Etiologies and Clinical Patterns of Hypopituitarism in Sudanese Children

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Introduction

❖ Hypopituitarism is a rare condition where there is deficiency of one or more pituitary hormones . The clinical manifestations of hypopituitarism depend upon the cause as well as the type and degree of hormonal insufficiency. Congenital causes can be due to developmental defects or genetic mutations. Acquired causes include brain tumors , head trauma and irradiation and various causes of brain insult such as inflammatory and infiltrative cause. **[1-3]** Diagnosis and management could be very challenging and requires professional endocrine care.

❖ We report the first data on etiological factors and clinical profiles of children with hypopituitarism from Sudan.

Subjects and Methods

This study was a descriptive, hospital based, retrospective study carried out in two major pediatric endocrinology centers in Sudan (Khartoum state) from January 2006 up to December 2014. Patients' records were reviewed and relevant demographical, clinical, hormonal and image data were collected using data collection sheets. The study was approved by The Ethical Committee and Research at Gaffar Ibn Auf and Soba hospital. Statistical analysis : Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 18. Frequencies and percentages were used as descriptive parameters for data analysis. Chi square test was used to evaluate the relationship between variables. For all tests, P. value < 0.05 was accepted as significant.

Results

The study included 156 patients. One hundred and one patients were males (M: F 1.8:1). The commonest age groups were those more than 10 years (adolescents) and represented 57.7 % of patients. Consanguinity was seen in 77.8 % of patients overall and in 91% of patients with congenital etiologies. The commonest clinical presentations were short stature and poor growth (93.5%) and delayed puberty (35.3%). Congenital causes (86.5%) were more prevalent than acquired causes (13.5%) (figure 1) , there were six family clusters with multiple pituitary hormone deficiency and three families with isolated growth hormone deficiency) IGHD) (table 1). Most of the congenital cases of multiple pituitary hormone deficiency (MPHD) were phenotypic for Prop1 mutation (77.5% of sporadic cases and 50% of inherited cases). Craniopharyngioma was the commonest acquired cause, seen in 16 (10.2%) patients. Growth hormone was the most frequent hormone deficient (89.7%), The number of patients with congenital IGHD were higher (46.1%) than those with congenital MPHD (37.1%) (figure 2). MRI brain findings were significantly abnormal in patients with congenital MPHD more than those with congenital IGHD.

Charts/Graphs/Pictures

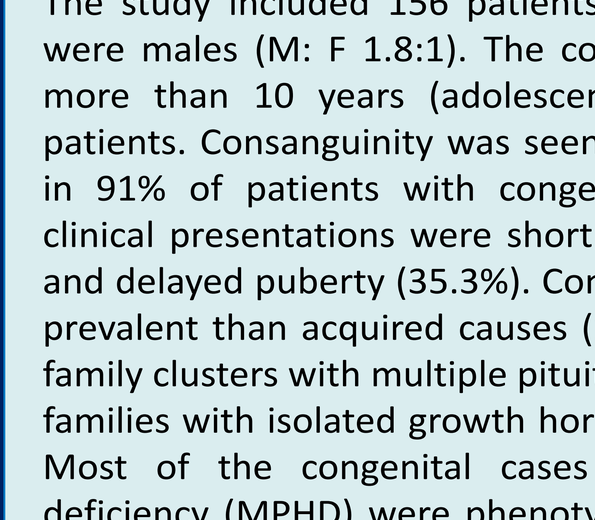

Figure 1 : patterns of pituitary hormone deficiency.

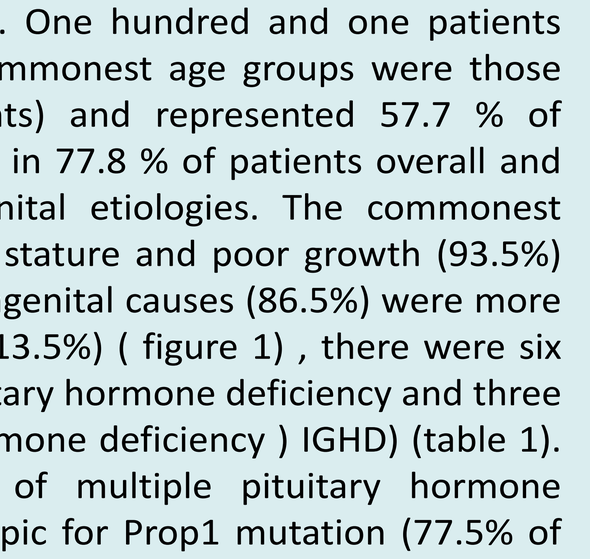

Figure 2: Types of hormone deficiencies in congenital cases

Family number	Number and gender of affected siblings	Hormones deficient	MRI brain	Phenotype
1	3 F M M	MPHD TSH,ACTH,GHD TSH,ACTH,GHD,ADH TSH,ACTH,GHD	Normal MRI except one patient had postmeningitic infraction	PROP1
2	2 M F	MPHD TSH, ACTH TSH,ACTH	Enlarged pituitary both patients	PROP1
3	2 M M	MPHD GHD,TSH GHD,TSH	Normal	PIT/PROP1
4	3 F F M	MPHD GHD,TSH GHD,TSH GH,TSH	Empty sella	PIT/PROP1
5	3 M M F	MPHD GHD,TSH GHD,TSH GHD,TSH	Not done	PIT/PROP1
6	2 F M	IGHD GHD,TSH,ACTH,PROLACTIN GHD,TSH,ACTH	Pituitary hypoplasia	PROP1
7	4 (two M)	IGHD	normal	
8	2 (two F)	IGHD	normal	
9	2 (two M)	IGHD	normal	

Discussion

- The number of patients diagnosed, when taking the nine years of the study period into consideration , was relatively large, with only a few other similar studies surpassing it the immediate explanation is the high rates of consanguineous marriages in the Sudanese population reflected in the percentage of cases with parents of 1st or 2nd degree cousinship (77.8%).

- In the literature hypopituitarism is mainly due to compressive pituitary tumors and/or secondary to their treatments (surgery or radiotherapy). Congenital hypopituitarism is less frequent. Its incidence is estimated between 1/4000 and 1/10,000 live births **[4].** In this study the number of patients with congenital causes outweighed those with acquired causes. Sporadic cases were observed in 66.6 % of the patients. Again, the high rates of consanguineous marriage may explain the larger magnitude of congenital causes.

- It is known in the litriture that structural pituitary abnormalities occur in approximately 50-70% of patients with congenital form of growth hormone deficiency (GHD) **[5].** Similar to our findings these abnormalities are more prevalent in patients with MPHD (90%) than in IGHD (20-50%)**[6].** Contrary findings were found in a study that described the clinico-radiological correlation in thirty one children (23 boys), aged 1-17 year **[7]** they observed almost similar prevalence of imaging abnormalities in IGHD and MPHD groups but they attributed this to the more number of patients with severe GHD (< 3 ng/mL) in IGHD group.

Conclusions

Congenital Hypopituitarism in populations with high rates of consanguineous marriage such as Sudan , maybe at a higher incidence than international data. Genetic studying is of great value in these populations

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