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BASELINE CHARACTERISTICS OF PATIENTS WITH GROWTH HORMONE DEFICIENCY

BÜYÜME HORMONU EKSİKLİĞİ OLAN HASTALARIN TEMEL ÖZELLİKLERİ

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ABSTRACT

Objective: The aim of this study was to describe the characteristics and the aetiological profile of patients with growth hormone deficiency (GHD)

Material and Method: Among randomly selected 320 cases with short stature with a height SDS<-3SD, 203 patients with diagnosis of GHD were evaluated with respect to their characteristics at diagnosis.

Results: 86 patients (42.4%) had idiopathic GHD, 79 patients (39%) had congenital GHD, 14 patients (6.9%) had defined syndromes with GHD and 10 patients (5%) had acquired GHD. Number of patients with isolated GHD was 154 (81.5%) and with multiple pituitary hormone deficiency (MPHD) was 35 (18.5%) among classified cases.

The most common accompanying hormone deficiency was TSH deficiency in GHD aetiologies with MPHD. Hypophyseal pathologies were most commonly seen in congenital and acquired GHD cases. Noonan syndrome was the most common syndrome with an accompanying GHD. The bone age delay was found to be over 2 years in congenital GHD. The mean IGF-1 SD score and the mean peak growth hormone stimulation tests' values were significantly low in congenital GHD.

Conclusions: Precise assessment of auxological, clinical and laboratory data could provide substantial value in the evaluation of severely short statured children with GHD.

Keywords: Severe short stature, children, aetiology, growth hormone deficiency

ÖZET

Amaç: Bu araştırmanın amacı büyüme hormonu eksikliği (BHE) olan hastaların karakteristik özelliklerinin ve etiyolojik profillerinin belirlenmesidir

Gereç ve Yöntem: Ağır boy kısalığı olan (boy SDS<-3SD) ve randomize seçilmiş 320 olgudan BHE tanısı olan 203 olgu ile araştırma yürütülmüştür

Bulgular: 86 hastada (%42,4) idiyopatik BHE, 79 hastada (%39) konjenital BHE, 14 hastada (%6,9) BHE eşlikli sendromlar ve 10 hastada (%5) edinsel BHE saptanmıştır. Sınıflandırılan olgular içinde izole BHE olan 154 (%81,5) ve çoklu hipofizer hormon eksikliği (ÇHHE) olan 35 (%18,5) olgu saptanmıştır.

ÇHHE olan BHE etiyoloji gruplarında en sık eşlik eden hormon eksikliği TSH eksikliğidir. Hipofizer patolojiler en sık konjenital ve edinsel BHE olgularında görülmektedir. BHE en sık Noonan sendromuna eşlik etmektedir. Konjenital BHE olgularında kemik yaşı gecikmesi 2 yıl ve üzeri saptanmıştır. Ortalama IGF-1 standart sapma skoru ve ortalama pik büyüme hormonu uyarı testi değeri konjenital BHE'de belirgin olarak düşük saptanmıştır.

Sonuç: Oksolojik, klinik ve laboratuvar verilerin titizlikle incelenmesi BHE'nin eşlik ettiği ağır boy kısalığı olan çocukların değerlendirilmesine önemli katkı sağlayabilmektedir.

Anahtar Kelimeler: Ağır boy kısalığı, çocuk, etiyoloji, büyüme hormone eksikliği

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INTRODUCTION

There are several aetiological causes of growth hormone deficiency (GHD), occurring at any level of the hypothalamic-pituitary axis causing growth hormone related growth retardation.

The prevalence of GHD differs between 1/3480 and 1/30,000 children according to the literature (1-8).

In a previous study (9), we analysed the aetiology of short stature in children with a height SDS<-3SDS. In this study, we aimed to describe the characteristics and the aetiological profile of GHD patients selected among those children. Auxological, demographic and endocrinological data are presented in relation to gender and the various aetiological diagnoses.

MATERIAL AND METHOD

This retrospective study was conducted in the Paediatric Endocrine Clinic of Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey. Randomly selected 320 severely short statured (height SDS<-3SDS) children with at least 12 months of follow-up were included in our previous study (9). Among those, 203 patients with a diagnosis of GHD were selected for this study.

Data collection

Identity records (birth dates, addresses, phone numbers), presence of parental consanguinity, mother's age at menarche, history of short stature and/or pubertal delay in the family, other familial diseases, history of precocious puberty, the height values of both mothers and fathers, the chief complaint of the patient at admission, type of birth, gestational age, anthropometric values at birth, birth complications, nutritional history, neuromotor developmental history, additional diseases and previous medications were all recorded from patients' files.

The anthropometric measurements, physical examination and pubertal findings and bone ages at admission and at follow-up were recorded from the files.

The pubertal sign was based on breast budding in females and a testicular volume of over 4 ml in males. Puberty was considered to be delayed with no sign of puberty at the age of 14 in males, and at the age of 13 in females (10). Pubertal development was assessed as recommended by Marshall and Tanner (11, 12).

Patients were divided into 2 groups according to Tanner staging to be used in comparison Tables; Stage 1 (prepubertal) and Stage >1 (pubertal).

Anthropometric measurements

Height, weight and head circumference

Ages at admission of all patients were calculated and recorded as decimal years. Three main groups were designated according to age at admission (< 5years, 5-10 years and >10years).

All data regarding height, weight and head circumference at admission of the patients were collected from patients' files. The height measurements of children and their parents in our clinic are done according to standard measurement rules by using a Harpenden stadiometer by the same auxologist. Weight measurements are done by using a scale which is sensitive to 100 grams. Body mass index (BMI) of patients were calculated by using height and weight values of the patients (kg/m^2). Height, weight and BMI SDS scores were calculated according to Turkish standards by Neyzi et al. (*13-15)* (Büyüyorum v1.3 programme was used for calculations).

SD scores of birth weight, height and head circumference were calculated according to the revised Fenton growth chart. For calculations, the Peditools Fenton 2013 programme was used (16).

Patients were divided into three groups; appropriate for gestational age (AGA), small for gestational age (SGA) and large for gestational age (LGA). Birth weight and/or length were between -2SD and +2SD in AGA, less than -2SD in SGA and greater than +2SD in LGA groups.

Target height calculation

Target height values for patients, of whom parental height values were present, were calculated according to the Tanner method (17). SD scores of these values were calculated by using Turkish standards (13-15).

Predicted adult height calculation

Predicted adult height (PAH) for each patient was calculated with the *Bayley-Pinneau* method by using the *Greulich-Pyle* atlas (18). The predicted adult height could not be calculated in males with a bone age below 7 years and in females with a bone age below 6 years. SD scores of predicted adult height values were calculated according to Turkish standards (13-15).

Formation of aetiology groups

Congenital GHD results from genetic errors, and may be associated with structural defects of the brain or with midline facial defects such as a cleft palate or a single central incisor. Several genetic defects have been identified so far. Acquired GHD can occur as a result of a variety of different causes including cranial trauma (perinatal or postnatal), central nervous system infections, tumours of the hypothalamic or pituitary region (pituitary adenoma, craniopharyngioma, glioma, germinoma, metastases), radiation therapy, infiltrative diseases (Langerhans cell histiocytosis, sarcoidosis, tuberculosis). If any other diagnosis cannot be established, the GHD aetiology is considered idiopathic. GHD can be associated with defined syndromes such as Turner's syndrome as well.

Isolated growth hormone deficiency is a condition due to a severe shortage or absence of growth hormone, whereas MPHD is an endocrine disorder due to a combination of pituitary hormone deficiencies. The diagnosis is established in a multi-step approach for each patient based on history, signs and symptoms, hormonal and radiological findings and genetic testing.

The aetiology groups for GHD were divided into 4 main groups to be used in comparison tables (19);

Group A: Idiopathic growth hormone deficiency
Group B: Congenital growth hormone deficiency
Group C: Acquired growth hormone deficiency
Group D: Defined syndromes with growth hormone deficiency
Group E: Unclassified

Since Group E constituted unclassified cases due to insufficient data, it was not used in comparison tables.

Further classification of GHD was done according to whether being isolated or MPHD:

Isolated GHD
Multiple pituitary hormone deficiency (MPHD)

Laboratory tests and methods
Calculation of bone age and bone age delay
Calculations of both bone age and bone age delay were done by using the *Greulich-Pyle* atlas. The delay in bone age was divided into 2 main groups to be used in comparison tables; bone age delay <2 years and bone age delay ≥2 years.

Hormonal tests and methods
Serum IGF-1 values
IGF-1 values were recorded from patients' files. In our clinic, the *Liaison® IGF-1 (313231) CLIA (chemiluminescent immunoassay) test (DiaSorin, Sallugia, Italy)* is used to assess the IGF-1 values in ng/ml. The SD scores of the results were calculated using the kit's data.

Serum IGFBP-3 values
IGFBP-3 values were recorded from patients' files. In our clinic, the *IMMULITE® test (Siemens, Malvern, PA, USA)* is used to assess the IGFBP-3 values in ng/ml. SD scores of the results were calculated using the kit's data.

Growth hormone provocation tests
GHD was defined as a serum peak GH concentration <10 ng/mL on provocation at two separate stimulation tests. GH stimulation tests were performed with various stimuli, such as insulin, L-dopa, clonidine, and glucagon. In prepubertal boys over 11 years, intramuscular testosterone depot injections were performed 7–10 days before GH testing; and in prepubertal girls over 10 years, oral conjugated oestrogen was prescribed for 3 days before testing.

Statistics
For statistical analysis SPSS 21.0 programme was used. *Pearsons's chi-square* and *Fisher's exact* tests were applied to sets of categorical data. *t*-test was performed for between-pairs comparison, and comparisons among groups were performed using analysis of variance. The *Mann–Whitney U* test was used when sample sizes were small and/or when the data did not approximate a normal distribution. The *LSD test* was used to find out which group differs from the others. Differences were regarded as significant when *P* value was <0.05.

RESULTS

Two hundred three (106 M/97 F) patients with a diagnosis of GHD were selected for this study. Among these, 86 patients (42.4%) had idiopathic GHD, 79 patients (39%) had congenital GHD, 14 patients (6.9%) had defined syndromes with GHD and 10 patients (5%) had acquired GHD (Table 1).

MPHD was found in 14% of cases with idiopathic GHD. The most common accompanying hormone deficiencies in those cases were TSH deficiency (75%), LH/FSH deficiency (25%) and ACTH deficiency (8%) respectively. MPHD was found in 25.3% of cases with congenital GHD. The most common accompanying hormone deficiencies in those cases were TSH deficiency (90%), LH/FSH deficiency (45%) and ACTH deficiency (15%) respectively. Twenty percent of acquired GHD cases had MPHD, and all of them were TSH deficient. Only one patient, who was both TSH and ACTH deficient, had MPHD within defined syndromes with the GHD aetiology group.

One hundred eighty-nine classified cases with GHD were also divided into subgroups; isolated GHD (n=154, 81.5%) and MPHD (n=35, 18.5%).

There was no statistical difference in means of gender, history of parental consanguinity and birth weight for gestational age distributions between GHD aetiology groups (p>0.05).

The mean age values at admission of idiopathic and acquired GHD aetiology groups were statistically higher than those of the congenital GHD aetiology group (p<0.05) (Table 2).

The mean height SD score of the idiopathic GHD group was statistically higher than that of the congenital GHD group (p=0.001) (Table 2).

The mean bone age delay at admission of the congenital GHD aetiology group was statistically found to be higher than that of the idiopathic GHD group (p<0.05) (Table 2).

The mean SD scores gathered after extraction between target height SD scores and height SD scores at admission revealed that the mean extracted SD score of the id-

Table 1: Aetiology of growth hormone deficiency (GHD).

Groups	n	%	M/F
Idiopathic GHD	86	42.4	44/42
Congenital GHD	79	39	41/38
Genetic causes (Pit-1, GH1, HESX-1 defects)[1]	3		1/2
Pituitary hypoplasia, Ectopic neurohypophysis	75		39/36
Central malformations	46		22/24
Others[2]	29		17/12
Others[3]	1		1/0
Acquired GHD	10	5	6/4
Tumour of the pituitary/hypothalamic region[4]	5		4/1
Cranial tumours distant from the hypothalamo-pituitary area[5]	1		1/0
Treatment for tumours outside the cranium[6]	2		1/1
Others[7]	2		0/2
Defined syndromes with GHD[8]	14	6.9	7/7
Unclassified	14	6.9	8/6
Total	203		

[1]Homozygous mutation in PROP1 (n=1), homozygous p.Val153Phe mutation in PIT1(POUF1) gene (n=1), homozygous deletion of exon 1-2 in PIT1(POUF1) gene (n=1), [2]Empty Sella (n=5), PVL,HIE (n=5), Partial empty sella (n=3), Chiari malformation (n=3), Arachnoid cyst (n=3), Corpus callosum hypoplasia (n=2), Cerebellar vermian atrophy (n=2), Spina bifida and hydrocephalus (n=1), Corpus callozum agenesis and trigonocephaly (n=1), Cortical atrophy (n=1), Pars intermedia cyst (n=1), Rathke cleft cyst (n=1), Moya Moya syndrome (n=1), [3]46,XX,t(13;14;9) karyotype (n=1), [4]Pituitary microadenoma (n=3), pituitary macroadenoma (n=1) Craniopharyngioma (n=1), [5]Medulloblastoma (n=1), [6]Wilms's tumour (n=2), [7]Autoimmune hypophysitis (n=1), Thalassemia major with bone marrow transplantation (n=1), [8]Noonan syndrome (n=4), Silver Russel syndrome (n=3), Perrault syndrome (n=1), Prader Willi syndrome (n=1), Rubinow syndrome (n=1), Seckel syndrome (n=1), Stuve-Wiedeman syndrome (n=1), Worster Drought syndrome (n=1), Joubert syndrome (n=1)

iopathic GHD group was statistically higher than defined syndromes with GHD groups ($p<0.05$) (Table 2).

There was no significant statistical difference among GHD aetiology groups according to their interpreted BMI SD scores and Tanner staging at admission ($p>0.05$).

The bone age delay was divided into two main groups: bone age delay below 2 years and bone age delay of 2 years and over. Patients with a bone age delay over 2 years were statistically higher in the congenital GHD group ($p<0.05$).

There was no statistical difference in means of gender, age at admission, history of parental consanguinity and birth weight for gestational age distributions between the isolated GHD and MPHD groups ($p>0.05$).

The mean birth height SD score of isolated GHD was statistically lower than the MPHD group ($p=0.001$) (Table 3).

The mean bone age delay at admission of the MPHD group was statistically found to be higher than the others ($p<0.05$) (Table 3).

There were no significant statistical differences between the isolated GHD and MPHD groups according to their interpreted BMI SD scores, Tanner staging and bone age delay groups at admission ($p>0.05$).

Mean IGF-1 SD score of the congenital GHD group was statistically found to be lower than other groups ($p<0.05$) (Table 4).

The mean peak growth hormone stimulation test value of the idiopathic GHD group was statistically higher than that of the congenital GHD group ($p<0.05$) (Table 4).

Mean IGF-1 SD score of MPHD group was statistically found to be lower than the isolated GHD group ($p<0.05$) (Table 5).

The IGFBP-3 SD score and the mean peak growth hormone stimulation test value of the MPHD group was significantly lower than that of the isolated GHD group ($p<0.001$, Table 5).

Table 2: Comparisons of birth data and patients' data at admission between GHD aetiology groups.

	Group A	Group B	Group C	Group D	F	p	*df*
Gestational week (mean±SD)	39.3±2.1	38.7±2.7	39.0±2.5	38.8±2.7	0.619	0.603	
Birth weight SDS (mean±SD)	-1.1±1.7	-0.8±1.6	-0.7±1.2	-1.2±2.0	0.566	0.638	
Birth height SDS (mean±SD)	-1.1±1.3	-0.4±1.7	-1.6±1.0	-1.9±2.4	1.985	0.125	
Age at admission (mean±SD)	9.1±3.7	7.7±4.3	11.3±4.2	8.1±5.6	2.952	0.034	**A>B C>B**
Height SDS at admission (mean±SD)	-3.8±0.9	-4.5±1.1	-4.0±0.7	-4.1±1.1	5.905	0.001	**A>B**
Weight SDS at admission (mean±SD)	-2.7±1.3	-3.1±1.6	-3.4±0.9	-3.5±1.9	1.871	0.136	
Head circumference SDS at admission (mean±SD)	-1.9±1.4	-2.1±1.9	-1.9±1.1	-2.6±1.8	0.306	0.821	
BMI SDS at admission (mean±SD)	-0.5±1.3	-0.5±1.7	-1.1±0.9	-1.1±2.3	1.113	0.345	
Bone age delay (mean±SD)	2.3±1.3	3.2±1.7	2.4±1.4	2.4±2.1	3.955	0.010	**B>A**
Predicted adult height (PAH) SDS (mean±SD)	-1.9±1.4	-2.3±1.8	-1.9±1.9	-2.9±1.8	0.588	0.625	
Target height (TH) SDS (mean±SD)	-1.5±0.8	-1.5±1.2	-1.5±0.9	-0.8±0.6	1.687	0.173	
Target height minus height SDS (mean±SD)	-2.4±1.3	-2.7±1.4	-2.3±1.1	-3.6±1.6	2.764	0.045	**A>D**

Table 4: Mean IGF-1 SDS, IGFBP-3 SDS and peak growth hormone stimulation test value comparisons between GHD aetiology groups.

	Group A	Group B	Group C		Group D		F	p	*df*
IGF-1 SDS (mean±SD)	-0.8±1.1	-1.5±1.3	-0.550	1.302	-0.769	1.464	4.186	0.007	**A>B C>B D>B**
IGFBP-3 SDS (mean±SD)	-0.5±0.9	-0.9±1.2	-0.671	0.699	-0.357	1.175	1.426	0.237	
Peak Growth Hormone Stimulation Test Value (mean±SD)	6.5±5.3	4.2±3.7	4.781	3.694	5.294	3.060	3.501	0.017	**A>B**

Table 5: Mean IGF-1 SDS, IGFBP-3 SDS and peak growth hormone stimulation test value comparisons between isolated GHD and MPHD groups.

	Isolated GHD	MPHD	t	p
IGF-1 SDS (mean±SD)	-0.9±1.0	-1.8±1.7	2.943	**0,006**
IGFBP-3 SDS (mean±SD)	-0.4±1.1	-1.3±1.1	4.037	**0,000**
Peak Growth Hormone Stimulation Test Value (mean±SD)	6.7±5.1	2.1±2.2	8.605	**0,000**

DISCUSSION

Idiopathic GHD was the most common aetiology of GHD in our study. Thomas et al. found idiopathic GHD as the most common aetiology of growth hormone deficiency (41%); followed by acquired GHD (35%), congenital GHD (20%) and defined syndromes with GHD (4%). Desai et al. also found the leading cause of GHD as idiopathic GHD (75%). So, our findings were consistent with the literature (20, 21).

Although there was a slight predominance of male patients in all the GHD aetiology groups in a study by Thomas et al., there was no statistical difference in gender in our study population. The male/female ratio of idiopathic GHD was found to be 2/1 in a study by Desai et al. Moreover, there was no statistical difference in gender distribution between GHD aetiology groups in our study ($p>0,05$). These findings were not consistent with the literature (20, 21). This might be related to a change in the perception and awareness of short stature in the society (22).

There was no statistical distributional difference in age at admission groups between GHD aetiology groups. Idiopathic, acquired GHD and defined syndromes with GHD cases tended to present at over 10 years of age; whereas congenital GHD cases had a tendency to present between 5-10 years of age. Besides, the mean age at admission of idiopathic and acquired GHD cases were statistically higher than that of congenital GHD, which is probably due to early presentation and recognition of short stature in the disease process.

There was no statistical distributional difference in history of parental consanguinity between GHD aetiology groups. The distribution of parental consanguinity was slightly higher in the acquired GHD group among others, with regard to a higher history of parental consanguinity rate than the general Turkish population found in our previous study (9).

There was no statistical difference in means of birth weight for gestational age distributions between GHD aetiology groups. The majority of the cases were AGA in all the GHD aetiology groups. Moreover, there was no statistical difference in mean gestational age at birth, mean birth weight SD scores and mean birth height SD scores between GHD aetiology groups. However, the mean birth weight SD scores of idiopathic and congenital GHD was statistically lower than that of acquired GHD in a study by Thomas et al.; which in fact was inconsistent with our findings (21). The mean height SD score of the idiopathic GHD group was statistically higher than that of the congenital GHD group in our study. There was no statistical difference in the mean weight, head circumference, target height, predicted adult height (PAH) and body mass index SD scores and the mean weight for height percentages of GHD aetiology groups at admission. Our study population was mostly regarded as normal according to their interpreted BMI SD scores and weight for height percentages. However, the mean target height SD score was statistically lower than other two groups in a study by Thomas et al. (21). Our findings support the argument that normal intrauterine growth is mostly independent from fetal pituitary hormones–unlike the critical role of the endocrine system in postnatal growth (23, 24).

There were no significant statistical differences among GHD aetiology groups according to their Tanner staging at admission. Cases were mostly prepubertal in all aetiology groups in our study.

The mean bone age delay at admission of the congenital GHD aetiology group was statistically found to be higher than that of the idiopathic GHD group. Moreover, patients with a bone age delay over 2 years were statistically higher in the congenital GHD group, when it was divided into two main groups. These findings may be related to a higher incidence of MPHD in the congenital GHD group.

Mean IGF-1 SD score of the congenital GHD group was statistically lower than other groups in our study, and the mean peak growth hormone stimulation test value of the idiopathic GHD group was statistically higher than that of the congenital GHD group as expected. But there was no statistical difference in mean IGFBP-3 SD scores among GHD aetiology groups.

Multiple pituitary hormone deficiency (MPHD) was found in 14 % of cases with idiopathic GHD. It was also found in 25.3% of congenital GHD, in 20% of acquired GHD and in 7.1% of defined syndromes with GHD. In a study by Thomas et al., MPHD was found in 13% of idiopathic GHD, in 50% of congenital GHD and in 52% of acquired GHD. As a consistent finding with Thomas et al. MPHD was found less in the idiopathic group; but the highest likelihood of MPHD in the congenital group was inconsistent with that study. In another study by Desai et al. MPHD was found in 12% of idiopathic cases; whereas it was found in 21% of organic GHD cases (20, 21). Our findings might be related to progressions in diagnostic procedures as more abnormalities are being diagnosed by imaging or at the gene level over time.

The most common accompanying hormone deficiencies in MPHD cases were TSH deficiency (75%), LH/FSH deficiency (25%) and ACTH deficiency (8%) respectively. MPHD was found in 25.3% of cases with congenital GHD. The most common accompanying hormone deficiencies in those cases were TSH deficiency (90%), LH/FSH deficiency (45%) and ACTH deficiency (15%) respectively. 20% of acquired GHD cases had MPHD and all of them were TSH deficient. Only one patient in defined syndromes with the GHD aetiology group, who was both TSH and ACTH defi-

cient, had MPHD. As a consistent finding with the study by Thomas et al.; the most common accompanying hormone deficiency in MPHD cases was TSH deficiency (21).

There was no statistical difference in means of gender, history of parental consanguinity and birth weight for gestational age distributions between the isolated GHD and MPHD groups. There was a slight distributional male predominance in the MPHD with accompanying TSH deficiency group. Both groups had higher distributions in admissions over 5 years of age. However, there was no statistical difference in the mean age at admission between both groups. There was no statistical difference in mean gestational age at birth and mean birth weight SD scores. Cases were mostly AGA. In a study by Lo et al., there were also no statistical differences in means of gender, birth weight for gestational age and mean age at admission when it was divided and compared between isolated partial GHD, isolated severe GHD and MPHD groups. Our findings for these 3 parameters were also consistent with the literature. However, in our study, the mean birth height SD score of isolated GHD was statistically lower than the other group (25). But this finding should be interpreted cautiously due to lack of birth length record data in our study population (9).

There were no significant statistical differences between the isolated GHD and MPHD groups according to their weight, height, head circumference and weight for height percentage values together with the mean target height, predicted adult height (PAH), body mass index and extracted SD scores at admission. Besides, cases were mostly normal according to their interpreted mean weight for height percentages and interpreted BMI SD scores and there were no statistical differences in both parameters between both groups in our study. As a consistent finding, Lo et al. also did not find statistical differences in mean target height SD scores between the isolated GHD and MPHD groups. However, in that study, the mean height SD score of the MPHD group was statistically lower than the other; which in fact is inconsistent with our finding. But it should also be kept in mind that our study population comprises only cases with severe short stature (25).

No matter how we could not find a significant distributional statistical difference between the isolated GHD and MPHD groups among bone age delay groups at admission; the mean bone age delay at admission of the MPHD group was statistically found to be higher than the other. In a study by Lo et al. the mean bone age delay of MPHD with the accompanying TSH deficiency group at admission was higher than the isolated partial and severe GHD groups. So, our finding was consistent with the literature (25).

There was no significant distributional statistical difference among Tanner staging groups at admission between the isolated GHD and the MPHD group. Cases were mostly prepubertal in our study population.

The mean IGF-1 & IGFBP-3 SD scores and the mean peak growth hormone stimulation test value of the MPHD group were significantly lower than that of the isolated GHD group. Lo et al. also found out that the mean IGF-1 SD score and the mean peak growth hormone stimulation test value of the MPHD group were significantly lower than the others (25).

CONCLUSION

The most common cause of growth hormone deficiency in this group was idiopathic GHD. In all the MPHD aetiology groups; the most common accompanying hormone deficiency was TSH deficiency. Hypophyseal pathologies were most commonly seen in congenital and acquired GHD cases. Noonan syndrome was the most common syndrome with an accompanying GHD. The bone age delay was found to be over 2 years in congenital GHD. The mean IGF-1 SD score and the mean peak growth hormone stimulation test value were low in congenital GHD. Precise assessment of auxological, clinical and laboratory data could provide substantial value in the evaluation of severely short statured children with GHD.

Ethics Committee Approval: This study was approved by the Ethical Committee of the Istanbul University School of Medicine (Meeting No:12 File No:2015/1272).

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