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Research Article

Thyroid Dysfunction in Patients with Type 2 Diabetes Mellitus attending Medical Outpatient/Inpatient Departments at a Tertiary Care Hospital

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ABSTRACT

Background & Objectives: Diabetes mellitus and thyroid dysfunction are the two most common endocrine disorders in clinical practice. The unrecognized thyroid dysfunction may adversely affect the metabolic control and add more risk to an already predisposing scenario for cardiovascular diseases. The objective was to find out the spectrum of thyroid dysfunction in patients of type 2 diabetes mellitus.

Materials and Methods: Seventy patients (40 female and 30 male) of age more than 30 years with type 2 diabetes mellitus were evaluated for one year visiting Nepal Medical College and Teaching Hospital. All the patients were evaluated for thyroid dysfunction by testing thyroid function test. The correlation of prevalence of thyroid disorder with gender distribution, age distribution, HbA_{1c}, duration of diabetes was evaluated. The observations and interpretations were recorded and results obtained were statistically analyzed.

Results: There was a high prevalence (27.1%) of thyroid disorders in patients of type 2 diabetes mellitus. Among all, the most common was subclinical hypothyroidism (20.0%) which was further found to be more in females (30.0%) and elderly patients (37.0%). Duration of diabetes had positive association with the incidence of thyroid disorders (P value 0.003).

Conclusion: Findings of this study suggests that thyroid disorders were commonly associated with diabetes mellitus among which subclinical hypothyroidism being the commonest. Moreover, thyroid disorders were more common in females and elderly population.

Keywords: Thyroid function, Type 2 Diabetes Mellitus, Subclinical hypothyroidism

INTRODUCTION

Diabetes mellitus is a major public health problem. Type 2 diabetes mellitus (DM) is the predominant form of diabetes worldwide, accounting for 90.0% of cases globally [1]. The world health organization (WHO) has projected that the global prevalence of type 2 DM will be more than double from 135 million in 1995 to 300 million by 2025 [2]. In this last two decades, type 2 DM is on the increasing trend, the degree of which differ between countries and different ethnic group within the individual country. A study done by Shrestha et al. in 2022 revealed the prevalence of DM to be 8.5% (95% CI 7.8% to 9.3%) [3]. The prevalence of thyroid disease in patients with diabetes is significantly higher as compared to that in the general population. This is reported as 13.4% and 6.8% with type 1 DM and type 2 DM respectively [4].

In a way thyroid dysfunction and type 2 DM are interlinked, moreover till now there are no internationally accepted guidelines for screening of thyroid dysfunction in type 2 DM patients. Type 2 DM patients with thyroid dysfunction are found to be more susceptible to ketosis and ketogenesis. Insulin resistance has been linked with subclinical hypothyroidism, which is in turn linked to impaired lipid balance and risk of development of metabolic syndrome [5]. There are only few studies in our country regarding relation of thyroid dysfunction in type 2 DM. Thus, this study was aimed to evaluate the spectrum of thyroid dysfunction in patients of type 2 diabetes mellitus in our settings.

MATERIALS AND METHODS

A prospective cross-sectional observational study was conducted in Nepal Medical College and Teaching Hospital (NMCTH), Attarkhel, Jorpati, Kathmandu for a year. The sample size was determined with the formula: Sample size: $n = z^2pq/d^2$ where, n = sample size, z = reliability coefficient for 95% confidence interval = 1.96, p = prevalence, 20%, q = 1-p = 80%, d = allowable error (d= 10%). Thus, the sample size was calculated as 61.46 patients. In view of minimum of 61 participants to be taken, 70 participants of type 2 DM were included in the study by convenience sampling technique. The inclusion criteria were patients with type 2 diabetes mellitus diagnosed as diabetes by American Diabetes Association (ADA) criteria[6] (new or old cases) and age more than 30 years. The exclusion criteria included type 1 diabetes mellitus, patients with gestational diabetes, drugs and steroids induced diabetes, all those who had proven thyroid disorder and on treatment, participants with history of pituitary surgery, irradiation and any suspected central nervous system lesion. These patients were excluded as we aim to evaluate the patients with type 2

diabetes mellitus only which would maintain the homogeneity of the sample population.

All patients of type 2 diabetes mellitus were screened after detailed history and physical examination at the hospital. Type 2 diabetes mellitus was diagnosed on the basis of ADA criteria. Blood sugar estimation was done by dry chemistry method in Vitros 250 by Johnson and Johnson. HbA_{1c} estimation was done by immunochromatography method on Nycocard reader. Differentiation with type 1 diabetes mellitus was made on the basis of age (30 years), as definite diagnosis with relevant blood investigations in our set up is difficult. Thyroid function tests were done by Enhanced Chemiluminescent immunoassay (ECI) method by Johnson and Johnson. Normal values are: fT3: 2.77-5.27 pg/mL, fT4: 0.78-2.19 ng/mL, TSH: 0.465-4.68 μIU/mL Patients were diagnosed to have: Overt hypothyroidism when TSH > 4.68 μIU/mL and FT4<0.78 ng/mL and or FT3<2.77 pg/mL.; Subclinical hypothyroidism when TSH >4.68 μIU/mL with normal FT3 and FT4; Overt hyperthyroidism when TSH <0.4μIU/mL and FT4 >2.19 ng/mL and or FT3> 5.27 pg/mL; Subclinical hyperthyroidism when TSH <0.4 μIU/mL with normal FT4 and FT4.[7]

A proforma was used to collect the information of the participants including name, age, sex address and previous medical history. A thorough physical examination was done including general examination and relevant systemic examination. The data was first recorded in the study proforma. Data were entered and analyzed by using IBM SPSS 20.0. Chi square test was used to show the association between the variables. P value less than 0.05 was considered statistically significant. Pearson coefficient of correlation (r) was done to correlate TSH among multiple parameters. The study population was divided into various subgroups according to the study objectives and relevant calculations were made. The study population was categorized broadly in more than or equals to 60 years and less than 60 years of age. Moreover, the diabetic patients were divided into three categories on the basis of duration of diabetes i.e. 0-5 years, 6-10 years and >10 years. Data were analyzed by using simple descriptive statistics like mean and standard deviation. Then results made were expressed in the form of tables, diagrams and graphs where appropriate. Ethical clearance was taken from Institutional Research/Review Committee (IRC) NMCTH with Ref 97-069/070.

RESULTS

During the study period of one year, total 70 participants were included in this study. Out of total participants, 40 (57.20%) were female and 30 (42.80%) were male. Among 70 diabetic patients, 51 (72.9%) patients had normal thyroid profile, 14 (20%) patients had subclinical hypothyroidism and 5 (7.1%) patients had overt hypothyroidism. There were no cases of hyperthyroidism either overt or subclinical (Table 1).

and few (n=37; 7.94%) from non-health professionals. Association between Socio-demographic characteristics and healthcare-seeking behavior shows, participants education level (p<0.0001) and morbid condition of diabetes (p=0.017) significantly associated with health care seeking behavior (Table 1). The prevalence of thyroid dysfunction was more among females than in males. In this study, 5 out of 30 male patients (16.6%) and 14 out of 40 female patients

(35.0%) were suffering from thyroid disorder. This study was statistically significant (P value = 0.048) according to Chi square test. The findings showed that females had statistically significant more prevalence of thyroid dysfunction than males.

Table 1: Types of thyroid disorder and their frequencies

Types of thyroid disorder	Frequency	Percent (%)
Subclinical hypothyroidism	14	20.0
Overt hypothyroidism	5	7.1
Subclinical hyperthyroidism	0	0.0
Overt hyperthyroidism	0	0.0
Normal	51	72.9
Total	70	100.0

Out of 43 patients who were below 60 years of age, 4 had thyroid disorders. Out of 27 patients who were more than or equals to 60 yrs of age, 15 had thyroid disorders which was statistically significant (P value <0.001). Age 60 and above had more thyroid dysfunction than below 60 years as shown in the table 2. TSH and age had statistically significant correlation (p value-0.0451) as per Pearson coefficient of correlation (r). Out of 30 male diabetics, 5 had thyroid dysfunction. 28.6% had subclinical hypothyroidism whereas 42.9% had overt hypothyroidism. All were above and equals to 60 years of age (P value < 0.001). Out of 40 female diabetics, 4 had subclinical hypothyroidism and were below 60 years of age group whereas 8 had subclinical hypothyroidism and 2 had overt hypothyroidism in the age group above and equals to 60 years.

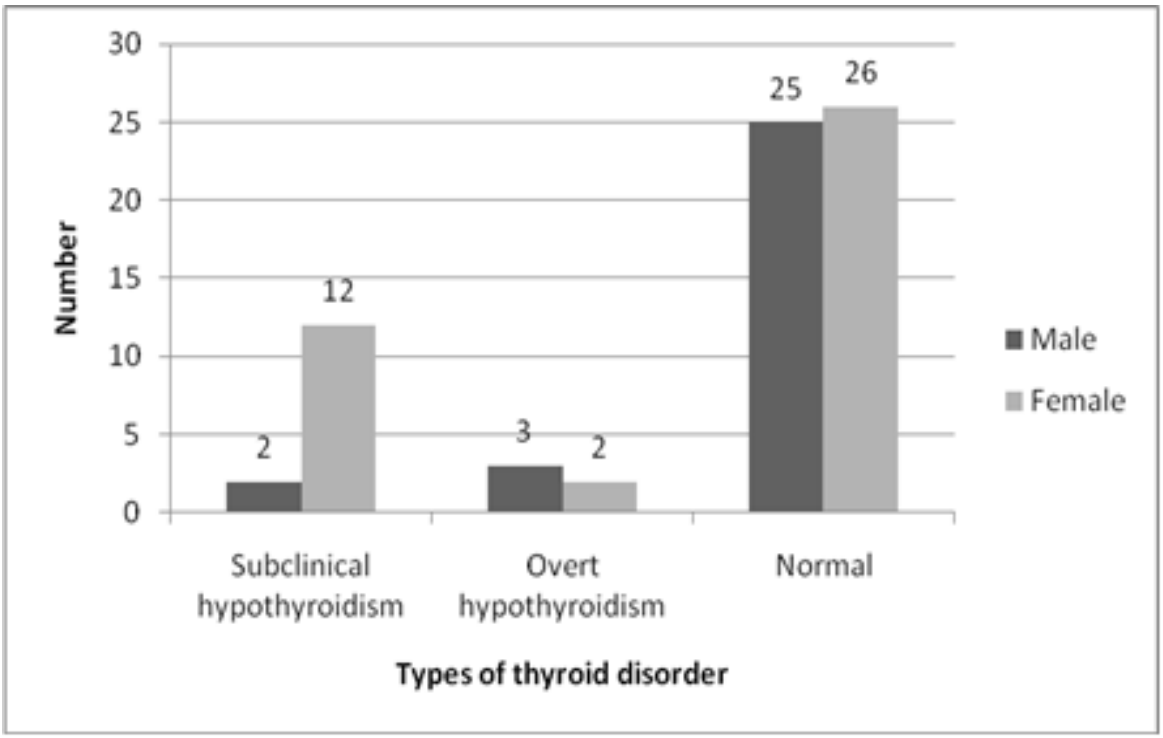

Figure 1: Gender wise distribution of thyroid disorder

Table 2: Age wise distribution of thyroid disorders

Age of the patients (years)	Types of thyroid disorder				P value
	Subclinical hypothyroidism (N/%)	Overt hypothyroidism (N/%)	Normal (N/%)	Total (N/%)	
<60 years	4 (9.3%)	0 (0.0%)	39 (90.7%)	43 (100.0%)	<0.001
≥60 years	10 (37.0%)	5 (18.5%)	12 (44.4%)	27 (100.0%)	
Total	14 (20.0%)	5 (7.1%)	52 (72.9%)	30 (100.0%)	

In this study, 70 patients were divided into three groups according to the duration of diabetes. Among them, 37 people were in the duration of 0-5 years, 21 were in 6-10 years duration and 12 had more than 10 years of duration of diabetes. This study showed, 6 patients had thyroid dysfunction in 0–5 years duration, 9 had thyroid dysfunction in 6-10 and 4 had thyroid dysfunction in more than 10 years of duration of diabetes. TSH and duration of diabetes had statistically significant correlation (p value-0.002) as per Pearson coefficient of correlation (r). Correlation is significant at the 0.01 level (2-tailed). This study showed the statistically significant association of thyroid dysfunction with the duration of diabetes (Chi Square = 16.29, p=0.003)

In this study, 84.3 % of patients were poorly controlled diabetes as suggested by HbA_{1c} ≥7% whereas 15.7% were controlled diabetes (HbA_{1c}< 7%). Eighteen patients with thyroid dysfunction belonged to ≥7% HbA_{1c} class whereas only 1 patient had < 7 % HbA_{1c}.

In this study, mean fT3 was 3.5987±0.9609 pg/mL, mean fT4 was 1.2801±0.4129 ng/mL and mean TSH was 7.5445±18.1436 μIU/mL. Mean value for fasting plasma glucose and post prandial glucose were 135.64±32.37 mg/dl and 224.43±48.73 mg/dl respectively. Mean age and duration of diabetes were 52.93±12.69 years and 6.67±4.49 years respectively. Mean duration of diabetes, TSH, fT3 and fT4 for subclinical hypothyroidism were 6.15±3.363 years, 6.8438±1.1491 μIU/mL, 3.0292±0.6116 pg/mL and 1.0700±0.25681 ng/mL respectively. Whereas, mean duration of diabetes, TSH, fT3 and fT4 for overt hypothyroidism were 9.40±7.668 years, 61.6200±40.922 μIU/mL, 2.540±.456 pg/mL and 0.6560±0.239 ng/mL respectively.

DISCUSSION

Diabetes mellitus, a common endocrine metabolic disorder, is one of the leading causes of death worldwide. Prevalence of thyroid disorder is also very high in general population and is second only to diabetes among all endocrine disorders. Thyroid disease is a pathological state that adversely affects diabetic control and is commonly found in most forms of diabetes mellitus which is associated with advanced age in type 2 diabetes mellitus and autoimmune diseases in type 1 diabetes mellitus [8]. Clinical relevance of thyroid diseases, especially in diabetic patients, significantly increases if it is associated with deteriorated function, which

can cause a number of problems with metabolic compensation of diabetes like increased frequency of hypoglycemia and development of potentially life-threatening ketoacidosis [9].

In the present study, out of the 70 diabetic patients, 19 (27.1%) patients had thyroid dysfunction and 51 (72.9%) patients were found to be euthyroid. The findings in this study is consistent with study of Khatiwada et al. done in B. P. Koirala Institute of Health Sciences, Dharan, Nepal who found that thyroid dysfunction is a common endocrine disorder in diabetic patients, where they reported that 35.41% of type 2 diabetic patients had thyroid dysfunction [10]. In another study done by Pashupathi et al. in India, prevalence of thyroid dysfunction was 45% among type 2 diabetics [11]. Papazafiropoulou et al. in their study, done in Greek diabetic population showed that thyroid dysfunction was 12.3% [12]. In a study done in Ghana, by Tagoe et al. among 60 type 2 diabetic patients, prevalence of thyroid dysfunction was 10.1%[6]. These findings showed that thyroid dysfunction in type 2 diabetes mellitus differs as per geographical areas and the prevalence of thyroid dysfunction is higher in Asia and also in South Asian region including Nepal.

The most prevalent disorder in diabetic patients in this study was subclinical hypothyroidism, occurring in 20% followed by overt hypothyroidism in 7.1%. These results were in concordance with Khatiwada et al [10]. In their study, subclinical hypothyroidism (26.5%) was followed by overt hypothyroidism (5.5%). In Al-Wazzan et al. study which was done in Kuwait, 204 were diagnosed as having thyroid dysfunction among 1580 type 2 diabetic patients, the most common dysfunction was subclinical hypothyroidism 45.1% followed by overt hypothyroidism in 20.1%, subclinical hyperthyroidism was 13.2% and overt hyperthyroidism was 5.9% [13]. Thus, this showed that subclinical hypothyroidism is the most common associated thyroid disorder in diabetes mellitus patients. In our study, prevalence of thyroid disorders was more in females as compared to males (35% vs.16.7%) which when evaluated statistically was significant. These results were in accordance with study of Papazafiropoulou et al. which showed thyroid dysfunction was more likely in females as compared to males (78.4% vs 21.6%) [12]. Likewise, Khatiwada et al. also reported higher prevalence of thyroid dysfunction in females (42.85%) than in males (30.04%) [10]. In this study, we found no patients with hyperthyroidism which was present in most of the studies mentioned above. This may be probably due to small sample size. Thus, the prevalence of thyroid disorder in diabetic patients is strongly influenced by female gender likely due to a combination of factors, including sex differences in immune function and hormonal fluctuations.

Out of 19 diabetic patients who had thyroid disorder, 4 patients belonged to age group of <60 years, 15 patients belonged to age group ≥60 years. Thus, the age specific trend in the prevalence of thyroid disorder was found to be highest in the age group of ≥60 years. This is in accordance with the studies of Ravishankar et al. where they found 34.4% patients with thyroid disorders over the age of 60 years compared to that of 26.4% below the age of 60 years [14]. Furthermore, Jain et al. found that, out of 32 diabetic patients who had thyroid disorder, 6 (18.75%) patients belonged to age group of <50 years, 8 (25%) patients belonged to age group of 50-60 years and 18 (56.25%) patients belonged to age group >60 years [15]. The age specific trend

in the prevalence of thyroid disorder was found to be highest in the age group of >60 years. The reasons behind this phenomenon is believed to be due to age related changes in thyroid gland, increased incidence of autoimmune thyroiditis in elderly and changes in pituitary-thyroid axis function[16].

Among 70 diabetic patients, majority of the patients had poorly controlled diabetes as 84.3% patients had HbA1c ≥7% whereas only 15.7% had HbA1c <7%. In our study, out of 19 diabetic patients who had thyroid disorder, 1 had HbA1c<7% and 18 had HbA1c ≥7%. The prevalence of thyroid disorder was found to be more in patients with HbA1c ≥7% as compared to patients with HbA1c<7%. However, the results were not statistically significant (p value=0.318) as 84.3% patients were poorly controlled diabetes. These results are comparable with the studies like Schlienger et al. where they observed that patients with poorly controlled diabetes i.e. HbA1c ≥12% were having low T3 levels [17]. Uncontrolled diabetes and thyroid dysfunction often found to occur together due to shared risk factors like obesity and autoimmune processes. Moreover, both conditions involve dysregulation of the endocrine system, impacting glucose metabolism and exacerbating each other.

In our study, out of 19 diabetic patients who had thyroid disorder, 6 had duration of diabetes less than 5 years, 9 had duration of diabetes 6-10 years and 4 had duration of diabetes more than 10 years. This showed that prevalence of thyroid disorder was significantly correlated with the duration of diabetes. This result was in concordance with Geffari et al. study done in an Arabian population, in which they found significant relationship between presence of thyroid dysfunction and duration of diabetes (p value-0.032) [18].

This study has got limitations which are as follows: i) this is a single centered study so the result might vary according to geographical areas ii) this is just a single study containing few numbers of patients, hence any conclusion from the study will be difficult to make and a study with large sample size is required iii) this study lacked the control group without diabetes mellitus.

CONCLUSION

In conclusion, this study showed a high prevalence of thyroid disorder in type 2 diabetes mellitus patients with most common being subclinical hypothyroidism. Thyroid disorder was predominantly present in females. Thyroid dysfunction was seen more in the elderly age group. This study showed positive relationship between prevalence of thyroid dysfunction with duration of diabetes, which was not shown by majority of the studies done before. The high prevalence of abnormal thyroid hormone levels may be due to local environmental factors or may be due to some genetic link. Further studies are necessary to elucidate the cause and the role of abnormal thyroid hormone levels in our population.

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