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Original Article

Evaluation of Subclinical Thyroid Dysfunction in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Objective: To evaluate subclinical thyroid dysfunction in Type II Diabetes Mellitus patients compared to healthy individuals.
Study Design: Cross-sectional study.
Place and Duration of Study: Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology, Rawalpindi Pakistan, from July 2021 to May 2022.
Methodology: A total of 437 participants, of which 207 had Type II Diabetes Mellitus and 230 had no comorbidities, were included in the study. Thyroid hormone levels were analyzed from serum samples by chemiluminescent method on automated immunoassay analyzer (Advia centaur). Mann-Whitney U test was applied to compare thyroid hormone levels between both groups, and *p*-value of ≤0.05 was regarded as significant. For risk assessment, frequency and odds ratios, with 95% confidence interval, were determined.
Results: There was a significant difference in the medians of Thyroid Stimulating Hormone (*p*=0.002) and total Triiodothyronine (T3) (*p*=0.004), while no significant difference was observed in the medians of Free Thyroxine (fT4) (*p*=0.573) between patients with Type II Diabetes and healthy participants. Diabetic participants had a higher frequency of subclinical thyroid dysfunction than healthy individuals (36% vs 1.3%). Diabetic patients had a greater risk of subclinical thyroid dysfunction than healthy participants (OR: 2.62 vs 0.06) while female participants risk of thyroid dysfunction was higher than males.
Conclusion: Risk of subclinical thyroid dysfunction was greater in Type II Diabetes Mellitus patients while subclinical hypothyroidism was the most common thyroid dysfunction.

Keywords: Endocrinology, Thyroid Disorders, Thyroid Function Tests, Type 2 Diabetes Mellitus.

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INTRODUCTION

Type II Diabetes Mellitus (T2DM) and thyroid disorders (TD) are two major endocrine abnormalities, that are known to effect each other.[1,2] T2DM contributes to over 60% of the world's diabetic population.[3] According to the International Diabetic Federation, over 33 million (26.7%) individuals in Pakistan have diabetes.[4,5] T2DM affects thyroid gland functionality at the level of hypothalamic regulation of TSH release, while in peripheral tissues, it causes impairment in the conversion of thyroxin (T4) to triiodothyronine (T3).[6,7] Hyperglycemia results in decreased levels of T3 and Thyroxine-5'deiodinase, increased reverse triiodothyronine (rT3) and abnormal level of T4.[8] Insulin resistance is also linked to hyperthyroidism and hypothyroidism, which is speculated to be the cause of poor glucose metabolism in T2DM.[9] As the prevalence of T2DM is very high in Pakistan and expected to worsen in the coming yeas,[10] therefore, our study was designed with the aim to evaluate thyroid hormone levels in T2DM patients compared to healthy individuals in Pakistani population.

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METHODOLOGY

This cross-sectional study was performed at Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan, from July 2021 to May 2022. Institutional Review Board of AFIP approved the study (IRB no. BS AHS/CHP-6/READ-IRB/21/633). Sample size of 207 was estimated by using WHO Calculator with 95% confidence interval with prevalence of thyroid disorders in T2DM found to be 16% from literature.[11] We enrolled 207 patients with T2DM and 230 healthy participants, using non-probability sampling technique.

Inclusion Criteria: We enrolled patients of either gender, diagnosed with T2DM, aged more than 18 years while non-diabetic healthy individuals of similar age and gender were included.

Exclusion Criteria: Patients less than 18 years of age, pregnant women, diagnosed with thyroid disorders or previous history of neck trauma or surgery were excluded.

After receiving informed written consent from participants, blood samples were taken, with whole blood collected in EDTA for HbA1C estimation and serum separator tube for TSH, T3 and fT4 level estimation. HbA1C was analyzed through capillary electrophoresis on Sebia Capillary 3 OCTA and thyroid hormone levels were analyzed through solid phase, enzyme labeled chemiluminescent immunoassay on ADVIA centaur. Collected data was analyzed through Statistical Package for the Social Sciences (SPSS) version 26. Normality of data was checked by applying Shapiro-Wilk test. Quantitative variables were represented as Median (IQR) as data was non-parametric. Mann-Whitney U test was applied to compare demographic variables and thyroid hormone levels with *p*-value of ≤0.05 regarded as significant. Frequencies of thyroid disorder and odds ratios were determined for risk estimation among patients.

RESULTS

A total of 437 individuals were included for analysis, further divided into two categories, with 207 being T2DM patients, of which 103(49.76%) were male and 104(50.24%) were female, and 230 being healthy individuals, of which 115(50%) were males and 115(50%) were females. As assessed by Shapiro-Wilk test, distribution of data was non-parametric. There was a significant difference in the medians of TSH (*p*-value=0.002), T3 (*p*-value=0.004), and HbA1C (*p*-value<0.001), between patients with T2DM and healthy individuals, although no statistically significant difference was observed in the medians of fT4 (*p*-value=0.573) Table-I.

Out of 207 patients with T2DM, 75(36.23%) patients had subclinical thyroid dysfunction and 3(1.3%) out of 230 healthy individuals were found to have subclinical thyroid dysfunction. Out of 75 subclinical thyroid dysfunction cases among patients with T2DM, 55(73.33%) had subclinical hypothyroidism while 20(26.67%) had subclinical hyperthyroidism, as shown in Table-II.

Females had more thyroid dysfunction than males, as among 78 individuals having abnormal thyroid function, 54(69%) were females and 24(31%) were males. Odds ratio with 95% confidence interval for risk of subclinical thyroid dysfunction was higher in patients with T2DM than healthy individuals, as shown in Table-III. The odds ratio for risk estimation of subclinical thyroid dysfunction according to gender with 95% confidence interval revealed odds ratio for male participants was 0.57 and for females, 1.51, indicating greater risk of subclinical thyroid dysfunction for females.

Table-I: Comparison Between Patients with T2DM and Healthy Participants Without T2DM (n= 437)

Test	With T2DM Median (IQR) n=(207)	Without T2DM Median (IQR) n=(230)	*p*-value
HbA1c %	7.00(2.30)	5.30(0.40)	<0.001
TSH mIU/L	2.10(4.40)	1.80(1.63)	0.002
Total T3 nmol/L	1.50(0.50)	1.50(0.50)	0.004
fT4 pmol/L	15.10(3.70)	14.90(3.13)	0.57

Table- II: Frequency of Subclinical Thyroid Disorders in Patients with T2DM (n= 437)

Thyroid Dysfunction	Frequency n (%)
Subclinical Hypothyroidism	55 (73.33%)
Subclinical Hyperthyroidism	20 (26.67%)

Table-III: Risk Estimation of Subclinical Thyroid Dysfunction (n=437)

Subclinical Thyroid Dysfunction	With T2DM n=207	Without T2DM n=230	Male n=218	Female n=219
Present	75(36%)	3(1%)	24(11%)	54(25%)
Not present	132(64%)	227(99%)	194(89%)	165(75%)
Odds ratio (95% CI)	2.62 (2.26-3.01)	0.06 (0.02-0.19)	0.57 (0.40-0.81)	1.51 (1.25-1.81)

DISCUSSION

Our study found that patients with T2DM had higher risk of subclinical thyroid dysfunction, particularly subclinical hypothyroidism, compared to individuals without T2DM. Additionally, females with T2DM had a higher incidence of thyroid dysfunction than males. According to literature, serum fT3 and fT4 levels did not differ significantly between either group, with only serum TSH levels being different, similar to our study, with frequency of thyroid disorders in T2DM found to be higher than individuals without T2DM, while females had more thyroid dysfunctions than males among patients with T2DM.[12,13] Another study reported that serum T3 levels were low in patients with T2DM and fT4 levels were same in both groups, similar to our study, but unlike our findings, this study reported that serum TSH levels were similar in both groups.[14] This difference may be due to different test used as in our study, HbA1C (capillary electrophoresis technique) was used to differentiate between presence or absence of T2DM while in other studies fasting plasma glucose estimation and patient history was used. Subclinical

hypothyroidism has emerged as the most common thyroid disorder found in literature with frequency of subclinical hypothyroidism being 12%, clinical hypothyroidism 0.7%, subclinical hyperthyroidism 0.3%, and clinical hyperthyroidism as 0.3% in individuals with T2DM who had no previously known thyroid dysfunction.[15,16] Indeed, one study found that thyroid dysfunction affects 12.3% of the general population diagnosed with T2DM, with women more affected than males,[17] similar to recent studies which reported that thyroid disorders were strongly linked with female gender, central obesity, and duration of Type II Diabetes Mellitus of more than 5 years,[18,19] similar to our study which showed subclinical hypothyroidism was the most common disorder among patients with T2DM and females were more at risk for thyroid dysfunction than males.

LIMITATION OF STUDY

Our study was a single center study and only a small sample of patients with T2DM was included. Multicenter studies with large sample size and subjects from other geographic locations of Pakistan may be enrolled and analyzed to explore further statistical and pathological associations.

CONCLUSION

We found the frequency of subclinical Thyroid dysfunction to be greater among patients with T2DM and subclinical hypothyroidism was the most common thyroid disorder with risk of subclinical Thyroid dysfunction higher in female patients of T2DM.

Conflict of Interest: None.

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Authors' Contributions:

Following authors have made substantial contributions to the manuscript as under:

MAM & MA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

ZHH & AB: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

MUM & MY: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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