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ORIGINAL ARTICLE

Etiological Classification of Short Stature in Children over 5 Years Old

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Abstract

Background: Short stature is a common problem in childhood, which may be a normal variant of growth or the result of pathologic conditions. Determination of the etiological factors would lead to more appropriate assessment and clinical approach for patients.

Objective: The aim of this study is to describe the etiologies of short stature among children.

Materials and Methods: An Observational Cross-Sectional study was conducted in 92 children older than 5 years with short stature. They are selected from Pediatric Endocrinology Clinic, Tishreen University Hospital between September 2020 and September 2021. Weight and height were measured and target height was calculated. Samples of blood, urine, stool were taken and appropriate investigations were performed.

Results: A total of 92 children, 42 males (45.7%) and 50 females (54.3%) with mean age 8.8 ± 2.7 years were included in the study. Out of the 92 children, 57(62%) were normal variants including familial short stature (44.6%) and constitutional growth delay (17.4%). Endocrine causes were founded in 14 cases (15.2%) which included hypothyroidism (8.7%), growth hormone deficiency GHD (4.3%) and vitamin D-resistant rickets (2.2%). Other causes of short stature were as follows: infection with Helicobacter pylori (9.8%), Celiac disease (6.5%), and malnutrition (4.3%).

Keywords

Short stature, Endocrine, Constitutional growth delay

Introduction

Growth is a complex biologic process which is affected by multiple factors including: genetic, hormonal, nutritional, and psychosocial factors, and the relative significance of them might vary in different populations [1,2].

Short stature is defined as a child whose height is 2 standard deviations (SD) or more below the mean for the same sex and chronologic age. Approximately, 3% of the population in the world is short [3].

Short stature may be either a variant of normal growth or the first manifestation of wide variety of underlying pathologic conditions which require early diagnosis and treatment [4]. Variants of normal growth include familial short stature, constitutional delay of growth and puberty, idiopathic short stature and small for gestational age with catch-up growth [5]. Pathological causes of abnormal growth include nonendocrine and endocrine disorders. Nonendocrine causes include: systemic diseases and their management, undernutrition, metabolic disorders, and genetic syndromes such as Turner Syndrome and Noonan syndrome [6,7].

Endocrine causes include growth hormone (GH) deficiency, hypothyroidism, and Cushing syndrome. Growth hormone deficiency (GHD) is responsible for short stature in 5% of the cases, whereas hypothyroidism constitutes 8-10% of the etiologies of short stature [8].

Short stature is one of the most common reasons for referral to a pediatric endocrinologist. It will not only affect the height of children, but also lead to varying degrees of psychological disorders [9]. Early identification

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of abnormal growth and referral to specialist promptly offer children the chance for appropriate management and improved outcomes [9]. While literature is replete with studies on short stature, the relative significance of the previous different factors that affect growth velocity varies in different populations. To our best of knowledge, etiologies of short stature in Syrian children weren't previously reported. Therefore, the objective of the study was to determine the underlying etiologies of short stature in children older than five years.

Patients and Methods

Study population

After approval by local research ethics committee, an Observational Comparative Cross-Sectional study was conducted in 328 patients seen at Pediatric Endocrinology Clinic, Tishreen University Hospital over a period of one year from September 2020 to September 2021 with a complaint of short stature.

Inclusion criteria were as follows: Children older than five years with short stature according to the definition.

Non-inclusion criteria: Patients with pulmonary, cardiac, kidney diseases that may affect the growth, presence of cerebral atrophy, mental retardation or polymal formative genetic syndrome.

Complete history, review of systems, and physical examination including Tanner staging were performed to categorize the cause of short stature. Weight and height were measured, standard deviation (SD) of the height was detected, and target height was calculated.

The following tests were performed in all patients: complete blood count (CBC), erythrocyte sedimentation rate (ESR), hepatic and renal function test, thyroid stimulating hormone (TSH), cortisol and insulin like growth factor1 (IGF-1), screening for celiac disease by serologies (tissue transglutaminase immunoglobulin A IgA), and helicobacter pylori stool antigen test. Urine and stool samples were obtained for analysis. However, the results were not significant in the study. Contrast-enhanced magnetic resonance imaging of the brain was performed in certain cases to exclude hypothalamic -pituitary dysfunction.

Cortisol was administered to all patients and was not mentioned because it had no role in the research.

IGF1 is a rational alternative to growth hormone and currently approved because it is more accurate, safe and easy to perform than growth hormone induction.

Ft4 was measured only for patients with abnormal TSH.

Total IgA wasn't measured because we don't have it.

Constitutional delay of growth was diagnosis by familial history and excluded other pathological causes.

Genetic study was conducted for a limited number of patients due to the lake of financial means.

Statistical analysis

Statistical analysis was performed by using IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations (SD), median, frequency count which represents a measure of number of times that an event occurs and percentages which are calculated by dividing the value by the total value and then multiply the resultant by 100.

Results

A total of 236 children were excluded of the study, of which; 65 were younger than five years, 45 with normal SD of the height, 69 with SD: -1 to -2 of the height, and 57 were incomplete for height information filling.

The study included a group of 92 children who fulfilled the criteria of short stature. Age ranged from 5 to 14 years, with mean age of 8.8 ± 2.7 years. The most frequent age group was 6-8 years (26.1%), followed by 12-14 years (20.7%). Female represented 54.3% of the study sample and males were 45.7%. Patients were classified according to SD of the height as follows: -2 to -3 (74 cases), and > -3 (18 cases), table 1.

As shown in table 2, familial short stature (44.6%), and constitutional delay of growth (17.4%) represented the most frequent etiologies of short stature.

The most common endocrinological causes were hypothyroidism (8.7%), followed by GHD (4.3%) and vitamin D-resistant rickets (2.2%). Other causes of short stature included: Helicobacter pylori infection (9.8%), celiac disease (6.5%), malnutrition (4.3%), Ehlers-Danlos (1.1%), asthma (1.1%), Silver-Russell (1.1%), recurrent urinary infection (1.1%), and TORCH infection (1.1%).

Children with SD of height < -3 were distributed into normal and pathological variants as follow: constitutional

Table 1: Demographic characteristics of the study population with short stature.

Variable	Result
Age (years)	**Range 5-14 (mean 8.8 ± 2.7)**
Age group	**Frequency**
5-6	16 (17.4%)
6-8	24 (26.1%)
8-10	18 (19.6%)
10-12	15 (16.3%)
12-14	19 (20.7%)
Sex	
Male	42 (45.7%)
Female	50 (54.3%)
SD of the height, n (%)	
-2 to -3	74 (80.43%)
< -3	18 (19.57%)

Table 2: Distribution of the study population according to the etiology.

Etiology	Result
Familial short stature	41 (44.6%)
Constitutional delay of growth	16 (17.4%)
Helicobacter pylori infection	9 (9.8%)
Hypothyroidism	8 (8.7%)
Celiac disease	6 (6.5%)
Malnutrition	4 (4.3%)
Growth hormone deficiency (GHD)	4 (4.3%)
Vitamin D-resistant rickets	2 (2.2%)
Others*	5 (5.5%)

delay of growth (3 cases: 3.26%), familial short stature (7 cases: 7.6%), helicobacter pylori infection (3 cases: 3.26%), celiac disease (2 cases: 2.17%), malnutrition (2 cases: 2.17%) and asthma (1 case: 1.1%).

Discussion

In the recent years, children's growth issue has received increasing attention with the socioeconomic development. Understanding of the factors that influence the growth and taking preventive measures is essential to improve the final outcome.

The current study of 92 children showed that familial short stature, and constitutional delay of growth were the most frequent causes of short stature(62%), followed by endocrinological causes(15.2%), (Hypothyroidism, Growth hormone deficiency (GHD) Vitamin D-resistant rickets) of which hypothyroidism represented the most frequent etiology. The results of current study are consistent with the previous studies.

Sultan, et al. found in a study conducted in 214 patient with short stature that five most common etiological factors are: constitutional (17.3%), familial (15%), malnutrition (9.8%), celiac disease (6.5%), and growth hormone deficiency (6.1%) [10].

Shiva, et al. demonstrated in a study conducted in 244 patients with short stature that normal variants including familial and constitutional constituted 53.3% of the etiology in short patients. Endocrinological causes represented 8.6% which include GHD (6.1%) and hypothyroidism (2.5%) [11].

Hussein, et al. showed that 63.6% of children with short stature had normal variants of them, 42% had familial short stature, 15.8% had constitutional growth delay, and 5.5% a combination of both. Endocrinological causes accounted for 26%, of them GHD was presented in 11.8% [12].

Conclusion

There are many supposed factors might be responsible for potential causes for short stature, and normal variants are the most frequent etiologies.

Recommendations

We emphasize the importance of monitoring growth pattern of the child over the time by using age and sex specific growth charts to ensure that the child is growing at an appropriate rate, and initiating investigations in presence of growth disorder.

Declarations

Competing of Interests

All the authors do not have any possible conflicts of interest.

Ethical consideration

After discussing the study with the parents, all of them gave a complete and clear informed consent to participate in the study. This study was performed in accordance with the Declaration of Helsinki.

Availability of data and materials

Most of the data was in the article, and other data can be asked from the corresponding author.

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Author contributions

All authors performed the measurements and wrote the article. Literature review was done by Dr. Suhad Abdullah, and all authors performed analytic calculations and performed the numerical simulations.

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