

Thyroid function in type 2 diabetes mellitus

Sajeda Afrin¹, Chandra Rani Sarkar², A.T.M Zoadur Rahim Zahid³, Neaz Ahmed⁴

Abstract

Background: Type 2 Diabetes Mellitus (T2DM) and thyroid disorder are common endocrine disorders that affect major population worldwide. Subclinical hypothyroidism is common among T2DM. **Objectives:** To observe thyroid stimulating hormone (TSH), total thyroxine (TT₄), free thyroxine (FT₄), total triiodothyronine (TT₃), free triiodothyronine (FT₃) levels in newly diagnosed T2DM. **Methods:** This cross sectional study was conducted from July 2014 to June 2015. For this, 50 newly diagnosed T2DM patients aged 30 to 50 years of both sexes were enrolled from the Out Patient Department of Endocrinology, Rangpur Medical College and Diabetic Association, Rangpur. Fifty age matched non-diabetic healthy subjects of both sexes constituted control. Serum TSH, TT₄, FT₄, TT₃, FT₃ levels were estimated to observe thyroid function. All these hormones were estimated by ELISA method. For statistical analysis independent sample “t” test was performed. **Results:** Serum TSH was significantly higher (p<0.001) and serum TT₄, FT₄, FT₃ levels were significantly lower (p<0.001) in T2DM compared to control. Eight (16%) of T2DM were hypothyroid. **Conclusion:** From this study it can be concluded that altered thyroid status leading to hypothyroidism may be associated with T2DM.

Key word: Type 2 Diabetes Mellitus, TSH, TT₄, FT₄, TT₃, FT₃.

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For Authors Affiliation, see end of text.
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Introduction

D iabetes mellitus is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin¹. Worldwide over 380 million people were estimated to have T2DM in 2013². T2DM poses a major global health threat, both in the developed and developing countries³. Diabetes Mellitus and thyroid disorders are endocrine disorders that are interrelated to each other⁴. The relationship between Diabetes Mellitus and thyroid disorders is characterized by a complex interdependent interaction. A higher frequency of retinopathy, nephropathy,

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cardiovascular diseases and also subclinical hypothyroidism complications were observed in T2DM⁵. Subclinical hypothyroidism being the most common disorder in T2DM⁶. TT₄, TT₃ secretion is controlled primarily by TSH, secreted from anterior pituitary gland⁷. Thyroid hormones are necessary for normal glucose metabolism. Hyper or hypo secretion of thyroid hormones can alter glucose homeostasis⁵. Thyroid disorders not only worsen the metabolic control but also affect the management of diabetes⁸. Therefore, diabetes patients need to be screened for thyroid dysfunction. American diabetic Association (ADA) has proposed the people with diabetes to be checked for thyroid disorders⁹. The magnitude of health problems related to diabetes

mellitus in our country has been increasing rapidly. Majority of the people are not aware about their health hazards caused by Diabetes Mellitus as well as thyroid dysfunction. Although thyroid disorders are increasing among T2DM but it is frequently overlooked and not diagnosed properly in the early stage. Only one study on hypothyroidism among T2DM is available¹⁰. Therefore, the present study has been designed to assess thyroid disorder among T2DM and thereby to develop awareness about thyroid dysfunction in newly diagnosed T2DM.

Methods

This is a cross sectional analytical study conducted in Department of Physiology, Rangpur Medical College, Rangpur from July, 2014 to June, 2015. Protocol of this study was approved by ethical review committee of Rangpur Medical College. A total number of 100 subjects, aged 30 to 50 years of both sexes and similar socio-economical condition were included in this study. Among them, 50 were apparently healthy subjects and 50 were newly diagnosed T2DM patients, selected from Out Patient Department (OPD) of Endocrinology, Rangpur Medical College and Diabetic Association, Rangpur. The objectives, nature, purpose and benefit of the study were explained to the subjects in details. Informed written consent was taken from all participants. All the subjects were excluded from known thyroid disorders, treated Type 2 Diabetes Mellitus and T2DM with other complications.

After 8-10 hours overnight fasting and 2 hours after ingestion of 75 gm glucose, each time 5 ml of venous blood was drawn from medial cubital vein by sterile disposable syringe. Serum glucose was estimated by enzyme method¹¹. Serum TSH, TT₄, FT₄, TT₃ and FT₃ were estimated by ELISA method¹². Data were expressed as mean \pm SE and were analyzed by independent sample 't' test. p value <0.05 was taken as level of significance.

Results

The mean serum TSH level was significantly higher ($p < 0.001$) and the TT₄, FT₄, TT₃ and FT₃ levels were significantly lower ($p < 0.001$) in T2DM than those of non-diabetic group (Table I). Eight (16%) patients were found with developing hypothyroidism but none of control group had hypothyroidism (Figure 1).

Table I : Serum TSH, TT₄, FT₄, T₃ and FT₃ levels in different groups (n=100)

Variables	NDG (n=50)	DG (n=50)
TSH (mIU/L)	3.04 \pm 0.08	5.34 \pm 0.23***
TT ₄ (μ g/dl)	8.05 \pm 0.17	3.91 \pm 0.15***
FT ₄ (ng/dl)	1.56 \pm 0.05	0.71 \pm 0.04***
TT ₃ (ng/ml)	1.25 \pm 0.03	0.80 \pm 0.02***
FT ₃ (pg/ml)	3.28 \pm 0.03	2.59 \pm 0.07***

Data were expressed as mean \pm SE. Statistical analysis was done by independent sample 't' test for comparison between groups. *** = $p < 0.001$. TSH = Thyroid Stimulating Hormone. TT₄ = Total Thyroxine. TT₃ = Total Triiodothyronine. FT₄ = Free Thyroxine. FT₃ = Free Triiodothyronine. NDG = Non-diabetic group, DG = Diabetic Group.

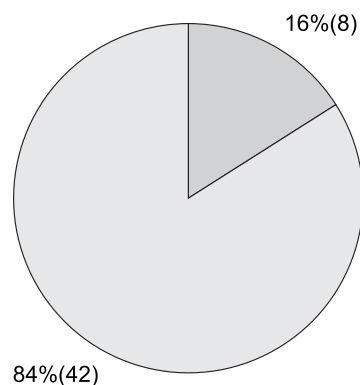


Figure 1: Pie chart showing the frequency of hypothyroidism (in %) in diabetic group. Cut point for TT₄=4.4–10.8 μ g/dl²⁰, TT₃=0.69–2.02 ng/ml²⁰, FT₄=0.8–2.0 ng/dl²⁰, FT₃=1.4– 4.2 pg/ml²¹, TSH=0.3–6.2 mIU/L²⁰

Discussion

In the present study, serum TSH level was found significantly increased but serum TT_4 , FT_4 , TT_3 and FT_3 levels were found significantly decreased in newly diagnosed T2DM than that of control subjects. Moreover, 16% of the patients presented with hypothyroid status. This finding is consistent with others^{3,8,10,13}. In contrast, some other researchers did not find any significant change of serum TSH in T2DM¹⁴. Even some studies found lower levels of serum TSH and higher levels of serum TT_4 and TT_3 in T2DM than that of control group^{15,16}.

It has been suggested that altered thyroid status in T2DM is linked to alteration of hypothalamo-pituitary-thyroid axis causing decreased formation of TT_4 and TT_3 . Also there is less activation of AMPK (5'-Adenosine Mono Phosphate activated Protein Kinase) in T2DM that also causes decreased formation of thyroid hormones.⁸ Decrease levels of thyroid hormones cause increased TSH release from anterior pituitary gland by feedback mechanism^{10,13,17}. Most of the T2DM patients were obese who might have increased level of leptin. This increased level of leptin develops leptin resistance centrally that causes decreased formation of thyroid hormones and increase TSH secretion by feedback mechanism in T2DM⁸.

Moreover the binding affinity of TT_4 is increased in T2DM that causes decrease formation of FT_4 in blood^{13,17}. In T2DM, Thyroid Hormone Binding Inhibitor (THBI) also produces that inactivates extra thyroidal conversion enzyme (T_{4-5} -deiodinase). By this way, reduce conversion of TT_4 to TT_3 in target tissue^{18,19}. There is also the degradation rate of TT_3 is more than TT_4 in T2DM. These all factors are responsible for decrease T_3 level^{3,13}. T2DM are also associated with obesity, stress, infection that caused changes in hypothalamo-pituitary-thyroid axis lead to decrease level of thyroxine and triiodothyronine and increased TSH level in T2DM⁸.

In the present study, the hypothyroidism developed in some of newly diagnosed T2DM patients may be due to alteration in hypothalamo-pituitary-thyroid axis that may cause decreased formation of thyroid hormones. The lower level of free T_4 in blood in T2DM may develop due to increase binding affinity of T_4 . All these factors may cause decrease thyroid hormone levels and increase TSH release by feedback mechanism.

Conclusion

From this study it can be concluded that hypothyroidism may develop in newly diagnosed T2DM. Therefore routine examination of serum TSH, TT_4 and TT_3 may be helpful to prevent complications like hypothyroidism in newly diagnosed T2DM.

Conflict of interest None

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Author Affiliations

1. *Sajeda Afrin, Lecturer, Department of Physiology, Rangpur Medical College, Rangpur. email: sajedaaftrin82@gmail.com. Cell: +8801763800898
2. Chandra Rani Sarkar, Professor and Head, Department of Physiology, Rangpur Medical College, Rangpur.
3. A.T.M Zoadur Rahim Zahid, Associate Professor, Department of Physiology, Rangpur Medical College, Rangpur.
4. Neaz Ahmed, Assistant Professor and Head, Department of Biochemistry, Rangpur Medical College, Rangpur.

*For correspondence

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