



Evaluation of Thyroid Function Test in kids with Insufficient Growth Hormone

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تقييم اختبار وظائف الغدة الدرقية لدى الاطفال اللذين يعانون من قصور هرمون النمو

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ABSTRACT

Background:

The purpose of this study is to demonstrate the effects of thyroid hormone testing and other variable biochemical on childhood growth hormone insufficiency.

Materials and Methods:

There are thirty (30) kids in the growth hormone deficiency group and thirty (30) kids in the control group, ages five to twelve. The demographic data of every participant is documented. Blood samples are obtained for the following types of laboratory analysis: Serum total T3, total T4, and TSH growth hormone levels were measured using kits. While the quantification of fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG), high density lipoprotein HDL, low density lipoprotein LDL, and very low density lipoprotein VLDL was done automatically.

Results:

While there no statistically significant was difference in FBS, TC, HDL, or LDL between the children with GHD and the control group across the several sets of biochemical data, there is a very noticeable reduction in TT4 and TSH in GH deficient children when compared to the control group. There was no statistically significant difference between the two groups about to TT3 .

Conclusion:

The findings lead us to the conclusion that a key contributing factor to children's lack of growth hormone is thyroid hormone imbalance, and that early diagnosis of both the thyroid gland and growth hormone levels in children is crucial to preventing short stature in them.

Key words: Growth Hormone, Thyroid function test , FBS, Lipid profile, GHD_.



INTRODUCTION:

Somatotropin, known as growth hormone (GH), is a polypeptide chain consisting of 191 amino acids, two di-sulfide bridges, and a molecular weight of 22 kDa. [1]. The primary goal of GH is to improve children's longitudinal growth. It does, however, have a broad effect on fat, muscle, and bone tissue, as well as several other body organs. Thanks to its interaction with insulin-like growth factors (IGFs), GH can either directly or indirectly alter tissues and organs [2]. When a child's height is two standard deviations (SD) or less below the range for children of that aged and gender, it is deemed that the child has short stature. [3]. This problem, can have a number of underlying reasons, such as genetic, environmental, or chronic health issues, is common in children who are small in stature. One of the most common reasons of low height is either congenital or acquired growth hormone deficiency [4]. Short stature can be diagnosed by a combination of physical examination and laboratory testing; but, before short stature can be treated, the right diagnosis and underlying reason must be found [5]. A medical condition called growth hormone deficit (GHD) is caused by a shortage of growth hormone and usually manifests in childhood or infancy. As to the findings, brain abnormalities are the most common occurrence in 75% of cases of this disease, with no known cause [6]. It is possible for GHD to coexist with the lack of further anterior or posterior hormonal deficiencies. GHD, a rare yet important cause, it has been connected to children's low height [7]. Currently, growth hormone deficiency is diagnosed by neuroradiological, biochemical, auxological, and clinical testing. Provocative GH secretion testing using pharmacological or physiological stimulation is used to confirm GHD. Thyroid dysfunction is defined as a changed blood level of thyroid stimulation hormone (TSH) in the context of Thyroid hormones: normal or changed. Thyroid dysfunction is a serious public health concern that can be impacted by racial, environmental, and iodine intake patterns [8]. Hypothyroidism and hyperthyroidism are two prevalent thyroid diseases; the former is significantly more common than the latter. Hypothyroidism, with a clinical formula of 0.2% in mature males and 2% in adult women, is a highly prevalent condition. The clinical topographies of hypothyroidism are influenced by the patient's age, the existence of concomitant illnesses, and the rate at which the ailment progresses [9]. Developmental delay has thyroid-stimulating hormone (TSH) as a secondary factor. This hormone is produced by the pituitary gland. Adrenocorticotrophic hormone (ACTH) stimulates the thyroid gland to produce the hormone that regulates the body metabolic functions and the adrenal gland to produce cortisol[10]. Growth hormone stimulates lipolysis in adipose tissue, which results in a notable release of free fatty acids into the bloodstream [10]. Children with GHD are more likely to experience lipid problems. Conversely, there is an inverse relationship between GH levels and the amount of abdominal fat [11]. Abnormal lipid and glucose metabolism, together with an increase in belly fat, are the consequences of GHD [12]. Development hormone deficiency (GHD) can occur at any stage of life, from infancy to old age [13]. The purpose of this study is to demonstrate the effects of thyroid hormone testing and other biochemical processes (lipid profile) on childhood growth hormone insufficiency.



MATERIALS AND METHODS:

Participants in this study were thirty (30) children who are attend the center teaching hospital of pediatrics in 2023 and thirty (30) kids between the ages of five and twelve in the control group. Thirty (30) children had growth hormone insufficiency.

Every participant's age, height, weight, and BMI were noted along with their other demographic data. Blood samples were obtained for the following types of laboratory analysis: Serum total T3, total T4, and TSH levels were measured using Mini Vidas and Biomerix Kits. Growth hormone levels were ascertained by measuring cheliumenesence. While the quantification of FBS, TC, TG, HDL, LDL, and VLDL was done automatically.

The registration of the acquired data and the entire statistical procedure are finished with the help of the Microsoft Office Excel 2010 Worksheet. The t-test at P-value determines differences that are statistically significant at < 0.05 .

RESULTS AND DISCUSSION

Growth hormone deficiency (GHD) is a medical condition caused by insufficient growth hormone and can begin in infancy or youth. Brain abnormalities are the most prevalent symptom and the underlying etiology of the illness is unclear in 75% of cases [14]. As can be seen in Table 1 showed that, although the growth hormone deficient children's high weight and body mass index had significantly decreased, there was no appreciable age difference between them and the control group. This is in line with a different study. This suggests that height has a substantial impact and is compatible with another severe type of growth retardation, namely severe slowing of growth (high velocity 5th percentile of age), in the absence of a convincing alternative explanation [15].

I agree with this study, which demonstrates that the high-dose group underwent greater changes in height, body weight, and bone age than the low-dose group did after six months of treatment [16].

According to a different study, GHD may present alone or in combination with other anterior or posterior hormonal issues. Despite being rare, GHD has been shown to be a major factor in the childhood syndrome known as minors [17].



Table (1): shows the anthropometric measurements of control and GHD children

Parameters	Children with newly diagnosis GHD	Control group	P-value
	Mean±SD	Mean±SD	
Number	30	30	
Age(year)	8.4 ± 2.44	8.4 ± 2.61	N.S
High(cm)	109.9 ± 11.12	122.9 ± 14.4	**H.S
Weight(kg)	19.18 ± 4.5	27.31 ± 9.68 2	**H.S
BMI (kg/m ²)	16.36 ± 2.83	23.15 ± 3.7	**H.S

NS is no significance differences.

*p<0.05 is a significant.

**p<0.01 is a high significant

Variable statistics demonstrate how thyroid hormones control how big a person gets [18].

Regarding TT3, there was no discernible difference between the two groups in Table (2). On the other hand, GH-deficient kids had far lower TT4 and TSH levels than the control group, while newly diagnosed children, growth hormone deficient children, and the control group showed a very significant increase in TT4 and TSH. With respect to the thyroid profile findings, there is no discernible variation in the TT3 levels between the GHD and control subjects. Its TSH and TT4 concur with the results of another study [19] that the most common condition is TSH insufficiency. The next most frequent interval between the development of further pituitary hormone insufficiency and the diagnosis of GHD was 31% for TSH. TSH levels in the group as a whole did not change substantially following the commencement of GH treatment, whereas FT4 levels declined after the second year of GH medication (p 0.01) and stayed below baseline until the conclusion of observation (p 0.01, after both the third and fourth years of treatment). Based on baseline pubertal status, only statistically significant rises in TSH and TT4 levels are observed with GH treatment in prepubertal children [20,21]. Even after accounting for variations in SDS height and bone age, multiple regression analysis showed that the average GH dosages given during the first two years of GH treatment were independently (R = 0.218, p 0.05) related with changes in TT4 levels during this period (TT4(2 years – baseline)).



Table (2): Comparison of the thyroid hormone profiles in kids with GHD and controls

Parameters	Children with newly diagnosis GHD	Control group	P-value
	Mean±SD	Mean±SD	
TT3(mMole/L)	1.96 ± 1.0	2.0 ±0.82	N.S
TT4(mMole/L)	55.27 ± 15.4	101.4± 25.78	**H.S
TSH(mIU/ml)	12.7 ±12.49	2.8±2.58	**H.S

NS is no significance differences.

*p<0.05 is a significant.

**p<0.01is a high significant

The anti-lipolytic effects of hyperinsulinemia can also be countered by growth hormone [22]. While total cholesterol (TG) is considerably reduced in the GHD children's group compared to the control group, Table 3 shows that no statistically significant difference was found in FBS, TC, HDL, or LDL between the GHD children and the control group in any of the several sets of biochemical data. GH induces lipolysis by blocking the absorption of insulin and raising glucose levels mostly in muscle but also in the liver [23]. Furthermore, GH plays a critical role in regulating lipoprotein metabolism [24].

Consistent with previous studies, our results shows that children with GHD had higher TG levels. It is now thought that growth hormone increases lipolysis, lowers tissue lipid content, and modifies the rate at which adipocyte fat dissolves via activating the -adrenergic receptor in adipocytes [25].GH promotes blood lipid metabolism, reduces the pace of LDL-C production, and improves the liver's capacity to absorb LDL. It also regulates the degree of hepatic LDL-C receptor mRNA expression [26]. Because of liver's capacity to breakdown and reduce lipids is compromised in GHD patients, children with the disorder have much higher levels of lipids than children without it [27]. Furthermore, it has been observed that rhGH therapy significantly enhanced the metabolism of fats in kids with GHD. Further research is needed to determine other potential mechanisms in GHD children that could lead to dyslipidemia [28]. Children with growth hormone deficit (AOGHD) have been reported to have impaired glucose and insulin resistance in addition to increased liver glucose production.



Table (3): differences in biochemical markers between GHD and control children.

Parameters	Children with newly diagnosis GHD	Control group	P-value
	Mean±SD	Mean±SD	
FBS (mg/dl)	79.9±5.14	81.1± 5.34	N.S
TC(mg/dl)	150.43±33.4	161.46±21.75	N.S
TG(mg/dl)	86.5±6.99	90.6±2.2	*S
HDL(mg/dl)	53.1±5.2	52.4± 5.4.	N.S
LDL(mg/dl)	80.03±30.65	90.94±22.0	N.S

NS is no significance differences.

S, significance differences

*p<0.05 is a significant.

**p<0.01 is a high significant

The idea underlying growth hormone deficit (GHD) is that kids with low GH levels react to stimuli by producing less GH than kids with normal GH levels.

When comparing children with growth hormone insufficiency to those in the control group, Table 4 demonstrates a highly significant decline in growth hormone. Children with GHD usually grow slowly, gaining less than 2 inches annually. It may take till the child is 2 or 3 years old to notice the slower pace of growth. Compared to most or all children of the same age and gender, they will be noticeably tiny. The main cause of GHD is mainly unknown. It could result from an injury or medical condition, or it might be innate. . In addition, serious brain injury [29] might cause GHD. The roles of insulin-like growth factor-1 (IGF-1), IGFBP 3, and growth hormone (GH) in the diagnosis of growth hormone is seen . A pubertal development delay may or may not occur in people with short stature (SS), both familial and non-familial. The most common conditions for which human growth hormone is give , are Turner's syndrome, chronic renal failure, and childhood low stature caused by GHD .Growth hormone [30] is one of the hormones that is most commonly supplemented.

It is commonly recognized that growth hormone (GH) affects many aspects of metabolism, including glucose and lipid homeostasis [31,32]. The findings lead us to the conclusion that a key contributing factor to children's lack of growth hormone is thyroid hormone imbalance, and that early diagnosis of both the thyroid gland and growth hormone levels in children is crucial to prevent short stature in them.



Table (4) Growth Hormone Level between Children with GHD and Control

Parameters	Children with newly diagnosis GHD	Control group	P-value
	Mean±SD	Mean±SD	
GH (ng/ml)	0.332± 0.36	1.27± 0.7	**H.S

NS, no significance differences.

*p<0.05 is significant.

**p<0.01 is highly statistically significant

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Conflict of interests.

There are no conflicts to declare.

References

- [1] G. Baumann, "Growth hormone isoforms". *Growth Hormone & IGF Research*, Vol. 19 no 4 pp. 333-340. 2009.
- [2] H. Green, M. Morikawa, and T. Mxon, "A dual effector theory of growth-hormone action". *Differentiation*, Vol. 29, no 2 pp. 195-198.
- [3] D. Alan "Causes of short stature." Up To Date online 14, 2019.
- [4] M. Haymond, et al., "Early recognition of growth abnormalities permitting early intervention". *Acta Paediatrica*, Vol. 102, no 8, pp. 787-796. 2013.
- [5] N. Albalawi, et al., "Short Stature in Children". *The Egyptian Journal of Hospital Medicine*, Vol. 70, no 2, pp. 228-233. 2018.
- [6] B Rikken 1, J van Busschbach, S le Cessie, W Manten, T Spermon, R Grobbee, J M Wit "Impaired social status of growth hormone deficient adults as compared to controls with short or normal stature". *Clinical Endocrinology*. Vol. 43, no 2, pp. 205-211. 1995.
- [7] D., Mehul T., and N. Malhotra. "A review of growth hormone deficiency." *Paediatrics and Child Health*. Vol. 29, no 7, pp. 285-292. 2019.
- [8] D, Daniel, K. Tesfa, and B. Biadgo "Thyroid dysfunction and cytological patterns among patients requested for thyroid function test in an endemic goiter area of Gondar, North West Ethiopia." *International Journal of Endocrinology* 2019.
- [9] M., Sudeb, et al. "A study of prevalence of primary hypothyroidism in recently diagnosed type 2 diabetes mellitus in a tertiary care hospital." *Int J Sci Rep* vol.1, no2, pp 105-112. 2015.
- [10] Z., Yuchao, et al. "The effect of growth hormone on lipid accumulation or maturation in adipocytes." *Cellular Physiology and Biochemistry* vol.39, no6, pp: 2135-2148. 2016.



- [11] V., Alessandra, C. Guzzetti, and S. Loche. "New aspects of the physiology of the GH-IGF-1 axis." *Hormone Resistance and Hypersensitivity* vol. 24, pp. 96-105. 2013.
- [12] B. Bengtsson, et al. "Cardiovascular effects of GH". *Journal of endocrinology*, Vol. 152, no 1, pp 1-3. 1997.
- [13] C., Manuela, and M.T. Dattani. "Progression from isolated growth hormone deficiency to combined pituitary hormone deficiency." *Growth Hormone & IGF Research* Vol. 37, pp. 19-25. 2017.
- [14] C., Manuela, and M.T. Dattani. "Progression from isolated growth hormone deficiency to combined pituitary hormone deficiency." *Growth Hormone & IGF Research* Vol. 37, pp. 19-25. 2017.
- [15] B. Rikken, et al, "Impaired social status of growth hormone deficient adults as compared to controls with short or normal stature". *Clinical Endocrinology*, Vol. 43, no 2, pp. 205-211. 1995.
- [16] D., Mehul T., and N. Malhotra. "A review of growth hormone deficiency." *Paediatrics and Child Health*, Vol. 29, no 7, pp: 285-292. 2019.
- [17] R. Rosenfeld, "Is growth hormone deficiency a viable diagnosis?. *The Journal of Clinical Endocrinology & Metabolism*, Vol. 82, no 2, pp: 349-351, 1997.
- [18] Y. Xue, et al, "An examination of the effects of different doses of recombinant human growth hormone on children with growth hormone deficiency". *Experimental and therapeutic medicine*, Vol. 11, no 5, pp: 1647-1652, 2016.
- [19] W.S., Ewelina, et al. "Thyroid function in children with growth hormone deficiency during long-term growth hormone replacement therapy." *Central European Journal of Immunology*, Vol. 43, no 3, pp: 255-261. 2018.
- [20] R Valcavi 1, F Valente, C Dieguez, M Zini, M Procopio, I Portioli, E Ghigo. "Evidence against depletion of the growth hormone (GH)-releasable pool in human primary hypothyroidism: studies with GH-releasing hormone, pyridostigmine, and arginine." *The Journal of Clinical Endocrinology & Metabolism*. Vol. 77, no 3, pp: 616-620. 1993.
- [21] E., Witkowska-Sędek; A. Borowiec; A., Majcher; M., Sobol; M., Rumińska; B. Pyrzak. Thyroid function in children with growth hormone deficiency during long-term growth hormone replacement therapy. *Central-European journal of immunology*, Vol. 43, no 3, p. 255, 2018.
- [22] E., Witkowska-Sędek; et al. "Thyroid function in children with growth hormone deficiency during long-term growth hormone replacement therapy." *Central European Journal of Immunology* Vol. 43, no 3, pp: 255-261. 2018.
- [23] M., Wabitsch; et al. "In vitro effects of growth hormone in adipose tissue." *Acta Pædiatrica* Vol. 83, pp: 48-53. 1994.
- [24] P.E., Lobie "Signal transduction through the growth hormone receptor. In: Bengtsson BA (ed). *Growth Hormone*". Kluwer Academic Publishers: Boston, pp 17–35.1999.
- [25] S.Y., Nam ; P.E.,Lobie . "The mechanism of effect of growth hormone on preadipocyte and adipocyte function". *Obes Rev* pp:1:73–86. 2000.
- [26] F.U, Chun-Jiang; X.K., Wang; C.M., Yang; H.Y., Wang; Y.Q., Fang, W.B., Shi."Effects of recombinant growth hormone on serum lipid levels and hepatic LDL receptor mRNA of rabbits". *Acta Acad Med Militaris Tertian*, pp: 27:753–5. 2005.
- [27] L., Roberto, et al. "Cardiac mass and function, carotid artery intima-media thickness, and lipoprotein levels in growth hormone-deficient adolescents." *The Journal of Clinical Endocrinology & Metabolism*, Vol. 86, no 3, pp: 1061-1065. 2001.
- [28] C., Ming, et al. "Effect of recombinant human growth hormone therapy on blood lipid and carotid intima-media thickness in children with growth hormone deficiency." *Pediatric research* Vol. 83, no 5, pp: 954-960.2018.

