



Assessment of Thyroid Dysfunctions in Type 2 Diabetes Mellitus Patients in Surman, Western-Libya

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Abstract: Diabetes mellitus (DM) and thyroid dysfunction (TD) are the two most common endocrine disorders in clinical practice. The study aim to find out the prevalence of thyroid disorders in type 2 diabetes mellitus patients. In a cross-sectional study 369 diagnosed type 2 DM patients, of which 203 are males and 166 are females, age ranged from (18 to 73) were enrolled, from July 2016 to July 2016. Their demographic data were obtained by through a questionnaire. Serum FT3, FT4, TSH and thyroid Antibodies (Tg-Ab, AM-Ab and TR-Ab) were measured using TOSOH, ELISA and enzymatic methods respectively. Out the 369 type 2 DM patients, of whom 9.5% are thyroid disorders, 2.3% have hypothyroidism, 5.0% subclinical hypothyroidism and 2.2% hyperthyroidism. Thyroid disorders are more common in female's 16.5:1 fold. Compared with the control group, hypothyroid and subclinical hypothyroid DM patients have significant increase in TSH while significant decreases were observed in FT3 and FT4. TSH was significantly lower while FT3 and FT4 were significantly higher in hyperthyroidism DM patients. Moreover 23.3% of hypothyroidism has positive Tg-Ab, 23.3% has AM-Ab and 100% of hyperthyroidism has positive TR-Ab. The data suggested that, the prevalence of thyroid diseases is common in type 2 DM Libyan patients. Autoantibodies are the main causes of thyroid dysfunction, therefore, could predict and increase risk of thyroid disease, especially in females.

Keywords: Type 2 Diabetes Mellitus, Thyroid Dysfunction, Autoantibodies, Libya

1. Introduction

Thyroid disorders are the most common endocrine dysfunctions. The total prevalence of these disorders estimated to be 200 million worldwide ¹. Diabetes mellitus is an important health problem affecting major population worldwide. It is associated with chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism ². ³. Thyroid diseases and diabetes mellitus are most common endocrinopathies encountered in clinical practice. Diabetes and thyroid disorders have been shown to mutually influence each other and an association between these two conditions

has been reported in literature ⁴. Thyroid dysfunction in diabetes mellitus manifests either as hypothyroidism (clinical or subclinical) or hyperthyroidism (clinical or subclinical) and is reflected in the circulating levels of thyroid hormones, namely tri-iodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) which might have an impact on blood glucose homeostasis ^{5, 6}. Various complexes as biochemical, genetic, hormonal and pathophysiological mechanisms encountered in influences of the mixed endocrine and non-endocrine disorders involved in the mechanism ⁷. Thyroid diseases affect approximately 10 to 15% of the patients with diabetes, whereas in non-diabetes,

the prevalence is approximately 6% because patients with one organ-specific autoimmune disease are at risk of developing other autoimmune disorders. On one hand, thyroid hormones contribute to the regulation of carbohydrate metabolism and pancreatic function. And on the other hand, diabetes affects thyroid function tests to variable extents⁸. Thyroid disorders are the most common condition which affects the endocrine system second to diabetes mellitus. As a result, it is common for an individual to be affected by thyroid diseases and diabetes^{9, 10, 11}. The problems with interpretation of serum TSH, T4 and T3 have been recognized. Various studies reported that thyroid disorders vary according to age, genders, ethnic and geographical areas^{12, 13}. Therefore our study plan was to compare the FT3, FT4 and TSH levels in type 2 diabetic patients with respect to different age and gender groups in the population of Surman, Western, Libya.

2. Materials and Methods

A cross-sectional study was conducted in type 2 diabetes mellitus patients who attending the out patients clinic at Surman General Hospital, in Libya, from July 2015 to July 2016. Patients with other endocrine diseases and autoimmune were excluded. A (n 369) type 2 DM patients were included, (n 203) males and (n 166) females, age ranged from (18 to 73) years old. Venipuncture blood (5 ml) was collected from each participant. Sera were obtained by centrifugation at 3000 rpm, and then kept at -20°C till used.

3. Ethical Consideration

The ethical approved was taken from local authorities committee (Ministry of Health), and all patients were be informed by the aim of the study, samples and information were used anonymously.

4. Methodology

The laboratory investigations FT3, FT4 and TSH were measured using complete (for FT3 and FT4) and sandwich (for TSH) immunochemistry techniques in fully automated immunoassay analyzer (TOSOH). Microplate immunometric assay was used to estimate (Tg-Ab, AM-Ab and TR-Ab), absorbance of tests were measured using ELISA reader spectrophotometer (Techan). The quality assurance and assay

accuracy were assured by using normal and pathological control sera.

5. Statistical Analysis

The Student's *t*-test and ANOVA were employed to compare differences between the means of continuous variables. Person's correlation was used to associate between study parameters and variables. Results expressed as Mean±SD and percentage. *P*-values ≤0.05 was considered statistically significant. Data were analyzed by statistical package of social science (version 21.0; SPSS Inc.).

6. Results

The analyses of frequency showed that, out of 369 type DM patients, 35(9.5%) have thyroid disorders, of which 5.0% was subclinical hypothyroidism followed by 2.3% hypothyroidism and 2.2% hyperthyroidism, presented in figure 1.

As we have shown by ANOVA analyses results, it was found that, both hypothyroidism and subclinical hypothyroidism have significantly lower FT3 and FT4 (1.52 ± 0.56 , 2.62 ± 0.32 and 0.49 ± 0.24 , 0.90 ± 0.12) in comparison with control group (Euthyroid) (2.64 ± 0.38 and 1.80 ± 0.24) respectively, with *p*-value <0.05, which presented in table 1.

Table 3 and 4 showed, the prevalence of autoantibodies among subtypes of thyroid dysfunction, out of 35 type 2 DM of which 7(23.3%) of hypothyroidism have positive Tg-Ab and 7(23.3%) have positive AM-Ab. Moreover 5(14.3%) of hyperthyroidism have positive TR-Ab. All positive autoantibodies (TG-Ab, AM-Ab and TR-Ab) are found in females with 100%.

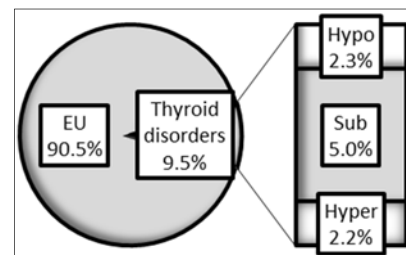


Figure 1. Frequency of thyroid disorders.

Eu= Euthyroid, Hypo= Hypothyroidism, Sub= Subclinical hypothyroidism, hyper= Hyperthyroidism

Table 1. Comparison of mean thyroid hormones and FBG in different classes of thyroid disorders.

| Characteristics | FBG | FT3 | FT4 | TSH |
|---------------------------|----------------|------------------|------------------|------------------|
| Control group (Euthyroid) | 212±70.5 | 2.64±0.38 | 1.80±0.24 | 2.65 ±0.38 |
| Hypothyroidism | 202±27.5 ** | 1.52 ±0.56 ** | 0.49±0.24 ** | 7.63±3.70 ** |
| Sub-hypothyroid | 211±50.6 ** | 2.82±0.32 | 0.90±0.12 * | 4.66±0.31 ** |
| Hyperthyroidism | 219±22.5 * | 7.63 ±0.14 ** | 9.43 ±6.88 ** | 0.09 ±0.03 ** |

* Significant, ** highly significant. Results expressed as Mean±SD, significant differences considered as *p*-value ≤0.05

Table 2. Gender wise comparison of thyroid hormones and FBG.

| Characteristics | Males | Females | P-values |
|-----------------|-----------|-------------|----------|
| | Mean±SD | Mean±SD | |
| FT3 (pg/ml) | 2.08±0.33 | 2.83±0.13 | 0.033 |
| FT4 (ng/dl) | 1.15±0.24 | 1.42 ± 0.20 | 0.146 |
| TSH (μIU/ml) | 1.87±0.91 | 2.57±0.16 | 0.000 |
| FBG mg/dl | 210±54.0 | 218±82.0 | 0.220 |

Results expressed as Mean±SD, significant differences considered as p-value ≤0.05

Table 3. Frequency of autoantibodies in different classes of thyroid disorders.

| Characteristics | Tg-Ab | | AM-Ab | | TR-Ab | |
|------------------|----------|-----------|----------|----------|----------|-----------|
| | +ve | -ve | +ve | -ve | +ve | -ve |
| Hypothyroidism | 7(23.3%) | - | 7(23.3%) | - | - | - |
| Subclinical Hypo | - | 23(65.7%) | - | 23(65.7) | - | 23(65.7%) |
| Hyperthyroidism | - | - | - | - | 5(14.3%) | - |

+ve = positive result –ve = negative result

Table 4. Frequency of autoantibodies in different classes of thyroid disorders among gender.

| Characteristics | Tg-Ab | | AM-Ab | | TR-Ab | |
|---------------------------|-------|--------|-------|--------|-------|--------|
| | Male | Female | Male | Female | Male | Female |
| Control group (Euthyroid) | - | - | - | - | - | - |
| Hypothyroid | - | 100% | - | 100% | - | - |
| Sub-clinical hypo | - | - | - | - | - | - |
| Hyperthyroid | - | - | - | - | - | 100% |
| Total | 100% | 100% | - | 100% | - | 100% |

7. Discussion

Insulin and thyroid hormones influence metabolism of carbohydrates, proteins, and lipids, hence their interrelation between DM and thyroid disorders^{7, 14, 15}. Several studies have been published, investigated the association between diabetes and thyroid dysfunction. Therefore the present study carried out to evaluate the prevalence of thyroid disorders among type 2 DM in Libyan population, moreover to associate between thyroid disorders and autoantibodies.

The analyses of frequency showed that, the prevalence rate of thyroid disorders in type 2 DM Libyan population was 9.5%, 5.0% is subclinical followed by 2.3% hypothyroidism and 2.2% hyperthyroidism. Thyroid disorders are more common in female than male 16.5:1 fold. In fact that, several epidemiological studies reported that, high prevalence of thyroid disorders (27.8%) among type 2 DM in India, and other study done in Spain reported 32.4% prevalence of thyroid disorders. These findings indicated that, type 2 DM Libyan population has low prevalence of thyroid disorders in comparison with other populations.

Interestingly, the present study observed significant higher in TSH and FT3 among type 2 DM females in comparison with males *p*-value (0.000 and 0.033) respectively. Concurrent with previous finding that, estrogen hormone has direct role in thyroid follicular cells, and its role in thyroxine binding globulin (TBG)¹⁶, explain higher level of TSH and FT3 in type 2 DM females.

The present study provide evidence that, both hypothyroidism and subclinical hypothyroidism type 2 DM patients have significantly lower FT3 and FT4 level, while

significantly higher was observed in mean TSH level when compared with control group (euthyroid). Concurrent with previous studies report, hypothyroidism is caused by insulin resistance, which led to less response of peripheral muscles to thyroid hormones¹⁷. On the other hand abnormality of thyroid hormones level attributed to insulin resistance, which decrease conversion of T4 to active T3, also reduced hypothalamus thyrotropin releasing hormone (TRH) in DM patients. In fact that, hypothyroidism result in lipid dysfunctions, so could magnify the cardiovascular disease and endothelial dysfunction in DM patients¹⁸.

Controversial findings have been documented regarding subclinical hypothyroidism, one reported an association between type 2 DM and hypothyroidism, other conflicting findings^{3, 17}. Therefore further investigations are recommended. Concurrent with previous findings, thyroid dysfunctions most probably caused by autoimmunity and may be associated DM. Moreover thyroid dysfunction has greater impact on dyslipidemia and cardiovascular disease. Out of 35 of thyroid dysfunction patients, of whom 94.3 are female and 5.7 are male. TG-Ab and AM-Ab were found in 23.3% and 23.3% among hypothyroidism female respectively, while autoantibodies were not found in subclinical hypothyroidism. Moreover, all hyperthyroidism females have positive TR-Ab.

In addition several studies reported that, patients with specific autoimmune disease at higher risk of developing other autoimmune disorders, indeed that thyroid disorders are more common in female, interpreted higher thyroiditis among female. Similarity of several studies reported, thyroiditis is most common disorders in type 2 DM patients with hypothyroidism¹⁹.

8. Conclusion

In conclusion, the results of present study suggest that, the prevalence of thyroid diseases is common in DM Libyan patients. Furthermore, autoantibodies are the main causes of thyroid dysfunction, therefore, could predict and increase risk of thyroid disease, especially in females. Meanwhile, routinely monitoring is recommended for diagnostic, prevention and management of related complications in type 2 DM Libyan population.

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Conflict of Interest

The authors declare that no conflict of interest related to this manuscript.

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