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Is childhood short stature effect on thyroid and kidney functions?

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ABSTRACT

Background: Growth process is a combination of several factors, including genetic, environmental, nutritional, metabolic and health problems including thyroid and renal diseases, and this process depends mainly on age and gender. A set of standard data ranges (head circumference, height, and weight) are determined at each stage of natural growth, and if the growth pattern less than these ranges, this leads to short stature and growth failure .

Methods: Serum triiodothyronine (T_3) , thyroxine (T_4) and thyroid stimulating hormone (TSH) concentrations were assayed by using the Japanese TOSHO AIA-360 Automated Immunoassay Analyzer, also glucose, creatinine and urea were estimated by using BIOLABO kits (France) in 30 healthy children as control group and 60 patients with short stature , age range (5 - 14) years.

Purpose: This study aimed to evaluate some biochemical parameters related to thyroid and kidney to determine the extent to which the parameters are affected by this disease, which reflect function imbalance of the relevant organs, and to use it as a diagnostic tool that helps in the early treatment and follow-up of the short stature state.

Results: The results showed that all biochemical parameters were studied representing by the concentrations of T_3, T_4, TSH, glucose urea and creatinine did not show any significant difference in children with short stature compared to the control group. However, TSH, creatinine and urea showed an increase by (31.8 %,),(6.1 %) and (2.7 %) respectively, while a decrease in the concentration of T_3 was observed by (9.4%) in children with short stature compared to control group.

Conclusions: It appears that, the condition of short stature in children does not have a clear effect on kidney and thyroid functions, as well as regulation mechanism of thyroid hormones secretion by TSH.

Keywords: *Growth, Short stature, Thyroid, Kidney.*

INTRODUCTION

The growth process is a combination of several factors, including genetic, environmental, nutritional, behavioral, metabolic and health problems, and depends mainly on age and sex. A group of standard criteria (head circumference, height, and weight) are determined at each stage of normal growth, and if the growth pattern within these criteria indicates good general health, but when it is less, this leads to short stature and slow growth. Clinical evaluation of children with short stature includes medical, social, and family history, physical examination, and most importantly, interpretation of the growth curve [1].

The thyroid gland secretes two main hormones, triiodothyronine (T_3) and tetraiodothyronine (T_4) is also called thyroxine .Thyroid hormones bind to proteins when they are released into the bloodstream, but a small amount of the hormones remains unbound (free) and are called FT_3 and FT_4 and are biologically effective [2]. Thyroid hormones are iodinated derivatives of the amino acid tyrosine and their functions are similar, but they differ in the effectiveness and speed of their effect. T_3 is four times more effective than T_4 and has less affinity for the proteins that transport it, so it is released quickly, while T_4 has larger affinity and binds strongly to transport proteins, so its release is slower. Therefore, the effect of T_3 is stronger and faster than T_4 on the target cells, but the period of its stay in the blood is shorter, as the half-life of T_4 is about 7 days but T_3 is between 10 and 24 hours. Concentration of T_3 is less compared to T_4, where level of T_3 in plasma is about (0.12) micrograms/dL, while T_3 reaches (8) micrograms/dL, and the daily secretion rate of T_4 is about (80-90) micrograms, while T_3 is (4-5) micrograms. T_4 is converted to T_3 in peripheral tissues by deiodinase enzyme. Most of the T_3 inside the pituitary gland cells is derived from T_4, so this gland is more sensitive to changes in the concentration of plasmaT_4 than the T_3 [3].

Thyroid-stimulating hormone (TSH), also called thyrotropin, is a peptide consisting of alpha and beta chains. Its half-life is about (600 minutes and its normal level in the blood is (2) units/ml. TSH stimulates the thyroid gland to secrete its hormones (T_4 and T_3) by increasing the degradation of thyroglobulin (TG), increasing the activity of the iodide pump, adding iodine to tyrosine to form

thyroid hormones, and also increases the size and number of thyroid gland cells, which contributes to increasing its secretory activity [4].

Thyroid hormones is regulated through the hypothalamus-pituitary-thyroid axis, which depends on the negative feedback system, as TSH is produced and secreted from the anterior pituitary gland by stimulating of the thyrotropin-releasing hormone (TRH), the latter is tripeptides produced from the hypothalamus [5].

Thyroid hormones play an important role in regulating vital processes in the body such as growth, metabolism, and organ functions [6]. Normal levels of thyroid hormones accelerate the growth of the body, especially in children, while their decrease stops or slows down growth, and at the same time causes the closure of the epiphysis, so the height of the person is somewhat short in the case of hypothyroidism. Thyroid hormones also have an important role in promoting the development of the brain and its growth during pregnancy and the first months after birth, as the deficiency of these hormones in this period leads to mental retardation and lack of physical growth, which is called cretinism, and this condition is incurable unless it is treated during the first months of life [7].

About one-third of children suffer from growth failure if they suffer from chronic kidney disease (CKD). This may be due to other influencing factors such as anemia, loss of appetite, and an imbalance of phosphorus and calcium due to disturbances in parathyroid hormones and vitamin D_3 and renal osteodystrophy, In addition renal tubular acidosis (RTA) also causes poor growth in children, and in this case alkaline treatments have a beneficial effect in achieving normal height [8].

MATERIALS AND METHOD

In all patients with Short stature and controls, 5 ml of blood was obtained from peripheral venous and dispensed into plain tube, leaved at 37 °C for 20 min., then centrifuged at 3000 rpm and sample sera were pipetted off and stored at - 20°C.

Serum triiodothyronine (T_3), thyroxine (T_4) and thyroid-stimulating hormone (TSH) concentrations were assayed by using TOSHO AIA-360 Automated Immunoassay Analyzer from Japan. In addition that, glucose, urea and creatinine concentrations were determined by BIOLABO kits, from France.

All parameters were evaluated in short stature patients (60) from the Al-Wafa Center for Endocrinology and Diabetes in Mosul city and (30) healthy children who served as the control group , equally distributed between both sexes and whose age varied from (5 - 14) years from (September 2022 – February 2023). Control group and patients were divided into two age groups (less than and more than 10) years.

SSPS program, version (23), based on the T-test and Duncan's multiple range test, was used to statistically evaluate the findings. The mean (M) and standard deviation (SD) of the results were used to express the values. We used two levels of probability, $p \leq 0.01^{**}$ and $p \leq 0.05^{*}$ to determine statistically significant differences [9].

RESULTS

It was found from current study that there were not effect of short stature on the studied parameters, as table (1) showed that the thyroid hormones represented by triiodothyronine (T_3), thyroxine hormone (T_4), thyroid stimulating hormone (TSH), as well as glucose concentrations did not show any significant difference in the group of children with short stature compared to the control group. However, thyroid stimulating hormone showed an increase of (31.8%), while a decrease in the concentration of triiodothyronine was observed by (9.4%) in children with short stature.

With regard to the study of some biochemical parameters related to kidney function, the results of the current study showed that no significant differences in the concentrations of both urea and creatinine between the children with short stature and control group, but they showed a slight increase of percentages amounting to (2.7%) and (6.1%). %) respectively.

Table 1. Values of biochemical parameters in children with short stature compared to control group.

Parameters	Control n=30 M±SD	Patients n=60 M±SD	Percentage change
Tri-iodothyronine (T_3) ng/ml	1.2 ± 0.3	1.1 ±0.5	-9.4%
Thyroxin Hormone (T_4) µg/ml	94.2 ± 21.1	93.5 ± 21.3	-0.85%
Thyroid Stimulating Hormone (TSH) mIU/ml	2.4 ± 0.7	3.19 ± 2.8	+31.8%
Glucose mmo/L	4.6 ± 0.6	4.6 ± 0.4	+ 0.23%
Urea mmol/L	4.01 ± 0.6	4.12 ± 1.4	+2.7%

Creatinine µmol/L	64.1 ± 15.9	68.2 ± 9.5	+6.1%

It is noted from the results of our study that all the biochemical parameters were not or slightly affected by short stature. In addition, it was noted that not all children with short stature showed these little changes in those parameters. Table (2) showed the percentage of the number of children with short stature in whom the concentrations of the studied parameters were within and out of the normal range.

Table 2. Percentage of children's number with short stature and their concentration of biochemical parameters within and outside the normal range.

Parameters	Normal range (NR)	Patients within NR Mean ± SD	Number's percentage	Patients out of NR Mean ± SD	Number's percentage
Tri-iodothyronine (T_3) ng/ml	0.81-1.4	1.1 ± 0.2	%82	1.76 ± 0.12	%18
Thyroxin Hormone (T_4) µg/ml	52.1-136.4	88.4 ± 11.03	%88	142.3 ± 2.5	%12
Thyroid Stimulating Hormone (TSH) mIU/ml	0.8-3.9	2.33 ± 0.8	%87	9.5 ± 4.8	%13
Glucose mmo/L	3.7-5.6	4.5 ± 0.5	%91	5.8 ± 0.25	%9
Urea mmol/L	2.7-5.2	3.7 ± 0.8	%87	6.7 ± 1.4	%13
Creatinine µmol/L	49.2-87.2	68.8 ± 10	%89	88.5 ± 0.5	%11

DISCUSION

In general, some scientific studies indicate that the relationship between the thyroid-pituitary axis and short stature is not completely clear and requires further research and study [10] [11]. It is clear from the results shown in table (2) that approximately 88% of children with short stature were not affected by their thyroid function, and this result is consistent with some previous studies[12] [13]. It is also noted that (91%) of these patients had glucose levels within the normal range, which is in line with some studies [14] [15].

Some studies contradicting our results indicated an increase in triiodothyronine in short people[16] , and the reason for this is due to the conversion of thyroxine (T_4) to triiodothyronine (T_3) in peripheral tissue by deiodinase enzyme .Also this condition found in a state called thyroid hormone resistance (THR), which occurs due to genetic mutations in the hormone receptors, most of which are in the thyroid receptor beta (TR-beta). This condition is characterized by an increase in both hormones T_3 and T_4 accompanied by normal or slightly elevated levels of the thyroid stimulating hormone (TSH) [17]. Other studies reported a low level of total T_3 in these patients,

which is in line with the results of the current study [18], and the reason for this is due to a destitution of tissue mass and thus a low of basal metabolic rate (BMR) , which means less need for the hormone triiodothyronine [19].

From the above, it is clear that there is no fixed relationship between the role of the thyroid gland and short stature, and this may be due to the availability of many interconnected factors in their effects, such as genetic, environmental, nutritional, physiological, metabolic, pathological and therapeutic factors, as well as behavior related to with daily activity such as exercise, sleep pattern, psychological comfort and individual differences such as height, weight and age [20] [21] [2] [22].

It appears from Table (2) that (88%) of children with short stature did not have affected kidney function, and this result was consistent with some previous studies [23]. Many studies indicated that there is a relationship between short stature and kidney failure, but this relationship goes in two opposite directions. The first, is the weakest in terms of its probability of occurrence and spread , goes in the direction that short stature is a cause of kidney failure and the reason for this is likely to be that individuals who suffer from short stature can they may have high levels of creatinine because their ratio of muscle mass to body size is higher than that of normal individuals, and since creatinine is a by-product of the metabolic process in the muscles, therefore, increasing muscle mass can lead to increased creatinine production. In addition, the kidneys play a crucial role in filtering urea, creatinine, and uric acid from the blood, and short individuals may have relatively smaller kidneys, which may affect their ability to eliminate these wastes efficiently. The second trend, which is the most accepted and seen in clinical cases of short stature , is that kidney failure is a cause of short stature, and one of the possible explanations is that some genetic conditions or syndromes associated with short stature may also affect kidney growth and function such as some genetic disorders can lead to structural abnormalities in the kidney, impairing its ability to effectively filter these wastes [24] [25] [8] [26].

In addition, hormonal imbalances or disturbances in the growth hormone axis can contribute to short stature [27]. Some studies have indicated that performing a growth hormone stimulation test (GHST) is not necessary when there is a clear alternative diagnosis for short stature, such as chronic renal insufficiency, as well as genetic syndromes, including Turner syndrome, Noonan syndrome, and Prader-Willi syndrome (PWS) [23]. In general, according to the results of the current study, it excludes the possibility that kidney failure is one of the causes of short stature in the sample of patient children in our study.

CONCLUSION

From this report it appears that, determination of thyroid hormones , TSH and some biochemical parameters related to renal functions in patients with short stature were no or slightly useful markers in the management of this disease .

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ETHICAL STATEMENT

This study has received permission from the ethical commission of the ministry of health and environment.

CONFLICT OF INTEREST

The authors state that they have no interests that conflict.

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