Introduction

Shortened height that is considerably shorter than the average height for a certain age, racial group, gender, or family is termed as short stature. Short stature may or may not be the result of a certain medical condition. The causes that may lead to the development of short stature can be classified into different categories: chronic diseases, familial short stature, and constitutional short stature.[5] The skeletal dysplasia is one of the causes of short stature, which are a large group of disorders characterized by short stature (mainly disproportionate) and malformations of bone and cartilage.[6] The clinical severity ranges from mild short stature to lethal forms.

Common clinical presentations of skeletal dysplasia are growth retardation, whether proportionate or disproportionate, large or small head, short arm and trunk, anomalies of the hands and feet, chest anomalies such as pear-shaped chest and narrow thorax, and recurrent fracture, i.e., osteogenesis imperfecta.[7,8]

Not many studies have been performed in the patients suffering from short stature for the evidence of skeletal dysplasia. Skeletal dysplasia among the general population has not been studied very

Abstract

Objective: To determine the frequency of skeletal dysplasia in children with short stature presenting to the endocrine clinic of a tertiary care hospital. Methods: This descriptive cross-sectional study was performed in the Outpatient Department of Endocrinology of National Institute of Child Health, Karachi, for 6 months of duration. A total of 200 children coming to endocrine OPD of NICH of either gender, having the age less than 14 years and height more than -2.5 SD below the mean (<3rd percentile), and growth failure (<4 cm/yr) were enrolled. A complete general physical examination including height, weight, fronto-occipital circumference (FOC), arm span, and U/L (upper/lower) segment ratio (using SI units and SDS) was performed. Results: Out of 200 children with short stature, skeletal dysplasia was diagnosed in 23 (11.5%) children with the mean age of 4.7 (±3.7) years. Proportion of skeletal dysplasia among short stature was high in females. Out of 75 girls, skeletal dysplasia was diagnosed in 10 (13.3%) girls, while out of 125 boys, skeletal dysplasia was diagnosed in 13 (10.4%) boys, whereas when we see proportion among skeletal dysplasia out of 23 children of skeletal dysplasia, 13 (56.5%) were boys, while 10 (43.5%) were girls. Conclusion: In this study, skeletal dysplasia was diagnosed in 11.5% children with short stature with the mean age of 4.7 years. It is concluded that the frequency of skeletal dysplasia in this institute is fairly high.

Keywords: FOC, osteochondrodysplasias, pediatric, short stature, skeletal dysplasia

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extensively as well, so there is a possibility of underestimation of skeletal dysplasia among short-stature people. Skeletal dysplasia knowledge has seen improvements in the literature in the recent past. Different genetic mechanisms that underlie the development of skeletal dysplasia have been identified, and multiple patterns of skeletal dysplasia have also been described. Two genes named as SHOX (short-stature homeobox) and FGFR3 (fibroblast growth factor receptor 3) are known to be the responsible factors to the emergence of phenotypic variability to isolated short stature in the form of dyschondrosteosis and hypochondroplasia, respectively. Therefore, the occurrence of skeletal dysplasia is very much underrated in people with idiopathic short stature attributed to short gestational age. Our hypothesis in this study is that the prevalence of skeletal dysplasia among children with short stature is much more common than the previous data have suggested. With the help of this study, we are able to identify the burden as well as the trend of skeletal dysplasia in our population, which can be useful in planning strategies of these patients regarding their social benefits and genetic counseling.

Material and Methods

This descriptive cross-sectional study was conducted at National Institute of Child Health (NICH), Karachi. The duration of study was 6 months, from September 2016 to February 2017. Children referred to the Outpatient Department of Endocrinology with height less than 2 SDs or below third percentile for their gender and age belonging to any gender and age less than 14 years were included in this study. Similarly, children with other findings such as kyphoscoliosis and contractures were also part of the study. Exclusion was based upon the following criteria: patient on regular blood transfusion for beta thalassemia, and children with renal impairment or undergoing antidiabetic therapy for type 1 diabetes mellitus. Sample size was calculated using the reference study conducted by Shiva S et al. Sample size calculation was performed using the non-probability consecutive type of sampling technique.

Ethical approval was obtained from the hospital ethics committee. All patients were informed about the mechanism and purpose of the study, and inclusion was based on the informed consent of the patient or his/her guardian. At presentation to the outpatient department, a detailed history session was conducted. History included prenatal history, history of the childhood, birth, whether or not twin pregnancy, infections occurred during gestation, gestational age, history of any birth-related complications such as birth trauma or birth asphyxia, any congenital deformity, history of developmental milestones, history of children’s school performance, and history of breast feeding. Moreover, other comorbidities were also ruled out during history such as CNS neoplasia, chronic illness, repeated infections, drug history, and any surgical procedure.

A complete general physical examination including height, weight, fronto-occipital circumference (FOC), arm span, and U/L (upper/lower) segment ratio (using SI units and SDS) was performed. Measurement of height was taken by making the child’s head in Frankfurt plane with heel, buttocks, shoulder, and occiput touching the vertical board. To measure the accurate height, upward pressure was applied on the mastoid. The measurements taken were plotted on the Tanner and Davies chart. Percentile position with respect to age and standard deviation scores was used to express the height of each patient. Other measurements included arm span, upper and lower body segments, and sitting height.

Children having disproportionate upper/lower (U/L) segment ratio more than or less than normal, FOC more than or less than 2 SDs, having dysmorphic features, and chest, back, or limbs deformities were clinically separated for radiological evaluation by skeletal survey. Children >6 months of age and infantogram in children <6 months of age were separated to confirm the diagnosis of skeletal dysplasia. Other biochemical investigations were also conducted where there was a need. This information was collected and entered into the pro forma.

Data were analyzed using SPSS version 25.0. Frequency and percentage were calculated for qualitative/categorical variables including gender, socioeconomic status, and skeletal dysplasia.

Mean, standard deviation, and 95% confidence interval were computed for quantitative data like age, height, and weight. Data were stratified based on sex, age, and socioeconomic status to see the effect of these on outcome, and Chi-square test was applied to compare proportion of gender, age-groups, and socioeconomic status between children with and without skeletal dysplasia. For quantitative variables, Mann–Whitney U test was applied to compare median weight and height between children with and without skeletal dysplasia.

Results

A total of 200 children with short stature were included in this study. Age distribution of the patients is presented in [Figure 1]. The mean age of the patients was 8.34 ± 3.98 years (95% CI: 7.78 to 8.89); similarly, mean height and weight of the patients are also presented in Table 1. Out of 200 cases, 125 were male and 75 were female. The male-to-female ratio was 1.7:1 [Figure 2]. The majority of children (98 (49%)) presented belonged to poor families (monthly income less than Rs. 10,000), while 81 (40.5%) families earned 10,000–50,000 monthly and 21 (10.5%) families earned >50,000 per month [Figure 3]. Frequency of skeletal dysplasia in children with short stature

![Table 1: Demographic characteristics of the study patients (n=200)](image-url)
was observed in 23 cases. With respect to gender, the rate of skeletal dysplasia was slightly high in females among children with short stature, i.e., 10/75 (13.3%) girls and 13/125 (10.4%) boys, and there was no statistically significant difference between gender (13.3% vs. 10.4% \( P = 0.529 \)), whereas out of 23 children of skeletal dysplasia, 13 (56.5%) were boys, while 10 (43.5%) were girls.

Skeletal dysplasia was 28.1% (16/57) in 1 to 5 years of age, 7.1% (5/70) in 6 to 10 years of age, and 2.7% (2/73) in above 10 years of age. The rate of skeletal dysplasia is significantly high in below 6 years of age compared to that in above 5 years of age (\( p = 0.0005 \)), showing early presentation of children. The frequency of skeletal dysplasia was not statistically significant among socioeconomic groups (\( p = 0.071 \)). The mean age ± SD of children with skeletal dysplasia was 4.7 ± 3.7 years. The mean height ± SD of children with skeletal dysplasia was 80 ± 20.5 cm, while the mean height of the children without skeletal dysplasia was 107.56 ± 19.9 cm, which shows that the mean height of children was significantly low in those children who had skeletal dysplasia. The mean weight of children with skeletal dysplasia was 10.4 ± 5.49 kg, and the mean weight was significantly low in children with skeletal dysplasia.

The types of skeletal dysplasia are given in Table 2. Achondroplasia was the most common type of skeletal dysplasia found in 9 (39.1%) children, and the second common type was mucopolysaccharidosis, i.e., 7 (30.4%).

### Discussion

The results of this study have shown that skeletal dysplasia had significantly high frequency (11.5%) among children with short stature. This was not possible to diagnose in the periphery and children presented in the endocrine clinic because of insufficient growth hormone. Skeletal dysplasia has very subtle clinical features, and these are very commonly missed by the physicians. Moreover, radiological diagnosis and findings of skeletal dysplasia are also very difficult to apprehend and require expert clinical skills. It can be suggested that every child presenting with growth anomaly, arm span, and short or large hands and feet should be examined clinically. Before a child is classified as an idiopathic short-stature patient, an X-ray should be performed in case no other etiology is certain. Moreover, consideration should be given in case one of the parents has a height less than -2 SDs, as it has been shown that the frequency of skeletal dysplasia increases in such scenarios of idiopathic short stature. In this study, however, those patients were included who had a final height of less than -2.5 SDs or height more than 2.5, but below the target height, skeletal dysplasia diagnosed in a close relative or clinical features of skeletal dysplasia are found. In this study, a major portion of the patients had metaphyseal or epiphyseal defect, isolated lumbar spinal stenosis, small epiphysis, or short neck of femur, and all these features did not meet the criteria to be considered as skeletal dysplasia.

The incidence of congenital malformations was very high in this part of the world. A high rate of consanguinity in our area is one of the factors for this high occurrence of skeletal dysplasia.

Skeletal dysplasias involving primarily the spine (e.g., spondyloepiphyseal) often are associated with a decreased U/L ratio for age; those involving especially the long bones (e.g., achondroplasia) often are associated with an increased U/L.

| Types                          | Total | Male | Female |
|-------------------------------|-------|------|--------|
| Achondroplasia                | 9     | 6    | 3      |
| Mucopolysaccharidosis         | 7     | 5    | 2      |
| Pseudoachondroplasia          | 2     | 0    | 2      |
| Osteopetrosis                 | 2     | 1    | 1      |
| Osteogenesis imperfecta       | 1     | 0    | 1      |
| Chondrodysplasia              | 1     | 1    | 0      |
| Spondyloepiphyseal dysplasia  | 1     | 0    | 1      |
ratio. This hospital-based study was conducted in children with short stature. The mean (±SD) age of children was 8.3 (±3.9) years. Gender distribution shows male predominance, i.e., male/female = 1.5:1. Other independent reviews on growth retardation revealed that boys outnumbered girls by 2.5:1[11] and 2.7:1[12].

Out of 200 children with short stature, skeletal dysplasia was diagnosed in 11.5% children with the mean age of 4.7 (±3.7) years. This percentage is very high compared to that of other studies. Skeletal dysplasia has been estimated to be 4.9% in one of the studies conducted in Iran (Shiva S N. A., Etiology of Short Stature in East Azerbaijan, Iran, 2009). The proportion of skeletal dysplasia was high in males. Out of 23 children of skeletal dysplasia, 13 (56.5%) were boys, while 10 (43.5%) were girls. Iranian study reported that skeletal dysplasia in boys was 4%, and in girls it was 4.5%. The mean height of children with skeletal dysplasia was 80 ± 20.5 cm (Min - Max = 51 – 122 cm), while the mean weight of children with skeletal dysplasia was 10.4 ± 5.6 kg (Min - Max = 4 – 28 kg). Achondroplasia was the most common type of skeletal dysplasia found in 9 (39.1%) children.

Identification of skeletal dysplasia is highly beneficial among the short-stature patients. These benefits include orthopedic surveillance required in certain types of skeletal dysplasia, skeletal dysplasia can reduce targeted final height, and also skeletal dysplasia can affect the pubertal growth spurt. Therapeutic implications can also be made on the basis of identification of skeletal dysplasia. Thus, many types of generalized skeletal dysplasias can lead to the development of short stature in children. To manage these types of patients, a multidisciplinary approach is required which includes seeking help from other allied health departments to work with the patients and their parents to make different amendments in work and home appliances as per their needs. This ultimately will result in autonomy of the patients and their parents and will enable them to reach their potential. Education of healthcare personnel regarding this condition should be provided so that patients can live their lives without having the fear of discrimination and stigma, as it has been known to be attached to these dwarfish anomalies.

**Conclusion**

In this study, skeletal dysplasia was diagnosed in 11.5% children with short stature with the mean age of 4.7 years. It is concluded that the frequency of skeletal dysplasias in this institute is fairly high. Detection of a large number of cases in a short period with a high proportion of skeletal dysplasias, male preponderance, and low mean age are the important highlights of this study.

**Data availability statement**

Any additional data can be requested from the corresponding author.

**Ethical approval**

Ethical considerations were fulfilled before the commencement of the study.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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