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Research Article

Co-occurrence of type 2 diabetes mellitus and thyroid metabolic disorders in Bangladeshi population

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Abstract: Studies have found that diabetes and thyroid disorders tend to co-occur in patients. Although this co-occurrence have been observed mainly in type 1 diabetes mellitus (T1DM), thyroid dysfunctions also co-occur in type 2 diabetes mellitus (T2DM) to a significant level. In the present study, we have investigated different thyroid function markers in 50 T2DM patients and 50 healthy age-sex matched controls of an urban population with mean±SD age of 41.86±6.43 and 41.54±7.88 respectively. Fasting blood glucose (FBG) (13.34±2.52 *vs*. 4.45±0.53) as well as mean glycosylated hemoglobin, $HbA1_c$ (%) (13.15±1.81 *vs*. 4.49±0.644) were significantly ($p<0.001$) higher in T2DM patients than control subjects. We found that serum levels of thyroid stimulating hormone (TSH) (1.22±0.74 vs. 1.74±1.07; $p<0.01$) and free T_3 (FT_3) (0.99±0.24 *vs.* 2.74±0.75; $p<0.001$) were significantly lower in T2DM patients than that of control subjects. However, we did not find any significant difference in case of the serum levels of freeT4 (FT_4) (15.42±2.90 *vs*. 15.61±2.98) between the T2DM patients and control subjects. We found that levels FBG and $HbA1_c$ were abnormally high and serum FT_3 was abnormally low in T2DM patients. On the other hand, levels of TSH, FT_4, anti-thyroglobulin (TG) and anti-thyroid peroxidase (TPO) were all almost within the normal range in T2DM patients. A significantly lower anti-TG level was found in T2DM patients than control (33.44±5.25 *vs*. 35.64±4.0; $p<0.05$). This study revealed a significant negative correlation of serum FT_3 with FBG and $HbA1_c$ (r=-0.789**, p=0.000 and r=-0.820**, p=0.000 respectively) irrespective of the groups. Findings of the present study on a small size of Bangladeshi population indicate the possibility of low FT_3 syndrome in T2DM patients in which thyroid autoimmunity was not related.

Keywords: Type 1 diabetes mellitus, Type 2 diabetes mellitus, Thyroid hormones, Autoimmunity, Fasting blood glucose

INTRODUCTION

Diabetes mellitus is a condition of impaired carbohydrate metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissue to insulin. It is one of the commonest metabolic disorders that is characterized by hyperglycemia (high blood sugar) and other signs, as distinct from a single illness and its incidence is rapidly increasing all over the world [1]. Recently global estimates of diabetes prevalence clearly indicate an overall increase of diabetes in the developing countries [2]. In the simplest terms, diabetes mellitus results when pancreatic beta cells fail to maintain adequate insulin secretion to prevent hyperglycemia. The World Health Organization recognizes three main forms of diabetes: type 1, type 2, and gestational diabetes (occurring during pregnancy), [3] which have similar signs, symptoms, and consequences, but different causes and population distributions. Type 1 Diabetes mellitus—formerly known as insulin-dependent diabetes (IDDM), childhood diabetes or also known as juvenile diabetes, is usually due to T-cell mediated autoimmune destruction of the pancreatic beta cells which produce insulin. Type 2 diabetes mellitus—previously known as adult-onset diabetes, maturity-onset diabetes, or non-insulin-dependent diabetes mellitus (NIDDM)—is due to a combination of defective insulin secretion and insulin resistance or reduced insulin sensitivity (defective responsiveness of tissues to insulin), which almost certainly involves the insulin receptor in cell membranes. Type 2 is characterized by tissue-wide insulin resistance and varies widely. Type II diabetes is far more common than type I, accounting for about 90 percent of all cases of diabetes mellitus. In most cases,

the onset of type II diabetes occurs after age 30, often between the age of 50 and 60 years and so is regarded as adult diabetes. Diabetes mellitus type 2 is often associated with obesity, hypertension and elevated cholesterol (combined hyperlipidemia), and some metabolic syndromes including endocrinological ones. Gestational diabetes is similar to type 2 diabetes, in that it involves insulin resistance; the hormones of pregnancy cause insulin resistance in those women genetically predisposed to developing this condition. In all types of diabetes mellitus, metabolism of all main food stuff is altered. The basic effect of insulin resistance on glucose metabolism is to prevent the efficient uptake and utilization of glucose by most cells of the body, except those of the brain. As a result, blood glucose level increases, their utilization by cells is lowered, and utilization of fats and proteins is increased, instead [3].

A combination of genetic and environmental factors causes the underlying beta-cell failure. In type 1 diabetes, a T-cell–mediated autoimmune response against beta cells appears to be the main disease mechanism, whereas insulin resistance is the key metabolic abnormality in type 2 diabetes.

Glucotoxicity, oxidative stress, and cytotoxic cytokines lead to further damage, which eventually results in beta-cell death if the process is not countered by effective self-repair and therapeutic interventions [4]. The criteria for diagnosing diabetes mellitus had been issued by consensus panel of experts from the National Diabetes Data Group and the WHO. They reflect the epidemiological and metabolic evidences and are based on fasting plasma glucose, blood sugar response to the oral glucose load and various diabetes-specific complications [5]. The American Diabetes Association recommends use of hemoglobin A1c (HbA1c or A1c) determinations to monitor glycemic control in known diabetic patients. As there is not a "gold standard" assay and because many countries do not have ready access to the test, an A1c determination is not recommended for the diagnosis of diabetes mellitus. However, because the A1c accurately reflects the mean blood glucose concentration over a 1-3 month period and correlates well with the development of diabetic complications, it may in future become established as a test for the diagnosis of diabetes [6].

Like diabetes, diseases of the thyroid gland are also amongst the most abundant endocrine disorders in the world, second only to diabetes [7]. Thyroid disorders can have a significant effect on blood glucose levels and, if left untreated, can affect diabetes control. Hyperthyroidism is typically associated with worsening glycemic control and increased insulin requirements. Hypothyroidism can decrease the insulin requirement in patients with diabetes. All over the world researchers have found that there is a higher incidence of thyroid dysfunctions among diabetic patients, which can complicate the metabolic disturbances to a significantly dangerous level [8]. Hyperthyroidism and hypothyroidism occurs in about 2% and 1% of the population respectively. Studies have found that diabetes and thyroid disorders tend to co-occur in patients. Almost one third of people with type 1 diabetes have been found to have thyroid disease. This is because both the T1DM and the most common thyroid disorders are autoimmune diseases, in which the immune system attacks a gland or organ of the body. In T1DM patients, thyroid dysfunctions may be due to underlying genetic predisposition which leads to the coexistence of autoimmune destruction of pancreatic islet cells as well as thyrocytes [9, 10]. In T2DM the association with thyroid diseases are largely unexplained, although it may relate to old age, and also possibly the fact that some T2DM are actually T1DM patients having a very slow-onset, and so having the same genetic predisposition as T1DM [8].

Many reports have shown that only clinical assessment might not be able to detect all the cases of thyroid dysfunctions as a large percentage of them are subclinical [8, 11, 12], which can only be diagnosed by biochemical assessment. As diabetes is a major public health problem, any disorder that may even be weakly associated with it, needs special attention.

In 1995 a randomly selected group of 1310 adult diabetic patients attending a diabetic outpatient clinic at Scotland received annual screening for thyroid diseases, by estimating serum free thyroxin and TSH concentrations. The overall prevalence of thyroid disease was found to be 13.4%, and was highest (31.4%) in Type1 diabetic females and the lowest in Type2 diabetic males (6.9%). Kabadi *et al*. indicated that thyroid hormone metabolism may be altered in Diabetes mellitus with a fall in serum T_3 level and reciprocal rise in rT_3. Serum T_3 and rT_3 concentration may serve as indicator of metabolic control in Diabetes mellitus [13, 14]. A low T_3, syndrome is a common finding in nonthyroidal illness as well as in Diabetes mellitus which is characterized by normal or slightly elevated T_4, Low T_3, increased rT_3, and normal TSH [15]. Hypothyroidism must be ruled out in these patients because failure to treat hypothyroidism in this group of patients could be catastrophic. Occasionally T4 is elevated and confused with hyperthyroid status. Some scientists have found the correlation between different degree and duration of metabolic control and thyroid hormone levels in type 1 and type 2 diabetics. According to them rT_3 and rT_3/T_3 ratio were significantly increased both in type 1 and type 2 diabetics. T_3 and T_4 were significantly lower in type 2 diabetics than in the controls. Significant positive correlations of HbA_{1c} to rT_3 and to rT_3/T_3 ratio were found in type 1 and in type 2 diabetics. There was no correlation between glycemia (BG), relative body weight (RBW) and thyroid hormones. These data suggest that the alterations of thyroid hormones in type

1 and type 2 diabetes mellitus reflect the degree of control better than the hyperglycemia and the duration of metabolic unbalance. Researchers in Japan stated that the same or a very closely related auto antigen(s) in both islet beta cells and thyroid follicular cells was present in NIDDM [16].

In a developing country like Bangladesh most of the researches are directed towards the control of the infectious diseases, with little attention to chronic diseases like diabetes coming lower in the ranks of priority, even though they may add to the mortality as well as to the morbidity. Different studies on thyroid function have already been conducted in the young diabetic group at BIRDEM (Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders). In all the studies, concentration of total T_3 was decreased significantly. In a study T_4 was unchanged but in another study it was slightly decreased. The decrease in T4 was probably due to higher glucose level of the diabetic subjects. TSH (Thyroid stimulating hormone) was normal in all the studies. These studies show that T_3 and T_4 were decreased with progressive rise in the percentage of HbA1c and a positive correlation was found between thyroid hormone metabolism and serum insulin. But no such work was done on Type 2 diabetic patients. Most of the studies that were done assessed only the prevalence of thyroid disorders among diabetic population, and they showed significant change in T_3, T_4 and TSH level with blood glucose. But total T_3 and T_4 might vary with the change in thyroid binding proteins (TBP) or presence of drugs that modify the total T_3 and T_4 but not the amount of free hormone. If TBP is normal in the subject then these are the reliable indices of thyroid function. However, freeT_3 and T_4 are not bound to TBP and these are the most important parameters to elucidate thyroid dysfunction in the group, which were not included in the previous studies. Thyroid antibodies, for example, Anti-TG (Anti-thyroglobulin), Anti-TPO(Anti-thyroperoxidase) for investigating the association of thyroid auto antibodies were not done in the previous studies on the diabetic population. As most of the studies of Bangladesh regarding this were done only on the young diabetic population but not on the over 30 age groups, we were interested to do the work on Type 2 diabetic patient who were between the age range of 30 to 55 years.

In the present study, we studied the interference of thyroid auto-antibodies in the thyroid dysfunction of Type 2 DM patients, by measuring the TSH, FT_3 (Free T_3), FT_4 (Free T_4), Anti-TG and Anti-TPO antibody to provide adequate treatment to all those patients who were found to have thyroid dysfunctions. We also investigated the lipid profile, which may be the risk factor of obesity and CVD in Type 2 diabetic patients in Bangladesh. This was done by measuring the Total cholesterol, Triglyceride, HDL-cholesterol and LDL-cholesterol level of Type 2 diabetic patients.

MATERIALS AND METHODS

Study Site

The study was conducted at the Research Division of Bangladesh Institute of Research and Rehabilitation in Diabetes Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh, catering patients not only from the Dhaka but also from other parts of the country. Hence a population taken from these hospitals all over the country would be representative of most of the population in Bangladesh.

Target Population

Patients

A total number of 50 Type 2 diabetic patients, out of which 34 were male and 16 were female, attending the BIRDEM outpatient department were included in this study.

Controls

50 healthy age and sex matched volunteers without family history of thyroid disease and without diabetes up to second generation were taken as control, out of which 17 were female. Both groups were between the ages of 30-55 years. Thus the studied subjects consisted of the following groups:

Group I: Control subjects (n=50)
Group II: Type 2 subjects (n=50)

Sampling method

Random convenient sampling was done.

Sampling Frame and Sampling Process including Criteria for Subject Selection

Sample collection was done by convenient sampling in which the patients attending the respective departments were chosen as per convenience after taking proper informed consent.

Inclusion criteria

- Patients attending BIRDEM with history of diabetes or found to be diabetic on assessment at presentation.
- Patients admitted in the Medical wards in BIRDEM with history of diabetes or found to be diabetic on assessment at presentation.
- Patients who were between the age group of 30-55 years.
- Patients who were willing to participate in the study.
- Patients who gave informed consent.

Exclusion criteria

- Patients not willing to participate in the study.
- Patients who were below age 30.
- Patients who were on medication that are known to modify the thyroid functions e.g. lithium, amiodarone, etc.

- Patients who were already known to suffer from hypo/hyperthyroidism, were also excluded.
- Patients who had undergone surgery of the thyroid gland.
- Patients who had exposure to radiation of the thyroid gland.
- Patients of drug-induced hyperglycemia, e.g. high dose steroids, pentamidine, diazoxide, etc.

Laboratory Methods

Collection of blood samples

Each subject was requested to fast overnight prior to collection of blood. Clinical examination were done on a predefined morning and 6 ml blood sample was aseptically drawn from the antecubital vein of the subject under fasting condition by using 10 ml disposable syringe. For estimation of HbA1c, 1ml of blood aliquot was taken in a test tube containing EDTA and the resulting solution was mixed gently. The rest of the blood sample was taken in a separate test tube for preparation of serum.

Preservation of samples

Collected blood sample was allowed to clot and after 10 minutes serum was separated by centrifugation at 3000 rpm, for 5-10 minutes at room temperature. The separated serum was collected in eppendorf tube and then preserved at -40^{0}C for further biochemical analysis. The following laboratory investigations were done for each of the study subject:

Estimation of serum was performed using glucose by glucose-oxidase method, estimation of glycosylated Hemoglobin (HbA1c) by HPLC method, estimation of serum Triglycerides by enzymatic colorimetric method, estimation of serum cholesterol by enzymatic method (Cholesterol oxidase/Peroxidase method), estimation of serum high density lipoprotein (HDL) by enzymatic method, estimation of serum free T_3, free T_4, and TSH were determined by Abbott AXSYM System auto analyzer. Estimation of thyroid stimulating hormone (TSH), free T_3 (FT $_3$) and free T_4 (FT $_4$) were carried out by microparticle enzyme immunoassay (MEIA) method. Measuring of Anti-TPO antibody from the serum and anti-TG antibody from the serum was done IMMULITE 1000 Analyzers.

RESULTS AND DISCUSSION

Age and sex distribution of study population

This study was conducted on 100 subjects between the age group 30-55 years, in which 50 subjects with history of diabetes and/or positive clinical assessment of diabetes at the BIRDEM Hospital out-patient or in-patient departments and later confirmed as Type 2 Diabetes Mellitus (T2DM) patients through laboratory investigation of fasting blood glucose (FBG) levels were included. Another 50 healthy age and sex matched volunteers without family history of thyroid disease and without diabetes up to second generation and again confirmed through investigation of FBG levels were taken as control. The mean±SD age of the T2DM patients was 41.86±6.43 (range 30-55) years, while the mean±SD age of control was 41.54±7.88 (range 30-55) years. Out of 50 patients 34 (68%) were males and 16 (32%) were females. Among control subjects 32 (64%) were males and 18 (36%) were females (Table 1).

Table 1: Age and sex distribution of study population

Variables		Type 2 DM patients (n=50)	Controls (n=50)
Age	Years	30-55years	30-55years
	Mean±SD	41.86±6.43	41.54±7.88
Sex Distribution	Male	34 (68%)	32 (64%)
	Female	16 (32%)	18 (36%)

Glycemic status of the study subjects

FBG levels in the study subjects confirmed the patients as T2DM patients and healthy controls as non-diabetic

According to National Diabetes Data Group and the WHO, fasting plasma glucose is suitable for the diagnosis of diabetes mellitus [17]. We found a highly significant difference of FBG levels between the patients and control population (***p<0.001) with the FBG levels abnormally high (in the patients and normal in the control populations (13.34±2.52 *vs.* 4.45±0.53) (Figure 1). Thus, this data confirms that the patients belonged to the T2DM and the control population was non-diabetic. Data, in each case, were analyzed by Student's t-test using SPSS 11.5 version and results, in each case, were presented as mean±SD and a p-value <0.05 (*), or <0.01 (**) or <0.001 (***) was considered as significant.

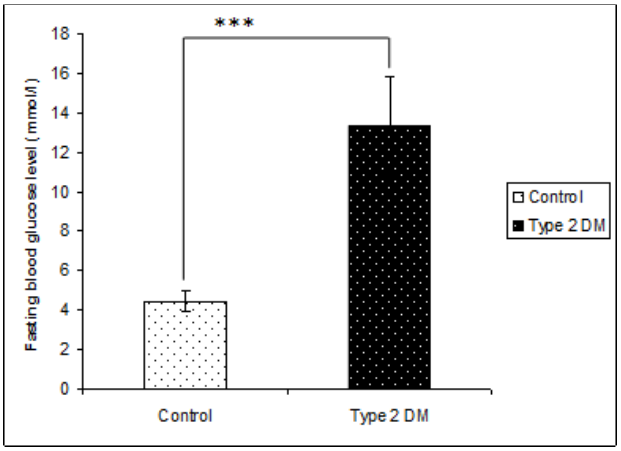

Fig. 1: Fasting blood glucose status in the study population

Abnormally high blood $HbA1_c$ levels in T2DM patients reflected that they had uncontrolled blood glucose levels

In diabetes with hyperglycemia, the increase in glycosylated hemoglobin is usually caused by an increase in $HbA1_c$. Determination of HbA_{1c} is an index of average blood sugar level for the 2-3 months period before the test. The major advantage of measuring glycosylated hemoglobin is that the specimen can be collected without regard to when the patient last ate. Glycosylated hemoglobin (HbA1c) test could be used for the diagnosis of uncontrolled diabetes mellitus [18, 19]. Diabetes affected individuals HbA1c levels highly correlated with adverse clinical outcomes (e.g., retinopathy) as were the case with fasting plasma glucose or postprandial plasma glucose levels and were as reproducible as fasting plasma glucose levels. In the present study, we found that blood levels of HbA1c in the T2DM patients were significantly higher than that of the non-diabetic control population with the HbA1c levels much higher than the normal level in the T2DM patients and normal (within the normal range) in the non-diabetic control population (13.15±1.81 *vs*. 4.49±0.644) (Figure 2).

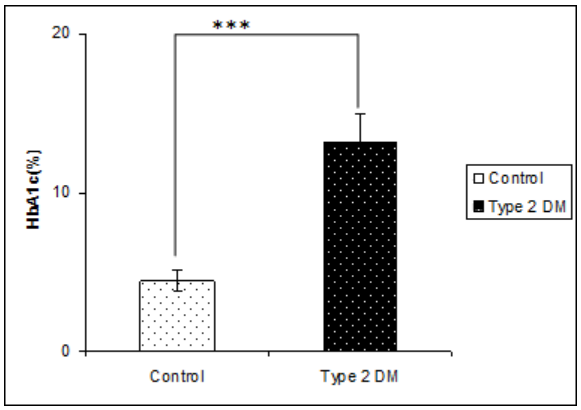

Fig. 2: HbA_{1c} (%) status in the study population

50 T2DM patients and 50 non-diabetic subjects were included in our study.

Thyroid function status of the study subjects

Normal levels of serum TSH were observed in T2DM patients

In the present study, we observed that serum mean TSH levels were within the normal range (0.47-5.01µIU/ml) in the T2DM patients. However, serum levels of TSH were significantly lower in T2DM patients than that of non-diabetic control population (1.22±0.74 *vs*. 1.74±1.07**)** (Figure 3).

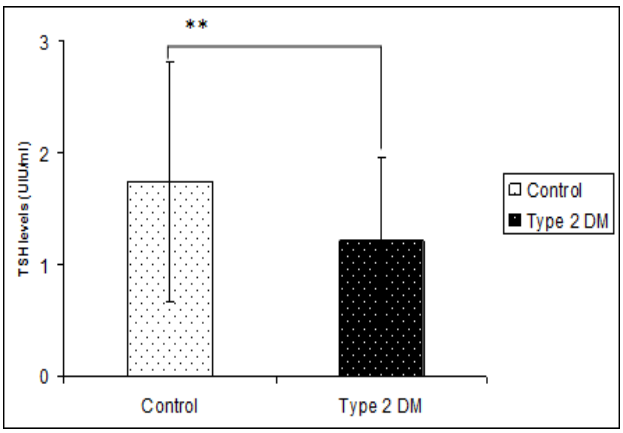

Fig. 3: Serum TSH levels of the study population

Low levels of serum Free T_3 (FT3) were observed in T2DM patients

We found that serum FT_3 was significantly lower in T2DM patients ($p<0.001$) than that of non-diabetic control group (0.99±0.24 *vs.* 2.74±0.75) as shown in Figure 4. This data showed that the levels of serum FT3 in T2DM patients were all much below the lower limit of the normal range.

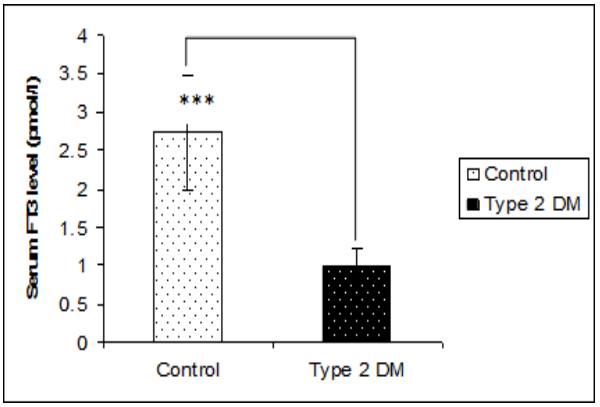

Fig. 4: Serum FT3 levels of the studied population

Normal levels of serum FT_4 were observed in the T2DM patients

When we examined the serum levels of FT4, we did not find any significant difference of FT_4 levels between T2DM patients and non-diabetic control population (15.42±2.90 *vs.* 15.61±2.98) (Figure 5). This data also revealed that serum FT4 levels in T2DM patients were within the normal range.

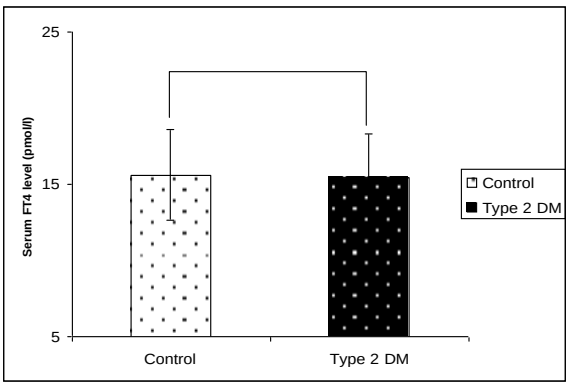

Figure 5 Serum FT_4 levels of the studied population

Normal levels of anti-TG and anti-TPO auto antibodies were found inT2DM patients

In the present study, we observed that both serum anti-TG and anti-TPO levels were within the normal range (<40 IU/ml and <35 IU/ml) in the T2DM patients. However, serum levels of anti-TG were significantly lower in T2DM patients than that of non-diabetic control population (33.44±5.25 *vs.* 35.64±4.00) (Figure 6). But we did not find any significant difference of anti-TPO levels between T2DM patients and non-diabetic control population (28.58±4.01 *vs.* 28.66±5.32) (Figure 7).

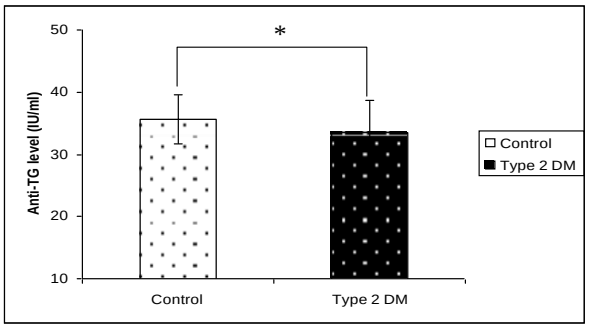

Fig. 6: Anti-TG status of the study population

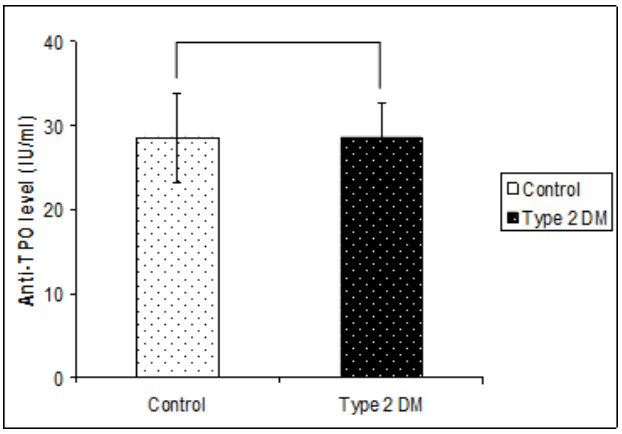

Fig. 7: Anti-TPO status of the study subjects

Correlation of serum FT3, FT4, TSH, Anti-TG, Anti-TPO with FBG and HbA1c in the study subjects

Irrespective of groups, either patients or control, fasting serum glucose (FBG) and HbA1c showed negative correlation with serum FT3 (FSG: r= -.789, p=.000; HbA1c: r= -.820; p=.000). Fasting serum glucose (FBG) and HbA1c also showed slight negative correlation with serum TSH (FSG: r=-.243, p=.015; HbA1c: r=-.278, p= 0.005).On the other hand, Anti-TG antibody showed slightly negative correlation with fasting blood glucose and HbA1c level, where in FBG: r=-.217, p=.030 and in HbA1c: r=-.243, p=.015.

Table 2: Correlation of serum FT3, FT4, TSH, Anti-TG, Anti-TPO with FBG and $HbA1_c$ in the study subjects

Group	$FreeT_3$		$Free\ T_4$		TSH		Anti-TG		Anti-TPO	
	R	p	r	P	r	P	r	p	r	P
FBG	-0.789**	0	-0.066	0.517	-0.243*	0.015	-0.217*	0.03	-0.056	0.577
$HbA1_c$	-0.820**	0	0.001	0.99	-0.278**	0.005	-0.243*	0.015	-0.018	0.856

**: Correlation is significant at the 0.01 level (2-tailed), *: Correlation is significant at the 0.05 level (2-tailed)

We examined the total cholesterol and HDL-cholesterol levels of both group, and from these we calculated the value of LDL-cholesterol with the help of following formula:

LDL-cholesterol (mg/dl) = Total cholesterol-Triglycerides/5 - HDL-cholesterol

Lipid profile of the study subjects

No significant difference was observed in triglyceride levels of both groups and both of them were in normal range (125.14±14.38 *vs.*125.68±17.23) (Table 3) whereas serum total cholesterol levels in T2DM patients were significantly higher than that of control (156.36±16.61 *vs.* 147.86±19.50) (Table 3). Again, serum HDL-cholesterol levels were significantly lower in Type 2 patients compared to normal (34.72±5.75 vs.40.62±4.78) and LDL-cholesterol were significantly higher in Type 2 diabetic patients when compared to control population (96.61±17.35 vs. 82.10±20.27) (Table 3).

Table 3: Lipid profile of the study subjects

Group	TG (mg/dl)	Cholesterol (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
Control (n=50)	125.68±17.23	147.86±19.50	40.62±4.78	82.10±20.27
T2DM (n=50)	125.14±14.38	156.36±16.61*	34.72±5.75***	96.61±17.35***

Regarding the levels of $HbA1_c$, we found that abnormally high blood $HbA1_c$ level in T2DM patients than that of the non-diabetic control population with the $HbA1_c$ levels in T2DM patients much higher above the normal upper limit and normal (within the normal range) in the non-diabetic control population (13.15±1.81 *vs*. 4.49±0.644), which clearly concluded that all of the T2DM patients were in uncontrolled disease condition. People with diabetes experience thyroid disorders more frequently than the general population [7]. Researchers have found that significant changes occur in serum T3, T4 and TSH levels in diabetic patients with the changes in blood glucose levels. But the total T3 and T4 may vary with the change in thyroid binding proteins (TBP) or presence of drugs that modify the total T3 and T4 but not the amount of free hormone. Our data showed serum mean TSH levels were within the normal range (0.47-5.01µIU/ml) in the T2DM patients although the values were significantly lower in T2DM patients than that of non-diabetic control population (1.22±0.74 *vs*. 1.74±1.07**)**. But when we examined the serum levels of FT4, we did not find any significant difference of FT_4 levels between T2DM patients and non-diabetic control population (15.42±2.90 *vs.* 15.61±2.98). This data also revealed that serum FT4 levels in T2DM patients were within the normal range. Then we examined the serum levels of FT3 in the study population. We found that serum FT3 levels were significantly lower in T2DM patients ($p<0.001$) than that of non-diabetic control group (0.99±0.24 *vs.* 2.74±0.75). This data showed that the levels of serum FT3 in T2DM patients were all much below the lower limit of the normal range. With this end we could say that the T2DM populations of our study were all suffering from low FT_3 syndrome. According to UM Kabadi *et al*. [14] in their study the serum TSH level was normal and mean serum T_3 became significantly low. He also postulated that serum FT_4 were normal in this condition and he designates the condition as "low FT_3 syndrome". These results are consistent with those reported in some other studies [20, 21].

One of the major aims of the present study was to find the association of low FT_3 with the thyroid auto antibodies like anti-TG and anti-TPO. In T1DM patients, thyroid dysfunctions may be due to underlying genetic cause. Researchers in Jordan have found that both anti-TPO and anti-TG autoantibody are positive in T2DM patients with sub clinical hypothyroidism when compared with control. But in our present study, subjects were suffering from low FT_3 syndrome not from sub clinical hypothyroidism. Our data clearly showed that both serum levels of anti-TG and anti-TPO autoantibodies were within the normal range (<40 IU/ml and <35 IU/ml respectively) in the T2DM patients. Although serum levels of anti-TG were significantly lower in T2DM patients than that of non-diabetic control population (33.44±5.25 *vs*. 35.64±4.00), we did not find any significant differences of anti-TPO levels between T2DM patients and non-diabetic control population (28.58±4.01 *vs.* 28.66±5.32). So, it reveals that in our population autoimmunity doesn't seem to be the major factor in the development of low FT_3 syndrome.

A significantly negative correlation was found between fasting blood glucose and serum T_3 levels [13, 22]. To explore the association of lowered FT3 with the increase of diabetes disease condition, correlation of thyroid hormones were done with FBG and HbA1c. A highly significant negative correlation of FT3 with FBG and HbA1c were found (r=-0.789**, p=0.000 and r=-0.820**, p=0.000 respectively) irrespective of the groups. These observations indicated that uncontrolled hyperglycemia may contribute to the development of low FT3 syndrome in T2DM patients in our study population [23]. In our study, we did not observe any significant difference in the TG levels between the T2DM patients and non-diabetic control population and levels of TG in both the groups were within the normal range (125.14±14.38 *vs.*125.68±17.23). We also found that all of our T2DM patients had normal levels of total-cholesterol (156.36±16.61 *vs.* 147.86±19.50), LDL-cholesterol (96.61±17.35 *vs.* 82.10±20.27) and HDL-Cholesterol (34.72±5.75 *vs*.40.62±4.78), although total-cholesterol and LDL-cholesterol level was significantly higher in T2DM patients and HDL-Cholesterol were significantly lower when compared to control. Most studies show that patients with type 2 diabetes have more triglyceride, less HDL cholesterol and an excess of small, dense LDL particles than non-diabetics [24, 25]. Our study revealed that lipid profile of T2DM patients in Bangladesh was not within the risk range for obesity and CVD adding further risks to them. However, the population size of the present study was small and more studies with a large population size of T2DM patients would be required to make a clear cut conclusion regarding the risk of obesity and CVD for T2DM in Bangladesh. Eventually, we can conclude that we observed the co-occurrence of low FT_3 syndrome may in T2DM patients in Bangladesh and thyroid

autoimmunity may not contribute to this development of low FT_3 syndrome. Finally, the lowering of FT_3 in diabetic subjects seems to be related with their degree of hyperglycemia. Further studies on a large scale population of T2DM patients in Bangladesh will be required to clearly explain their general pattern of thyroid dysfunction.

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