

Evaluation of short stature in paediatric age group in rural medical college

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Abstract

Introduction: Short stature is defined as height below 3rd centile or less than two standard deviations (SDs) below the median height for that age and sex according to the population standard. Approximately 3% children in any population will be short, amongst which almost 50% are having physiological short stature. The most common cause of short stature was found to be Idiopathic short stature.

Materials and Methods: All Patients attending the OPD and IPD in IMCHRC from May 2017 to April 2018 between the age group 2-12 years were included in the study. Height and Weight were plotted on appropriate growth charts and centiles determined. The Patients of short stature were identified by these charts. The detailed history, physical examination and X-ray for bone age of all the short stature cases were done. Thyroid profile, Growth hormone and other necessary and relevant investigations were done in selected cases.

Result: In the present study, Out of 3000 patients 124 were diagnosed as having short stature. This incidence is about 4.2% of the total population. Amongst 124 subjects diagnosed as short stature, 91.9% (114 cases) were having proportionate short stature while only about 8.1% (10 cases) were having disproportionate short stature. In 29.8% (37 cases) were Idiopathic (where no pathology was found).

Conclusion: Idiopathic short stature, including familial short stature and constitutional growth delay is the most common cause of short stature, also chronic systemic illnesses and endocrinal disorders, especially hypothyroidism were found to be on higher side.

Keywords: Short stature, Idiopathic short stature, Chronic systemic illness, Endocrinal disorder.

Introduction

Short stature is defined as height below 3rd centile or less than two standard deviations (SDs) below the median height for that age and sex according to the population standard; or even if the height is within the normal percentiles but growth velocity is consistently below 25th percentile over 6–12 months of observation.^{1,2} Approximately 3% children in any population will be short, amongst which half will be physiological (familial or constitutional) and half will be pathological.

Normal growth requires adequate nutrition along with various hormonal stimuli. The important hormones are: - Growth hormone (GH), Insulin-like growth factor (IGF)-1, Thyroid hormones, Sex steroids and other growth factors.

Previously the causes of Growth retardation in children were in order of frequency: Protein energy malnutrition (PEM), chronic systemic disease including Chronic anemia, Skeletal disorders, Constitutional and Familial short stature, Endocrine disorders, Intrauterine growth retardation, Chromosomal disorders, and miscellaneous. Majority of the short stature cases with endocrine problems had congenital Hypothyroidism

Causes of Short Stature

Proportionate Short Stature

Normal Variants (Idiopathic)

1. Familial
2. Constitutional delay in growth and puberty.

Prenatal Causes

1. Intrauterine growth restriction (placental, infections or teratogens)
2. Genetic disorders (chromosomal and metabolic disorders).

Postnatal Causes

1. Under Nutrition / Malnutrition
2. Chronic systemic illness:-
 - a. CHD,
 - b. Asthma,
 - c. Cerebral Palsy,
 - d. Diabetes Mellitus
 - e. Cystic Fibrosis,
 - f. Malabsorption,
 - g. Celiac Disease,
 - h. Chronic Malaria
 - i. Hemoglobinopathies
 - j. Chronic renal Failure,
 - k. Chronic Liver Disease
- l. Epilepsy
1. Psychosocial short stature (emotional deprivation)
2. Endocrine causes
 - a. Growth hormone deficiency/insensitivity
 - b. Hypothyroidism
 - c. Juvenile diabetes mellitus
 - d. Cushing's syndrome
 - e. Pseudo hypoparathyroidism
 - f. Precocious/delayed puberty.

Disproportionate Short Stature

With Short Limbs

1. Achondroplasia,
2. Hypochondroplasia,
3. Chondrodysplasia punctata,
4. Chondroectodermal dysplasia,
5. Diastrophic dysplasia,
6. Metaphyseal chondrodysplasia
7. Deformities due to osteogenesis imperfect/ Refractory Rickets.

With Short Trunk

1. Spondyloepiphyseal dysplasia,
2. Mucopolipidosis,
3. Mucopolysaccharidosis
4. Caries spine,
5. Hemivertebrae.

Idiopathic Short Stature

| Features | Familial short stature | Constitutional short stature |
|-------------------------------------|-------------------------------------|------------------------------|
| Sex | Both equally affected | More common in boys |
| Length at birth | Normal | Normal |
| Family history | Short stature | Delayed puberty |
| Parents stature | Short(one/both) | Average |
| Height velocity | Normal | Normal |
| Puberty | Normal | Delayed |
| Bone age (ba) and chronical age(ca) | Ba=Ca>height age | Ca>Ba=height age |
| Final height | Short(but normal for target height) | Normal |

Comparison of Short Stature among various causes

| | Familial | Constitutional | Hypothyroidism | G.H deficiency | CSI | Genetic | Skeletal |
|-------------------|--------------|-----------------------|-----------------|-----------------|----------------|-----------------|-------------------|
| Family history | +ve | -ve | +/-ve | -ve(usually) | -ve (usually) | +/-ve | -ve |
| M:F | Equal | >Boys | equal | equal | equal | equal | Equal |
| Length at birth | Below Normal | Normal | Normal | Normal | Normal | low | Low to normal |
| Ht.velocity | Normal | Mid childhood delayed | Delayed | Delayed | Normal/Delayed | Delayed | Normal |
| Ultimate Ht. | short | Normal | Short to Normal | Short | Normal | Short to Normal | Short to Normal |
| puberty | Normal | Normal to Delayed | Delayed | Delayed | Mild Delayed | Delayed | Normal to Delayed |
| H/O infection/CSI | -ve | -ve | +ve | -ve | +ve | -ve | +/- |
| Bone Age | CA=BA | CA=BA | Grossly delayed | Grossly Delayed | CA=BA | CA=BA | CA=BA |
| US:LS | Normal | Normal | Abnormal | Normal | Normal | Normal | Abnormal |
| Other Anamolies | -ve | -ve | +/- ve | +/- ve | +/- ve | +/- ve | +/- ve |
| MR | -ve | -ve | +ve | -ve | +/- ve | +/- ve | +/- ve |
| Thyroid profile | Normal | Normal | TSH increase | Normal | Normal | Normal | Normal |
| G.H | Normal | Normal | Normal | Low | Normal | Normal | Normal |

Prenatal Causes

Intrauterine Growth Restriction: Arrest of the fetal growth in early embryonic life causes reduction in total number of cells, leading to diminished growth potential in postnatal life. Although the majority of small for gestational age (SGA) infants show catch-up growth, about 20% may follow a lifelong pattern of short stature.

Genetic Syndromes: Although classic Turner's syndrome of 45, XO (gonadal dysgenesis) is often correctly diagnosed, it is not always appreciated that any phenotypic female with short stature may have a variant of Turner's syndrome. Thus, a karyotype determination should be performed for

every short girl if no other cause for short stature is found, especially if puberty is delayed. Other syndromes, e.g. Down syndrome, Noonan syndrome, Prader-Willi syndrome, Silver-Russell syndrome, Seckle syndrome, may be associated with short stature.

Endocrine Causes

Hypothyroidism: Untreated severe congenital hypothyroidism results in profound growth failure. With proper treatment, however, children with congenital hypothyroidism reach a height appropriate for their genetic potential.¹⁴ Acquired hypothyroidism during childhood may

also result in growth failure that can range from subtle to profound, depending on the severity and duration of the hypothyroidism. Growth failure may be the most prominent manifestation of hypothyroidism in children.¹⁵ Skeletal maturation is delayed in those children in whom the hypothyroidism was sufficient to retard growth, with the BA at diagnosis corresponding to the age at onset of the hypothyroidism.¹⁵ Body proportion is immature, with an increased upper-to-lower body segment ratio.

In those children with severe growth failure, treatment with thyroid hormone results in rapid catch-up growth with marked skeletal maturation. In cases of prolonged severe hypothyroidism, the advancement of skeletal maturation with treatment can exceed the growth acceleration, resulting in a compromised adult height.¹⁵

Growth Hormone Deficiency: Classic GH deficiency, either alone or in conjunction with other pituitary hormone deficiencies, might also have a characteristic profile. Male patients may have a small penis (microphallus) and if in the neonatal period, hypoglycemia. The neonate with a microphallus should be tested for hypopituitarism initially, whereas the older child should be evaluated if there is evidence of growth failure. Affected GH-deficient female patients do not have abnormalities of genital development; however, because hypoglycemia is often a component of hypopituitarism, it is still a clue. Children with classic GH deficiency are often said to have a pudgy, cherubic appearance, in part because height is usually more affected than weight and the Deficiency is associated with a characteristic distribution of fat in the face and abdomen

Type-1 Diabetes Mellitus: Although weight loss may occur immediately before the onset of clinically apparent insulin-dependent diabetes mellitus (IDDM), children with new-onset diabetes are frequently taller than their peer group, possibly because GH and insulin levels are increased during the preclinical evolution of the disease.⁷⁻⁹ Most children with IDDM, even those with marginal control,¹⁰ grow quite normally, especially in prepubertal years, although growth velocity may decrease during puberty.¹¹ However, growth failure can occur in diabetic children with long-standing poor glycemic control.^{12,13}

Rickets: In the past, Hypovitaminosis-D was a major cause of short stature and was often associated with other causes of growth failure, such as Malnutrition, prematurity, Malabsorption, Hepatic disease, or Chronic renal failure (CRF). Early detection and treatment of Rickets help to improve the sign of rickets.

Psychosocial Short Stature: An extreme form of failure to thrive is termed psychosocial dwarfism or emotional deprivation dwarfism.¹⁶⁻¹⁸ Most cases of failure to thrive can be traced back to a poor home environment and inadequate parenting, with improved weight gain and growth upon removal of the infant from the dysfunctional home.

Skeletal Dysplasias: The osteochondro dysplasias encompass a heterogeneous group of disorders characterized by intrinsic abnormalities of cartilage and bone. The family history is critical, although many cases are caused by de novo mutations, and this is generally the case in autosomal-

dominant achondrodysplasia and hypochondrodysplasia. Measurement of body proportions should include arm span, sitting height, upper and lower body segments, and head circumference.

Comparison with Child's Own Genetic Potential

- Mid-parental height for boys = $(\text{Mother's height} + \text{father's height})/2 + 6.5 \text{ cm} \pm 8 \text{ cm}$
- Mid-parental height for girls = $(\text{Mother's height} + \text{father's height})/2 - 6.5 \text{ cm} \pm 8 \text{ cm}$.

The target height is plotted on the growth chart at 18-20yrs of age. This gives the estimated target height for the child, and if the child is falling within the target height, the cause could be genetic or constitutional. Otherwise, it is considered abnormal.

Materials and Methods

All Patients attending the OPD and IPD in IMCHRC from May 2017 to April 2018 between the age group 2-12 years were included in the study. Height and Weight were plotted on appropriate growth charts and centiles determined. The Patients of short stature were identified by these charts. The detailed history, physical examination and X-ray for bone age of all the short stature cases were done. Thyroid profile, Growth hormone and other necessary and relevant investigations were done in selected cases. Parental height was noted and midparental height was plotted in the graph.

Projected Height: The projected height for a child older than two years is determined by extrapolating the child's growth along the current channel to the 18- to 20-year mark. If the child's bone age is delayed or advanced, then the projected height should be plotted based on the bone age rather than the chronologic age.

Study: Cross sectional study

Inclusion Criteria: All the cases who attended the OPD in the given time period.

Exclusion Criteria: Cases who refused to give consent for further investigation.

Outcome Measures: Percentage of patients with short stature was calculated, as well as etiological factors of short stature were evaluated.

Result

This study was done over a period of 1 year from May2015 to April 2016. Around 3000 patients coming to OPD and IPD screened for short stature. Out of 3000 patients 124 were diagnosed as having short stature. This incidence is about 4.2% of the total population.

Amongst 124 subjects diagnosed as short stature, 91.9% (114 cases) were having proportionate short stature while only about 8.1% (10 cases) were having disproportionate short stature. In 29.8% (37 cases) were Idiopathic (where no pathology was found).

The frequency of different causes of short stature is shown in table no.1.

In our study females 51.6% (64 cases) were found to be affected more than males 48.4% (60 cases). Ratio of Male:Female is 1:1.1

The most common causes of short stature was found to be Idiopathic short stature (including familial and constitutional delay) 29.8% (37cases). While chronic systemic illness were found to be the second most common cause of short stature 25.8% (32 cases).

Out of 124 patients, 14 patients (11.3%) were due to endocrinal causes. Amongst them, 07 cases (53.3%) were due to Hypothyroidism, where males were more affected 5 cases out of 7(62.5%) than female 3 cases out of 7(37.5%), while only 3 cases of Growth hormone deficiency were found (2 males and 1 female).

Amongst the chronic systemic illness as the cause of short stature 32 cases /124 (25.8%) were found. In this group majority of the cases 16/32 were due to Hemoglobinopathies, the rest of them were due to Celiac disease (2 cases), CHD (6 cases), chronic Malaria (2 cases) and Cerebral palsy (5cases). The next important causes of short stature was nutritional disorder (chronic malnutrition) which was 16.9% (21/124) amongst which females were more affected.

Table 1: Age distribution of cases studied with short stature

| Age Group (years) | No. of cases | % of cases |
|-------------------|--------------|--------------|
| 2 – 5 | 48 | 38.7 |
| 6 – 9 | 56 | 45.2 |
| 10 – 13 | 17 | 13.7 |
| 14 | 3 | 2.4 |
| Total | 124 | 100.0 |

Values are n (% of cases). Chi-Square value = 61.097, P-value = 0.001***. ***P-value<0.001.

Of 124 cases studied, 48 cases (38.7%) had their age between 2 – 5 years, 56 cases (45.2%) had their age between 6 – 9 years, 17 cases (13.7%) had their age between 10 – 13 years and 3 cases (2.4%) were of 14 years old. On one-sample Chi-Square test, the distribution of prevalence of short stature differs across various age groups (P-value<0.001).

The mean ± Sd of age of the entire study group was 6.5 ± 2.8 years. The minimum – maximum age range among the cases studied was 2–14 years.

Table 2: Sex distribution of cases studied with short stature

| Sex | No. of cases | % of cases |
|--------------|--------------|--------------|
| Male | 60 | 48.4 |
| Female | 64 | 51.6 |
| Total | 124 | 100.0 |

Values are n (% of cases). Chi-Square value = 0.129, P-value = 0.719^{NS}. NS-Non Significant.

Of 124 cases studied, 60 cases (48.4%) were males and 64 cases (51.6%) were females. The male to female sex ratio of the cases studied in the entire study group was 0.94: 1.00. On one-sample Chi-Square test, the distribution of prevalence of short stature did not differ significantly

between male and female group of cases studied (P-value>0.05).

Table 3: Distribution of etiology in the cases studied with short stature

| Etiology | No. of cases | % of cases |
|--------------|--------------|--------------|
| Idiopathic | 37 | 29.8 |
| CSI | 32 | 25.8 |
| Nutritional | 21 | 16.9 |
| Endocrine | 14 | 11.3 |
| Genetic | 10 | 8.1 |
| Skeletal | 10 | 8.1 |
| Total | 124 | 100.0 |

Values are n (% of cases). Chi-Square value = 32.290, P-value = 0.001***. ***P-value<0.001.

Of 124 cases studied, idiopathic was the most common etiology which was present in 37 cases (29.8%), 32 cases (25.8%) had CSI, 21 cases (16.9%) had nutritional etiology, 14 cases (11.3%) had endocrine etiology, 10 cases (8.1%) had genetic etiology and 10 cases (8.1%) had skeletal etiology. On one-sample Chi-Square test, the distribution of prevalence of short stature differs significantly various etiological factors (P-value<0.001).

Table 4: Distribution of cases with short stature according to proportionate and disproportionata stature

| Stature type | No. of cases | % of cases |
|------------------|--------------|--------------|
| Proportionate | 114 | 91.9 |
| Disproportionate | 10 | 8.1 |
| Total | 124 | 100.0 |

Values are n (% of cases). Chi-Square value = 87.226, P-value = 0.001***. ***P-value<0.001.

Of 124 cases studied, 114 cases (91.9%) had proportionate short stature and 10 cases (8.1%) had disproportionata short stature. On one-sample Chi-Square test, the distribution of prevalence of short stature differs significantly between cases with proportionate and disproportionata stature (P-value<0.001).

Table 5: Percentage of hemoglobinopathy cases in CSI group with short stature.

| Hemoglobinopathy | No. of cases | % of cases |
|------------------|--------------|--------------|
| Present | 12 | 37.5 |
| Absent | 20 | 62.5 |
| Total | 32 | 100.0 |

Values are n (% of cases). Chi-Square value = 2.000, P-value = 0.157^{NS}. NS-Statistically Non-Significant.

Of 32 cases studied with CSI, 12 cases (37.5%) had hemoglobinopathy and 20 cases (62.5%) did not have it. On one-sample Chi-Square test, the distribution of prevalence of short stature did not differ significantly between cases with hemoglobinopathy and cases without hemoglobinopathy (P-value>0.05).

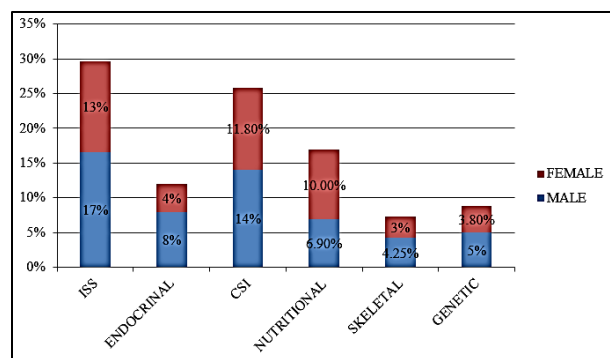


Fig. 1

Discussion

Comparison of different causes of short stature in different studies

| | B.J.W. Hospital Mumbai | Pakistan | IMCHRC. Indore |
|-------------|------------------------|-----------|----------------|
| ISS | 15(10.7%) | 82(38.3%) | 37(29.8%) |
| CSI | 23(16.4%) | 26(12%) | 32(25.8%) |
| Endo | 15(10.7%) | 33(15.9%) | 14(11.3%) |
| Nutritional | 42(30%) | 24(9.8) | 21(16.9%) |
| Skeletal | 16(11.4%) | 12(5.6%) | 10(8.1%) |
| Genetic | | | 10(8.1%) |

| | Age | Weight | Height | MAC | H.C |
|--------|------|--------|--------|------|-------|
| Mean | 6.61 | 16.21 | 103.55 | 15.8 | 48.97 |
| SD(±2) | 2.53 | 4.37 | 18.34 | 7.98 | 3.91 |

As growth is an important and essential biological feature of childhood. Any cause leading to delayed growth and ultimately short stature, is a cause of concern for parents and the child. It is found that short stature is the reflection of many hidden diseases.

Short stature has been studied worldwide, but different studies showed variations in the prevalence of major causes of short stature, reason being different (geographical, racial, genetic, environmental or, socioeconomic). Therefore, problem of short stature is important and requires early diagnosis, determination of causes and early intervention.

In the present study, Out of 3000 patients 124 were diagnosed as having short stature. This incidence is about 4.2% of the total population.

Idiopathic short stature, including familial short stature and constitutional growth delay is the most common causes of short stature, also chronic systemic illnesses and endocrinal disorders, especially hypothyroidism were found to be on higher side as compared to the studies done in Pakistan and Iran.

Out of total no. of patients (3000) coming to OPD and IPD, 124 patients were found to have short stature (n=124) ie-Height below 3rd percentile or Ht. <-2SD for that age, sex and group of population.

In our study, out of 124 patients, 60 were male children and 64 were females. The difference was not much

significant, while in other studies males outnumbered females significantly.

It has been noticed that ISS (FSS+CGD) was the commonly causes for Short stature out of 124 children, 37 children (29.8%) had short stature which was familial or without any obvious cause. This was in agreement with other studies.

Our centre is a rural medical college, hospital providing tertiary care. Due to this many patients, coming from rural population, having chronic systemic illness are hospitalised. Due to this reason, children with chronic disease were found to be more in number leading to short stature. Out of 124 children,32 were amongst this group(25.8%).This reading was very high as compared to the studies done in Iran and Pakistan where it was 10-12%. Amongst the 32 patients with chronic systemic illness, 16 patient (12.9% of the total patients and almost 50% of this group patients) were of Hemoglobinopathies leading to short stature. This is alarming finding as compared to the other studies. The reason being that, there is a tribal area near this centre, from where many patients are coming to this centre for treatment. Tribal community is known to have genetic predisposition for hemoglobinopathies which are leading to short stature. The other causes among these group were CHD-6/32, Chronic Malaria 2/32, cerebral palsy 6/32 and 2 cases of celiac disease. These patients though have short stature, the bone age is not grossly delayed as compared to the endocrinal causes.

The next major cause of short stature is the endocrinal cause. There were 15 out of124 patients with endocrinal disorders leading to short stature which comes to 12.1% of the total patients, which is less compared to other studies done in Pakistan where it was 15.9%

In our study the cases of congenital Hypothyroidism leading to short stature were more than the GHD patients. Patients with hypothyroidism were 6.4% (7 cases) of total 124 patients while 3.2% (4 cases) of patients had DM and only 2.41% (3 cases) of patients were detected with GHD.

Amongst these endocrinal causes hypothyroidism was the leading cause. 7 cases showed gross delay in bone age and TSH was higher while in 3 cases of GHD, 2 patients had Pituitary hypoplasia seen in MRI (Brain) and 1 patient had a CNS tumor (crainophayngioma), which was operated and the patient was put on Growth hormone. In the other 2 cases, the 2 consecutive provocative tests showed GH conc. of <10^ug./l. Also of these 3 patients, 2 were boys and 1 was girl with short stature.

4 patients of DM were treated at this centre who also had short stature but bone age was not grossly delayed.

Our study also showed nutritional causes to be an important leading to short stature. Previously due to low awareness and education level of people in rural area, poor socioeconomic status or poor medical help, the no. of patients of SAM were more leading to stunting and wasting. In our study there were 21/124 patients who had malnutrition leading to short stature (16.9% of the total). They had delayed bone age and height was <-3SD.

Chromosomal disorders are also known to cause short stature. In our study also we had 14 cases of chromosomal disorder who were almost 8.87% of the total cases almost in agreement with other studies.

Amongst these patients 6 patients of down syndrome were the common ones amongst them. Being a medical college hospital many syndromic patients are referred for multidisciplinary care.

Skeletal causes of short stature were least among the causes of short stature. There were 9 cases (7.25%) of skeletal disorder which lead to disproportionate short stature, which was similar to other studies done. Out of 9 cases- 2 patient of rickets, 2 case of Chondroplasia and 1 each of TB spine, Achondroplasia, Perth's disease, fluorosis.

Conclusion

Constitutional growth delay and Familial Short stature which are still the leading causes of short stature in children. But chronic systemic illness are on the rise, which can be treated if diagnosed early and treated promptly. Patient with cong. Hypothyroidism can be diagnosed earlier by Neonatal screening programme, and the incidence can be brought down, while genetic counselling may help to reduce chromosomal disorders and hemoglobinopathies, which will decrease its incidence and ultimately also short stature.

Conflict of Interest: Nil.

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