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Prevalence of Growth Hormone Deficiency in Children with Short Stature

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ABSTRACT— The study was conducted to evaluate the prevalence of growth hormone deficiency in children with isolated short stature. An observational study comprised (110) short children aged (3-15) year with current height > 2SD below the mean of comparable age and gender, who do not have any symptoms related to diseases that affect growth or specific dysmorphic features of genetic syndromes. Evaluation of children included detailed personal and family history, physical examination, growth analysis, radiological (bone age), laboratory tests, and growth hormone (GH) stimulation test. GH concentration less than 10 ng/ml has been used to support the diagnosis. Low level of GH was found in (59) children, accounted for (53.6%). Males outnumbered females (39, 20) respectively with male to female ratio 1.95:1. The study showed late referral of children, 34% had first referral after the age of 10. Bone age was shown delayed for chronologic age in 66%. Celiac disease and hypothyroidism did not account for a considerable percentage of short stature in the current study (1.8, 0.9) respectively. Growth hormone deficiency is not uncommon in children with short stature. There is delay of referral of short-statured children for the diagnosis and treatment, awareness of growth monitoring helps improves referrals. Early initiation of therapy with GH may aid in achieving final adult height and lower the psychologic impacts. Further researches are recommended to detect IGF-1 and to study consequences of GHD and the safety of therapy.

KEYWORDS: Bone age, hormone deficiency, hypothyroidism.

1. Introduction

Growth is a good indicator of a child's health. [1] Growth deviations may be expressed as standard deviation (SD) from the normal population mean for children of comparable age and sex, [2] children classified as short-statured are those with heights >2 SD below the mean. Short stature (SS) is a common pediatric concern. It results from an intricate process 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. [3] Variants of normal growth include constitutional growth delay and familial short stature. Pathological causes include endocrine diseases, genetic conditions like Achondroplagia, Turner and Noonan syndromes and chronic diseases. Children in whom no specific cause identified, diagnosed as idiopathic short stature.

Growth hormone deficiency (GHD) is an important and treatable endocrine cause of short stature, the prevalence of GHD in children with SS ranges from 2.8% to 69%. [4,5,6] Knowing the prevalence would greatly help in streamlining the screening of children with GHD. [4] The diagnosis of GHD in childhood is challenging, in large part due to the lack of a true gold standard and the relatively poor performance of available diagnostic testing. [7] Early initiation of growth hormone can often boost growth in short-statured children with hormone deficiency, therefore the diagnosis of GHD should be done as soon as possible. This

study was carried out to know the prevalence of growth hormone deficiency in short- statured children referred to the Pediatric Endocrine Clinic.

2. Methods

An observational study was conducted to study the prevalence of growth hormone deficiency in short-statured children referred to the Pediatric Endocrine Clinic in Almawani teaching hospital from October 2015 to October 2017. The study population comprised (110) short children with current height > 2SD below the mean of comparable age and gender, aged (3-15) year who do not have any symptoms related to diseases that affect growth or specific dysmorphic features of genetic syndromes. Children with identified causes of SS excluded in the study. Evaluation of children included detailed personal and family history, physical examination, growth analysis, radiological (bone age), laboratory tests, and growth hormone stimulation test was performed. Growth hormone concentration less than 10 ng/ml considered as low. In the current study, oral Clonidine was given at a dose of 0.15 mg/m2, two blood samples were taken at 0 and 90 minutes to detect growth hormone level.

3. Results

One hundred and ten short- statured children were involved in the study, (60) were males (54.5%) and (50) females (45.5%) with male to female ratio: 1.2:1 as shown in table 1. Low level of GH found in (59) children, accounted for (53.6%). Males outnumbered females (39, 20) respectively with male to female ratio 1.95:1 (table2). Figure (1) shows the age of referral of short children with GHD. Figure 2 represents the sex distribution of short-statured children. Among 110 short children, bone age found delayed in 73 (66.3%) as presented in table3. Screening for celiac disease in the study population was positive in two patients constituted 1.8 %, while hypothyroidism detected in only one child (0.9%).

Table 1. Age and sex distribution of the study population

Age (years)	Male	Female	Total
< 5	23 (38.3%)	17 (34%)	40 (36.3%)
5-10	15 (25%)	19 (38%)	34 (30.9%)
>10	22 (36.6%)	14 (28%)	36 (32.7%)
Total	60 (100%)	50 (100%)	110 (100%)

Table 2: Age and sex distribution of children with deficient GH

Age (years)	Male	Female	Total
< 5	9 (23%)	3 (15%)	12 (20.3%)
5-10	17 (43.5%)	10 (50%)	27 (45.7%)
> 10	13 (33.3%)	7 (35%)	20 (33.8%)
Total	39 (100%)	20 (100%)	59 (100%)

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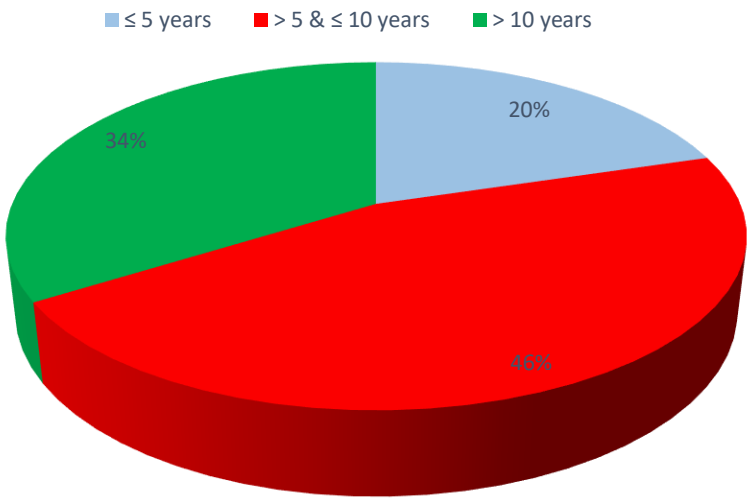

Figure 1: Age of referral of short- statured children with GHD

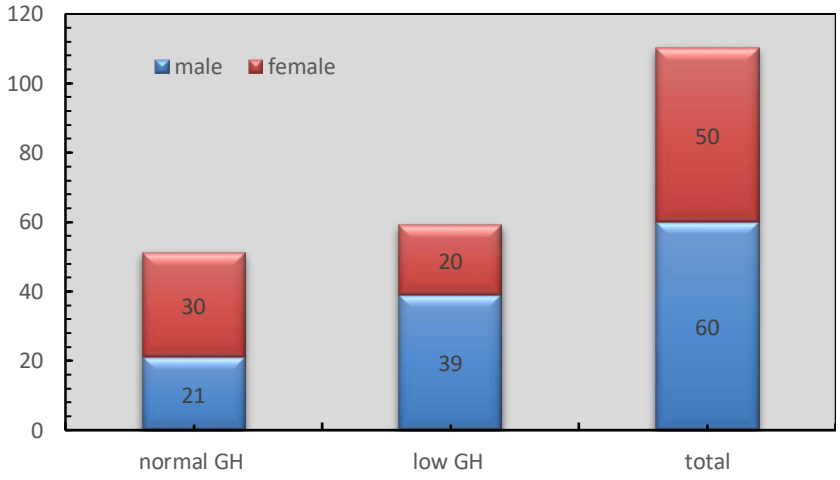

Figure 2: Sex distribution of short-statured children

Table 3. Bone age in the study population

Bone age	Short children	GH=normal	GH=low
Normal	37 (33.63%)	17 (33.33%)	20 (33.89%)
Delayed	73 (66.36 %)	34 (66.66%)	39 (66.10%)
Total	110 (100%)	51 (100%)	59 (100%)

4. Discussion

The aim of the current study was to evaluate the prevalence of GH in children with isolated short stature

with heights > 2SD below the mean of comparable age and gender. Growth hormone is an important treatable cause of short stature, treatment with GH should be started as soon as hormone deficiency is diagnosed. Delayed treatment decreases the chance of achieving final adult height. Literature review revealed increasing number of studies and reviews in recent years dealing with short stature and GHD [8,9,10,11] In the current study including 110 children, low growth hormone responses to provocative stimuli was found in 59 children (53.6%), this relatively high result may be because of the relatively small size of the study population which involved only children referred to the specialized endocrine clinic. Hussein A. et al, in a study done in Egypt, reported that 11.8% of short-statured children had GHD. [12] In a similar study in Korea, Song KC et al found GHD in (38.9%) of pathologic short stature. [13]

More male short children referred to the endocrine clinic than short females. For children with GHD male to female ratio was 1.95:1. This is in agreement with a study in Pakistan by Lashari SK et al in which boys outnumbered girls with ratio of 2.7: 1 [14] Parents may think that short girls are more socially accepted than short boys. The study showed late referral of children, a significant number with deficient GHD (34%) had first referral after the age of 10. In the primary health care centers, regular measurements of growth parameters done when the child brought for immunization. After 2 years of age, unfortunately pediatricians and primary health care physicians focus on child's body weight although growth charts are readily available for height measurement. Further, parents' concerns about their child's short height increase as the child reaching adolescence. At this late age of referral, the growth potential diminished and the response to GH therapy becomes limited, hence awareness of growth monitoring would help improve the referral for the diagnosis and treatment of children with short stature and GHD. Bone age delayed for chronological age detected in 66.10% of GH- deficient children. Celiac disease did not account for a considerable percentage of the study subjects (1.8%). In a study done in Saudi Arabia, Al- Jurayyan et al reported celiac disease in 10% of non-genetic cases of short stature. [15] Hypothyroidism was detected in only one child (0.9%). Short-statured children may exhibit psychological impacts; they may have depression or low self-esteem especially those who are very self-conscious about their height; psychological benefits will be greater with early initiation of GH treatment.

5. Conclusion and Recommendation

- Growth hormone deficiency is not uncommon in children with short stature.
- There is a delay of referral for short stature and GH diagnosis and treatment.
- Awareness of growth monitoring helps improve referrals of children.
- Early initiation of therapy with GH may aid in achieving final adult height and lower the psychologic impact.
- Further researches are recommended to measure IGF1and to study consequences of GHD and safety of therapy.

6. Author Contribution

All authors have contributed. Supervision of the work and submission done by Dr. Miami K. Yousif.

7. Conflict of interest

None declared

8. Funding

None

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