Research Article

A controlled study on the prevalence of underactive thyroid in type 2 diabetes

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Abstract

Background: The term "thyroid diabetes" depicts the effect of excess thyroid hormones in the progressively worsening glucose control. Subclinical hypothyroidism is most commonly present in females than males, reaching a prevalence of up to 20% in older females. Hashimoto's thyroiditis and Graves' disease are the principal causes of hyper- and hypothyroidisms.

Objectives: (1) To study the prevalence of hypothyroidism in diabetes and to evaluate the etiologic evidence of triglycerides on prevailing cardiovascular risk and metabolic syndrome. (2) To determine the mean levels of fasting blood sugar (FBS), HbA1c, triiodothyronine, serum thyroxin, and thyroid-stimulating hormone. (3) To evaluate the hemoglobin levels and to establish the prevalence of anemia in diabetic patients with hypothyroidism. (4) To determine the mean age and male/female ratio in diabetic patients with hypothyroidism.

Materials and Methods: This study was a hospital-based case–control study carried out at Department of General Medicine, Owaisi Hospital and Research Center, Deccan College of Medical Sciences, Hyderabad, India. A total of 76 patients (63 women and 13 men) were enrolled in the study along with 38 control participants after explaining the study process and taking an inform consent. Blood samples were collected on the basis of history of diabetes noted for these patients.

Results: Among 76 patients included in the study, 38 patients were having diabetes and hypothyroidism and the rest of them had normal diagnostic profile. The mean age was found to be 33.5 ± 13.8, and 18.5% men and 81.5% women were having hypothyroidism along with diabetes. The thyroid profile of patients with diabetes showed a remarkable increase in thyroid-stimulating hormone and this was considered to be the hypothyroidism as the mean level in the patients was 15.4 ± 17.1.

Conclusion: In this study, diabetic patients with hypothyroidism showed increased FBS, HbA1c levels as the Hb levels were decreased whereas the triglyceride levels were increased from moderate to high, which in turn increased the susceptibility to cardiovascular risk and metabolic syndrome. Therefore, patients need timely cardiac monitoring and life style modification to avert the metabolic syndrome and cardiovascular risk.

KEY WORDS: Hypothyroidism, diabetes, anemia, triglycerides

Introduction

The term "thyroid diabetes" was first coined in a previous work, which represents the effect of excess thyroid hormones in relationship to progressively worsening glucose control. Subclinical hypothyroidism is most commonly present in females than males, reaching a prevalence of up to 20% reaching in older females. Hashimoto's thyroiditis and Graves' disease are the principal causes of hyper- and hypothyroidisms.[1]

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Insulin secretion is directly under the control of thyroid hormones. Generally, pathophysiology of hypothyroidism indicates that there is a decrease in the glucose-induced insulin secretion by beta cells and their response to glucose or catecholamine is increased due to the increased beta cell mass. Besides, insulin clear-out is increased in thyrotoxicosis.[2]

Diabetes mellitus has been explored to be linked with hypothyroidism (Hashimoto's thyroiditis) or thyroid over activity (Graves's disease). A meta-analysis reported 11% thyroid dysfunction in diabetes. The main cause of thyroid dysfunction in

patients with diabetes is autoimmunity. Mismanaged diabetes, both type 1 and type 2, may result in low T3 (triiodothyronine) state, which is expressed by low serum total and free T3 levels but may show near-normal serum T4 (serum thyroxin) and thyroid-stimulating hormone (TSH) concentrations. The correlation between type 2 diabetes and thyroid dysfunction has been a known fact that may be responsible for the diverse facts of metabolic syndrome including atherosclerosis, and increased blood pressure and related cardiovascular disorder.[2]

Hypothyroidism is common in iodine-replete areas and study by Asvold et al.[3] showed that 0.2%–0.5% patients had biochemically overt hypothyroidism and 4%–10% patients had subclinical hypothyroidism, which suggests that subclinical hypothyroidism may be linked with an increased risk of coronary artery disease, adverse pregnancy outcomes, and development of clinical hypothyroidism.

In a study by Garduno-Garcia et al.[4] revealed that since the 1970s a relation has existed between thyroid dysfunction and cardiovascular mortality. Various studies showed that subclinical hypothyroidism increases the risk of cardiovascular disease. Even more disputable is the association between subclinical hypothyroidism and insulin resistance.[4] Not long ago metformin had been reported to interfere with thyroid hormone. This can be seen by low levels of serum thyrotropin to subnormal levels in patients with hypothyroidism in balanced levothyroxine (T4) treatment.[5]

Thyroid hormone triggers erythrocyte sedimentation productivity, and hypothyroidism often results in hypoproliferative erythropoiesis. In accompaniment, thyroid hormone upgrades albumin metabolism and albumin degradation is decreased in hypothyroidism.[6] In a study conducted by Das et al.,[7] which was conducted on 23 patients with erythropoiesis and 21 with hypothyroidism and included timely hematologic evaluation, bone marrow morphology and serum iron levels, showed that the patients with hypothyroidism had remarkable reduction in red blood cell mass per kilogram of body weight. The existence of anemia in many of these patients was not evident from hemoglobin and hematocrit values due to associated reduction of plasma volume. Some studies suggested in the study by Hsieh et al.[8] show that obesity is one of the major factors associated with metabolic syndrome. The World Health Organization elucidates that metabolic syndrome is a collection of disorders associated with existence of diabetes, impaired glucose tolerance, fluctuating fasting blood sugar (FBS), or resistance of insulin and any two of the following abnormalities: central obesity, high triglyceride levels, and hypertension.Type 2 diabetes is associated with atherosclerosis and hyperglycemia. Long-term hyperglycemia causes glycosylation of all proteins, mainly matrix and collagen cross-linking, which may result in endothelial dysfunction, leading to progression of atherosclerosis whereas high triglyceride levels are also a major contributing factor of cardiovascular disease.[9] A study by Nathalie et al.[10] showed that older Taiwanese population have higher prevalence of metabolic syndrome in persons with hypothyroidism when associated with those with hyperthyroidism.

Aims and Objectives

(1) To study the prevalence of hypothyroidism in diabetes and to evaluate the etiologic evidence of triglycerides on the prevailing cardiovascular risk and metabolic syndrome. (2) To determine the mean levels of FBS, HbA1c, triiodothyronine, serum thyroxin, and TSH. (3) To evaluate the hemoglobin levels and to establish the prevalence of anemia in diabetic patients with hypothyroidism. (4) To determine the mean age and male/female ratio in diabetic patients with hypothyroidism.

Materials and Methods

The present study is a hospital-based case–control study carried out at the Department of General Medicine, Owaisi Hospital and Research Center, Deccan College of Medical Sciences, Hyderabad, India. Patients visiting the inpatient Department of General Medicine in Owaisi Hospital and Research Center from July 2014 to October 2014 (3 months) were selected for this study. All patients selected had a history of type 2 diabetes and elevated TSH and HbA1c levels. We also assessed the hemoglobin (Hb) levels. These values were documented on a predesigned and pretested pro forma. Thyroid profile details included T3, T4, and TSH and diabetic profile included HbA1c, triglycerides, FBS, and complete blood count.

All these parameters were investigated, recorded, and then a comparison was made between diabetic hypothyroid patients and control participants. Later, the results were collected and presented in graphs and tables, showing the values as mean ± standard deviation.

A total of 76 patients were enrolled in the study along with the 38 controls after explaining the study process and taking an inform consent. Blood samples were collected on the basis of history of diabetes of these patients. Among the participants 63 were females and 13 were males. Exclusion criteria were (1) patients aged below 10 years, (2) patients admitted to emergency department, and (3) patients who underwent thyrodictomy. Statistical analyses were carried out using Microsoft Excel, Epi Info 7, and Microsoft Word.

Results

Among 76 patients included in this study, 38 patients were diabetic and hypothyroid; rest the 38 patients had normal diagnostic profile. The mean age of the patients with hypothyroidism and diabetes was 33.5 ± 13.8 whereas that of the patients with control profile was 32.1 ± 13.4 [Table 1]. There were 55.3% patients with diabetes and hypothyroidism who were under the age group of 10–34 years and 44.7% patients were above 35 years whereas the control group had 52.6% patients under the age group of 10–34 years and 47.4% above the age of 35 years.

Among diabetic patients with hypothyroid, 18.5% were men and 81.5% were women. The control group consisted of 15.7% men and 84.3% women. The frequency of men having hypothyroid diabetes was 7 and women was 31; this proves that the hypothyroid diabetes is more common in women than

Table 1: Age in diabetic hypothyroid patients

Range (years)	Frequency (%)		Mean ± standard deviation	
	Diabetic hypothyroid patients	Control	Diabetic hypothyroid patients	Control
10–34	21 (55.3)	20 (52.6)	33.5 ± 13.8	32.1 ± 13.4
Above 35	17 (44.7)	18 (47.4)		

Table 2: Sex ratio in diabetic hypothyroid patients

	Diabetic hypothyroid patients		Control group	
	Males	Females	Males	Females
Frequency	7	31	6	32
Percentage	18.5	81.5	15.7	84.3

in men, as shown in Table 2.

The thyroid profile of patients with diabetes showed a remarkable increase in TSH and hypothyroidism was considered if the mean level in the patients was 15.4 ± 17.1 whereas the reference range was between 0.4and 7.0 μIU/ml and the control group had a mean level of 3.78 ± 1.27. The triiodothyronine (T3) showed a mean level 0.91 ± 0.10 and the normal ranges were between 0.8 and 1.9 mg/ml; the control group and diabetic patients with hypothyroidism mostly had normal T3 levels. The mean level of T4 (serum thyroxin) in hypothyroid diabetes patients was 76.1 ± 17.2 whereas that of control group was 77.5 ± 14.6 [Table 3].

The hemoglobin mean level in diabetic patients with hypothyroidism was 9.7 ± 1.7 whereas that in the control group was 13.7 ± 1.3; the normal range for the hemoglobin is was 12.0–15.0 gm/dl, as shown in Table 4. It can be seen that 15.7% diabetic patients with hypothyroidism fall under the normal hemoglobin category but 84.2% diabetic patients with hypothyroidism fall under anemic category; the mean levels of the patients were very low when compared to normal range. This shows that most of the diabetic patients with hypothyroidism were anemic.

The triglyceride level fluctuated in the control group also. It can be seen that 65.7% control group and 28.9% diabetic patients with hypothyroidism fall under the borderline range of 150–199 mg/dl whereas 71% diabetic patients with hypothyroidism are in high-value range of 200–499 mg/dl [Table 4]. The mean triglyceride level of hypothyroid diabetes is 256.02 ± 65.4, as shown in Table 5, which is high when compared to that of the control group, which is having a mean of 154.1 ± 9.21. This indicates that patients with diabetes and hypothyroidism have high cardiovascular risk and metabolic syndrome.

The normal range of FBS is 70–100 mg/dl. In early diabetic stages patients the normal level of FBS is 101–126 mg/dl whereas it is more than 126 mg/dl in patients with established diabetes. The mean FBS value in patients with diabetic hypothyroid in the current study was approximately 177.16 ± 37.7 and the mean value exhibited by the control group was 82.3 ± 6.58, as shown in Table 6. Almost 100% of the control group participants have the normal FBS values, 7.8% patients fall under the early diabetic stage, and 92.1% patients have established diabetes.

The mean HbA1c levels in patients with diabetic hypothyroidism and with control group were approximately

Table 3: Thyroid hormone levels in study and control groups

	T3 (serum Tri-iodothyronine)	T4 (serum thyroxin)	Thyroid-stimulating hormone (TSH)
Normal ranges	0.8–1.9 mg/ml	50–120 mg/ml	0.4–7.0 μIU/ml
Diabetic hypothyroid patients	0.91 ± 0.10	76.1 ± 17.2	15.4 ± 17.1
Control group	0.88 ± 0.07	77.5 ± 14.6	3.78 ± 1.27

Table 4: Hemoglobin levels (Hg) in diabetic hypothyroid patients

Range	Frequency (%)		Mean ± standard deviation	
	Diabetic hypothyroid patients	Control	Diabetic hypothyroid patients	Control
Normal (12.0–15.0 gm/dl)	6 (15.7)	35 (92.1)	9.7 ± 1.7	13.7 ± 1.3
Anemic (below 12.0 gm/dl)	32 (84.2)	3 (7.8)		

Table 5: Triglyceride levels in diabetic hypothyroid patients

Range	Frequency (%)		Mean ± standard deviation	
	Diabetic hypothyroid patients	Control	Diabetic hypothyroid patients	Control
Normal (≤150 mg/dl)	0 (0)	13 (34.2)	256.02 ± 65.4	154.1 ± 9.12
Borderline (150–199 mg/dl)	11 (28.9)	25 (65.7)		
High (200–499 mg/dl)	27 (71)	0		

Table 6: Fasting blood sugar levels in diabetic hypothyroid patients

Ranges	Frequency (%)		Mean ± standard deviation	
	Diabetic hypothyroid patients	Control	Diabetic hypothyroid patients	Control
Normal (70–100 mg/dl)	0 (0)	38 (100)	177.16 ± 37.7	82.3 ± 6.58
Early diabetic (101–126 mg/dl)	3 (7.8)	0		
Established diabetes (≥126 mg/dl)	35 (92.1)	0		

Table 7: HbA1c levels in diabetic hypothyroid patients

Range	Frequency (%)		Mean ± standard deviation	
	Diabetic hypothyroid patients	Control	Diabetic hypothyroid patients	Control
Normal (≤5.7%)	0 (0)	38 (100)	10.4 ± 5.5	4.45 ± 0.56
Prediabetic patients (5.7%–6.4%)	0 (0)	0		
Diabetes (≥6.5%)	38 (100)	0		

10.4 ± 5.5 and 4.45 ± 0.57, respectively [Table 7]. Almost 100% individuals with diabetic hypothyroidism have the HbA1c levels ≥6.5% whereas 100% in control group have the levels within the range of normal limits, that is, ≤5.7%.

Discussion

In a study by Rotondi et al.,[11] the mean age was 46.2 ±12.2 whereas in the present study it was 33.5 ± 13.8; both the study patients had raised TSH. There was prevalence of hypothyroidism in India at age of 33 years whereas it was 46 years in Italy.The sex ratio in contemporary study was 31:7 (women/men) in diabetic patients with hypothyroidism and was 32:6 in a control group, whereas a study by Christy et al.[12] showed a sex ratio to be 24:6 (women/men), determining predominance of females in hypothyroidism. Triiodothyronine levels in an existing study were normal in both the diabetic and the control patients. A study by Alevizaki et al.[13] revealed that T3 levels are closely associated with the subcutaneous fat deposition but there is no evidence of subcutaneous fat deposition in the subjects as the triiodothyronine levels appear to be normal. However, T4 levels in this study were normal in both patients with diabetes and control group; this was a major outcome as none of the patients received thyroxin sodium but elevated TSH levels were observed in patients with diabetes and there was an increase up to 15.4 ± 17.1 μIU/ml, which shows the hypothyroidism. In a study by Christy et al.,[12] a sharp elevation (34.12 ± 13.6 μIU/ml) in the TSH levels was seen.

The mean hemoglobin level in this study was 9.7 ± 1.7, which was lower than the normal reference range whereas many studies have shown that an increased HbA1c level is linked with iron-deficiency anemia.[12] Approximately 84.2% diabetic patients with hypothyroidism were found to be anemic. This might be due to the elevated HbA1c levels. The mean HbA1c levels in this study were 10.4 ± 5.5, which was much more elevated when compared to the reference range. In a study by Christy et al., the mean HbA1c level in anemic cases is 6.57 ± 0.69, which is slightly higher than the normal range but the current study shows high mean levels when compared to Chisty's study.[12] There may be chances that HbA1c levels may come down to the normal range after treatment with the thyroid replacement therapy.

The mean triglyceride level of 209.3 ± 40.1 was observed in a study conducted by Alevizaki et al.[13] whereas in the present study, it was 256.02 ± 65.4, which is quite higher. This implies that the patients with both diabetes and high triglyceride levels have increased chances of cardiovascular risks and metabolic syndrome. A study by Uttra et al.[9] showed that 31% patients had high triglyceride level whereas in our study it was 71% .

In our study, the mean fasting blood sugar was 177.16 ± 37.7 whereas the fasting blood glucose levels in the study by Pistrosch et al.[14] in healthy control subjects and patients with diabetes were 88.5 ± 7.2 and 133.8 ± 12.6. In our study, the levels were 177.16 ± 37.7 and 82.3 ± 6.58 for diabetic patients with hypothyroidism and control subjects.

Conclusion

There was a significant correlation between fasting plasma glucose levels and HbA1c. Both FBS and HbA1c levels increased in diabetic patients with hypothyroidism. Incidence of hypothyroidism and anemia was more in females. This study shows that increase in HbA1c levels is associated with anemia. We conclude that high levels of triglycerides (moderate to high) in diabetic patients with hypothyroidism may increase the chances of cardiovascular risk and metabolic syndrome. Hence timely cardiac monitoring and life style modification of patients may avert the metabolic syndrome and cardiovascular risk, which may improve the quality of life of the patients. The impact of thyroid alterations on glucose metabolism has been known for a long time. Patients with hypothyroidism have fluctuating glucose levels and management of hypothyroidism may improve the diabetic control. In this study, females were found to be more prone to hypothyroidism, perhaps timely thyroid checkup may reveal thyroid functioning and may be advisable to maintain and improve thyroid functioning.

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