Estimation of Thyroid Function Tests in Type 2 Diabetes Mellitus

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Abstract—**Background and Objectives: Type 2 diabetes mellitus (T2DM) is an endocrine and metabolic disorder caused by insulin resistance, insulin hormone deficiency, and impaired insulin production form pancreatic beta cells. Thyroid hormones play a key role in glucose metabolism via several mechanisms. This study aimed to estimate the serum thyroid hormone levels in type 2 diabetic patients.**

Methods: The current case and control study was carried out in Erbil city. Blood specimens were collected from 100 subjects divided into two groups (50 case , 50 control). Each group consisted of (32 females and 18 males). The separate serum was used to determine the levels of thyroid stimulating hormone and thyroid hormones in diabetic patients and control subjects.

Results: The results demonstrated that the serum thyroid hormones were significantly lower in patients with type 2 diabetes compared to healthy subjects. The mean ± SE was (3.58 ± 0.06) pmol/L and (14 ± 0.34) pmol/L, for triiodothyronine and thyroxine in type 2 diabetic patients, respectively. In addition, there was a significant difference in serum thyroxine levels among the grades of body mass index values in the case group.

Conclusion: The study result concluded that type 2 diabetes mellitus could cause thyroid dysfunctions. It demonstrated that chronic hyperglycemia status in diabetes mellitus had a significant effect on serum thyroid hormone concentration.

Index Terms— **Type 2 diabetes mellitus, Thyroid hormones, and Thyroid stimulating hormone.**

I. INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders known as diabetes characterized by a high level of glucose in the blood (hyperglycemia) (García, 2017). It results from imperfection and defects in insulin secretion from beta cells of the pancreas, the function of insulin on the target cells, or both (American Diabetes Association, 2010). The most common signs and symptoms of DM are weight loss, polyuria, and polydipsia (Lal, 2016). Type 2 diabetes mellitus (T2DM) is a metabolic disorder caused by a combination of two main factors: defective insulin secretion pathway (insulin hormone deficiency) and the inability of insulin-sensitive tissues to respond to the insulin hormone (Roden and Shulman, 2019). It is closely related to a family history of diabetes mellitus, obese individuals, lack of physical activity, and age more than 35 years old (Sirdah, 2015).

The largest endocrine gland in the body is the thyroid gland, which is known as a butterfly-shaped gland (Jawad et al, 2016). The weight of the thyroid gland is approximately between 15-20 g, but the weight of the gland would be different depending on the gender as the thyroid gland in males has more weight than in females (Benvenga et al, 2018). The thyroid gland synthesizes several necessary hormones including triiodothyronine (T3), thyroxine (T4), and calcitonin (Shahid et al, 2022). Thyroid hormones have played an essential role in controlling the catabolism of carbohydrates, protein, and fat in all cells, regulating body temperature, and they are one of the most important hormones during the growth phase in infancy and childhood (Jawad et al, 2016). Calcitonin regulates the calcium homeostasis.

The insulin or thyroid hormones metabolism can result in functional abnormalities of one another as thyroid hormones are insulin antagonists, affect indirectly insulin activity, and play an essential role in the sensitivity of insulin, while insulin is an anabolic hormone that plays a key role to raise the value of FT4 and suppressing the level of FT3 by inhibiting the conversion of thyroxine to triiodothyronine in the liver (Ramesh et al, 2015; Ray and Ghosh, 2016; Acharya et al, 2017).

Diabetes mellitus and thyroid dysfunctions are the most common endocrine diseases seen in the general population, according to American Diabetes Association have a strong relationship between diabetes and thyroid diseases (Al-Geffari et al, 2013).

Thyroid disorders have a higher prevalence in diabetes patients than in non-diabetes participants, especially hypothyroidism was frequently observed in individuals with type 2 diabetes mellitus (Distiller et al, 2014; Kalra, 2014). The present study aims to evaluate serum levels of thyroid function tests in both diabetic and non-diabetic.

II. MATERIALS AND METHODS

This case-control study was designed to investigate the serum thyroid hormones levels in participants with and without diabetes mellitus. The sample collection was conducted from October (2021) to January (2022) in different medical health centers in Erbil city. The individuals in this study divided into two groups; 50 cases and 50 controls. Both groups consisted of (18 males and 32 females). The case participants had previously received a diagnosis of T2DM from by a specialized physician (endocrinologist). The simple random sampling used to select individuals for the study.

A. Collection of Specimens

The standard phlebotomy method used for collecting the peripheral blood samples, 5 ml of early morning venous blood samples were drawn and then transfer into two tubes: a gel tube used for estimating thyroid function test and fasting blood sugar

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(FBS) and an EDTA tube used for investigating of glycated hemoglobin (HbA1c). At room temperature, a gel tube was incubated approximately 10 minutes, then the serum was separated by centrifugation at 4000 rpm for eight minutes. The Cobas C 311 and sandwich ELISA devices were used for investigating the biochemical parameters.

B. Statistical Analysis

The statistical package for social science (SPSS) (Version 26) software was used for analyzing the data. In the study, all the selected variables were presented as mean ± standard error. The thyroid stimulating hormone, free triiodothyronine, and free thyroxine were compared between diabetic and non-diabetic by using an independent t-test. The Chi-square test is used for estimating qualitative data by frequency and percentage. The Pearson correlation coefficient test was used for measuring the statistical relationship (liner relationship) between two numerical variables. The probability value (P-value ≤ 0.05) statistically means a significant difference, while a P-value of less than 0.001 statistically means a highly significant difference, however a P-value more than 0.05 was considered that non-significant difference.

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III. RESULTS

A. Participants Demographic Characteristics

Table (1) provides the number and percentage of genders, ages, and family history of thyroid disorders for both diabetic and non-diabetic groups. Both groups included 50 participants, it consisted of 32 females and 18 males. Several patients with T2DM have a family history of TDs.

TABLE 1: COMPARISON OF THE DEMOGRAPHIC CHARACTERISTICS BETWEEN BOTH GROUPS.

Demographic Characterizes	Case No. 50 No. (%)	Control No. 50 No. (%)
Gender		
• Males	18(36%)	18(36%)
• Females	32(64%)	32(64%)
Age-group		
• 40-49 years	13(26%)	13(26%)
• 50-59 years	21(42%)	21(42%)
• 60-69 years	16 (32%)	16(32%)
Family history of TDs		
• Yes	12 (24%)	13 (26%)
• No	38 (76%)	37 (74%)

B. Result of Hormones Between Diabetics and Non-Diabetics Participants

The mean ± SE of TSH was (2.09 ± 0.29) in the diabetic participants, while in the non-diabetic was (1.99 ± 0.25). Statistically, there was no significant difference in mean serum TSH level between type two diabetic and non-diabetic participants. The mean ± SE of FT3and FT4, was (3.58 ± 0.07) and (14 ± 0.34) in the case group, receptively. Regarding the control, the mean ± SE for FT3 was (4.47 ± 0.07) and FT4 was (16.90 ± 0.43). The data analysis showed a statistically high significance difference (P-value ≤ 0.001) in the serum FT3 and FT4, concentrations when comparing type two diabetic patients with healthy individuals.

TABLE 2: COMPARISON OF BIOCHEMICAL PARAMETERS BETWEEN DIABETIC PATIENTS AND CONTROL GROUP.

Biochemical parameters	Case No. 50 Mean ± SE	Control No. 50 Mean ± SE	P-value
TSH (µIU/mL)	2.09 ± 0.29	1.99 ± 0.25	0.804 *
FT3 (pmol/L)	3.58 ± 0.06	4.47 ± 0.07	**0.001***
FT4 (pmol/L)	14 ± 0.34	16.90 ± 0.43	**0.001** *

*By t-test for two independent samples.

C. Investigation of Serum Thyroid Function Test Between Both Genders With Type 2 Diabetes Mellitus

Table (3) shows that there was no significant difference according to gender in the concentrations of thyroid function test among case participants. The (P-value ≥ 0.05) for these biochemical parameters in this study.

TABLE 3: COMPARISON OF THE SERUM THYROID HORMONES FUNCTIONS BETWEEN BOTH GENDERS WITH TYPE TWO DIABETES.

	Case Gender		
Biochemical Parameters	Males No. 18 Mean ± SE	Females No. 32 Mean ± SE	P-value
TSH(µIU/mL)	1.59 ± 0.21	2.37 ± 0.42	0.194 *
FT3(pmol/L)	3.73 ± 0.81	3.49 ± 0.09	0.104 *
FT4(pmol/L)	14.70 ± 0.78	13.60 ± 0.29	0.127 *

*By t-test for two independent samples.

D. Association Between Family History of Thyroid Disorders and The Serum TSH, FT3, and FT4, in T2DM patients

The result of a family history of thyroid disorders showed that there was a significant difference in the serum concentrations of TSH and FT3 between diabetic patients with a family history of TDs and diabetic patients without a family history of TDs, while free thyroxine statistically, there was no significant difference in their serum concentrations between T2DM patients with a family history of TDs and patients without a family history of TDs.

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TABLE 4: MEAN ± SE OF TSH, FT3, FT4 BETWEEN DIABETIC PATIENTS DEPENDING ON FAMILY HISTORY OF TDS.

Biochemical Parameters	Family History of TDs		
	Yes No. 12 Mean ± SE	No No. 38 Mean ± SE	P-value
TSH(µIU/mL)	3.20 ± 1.04	1.75 ± 0.16	**0.030***
FT3(pmol/L)	3.27 ± 0.17	3.68 ± 0.07	**0.009***
FT4(pmol/L)	13.12 ± 0.29	14.28 ± 0.43	0.153*

*By t-test for two independent samples.

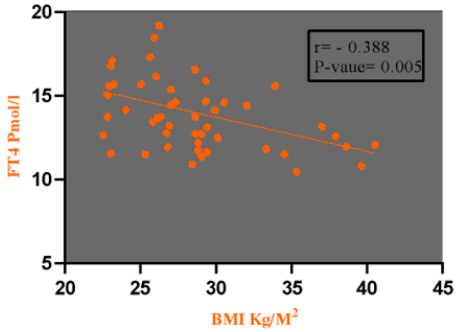

Figure 1: Shows the correlation coefficient between Body Mass Index and thyroxine (FT4) among the case group.

IV. DISCUSSION

Thyroid hormones are the two main metabolic hormones synthesized by the thyroid gland, thyroid stimulating hormone (TSH) regulates the biosynthesis pathway of thyroid hormones by the feedback mechanism system in the body, which is released by the anterior pituitary gland (Shahid et al, 2022). The statistical analysis in this study indicated that there was no significant difference in the mean serum level of thyroid stimulating hormone (P-value ≥ 0.05) between type 2 diabetic patients and control individuals as shown in Table (1). The same result was obtained by other research study (Saeed, 2018; Hmood et al, 2020). In this study, the triiodothyronine result showed that the serum free triiodothyronine concentration in type 2 diabetic individuals was lower than in healthy subjects, statistical evaluation (P-value ≤ 0.001) indicated a highly significant difference between the mean FT3 serum level between case and control groups as present in Table (2), this result is in agreement with the result obtained by other researchers (Afrin et al, 2017; Akka et al, 2017). Regarding the thyroxine, statistical evaluation as FT3, the result demonstrated that when comparing the serum level of FT4 between diabetic and non-diabetic participants, the level was reduced in diabetic patients. The same results were reported by several research studies (Afrin et al, 2017; Jiffri, 2017; Hmood et al, 2020). In type 2 diabetes mellitus chronic hyperglycemia affects endocrine and non-endocrine organs, regarding the thyroid gland, it alters the hypothalamus-pituitary-thyroid axis and feedback mechanism system that causing reduced triiodothyronine and thyroxine production (Rai et al, 2013). Based on the result of thyroid hormones, this study discussed that most patients with type 2 diabetes are at risk for developing secondary hypothyroidism, which is a form of hypothyroidism characterized by low or normal serum TSH concertation and reducing thyroid hormones serum levels. The same finding was performed by other investigators (Demitrost and Ranabir, 2012). Thyroid function tests between males and females among diabetic patients showed that gender had non-significant effect (P-value ≥ 0.05) on serum concentrations of thyroid stimulating hormone, free triiodothyronine and free thyroxine as present in Table (2). The same result was performed in other studies, which reported that there was no significant difference in the mean of serum thyroid function tests between males and females in the diabetic group (Abidia et al, 2015; Saeed, 2018). In general, the prevalence of thyroid disorders is higher among females than in males due to it related to its autoimmune nature in females, and the interaction between thyroid hormones and the female sex hormones such as estrogen and progesterone (Baksi and Pradhan, 2021).

However, this discussion is the opposite this study result may be related to sample size, environment, and area. Regarding the family history of thyroid disorders, the statistical evaluation noted that the mean serum TSH concentration was significantly higher in diabetic patients with a family history of TDs than in diabetic patients without thyroid disorders family history, while an inverse result was observed that the serum concentration of free triiodothyronine was significantly lower in case participants with a family history of TDs than in diabetic patients without a family history of TDs as present in Table (3). In addition, the result of thyroxine showed that there was non-significant difference in the serum FT4 concentration between patients with a family history of thyroid disorders and diabetic patients without a family history of thyroid disorders. This present case-control study is consistent with studies reported by Schroner with his colleagues (2006) demonstrated that the prevalence of thyroid disorders was higher in diabetic patients with a family history of thyroid disorders. A positive family history of thyroid dysfunctions among type 2 diabetes was one of the most common risk factors for developing thyroid disorders due to a heredity root like a mutation of several genes e.g., TPO and Tg that increased the chance of the development of thyroid diseases as hypothyroidism (Al-Geffari et al, 2013). It is in agreement with the present study result. Inverse significant correlation between BMI values and FT4 levels that means the concentrations of free thyroxine reduced with the elevated value of body mass index due to in obese individuals altered metabolic rate and energy balance. Several studies concluded a positive non-significant correlation between BMI categories and thyroid hormones, which is in disagreement with the present study correlation result of thyroid hormones serum levels with the values of body mass index (Udiong et al, 2015; Binobead et al, 2019).

CONCLUSION

Based on the results, this study concluded that serum thyroid hormone concentrations are lower in diabetic individuals than in healthy subjects. The prevalence of secondary hypothyroidism was common among patients with type 2 diabetes mellitus. Chronic hyperglycemia can affect the serum thyroid hormones concentration. The thyroxine serum

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concentrations were significantly correlated with BMI values in diabetic patient.

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