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An Etiologic Evaluation of Children with Short Stature in Gorgan (Northeast Iran), 2005

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Growth is an important biological process during childhood. Short stature is the most common cause of a child to be examined by an endocrinologist. This cross-sectional study was performed to determine the short stature causes in children aged 6-14 years old in 2005 who were referred to Talghani Medical-Educational Center. Demographic characteristics, history of any serious problem (prematurity), clinical feature, biochemical and endocrinological test results and radiological findings were evaluated. Standard Deviation Score (SDS) was calculated and written down in an information recording form. From 100 children under study (66%) were girls with the average age of 10.84 year. Their average of bone age was 8.4 year. Most common causes for short stature were constitutional (57%), growth hormone deficiency (30%) and familial (8%).There was not significant difference between two sexes in this view. According to the findings, after ruling out of Constitutional and familial causes, we strongly recommended the provocative growth hormone test for early detection and timely prevention of permanent short stature.

Key words: Short stature, etiology, children, Gorgan, Iran

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INTRODUCTION

Growth is a complex process and influenced by genetic background, different functions of endocrine system, nutrition, effect of any chronic disease and the level of individual physical activity (Kamboj, 2005). There are many ways to evaluate the growth pattern; one of them is intermittent height measurement. The short stature is a term applied to a child who is two standard deviations or more below the average height for children of that gender and chronologic age (and ideally of the same racial-ethnic group). This translates into being below the third percentile for height (Cakan and Kamat, 2007). Of course; we should pay attention to inconsistency of a child and parents' height in spite of having normal growth chart. So corrected average height of parents is helpful for determining the child's normal growth. This scale for males is the average of parents' height plus 6.5 cm and for females is the average of parents' height minus 6.5 cm and if a child is two standard deviation (i.e., 10 cm) shorter than this scale, it means that the child is short (Kamboj, 2005; Memon, 2005; Styne and Claser, 2002). In most cases, the short stature is caused by physiologic factors such as constitutional or familial, but it may happen after serious and curable diseases and sometimes it may be the only sign of a systematic disease (Afsharpeyman and Moaieri, 2004). Although growth disorders manifest as unspecific signs and often are ignored by parents, they could be the first key to lead a physician to diagnose a special disease. Growth changes can be used as a sensitive marker for general health and deviation of health may manifest abnormal growth at first. So, careful evaluation of the growth pattern in every visit during childhood is necessary (Charles and Brook, 1995).

Due to occurrence of psychogenic problems for the child with short stature and its effect on child's life, early diagnosis before epiphyseal closure can be useful in treatment and restoring of normal growth pattern. Since, Growth affected by race, life style and nutritional, cultural and socioeconomic status, it is thought that the etiology of short stature in children to be different in developing countries than developed. In order to find out the incidence of different etiologies causing short stature in our population, this study was undertaken.

MATERIALS AND METHODS

This was a cross-sectional study which was carried out to determine the frequency distribution of short stature causes in 100 short children (who were referred to Taleghani pediatrics Medical-Educational center in Gorgan) in 2005.

The studied cases were all children aged 6-14 who were referred to Talghani pediatrics hospital in order to follow up their problem. According to the routine program, the height of all children were measured and everyone with the height under 3rd Percentile curve, on the basis of age and sex, enrolled into the study (n = 100).

Then, the history of major diseases in child and her/his family was evaluated. After careful examination, wrist radiography and determining of the height age, type of the short stature was specified as below:

Constitutional: height age = bone age < calendar age

Familial: height age < bone age = calendar age

Endocrine: height age < bone age < calendar age

In addition, for every child on the basis of following formula, Standard Deviations Score (SDS) was determined:

$$SDS = \frac{X - Y}{SD}$$

Where:
X = The true height of child,
Y = The mean height for the age and sex,
SD = Standard Deviation.

Then, for the -2 < SDS < -1; CBC, BUN and creatinine and for the SDS ≤ -2 serum level of growth hormone, T4 and TSH were also measured. In shorter children (under the 3rd percentile), provocative growth hormone test with clonidine and propranolol were repeated two times. In children admitted to hospital, the night before, the fasting blood sample was taken for the baseline measuring and fasting growth hormone and thyroid function tests, CBC, Urea and creatinine tests in the next morning were done. Then, clonidine and propranolol were administered to and samples were taken again in order to measure the growth hormone in 30, 60, 90 and 120 min intervals after drug administration.

Growth hormone level under 10 ng dL^{-1}, in any of the samples, was considered as growth hormone deficiency.

In regard to thyroid function, thyroxin less than 7.5 and TSH more than 5 were considered as hypothyroidism. If a female had a SDS< -3, karyotype must be done.

Gathered data entered into information recording form and Coded. Data was analyzed in statistical software, SPSS (ver: 13), using χ^2 and t-student tests.

RESULTS

Cases participated in this study were 100 children aged 4-16 suffering from short stature. Sixty six percent

(n = 66) of all were female. The average age was 10.84±2.25 year. The minimum and maximum measured height was 97 and 134 cm. The average height of children and their fathers and mothers were 120.67±8.59, 170.56±4.87 and 162.6±4.87 cm, respectively. There was not significant difference in height, bone and calendar age between two sexes (Table 1). The results of the wrist radiography showed that the average of the children bone age was 8.14±2.32. Ninety four percent of them had bone age less than calendar age. The average of patients' SD score was -4.16±1.32. With consideration of children's age, height growth curve, bone age and test results, common causes of short stature were constitutional (57%) growth hormone deficiency (30%), genetic or Familial (8%), hypothyroidism (3%), respectively (Table 2). There wasn't any significant difference between sex groups in regard to short stature causes ($p>0.05$). Comparing the average of the bone age among three common causes of short stature showed that, the children with the growth hormone deficiency had the lowest bone age (6.55±1.76) and the children with constitutional short stature had a bone age lower than the children suffering from familial short stature. These differences were statistically significant ($p<0.05$) (Table 3). Furthermore, the findings showed a significant difference between the SDS average and different type of short stature ($p<0.05$). The children suffering from familial short stature had the lowest SDS (-4.85±1.26) (Table 3).

Table 1: The average of bone age, child and parent's height and SDS score in two sexes

Characteristics	Male	Female	p-value*
Calendar age	10.79±2.32	10.86±2.22	0.884
Bone age	7.89±2.19	8.26±2.39	0.456
Child's height	120-92.00±9.25	120.54±8.26	0.834
Father's height	171.35±4.79	170.19±4.9	0.263
Mother's height	164.20±4.68	161.83±4.79	0.019
SDS	-4.30±1.4	-3.88±1.09	0.134

*p-value >0.05 was considered non significant

Table 2: Proportional frequency causes of short stature in two sexes

Causes of short stature	Female (%)	Male (%)	Total
Constitutional	54.5	61.8	57
Growth hormone deficiency	28.9	32.4	30
Hypothyroidism	3.0	2.9	3
Genetic	10.6	2.9	8
Prematurity	1.5	-	1
Terner syndrome	1.5	-	1
Sum	100.0	100.0	100

Table 3: The average of bone age and SDS in different causes of the short stature

Causes of short stature	Bone age	SDS
Constitutional	8.54±1081	-3.82±1.22
Growth hormone deficiency	6.55±1.76	-4.67±1.35
Hypothyroidism	8.66±1.53	-3.63±1.58
Genetic	11.69±2.71	-4.85±1.26

DISCUSSION

The bulk of studies all over the world had shown that constitutional growth delay, familial short stature and GH deficiency are the most frequent causes of short stature and it is in according to present study (Soheylekhah and Halvaii, 2001; Nakhjavani *et al*., 2001; Moaieri and Aghighi, 2004; Fanny *et al*., 2002; Shu *et al*., 2002).

Although the short stature causes reported in all above-mentioned studies, confirm our study, but the difference in rank of causes can be due to studied cases and settings. For example, Fanny *et al*. (2002) study was done on the patients who were referred to the genetic center with specific patient concern; while, the present study is carried out in a general center with serving of non specific patient concern.

In a study done by Biswas (2005) mentioned that malnutrition, primary hypothyroidism, familial causes, lung and abdominal tuberculosis, malabsorbtion syndromes and intrauterine growth retardation to be the most common reasons of the short stature. Constitutional causes and deficiency of growth hormone with prevalence of 1.5 and 2.5% were respectively uncommon causes of short stature. Prevalence of malnutrition and low socioeconomic and health levels in India could be one the reasons for the difference between present study and above-mentioned study.

Findings related to the average of bone age showed that the children suffering from growth hormone deficiency had the lowest bone age average and followed by children suffering from constitutional and genetic causes, Even though Moeiri's findings showed the short stature caused by hypothyroidism had the lowest bone age. The reason for the difference can be caused by the different range of ages in these studies. In another study children were 4-18 years; while the group age in this study was between 6-14 years. The results related to the SD score demonstrated that SDS average of the patients suffering from constitutional short stature was significantly higher than the others. In Moaieri and Aghighi (2004), the highest SD score is related to the genetic cause and then the constitutional and hormonal causes, respectively. Differences in studied groups can be the cause of different results in theses two above-said studies, because they were accomplished in the referring centers in which the patients suffering from severe and special disorders with significant short stature. In relation to gender prevalence of short stature, the results of the present study demonstrated that female's ratio was more than of males. These findings are confirmed by Afsharpeyman and Moaieri (2004), Soheylekhah and Halvii (2001) and Karamzadeh (1997) results whereas;

Nakhjavani *et al.* (2001) and Undasy and Feldkamp (1994) showed the opposite results that is, males preference. Ferry (2006) believes that the reason of higher prevalence of short stature among males is due to further seeking of medical care by parents of male children than females.

CONCLUSION

Since, the most common short stature causes were constitutional, hormonal and familial, it is recommended that in children with the height growth delay (<3rd percentile) more studies (SDS and bone age) should be done and if SDS<-2 and bone age dilation is present, careful systematic studies and gonadal tests should be done. With early diagnosis and prompt treatment, before epiphyseal closure, we can prevent short stature in children

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