

MONITORING OF THYROID HORMONES LEVELS IN DIABETIC MELLITUS TYPE 2 PATIENTS CONTROLLED AND UNCONTROLLED IN SANA'A, YEMEN

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ABSTRACT

Background: Diabetes mellitus (DM) is a common endocrine metabolic disorder and variety of thyroid abnormalities may coexist and interact with DM that appears to influence thyroid function. **Objective:** Therefore, the study aimed to monitor the thyroid hormones levels in DM type 2 patients controlled and uncontrolled in Sana'a, Yemen. **Methods:** The study included 150 subjects from major public hospitals in Sana'a city, Yemen. 50 were diagnosed with DM type 2 controlled as group I and 50 were diagnosed with DM type 2 uncontrolled as group II. 50 were healthy volunteers as control group. The biochemical parameters namely Fasting Blood Sugar (FBG) and Glycated Hemoglobin (HbA1c) were assayed in three groups. On the other hand, thyroid hormones levels namely thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) were monitored in the same groups. Data obtained were analyzed using suitable statistical tools. **Results:** The levels of thyroid hormones in DM type 2 patients controlled and uncontrolled were recorded. The mean of TSH, FT3, and FT4 levels were recorded in three groups. The results were (1.83 ± 0.791 mU/L, 3.0 ± 2.2 mU/L, 1.83 ± 0.85 mU/L); (3.47 ± 0.78 Pg/mL, 2.9 ± 0.74 Pg/mL, 4.1 ± 0.71 Pg/mL); (1.1 ± 0.212 ng/dl, 1.01 ± 0.33 ng/dl, 1.2 ± 0.14 ng/dl), respectively. The results were observed that different significant ($p < 0.05$) in TSH and Free T3 levels between groups I and II. While different significant ($p > 0.05$) in FreeT3 and Free T4 between group I and III. Also, the different significant in three hormones levels between group II and III. On the other hand, the present study showed 20 % of patients had thyroid dysfunction. 17 % of hypothyroidism and 3% of hyperthyroidism. However, 2% of hypothyroid in controlled patients and 15 % of hypothyroid in uncontrolled patients, while 2% of hyperthyroidism was found in controlled patients and 1 % of hyperthyroidism was recorded in uncontrolled patients. **Conclusion:** The study outcome concluded that the thyroid dysfunction may progressive in DM type 2 patients uncontrolled as complication.

KEYWORDS: Diabetic mellitus, type 2, thyroid hormones, monitoring, controlled, uncontrolled.

INTRODUCTION

Diabetes mellitus (DM), a common endocrine metabolic disorder, is a leading cause of death worldwide.^[1] Variety of thyroid abnormalities may coexist and interact with DM that appears to influence thyroid function in at least two sites, one at the level of hypothalamic control of thyroid stimulation hormones release and other at the conversion of thyroxine (T4) to 3,5,3 Triiodothyronine (T3) in the peripheral tissue. Defects in carbohydrate metabolism machinery and consistent efforts of the physiology system to correct the imbalance in carbohydrate metabolism place an overexertion on the endocrine system, continuing deterioration of endocrine control exacerbate the metabolic disturbance and leads primarily to hyperglycemia.^[2]

Marked hyperglycemia causes reversible reduction of the activity and concentration of hepatic T₄-5- Deiodinase, low serum concentration of T3, elevated levels of reverse T3 and low normal, or high level of T4.^[3] Since thyroid hormone regulate metabolism and diabetes can alter metabolism of food stuff, the metabolism of organism may be further affected of the combination of thyroid disease and diabetes, thyroid disorders are also very common in the general population and it is second only to diabetes as the most common condition to affect the endocrine system. As a result it is common for an individual to be affected by both thyroid disease and diabetes.^[4]

In several countries of the world information's on the actual prevalence and incidence of DM are available the problem of thyroid disorder which have been reported in

over 110 countries of the world with 1.6 billion people at risk. Many of studies have estimated the prevalence of thyroid dysfunction among DM patients to be varying from 2.2 to 17 %.^[3,4,5]

Our study aimed to monitor the thyroid hormones levels in DM type 2 patients controlled and uncontrolled in Sana'a, Yemen.

MATERIALS AND METHODS

2.1 Study design: This study was conducted among individuals who came to medical clinic in major public hospitals in Sana'a city previously diagnosed as DM type 2. The subjects were divided into three groups, the first group was 50 DM type 2 controlled, the second group was 50 DM type 2 uncontrolled, and the third group was 50 healthy non-diabetic people as control.

2.2 Ethical issues: Subjects received a simple explanation of the aim of the study and asked to participate. If they agreed, the sample was collected and an interview was conducted. Confidentiality of the collected data was achieved by keeping data record in a locked room with limited access to the research team only. Clinical information was obtained from the patients. Information included the name, sex, age, body mass index (BMI), duration of diabetic, chronic diseases associated, and drug admiration.

2.3. Inclusion and exclusion criteria

The inclusion criteria included, cases of DM type 2 controlled with an HbA1c less than or equal to 7 and with age more than 30 years and less than 70 years. Cases of DM type 2 uncontrolled with an Glycated hemoglobin (HbA1c) more than 7 aged more than 30 years and less than 70 years. On the other hand, the subjects with previous history of thyroid disease, and other diseases or medications effect on thyroid function.

2.4. Sample collection: After obtaining the consent of cases and controls participation as voluntaries in the study and obtain required patient details. 7 ml of blood was collected from antecubital vein after fast overnight 8-

12 hours. Blood was collected in EDTA vacutainer (2ml) and plain vacutainer (5ml). Blood collected in plain vacutainer was processed to obtain serum and following parameters were estimated namely serum fast blood sugar, serum free T3 level, serum free T4 level, and serum TSH level. Blood collected in EDTA tube was used for estimation of: HbA1c.

2.5. Assay of glucose and glycated hemoglobin

The blood glucose namely Fasting Blood Sugar (FBS) was estimated based on enzymatic method using photometric method. On the other hand, the HbA1c was assayed by immunoturbidimetry method.^[6,7]

2.6. Assay of thyroid hormones levels: The thyroid hormones levels in serum namely Thyroid-stimulating hormone (TSH), free triiodothyronine (FT3) thyroxine (FT4) and were measured by Chemiluminescence method. The principle assay included a one-step enzyme immunoassay sandwich method with final fluorescent detection (ELFA).^[6] All assay steps were performed automatically by the COBAS instrument.^[8]

2.7. Statistical analysis: Statistical Package for Social Sciences (SPSS, Version 18) software was used for the statistical analysis. The differences between the groups were tested for significance by Z-test, and one-way analysis of variance (ANOVA) test were used. The relationship between variables was analyzed by Pearson's correlation tests. Differences and correlations were considered significant at $p < 0.05$.

3. RESULTS

1.1. Subjects characteristics: The background information of the clinical history for the 150 samples in three groups were summarized in (Table 1). The group I was DM type 2 controlled, the group II was DM type 2 uncontrolled and the group III was health control group. The personal data namely age, sex, and Body Mass Index (BMI) was recorded and results showed that the age of the patients included in this study between 36 to 53 years with 1:1.4 male: female ratio (Table 1).

Table 1: Subjects characteristics

Parameters	Group I n=50	Group II n=50	Group III n=50
Age	46.4±6.8	46.9±7.5	40±3.8
Sex			
• Male	22	30	26
• Female	28	20	24
BMI	22.8 ± 3.33	27 ± 2.3	21 ± 2.51

3.2. Levels of glucose and HbA1C in DM type 2 controlled and uncontrolled

The levels of FBS, and HbA1C were investigated in DM type 2 controlled as group I and uncontrolled as group II and summarized in Table .2. In the group I, the results presented show the mean of the FBG level was 141 ± 41 mg/dl while the mean of the HbA1C level was 6.3 ± 0.56

%. On the other mean, significant increase ($p < 0.05$) in FBS level in comparing with the group III (control health group) namely 84 ± 12.3 mg/dl that was non- within to normal range (70 – 110 mg/dl), also significant increase ($p > 0.05$) in HbA1c in comparing with control group (Table .2). However, in the group II. according to biochemical assays for FBS, and HbA1C and the results

proved significant increase ($p < 0.05$) in all parameters namely 209 ± 81 mg/ml and $10.23 \pm 1.7\%$, respectively in comparing with group III (Table 2).

Table 2: Assay of blood glucose and glycated hemoglobin in DM type 2 patients controlled and uncontrolled

Parameters	Group I	Group II	Group III
FBS mg/dl	$141 \pm 41^*$	$209 \pm 81 \text{ €}$	84 ± 12
HBA1C%	$6.3 \pm 0.56^*$	$10.23 \pm 2 \text{ €}$	4.3 ± 0.62
* : Different significant between group I and III ($p < 0.05$)			
€ : Different significant between group II and III ($p < 0.05$)			

3.3. Level of thyroid hormones in DM type 2 controlled and uncontrolled

The levels of thyroid hormones in DM type 2 controlled and uncontrolled were assayed. The mean of TSH, FT3, and FT4 levels were recorded in both groups and the results were (1.83 ± 0.791 mU/L, 3.0 ± 2.2 mU/L); (3.47 ± 0.78 Pg/mL, 2.9 ± 0.74 Pg/mL); (1.1 ± 0.212 ng/dl, 1.01 ± 0.33 ng/dl), respectively. The results were

observed that different significant ($p < 0.05$) in TSH and FT3 hormones levels between groups I and II. While significantly statistically different ($p < 0.05$) in FT3 and FT4 between group I and III. On the other hand, the significantly statistically different ($p < 0.05$) in three hormones levels between group II and III. In brief, all the means of levels of thyroids hormones were according to normal range.

Table 3: Assay of thyroid hormones levels in DM type patients controlled and uncontrolled

Hormones	Group I	Group II	Group III
TSH mU/L	$1.83 \pm 0.791^*$	$3.0 \pm 2.2 \text{ €}$	1.83 ± 0.85
FT3 Pg/mL	$3.47 \pm 0.78 +$	$2.9 \pm 0.74 \text{ €}$	4.1 ± 0.71
FT4 ng/dl	$1.1 \pm 0.212^* +$	$1.01 \pm 0.33 \text{ €}$	1.2 ± 0.14
*:Different significant between group I and II ($p < 0.05$) € : Different significant between group II and III ($p < 0.05$)			
+:Different significant between group I and III ($p < 0.05$)			

On the other hand, the results proved that the patients which have hypothyroidism in DM type 2 controlled was 4 % and 4% of hyperthyroidism, while in DM type 2 uncontrolled were 30 % of hypothyroidism and 2% of hyperthyroidism (Figure 1 and 2).

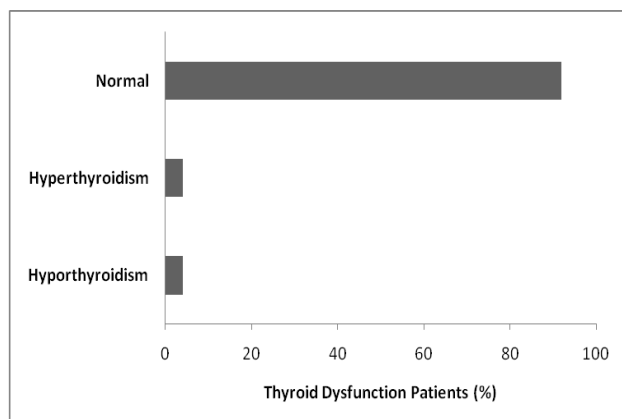


Figure 1: Percent of patients that have hyperthyroidism and hypothyroidism in DM type 2 controlled

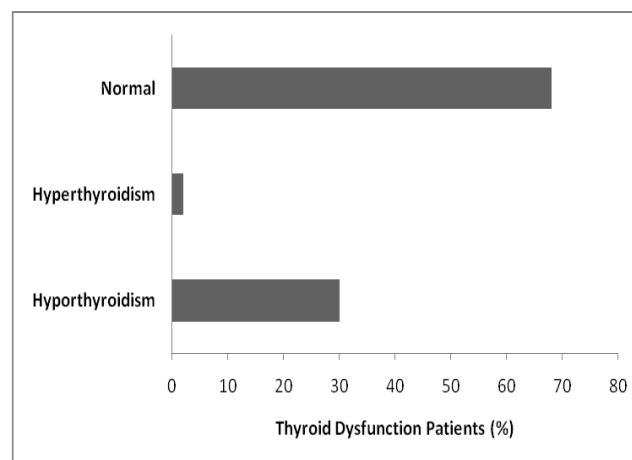


Figure 2: Percent of patients that have hyperthyroidism and hypothyroidism in DM type 2 uncontrolled.

According to the interpretation of the results as shown in the (Table 4), further described of the cases of hypothyroidism and hyperthyroidism in this study was as follows: 7 with sick euthyroid syndrome, 3 for each male and female in DM type 2 uncontrolled and 1 female in DM type 2 controlled, 6 with subclinical hypothyroidism that were 3 females and 2 males in DM type 2 uncontrolled, and 1 female found in controlled. 4 with overt hypothyroidism that were 2 females, and 2 males in DM type 2 uncontrolled, 2 females with overt hyperthyroidism were found only in controlled, while 1

male found only in uncontrolled showed the features subclinical hyperthyroidism (Figure 4).

Table 4: Classification of thyroid dysfunction in subjects with DM type 2 patients controlled and uncontrolled

Feature	Group I	Group II
Overt hypothyroidism		
Male	---	2
Female	---	2
Subclinical hypothyroidism		
Male	1	3
Female		
Overt hyperthyroidism		
Male	2	---
Female		---
Subclinical hyperthyroidism		
Male	---	1
Female	---	---
Sick euthyroid syndrome		
Male	---	3
Female	1	3
Note : overt hypothyroidism TSH increased , FT3 decreased , FT4 decreases ; subclinical hypothyroidism TSH increased , FT3 normal , FT4 normal ; overt hyperthyroidism TSH decreased , FT3 increased , FT4 increased ; subclinical hyperthyroidism TSH decreased , FT3 normal , FT4 normal ; sick euthyroid syndrome TSH normal, FT3 decreased , FT4 normal. ^[9]		

4. DISCUSSION

Present study was conducted to evaluate the thyroid hormone levels in DM type 2 controlled and uncontrolled patients. Different significant ($p < 0.05$) in TSH hormone level was found between group I and II, also between groups II and III. The most important finding in this study was that TSH was higher in DM type 2 uncontrolled compared to DM type 2 controlled and normal groups. This finding is similar to the study by Swamy *et al.*^[10] In addition, this finding was explained by poorly diabetic control interfere with thyroid axis.^[11-13] Also our finding was in agreement by previous studies.^[14,15] The results were observed that different significant ($p < 0.05$) in TSH and free T3 hormones levels between groups I and II. This finding was in agreement by previous studies.^[16] They reported, poorly controlled diabetes result in a low T3 state and a loss of TSH response to TRH. Low level of FreeT3 in group II was found compared with group I and III. , a significant difference ($p < 0.05$) was observed between both , this variation was observed between level of FreeT3 in group I and II compared to group III. The variation is due to poorly controlled diabetes which results in a low T3. This due to influence of diabetes mellitus at the conversion of T4 to T3 in the peripheral tissues and this finding was in agreement with other studies.^[3,17] They reported that alteration in thyroid hormones indicate the characteristic of low T3 syndrome and this is due to marked hyperglycemia that causes reversible reduction of the activity and hepatic concentration of T4-5-deiodinase, low serum concentration of T3, elevated

levels of reverse T3 and low, normal, or high level of T4.^[18,19] Which a characteristic finding of low T3 syndrome same conclusion was reported in other studies.^[20, 21]

Different significant ($p < 0.05$) in free T3 and free T4 between group I and III. On the other hand, the different significant in three hormones levels between group II and III. Suzuki *et al.* attributed the abnormal thyroid hormones levels found in diabetes to the presence of thyroid hormones binding inhibitor (THBI), an inhibitor of extra thyroidal conversion enzyme (5'-deiodinase) of T4 to T3 and dysfunction of the hypothalamus-pituitary-thyroid axis. These situations way prevail in diabetics and would be aggravated in poorly controlled diabetics. Stress, which is associated with diabetes, may also cause changes in the hypothalamus anterior pituitary axis in these diabetics.^[22]

There are few studies on the prevalence of thyroid dysfunction in diabetes. Some studies have targeted only DM type 1, while other only DM type 2. The prevalence of thyroid dysfunction varies among different population. The Fremantle diabetes study found a prevalence of subclinical hypothyroidism of 8.6% in women with DM type 2 in Australia^[23], in Jordan by Radaideh *et al.* found the overall prevalence of thyroid disease in DM type 2 was 12.5%.^[24] Greek study also presented the prevalence of thyroid dysfunction in DM type 2 to be 12.3%.^[25] The present study shows that 40 % of diabetic patients have thyroid dysfunction. 34 % of them are

hypothyroid and 6 % of them are hyperthyroid. However, 4% of hypothyroid in controlled and 30% of hypothyroid in uncontrolled, while 4% of hyperthyroid was found in controlled and 2 % of hyperthyroid was recorded in uncontrolled. This results were consistent with the other studies.^[26 - 28]

Further analysis shows 14 % patients show biochemical features of sick euthyroid (FT3 is below normal range with normal FT4, TSH level) 2% of them are female in DM type 2 controlled and 12 % of them are 6% for each male and female in DM type 2 uncontrolled. 12 % patients show features subclinical hypothyroidism (TSH level in the range of above normal range mIU/ml with normal FT4 and FT3 level) 2% of them are female found in controlled and 6% of them are female and 4% are male found in uncontrolled. 8% overt hypothyroidism (TSH level is above normal range while FT3 and FT4 levels are below normal) 4% for each male and female are all in uncontrolled. 4 % patients are female found only in controlled show the features of overt hyperthyroidism (FT4 level well above normal range along with low TSH). While 2% patients are male found only in uncontrolled show the features subclinical hyperthyroidism (only biochemical low level of TSH with normal FT3, FT4 level). which is similar to study by ^[29] and many other previous studies.^[12,20,29] Sick euthyroid and subclinical hypothyroidism are commonest disorder in this study (14% and 12%) respectively, This comes in accordance with other studies ^[15] which revealed higher incidence of subclinical hypothyroidism among all other patterns of thyroid dysfunction in diabetes mellitus type 2, In Al Wazzan et al study, sick euthyroid syndrome constituted 15.7% of those with abnormal thyroid function in DM type 2 patients .which is similar to many other previous studies like.^[12,22, 29, 31] The hyperglycemia seen in DM type 2 is known to have negative effects on thyroid function precisely blunting the pituitary TSH response to stimulation by hypothalamic thyroid release hormone (TRH). This may be due to possible alteration of post translational glycosylation of TRH thus affecting the biological activity. It also affects the conversion of T4 to T3 in the peripheral tissue.^[32]

In our study show high percentage of thyroid dysfunction was found in female 24 % while 16 % male. These observations are consistent with the other studies.^[14, 31,33] In this study did not show any correlation between thyroid hormone levels and FBS, HbA1c, which can be explained by that majority 68 % in DM type 2 uncontrolled and 92 % in controlled were euthyroid.

CONCLUSION

In conclusion, thyroid disease is a pathological state that adversely affects diabetic control and is commonly found in most forms of DM which is associated with DM type 2. Good glycemic control and dietary modification are usually enough for prevention the thyroid dysfunction in DM. On the other hand, the study outcome concluded

that the thyroid dysfunction may progressive in DM type 2 patients uncontrolled. Altered thyroid hormones have been described in patients with diabetes especially these with poor glycemic control in DM patients.

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