Craniofacial proportions and anthropometric measurements among growth hormone deficient Egyptian children

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ABSTRACT

Introduction: Untreated children with growth hormone deficiency (GHD) have typical somatic features, including short stature, acromicria and distinctive craniofacial features including small head circumference.

Patients and Methods: By using a cross sectional study design, we investigated the effect of GHD on craniofacial growth with photographic facial morphometrics & various anthropometric measurements, in 20 children with GHD compared with 20 healthy children and normal first degree relatives of the same age and sex group.

Results: Untreated children with GHD had retarded facial height & width ($p<0.01$) compared with the control group. Moreover all anthropometric measurements (weight, height, head circumference, sitting height, arm span and sub-ischial leg length) were reduced in GHD children in comparison to controls ($p<0.01$) except ear length which was above 3rd percentile. Also small head circumference for chronologic age and for height age was observed in GHD children ($p<0.01$). In addition small hands and feet for age (below 3rd percentile) were found in untreated GHD children when compared with normal controls. This report validates & quantifies the clinical impression of foreshortened facies in GHD children.

Key Words:

Growth hormone deficieny, anthropometric measurements, craniofacial proportion.

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INTRODUCTION

The mechanism regulating craniofacial growth & development are complex interactions between genes, hormones, nutrients and epigenetic factors that will give the craniofacial bone its final morphology, while any disturbances in this mechanism may result in deviating growth pattern[1]. Untreated children with GHD have typical somatic features, including small head circumference [2]. The clinical studies have found global delays in all linear craniofacial dimensions

mostly in anterior facial height, predominantly the lower third[3]. Greater retardation in the mandible than the maxilla results in a retrognathic mandible.[4]

David et al[5] had found small total vertical anterior facial proportions in untreated children with GHD than normal relatives and controls (the vertical proportions of triangles 5—8—24 and 15—23—22 on frontal and lateral images respectively but a measure of mid facial height (triangle 5—8—25) was not significantly reduced suggesting that the deficit in overall anterior facial height was localized to lower face. Also they noticed that untreated children with GHD had smaller facial width compared with normal subjects (triangle 5—8—27).

Zachmann et al.[6] had shown that simple anthropometric measurements may be of help in differentiation of various types of GHD. They found in all studied groups that standing height, sitting height and sub-ischial leg length were equally retarded, and bihumeral width was more retarded than biiliac width, the head was relatively large and fat tissue was increased with subscapular skin folds being greater than triceps skinfolds indicating relative obesity of the trunk, muscle and / or bone mass was reduced (arm and calf circumference).

In this study we assess the craniofacial deficit and acral growth found in untreated children with GHD by using photographic morphometric analysis and anthropometrics and compare them with the values obtained for normal age and sex matched children, in order to validate and quantify the clinical impression of foreshortened facies in GHD children.

PATIENTS AND METHODS

The subjects of this study were recruited from the outpatient endocrine clinic of Ain Shams University Children′s Hospital during the period from June 2006 to August 2007. Children were defined as GH deficient if they had failed to achieve a stimulated GH level > 10 ng/ml in response to two GH secretagogues. Subjects with syndromic short stature, dysmorphology or a history of craniofacial surgery were excluded. They were 10 boys and 10 girls with their age ranging from 5 to 15 years with a mean value of 10.22 (±3.91) years. Twenty healthy subjects were enrolled as a control group (14 unrelated healthy children and 6 first degree relatives of the patients with normal level of GH). Their ages ranged from 5 to15 years with a mean value of 10.26 (±3.21) years. An informed consent was obtained from all participants and / or their guardians prior to the study.

- Various anthropometric measurements were taken including: Height, weight, head circumference, sitting height, arm span, ear length, hand length and foot length.

Measurements were plotted on appropriate charts and standard deviation scores were calculated using genotropin auxology calculator English version 2.0 developed by Pharmacia & Upjohn, 1999.[7-9]

- Growth hormone response was tested on two occasions with two provocation tests (Insulin & L.dopa) (Axysm device, ELISA).

Facial morphometry:

1. Front and lateral photographs of

the face and head of subjects were obtained with subjects instructed to hold their expression in as relaxed a manner as possible without smiling[10], only photographs of sufficient quality to allow accurate measurements of all landmark points under investigation were included in the analyses.

2. Images were analyzed by using Image - ProPlus (Media Cybernetics, Silver Spring, Md) software (Quick Basic Program).
3. Facial features were analyzed by using the triangulation method developed by Bookstein[10], (Figure 1).
4. Mean shapes of triangles defined by three landmarks were analyzed by using 22 landmark points previously used to study facial morphometry in persons with Laron syndrome (2,12), (Figure 1). In brief, using triangle Δ 15-23-22 as an example, two strategic reference points are chosen and digitized. Point 15 is assigned the value of the origin (0,0), and point 23 is given the value (1,0) in a Cartesian (X,Y) system.

The triangulation method uses an internal relative scale by arbitrarily assigning the base of the triangle, 15-23, a standard length of 1. Thereafter, the digitized (X,Y) coordinates of any other point (eg 22) represent a relative distance and direction from the established axis and contain all the information about the shape of the triangle. Each triangle of the sample can be standardized in this manner, and the shape of the triangle can be represented by the average of its shape co-ordinates. By comparing the average values of the (X, Y) coordinates of the normal control population with untreated children for GHD, one can assess craniofacial deficits.

Statistical analysis:

Morphometry of each landmark (triangle) was compared between the two groups by use of multivariance. When this analysis showed significant differences, a contrast method was used to assess which of the coordinates, X or Y or both, differed pair wise between the groups. The anthropomorphic data were tabulated, coded then analyzed using SPSS computer software version 12.0. The relationship between different parameters was assessed using student t-test, Mann- Whitney test. A p value < 0.05 was considered statistically significant while a p value < 0.01 or < 0.001 were considered high significant analysis.

RESULTS

The results of the present study are listed in Tables 1- 5 and Figures 1- 3. Regarding the demographic characteristics of the GHD children and the control group, no significant difference was found in age or gender distribution between GHD children and the healthy ones ($p>0.05$) (Table1). Also there was no significant difference in BMI (SDS) between untreated GHD children and controls ($p>0.05$) (Table 4). On comparing the facial morphometric measures of the patients and the control group, a highly significant decrease in the vertical proportions (Y axis) of Δ 5-8- 24 and Δ 15-22-23 on frontal and lateral images respectively was found in the GHD children and the control group ($p<0.01$) (Table 2, Figure 3). On the other hand vertical proportion of Δ 5-8-25, a measure of mid-facial height was not different between GHD children and control group ($p>0.05$) (Table 2), suggesting that the defect in overall

anterior facial proportion was localized to lower face leading to retrognathic mandible. Moreover untreated children with GHD had a significantly smaller facial width (X axis) compared with the controls and significantly smaller horizontal proportion (X axis) of Δ 5- 8 -27 ($p < 0.05$) and Δ 15-22-23 ($p < 0.01$) (Table 3, Figure 3). There was no significant difference between cases and controls as regards horizontal proportion of Δ 5-8-24 and Δ 5-8-25 ($p > 0.05$) (Table 3) indicating no affection of mid-facial width in GHD children. Our study had shown that head circumference SDS remained disproportionately small when corrected for height age (SDS = -1.23, $p < 0.05$), (Table 5). However, head circumference SDS was insignificantly retarded in comparison to height SDS, in other words they were more or less similarly retarded (Table 4). As regards anthropometric measurements the standing height SDS, sitting height SDS, arm span and sub-ischial leg length SDS for chronological age were highly significantly retarded in GHD children compared to controls ($p < 0.01$) (Table 4, Figure 2). Both hand and foot lengths among untreated children with GHD revealed that 50-60 % of GHD children were below 3rd percentile for age. 12 (60%) cases had hand length below 3rd centile as compared to two controls (10%). Six cases (30%) were above 3rd centile compared to 14 (70%) controls. The remaining two cases (10%) had a hand length at exactly the 3rd centile as opposed to four controls (20%). As regards foot length, 10 cases (50%) were below 3rd centile as compared to one control (5%). Four cases (25%) had foot length above 3rd centile and six (30%) were at 3rd centile in comparison to 17 controls (85%) and two controls (10%) respectively.While there was no significant difference between cases and controls as regards ear length, where 80% of cases (n=16) were above 3rd percentile compared to 100% (n=20) of the controls.[7,8]

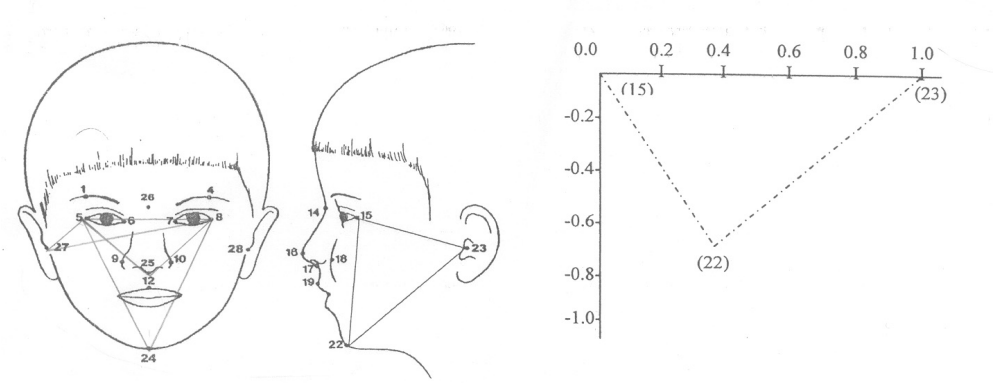


Fig. 1: Twenty- two facial points or landmarks were selected for morphometric analysis. These points were chosen because they are readily identified on photographs and have previously been shown to describe facial changes in other craniofacial syndromes adequately. Shape coordinates of the triangle with vertices 15 (exocanthion), 23, and 22 (ganthion). The scale of the triangle is standardized by assigning the base, vertices 15 and 23, a standard length of 1.0 by fixing point 15 at (0,0) and point 23 at (1,0) in a Cartesian model. All the information about the shape of the triangle is contained in the co-ordinates (X, Y) of point 22 relative to points 15 and 23.[2,12]

Table 1: Comparison between the demographic characteristics of untreated children with GHD and control group.

Variables	GHD group n = 20	Control group n = 20	p value
Age (yrs) mean (SD)	10.22 (3.91)	10.26 (3.21)	>0.05
Range	5-15	5-15	
Gender (M/F)	1/1	1.1/1	

Table 2: Comparison between GHD children with control group as regards facial morphometric vertical height (Y axis).

Triangle	GHD group n = 20 Mean (SD) Coordinate Y	Control group n = 20 Mean (SD) Coordinate Y	T test	p value
15-22-23	1.035 (0.086)	1.272 (0.043)	11.547	<0.01
5-8-24	1.0313 (0.069)	1.313 (0.148)	7.36	<0.01
5-8-27	0.244 (0.056)	0.293 (0.040)	3.367	<0.05
5-8-25	0.495 (0.071)	0.518 (0.058)	-1.42	>0.05

Table 3: Comparison between GHD children with control group as regards facial morphometric horizontal imensions (X axis).

Traingle	GHD group n = 20 Mean (SD) Coordinate X	Control group n = 20 Mean (SD) Coordinate X	T test	p value
15-22-23	0.227 (0.039)	0.336 (0.055)	7.061	<0.01
5-8-24	0.5	0.5		>0.05
5-8-25	0.5	0.5		>0.05
5-8-27	0.114 (0.060)	0.166 (0.557)	2.81	<0.05

Table 4: Comparison between GHD children and control group as regards anthropometric measurements.

Variables	GHD group n = 20 Mean (SD)	Control group n = 20 Mean (SD)	T test	p value	S
Height (SDS)	-3.29 (1.2)	-0.58 (1.2)	-6.269	<0.01	HS
BMI (SDS)	-1.07 (1.5)	-0.3 (0.9)	-1.8	>0.05	NS
HC (SDS)	-2.915 (1.8)	-0.31 (2.9)	-3.614	<0.05	S
Arm span (SDS)	-3.250 (1.4)	-0.555 (1.3)	-6.0	<0.01	HS
Sitting height (SDS)	-4.110 (1.328)	-1.480 (1.898)	-5.796	<0.01	HS
Sub-ischial leg length (SDS)	-1.935 (1.149)	0.46 (1.399)	-5.878	<0.01	HS

HC = Head Circumference
SDS= Standard Deviation Score
S = Significant
HS = Highly significant
NS = Non significant

Table 5: Comparison between head circumference SDS for height age of GHD group and control group.

Variable	GHD group n = 20 Mean (SD)	Control group n = 20 Mean (SD)	T test	p value	S
HC for HA	-1.23 (1.8)	0.52 (1.51)	-3.591	<0.05	S

HC = Head Circumference
HA = Height Age
S = Significant

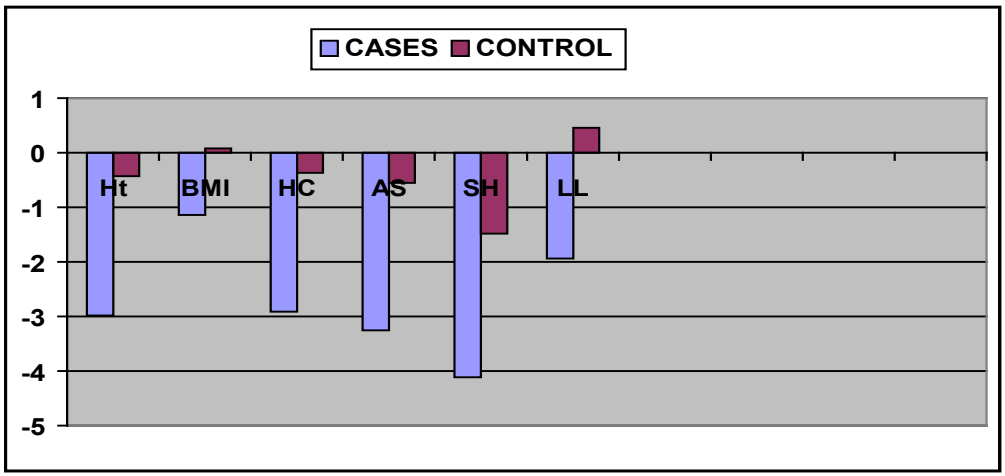
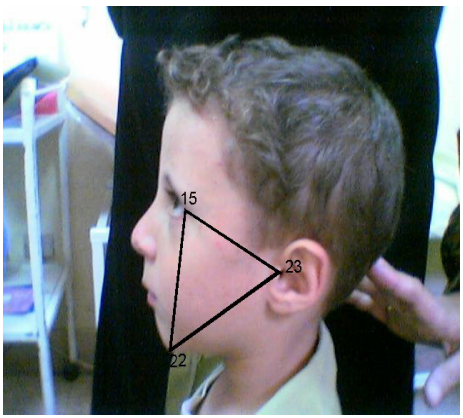


Fig. 2: Comparison between GHD children & control group as regards anthropomorphic measurements (SDS).

Ht = Height
BMI = Body Mass Index
HC = Head Circumference
AS = Arm Span
SH = Sitting Height



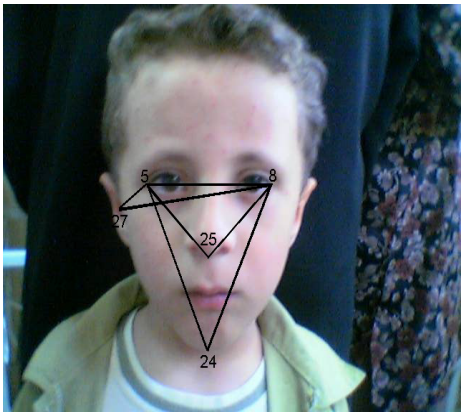


Fig. 3: Photographs of seven years old patient.

Triangle 5, 8, 27 Frontolateral
Triangle 15, 22, 23 Lateral
Triangle 5, 8, 25 Frontal
Triangle 5, 8, 24 Frontal

DISCUSSION

Untreated children with growth hormone deficiency (GHD) have typical somatic features including short stature, acromicria and distinctive craniofacial features including small head circumference.[2,12]

The results of this study demonstrate that the retardation in growth in GHD children affects not only height and weight but also the development and growth of the face, as proved by the retarded facial height and width ($p<o.o1$) compared with healthy controls. This is in agreement with David et al.[5], Schaefer et al.[2]

Our study found delay in linear craniofacial dimensions especially the lower third of the face which resulted in greater retardation in the mandible than the maxilla giving rise to retrognathic mandible as evidenced in measurements of (Y,X axes) in triangles (Δ 15-23-22, Δ 5-8-24 , Δ 5-8-27). The craniofacial deficits found in untreated children with GHD by using photographic morphometric analysis are in agreement with several previous studies which used cephalometric, facial molds[3,5] and another study that used morphometrics[4]. These results have consistently found global retardation of the craniofacies in particular reduction in anterior facial height, width and depth.[3]

As regards anthropomorphic measurements, height SDS as well as head circumference SDS, arm span SDS, sitting height SDS and sub-ischial leg length SDS were all significantly retarded in comparison to the control group. This also applied to the hand and foot lengths as 60% and 50% of patients had hand and foot lengths respectively below 3rd centile. Head circumference SDS for height age was also significantly retarded in the studied patients (Table 5).

When head circumference SDS for chronological age was compared to height SDS for chronological age, no significant difference was found ($p>0.05$). In other words they were not disproportionately retarded, this comes in disagreement with Guevara-Aguine et al.[13], Schaefer et al.[2] stated that the comparison between head circumference SDS and height SDS is inappropriate because of the different magnitudes of growth in head size and body length, for example, there is a 12% increase in head circumference from 2 years to maturity in males while there is greater than 100% increase in stature during this time. Thus the head is not relatively large but normal for body size so the impression of macrocephaly particularly in young children appears to reflect the reduction in vertical dimension of the face, the hypoplastic nasal bridge and the normal width and height of the forehead.

In spite of the fact that head circumference SDS for height age and for chronological age was retarded (-1.23 (1.8), -2.92 (1.8) respectively), it was relatively less retarded, or relatively large in comparison to standing height SDS, sitting height SDS, arm span SDS and sub-ischial leg length SDS (Table 4) and this was in consistency with David et al.[5]

Moreover BMI SDS for chronological age was found to be considerably less retarded than other anthropometric measures and this was in agreement

with other studies[6]. Notably, standing height, sitting height, arm span and leg length SDS were not equally retarded in the studied population (Table 4). This might be due to the absence or presence of testosterone / estrogen which can modify the action of human growth hormone[14]. Hand and foot sizes in most of the studied children were below 3rd percentile and this comes in agreement with David et al.[5]

CONCLUSION

Our data suggest that GHD children have characteristic anthropomorphic differences from normal children of the same chronological age and that GHD affects the growth of the limbs and vertebral column more than that of the skull. These findings warrant a further longitudinal study of the effect of GH therapy on craniofacial and body proportions especially in population receiving GH from a younger age and for prolonged periods.

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