



**THYROID DYSFUNCTION IN PATIENTS WITH DIABETES  
MELLITUS: A RETROSPECTIVE STUDY**

**Amit Kumar Dixit<sup>1\*</sup>, Ranjit Kumar Dey<sup>1</sup>, Rohit Kumar Ravte<sup>2</sup>, Ashok Kumar Panda<sup>2</sup>,  
Sanatan Rai<sup>2</sup>, Naushin Afrin<sup>2</sup>, Jayram Hazra<sup>2</sup>**

<sup>1</sup>Department of Pathology and Biochemistry, National Research Institute of Ayurvedic Drug Development (NRIADD), CCRAS, Ministry of AYUSH, Government of India, 4 CN Block, Sec-5, Bidhannagar, Kolkata-700091, West Bengal, India

<sup>2</sup>Hospital Division, NRIADD, Ministry of AYUSH, Government of India, 4 CN Block, Sec-5, Bidhannagar, Kolkata-700091, West Bengal, India

Article Received on 16/01/2015

Article Revised on 06/02/2015

Article Accepted on 26/02/2015

**\*Correspondence for**

**Author**

**Dr. Amit Kumar Dixit**

Department of Pathology and Biochemistry, National Research Institute of Ayurvedic Drug Development (NRIADD), CCRAS, Ministry of AYUSH, Government of India, 4 CN Block, Sec-5, Bidhannagar, Kolkata-700091, West Bengal, India

**ABSTRACT**

Thyroid dysfunction is one of the common endocrinopathy encountered in diabetes mellitus, which affects the basal metabolic rate of the individual. Early detection and treatment of thyroid dysfunction in type-2 diabetes mellitus can prevent risk for various metabolic disorders. The rationale of this study was to study the prevalence of thyroid dysfunction in patients with type-2 diabetes mellitus. Necessary data was collected from the medical archives of 60 patients (43 female and 17 male) with diabetes mellitus registered in Department of Pathology and Biochemistry of Ayurveda hospital established at Kolkata, India. The mean ages of female and male subjects were  $41.2 \pm 5$  and  $44.2 \pm 8$  years respectively. Out the 60

diabetes mellitus patients, 36 with euthyroid, 9 with subclinical hypothyroidism, 10 with hypothyroidism, 4 with subclinical hyperthyroidism and 1 with hyperthyroidism were identified. In conclusion, the result suggest that the prevalence of thyroid disorder is quite high in female patients with type-2 diabetes mellitus and most of them have subclinical hypothyroidism, and most of these patients were above 40 years of age. This is a preliminary study with a small sample size, hence, larger epidemiological studies is required to find out the actual prevalence and incidence of thyroid dysfunction in patients with diabetes mellitus.

**KEYWORDS:** Thyroid dysfunction; diabetes mellitus; triiodothyronine; thyroxine; TSH.

## INTRODUCTION

Diabetes mellitus is a group of etiologically different metabolic defects characterized by hyperglycemia resulting from defect in insulin secretion as well as insulin action or both. Occasionally other endocrine disorders like abnormal thyroid hormone level are found in diabetes. Thyroid dysfunction is one of the common endocrinopathy encountered in practice, which affects the basal metabolic rate of the individual.<sup>[1]</sup> Thyroid disorders other than iodine deficiency disorders in the form of thyroiditis, hypothyroidism or autoimmune thyroid dysfunctions are on rise.<sup>[2]</sup> The WHO estimates that substantially greater than 190 millions suffer from iodine deficiency disorders in world.<sup>[3]</sup> Thyroid dysfunction is primarily conditions that affect the amount of thyroid hormones being produced in the body. Excess production leads to hyperthyroidism while diminished production leads to hypothyroidism. They affect synthesis, mobilization and degradation of lipids, although degradation is influenced more than synthesis.<sup>[4]</sup> Thyroid dysfunction particularly hypothyroidism is associated with dyslipidemia which increase the risk of hypertension, endothelial dysfunction, and cardiovascular diseases.<sup>[5,6]</sup> Prominent cardiovascular features such as tachycardia, arrhythmias, congestive cardiac failure, and systolic hypertension are well recognized manifestations of thyrotoxicosis.

Early recognition and treatment of thyroid dysfunction in patients with diabetes mellitus will attenuate metabolic disorders and improve general wellbeing. The studies focusing on the association between thyroid dysfunction and diabetes mellitus are sparse. Therefore, this retrospective study has been undertaken to estimate the relationship between thyroid dysfunction and diabetes mellitus.

## MATERIALS AND METHODS

**Chemical:** The diagnostic kits of glucose were procured from Siemens Ltd, (Gujrat India). All the reagents were stored at 2-8°C after procurement. The ELISA kits for T<sub>3</sub>, T<sub>4</sub>, and TSH were procured from Monobind Inc. (California, USA).

**Subjects:** It is a retrospective study based on the available biochemical data of patients visiting the Biochemistry department for the diagnosis diabetes mellitus and thyroid dysfunction, after prescription and medication from OPD and IPD of the Ayurveda hospital at Kolkata, India. A total of 60 thyroid patients (43 females and 17 males) were randomly

selected from the medical records. Patients reported with other ailments and metabolic disorders were excluded from the study. The individual information about clinical symptoms, weight, height and diagnosis by the hospital physicians were well documented in medical records of the hospital.

**Estimation of blood sugar:** Venous blood samples were collected from all the subjects. The plasma was used for analyzing FBS and PPBS. Plasma glucose was measured by Glucose oxidase and peroxidase (GOD-POD) method. It is based on the principle that glucose is oxidized by glucose oxidase into gluconic acid and hydrogen peroxide. Hydrogen peroxide in presence of peroxidase oxidizes the chromogen 4-aminoantipyrine/ phenolic compound to a red colored compound. The intensity of the red colored compound is directly proportional to the glucose concentration and is measured at 505 nm using a semi-automated biochemistry analyzer (Robonik, Mumbai, India).

**Estimation of T<sub>3</sub>, T<sub>4</sub> and TSH:** Venous blood samples were collected from all the subjects in the morning after fasting overnight. The assay of T<sub>3</sub> and T<sub>4</sub> was performed on the basis of competitive method of enzyme linked immuno sorbent assay (ELISA) (Lisa Plus, Aspen Diagnostics, Mumbai, India), while TSH was assayed through sandwich method. Classification of the values was based on the following criteria.

- 1) Normal, when the total T<sub>4</sub> and TSH are in the normal range
- 2) Hypothyroidism-when total T<sub>4</sub> < 4.4 µg/dl and TSH > 5.5 mIU/ml.
- 3) Subclinical hypothyroidism when T<sub>4</sub> is within normal limits but TSH > 5.5 mIU/ml.
- 4) Subclinical Hyperthyroidism when T<sub>4</sub> is within normal limits but TSH < 0.4 mIU/ml.
- 5) Hyperthyroidism when T<sub>4</sub> is > 11.6 µg/dl but TSH < 0.4 mIU/ml.

**Statistical analysis:** The data obtained was analyzed for significance between the groups by one-way analysis of variance (ANOVA) by using statistical software program “SPSS evaluation version 19”.

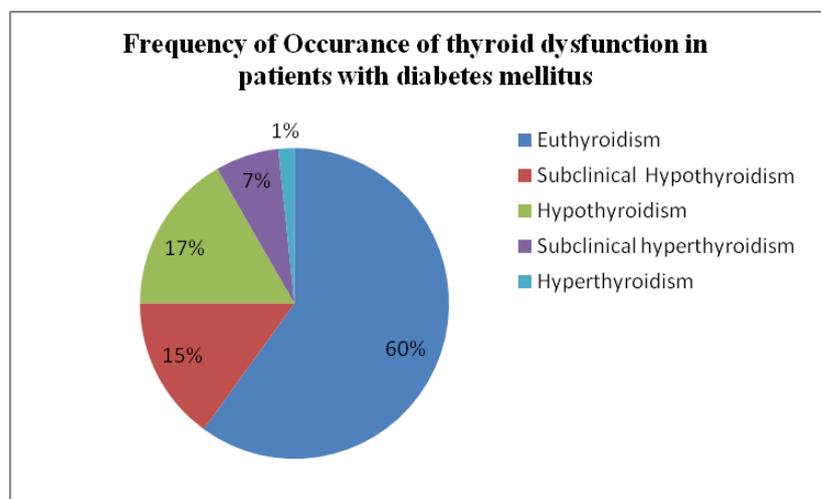
## RESULTS

Results of the present retrospective study showed that among 60 patients with diabetes mellitus included in this study, female and male were 43 and 17, respectively (**Table 1**). Results showed that, all individuals selected for the study were with diabetes mellitus. The normal reference range considered for each parameter was already established reference value of our laboratory. Results showed that out the 60 diabetes mellitus patients, 36 with

euthyroid, 9 with subclinical hypothyroidism, 10 with hypothyroidism, 4 with subclinical hyperthyroidism and 1 with hyperthyroidism were identified (**Fig.1**).

**Table 1: Gender distribution, age and glucose level of patients with diabetes mellitus.**

Gender	No. of patients	Mean age in years	Mean FBS (mg/dl)	Mean PPBS (mg/dl)
Female	43	41.2 ± 5	135 ± 5.6	218 ± 25
Male	17	44.2 ± 8	140 ± 6.3	232 ± 14



## DISCUSSION

Diabetes mellitus and thyroid diseases are the two common endocrinopathies seen in the adult population. With insulin and thyroid hormones being intimately involved in cellular metabolism and thus excess or deficit of either of these hormones could result in the functional derangement of the other.<sup>[7]</sup> Furthermore, insights are being developed into the complex interactions, at the phenotypic and molecular levels, between thyroid dysfunction and cardiovascular risk. Thus, our understanding has shifted from the simplistic concept of thyroid dysfunction as a benign disorder of hormone secretion to a more complete appreciation of its multiple deleterious effects on cardiovascular and metabolic function.<sup>[8, 9, 10]</sup> Subclinical hypothyroidism is defined as an elevated TSH concentration in the presence of normal thyroid hormones.<sup>[11]</sup> With the advent of sensitive assays for TSH measurements subclinical hypothyroidism will increasingly be diagnosed in healthy individuals with no overt features of thyroid disease. The clinical features of thyroid disorders tend to be nonspecific and fewer in elderly compared to younger patients and the symptoms are often confused with normal ageing process and coexisting diseases which may result in greater number of elderly patients being undiagnosed.<sup>[12]</sup> The serum T<sub>3</sub> levels, basal TSH levels and

TSH response to thyrotropin releasing hormone (TRH) may all be strongly influenced by the glycaemic status in euthyroid patients with diabetes mellitus. Diabetes of either type, if not properly controlled may induce a “Low T<sub>3</sub> state” characterized by low serum total and free T<sub>3</sub> levels, increase in reverse T<sub>3</sub> (rT<sub>3</sub>) but near normal serum T<sub>4</sub> and TSH concentrations. Low serum T<sub>3</sub> is due to reduced peripheral conversion of thyroxine (T<sub>4</sub>) to tri-iodothyronine (T<sub>3</sub>) via 5' monodeiodination reaction. Poorly controlled diabetes may also result in impaired TSH response to TRH or loss of normal nocturnal TSH peak. TSH responses and “low T<sub>3</sub> state” may normalize with improvement in glycaemic status.

Results showed higher prevalence of thyroid dysfunction in females which is in accordance with the earlier studies.<sup>[2,13,14]</sup> It may be due to a sex difference in the prevalence of autoimmune diseases. Thyroid management in people with diabetes mellitus starts with a thorough evaluation that aims to identify secondary causes that might contribute to the abnormal metabolism.<sup>[15,16,17,18,19]</sup> Medication alongwith dietary modifications are the cornerstones of management. Realizing the fact that individuals with thyroid dysfunction have a high probability of developing cardiovascular and cerebrovascular disease, it is essential that an individual who has diabetes should take care of his thyroid function.<sup>[20, 21, 22, 23]</sup>

In conclusion, the results suggest that there is inter-dependence between insulin and thyroid hormones for normal cellular metabolism so that diabetes mellitus and thyroid diseases can mutually influence the other disease process. When diabetes occurs in euthyroid individuals, it results in altered thyroid function tests with no clinical dysfunction. The prevalence of thyroid disorder is quite high in female patients with type-2 diabetes mellitus and most of them have subclinical hypothyroidism, and most of these patients were above 40 years of age. This is a short preliminary study with a small sample size, and larger epidemiological studies is required to find out the actual prevalence and incidence of thyroid dysfunction in patients with diabetes mellitus.

#### **COMPETING INTERESTS**

The authors declared that they have no competing interests.

#### **ACKNOWLEDGEMENT**

The authors are grateful to Dr. A. Mitra, Dr. KK Ratha, Mr. S.C. Pandey, Mr. Kartik Hazra staff of National Research Institute of Ayurvedic Drug Development, Kolkata for their support, encouragement, cooperation and skillful technical assistance.

**REFERENCES**

1. Thakkar NV and Jain SM. The impact of diabetes on thyroid dysfunction and outcomes in a native Indian female population. *Thyroid Science*, 2011; 6(4): 1-9.
2. Regmi A, Shah B, Rai BR and Pandeya A. Serum lipid profile in patients with thyroid disorders in central Nepal. *Nepal Med Coll J*, 2010; 12(4): 253-256.
3. WHO/ICCIDD/UNICEF. Assessment of iodine deficiency disorders and monitoring their elimination. 2nd edition. Geneva: WHO. 2001
4. Ridgway EC. Modern concepts of primary thyroid gland failure. *Clin Chem*, 1996; 42: 179-182.
5. Pucci E, Chiovalto L and Pinchera A. Thyroid and lipid metabolism. *Inter J Obesity*, 2004; 24: 109-12.
6. Estienne V, Duthoit C, Reichert M, et al. Androgen-dependent expression of Fc̄RIIB2 by thyrocytes from patients with autoimmune Graves' disease: a possible molecular clue for sex dependence of autoimmune disease. *Fed Am Soc Experiment Biol*, 2002; 16: 1087-1092.
7. Cutolo M, Sulli A, Capellino S, et al. Sex hormones influence on the immune system: basic and clinical aspects in autoimmunity. *Lupus*, 2004; 13(9): 635-638.
8. Jiskra J, Limanova Z and Antosova M. Thyroid disease, dyslipidemia and cardiovascular risk. *Vnitr Lek*, 2007; 53: 382-5.
9. Fernandez-Real JM., Lopez-Bermejo A, Castro A, et al. Thyroid function is intrinsically linked to insulin sensitivity and endothelium dependant vasodilation in healthy euthyroid subjects. *J Clin Endocrinol Metab*, 2006; 91(9): 3337-3343.
10. Hage M, Zantout MS and Azar ST. Thyroid disorders and diabetes mellitus. *J Thyroid Res*, 2011; 1-7.
11. Biondi B and Cooper DS. The clinical significance of subclinical thyroid dysfunction. *Endocr Rev*, 2008; 29: 76-131.
12. Parle JV, Maisonneuve P, Sheppard MC, Boyle P and Franklyn JA. Prediction of all-cause and cardiovascular mortality in elderly people from one low serum thyrotropin result: a 10-year cohort study. *Lancet*, 2001; 358: 861-865.
13. Sisk J. Thyroid disease in women. *Thyroid*, 2005; 17: 34-8.
14. Limbu YR, Rai SK, Ono K et al. Lipid profile of adult Nepalese population. *Nepal Med Coll J*, 2008; 1: 4-7.
15. Cabral MD, Costa AJL, Santos M and Vaisman M. Lipid profile alterations in subclinical hypothyroidism. *Endocrinologist*, 2004; 14: 121-125.

16. Liberopoulos EN and Elisaf MS. Dyslipidemia in patients with thyroid disorders. *Hormones*, 2002; 1: 218-23.
17. Packard C, Nunn A and Hobbs R. High density lipoprotein: guardian of the vascular system. *Inter J Clin Practice*, 2002; 56: 761–71.
18. Duntas LH. Thyroid disease and lipids. *Thyroid*, 2002; 12: 287-293.
19. Ladenson PW, Singer PA, Ain KB, Bagchi N, Bigos ST, Levy EG, et al. American Thyroid Association guidelines for detection of thyroid dysfunction. *Arch Intern Med*, 2000; 160: 1573-1575.
20. Mouradian M and Abourizk N. Diabetes mellitus and thyroid disease. *Diabetes Care*, 1983; 6: 512-520.
21. Satish R and Mohan V. Diabetes and thyroid diseases: a review. *Int J Diab Dev Countries*, 2003; 23(4):120-123.
22. Brenta G. Diabetes and thyroid disorders. *Br J Diabetes Vasc Dis*, 2010, 10: 172-177.
23. Dixit AK, Dey RK, Suresh A, Mitra A, Upadhyay SN, Hazra J. Lipid profile of patients with thyroid dysfunction in Ayurveda hospital. *Inter J Bio Res*, 2014; 5: 241-243.