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Incidence of Growth Hormone Deficiency in Holy Karbala City

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Abstract

Background: Short stature is a major health problem in pediatric age group that needs health assessment to reach the cause. One of the treatable causes of short stature in pediatric is growth hormone deficiency which is either acute or chronic.

Aim of study: To assess the incidence of G.H.D in pediatric patients with short stature in Al-Hassan centre of endocrinology and diabetes in Karbala province.

Results: Incidence of growth hormone deficiency was 1/2500 of total target population with male to female sex predilection 1.3/1.

Conclusion: Relatively higher incidence of growth hormone deficiency comparable with other studies may be partly to include patients from areas outside the province. Due to lack of treatment in their regions and may be partly due to need for more strict criteria in laboratory works like usage of two provocation tests instead of one. With use of priming test in adolescent patients to increase the specificity of the provocation test.

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Introduction

Growth Hormone Deficiency

GHD has a prevalence of ~1 in 4000 during childhood. Although rare, it is an important diagnosis because therapy with recombinant human GH (rhGH) is very effective and a missed diagnosis will result in a poor outcome [1]. The diagnosis includes growth assessment, biochemical investigation of the GH/IGF-I axis and imaging of the hypothalamo-pituitary area. Before evaluation of the GH/IGF-I axis, other diagnoses, such as familial short stature, hypothyroidism, Turner syndrome, coeliac disease, chronic illness such as Crohn's disease and skeletal dysplasias, should be excluded [2].

The GH axis is more susceptible to disruption by acquired conditions than are other hypothalamic-pituitary axes. Recognized causes of acquired GH deficiency include the use of radiotherapy for malignancy, meningitis, histiocytosis, and trauma [3].

GH deficiency should be suspected in children with severe postnatal growth failure [4].

Criteria for growth failure include:

- Height below the 1st percentile for age and sex.
- Height >2 SD below sex adjusted mid-parental height.
- Acquired GH deficiency can occur at any age, and when it is of acute onset, height may be within the normal range.

But use of height velocity parameter in I.G.H.D with the absence of short stature, a height velocity more than 2 SD below the mean over 1 year or more than -1.5 SD sustained over 2 years that may occur in GHD presenting in infancy or in organic acquired GHD.

- Signs indicative of an intracranial lesion.
- Signs of multiple pituitary hormone deficiency (MPHD).
- Neonatal symptoms and signs of GHD. GHD can be isolated (IGHD) or a component of MPHD.

The presentation in the neonatal period is with hypoglycaemia, prolonged conjugated hyperbilirubinaemia and micropenis. Birth size is typically within the normal range, although there may be a reduction of ~10% that occurs typically late in pregnancy. Growth velocity is reduced during the first year of life in children with severe GHD but the phenotype evolves after 1 year of age in those with mild GHD [5].

The earliest manifestations are a reduction in height velocity followed by a reduction in height SDS adjusted for mean parental height SDS. the time taken depending on the severity and duration of GHD. A child with GHD often has midface hypoplasia, hypotonia, a high-pitched voice, immature appearance, delayed dentition, thin sparse hair, slow nail growth and truncal adiposity. GHD is also associated with effect on cognition [5].

A strong clinical suspicion is important in establishing the diagnosis because laboratory measures of GH sufficiency lack specificity. Observation of low serum levels of IGF-1 and the GH-dependent IGF-BP3 can be helpful, but IGF-1 and IGF-BP3 levels should be matched to normal values for skeletal age rather than chronological age [6].

Definitive diagnosis of GH deficiency traditionally requires demonstration of absent or low levels of GH in response to stimulation. A variety of provocative tests have been devised that rapidly increase the level of GH in normal children. These include administration of insulin, arginine, clonidine, or glucagon. In chronic GH deficiency, the demonstration of subnormal linear growth, a delayed skeletal age, and low peak levels of GH (<10 ng/mL with 2 pharmacologic test).

In acute GH deficiency, a high clinical suspicion of GH deficiency and low peak levels of GH (<10 ng/mL with 2 pharmacologic tests [7].

Some studies indicate that a majority of normal prepubertal children fail to achieve GH values >10 ng/mL with 2 pharmacologic tests. The researchers suggest that 3 days of estrogen priming should be used before GH testing to achieve greater diagnostic specificity [2]. In addition to establishing the diagnosis of GH deficiency, it is necessary to examine other pituitary functions. Levels of TSH, free thyroxine, ACTH, cortisol, gonadotropins, and gonadal steroids might provide evidence of other pituitary hormonal deficiencies. Antidiuretic hormone deficiency may be established by appropriate studies [8].

Patients and Methods

A cross sectional study conducted in Alhassan specialized centre for diabetes and endocrinology in Al-Hussein teaching hospital in Karbala. Many patients were evaluated for short stature during the period between Jan, 2017 to Dec, 2018 only 768 patients had been received growth hormone replacement therapy in outpatient clinic less than 15 years old. For each one an auxologic parameters done (height, weight and mid parental height on growth chart according to age and gender).Further evaluation to whom matching criteria of short stature (below 2.25 standard deviation for height, or 2 standard deviation below expected gender adjusted mid-parental height) bone age assessed by Tanner-Whitehouse II method (TW II) and investigation as renal function, thyroid function, coeliac screen, blood picture and other sophisticated evaluation if indicated according to patient condition to rule out underlying organic causes of short stature. Growth hormone level assessment is mandatory in form provocation test with clonidine 5 mcg\kg (blood sample from fasting patient before administration of clonidine dose then at least two blood samples after one and two hours of clonidine administration with clinical observation of vital sign and blood sugar to avoiding any complication). GH deficiency considered for responses < 10 ng/ml; results must be interpreted in the context of auxologic data. Because GH levels rise during puberty, many children who fail provocative GH stimulation testing before puberty may have normal results after puberty or when primed with gonadal steroids [9].

Results

In these three years (2017, 2018 and 2019),781 patients were evaluated and registered as short stature with growth hormone deficiency. Only 652 patients were included in our study and received growth hormone replacement therapy when available in our specialized centre for endocrinology, their age were 5-15 years. Newly diagnosed cases 117, 251 and 284 in that three consecutive 2017, 2018 and 2019. Total population of pediatric age group between 5-15 years, was 485208, 498081 and 511187 in that three consecutive were registered in statistical unit in holy Karbala health department. Incidence for each year calculated as in figure 1, and average of these three years was 1\2500 as in figure 2.

The gender predilection was males predominant in 2017 and 2019, while in 2018 females were predominant.as average males were predominant in these three consecutive years as showing in table 1 and figure 3. While figure 4 show predominantly males affected than females in ratio 1.3:1 (male:female ratio).

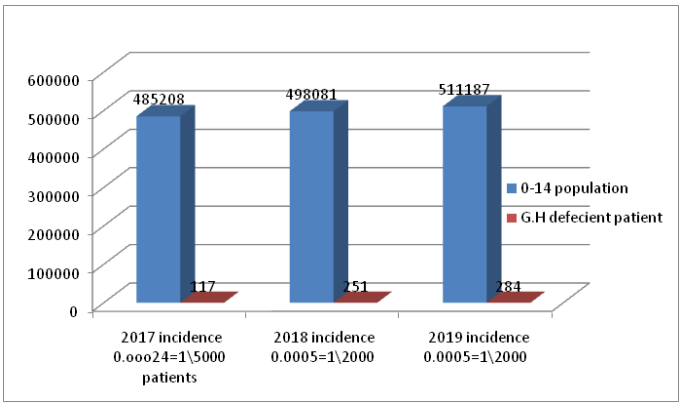

Figure 1: Incidence of growth hormone deficiency in Karbala at 2017, 2018 and 2019.

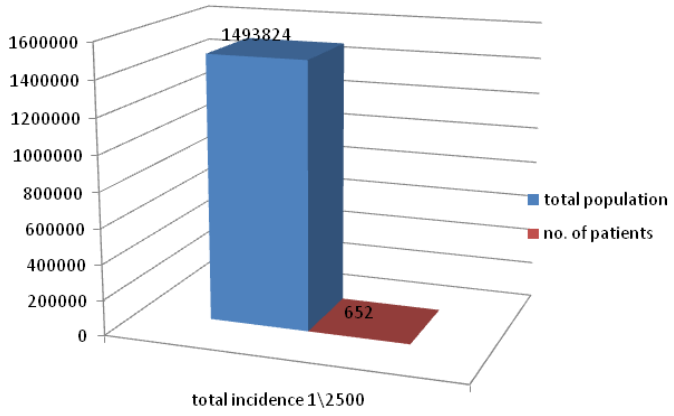

Figure 2: Mean of the incidence of growth hormone deficiency in Karbala at 2017, 2018 and 2019.

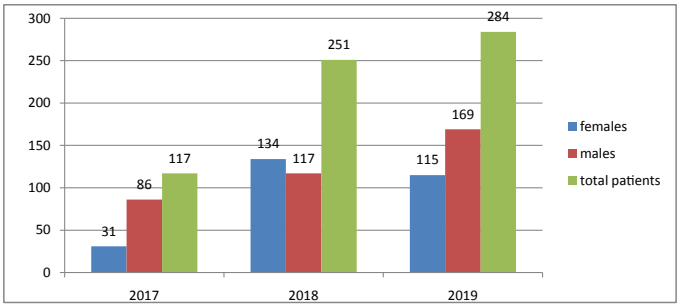

Figure 3: Number of newly diagnosed growth hormone deficiency males and females during 2017, 2018 and 2019.

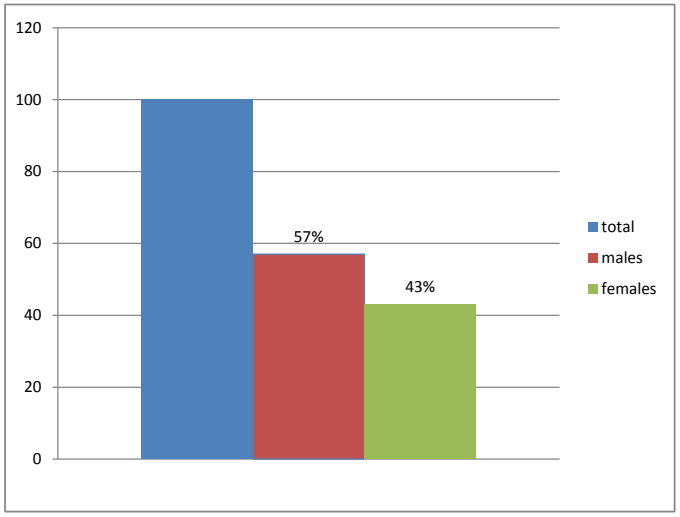

Figure 4: Percent and male:female ratio 1.3:1.

Table 1: Number of newly diagnosed growth hormone deficiency males and females during 2017, 2018 and 2019.

Year	Total number	Number of Males	Number of Females
2017	117	86	31
2018	251	117	134
2019	284	169	115
	652	372	280

Discussion

Incidence of growth hormone deficiency in our centre was 1/2500 of population at risk aged between 5-15 years while prevalence of GHD in the United States is at least 1:3480 [10].

Short stature and growth failure in children and adolescents AD Rogol, GF Hayden incidence of one in 3,000 to 9,000 [11]. Both of these studies are lower than our result, mostly due to some patient from other neighbouring city, especially when treatment unavailable in other centres.

Male: female ratio in our study was 1.3:1 which is similar to study done in King Khalid University Hospital (KKUH), King Saud University (KSU), Riyadh, Saudi Arabia. Their age ranged between 2 years and 6 months to 14 years. The male to female ratio was 1.3:1 [12].

Recommendations

- Further research to evaluate short stature cases using more strict exclusion criteria regarding the patients not recorded in province statistics.
- Provide updated investigations to evaluate short stature cases based upon strict clinical and auxological criteria with use of 2 provocation test as lab. Parameter and giving priming sex hormone dose to adolescent patients [13].
- Provide recommended treatment to short stature cases continuously as requirement.

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