Original Article

Hypothyroidism in diabetes mellitus patients in Eastern Nepal

Robin Maskey, Dhana Ratna Shakya[1], Jouslin Kishore Baranwal[2], Poonam Lavaju[3], Prahlad Karki, Shyam Krishna Poudel

Departments of Internal Medicine, [1]Psychiatry, [2]Biochemistry, and [3]Ophthalmology, B. P. Koirala Institute of Health Sciences, Dharan, Nepal

ABSTRACT

Context: The coexistence of diabetes mellitus (DM) with hypothyroidism is a known clinical observation. **Aims:** To estimate prevalence and co-relate that of hypothyroidism in patients with DM in relation to the age and sex, the lipid profile, body mass index visiting diabetes clinic and inpatients in B. P. Koirala Institute of Health Sciences. **Settings and Design:** The hospital-based descriptive study. **Materials and Methods:** Two hundred and seventy-one known or newly detected cases of DM aged more than 15 years were selected randomly from September 2012 to September 2013 and subjected to evaluation for thyroid function – clinically and biochemically and other relevant investigations were done. **Statistical Analysis Used:** For descriptive statistics mean, standard deviation, percentage, proportion were calculated. For inferential statistics following test were carried out at the level of significant 0.05 where confidence interval is 95%. The statistical operations were done through Statistical Package for the Social Sciences version 10. **Results:** Of 271 subjects, the prevalence of hypothyroidism (clinical and subclinical) in diabetics was, 4.05% (11/271) with females preponderance, of which 7 (30.4%) were clinically hypothyroid and 4 (17.4%) were subclinical hypothyroid. One (4.3%) patient had subclinical hyperthyroidism. The mean age at diagnosis of type 2 DM was 51–60 years. 8.69% of diabetics with primary hypothyroids were having morbid obesity. High-density lipoprotein among different thyroid status were statistically significant ($P = 0.042$). **Conclusions:** Hypothyroidism is not uncommon in diabetes, and we found body mass index, mean triglyceride and cholesterol levels were more in those diabetic patients having coexisting hypothyroidism.

Key words: Diabetes mellitus, Eastern Nepal, hypothyroidism

Introduction

It has been estimated that the prevalence of diabetes in adults worldwide was 4.0% in 1995 and will rise to 5.4% by the year 2025. It is higher in developed than in developing countries. The number of adults with diabetes in the world will rise from 135 million in 1995 to 300 million in the year 2025.[1] Nepal has the highest prevalence of prediabetes among SAARC countries[2] with diabetes mellitus (DM) prevalence among urban 25.9% versus rural 3.1%.[2] According to a study done among 11,394 participants in five areas of eastern Nepal (Dharan, Tarahara, Damak, Biratnagar and Birtamod), 3–8% had diabetes.[3]

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The prevalence of hypothyroidism among people with diabetes ranges from 0.2% to 6% depending on age and sex.[4] Ganz and Kozak[5] at Joslin's clinic, reviewed the records of 60,703 patients with diabetes from 1957 to 1972 and reported 114 (0.19%) cases of hypothyroidism. The Indian study done at GND Hospital, Amritsar,[6] of 184 cases of T2DM showed thyroid disease (TD) present in 78 (40.4%) cases.

The ability to diagnose and treat unsuspected hypothyroidism in these populations may greatly enhance the quality of life. Hence, the detection of such cases is of great importance where hypothyroidism contributes to morbidity and where it is the cause for poor control of the associated conditions. There is limited data both about diabetes and endocrine disorders in Nepalese context and more so about the

Corresponding Author: Dr. Robin Maskey, B. P. Koirala Institute of Health Sciences, Dharan, Nepal. E-mail: drmaskey@gmail.com

relationship between diabetes and hypothyroidism. Hence, we tried to explore the prevalence of hypothyroid and co-relation of the both with this study.

Subjects and Methods

This was a hospital-based descriptive study conducted among consecutive diabetic out-patients and inpatients from September 2012 to September 2013 at Department of Internal Medicine of B. P. Koirala Institute of Health Sciences, Dharan, Nepal. DM Patients diagnosed as per the American Diabetes Association (ADA)[7] and age 15 years and above giving informed written consent were enrolled. Those patients with gestational and secondary diabetes, those not giving the consent and hypothyroidism arising as a result of thyroid surgery or radiotherapy were excluded.

Diabetes mellitus was diagnosed according to ADA diagnostic criteria 2010,[7] as follows:

- Fasting plasma glucose ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h (in the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day).

OR

- Symptoms of hyperglycemia and a casual (random) plasma glucose ≥200 mg/dl (11.1 mmol/l). Casual (random) is defined as any time of day without regard to time since last meal. The classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss.

OR

- Two hour plasma glucose (postprandial plasma glucose PP) ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test. The test should be performed as described by the World Health Organization using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water (In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day).

  OR

  - Glycated Hemoglobin (HbA1c) ≥6.5%.

They were subjected to evaluation for thyroid function with history, clinical examination and investigations including thyroid function test. Diagnosis of hypothyroidism was based on values given in Table 1. Patients are already known to have both DM and hypothyroidism were also included. Every patient's blood sample was collected for measurement following standard package of diabetes investigations, including: FBS, PPBS, serum urea and creatinine, routine urine examination, lipid profile (total cholesterol, high-density lipoprotein (HDL), triglycerides, low-density lipoprotein, and very low-density lipoprotein), serum sodium and potassium, electrocardiography, Chest X-ray. HbA1c was evaluated using immunochromatogaraphy method with NYCO CARD READER II fully automated HbA1c analyzer system. Serum thyroid-stimulating hormone, T3, T4 were measured by chemiluminescence immunoassay (CLIA) method. CLIA utilizes 0.3 ml of the refrigerated serum from serum separator tube. For patients having both the conditions AMA or anti-TPO antibodies were not done because our institute do not have facilities to do this test.

Table 1: Thyroid status groups

Thyroid status	Total (*n*=23) (%)
Euthyroid	11 (47.8)
Subclinical hypothyroidism	4 (17.4)
Clinical hypothyroidism	7 (30.4)
Subclinical hyperthyroidism	1 (4.3)
Total	23 (100)

Results

Two hundred and seventy-one known or newly detected cases of DM aged more than 15 years were selected randomly from the patients attending to B. P. Koirala Institute of Health Sciences from September 2012 to September 2013. Among them, only 23 patients (8.48%) were found to have thyroid disorders.

Of 271 subjects, hypothyroidism and diabetes was observed to occur together in 11 patients, of which 7 (30.4%) were clinically hypothyroid and 4 (17.4%) were subclinical hypothyroid. One (4.3%) patient was found to have subclinical hyperthyroidism. Thus, the prevalence of hypothyroidism (clinical and subclinical) in diabetics was 4.05% (11/271). We found the majority of subjects were females [Figure 1].

Majority of patients were between 51 and 60 years of age group with female preponderance [Figure 2].

Among 23 subjects 30% of were from Hilly ethnic groups/Mongols followed by 21.7% Brahmins, and 13% others [Table 2].

Thus, the difference in use of oral antidiabetic drugs in different thyroid status was not statistically significant and was more (47.8%) in euthyroid status subjects [Figure 3].

Insulin was used more (17.3%) by primary hypothyroid subjects than others [Figure 4].

We found more number of patients with good glycemic control among euthyriod diabetic compared to diabetic patients with clinical hypothyroidism and subclinical hyperthyroidism [Figure 5].

About 30.4% had prehypertension among euthyroid diabetics followed by 26%, 17.3% and 4.34% in clinical hypothyroidism, subclinical hypothyroidism, and subclinical hyperthyroidism respectively. Stage 1 hypertension was present only inneuthyroid diabetics and stage 2 hypertension in 4.34% of both euthyroid and clinical hypothyroidism diabetics [Figure 6].

When body mass index (BMI) ≥23 kg/m^2 (as recommended for Asians) is taken as the determining factor for overweight, we found 21.7% of euthyroid diabetics patients were obese, 8.69% overweight and 4.34% morbid obese. Whereas 4.34% were overweight among diabetics with subclinical hypothyroids, primary hypothyroids and subclinical hyperthyroids. 8.69% of diabetics with primary hypothyroids were having morbid obesity [Figure 7].

Table 2: Caste/ethnicity distribution

Caste-ethnicity groups	Number (%)
Brahmins	5 (21.73)
Chhetris	1 (4.34)
Newars	4 (17.40)
Hilly ethnic groups/Mongols	7 (30.43)
Native Terai ethnic groups	1 (4.34)
Disadvantaged/dalits	2 (8.70)
Others	3 (13.04)
Total	23 (100)

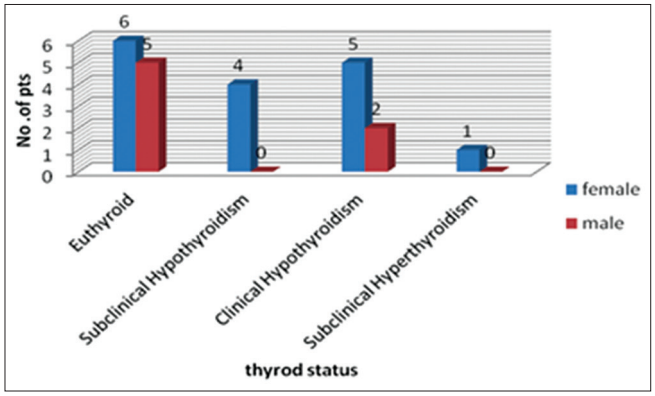

Figure 1: Thyroid status groups

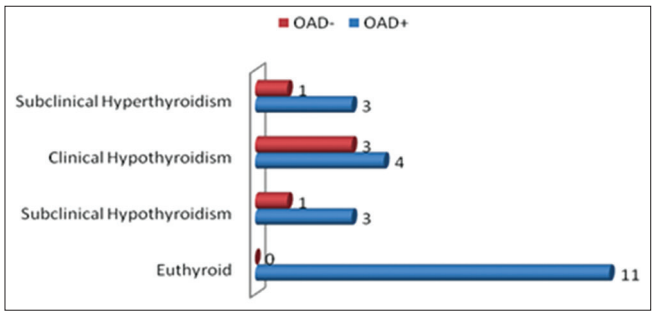

Figure 3: Use of oral anti diabetic drugs in type 2 diabetes with different thyroid status

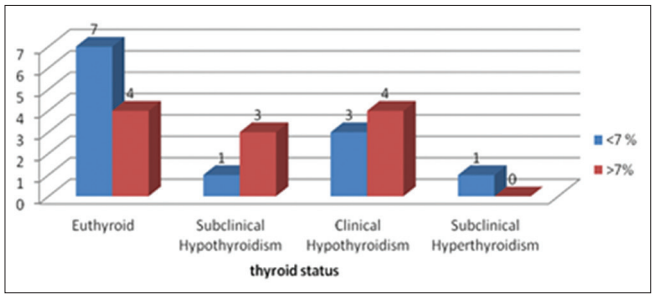

Figure 5: Glycemic status amond different thyroid disorders

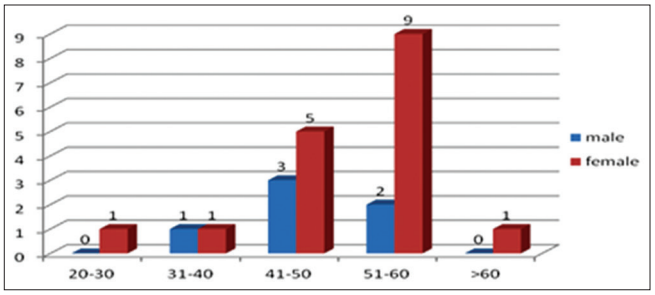

Figure 2: Distribution of subjects as per age and sex

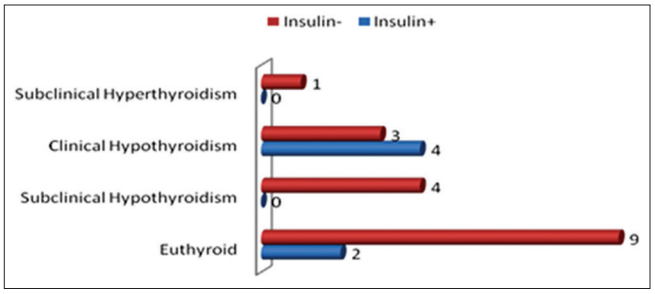

Figure 4: Use of Insulin in type 2 diabetes with different thyroid status

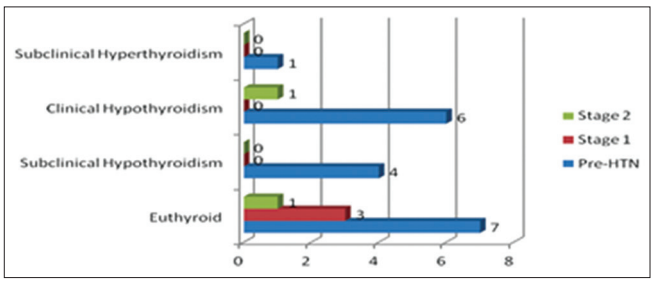

Figure 6: HTN among type 2 diabetes mellitus with different thyroid status

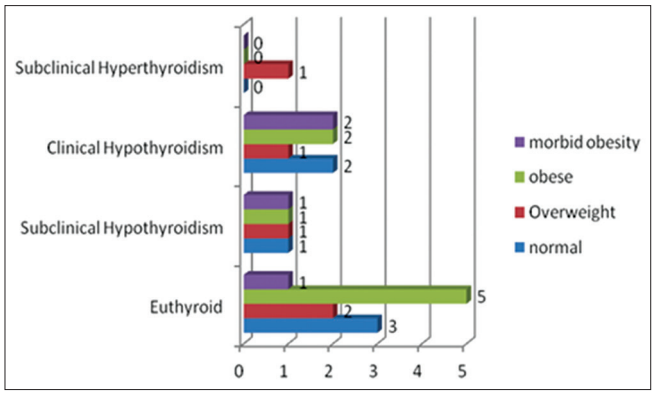

Figure 7: Body mass index among type2 diabetes mellitus with different thyroid status

We found diabetics with high or low HDL among different thyroid status were statistically significant ($P = 0.042$) [Table 3].

Table 3: Analysis among subjects with thyroid disorders in diabetes

Parameters (n=23)	Mean±SD	P
Age	54.43±8.7	0.443
T3	1.45±0.7	0.000
T4	7.42±4.27	0.000
TSH	10±16.2	0.05
Fasting blood glucose	126±31.04	0.639
PPBS	219±64	0.194
HbA1c	6.7±1.4	0.699
Height	157±7.5	0.692
Weight	64±10	0.912
BMI	26.2±4.2	0.855
Total cholesterol	185±39	0.30
HDL	43±23	0.042
LDL	107±37	0.410
Triglycerides	169±71	0.478

SD: Standard deviation, TSH: Thyroid-stimulating hormone, PPBS: Postprandial blood sugar, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HbA1c: Glycated hemoglobin

Discussion

The coexistence of DM with hypothyroidism is a known clinical observation. Various meta-analyses done show the prevalence of hypothyroidism in the general population to be about 1%. Routine screening of thyroid function in diabetics gives a greater yield - 5–15 times than that found in the general population. In addition to identifying undiagnosed clinically hypothyroid patients, it identifies an at risk group with subclinical hypothyroidism that constitutes more than two-thirds of total hypothyroidism in diabetic.

Thyroid function done in 298 type 2 diabetics showed[8] (12.7%) suffered from thyroid dysfunction – 10.7% had hypothyroidism (>2/3rd sub clinical) and 2% had hyperthyroidism. In 31 cases (10.4%) the diagnosis was performed *de novo*. TD was more prevalent among females and elderly.[9]

Numerous studies have been done on the prevalence of hypothyroidism (clinical and subclinical) in diabetics and relation between them regarding various parameters. In type 2 diabetics, the prevalence of clinical hypothyroidism was 4.05% in present study, and 6.4%, 4.0% and 1.7% in other studies. Feely and Isles.[11] reported a 4% prevalence of clinical hypothyroidism in diabetics. They also noted increased prevalence (5%) in women with diabetes who were older than 60 years [Table 4].

Table 4: Clinical hypothyroidism in diabetics

Clinical hypothyroidism	Total
Present study	4.05
Michalek *et al.*[4]	6.4
Hecht and Gershberg[10]	1.7
Feely and Isles[11]	4.0

We found most patients of 51–60 years of age. In the study of 120 T2DM patients at Hyderabad,[12] hypothyroidism was seen in 32 (27%, 10% being subclinical), of which 80% were females. 70% of patients with hypothyroidism were between 40 and 60 years age. The lower prevalence of clinical hypothyroidism in our study may be due to less sample size and study population belonging to different race and ethnicity.

The caste ethnicities were classified as per the system of "Government of Nepal, 2007 for Free Health services, District Health Service Report 2064". Hilly ethnic groups and mongols exceeded other caste/ethnicity groups among diabetics, followed by Brahmins and disadvantages/dalit which is similar to findings of other studies from same institute.[13] The reason for dominance of Mongols in Dharan is due to majority of population are of Mongols.

When BMI ≥ 23 kg/m^2 (as recommended for Asians)[14] is taken as the determining factor for overweight, we found 21.7% of euthyroid diabetics patients were obese, 8.69% overweight and 4.34% morbid obese. Whereas 4.34% were overweight among diabetics with subclinical hypothyroids, primary hypothyroids and subclinical hyperthyroids. 8.69% of diabetics with primary hypothyroids were having morbid obesity [Figure 7].

We found diabetics with high or low HDL among different thyroid status were statistically significant ($P = 0.042$).

Limitations of our study are as follows:

- The sample size was small
- Subjects were clinic diabetes patients of hospital setting.

Recommendations in future are as follows:

- We found even small number of hypothyroidism in diabetic subjects, but the burden is increasing

- Awareness about the thyroid disorders should be raised among medical staff, other medical professionals, and other staffs through various regular awareness raising programs
- Further Research is a must to elaborately look into different aspects of this problem.

Conclusion

Hypothyroidism is not uncommon in diabetes, and every diabetic patient should be screened for hypothyroidism. We found body mass index, mean triglyceride and cholesterol levels were more in those diabetic patients having coexisting hypothyroidism.

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