Research Article

Study of thyroid function in type 2 diabetic and non-diabetic population

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Abstract

Background: Diabetes mellitus (DM) is a common endocrine metabolic disorder and is one of the leading causes of death worldwide. Thyroid disorders are also very common in the general population and are 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 diseases and diabetes.

Objective: To compare the prevalence of thyroid dysfunction in type 2 diabetic patients and healthy controls.

Materials and Methods: This study comprises 200 subjects including 100 type 2 diabetic patients and 100 controls, in whom serum-fasting glucose, serum triiodothyronine (T_3), thyroxine (T_4), and thyroid-stimulating hormone (TSH) were measured.

Result: Among the 100 type 2 diabetic patients studied, 32% of the patients had abnormal thyroid hormone levels and 68% had normal thyroid hormone levels. Among the 32% of diabetic patients with abnormal thyroid hormone levels, 22% of them had hypothyroidism (8% clinical hypothyroidism and 14% subclinical hypothyroidism) and 10% had hyperthyroidism (4% clinical hyperthyroidism and 6% subclinical hyperthyroidism). All the controls were found to have normal thyroid hormone levels.

Conclusion: There is high prevalence of thyroid dysfunction in type 2 diabetic patients as compared to healthy controls. Hypothyroidism was found more common than hyperthyroidism. Therefore, detection of abnormal thyroid hormone levels in the early stage of DM may help patients improve the quality of life and reduce the morbidity rate.

KEY WORDS: Type 2 diabetes mellitus, hyperthyroidism, hypothyroidism

Introduction

Diabetes mellitus (DM) is defined as a heterogeneous group of diseases, characterized by a state of chronic hyperglycemia, resulting from a diversity of etiologies, environmental and genetic, acting jointly. The underlying cause of diabetes is the defective production or action of insulin, a hormone that controls glucose, fat, and amino acid metabolism.[1]

DM is a significant health problem affecting major population worldwide. A recent study by the World Health Organization (WHO) estimated that the worldwide prevalence of diabetes in 2002 was 170 million, with the number predicted to grow to 366 million or more by 2030. The major underlying causes of the epidemic are thought to be due to adoption of a sedentary lifestyle, the consumption of non-traditional foods, and a genetic predisposition to the disease. India has the dubious distinction of being home to the largest number of people suffering from diabetes in any country. Despite great strides made in understanding and for management of diabetes, the disease and its related complications are increasing unabated.[2]

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DM on long term is associated with vascular complications that are responsible for increased morbidity and mortality among diabetic subjects. New addition to these complications is the thyroid dysfunction, which is evidenced by the recent studies.[3]

Thyroid disorders are also very common in the general population and are 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 diseases and diabetes. The first reports showing the association between diabetes and thyroid dysfunction were published in 1979. Since then, a number of studies in different countries have tried to estimate the prevalence of thyroid dysfunction among type 2 diabetic patients.[4]

The diagnosis of thyroid dysfunction in diabetic patients based solely on clinical manifestations can be difficult because poor glycemic control can produce features similar to hyperthyroidism, such as weight loss despite increased appetite and fatigue. Severe diabetic nephropathy can be mistaken for hypothyroidism because patients with this condition may have edema, fatigue, pallor, and weight gain.[5]

So it is important to evaluate diabetic population regarding thyroid diseases clinically or subclinically, as one condition can worsen the other if left untreated in form of worsening of DM and dyslipidemias and causing diverse complications. Therefore, it is imperative to screen diabetic population regarding thyroid diseases.[6]

Materials and Methods

This study comprises 200 subjects including 100 type 2 diabetic patients and 100 controls. All the patients in the diabetic group were confirmed diabetics who previously had fasting blood glucose levels >120 mg/dL on more than two occasions based on the American Diabetes Association (ADA) 2010 criteria for diagnosis of DM,[7] and who were receiving treatment such as insulin, glybenicide, glucophage, or physical exercise therapy for DM. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were investigated by a self-administered questionnaire. The study excluded the patients with history of type 1 DM, those with known history of thyroid dysfunction, and those with liver disease, renal disease, hypertension, and pregnancy.

Age- and sex-matched healthy volunteers without a history of diabetes and with normal blood sugar were considered to be control subjects. All subjects were informed about the objectives of the study and their roles in the study.

Biochemical Investigations

Under all aseptic precautions, using a sterile disposable syringe, about 4 ml of venous blood drawn from subjects who were on overnight fasting was kept in a plain vacutainer and centrifuged, and then serum was separated, which is used for the estimation of serum fasting glucose and thyroid profile. Serum fasting glucose was measured by glucose oxidase and peroxidase (GOD–POD) method,[8] and serum T_3, T_4, and TSH were estimated by chemiluminescence immunoassay method (CLIA).[9]

Classification of the values into high, low, or normal thyroid hormone level was based on the following criteria. Subjects classified as having high levels of thyroid hormones had T_3 values > 2 ng/ml, T_4 value > 12 μg/dl, or TSH < 0.2 μIU/ml or all. Those classified as having hypothyroidism had T_3 values < 0.5 ng/ml, T_4 values < 4.8 μg/dl, or TSH values >5.4 μIU/ml or all. Subject grouped as normal had T_3, T_4, and TSH values within the range 0.5–2.0 ng/ml, 4.8–11.6 μg/dl, and 0.28–5.45 μIU/ml, respectively.

Statistical Analysis

Results are expressed as mean ± SD, range values for continuous data, number, and percentage for discrete data. Prevalence of thyroid dysfunction was expressed as percentage with 95% confidence interval (CI). Unpaired *t*-test was used for two-group comparison. For all the tests, *p*-value of <0.05 was considered for statistical significance.

Results

Among the 100 type 2 diabetic patients studied, 47 were males and 53 were females with mean age of 55.5 ± 6.2 years. Among the 100 healthy controls studied, 49 were males and 51 were females with mean age of 49.8 ± 6.5 years.

As shown in Table 1, among the 100 type 2 diabetic patients studied, 32% of the patients had abnormal thyroid hormone levels and 68% had normal thyroid hormone levels. Among the 32% of diabetic patients with abnormal thyroid hormone levels, 22% of them had hypothyroidism (8% clinical hypothyroidism and 14% subclinical hypothyroidism) and 10% had hyperthyroidism (4% clinical hyperthyroidism and 6% subclinical hyperthyroidism). All the controls were found to have normal thyroid hormone levels.

Statistical analysis by student's *t*-test [Table 2] shows that the serum levels of T_3 and T_4 decreased (statistical significance $p < 0.001$), whereas serum TSH level increased (statistical significance $p < 0.001$) in 22% diabetic patients when compared to healthy controls. The serum levels of T_3 and T_4 increased (statistical significance ($p < 0.001$), whereas serum TSH level decreased (statistical significance $p < 0.001$) in 10% type 2 diabetic patients when compared to healthy controls.

Table 1: Prevalence of thyroid dysfunction among diabetic patients and healthy controls

Thyroid status	Diabetic patients (n = 100)	Healthy controls (n = 100)
Hypothyroid	22	0
Hyperthyroid	10	0
Euthyroid	68	100
Total	100	100

Table 2: Comparison of thyroid hormone levels among diabetic patients with hypothyroidism, hyperthyroidism, and controls

Parameters		Healthy controls (*n* = 100)	Diabetic patients with hypothyroidism (*n* = 27)	Diabetic patients with hyperthyroidism (*n* = 15)	*p*-value
T3 (ng/ml)	Mean ± SD	1.16 ± 0.46	0.36 ± 0.73	3.07 ± 0.73	< 0.001 HS
	Range	0.20–2.4	0.0–1.48	1.90–4.40	
T4 (μg/dl)	Mean ± SD	7.53 ± 2.34	3.30 ± 2.18	16.69 ± 6.60	<0.001 HS
	Range	2.81–13.6	0.80–9.8	4.22–27.8	
TSH (μIU/ml)	Mean ± SD	2.78 ± 4.29	42.4 ± 35.53	0.03 ± 0.05	<0.001 HS
	Range	0.10–38.1	8.8–127.2	0.00–0.1	

Discussion

DM is a complex and multifactorial disease. The metabolic dysregulation associated with diabetes causes secondary pathophysiologic changes in multiple organ systems that impose a heavy burden of morbidity and mortality from macrovascular and microvascular complications.[2]

DM and thyroid disorders are the two common endocrinopathies seen in the adult population. Recent studies have shown a very high prevalence of thyroid dysfunction in type 2 DM. Insulin and thyroid hormones are intimately involved in cellular metabolism and thus excess or deficit of either of them may result in the functional derangement of the other.[10]

This study shows a very high prevalence of thyroid dysfunction among type 2 diabetic patients, hypothyroidism being more common than hyperthyroidism. Our results are in accordance with Pasupathi et al.,[2] Swamy et al.,[3] Singh et al.,[4] Mazin et al.,[11] Udiong et al.,[12] Bassyouni et al.,[13] and Shaikh et al.[6]

DM appears to influence thyroid function in two sites; first, at the level of hypothalamic control of thyroid-stimulating hormone release and second, at the conversion of T_4 to T_3 in the peripheral tissue. Marked hyperglycemia causes reversible reduction of the activity and hepatic concentration of $T_{4/5}$ deiodinase, causing low serum concentrations of T_3 and elevated levels of T_4. DM is associated with increased insulin level and C-peptide level. Insulin is an anabolic hormone known to enhance TSH turnover, which is protein in nature. Recently, C-peptide has been shown to enhance Na^+/K^+ ATPase activity, an action that may also increase protein synthesis. Such an action would induce increased turnover of TSH, a protein hormone. Stress, which is associated with diabetes, may also cause changes in the hypothalamus–anterior–pituitary axis in diabetics. It appears that the presence of subclinical hypothyroidism and hyperthyroidism may result from hypothalamus–hypophyseal–thyroid axis disorders.

The abnormal thyroid hormone levels may be the outcome of the various medications the diabetics were receiving. Insulin, an anabolic hormone, enhances the levels of FT_4 and suppresses the levels of T_3 by inhibiting hepatic conversion of T_4 to T_3. Some of the oral hypoglycemic agents such as the phenylthioureas are known to suppress the levels of FT_4 and T_4, while raising the levels of TSH. Many investigators reported that the treatment of diabetes with sulfonylurea lead to an increased incidence of goiter and hypothyroidism.[13,6]

Autoimmunity is a common feature in type 1 diabetes. But several studies have demonstrated a higher prevalence of thyroid auto-antibodies such as anti-TPO, anti-TG, and anti-GAD-65 in type 2 DM. Presence of significantly higher positive thyroid auto-antibodies in type 2 DM patients denotes the important role of autoimmunity in the development of thyroid dysfunction among type 2 DM.[13,14]

Studies have shown that there are higher incidences of different types of abnormal thyroid morphology (size and structure), for example, diffuse goiter, multinodular goiter, and solitary nodule among type 2 diabetics. Increase in incidence of abnormal thyroid morphology, uncontrolled hyperglycemia associated with osmotic diuresis, could play a major role in thyroid gland enlargement. Hyperinsulinemia as a growth factor associated with insulin resistance may be another mechanism for thyroid gland enlargement.[13]

Conclusion

Thus, this study shows high incidence of abnormal thyroid hormone level among type 2 diabetic subjects. Failure to recognize the presence of abnormal thyroid hormone levels in diabetes may be a primary cause of poor management often encountered in some treated diabetic patients. Therefore, there is need for the routine assay of thyroid hormones in particularly those diabetic patients whose conditions are difficult to manage. This study shows a high incidence of abnormal thyroid hormone levels among diabetic patients. In conclusion, our findings demonstrate that detection of abnormal thyroid hormone levels in addition to other biochemical variables in the early stage of diabetes will help patients improve their health and reduce their morbidity rate.

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