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Evaluation of thyroid profile in patients with type 2 diabetes mellitus in a tertiary care hospital in Nepal

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ABSTRACT

Background

Diabetes mellitus and thyroid disorders are among the two most common endocrine disorders encountered in clinical settings. These two disorders are shown to influence each other, and scholars generally report an association between both conditions. Uncontrolled thyroid disorders can result in abnormal glycemic control in diabetic patients. Thyroid disorder is mainly manifested in patients suffering from diabetes and is associated with increased age, especially in type 2 diabetes. This study aims to establish the prevalence of thyroid disorder in type 2 diabetes mellitus, to estimate fasting blood glucose levels, and to detect glycated haemoglobin (HbA1c) levels in euthyroid, hypothyroid, and hyperthyroid subjects.

Material and methods

The present hospital-based cross-sectional study was conducted on 66 subjects aged 21 to 80. The thyroid hormones were evaluated using the ELISA method, and HbA1c was estimated using the High-performance liquid chromatography (HPLC) method.

Results

The present study showed the majority of participants were 41-60 years old and had a higher prevalence of hypothyroidism (21.21%) in type 2 diabetes mellitus (T2DM), but the prevalence of hyperthyroidism was lower, 10.60% in T2DM.

Conclusion

T2DM was found to be more common among older adult groups (41-60 years). Hypothyroidism was more prevalent compared to hyperthyroidism in diabetes mellitus. Therefore, timely diagnosis should be made to prevent complications of thyroid disorders in diabetic individuals.

Keywords
Euthyroidism, glycated hemoglobin, Type 2 diabetes mellitus, thyroid disorders

Background

Diabetes mellitus (DM) and thyroid dysfunction (TD) are among the most common endocrinopathies that are encountered in clinical practice and frequently coexist. A higher prevalence of TD is seen in patients suffering from T2DM than in non-diabetic individuals, and its prevalence in Kathmandu, Nepal, is 27.94% [1-3]. Various metabolic, inherited, and hormonal abnormalities intermingle, leading to the pathophysiological relationship between T2DM and thyroid illness [4].

Diabetes alters the action of thyroid hormones by influencing the levels of thyroid-stimulating hormone (TSH) and hinders the ability of peripheral tissues to convert thyroxine (T4) to triiodothyronine (T3) [5, 6]. Furthermore, in diabetic patients with normal thyroid function, long-term hyperglycemia may contribute to the development of thyroid illness [5]. Insulin resistance (IR) and/or decreased insulin production fluctuation in people with type 2 diabetes (T2DM), which results in hyperglycemia [6]. Conversely, chronic hyperglycemia might be a factor in the onset of thyroid disease [5].

Patients with diabetes mellitus have an increased prevalence of thyroid dysfunction compared to non-diabetic individuals, among whom hypothyroidism is the most prevalent disorder. Studies have found varying degrees of prevalence of thyroid hormone abnormalities in people with T2DM [2, 3].

Since undiagnosed thyroid dysfunction can alter metabolic controls in diabetic patients and raise pre-existing cardiovascular risk, diagnosing and treating thyroid abnormalities in these individuals may improve glycemic control, lower cardiovascular risk, and improve overall health and well-being [7, 8]. Thus, this study aims to estimate fasting plasma glucose and HbA1c in euthyroid subjects and in patients with a thyroid disorder and determine the prevalence rates of thyroid dysfunction in T2DM.

Material and methods

Study design and the participants

The present cross-sectional study was conducted at BP Koirala Institute of Health Sciences, Dharan, Nepal, from March to May 2024. Study samples were collected from its central laboratory. The present study included 76 patients visiting the medicine inpatient and outpatient departments, with their ages ranging from 21 to 80 years of both genders. Patients were selected by a non-probability sampling method using a consecutive sampling technique and were informed about the objective of the study; in addition, consent was taken from all the participants.

Experimental procedure and data collection

Participants were advised to visit the hospital laboratory in a fasting condition. A venous blood sample was obtained by venipuncture from the cubital vein under aseptic conditions. Two ml of blood was collected in EDTA tubes for HbA1c estimation, which was done using high-performance liquid chromatography (HPLC) methods. The remaining blood was centrifuged, serum was separated, and free T3 (fT3), free T4 (fT4), and TSH were analyzed using ELISA. Reference ranges provided by kits for thyroid hormones were fT3 (2.00–4.2 pg/ml), fT4 (8.90-17.20 pg/ml) and TSH (0.30-4.5 μIU/ml), fasting blood glucose (FBG) (70-110 mg/dl), and HbA1c (4.0-5.6%).

Inclusion criteria

Individuals who were diagnosed with T2DM the patients who were undergoing diabetic treatment, those who were consuming anti-hypoglycemic agents, or individuals having FBG ≥126 mg/dl on more than two separate occasions or HbA1C ≥7%, and patients who had given consent for this research.

Exclusion criteria

Patients who were experiencing diabetic complications and had a history of thyroid dysfunction, including those who had undergone thyroidectomy and taken anti-thyroid medications, were excluded. In addition, the patients who had Graves' disease, thyroid carcinoma, radiation exposure, toxic multi-nodular goiter, toxic adenoma, or gestational hyperthyroidism. Individuals who were not willing to participate in the study.

Ethical committee approval and informed consent

Ethical Committee of the BP Koirala Institute of Health Sciences, Dharan approved the study. Consent was obtained from the participants prior to the study. This study was done according to the declaration of Helsinki.

Data interpretation and statistical analysis

After obtaining the laboratory results, an analysis was done using the Statistical Package for the Social Sciences (SPSS) version 16. Descriptive statistics were represented as mean ± standard deviation (SD) with 95% confidence intervals for continuous data (age, fT3, fT4 and TSH, fasting blood glucose, HbA1c), and the frequency number was used to depict the categorical data (gender).

Results

The current study includes diabetic subjects whose ages range from 21 to 80 years and whose mean age was 52.07. Among the study participants, 31 (46.96%) were male and 35 (53.04%) were female. Furthermore, the majority of the study participants belong to the age group 41-60 years (53.03%), but the least number of participants belong to the age group of 21-40 years (21.21%) (Table 1).

Table 1: Age and gender distribution of study participants

Age	Male		Female		Total	
	n	(%)	n	(%)	n	(%)
	31	46.96	35	53.04	66	100
21-40	10	15.15	4	6.06	14	21.21
41-60	10	15.15	25	37.87	35	53.03
61-80	11	16.66	6	9.09	17	25.75

Table 2: Biochemical Parameters of the Study Group

Parameters	Mean ± SD		
	Euthyroid n=45(68.18%)	Hypothyroid n=14 (21.21%)	Hyperthyroid n=7 (10.60%)
fT3	3.09± 0.60	2.90±0.58	4.79±1.99
fT4	12.42± 1.25	11.32±3.03	16.36±4.50
TSH	2.64±1.04	6.92±3.54	2.36±1.37
FBG	122.22±63.34	109.88±9.64	138.95±23.64
HbA1c	7.81±1.90	6.73±0.88	7.32±0.96

Among 66 patients having T2DM, 68.18% had normal thyroid function (euthyroid), 21.21% were hypothyroid patients, and the rest 10.60% were hyperthyroid patients. The overall prevalence of thyroid disorder was 31.81%, including both hypothyroidism and hyperthyroidism, which is shown in Table 2.

The mean values of fT3 and fT4 were 3.09± 0.60 and 12.42± 1.25 in euthyroidism, whereas the values are lower in hypothyroidism and higher in hyperthyroidism. The mean value of TSH was 2.64±1.04 in euthyroidism, whereas it increased in hypothyroidism and decreased in hyperthyroidism. When comparing fasting blood glucose (FBG), it is 122.22±63.34 in euthyroidism, whereas the value is lowered in hypothyroidism and is raised in hyperthyroidism. Similarly, HbA1c is decreased in hypothyroidism as well as in hyperthyroidism compared to that in euthyroidism.

Discussion

Type 2 diabetes mellitus (T2DM) and thyroid dysfunctions are among the most commonly manifested endocrine disorders in clinical practices and often frequently coexist [2]. As compared to the young age group (aged 21-40 years), older age groups (41-60 years) had higher chances of being diagnosed with type 2 diabetes mellitus. With advancing age, the body's composition is changed, with a rise in body mass and a deranged lipid profile. Increased abdominal fat is associated with hyperinsulinemia or insulin resistance (IR) [9-10]. T2DM is one of the factors that influence the development of thyroid dysfunction, and the latter can occur in the form of hypothyroidism or hyperthyroidism and can contribute to diabetic complications like retinopathy, neuropathy, and the progression of cardiovascular disease [4].

In this study, the majority of the T2DM patients, 68.18%, were euthyroid subjects. Among the thyroid disorders in diabetic subjects (31.81%), hypothyroidism was more prevalent, which is 21.21%. In contrast, the prevalence of hypothyroidism was only 10.60%, which is in agreement with the work by Ghimire S et al. [3]. In a similar type of study conducted in India, a lesser hypothyroidism (13.9%) in T2DM was observed [11]. A study has demonstrated the duration of diabetes, which may act as a contributing element in the development of thyroid dysfunction in individuals with T2DM [12]. The mean levels of TSH were slightly higher in hypothyroidism (6.92±3.54) but lower in hyperthyroidism (2.36±1.37). However, FBG was lower in hypothyroidism (109.88±9.64) but higher in hyperthyroidism (138.95±23.64) compared to that in euthyroid subjects. Similarly, the value of HbA1c was lower in hypothyroidism but higher in hyperthyroidism. Thyroid hormones influence glucose homeostasis. These helps develop pancreatic β-cells and regulate glucose homeostasis involving multiple organs such as the liver, gastrointestinal tract, pancreas, adipose tissue, skeletal muscles, and the central nervous system [13].

Studies have found insulin resistance (IR) in both hypothyroid and hyperthyroid diabetic patients. An increased level of insulin escalates the levels of T4 but minimizes the levels of T3 by inhibiting a change of T4 to T3 in the liver [7]. Thyroid hormone-binding inhibitors, which suppress the formation of T3 from T4 may also be the cause of hypothalamo-pituitary thyroid axis dysfunction and the effect of poorly managed diabetes on thyroid hormone concentration [14]. Increased concentration of thyroid hormones in the bloodstream in the case of hyperthyroidism is linked to impaired glycaemic control, such as insulinopenia and hyperglycemia.

How thyroid hormones affect glucose metabolism and lead to glucose intolerance and T2DM is a complex mechanism. Thyroid disorders, both hyperthyroidism and hypothyroidism, may lead to glucose intolerance. Thyroid hormones affect glucose metabolism by acting on various organs such as the gastrointestinal tract, liver, muscle, etc. These increase gastrointestinal motility and stimulate the absorption of monosaccharides, such as glucose, from the intestine. In hepatic cells, these increase the action of phosphoenolpyruvate carboxykinase, which induces gluconeogenesis, leading to hyperglycemia [15]. Thus, thyroid hormones lead to hyperglycemia either directly through hepatic gluconeogenesis or indirectly by hepatic glycogenolysis through glucagon or catecholamines, as thyroid hormones also increase the release of glucagon, a catabolic hormone, from the alpha cells of the pancreas [4, 15]. Increased glycogenolysis and hepatic glucose output stimulate hyperinsulinemia and glucose intolerance, which results in peripheral insulin resistance [4]. Glycated haemoglobin (HbA1c) is one of the most reliable indicators of average glycemic control during two to three months [16]. It is directly affected by glucose metabolism and blood glucose levels. An abnormal glucose homeostasis is associated with hyperinsulinemia that may result in insulin resistance and is linked to a transient rise of glucose in the blood, which in turn contributes to haemoglobin glycation. Hypothyroid patients manifest increased blood glucose levels, and an altered RBC turnover is responsible for altered HbA1c levels in such patients [17]. The present study showed lower levels of HbA1c in patients with hypothyroidism, which may be due to the effect of thyroid hormone medication on hypothyroid patients [18]. Similarly, hyperthyroid patients also showed lower levels of HbA1c compared to those in the euthyroid group, which may be due to excessive glycation of hemoglobin by malondialdehyde, a

lipid peroxidation product induced by excessive thyroid hormones [19, 20].

Patients with T2DM are more prone to developing thyroid disorders, which are even exaggerated in chronic diabetes mellitus and females. Timed diagnosis and treatment of thyroid disorder in diabetes mellitus can improve the morbidity as well as help prevent the worsening of diabetic complications.

Conclusion

T2DM was relatively less prevalent in younger populations and most common in this study's 41-60 age group. An occurrence of hypothyroidism was revealed to be relatively increased in diabetes mellitus (21.21%) compared to that of hyperthyroidism. Patients with hypothyroidism showed low levels of fT4 and fT3 but with higher values of FBG and HbA1C compared to those of hyperthyroid patients. Hence, proper screening and diagnosis should be established to aid in the management of this disorder treatment procedure and prevention of complications of thyroid disorder and diabetes mellitus.

Limitation and future scope of the study

The study of insulin resistance, anti-thyroid peroxidase (anti-TPO) antibody, and estimation of lipid profile has not been done in this study. Therefore, the effect of insulin resistance, dyslipidemia, and anti-TPO antibodies in developing thyroid dysfunction among T2DM patients could not be assessed.

Relevance of the study

This cross-sectional study revealed a higher prevalence of hypothyroidism in T2DM. Findings of the current study suggest a large-scale research is required to explore age wise prevalence of hypothyroidism or hyperthyroidism in T2DM.

Abbreviations

Diabetes mellitus (DM), enzyme linked immune-sorbent assay (ELISA), fasting blood glucose (FBG), free T3 (fT3), free T4 (fT4), Glycated haemoglobin (HbA1c), High-performance liquid chromatography (HPLC), thyroid dysfunction (TD), thyroid-stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3), and type 2 diabetes mellitus (T2DM).

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Authors' contribution

a. Study planning: SKY, BK
b. Data collection: SM, BK
c. Data analysis/ interpretation: SKY, SM
d. Manuscript writing: SKY, BK
e. Manuscript revision: SKY, SM
f. Final approval: SKY, BK
g. Agreement to be accountable for all aspects of the work: SKY, BK

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Availability of data and materials

All data underlying the results are available as part of the article.

Competing interests

The authors declare that there are no conflicts of interest to disclose in relation to this manuscript.

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