Thyroid Spectrum Disease in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: There is a complex underlying relation between diabetes mellitus and thyroid dysfunction. This is attributable to an array of complex intertwining biochemical, genetic and hormonal malfunctions mirroring this patho-physiological association. Autoimmunity has been implicated to be the major cause of thyroid-dysfunction associated diabetes mellitus. Hence, the current study aimed to establish the prevalence of thyroid dysfunction in type 2 diabetes mellitus.

Materials and Methods: The current study was carried out on 100 type 2 diabetes mellitus patients attending department of Internal Medicine, National Medical College, Birgunj from July 2018 to July 2019. After obtaining informed consent, socio-demographic, clinical and anthropometric data was collected as per a structured proforma. Also, blood was collected from each patient to obtain fasting blood sugar, post prandial blood sugar, Glycated hemoglobin, triiodothyronine, and thyroxine and thyrotropin levels. Statistical analysis was done as per standard protocol.

Result: The mean Body Mass Index of our patients was 24.88 (SD±2.26) kg/m^2 and body mass index was significantly associated with thyroid dysfunction (p value=.043).Thyroid dysfunction was present in 31% of patients. Also, thyroid dysfunction was significantly associated with fasting blood sugar, post prandial blood sugar and HbA1c levels.

Conclusion: Thyroid dysfunction has a high prevalence in type 2 diabetes mellitus. Hence, all type 2 diabetes mellitus must undergo screening for thyroid dysfunction for optimal patient management.

Keywords: Diabetes, Thyroid spectrum Disorder.

INTRODUCTION

Thyroid dysfunction and diabetes mellitus are the two most common endocrine disorders encountered in clinical practice. Thyroid disorders are common in the general population, and the prevalence increases with age. Thyroid disease is a pathological state that can adversely affect glycemic control in diabetics and has the potential to affect the health. Thyroid disease is found commonly in diabetes and is associated with advanced age, particularly in type 2diabetes mellitus (T2DM) and underlying autoimmune disease in type 1 diabetes. Insulin and thyroid hormones are intimately involved in cellular metabolism and thus excess or deficit of either of these hormones result in the functional derangement of the other.[1]

Diabetes and thyroid disorders have been shown to mutually influence each other and an association between both these conditions has been reported in previous studies.[2,3] Retrospective studies from Nepal shows about 30% prevalence of thyroid disorder in type 2 diabetes mellitus, subclinical hypothyroidism being the most common form.[4,5]

Inability to diagnose abnormal thyroid hormone levels in patients with diabetes is often a reason for poor diabetic management. If a patient is showing unexplained alteration in metabolic control, thyroid function tests should be performed. There is a continuing interest in the association between thyroid disorders inT2DM. Owing to a lack of local studies conducted to study the association between thyroid dysfunction and T2DM, the current study was undertaken.

MATERIAL AND METHODS

This is a cross-sectional prospective hospital based clinical study titled "Prevalence of thyroid dysfunction among type 2 diabetes mellitus patients" was conducted in Department of Internal Medicine, National Medical College & Hospital, Birgunj, Parsa, Nepal for a period of 12 months (July 2018 - July 2019). Non probability purposive sampling method was used. All consenting patients fulfilling the inclusion and exclusion criteria were subjected to a detailed history, anthropometric measurements and clinical examination. Subsequently blood was drawn after a fasting of 12 hrs for analysis of Fasting Blood Sugar (Glucose oxidase-peroxidase method); glycated hemoglobin (ion exchange resin method); T3, T4 and TSH (chemiluminescence immunoassay) levels. Blood was collected again after 2 hours of consuming non-standardized meal for Post prandial glucose estimation.

The results of thyroid function were classified by use of the following as normal reference range:

- TSH: 0.55-4.78 µIU/ml
- T3: 0.6-1.8ng/ml
- T4: 3.2-12.6 µg/dl

Thyroid dysfunction was classified into:

- Hypothyroidism: when T3, T4 were less and TSH greater than the reference ranges.
- Hyperthyroidism: when T3, T4 were greater and TSH

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less than the reference ranges.
- Subclinical hypothyroidism: when T3, T4 were within normal range and TSH greater than the reference ranges.
- Subclinical hyperthyroidism: when T3, T4 were within normal range and TSH less than the reference ranges

A total of 100 patients from department of Internal medicine (National Medical College and Teaching Hospital) fulfilling the inclusion and exclusion criteria were entered in the study.

Inclusion Criteria

1. All patients with type 2 diabetes mellitus (as per ADA criteria)[9] who are ≥ 20 years.

Exclusion Criteria

1. Type 1 diabetes mellitus.
2. Patients with gestational diabetes mellitus, pancreatitis and steroid induced diabetes.
3. Pre-existing cases of thyroid disorder.
4. Patients suffering from haemoglobinopathies and anemia.
5. Patients on amiodarone therapy.

Sugar Profile	Mean (±SD)
Fasting Blood Sugar (mg/dl)	180.93 (±23.82)
Post Prandial Blood Sugar (mg/dl)	261.66 (±57.43)
HbA1c (%)	07.85 (±01.19)

Table-1: Sugar profile of participants

Thyroid Profile	Mean (±SD)
T3 (ng/ml)	1.50 (±00.91)
T4 (µg/dl)	7.47 (±03.04)
Thyroid Stimulating Hormone (mIU/ml)	6.73 (±10.88)

Table-2: Thyroid Profile

This study was approved by the institutional review board of Department of Internal Medicine, National Medical College & Hospital, Tribhuvan University, Kathmandu, Nepal. Informed consent was obtained from all study participants and/or their caregivers.

All obtained data was recorded as per a premade proforma. Data analysis was done as per statistical standard protocol using IBM SPSS (version 20).Significance for association was obtained using Man-Whitney test (parametric and non-parametric set of data) and chi-square test (non-parametric sets of data). A statistically significant test result was considered when p value was ≤ 0.05.

RESULTS

The current prospective hospital based cross-sectional study was performed at National Medical College, Birgunj from July, 2018 to July, 2019. A total of 100 type II Diabetes Mellitus patients were included in the study. The mean (±S.D.) age of the patients in this study was 51.75 (SD±12.56) years. Maximum number (n=36; 36.00%) of cases were between 50-59 years of age. Female to male ratio of 1.38:1.0 was observed in our study. Females comprised 58.00% (n=58) and males comprised 42.00% (n=42) of study sample.

Body Mass Index of our patients were classified into underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) and obese (≥30) as per WHO expert consultation group which advocated in retaining previously proposed cutoff values for BMI stratification in Asian population due to lack of available local data.[10] The mean (±S.D.) BMI of our patients was 24.88 (SD±2.26) kg/m^2. Majority of the patients had normal BMI (n=58; 58%). (Figure-5) Also, BMI was significantly associated with Thyroid Dysfunction (p value=.043).

Sugar Profile

Mean values (±S.D.) of sugar profile observed in our

Thyroid Dysfunction	Sugar Profile		
	Mean FBS[1] (mg/dl)	Mean PPBS[2] (mg/dl)	Mean HbA1c[3] (%)
Absent (n=69; 69%)	177.12(±19.58)	248.80(±45.69)	7.51(±.54)
Present (n=31; 31%)	189.42(±29.92)	290.29(±70.17)	8.63(±1.76)
p value^	.024*	.002*	.001*

^p value obtained using Man-Whitney test (non-parametric and parametric set of data); *significant p-value(≤.05)
[1]FBS: Fasting blood sugar; [2]PPBS: Post Prandial Blood Sugar; [3]HbA1c: Glycated Hemoglobin

Table-3: Association of sugar profile with thyroid dysfunction

Thyroid Dysfunction	Duration of Diabetes		P-value^
	<5 years (N)	≥ 5years (N)	
Absent (n=69)	63	6	<.001*
Present (n=31)	6	25	

^p value obtained using Chi test; *significant p-value(≤.05)

Table-4: Duration of Diabetes and Thyroid Dysfunction

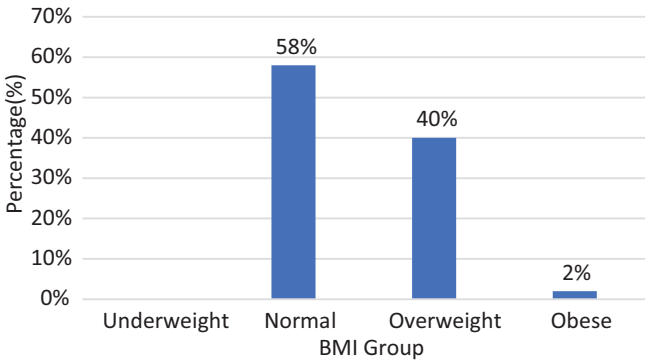

Figure-1: Bar Diagram: Body Mass Index Group

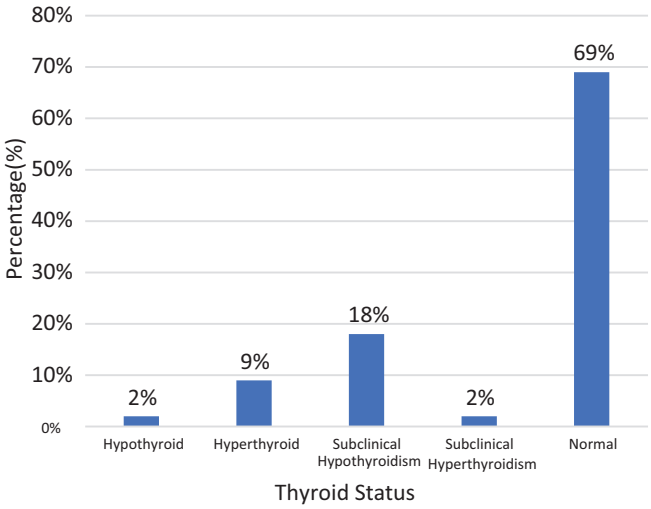

Figure-2: Bar Diagram: Pattern of Thyroid Dysfunction

patients are summarized in Table 1.

Thyroid Dysfunction

Mean values (±S.D.) of thyroid profile observed in our patients are summarized in Table-2.

Thyroid Dysfunction was present in 31% (n=31) of our patients. Pattern of thyroid dysfunction observed in our patients is summarized in Figure-2.

Association of sugar profile with thyroid dysfunction

Mean fasting blood sugar (p value .024), post prandial blood sugar (p value .002) and HbA1c levels (p value .001) was significantly elevated in patients with thyroid dysfunction when compared to patients without thyroid dysfunction. Thyroid dysfunction was significantly more prevalent in patients having diabetes mellitus for ≥5years when compared to patients having the disease for <5 years (p value <.001). Findings are summarized in Table-3 and Table-4.

DISCUSSION

Diabetes mellitus (DM) has an intersecting underlying pathology with thyroid dysfunction. The most probable mechanism leading to thyroid dysfunction in DM could be attributed to perturbed genetic expression of a constellation of genes along with physiological aberrations leading to impaired glucose utilization and disposal in muscles, overproduction of hepatic glucose output, and enhanced absorption of splanchnic glucose. These factors contribute to insulin resistance. Insulin resistance is also associated with thyroid dysfunction. Hyper- and hypothyroidism have been associated with insulin resistance which has been reported to be the major cause of impaired glucose metabolism in DM. Elevated levels of free circulating thyroid hormones produce hyperglycemia by causing polyphagia, enhancing glucose absorption from the gastro-intestinal tract, accelerating insulin degradation and stimulating glycogenolysis. By opposite action, reduced levels of the hormones in hypothyroidism may cause hypoglycemia.[1-4]

Thyroid Dysfunction was present in 31% of patients. This is in concordance with observations made by Bhusal et. al. and Demitrost et. al. who observed a prevalence of 35% and 31.2%, respectively in their studies.[11, 12] However, some studies differ with regards to prevalence of thyroid disorders in diabetic patients.[6, 13] Regional variations may account for the observed difference. Also, thyroid dysfunction was significantly associated with fasting blood sugar, post prandial blood sugar and HbA1c levels. This observation may be accounted by the worsening of sugar profile by abnormalities in thyroid function.[8]

Ogbonna et. al. concluded in their study that duration of diabetes was a risk factor for development of thyroid dysfunction.[14] Similarly, in our study thyroid dysfunction was significantly more prevalent in patients having diabetes mellitus for ≥5years when compared to patients having the disease for <5 years (p value <.001).

The mean age of the patients in our study was 51.75 (SD±12.56) years. Similar observation was made by Jalal et al. who observed a mean age of 51.38 (SD±7.42) years in their patients.[13] However, Bhusal et. al. reported a slightly higher mean age of 55.73 (SD ± 1.62) years in their study subjects.[11] Local demographic factors may account for the observed difference. Female to male ratio of 1.38:1.0 was observed in our study. Female preponderance has also been observed in several other studies.[11, 13]

Body Mass Index of our patients were classified into underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) and obese (≥30) as per WHO expert consultation group which advocated in retaining previously proposed cutoff values for BMI stratification in Asian population due to lack of available local data.[10] The mean Body Mass Index (BMI) of our patients was 24.88 (SD±2.26) kg/m^2. Bhusal et. al. observed a higher mean BMI of 27.66 (SD±5.67) kg/m^2.[11] Local demographic and lifestyle differences may account for observed difference. Interestingly, BMI of our patients had a significant association with thyroid dysfunction (p value=.043). Similar significant association was also observed by Demitrost et. al.[12] Variations of normal thyroid function are accompanied by differences in BMI perhaps due to the changes in the resting energy consumption. The high incidence of the pathological disorders in thyroid function combined with the strong influence of various environmental factors can increase weight and lead to

obesity.[16]

Hence, our study highlights the high prevalence of thyroid dysfunction in type 2 diabetes mellitus (T2DM) and underscores the importance of concurrent periodic evaluation of thyroid function in T2DM for optimal patient management.

CONCLUSION

Thyroid dysfunction has a prevalence of 31% in Type 2 diabetic patients. Body Mass Index has a significant association with thyroid dysfunction. Thyroid dysfunction was significantly associated with fasting blood sugar, post-prandial blood sugar and HbA1c levels. Small sample size of patients taken. Hospital based study which may be not representative of general population.

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