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Original Research Article

Thyroidal Hormonal Variations: A Neglected Entity in Type II Diabetes Mellitus

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Abstract:

Introduction: The co-existence of thyroid dysfunction in type 2 diabetes mellitus patients will worsen the macrovascular and microvascular complications, morbidity, mortality, and quality of life. Over the years it has been evident that there exists regards a strong relationship between thyroid and diabetes. The incidence of thyroid diseases differs in different diabetic population. Thyroid through its hormones exert a great influence on various organs in the body. Similarly insulin also plays a major role in various cellular metabolic activities. Hence, a deficiency or excess of the thyroid hormones are thought to alter the functional integrity of insulin

Aim and Objective: The objective of this study was to determine the prevalence of thyroid dysfunction among patients with Type 2 diabetes.

Methods: This Hospital based prospective cross sectional study was conducted from May 2022- May 2023. A total of 100 patients with type-2 diabetes who regularly attend the outpatient Endocrinology Department, GGH Ananthapuramu. A detailed history and examination was done after getting informed consent. Blood samples were collected and sent to the laboratory for the evaluation of thyroid profile.

Results: Thyroid dysfunction was found in 36%of the patients with Type 2 DM. Among 100 patients the prevalence of subclinical hypothyroidism was 18 %, primary hypothyroidism was 10 %, clinical hyperthyroidism 16 %.and 64 are in euthyroid state.

Conclusion: Thyroid Hormone testing is usually neglected in Type 2 Diabetes mellitus. Unidentified Thyroid Dysfunction will have impact on microvascular and macrovascular complications of Type 2DM. Thus, Routine Screening of Thyroid is advised in all patients of type 2 DM to reduce the morbidity and mortality.

Keywords: Thyroid Dysfunction, Type 2 Diabetes Mellitus, Hyperthyroidism, Hypothyroidism.

Introduction

The current understanding of the relationship between type 2 diabetes and thyroid dysfunction is lacking in clarity due to the intricate nature of the underlying mechanism. This complexity arises from the involvement of multiple variables, including the synthesis of thyrotropin releasing hormone (TRH), the circadian rhythm of thyroid stimulating hormone (TSH), insulin resistance, autoimmunity, and the utilisation of metformin. [1]

Diabetes mellitus is a significant global health issue that impacts large populations across the globe. The condition is distinguished by either complete or partial insufficiencies in the secretion of insulin and/or the effectiveness of insulin, which are accompanied by persistent high blood sugar levels and disruptions in the metabolism of carbohydrates, lipids, and proteins.[2] The thyroid gland is a highly vascular organ that ranges in colour from brown to red and has a hard firmness. It is situated anteriorly in the lower region of the neck and posteriorly to the

strap muscles. It extends from the level of the fifth cervical vertebra down to the first thoracic vertebra. [3] The morphology of the thyroid gland exhibits a range of shapes, ranging from a H to a U shape. It is composed of two lateral lobes that are connected by a median isthmus. The superior and inferior poles of these lobes are linked by this isthmus. The average height of the thyroid gland measures between 12 to 15 mm, and it is positioned above the second to fourth tracheal rings, as depicted in Figure 3. In certain cases, it is possible for the isthmus to be non-existent, resulting in the presence of two separate lobes of the gland. The lateral lobes of the thyroid gland typically have dimensions ranging from 50 to 60 mm, corresponding to a volume of approximately 8 to 10 ml. At the level of the oblique lines on the laminae of the thyroid cartilage, the superior poles of these lobes extend laterally.. At the level of the fifth tracheal cartilage, there is a lateral divergence observed in the lower poles. The weight of the thyroid gland exhibits variation, with an average range of 15 g to 30 g in adult individuals. Notably, it tends to be relatively heavier in females. During the menstrual cycle and pregnancy, there is an observed enlargement of the thyroid gland.[3]

The thyroid gland is responsible for the production of significant hormones, namely triiodothyronine (T3) and tetra-iodothyron (T4). Thyroid hormones are responsible for regulating various physiological processes, including metabolism, organ function, growth, brain development, fuel metabolism, body temperature, and reproduction. In contrast, the synthesis of thyroid hormones (T3 and T4) occurs within the follicular cells of the thyroid gland and is controlled by the production of thyroid-stimulating hormone (TSH) by the thyrotropes located in the anterior pituitary gland. The production of thyroid-stimulating hormone (TSH) is regulated by the release of thyroid-releasing hormone (TRH), which is synthesised by the hypothalamus. The hypothalamus and pituitary gland exert regulatory control over the secretion of hormones by the thyroid gland. The hypothalamus and pituitary gland reduce the production of thyrotropin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH) when the circulating levels of thyroxine (T4) reach an adequate threshold.[4]

Thyroid diseases and diabetes mellitus are prevalent endocrine disorders frequently observed in clinical settings, and their interrelationship has been well-documented. The coexistence of these conditions has been extensively reported.[5]

Unregulated type-2 diabetes mellitus has an impact on the levels of thyroid hormones, specifically plasma tri-iodothyronine (T3) and thyroxine (T4). However, it is common for underlying thyroid disorders to remain undiagnosed due to the similarity in clinical symptoms between thyroid disorders and diabetes. As a result, these disorders may be overlooked or mistakenly attributed to other medical conditions. Multiple studies have documented an increased incidence of thyroid disorders among individuals diagnosed with type-2 diabetes mellitus, with hypothyroidism being the most prevalent condition. Various potential explanations have been proposed to account for the observed correlation between diabetes mellitus and hypothyroidism. These include genetic factors, biochemical mechanisms, and hormonal influences.[6] Prevalence of thyroid dysfunction is greater in diabetes patients compared to the general population. Prevalence of thyroid dysfunction in general population is around 6.6-13.4%, while in diabetes population around 10-27%.[7]

The simultaneous presence of diabetes and thyroid disorders has the potential to exacerbate the susceptibility to diabetic retinopathy and diabetic nephropathy among individuals diagnosed with diabetes. The existing guidelines lack clarity and specificity regarding the recommended frequency of thyroid function monitoring in patients with Type 2 diabetes mellitus. The identification and management of thyroid dysfunction in individuals with diabetes has the potential to enhance glycemic control, mitigate cardiovascular risk, and enhance overall health and wellness. Hence, the present investigation was undertaken to ascertain the neglected entity of thyroid dysfunction among individuals diagnosed with type 2 diabetes mellitus.

Methods:

Study design: Hospital based prospective cross-sectional study

Study period: A period of one years from the date of approval of my publication work by Institutional Scientific and Ethical Committee. May 2022- May 2023.

Study setting: Endocrinology Department and Biochemistry Department, GGH Ananthapuramu.

Study subjects: A total of 100 patients with type-2 diabetes who regularly attend the outpatient Endocrinology Department, GGH Ananthapuramu were included in the study.

Sample size and Type:

Random Sampling (Sample)

It was estimated that 27% of people had Thyroid dysfunction in diabetics.[7] The size of the sample was determined based on the acquired prevalence, which was found to be 73%, at a confidence interval of 95% and an absolute precision of 10%.

$n = 4pq/L^2$ n = Minimum sample size
p = Prevalence in percentage
q = 100-p
L = Allowable error in percentage of prevalence.
Using the above formula and data,

p = 27
q = (100-p) =100– 27= 73 ;
L = 10%
Minimum sample (n) = $\frac{4x73 \times 27}{10x10}$ = 78.84

The minimum sample size 78 case by the following sampling method. But the convenience purpose 100 sample was obtained.

Known Type–2 diabetic patients were included in the study after getting informed consent.

Patients with type-1 diabetes, diabetic nephropathy, known history of thyroid dysfunction, pregnant women, patients with recent interventions: pulse corticosteroids and/or radioiodine, history of receiving any drug that may have caused thyroid dysfunction and with a history of hospitalisation for less than 6 months were excluded. After informed consent, 7 ml of blood was drawn from the ante cubital vein after 8-12 hours of fasting. Fasting Blood sugar was estimated by GOD POD method. Serum T3, T4, and TSH were evaluated by chemiluminescence. Based on the thyroid function profile, the target subjects were categorised into two main groups. The first group categorised as euthyroid included diabetic patients who had normal thyroid function profile, and the second group included diabetic patients with abnormal thyroid profile.

According to their thyroid profiles, the latter were categorised into four groups as follows:

1. Subclinical Hypothyroidism
2. Clinical / Overt Hypothyroidism
3. Subclinical Hyperthyroidism
4. Clinical / Overt Hyperthyroidism

Statistical Analysis: The data was tabulated and analysed. Statistical analysis was performed using SPSS version 15. Categorical variables were described as frequency (percentage), mean ± 1.96 * standard deviation was used for continuous parameters.

Ethical Clearance This study had been ethically approved by Research Ethic Committee from Government Medical College, Ananthapuram.

Results:

Table 1: Distribution of Thyroid Status among Type-2 Diabetes Patients

Sr. No.	Thyroid status	Frequency
1	Normal Thyroid	64
2	Primary Hypothyroidism	2
3	Subclinical Hypothyroidism	18
4	Hyperthyroidism	16

Table 2: Association on of Thyroid Disorders with Gender, Age and Duration of Diabetes, BMI among Type 2 Diabetes Patients

Variable	Gender		Age		Duration of Diabetes	
	Male	Female	<50 yrs	>50 yrs	≥ 5 yrs	< 5 yrs
No of diabetics with thyroid dysfunction	15	21	25	11	19	17
No of diabetics without thyroid dysfunction	23	41	13	51	18	46
Odds ratio	1.27		7.4895		2.8562	
95 % CI	0.5516 to 2.9392		2.8957 to 19.3708		1.2189 to 6.6927	
Chi square value	0.321		23.6		6.0072	
P value	P = 0.5713		< 0.00001		0.014248.	

Table 3: Mean and SD of Serum levels of FBG TSH, T4 and T3 among Type-2 Diabetes Patients

Thyroid status	FBG (mg/dl)	TSH (µmol/L)	T4 (nmol/L)	T3 (nmol/L)
Normal Thyroid	164.86 ± 4.87	2.40 ± 0.26	98.85 ± 4.52	1.20 ± 0.06
Primary Hypothyroidism	167.525 ± 3.25	35.01 ± 3.51	38.25 ±2.01	0.52 ± 0.03
Subclinical Hypothyroidism	158.3±8.2	38.23 ± 4.51	30.25±2.03	0.46 ± 0.02
Hyperthyroidism	177.16 ± 4.72	0.021 ± 0.004	210 ± 5.2	6.11 ± 0.35

A total 100 patients with Type 2 Diabetes were included in the study. Table 1 depicts Distribution of Thyroid Status among Type-2 Diabetes Patients. Among 100 patients The prevalence of subclinical hypothyroidism was 18 %, primary hypothyroidism was 10%, clinical hyperthyroidism 16% and 64 are in euthyroid state. Table 2 depicts Association on of Thyroid Disorders with Gender, Age and Duration of Diabetes, BMI among Type 2 Diabetes Patients. In the current study among the patients with thyroid disorders 21% were females. 15% were males .25% were <50 yrs of age and 11% were>50 yrs age. 17% were <5 yrs of duration of Type 2 DM.19% were > <5 yrs of duration of Type 2 DM. However statistical Significance found in Duration of Diabetes and age of patients. Table 3 shows, Mean and SD of Serum levels of FBG TSH, T4 and T3 among Type-2 Diabetes Patients. The result of the present study shows increase in the means of TSH primary hypothyroidism and subclinical

hyperthyroidism among Type-2 Diabetes Patients. While there was a highly significant decrease in the means of TSH level in diabetic with hyperthyroidism group.

Increase in the means of T4 level in diabetic with hyperthyroidism group (210±5.2 nmol/L) when compared to diabetic with Subclinical Hypothyroidism group (30.25±2.03), Primary Hypothyroidism (35.01±3.51)

Increase in the means of T3 level in diabetic with hyperthyroidism group (6.11±0.35 nmol/L). Decrease in the mean of T3 level in primary hypothyroidism and subclinical hyperthyroidism among Type-2 Diabetes Patients (0.52±0.03, 0.46±0.02).

Discussion

Epidemiological research in endocrinology has focused on thyroid dysfunction in type 2 diabetes patients in the recent decade. These studies examined prevalence. Hypothyroidism, which pathophysiology, aetiology, comorbidities in type-2 diabetes complications. This study has showed a high prevalence (36%) of thyroid dysfunction in patients with type 2 diabetes and this is correlated with other studies Pasupathi P et al, Singh et al Ajaz Ahmad Telwani, Reddy et al and Demitrost et al with prevalence of 45%, 30% 29% 29% and 31.2 % respectively. [8,9,10,11,12]

In this study Among 100 patients The prevalence of subclinical hypothyroidism was 18%, primary hypothyroidism was 10%, clinical hyperthyroidism 16 % and 64% are in euthyroid state. Type 2 diabetes and thyroid dysfunction share a pathophysiology. DM appears to affect thyroid function in two ways: hypothalamic regulation of TSH release and peripheral tissue conversion of T4 to T3. Hyperglycaemia lowers hepatic T4-5 deiodinase, lowers serum T3, raises reverse T3, and lowers, normalises, or raises T4. Thyroid hormones influence metabolism, and diabetes can change metabolism.[13,14] In diabetic individuals, it was discovered that there is a considerable decrease in the plasma levels of T3, as well as a significant increase in the levels of TSH.

The thyroid hormones have an insulin-opposing effect, which indirectly amplifies insulin's effects on the body. Diabetes mellitus causes a reduction in the production of thyroid stimulating hormone (TSH), which is ultimately accountable for the condition's characteristically low levels of thyroid hormone. The findings of this study indicated that people with type II diabetes were at a greater risk of developing hypothyroidism on a more regular basis. [15] Hyperthyroidism associated with increased glucose intestinal absorption, which enhancing glycogenolysis and gluconeogenesis. This leads to hyperglycaemia and the subsequent increase in glucose-stimulated insulin secretion. Furthermore, hyperthyroidism is associated with increased hepatic glucose output, reduced insulin action and increased ketoacidosis resulting from excessive thyroid stimulated lipolysis.[16,17] Thyroid hormones antagonize insulin action. Increases in plasma thyroid hormone levels (as for example in hyperthyroidism) impair the ability of insulin to suppress hepatic glucose production and to increase glucose uptake in muscle [18]. However, thyroid hormones oppose the action of insulin and stimulate hepatic gluconeogenesis and glycogenolysis.[19]

Diabetes management is complicated by hyperthyroidism and hypothyroidism. Undiagnosed thyroid problems may also affect diabetes and its complications. Subclinical hypothyroidism increased retinopathy and nephropathy in diabetics. Thus, diabetics may benefit from subclinical hypothyroidism therapy.[20]

Conclusion

According to recommendation from several endocrinology and thyroid organizations, TSH screening should be done first in patients attending healthcare facilities, not as mass screening in the community. Thyroid Hormone testing is usually neglected in Type 2 Diabetes mellitus. Unidentified Thyroid Dysfunction will have impact on microvascular and macrovascular complications of Type 2DM. Thus, Routine Screening of Thyroid is advised in all patients of type 2 DM to reduce the morbidity and mortality

Limitations of this study are as time period is limited and number of patients is limited results in large population are unpredictable.

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