem encountered by practicing pediatricians. It results from an intricate process which involves integration of genetic potential, functioning endocrine system, nutritional status, effects of chronic diseases and physical activity level. A disturbance at any point of these levels may affect growth adversely resulting in short stature which is defined by height or length below the 3rd centile or less than 2 standard deviation for that specific age and sex.1,2

Short stature is a result of various etiologies, which are categorized as normal variants and pathological causes. Normal variant short stature consists of Familial Short Stature (FSS) and Constitutional Growth Delay (CGD), while pathological causes are subdivided into endocrine diseases, clinically defined syndromes, chronic diseases, metabolic diseases and others.3

The final adult height in humans is controlled by multiple genes. In familial short stature, the final expected adult height is short but within the target range of height for the family.4
Constitutional Growth Delay (CGD) having subtle defects in Growth Hormone-Insulin like Growth Factor (GH-IGF) axis and higher energy expenditure, this increased metabolism may result in impaired tempo of growth. Puberty is delayed but the final adult height is usually not affected and remains in the lower parental target height zone. 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. Celiac disease is a prime example of a remediable cause of short stature especially in younger children.

Common endocrine disorders leading to short stature include hypothyroidism, cushing’s syndrome and growth hormone deficiency.

Short stature may also be seen with severe Intrauterine Growth Retardation (IUGR) and in large number of dysmorphic syndromes. Emotional deprivation is an important cause of retardation of growth. Idiopathic Short Stature (ISS) is considered when no causative disorder can be identified.

**METHODS**

This cross-sectional study was conducted at the pediatric endocrinology clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from January 2017 to August 2018. Children from both genders, 2-18 years of age having height below two Standard Deviation (-2SD) from the mean or less than 3rd percentile for age and sex who came in the clinic during the study period were included. Patients with contractures and kyphoscoliosis in whom height could not be measured and patient already on treatment were excluded. All the patient who came during the study period and matched with inclusion and exclusion criteria were enrolled in the study. Protocol was approved and ethical clearance was taken from the Institutional Review Board (IRB) of BSMMU. The patients and/or the parents were informed of the study design and the purpose of the study. All sorts of confidentiality were ensured. Informed written consent was taken.

A structured questionnaire gathered the data regarding particulars and anthropometric measurements of selected children. Birth history, family history of any short stature or pubertal delay, dietary history, history of any chronic disease was taken. After history taking anthropometric indices were measured. The weight was measured by using Bathroom scale and height was recorded by using locally made height board where two horizontal flat wooden boards, one for head-end and another for foot-end, was attached with a long vertical scale to nearest 0.5 cm. Values of height and weight were evaluated to categorize individuals nutritional status. Lower segment was measured from the pubic symphysis to the heel and upper segment was calculated by subtracting the lower segment from the height. Upper segment to lower segment ratio of the body was calculated to differentiate between proportionate and disproportionate short stature. Mid Parental height was taken in all patients for initial categorization. OFC was measured by measuring tape slipped over the head and passed around the occipital protuberance and supra orbital ridge and expressed in centimeter. Height for age, weight for age, weight for height, OFC for age, BMI for age was plotted on Center for Disease Control and Prevention (CDC) growth chart, Standard Deviation (SD) score was calculated and compared with CDC normal growth data for children. After doing clinical evaluation (history and examination), patients were advised to do some investigations.

All the patients were advised to do first line investigations which includes: complete blood count with ESR, urine R/M/E, serum creatinine, SGPT, thyroid function test and Xray for bone age. If the clinical features and first line investigations were suggestive patients were advised to do second line investigations which includes serum calcium, serum phosphate, serum alkaline phosphatase, serum parathormone, X ray wrist, knee and ankle, growth hormone stimulation test, chromosomal analysis.

The data were collected and compiled manually. The entered data were checked, verified and analyzed by Statistical Program for Social Science (SPSS software, version 22). The data were presented in tabular form. Unpaired t-test and chi-square test was applied for data analysis. A p-value less than 0.05 was considered as significant.

**RESULTS**

A total number of 100 short stature patients were enrolled in this study among them 47% were males and 53% were females. The male to female ratio was 0.92:1. Most common age group was 6-11 years.

**Table 1: Demographic profile of the study population (n=100).**

| Demographic profile | Number of patient (%) |
|---------------------|-----------------------|
| Age (years)         |                       |
| 2-5                 | 16 (16)               |
| 6-11                | 59 (59)               |
| 12-18               | 25 (25)               |
| Sex                 |                       |
| Male                | 47 (47)               |
| Female              | 53 (53)               |
| Residence           |                       |
| Rural               | 62 (62)               |
| Urban               | 38 (38)               |
| Socioeconomic condition |                 |
| (<10000 Tk)         | 10 (10)               |
| (10000-<30000 Tk)   | 54 (54)               |
| (30000-<50000 Tk)   | 30 (30)               |
| (>50000 Tk)         | 6 (6)                 |

Data were expressed as number and percentage.
Most of the patients (62%) were from rural area and 38% patients were from urban area, 54% patients belonged to a low socioeconomic background (with monthly family income of 10,000-<30,000 tk) (Table 1). Causes of short stature in this study was FSS (51% cases), CGD (14% cases), hypothyroidism (12% cases), GHD (8% cases), malnutrition (6% cases), genetic syndrome (5% cases) (among them 3 cases were turner syndrome and 2 cases were down syndrome); and rickets, skeletal dysplasia and IUGR comprised 1% cases each.

**Table 2: Etiology of short stature (n=100).**

| Etiology                                      | Total, n (%) | Male n(%) | Female n (%) | p value |
|-----------------------------------------------|--------------|-----------|--------------|---------|
| Normal variants of growth                     |              |           |              |         |
| Familial short stature (FSS)                  | 51(51)       | 21(41.17) | 30(58.83)    | 0.074ns |
| Constitutional growth delay (CGD)             | 14(14)       | 8(57.14)  | 6(42.86)     | 0.449ns |
| Endocrine                                     |              |           |              |         |
| Hypothyroidia (FSS)                           | 12(12)       | 4(33.33)  | 8(66.67)     | 0.102ns |
| Growth hormone deficiency (CGD)               | 8(8)         | 6(75)     | 2(25)        | 0.045** |
| Pathological short stature                    |              |           |              |         |
| Malnutrition (FSS)                            | 6(6)         | 4(66.66)  | 2(33.44)     | 0.248ns |
| Genetic Syndrome                              |              |           |              |         |
| Turner Syndrome                               | 3(3)         | -         | 3(100.0)     | -       |
| Down Syndrome                                 | 2(2)         | 1(50)     | 1(50)        | 1.000ns |
| Rickets                                       | 1(1)         | 1(100)    | -            | -       |
| Skeletal dysplasia                            | 1(1)         | 1(100)    | -            | -       |
| IUGR                                          | 1(1)         | 1(100)    | -            | -       |

IUGR=Intrauterine growth retardation
Statistical analysis was done by Chi-square test, ns=not significant, **= significant at p<0.05

**Table 3: Distribution of the study patients by height in relation to age and sex (n=100).**

| Age (Years) | Height (cm) (Mean) | Male | Female | p value |
|-------------|-------------------|------|--------|---------|
|             | Number | Mean height±SD (cm) | Number | Mean height±SD (cm) |
| 2-5         | 85.4   | 4 | 86.12±16.64 | 12 | 77.75±8.37 | 0.196 ns |
| 6-11        | 110.8  | 31 | 109.90±11.01 | 28 | 114.41±9.26 | 0.094 ns |
| 12-18       | 134.6  | 12 | 136.46±7.01 | 13 | 127.75±13.49 | 0.048** |

Statistical analysis was done by Unpaired t-test, ns=not significant, **= significant at p<0.05

**Table 4: Etiology of short stature in relation to severity.**

| Etiology               | Height SD<-2 to -3 | Height SD<-3 | P value |
|------------------------|--------------------|--------------|---------|
|                        | Mean height±SD (cm) | Mean height±SD (cm) |
| Familial short stature | 118.31±10.88       | 114.02±17.86 | 0.235 ns |
| CGD                    | 114.9±9.34         | 114.75±7.93  | 0.981 ns |
| Hypothyroidism         | 113.14±21.30       | 97.2±12.75   | 0.169 ns |
| Genetic Syndrome       | 122.16±19.63       | 101.5±4.94   | 0.258 ns |

Statistical analysis was done by Unpaired t-test, ns=not significant.
**All the patients of GHD and malnutrition were severely stunted.
**Panhypopituitarism, rickets, skeletal dysplasia and IUGR consisted only 1 patient each and also severely stunted.

Comparison of height of male and female patients of different age group showed that in the age group of 12-18 years, female patients were significantly shorter than male patients (p value 0.04) (Table 3). Comparison of
height between moderate and severe short stature patients of different etiologies showed that there was no significant difference (Table 4). Pathological short stature patients were severely underweight and NVSSS patients were moderately underweight (p value 0.001) (table 5).

Table 5: Association of demographic characteristics of children with normal variant and pathological short stature (n=100).

| Variable          | Normal variant SS (n=65) | Pathological SS (n=35) | p-value |
|-------------------|--------------------------|------------------------|---------|
|                   | n (%)                    | n (%)                  |         |
| Age (year)        |                          |                        |         |
| 2-5               | 9                        | 13.9                   | 7       | 20       | 0.686ns |
| 6-11              | 40                       | 61.5                   | 19      | 54.3     |         |
| 12-18             | 16                       | 24.6                   | 9       | 25.7     |         |
| Sex (M/F)         |                          |                        |         |
| Male              | 29                       | 44.6                   | 19      | 54.3     | 0.355ns |
| Female            | 36                       | 55.4                   | 16      | 45.7     |         |
| Residence         |                          |                        |         |
| Rural             | 42                       | 64.6                   | 20      | 57.1     | 0.462ns |
| Urban             | 23                       | 35.4                   | 15      | 42.9     |         |
| Socioeconomic class |                      |                        |         |
| (<10000 Tk)       | 5                        | 7.8                    | 5       | 14.3     | 0.250ns |
| (10000-<30000 Tk) | 37                       | 57.8                   | 17      | 48.6     |         |
| (30000-50000 Tk)  | 21                       | 31.3                   | 9       | 25.7     |         |
| (>50000 Tk)       | 2                        | 3.1                    | 4       | 11.4     |         |
| Height            |                          |                        |         |
| Moderate stunting | 38                       | 58.5                   | 14      | 40       | 0.078ns |
| Severe stunting   | 27                       | 41.5                   | 21      | 60       |         |
| Weight            |                          |                        |         |
| Normal            | 26                       | 40.0                   | 8       | 22.9     |         |
| Moderate underweight | 37                    | 56.9                   | 12      | 34.2     | 0.001** |
| Severe underweight | 2                      | 3.1                    | 15      | 42.9     |         |

Data were expressed as number and percentage. SS=Short stature, cm=centimeter Statistical analysis was done by Chi-square test, ns=not significant, **= significant at p<0.05

DISCUSSION

This cross-sectional study was conducted to know the etiology of short stature in children, who attended the pediatric endocrinology clinic with a height for age below the 3rd centile. In the present study 100 patients of short stature were enrolled, among them most common age group was 6-11 years, which is similar with other studies.16,17

Present study had 47 males and 53 females. The male to female ratio was 0.92:1. It is not similar with most of the studies done in different countries where males outnumbered the females.17,19 Increased incidence of short stature in females in this study may be due to the fact that, there is increasing awareness among people about health seeking and most of the families have only 1-2 child. So, parents are giving similar emphasis on female and male child.

Causes of short stature in this study were FSS (51%), CGD (14%), hypothyroidism (12%), GHD (8%), malnutrition (6%), genetic syndrome (5%). Among the genetic syndrome 3 cases were Turner syndrome, 2 cases were down syndrome. Rickets, skeletal dysplasia and IUGR comprises 1% cases each. These findings are similar with other studies. A study done in Egypt found FSS, CGD, GHD, hypothyroidism and IUGR 42%, 15.8%, 11.8%, 9.1% and 2% respectively.16 Another study done in Pakistan found FSS, hypothyroidism, GHD and CGD 21.3%, 17.2%, 10.7% and 6.6% respectively.17 FSS was the most common (51%) cause of short stature in this study which is similar with other studies.16,17 In some other studies CGD was the most common cause of short stature (33% and 17.3%).20,21 In the current study CGD comprised 14% cases, which was the second most common cause of short stature.

In this study FSS was more common in females than males (30% vs 21%) whereas in case of CGD males outnumbered females (8% vs 6%). This finding is similar with other studies.7,21,22 Current study showed that NVSSS was more common than pathological short stature (65% vs 35%) which is similar with other studies.16,23

If authors categorize the causes into three main etiological groups, the most frequent was NVSSS (FSS and CGD) followed by endocrinological and non-endocrinological group. In this study NVSSS comprised 65% cases, endocrinological causes were 21% and non-endocrinological causes were 14%, which is very much consistent with other studies done in different countries.7,16,23-25 But some other studies found non-endocrinological causes as the most common cause of short stature.17,21 From this point it is very much evident that the most common cause of short stature is normal
variant. So, early diagnosis and proper counseling helps the patients to save money from unnecessary investigations and also removes anxiety.

Endocrine diseases are usually less common cause of short stature in children, varied markedly in different studies, ranging from 5% to 35%. In this study endocrine diseases constituted 21% of cases. The most common endocrine cause in this study was hypothyroidism (12%) followed by GHD (8%) and panhypopituitarism (1%). The higher number of endocrine causes in this study may be due to the fact that this study was conducted in a pediatric endocrine clinic.

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%). Another study done in India found hypothyroidism and GHD 44.2% and 7.4% respectively. This findings were similar to this study which constitutes 12% and 8% respectively.

The most common non-endocrinological cause of short stature in this study was malnutrition (6%) which is similar with other studies ranging from 4.7-9.8%. One study found celiac disease (6.6%) as the most common non-endocrinological cause of short stature. But in this study there was no celiac disease case.

In the current study, genetic syndrome was found in 5% cases, among them 3 cases were Turner syndrome and 2 cases were Down syndrome. One study found genetic syndrome in 5.6% cases. In the present study, comparison of number of male and female patients of different etiologies were done which showed that GHD was significantly more in male patients (p value 0.04) (Table 2). These was similar with other studies.

Comparison of height between male and female patients of different age groups showed that in the age group of 12-18 years female patients were significantly shorter than male patients (p value 0.04) (Table 3). This is because of the fact that during this age linear growth is due to the pubertal growth spurt and male’s pubertal growth spurt is more than the females, so males are significantly taller than females.

In the current study, comparison of height between moderate and severe short stature patients of different etiologies were done which showed that there was no significant difference of height between moderate and severe short stature patients of different etiologies (Table 4).

Comparison of demographic characteristics of patients such as age, sex, residence, socioeconomic class, height and weight between normal variant and pathological short stature patients were done, among them only weight was significant (p value 0.001) (Table 5). Pathological short stature patients were severely underweight and NVSS patients were moderately underweight.

The limitations of this study include, this study was performed in a single centre, small sample size and failure to calculate and plot growth velocity which requires a regular follow-up at six months to twelve months interval, which was not possible in this cross-sectional study. Secondly, it was a hospital-based study where patients of specific diseases were referred. In Bangladesh there is not so much data regarding the etiology of short stature. This study will provide a baseline data which will help the future studies. A large scale, community-based study is needed to better delineate the cause of short stature in general population.

CONCLUSION

FSS and CGD were the leading cause of short stature in children. Endocrinological causes were the most common cause of short stature after normal variant. Among the endocrine cause hypothyroidism was most common followed by growth hormone deficiency. Adolescent females were significantly shorter than males and rural peoples were more likely to be short than urban people.

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