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The Role of insulin in the Regulation of thyroid function for type 1 diabetic patients

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Abstract

Background: The thyroid gland is classified as one of the important endocrine glands in the human body, as it is regulated by a hormone known as thyroid stimulating hormone (TSH) secreted by the anterior lobe of the pituitary gland. The thyroid gland acts to secrete the hormone thyroxine (T4). Then it converts to triiodothyronine (T3) which is responsible for many functions in the body, but the most important of these functions is regulating metabolism in the body. **Materials and Methods**: This study collected samples from healthy people (the first group) and people with T1D (the second group). Blood samples were taken from both groups after their members agreed to join the study, and biochemical markers were measured for all members of both groups in the serum samples, including random blood sugar (RBS), Insulin hormone (Ins. H.), C-peptide, TSH, T4, and T3. **Results**: After doing statistical analysis, the current study showed that there are clinically significant differences between the two groups, which are as follows: *An increase in the level of RBS and TSH in the second group compared to the first group and *A decrease in the level of Ins.H., C-peptide, T4 and T3 in the second group compared to the first group.

Conclusion: The study concluded that there is an association between the absence of insulin in patients with T1D and hypothyroidism. This study showed that insulin has an important role in the process of regulating the production of thyroid hormones.

Keywords: Type 1 diabetes, Thyroid hormones, hypothyroidism.

Introduction

Type 1 diabetes (T1D) is a mostly chronic disease caused by over-activity of the immune system, which leads to the destruction of the cells responsible for producing insulin (called beta cells) in the pancreas tissues (1). This disease is characterized by high glucose levels in the blood and affects people under 20 years of age, it is often classified as a hereditary disease. Over-activity of the immune system generates autoimmune diseases, of which T1D is considered one of these diseases, as the immune system produces special antigens that attack and destroy beta cells. In return, the immune system also produces antibodies to these antigens, the most famous and important of which are Antibodies to glutamic acid decarboxylase (Anti-GAD) (2). Under these pathological conditions, the insulin hormone (Ins.H.) production

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becomes absent from beta cells because it destroys it, leading to glucose elevation in the blood, characterized by various features such as tiredness, weight loss, unhealing cuts, thirstiness, etc. (3).

Ins.H. is the most important in glucose catabolism, it has a protein structure encoded by beta cells. Ins.H. is secreted parallel with C-peptide at a special mechanism, see Figure 1. At T1D diagnosis C-peptide more Ins.H. because it has a long half-life compared with Ins.H. in blood (4).

The thyroid gland is one of the endocrine glands in the body, as it is located in the lower part of the front of the neck. This gland is under the control and regulation of the thyroid stimulating hormone (TSH), which is secreted by the pituitary gland, which has a glycoprotein structure that targets the thyroid gland so that it can begin producing its hormones called thyroid hormones (5), see figure 2.

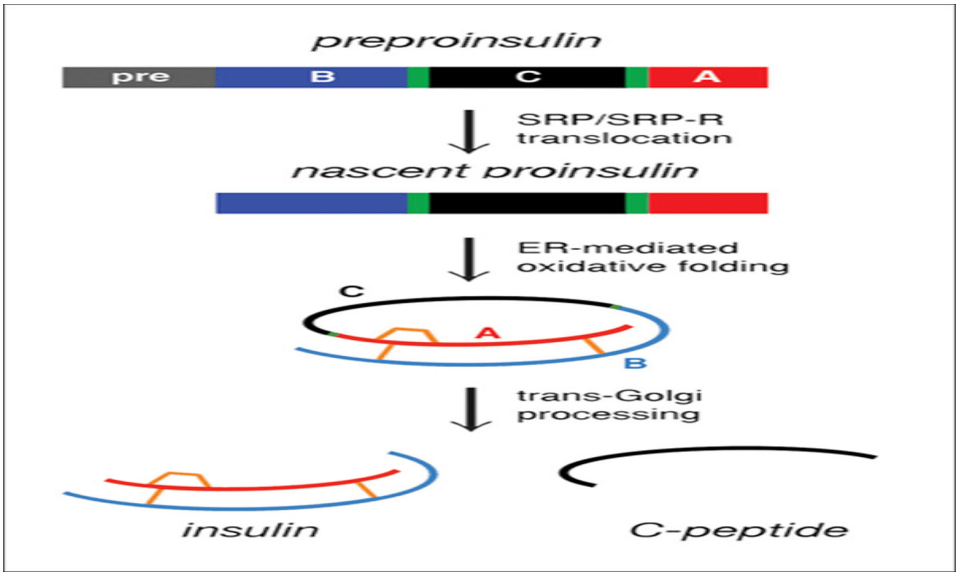

Figure 1 Ins.H. and C-peptide secretion mechanism (6)

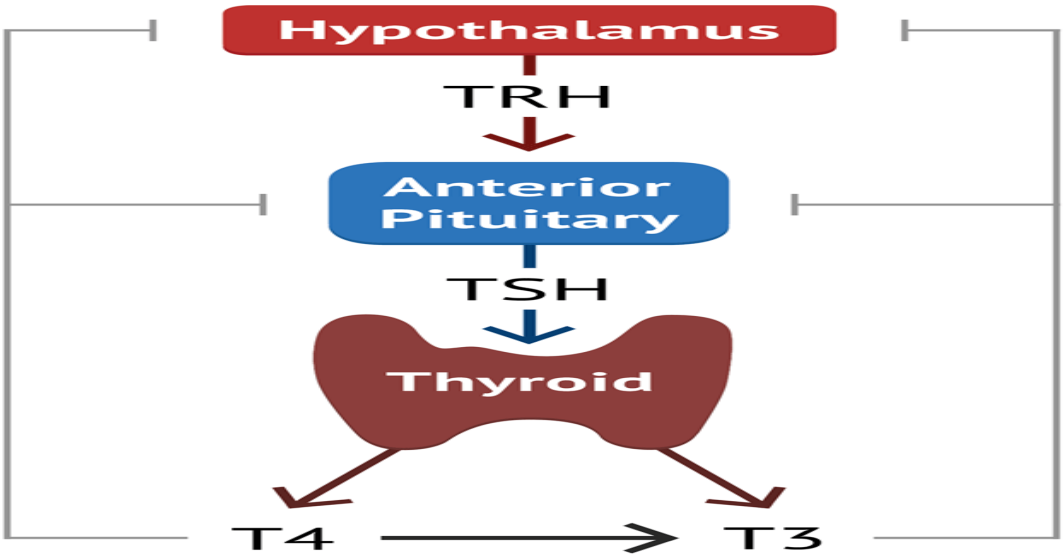

Figure 2. TSH, T4, and T3 secretion mechanism axis (7)

Thyroid hormones include two types of hormones thyroxine (T4) and triiodothyronine (T3), as the structure of these hormones is protein and has several functions, the most important of which are (8):-

-It works to regulate the body's metabolism
-It regulates body temperature
-It regulates the heartbeat
-It contributes to regulating protein synthesis in the body

On the other hand, the thyroid gland suffers from many disorders, including hyperthyroidism, hypothyroidism, nodules, and other disorders, but the most common disorder seen in the population is hypothyroidism (9). At hypothyroidism, the thyroid hormones become relatively lower than the level of TSH's effect on the thyroid gland. The most prominent causes of hypothyroidism are the presence of an auto-immune disease, receiving treatment for hyperthyroidism, taking certain medications, thyroid surgery, or radiation therapy. Also, symptoms begin to appear in patients with hypothyroidism, and the most common symptoms and signs are lack of concentration, fatigue, weight gain, facial swelling, etc. (10).

Our current study highlights and aims to clarify the nature of the effect of the loss of Ins.H. secretion in patients with T1D on the functions of thyroid hormones and the extent of the effect on it.

Experimental section

Design of the study

This study was designed according to the selection of study individuals and classified into 2 groups of individuals, as follows:-

*The first group: included the selection of 25 healthy individuals who did not suffer from any disease and were the age under 20 years, both males and females.

*The second group: included the selection of 25 individuals suffering from T1D and were the age under 20 years, both males and females.

T1D patients were diagnosed based on symptoms, signs, patient history, and clinical and laboratory examinations according to the conditions and characteristics stipulated by the American Diabetes Association Releases 2023 (11).

Ethics of the study

In the current study, study individuals were selected, and their pathological samples were collected in April 2024 at Al-Yarmouk Teaching Hospital/Iraq. The consent of all individuals was obtained verbally to be included in this study, and this study was conducted after the 2000 Helsinki Declaration on the Ethics of Scientific Research after approved via ethical committee approval in college (approval No. 309 in April 2024). This is to fully achieve scientific research ethics in this study.

Collect samples and measurements

After the study individuals were identified and diagnosed, their blood samples were collected, and then the blood samples were left in the water bath for 5 minutes to prepare them for the separation process using a centrifuge to obtain the serum samples. These serums were used to measure several biochemical parameters according to scientific measurement methods and kits from reputable companies according to the following table, see Table 1.

Table 1 The biochemical markers kit details

Biochemical marker	Principle test	Company name for the kit	Lot Number
Random blood sugar (RBS)	Spectrophotometer	SPINREACT	MDBSIS46-E - 03/05/17
Ins.H.	The enzyme-linked immunosorbent assay (ELISA)	ABCAM	ab278123
C-peptide	Solid phase ELISA	IBL International GMBH	RE53011
TSH	Kinetic Fluorescence Immunoassay	TOSOH	1007471001-017F - 01/17
T4	Kinetic Fluorescence Immunoassay	TOSOH	1007371001-017E - 01/17
T3	Kinetic Fluorescence Immunoassay	TOSOH	1007271001-110G - 11/20

Statistical analysis

This study depends on analyzing the data on the statistical analysis method known T-test, which depends on using the mean $\pm$ standard deviation (SD) value to compare the first and second groups according to the previous biochemical parameters determined in the table above. This statistical method shows the important values in the value differences of previous biochemical parameters between the two groups by showing a value called p-value as it is clinically important when it is equal to or less than 0.05, according to the SPSS program, version 18 for the year 2022 (12).

Results

Our current study showed that there are important clinically significant differences between the biochemical markers included in the study when comparing the two groups first group (healthy group) and the second group (T1D group). At current study used the statistical analysis method (T-test) for comparison between the groups. The differences were as follows:-

*An elevation in the levels of RBS and TSH for the second group compared to the first group.

*A decrease in the levels of Ins.H., C-peptide, T4, and T3 for the second group compared to the first group.

See Table 2 and Figures 3 and 4.

Table 2 The Comparison between First group (healthy group) and Second group (T1D group) according to various biochemical markers

Biochemical parameters	First group (healthy group) (No.25) Mean ± SD	Second group (T1D group) (No.25) Mean ± SD	p-value
RBS (mg/dl)	92.4 ± 19.1	133.4 ± 10.8	0.001*
Ins.H. (U/ml)	8.48 ± 5.6	0.7 ± 0.18	0.001*
C-peptide (ng/ml)	2.82 ± 1.3	0.91 ± 0.2	0.01*
TSH (µIU/ml)	2.73 ± 2.1	7.5 ± 2.4	0.03*
T4 (nmol/L)	106.5 ± 28.6	60.6 ± 4.7	0.001*
T3 (nmol/L)	2.47 ± 1.5	0.89 ± 0.41	0.01*

*Significant value (P-value less than 0.05)

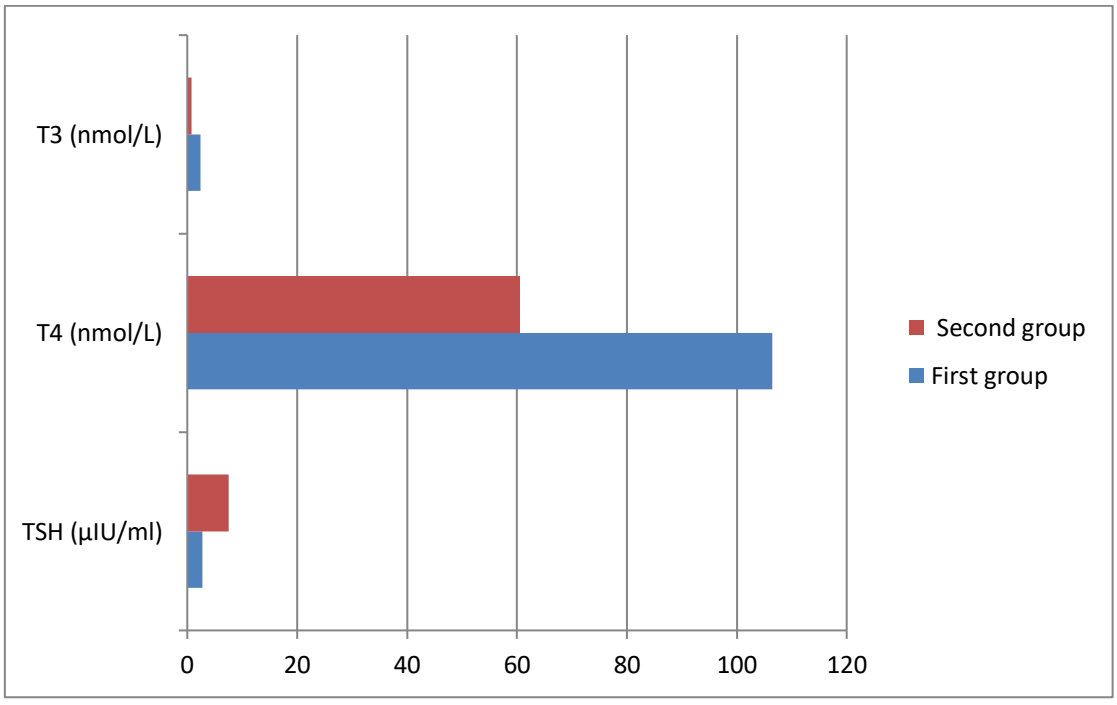

Figure 3 Comparison between First group (healthy group) and Second group (T1D group) according to various biochemical markers

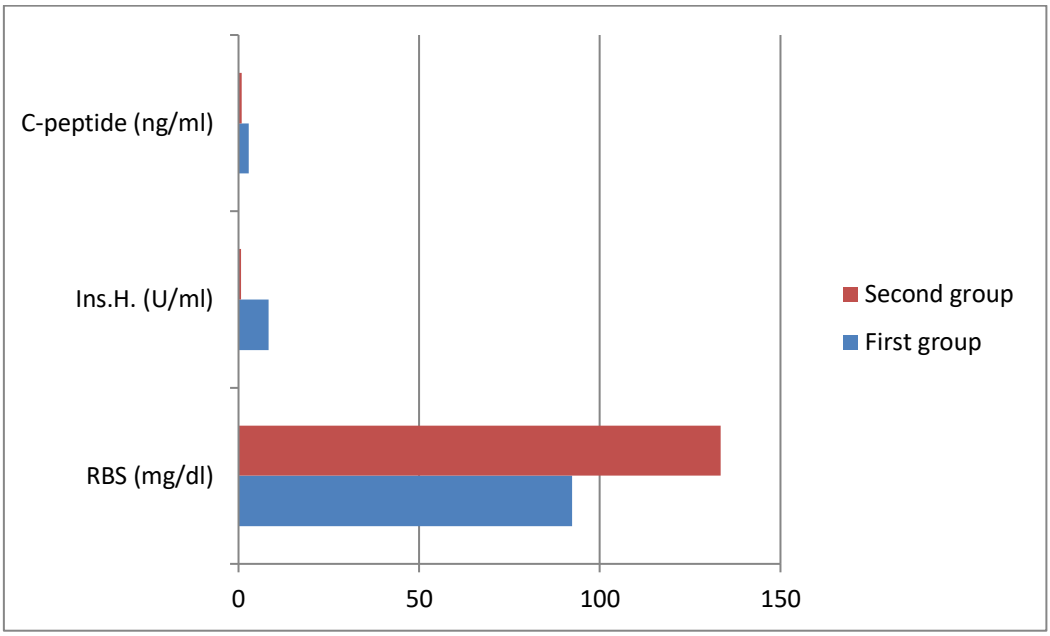

Figure 4 Comparison between First group (healthy group) and Second group (T1D group) according to various biochemical markers

Discussion

Any disruption in the human body's metabolic processes for vital compounds such as fats and proteins as a result of high blood glucose levels can result in metabolic diseases, the most important of which is diabetes, which is considered one of the most common chronic diseases. High glucose levels come from two main reasons: the inability of pancreatic beta cells to produce sufficient amounts of Ins.H. or failure of the body's cells to respond to the Ins.H. Self-destructive pancreatic beta cells characterize T1D, which accounts for 5-8% of all diabetic cases (11,12).

Thyroid hormones are considered essential for various functions such as growth and development, on the other hand, they play a key tool in the balance of energy (8). Thyroid hormones are secreted by the thyroid gland, and the thyroid gland is controlled by the hypothalamus-pituitary-thyroid -axis. The thyroid hormone has 2 forms: the T4 (called prohormone) and T3 (called biologically active) forms. Hypothyroidism is a common disorder in the population after diabetes, that is considered the second disorder of the endocrine system (6,13).

The study results show that the RBS and Ins.H. levels in T1D patients depend on the significant elevate of RBS and the significant reduction of Ins.H. of the T1D group (second group) when compared with the first group (healthy group). This RBS increase and Ins.H. decrease are considered suitable because this group is affected via T1D due to has family history. T1D disease is the most common genetic disease for young people. This disease has various characteristics such as tiredness, polyurea, and polydipsia.

The explanation for T1D is that it is an autoimmune disease due to the formation of anti-GAD. The anti-GAD can destroy the pancreatic beta-cells that lead to Ins.H. absence (14). Therefore, there is a direct relationship between the level of anti-GAD and the level of RBS because anti-GAD works to eliminate the very important role of Ins.H. in the process of sugar metabolism in the body. In other words, the

disorder of glucose catabolism, which is called T1D depends on Ins.H. doses for treatment (15).

The Ins. H presence has a significant role in regulating the alpha-thyroid hormone receptor (α-THR) production in the body, when Ins.H. decreases or is absent, this receptor production will be its expression in the tissues reduced especially the pituitary and hypothalamus glands. These conditions can lead to increased TSH secretion due to the feedback mechanism and lack of receptors of the pituitary gland for thyroid hormones. So, the present study explains significant TSH elevation in the T1D group compared healthy group with T4 and T3 decrease (This status is known as hypothyroidism). This occurred because the Ins.H. was reduced in the T1D group (16).

The present study results agree and demonstrate with (Armstrong et al. 2023) which demonstrated the Ins.H. effect on the thyroid hormones receptors and synthesis of TSH (16). In addition, this study shows the hypothyroidism state at T1D. This also implies that the lack or weakening of the existence of the α-THR can make the gland insensitive condition for the action of thyroid gland hormones through the short type feedback.

The thyroid gland remains in underactive conditions and does not secrete sufficient levels of the hormones, which is consistent and agrees with (Li et al. 2022) which demonstrated the relationship between hypothyroidism and T1D (17,18). It also the interpretation of the reduction in thyroid hormones at T1D compared with the healthy group. This has occurred due to the existence of autoimmune antibodies like anti-thyroglobulin (Tg) and Anti-thyroid peroxidase (TPO) (19). Auto-immune antibodies have a role in the thyroid hormones production inhibiting, which leads to hypothyroidism, this idea agrees with the results of our current study and agrees with Li, Yanli, et al (2022) and Moura Neto, Arnaldo, et al . (20,21).

In addition, the C-peptide marker was measured to evaluate pancreatic gland insufficiency because C-peptide has a longer half-life than Ins.H., and the study proved that C-peptide has lower levels in the second group in the study compared with the first group (22).

Conclusion

This study concluded to explain the importance of losing the Ins. H. in T1D patients and how it affects the production of thyroid hormones (T4 and T3), as we have shown that there is an important association between hypothyroidism and T1D disorders in young people.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all work aspects.

Conflict of Interest

There are no conflicts of interest in this study.

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