INTRODUCTION

The association between type 2 diabetes mellitus (T2DM) and thyroid dysfunction (TD) has been reported in medical literature since 1979. Many studies have reported varying prevalence (10%–24%) of TD in T2 DM. This could partially be due to variation in autoimmunity and iodine status. A previous study from India suggested a thyroid disease prevalence of 31.2% among T2 DM patients. The implication of TD on diabetes-related complications or cardiovascular risks is less documented. Iodine status in diabetic individuals in India has not been reported.

METHODS

We conducted an observational cross-sectional study. Consecutive one hundred patients with diabetes who attended our out-patient clinic were evaluated. Diabetes was defined as per the American Diabetes Association criteria (Fasting plasma sugar ≥126 mg/dl, postprandial blood sugar ≥200 or Glycated hemoglobin [HBA1c] ≥6.5% on 2 occasions). Those patients were on treatment for diabetes as well as for their co-existing comorbidities. Written informed consent for the study was obtained from all the patients. We excluded pregnant women or patients taking drugs that can alter thyroid function. Subclinical hypothyroid and overt hypothyroidism were diagnosed as per standard definitions. Results: Out of 100 patients were analyzed, 51 (51%) were male. Mean (±standard deviation) age was 45.4 ± 11.2 years, body mass index 24.1 ± 4.28 kg/m², and duration of diabetes 7.76 ± 5.77 years. The prevalence of subclinical hypothyroidism and overt hypothyroidism was 23/100 (23%) and 3/100 (3%), respectively. Thyroid autoantibody was positive in 13 (13.1%) patients. All patients were iodine sufficient. A trend toward increased neuropathy (r = 0.45) and nephropathy (r = −0.29) was associated with rising TSH. Conclusion: Almost one in four people living with diabetes are suffering from TD. Thus, routine screening should be implemented. Salt iodination program is a huge success in this part of the country.

Keywords: Diabetic peripheral neuropathy, electrochemical skin conductance, normative data, sudomotor function

Address for correspondence: Dr. Sujoy Ghosh, Department of Endocrinology, 242 A JC Bose Road, IPGMER, Kolkata, West Bengal, India. E-mail: drsujoyghosh2000@gmail.com

How to cite this article: Pramanik S, Ghosh S, Mukhopadhyay P, Bhattacharjee R, Mukherjee B, Mondal SA, et al. Thyroid status in patients with Type 2 diabetes attending a tertiary care hospital in Eastern India. Indian J Endocr Metab 2018;22:112-5.
Diabetic Retinopathy Study (ETDRS) Research Group diabetic retinopathy classification system. Blood samples were obtained for biochemical analysis: HbA1c, lipid profile, creatinine, free thyroxine (FT4) and thyrotropin (TSH), anti-thyroperoxidase antibody (anti-TPO), uric for the albumin-creatinine ratio (ACR) and urinary iodine. HbA1c was measured by high-pressure liquid pressure chromatography Biorad D10 method. Serum TSH, FT4, and anti-TPO were estimated by the electrochemiluminescence technique using commercially available kits from Siemens Diagnostics (Mannheim, Germany) with Immulite 1000 analyzer. The analytical sensitivity and total precision values for TSH and FT4 assays were 0.004 μIU/ml and 2.2%, 0.35 ng/dl and 2.7%, respectively. The laboratory reference ranges were TSH (0.4–4 μIU/ml) and FT4 (0.8–1.9 ng/dl) and the inter-assay coefficients of variation (CV) for the assays were 8.9% and 5.5%, respectively. The corresponding values for inter-assay CV, total precision and analytical sensitivity for anti-TPO were 10.5%, 7.6%, and <7 IU/ml. Urinary iodine was measured using Sandell-Kolthoff method (normal range >100 μg/L).

TD was classified as clinical hypothyroidism (C-Hypo) if TSH levels were >4 μIU/ml and FT4 levels were lower than 0.8 ng/dl; sub-C-Hypo (SC-Hypo) if TSH levels were >4 μIU/ml and FT4 levels ranged from 0.8 ng/dl to 1.9 ng/dl, SC-Hyper if TSH levels was lower than 0.4 μIU/ml and FT4 levels ranged from 0.8 to 1.8 ng/dl and clinical hyperthyroidism (C-Hyper) if TSH levels were lower 0.4 μIU/ml and FT4 levels were higher than 1.9 ng/dl. Anti-TPO levels >35 IU/mL was considered to be positive and suggested autoimmunity.

Discussion
Thyroid hormone itself affects intermediary metabolism and thus alter glucose homeostasis. Hypothyroidism leads to reductions in hepatic glucose output, gluconeogenesis, and peripheral glucose utilization thus predisposing to hypoglycemia. Use of medications for diabetes also alters thyroid function. For example, use of metformin has been shown to improve insulin sensitivity and reduce the need for insulin in patients with type 2 diabetes. However, metformin has also been associated with a reduction in thyroid hormone levels and an increased risk of thyroid dysfunction. This highlights the need for ongoing monitoring of thyroid function in patients with diabetes who are taking metformin.

Table 1: Clinical and demographic data of the studied population

| Characteristics (n=100) | Values |
|------------------------|--------|
| Age (years)            | 45.4±11.2 |
| Sex male:female        | 51:49 |
| BMI (kg/m²)            | 24.1±4.28 |
| Duration of diabetes (years) | 7.76±5.77 |
| Family history of diabetes/thyroid (%) | 62/3 |
| Addiction smoking/alcohol (%) | 19/11 |
| Goiter (1B or more) (%) | 5 |
| Acanthosis nigricans   | 43 |
| Grade I                | 30 |
| Grade II               | 11 |
| Grades III             | 2 |
| Retinopathy (ETDRS Classification) (%) | Mild NPDR 8 |
| Diabetic symmetric neuropathy (%) | 19 |
| Nephropathy albuminuria | Moderate 34 |
| Severe                 | 8 |
| HbA1c (%)              | 8.18±1.67 |
| Hypertension (%)       | 55 |
| Dyslipidemia (%)       | 91 |

BMI: Body mass index, ETDRS: Early Treatment Diabetic Retinopathy Study, NPDR: Nonproliferative diabetic retinopathy, HbA1c: Glycated hemoglobin.
shown to cause TSH suppression in patients receiving levothyroxine\(^5\) and insulin increases the level of FT4 while suppresses the level of T3 by inhibiting the hepatic conversion of T4 to T3.\(^6\) Worldwide there is variation in prevalence of TD, possibly due to differing iodine and autoimmunity status. Interestingly, none of our patients were suffering from iodine deficiency. The study result is consistent with the WHO statement\(^7\) in 2004 that India has gained optimal iodine nutrition although few studies\(^8,9\) form our state revealed inadequate iodine concentration in salt in 20%–32% of samples at the consumer level. The prevalence of thyroid autoimmunity was 13% among people with diabetes in our study.

Multiple studies revealed the increased prevalence of TD in type 2 diabetics. A recent meta-analysis\(^10\) of 61 studies performed worldwide described adjusted pooled prevalence of SC-Hypo in T2DM patients was 10.2%. Meanwhile, T2DM was associated with a 1.93-fold increase in the risk of SC-Hypo (95% confidence interval [CI]: 1.66, 2.24). However, the studies from India showed the much higher prevalence of TD. For example, Gurjeet\(^11\) reported 15% prevalence of SC-Hypo in type 2 diabetics in Punjab; Demitrost\(^12\) from Manipur reported the same to be 16.3%; Anil \textit{et al.}\(^13\) from South India found this prevalence to be 11.25% and recently Chaturvedi \textit{et al.}\(^14\) from Meerut reported this prevalence as high as 27%. Most of the studies\(^11-13\) from India also reported the prevalence of subclinical hypothyroid is higher in diabetics as compared with nondiabetics. The study describes 23% prevalence of SC-hypo in people with diabetes. This is consistent with the results of previously published reports. We did not have any control arm.

Results from previous meta-analysis\(^10\) reported SCH might affect the development of diabetic complications with an overall odds ratio of 1.74 (95% CI: 1.34, 2.28) for diabetic nephropathy, 1.42 (95% CI: 1.21, 1.67) for diabetic retinopathy, 1.85 (95% CI: 1.35, 2.54) for peripheral arterial disease, and 1.87 (95% CI: 1.06, 3.28) for diabetic peripheral neuropathy. We found a trend toward higher diabetic complications (neuropathy and nephropathy) with rising TSH. However, we did not find any difference in diabetes-related complications between euthyroid and SCH groups, possibly due to small sample size.

Given the huge burden of type 2 diabetes in India, we can speculate the burden of undiagnosed TD in the society. The exact mechanism for such high association is not clear. Again, whether treating these patients with levothyroxine will reduce their metabolic complications are beyond the scope of this study. The future large-scale longitudinal study is likely to answer these questions.

**Conclusion**

This study reveals about one in four people living with diabetes are suffering from TD in this part of the country, which might warrant routine screening. A trend toward increased neuropathy and nephropathy was associated with rising TSH. This study also implies huge success of salt iodization program in this part of the country.

**Financial support and sponsorship**

This study was funded by Endocrine society of Bengal.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Feely J, Isles TE. Screening for thyroid dysfunction in diabetics. Br Med J 1979;1:1678.
2. Gharib H, Tuttle RM, Baskim J, Fish LH, Singer PA, McDermott MT: Consensus statement. Subclinical thyroid dysfunction: A joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association and The Endocrine Society. J Clin Endocrinol Metab 2005;90:581-5.
3. Demitrost L, Ranabir S. Thyroid dysfunction in type 2 diabetes mellitus: A retrospective study. Indian J Endocrinol Metab 2012;16:S334-5.
4. Somwaru LL, Arnold AM, Joshi N, Fried LP, Cappola AR. High frequency of and factors associated with thyroid hormone over-replacement and under-replacement in men and women aged 65 and over. J Clin Endocrinol Metab 2009;94:1342-5.
5. Cappelli C, Rotondi M, Pirola I, Agosti B, Gandossi E, Valentini U, et al. TSH-lowering effect of metformin in type 2 diabetic patients: Differences between euthyroid, untreated hypothyroid, and euthyroid on L-T4 therapy patients. Diabetes Care 2009;32:1589-90.
6. Mannheim B. Extrathyroidal factor affecting thyroid hormone

---

**Table 2: Prevalence of thyroid dysfunction in type 2 diabetes**

| Thyroid function (n=100) | n (%) |
|-------------------------|-------|
| Euthyroid               | 74 (74) |
| SC-hypo                 | 23 (23) |
| C-hypo                  | 3 (3)   |
| SC-hyper                | 0      |
| C-hyper                 | 0      |

SC-hypo: Subclinical hypothyroidism, C-hypo: Clinical hypothyroidism, SC-hyper: Subclinical hyperthyroidism, C-hyper: Clinical hyperthyroidism

**Table 3: Prevalence of thyroid autoimmunity and iodine deficiency in type 2 diabetes**

| Parameters (n=100)                | n (%) |
|----------------------------------|-------|
| Anti TPO antibody positivity     | 13 (13) |
| Low urinary iodine (<100 µg/L)   | 0     |
| TPO: Thyroid peroxidase          |       |

**Table 4: Correlation between thyroid stimulating hormone and diabetic complications**

| Correlation between TSH and diabetic complications | With VPT | With urine ACR | With eGFR | With retinopathy |
|---------------------------------------------------|---------|---------------|-----------|-----------------|
| Coefficient of correlation (r)                     | 0.01    | 0.10          | 0.045     | 0.44            |
| TSH: Thyroid stimulating hormone, VPT: Vibration perception threshold, ACR: Albumin creatinine ratio, eGFR: Estimated GFR | TSH: Thyroid stimulating hormone, VPT: Vibration perception threshold, ACR: Albumin creatinine ratio, eGFR: Estimated GFR |
concentration. Rational Approach to Thyroid Diagnosis. Germany: Gmbh, Boehringer Mannheim; 1984. p. 2-4.

7. World Health Organization. Iodine Status Worldwide: WHO Global Database on Iodine Deficiency. Geneva: Department of Nutrition for Health and Development, World Health Organization; 2004.

8. Das DK, Chakraborty I, Biswas AB, Saha I, Mazumder P, Saha S, et al. Goitre prevalence, urinary iodine and salt iodisation level in a district of West Bengal, India. J Am Coll Nutr 2008;27:401-5.

9. Das DK, Chakraborty I, Biswas AB, Sarkar GN, Shrivastava P, Sen S, et al. Iodine deficiency disorders among school children of Dakshin Dinajpur District, West Bengal. Indian J Public Health 2005;49:68-72.

10. Han C, He X, Xia X, Li Y, Shi X, Shan Z, et al. Subclinical hypothyroidism and type 2 diabetes: A systematic review and meta-analysis. PLoS One 2015;10:e0135233.

11. Gurjeet S, Vikas G, Anu Kumar S, Neeraj G. Evaluation of thyroid dysfunction among type 2 diabetic Punjabi population. Adv Biore 2011;2:3-9.

12. Anil KR, Narashimha Shetty KR, Lalitha R, Shetty SB. Prevalence of thyroid dysfunction among type 2 diabetes subjects in South India. Int J Clin Cases Investig 2014;5:93-100.

13. Chaturvedi S, Nagtilak S, Parashar P, Rastogi A, Gupta A. Thyroid dysfunction and it’s relation with Type 2 diabetes mellitus in Meerut. Int J Sci Res 2016;7:305-7.