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Clinical, Anthropometric and Dynamic Clonidine Stimulated Growth Hormone Study in Short Stature Children.

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ABSTRACT

Background: Growth hormone is the important hormone controlling growth from birth to adolescence. Children with growth hormone deficiency usually present with severe short stature and correct diagnosis by provocative GH test is essential so as to treat such children with costly GH available now. **Aim:** To study the clinical profile, Anthropometric measurements, Growth Hormone dynamics, Thyroid functions test in short stature children. **Methods:** Children with height 2 standard deviation below the mean for the age (WHO Growth Charts up to 5 years and Agarwal DK et al growth reference after 5 years) and Children referred to short stature as the primary complaint were included in the study. Anthropometric measurements, clinical examination, dynamic clonidine provocative GH tests were done. **Results:** Out of 30 short children, 25 children (83%) were identified as having growth hormone deficiency as evidenced by subnormal growth hormone response (peak GH below 10ng/ml). 4 children (13%) were identified as having GH insensitivity (or) Laron's dwarfism in the form of supra-physiological level of serum GH. One child showed normal GH response. Among 25 children who showed GHD 3 of them also showed clinical hypothyroidism as evidenced by the rise of serum TSH level above 5.5 units/ml. **Conclusion:** Growth hormone abnormality was found to be the most common cause for pathological short stature (96%) when chronic systemic disorders were excluded.

Keywords: Short stature, growth hormone deficiency, dynamic growth hormone test.

INTRODUCTION

Short stature carries physical, mental and social stigma for the child and for the parents, which forms the main symptom needing a thorough and careful assessment by the health-personalles involved in pediatric practice. One of the important issues facing those concerned with the evaluation of short stature in India is, in regard with the use standards for evaluation. According to Goldstein and Tanner, national standards drawn from representative samples of population are ideal standards to use if these exist.[1] The diagnosis of growth hormone deficiency in children with short stature is based on clinical features and hormonal studies. Children with growth hormone deficiency usually present with severe short stature and a low growth velocity of less than4 cm/ year.[2,3] Alternative causes of poor growth need to be considered and excluded. One of the normal variants is idiopathic short stature, a group of short children with no definitely recognizable underlying disease. It is important to distinguish between the child with growth hormone deficiency and the short normal child. Growth hormone secretion is regulated by multiple physiologic factors, including age, onset of puberty, nutritional status, and body weight.[4-7] Growth hormone secretion is pulsatile and serum concentrations are low during the daytime. Thus, provocative tests of GH release, rather than single basal growth hormone estimation, are used to determine GH status. Electro chemiluminescent assay (ECLIA) is used to determine the level of growth hormone.[8]

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Aim

To study the clinical profile, Anthropometric measurements, Growth Hormone dynamics, Thyroid functions test in Short stature children.

MATERIALS AND METHODS

This prospective study was conducted in Kanyakumari Government Medical College. Children with height 2 standard deviation below the mean for the age (WHO Growth chart <5 years &

Agarwal DK et al growth reference after 5 years) and Children referred to short stature as the primary complaint were included in the study. Children with nutritional disorders, skeletal dysplasias, genetic syndromes, chromosomal disorder, chronic systemic diseases, chronic infections were excluded from the study. Clinical examination and history of the children were collected. Anthropometric data were collected. Study children were subjected to dynamic growth hormone test. Basal sample after overnight fasting and oral post clonidine 4 microgram/kg peak sample were collected separately. Growth hormone estimation was done by using ECLIA. TSH assay was done by using ECLIA.

RESULTS

Out of 30 short children, 25 children (83%) were identified as having growth hormone deficiency as evidenced by subnormal growth hormone response (peak GH below 10ng/ml). 4 children (13%) were identified as having GH insensitivity (or) Laron's dwarfism in the form of supra-physiological level of serum GH. One child showed normal GH response. Among 25 children who showed GHD 3 of them also showed clinical hypothyroidism as evidenced by the rise of serum TSH level above 5.5 units/ml. These 3 children were treated with Thyroxine for 6 weeks and subjected to repeat dynamic GH estimation test, which again showed subnormal response. Male: Female ration was found to be 1.07:1 with males numbering 15, females 14. Familial incidence of short stature with GH abnormality was found in 3 pairs (20%) of siblings, of which one pair had GH insensitivity syndrome. All these 3 pairs of children were born out of consanguineous marriages. 18 children (62%) were borne of consanguineous parentage. 3 children had birth asphyxia. Typical facial features of GH deficiency were found in 15 cases (51%) but truncal obesity was found in only one case.

Table 1: Distribution study children in age group.

Age groups	Affected Children	Percentage
< 3 years	2	7%
3 to 6 years	10	35%
7 to 9 years	5	17%
10 to 12 years	12	41%
Total	29	100%

Children with short stature were found to be clustered around the age of 10 to 12 years. In assessing the nutritional status of the study children the weight of these children was found to be within 0.66 S.D of the expected means weight. The mean US/LS ratio observed was 1.125 against the expected of 1.3 with p value of <0.05 suggestive of more shortening of torso compared to the limbs. The mean height age observed was 3.6 years compared to the mean chronological age of 7.6 years. The mean bone age observed was 5.9 years compared to the mean chronological age of 7.6 years.

Table 2: Distribution of Growth hormone level.

Growth Hormone deficiency, N=25		GH Insensitivity N=4		Normal Dynamics N=1	
Basal	Peak	Basal	Peak	Basal	Peak
0.86 ±0.6	1.70 ±1.4	28	28.3	4.6	12.6

Growth hormone dynamics was observed in 25 children with sub abnormal GH response, mean basal level 0.86 ±0.6, mean post clonidine peak 1.70 ±1.4. In 4 children with GH insensitivity, the GH dynamics observed was, mean basal level 28ng/ml, mean post clonidine peak 28.3ng/ml. Only one child showed normal GH dynamics in the form of basal GH 4.6ng/ml, post clonidine peak 12.6ng/ml.

DISCUSSION

In the present study GH abnormalities was found to be the most common cause for pathological short stature (96%) when nutritional and other chronic systemic disorders were excluded. The magnitude of this problem was comparatively more than that was observed by Desai M et al and Gupta S et al in North Indian population.[9,10] 83% of short children were found to be suffering from GH deficiency. 13% of short children were found to have GH insensitivity syndrome and only one child was found to have normal GH dynamics. Desai M et al in his series of 100 cases of GH abnormality found 89% were due to GH deficiency, 11% due to GH insensitivity syndromes.[9] Perinatal insults like birth asphyxia, forceps deliveries found only in 3 cases (12%) of GH deficiency in the present study, unlike the western studies, which observed 50-60% incidence.[11, 12]

Familial clustering observed was 20% in this study, less than what was observed by the Bombay based study 31% but more than that was observed by western investigators.[9, 10, 13]

High incidence of consanguineous parentage 62% was observed in this study. This is much higher than any other previous Indian studies. Consanguineous parentage was found in all cases due to GH insensitivity syndrome, Ganong et al also found similar incidence. Even though the typical morphological features of GH deficiency were found in 51% of cases, the truncal obesity was found only in one case. This may be due to the associated nutritional and environmental insults in our country.[14] There was no history suggestive of hypoglycemic attacks in any of these children. Herber et al identified 11 children with hypoglycemic attack out of 29 GHD children, all of them were less than 2 years old.[15]

According to Kaplan et al, degree of delay in bone age in GH deficiency is usually equivalent to delay in height age. But in the present study the retardation

of height age (53%) was more severe than that of bone age (41.9%).[16]

Colcaco et al in his study of 100 cases of GH abnormalities, found height age was more severely retarded that bone age in GH insensitivity syndromes unlike GH deficiency. In the present study it was observed more severe retardation of height age than bone age in both GH deficiency and GH insensitivity groups.[9]

CONCLUSION

Growth hormone abnormality was found to be the most common cause for pathological short stature (96%) when chronic systemic disorders were excluded. Using -2 SD of WHO reference chart below 5 years and Agarwal DK et al growth references above 5 years is effective in identifying maximum number of pathological short stature, which form the basis for sophisticated hormonal assays and further hormonal replacement if needed. It throws light on the maximum incidence of consanguineous parentage. Anthropometric measurements reveal marked retardation of torso growth.

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