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Research Article

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Analysis of Short Stature in Children

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Abstract

Growth is a continuous biologic process influenced by genetic, nutritional, environmental, and hormonal factors. Normal growth can occur only if the individual is healthy. Longitudinal growth assessment is essential in child care. Short stature can be promptly recognized only with accurate measurements of growth and critical analysis of growth data. The objective of this study was to assess the characteristics of patients referred to pediatric clinic because of short stature and determination of the etiology in tertiary care hospitals of Southeast Asia.

This is a retrospective study of patients referred to a pediatric clinic with short stature during the period March 2015 to March 2018. After a proper detailed medical history, growth analysis and physical examination, followed by a radiological (bone age) and laboratory screening (complete blood count, urine and stool analysis and also thyroid function). Growth hormone stimulation tests were performed when indicated. Magnetic resonance imaging (MRI) of the pituitary was performed if required. As well, celiac screening and small bowel biopsy were performed when appropriate.

During the period, two hundred and thirty eight patients were evaluated for short stature. Their age ranged from 3 years to 12 years. The male to female ratio was 1.3:1. The commonest etiology was genetic short stature found in 32 patients, while in the remaining patients, nutritional, endocrine, metabolic and other causes were noted.

Short stature was a common referral. A wide variety of etiological diagnosis was noticed with genetic short stature being the commonest. A wide variety of endocrine causes were evident, with growth hormone deficiency, as a results of different etiologies, being the commonest.

Keywords: Short stature; Etiology; Children; Growth

Abbreviations

CBC : Complete Blood Count
CDG : Constitutional Delay of Growth
ESR : Erythrocyte Sedimentation Rate
FSS : Familial Short Stature
GH : Growth Hormone
GHD : Growth Hormone Deficiency
ISS : Idiopathic Short Stature
IUGR : Intrauterine Growth Retardation
SDS : Standard Deviation Score
SS : Short Stature

Introduction

Short stature (SS) is one of the most common causes of referrals to pediatric endocrinologists. It is defined as a height of more than two standard deviations below the average for same age and sex [1,2].

Short stature is a common problem in children globally, especially in developing countries [3]. When compared with well-nourished and genetically relevant population, short stature is defined as height or length below 3rd percentile for that age and gender [4]. Statistically, this refers to children who are shorter than 97% of their age and gender matched peers.

The way by which the short stature influences the psychosocial

and educational function of short children is controversial [5,6]. Likewise, there is no compelling evidence to show an association between short stature and cognitive and psychosocial maladaptation or dysfunction [7].

Many of the patients referred with SS have no identifiable medical abnormality and are classified as constitutional delay of growth (CDG), familial short stature (FSS), or idiopathic short stature (ISS). However, in some cases it may be the only clinical manifestation of a systemic, endocrine or metabolic disorder [1,8,9,10]. Another disorder that may lead to malabsorption is tropical sprue, which is most common in Southeast Asia. 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 [11].

Methodology

This retrospective study was carried out between March 2015 and March 2018. All of the subjects referred to outpatient pediatric clinic of Tertiary care Hospitals of Southeast Asia with complaint of SS were recruited. Subjects that haven't completed at least 6 months follow up visit were excluded. At first a complete medical and growth history was taken and a thorough physical examination carried out. Seca balance with height measuring scale were used for weight and height measurements. National Center for Health Statistics (NCHS) growth charts were used for calculation of height Standard Deviation Score (SDS). Patients with normal physical examination and body height less than 2SDS below mean were followed only for their growth velocity and no laboratory test was done on them at beginning. Patients with a body height more than 2SDS below mean for same sex and age, underwent complete paraclinical evaluation including X-ray for assigning bone age, ESR, CBC, serum creatinine level, arterial blood gases, serum electrolytes and alkaline phosphatase, stool examination, urine analysis and culture, thyroid function tests, antigliadin and anti endomysial antibodies.

Patients with normal laboratory findings and growth velocity lower than 25% normal growth rate for the same sex and age, and also those with a body height more than 3SDS below mean, underwent GH provocative test. Bone survey was done when skeletal dysplasias were suspected. Finally after complete evaluation and suitable treatments (if needed), subjects who completed at least 6 months follow up were classified as: 1) Those who were not really short (body height less than 2SDS below mean and height velocity greater than 25%). 2) Those who were short (body height more than 2SDS below mean for same sex and age). The short patients were classified as following: 1) FSS (skeletal age proportional with chronologic age, short parents and no abnormal paraclinical findings), 2) CDG (shortness with normal growth rate, retarded skeletal age, positive family history of constitutional growth delay), 3) GH deficiency (severe SS, delayed skeletal maturation, low growth velocity, maximum GH level less than 10 ng/ml in two provocative tests with normal findings in all other laboratory tests), 4) Hypothyroidism, 5) Turner syndrome (based on karyotype), 6) Skeletal dysplasia (according to bone survey), 7) IUGR (intrauterine growth retardation with no appropriate growth rate after delivery), 8) Malnutrition, 9) ISS (shortness and delayed bone age with completely normal clinical and paraclinical findings and no abnormality in growth hormone study, 10) Other causes.

After gathering and classifying initial data, we used SPSS software version 16 for statistical analysis. T-test, Chi-Square, NPar Chi-Square statistical tests were used. Continuous data were presented as mean±SD and categorical data were presented as proportions. P-values less than 0.05 were considered statistically significant. According to the fact that all studies and therapies were based on patients, needs and we refused any unnecessary examinations and their private data will not be obtained by any factual or legal authorities, this research does not have any ethical problems.

Results

During 3 years time, 238 subjects were referred with complaint of SS. Eighteen of them were excluded because they did not complete at least 6 months follow up and 220 children and adolescents that were followed about 6-15 (mean 6.8±2.3) months, containing 67 (55.83%) boys and 53 (44.167%) girls, entered the final analysis. There was no statistically meaningful difference between the number of referred boys and girls (P=0.066). The patients were between 3-12 years of age (mean 9.7±3.7).

The mean height SDS of short patients was -4±1.24 which was -3.45±1.15 for short boys and -3.45±1.35 for short girls, the difference was not statistically meaningful (P=0.5).

Three of 220 short subjects were not para-clinically evaluated because they were referred after their first menstruation. Remaining 217 short subjects underwent complete examinations. The (Table 1) shows number and percentages of the patients based on their final diagnosis. No statistically meaningful difference (P=0.8) was observed between the age of short boys (9.9±4.1 years) and short girls (9.9±3.6 years). Most of the children had non-pathologic types of SS (FSS or CDG). Totally 35.48% of cases were due to non-pathologic types of SS. In this group, 53.25% were due to familial SS and 46.75% to CDG. The main etiology of nonpathologic SS was FSS in girls and in boys. Among the pathologic types, there were prenatal and postnatal causes with genetic disorders being the most common.

Table 1: Etiology of short stature in 217 short children

Etiology	No. of Patients (n)	Percentage (%)
A) Normal Variants		
Familial	41	18.89
CGD	36	16.59
B) Prenatal Causes		
IUGR	13	5.99
Genetic Disorders	32	14.75
C) Postnatal Causes		
Under Nutrition	20	9.22
Chronic Systemic Illness	21	9.68
Endocrine Disorders	29	13.36
Metabolic Disorders	25	11.52

The endocrine etiology are listed in (Table 2). It shows number and percentages of the common variants of endocrine disorders. The commonest between them is GH deficiency (5.99%) and then Hypothyroidism (3.23%).

Table 2: The endocrine etiology among 217 children with short stature

Etiology	No. of Patients (n)	Percentages (%)
GH Deficiency	13	5.99
GH Insensitivity	4	1.84
Type-1 DM	5	2.3
Hypothyroidism	7	3.23

The other observed causes which includes nutritional deficits, birth defects and systemic diseases are summarized in (Table 3).

Table 3: The other etiology among 217 children with short stature

Etiology	No. of Patients (n)	Percentages (%)
Chronic Systemic Illness	7	3.23
Malabsorption	11	5.07
Birth Defects	4	1.84
Cushing's Syndrome	4	1.84
Rickets	8	3.68
Coeliac Disease	6	2.76
Mucopolysaccharidoses	7	3.23

Discussion

Short stature is a common finding among general population and between 0.1% and 2.5% of people in different areas have a body height more than 2SDS below mean. Also the most common cause for referrals to pediatric clinics is SS, but in many of these patients there is no pathologic reason for their shortness. In our study many of short patients (35.48%) were placed in nonpathologic group (FSS or CDG) too, and in 64.52% of cases pathologic causes were found. Researches in other parts of the world have indicated that most of the SS cases are related to non-pathologic causes [2,12,13].

In our study there were no significant differences between numbers of two sexes, their ages at referral time, and their height SDS. But the portion of subjects that were not really short was higher in females than in males. It seems that in our society girls prefer to be tall but their parents do not have enough information about SS and steps of normal growth. Psychosocial adaptation and degree of parents' awareness are critical determinants in seeking for evaluation and treatment of SS [14]. It is important to know that the SS is a common complication in children born with IUGR [15]. These children have sevenfold greater risk of being short and 8% of them will have adult height less than -2SDS, which corresponds to 20% of short adult population [16]. In spite of other researches that have reported the incidence of GH deficiency (GHD) between 16% and 32% among short subjects in Iran the rate of GHD was not considerable (5.99%) among our short patients. In this research we used GH provocative tests for patients with a body height more than 3SDS below mean, delayed skeletal maturation and growth velocity less than 25% in at least 6 months follow up [17,18,19]. It seems that most of Turner cases diagnosed in endocrinology clinics were above ten years of age when they were referred because of SS. It was true in our study too [20,21]. The main limitation of our study was that a great number of our patients haven't completed the six months follow-up and were eliminated from the final analysis.

Conclusion

Short stature is a common indication for genetic evaluation. The differential diagnosis is broad and includes both pathologic causes of short stature and no pathologic causes. The purpose of evaluation for short stature is to provide accurate diagnosis for medical management and to provide prognosis and recurrence risk counseling for the patient and family. A great number of children referred with short stature to pediatric clinics of all tertiary care hospitals of Southeast Asia are not really short. Greater than half of short patients are normal variants of Short stature.

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