

A Comparative Study of Thyroid Hormone and Lipid Status of Patient with and without Diabetes in Adults

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ABSTRACT

Introduction: Lipid and thyroid function abnormalities are common in IDDM and NIDDM. Very few studies have addressed this issue in Bangladesh though Bangladeshi population is very much susceptible to patient with diabetes. **Aims:** To study on lipid profile and thyroid function in IDDM and NIDDM and the effect of glycemic control on it. **Patients and Methods:** This was a retrospective study carried out in the Dept. of Endocrinology, BIRDEM, Dhaka, Bangladesh during the period of January, 2012 to May, 2012. In this study, population consisted of 120 subjects (Age between 40 - 72 years; and Sex matched) divided into two groups: patient with diabetes 60 subjects (male-30, female-30) and patient without diabetes 60 subjects (male-30, female-30). Plasma glucose, HbA1c and serum lipids were measured by enzymatic method. Thyroid hormones were measured by a Chemiluminescent Micro particle Immunoassay (CMIA). **Results:** The statistical significance was evaluated by Student's t-test, Correlation-Coefficient test. All Values are given as mean \pm SD. The level of serum TSH in patient with diabetes (3.43 ± 2.71) was significantly ($p < 0.05$) increased compared to patient without diabetes subjects (1.98 ± 1.72). TSH levels were positively correlated with fasting plasma glucose ($r = 0.240$, $p < 0.05$), serum cholesterol ($r = 0.290$, $p < 0.020$) and triglyceride concentration ($r = 0.246$, $p < 0.05$). On the other hand, free T₄ levels were inversely correlated with postprandial blood glucose ($r = -0.256$, $p < 0.046$). **Conclusions:** It may be concluded that the lipid and thyroid function abnormalities with others socio-demographic and biophysical risk factors were more common in patient with diabetes cases rather than patient without diabetes cases. Therefore, further prospective studies with larger number of patients are required to strengthen the observations of the present study.

Keywords: NIDDM; IDDM; Glycosylated Hemoglobin; Lipid Profile; Hypo and Hyperthyroidism

1. Introduction

Hypothyroidism and hyperthyroidism are common causes of secondary dyslipidemia [1]. This observation is partly related to the hyperlipidemia known to be present in patients with both primary and secondary hypothyroidism [2]. Several cross-sectional studies have reported increased levels of total cholesterol and low-density lipoprotein (LDL) cholesterol in adults with sub clinical hypothyroidism compared with euthyroid controls [3]. In adults, increasing levels of TSH to be associated with increases in total cholesterol, LDL cholesterol and tri-

glycerides and with decreases in HDL cholesterol [4-6]. In healthy euthyroid adults, both serum TSH and the free T₄ value have been found to be positively associated with fasting and post load insulin concentrations and negatively associated with insulin sensitivity [7]. The present investigation is an attempt to study how patient with diabetes affects thyroid function and lipid metabolism in euthyroid individuals and conversely how thyroid diseases could affect glycemic control. Thyroid function is affected in patient with diabetes. Hypothyroidism among patient with diabetes has been frequently encountered [8,9]. The major disorders of thyroid gland are hyperthyroidism and hypothyroidism, which have been re-

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ported in over 110 countries of the world with 1.6 billion people at risk [10,11]. Defects in carbohydrate metabolizing machinery and consistent efforts of the physiological system to correct the imbalance in carbohydrate metabolism place an overexertion on the endocrine system. Continuing deterioration of endocrine control exacerbates the metabolic disturbances and leads primarily to hyperglycemia [12,13]. The adoption of a sedentary lifestyle, the consumption of non-traditional foods, and a genetic predisposition to the disease are thought to be the major underlying causes of the epidemic [14]. The influence of endocrine and non-endocrine organs other than the pancreas on NIDDM is documented. Occasionally, other endocrine disorders such as abnormal thyroid hormone levels are found in diabetes [15]. There is evidence from animal studies that the function of the thyroid gland itself may be altered in diabetes mellitus [16]. T_3 production from peripheral T_4 mono-denomination is impaired in uncontrolled diabetes mellitus and this impairment is correlated with the impairment of glucose utilization. Similar findings were later observed in another investigation by them on September 1979 and they emphasized that glucose uptake and utilization were important in the regulation of thyroid hormone metabolism by assessing thyroid hormone turn over in diabetic patient [17]. In untreated insulin requiring diabetic patients TSH remained suppressed and T_3 and T_4 remained low. Measurement of T_3 and T_4 are therefore not reliable indicator of thyroid status in the untreated insulin requiring patient with diabetes [18]. Regulation of TSH secretion is altered in NIDDM during decompensate state and normalizes when euglycemia achieved [19,20]. Concentration of free rather than total plasma hormones and other workers have observed that in contrast to free T_3 , free T_4 may be normal or even elevated in other non thyroidal diseases [21, 22].

2. Materials and Methods

This was a prospective study carried out in the dept. of Endocrinology, BIRDEM (Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine and Metabolic Disorders)-WHO collaborating center for prevention and control of diabetes. Dhaka, Bangladesh during the period of January, 2012 to May, 2012. In this study population consisted of 120 subjects (Age between 40 - 72 years; and Sex matched) divided into two groups: patient with diabetes 60 subjects (male-30, female-30) and patient without diabetes 60 subjects (male-30, female-30). General health characteristics such as Age, Sex, Smoking status, Family status, Family history, Treatment status and Biophysical characteristics (particularly as related to preference) were investigated by a self-administered questionnaire. All the patients in the patient with

diabetes group were confirmed diabetes who previously had fasting plasma glucose levels and plasma glucose at 2 hours of OGTT/After breakfast >7.0 mmol/L and >11.0 mmol/L, HbA1c $> 6.0\%$ and who were receiving treatment such as insulin, Diet, anti-diabetic drug or physical exercise therapy for NIDDM. In addition, none of the subjects had a history of previous thyroid disease.

Laboratory Procedure

Consent was taken for each subject and they were requested to fast overnight. Blood samples were collected by venepuncture from patients. The samples were allowed to clot and the Serum separated by centrifugation at 10,000 rpm for 15 minutes at room temperature. Serum samples were stored at -20°C until tested. Blood samples were treated as follows: For Free T_4 , TSH and lipid estimation 4 ml of blood was taken in a plain test tube and was separated by centrifugation. For glucose estimation 1 ml of blood was placed in a tube containing fluoride. For estimation of HbA1c 1 ml of blood was taken in a separate test tube containing EDTA. The plasma was separated and analyzed within a few hours of collection. Plasma glucose and serum lipids (triglyceride, total cholesterol and HDL cholesterol) were measured in the BIRDEM Biochemistry laboratory, Dhaka by enzymatic method and mentioned briefly. The LDL cholesterol was calculated from observed triglyceride, total cholesterol and HDL cholesterol by using Friedwald's formula (If triglyceride result is below 400 mg/dL). If triglyceride result is upon 400 mg/dL used direct LDL-C measurement method follow. The normal value of serum FT4 = (11.0 - 24.0) pmol/L and TSH = (0.40 - 5.0) IU/mL. Desirable levels of blood fats are: total cholesterol; below 200 mg/dL, HDL cholesterol; Men: above 40 mg/dL, Women: above 50 mg/dL. LDL cholesterol below 100 mg/dL.

3. Result

Information about the demographic characteristics of the study population was shown in **Table 1**. The mean Age of patient with diabetes subjects were $(43.70 \pm 11.17^{\text{NS}}$ years) where as patient without diabetes subjects were $(38.61 \pm 13.30$ years) (**Figure 1**). Body mass index were significantly ($p < 0.001$) increased in patient with diabetes subjects $(27.96 \pm 4.35 \text{ kg/m}^2)$ compared with that of patient without diabetes subjects $(23.97 \pm 3.01 \text{ kg/m}^2)$ (**Figure 2**). We observed that the markedly elevated hypertensive patients in patient with diabetes subjects 22 (36.67%), whereas the patient without diabetes subjects were 6 (10%). Exsmoker were markedly elevated in patient with diabetes subjects 7 (11.67%) compared with that of patient without diabetes subjects 4 (6.67%).

Table 2 shows the levels of various biochemical pa-

Table 1. Comparison of demographic characteristics of patient without diabetes and patient with diabetes subjects.

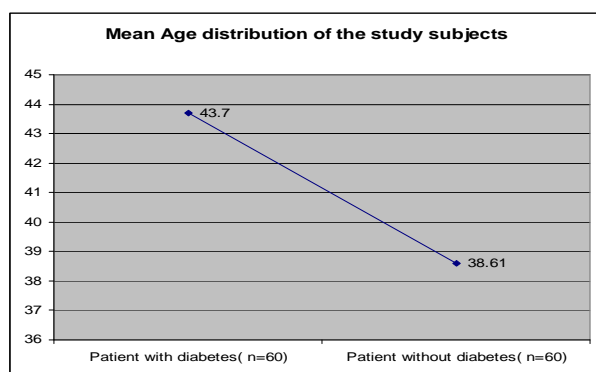
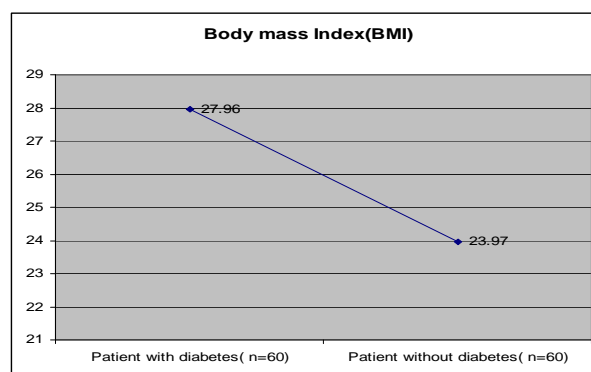
Parameter	Patient without diabetes subjects (n = 60)	Patient with diabetes subjects (n = 60)
Age (years)	38.61 ± 13.30	43.70 ± 11.17 ^{NS}
Sex: male	50%	50%
Female	50%	50%
EX-smoker	4 (6.67%)	7 (11.67%)
Current smoker	6 (10%)	3 (5%)
Non smoker	50 (83.33%)	46 (83.33%)
Tobacco leaf	6 (10%)	6 (10%)*
Hypertension	6 (10%)	22 (36.67%)*
Diabetes mellitus	0 (0%)	60 (100%)
Body mass index (kg/m ²)	23.97 ± 3.01	27.96 ± 4.35***

The statistical significance was evaluated by Student's t-test (paired sample t test). Values are given as mean ± SD from 60 subjects in patient without diabetes and patient with diabetes subjects. Patient without diabetes subject compared with patient with diabetes subjects, *p < 0.05, **p < 0.01, ***p < 0.001, ^{NS}Not significant.

Table 2. Comparison of biochemical changes in patient without diabetes and patient with diabetes subjects.

Parameter	Patient without diabetes subjects (n = 60)	Patient with diabetes subjects (n = 60)
Blood glucose fasting (mmol/L)	5.16 ± 0.80	8.24 ± 2.58***
Postprandial plasma glucose (mmol/L)	6.51 ± 0.95	12.86 ± 5.25***
HbA1c (%)	5.43 ± 0.39	9.27 ± 3.53***
Total cholesterol (mg/dl)	178.70 ± 33.81	199.45 ± 51.34**
Triglyceride (mg/dl)	155.35 ± 61.15	195.01 ± 52.40*
HDL-C (mg/dl)	39.46 ± 6.88	35.11 ± 7.71*
LDL-C (mg/dl)	106.71 ± 23.95	124.25 ± 38.54*
TSH (μIU/ml)	1.98 ± 1.72	3.43 ± 2.71*
FT ₄ (Pmol/L)	15.27 ± 6.68	16.78 ± 8.73 ^{NS}

The statistical significance was evaluated by Student's t-test (paired sample t test). Values are given as mean ± SD from 60 subjects in patient without diabetes and patient with diabetes subjects. Patient without diabetes subject compared with patient with diabetes subjects, *p < 0.05, **p < 0.01, ***p < 0.001, ^{NS}Not significant.

**Figure 1. Mean age of the study subjects (patient with diabetes and patient without diabetes).****Figure 2. Mean body mass index (BMI) of the study subjects (patient with diabetes and patient without diabetes).**

rameters in patient with diabetes and patient without diabetes subjects. Fasting plasma glucose (FPG) and post-

prandial (PPG) level, HbA1c, serum triglyceride, total cholesterol, LDL-C were significantly increased in pa-

tient with diabetes subjects FPG (8.24 ± 2.58 , $p < 0.001$), PPG (12.86 ± 5.25 , $p < 0.001$), HbA1c (9.27 ± 3.53 , $p < 0.001$), total cholesterol (199.45 ± 51.34 , $p < 0.01$), triglyceride (195.01 ± 52.40 , $p < 0.05$), LDL (124.25 ± 38.54 , $p < 0.05$) compared with that of patient without diabetes subjects (5.16 ± 0.80 , 6.51 ± 0.95 , 5.43 ± 0.39 , 155.35 ± 61.15 , 178.70 ± 33.81 , 106.71 ± 23.95) respectively, and HDL-C levels were significantly ($p < 0.05$) decreased in patient with diabetes subjects (35.11 ± 7.71 , $p < 0.05$) when compared with that of patient without diabetes subjects (39.46 ± 6.88).

Table 2 illustrates the levels of serum thyroid hormones in patient with diabetes and patient without diabetes subjects. The level of serum TSH was increased significantly ($p < 0.05$) in patient with diabetes subjects (3.43 ± 2.71) compared with that of patient without diabetes subjects (1.98 ± 1.72) (**Figure 3**). But FT₄ did not differ significantly in patient with diabetes subjects (16.78 ± 8.73) compared with that of patient without diabetes subjects (15.27 ± 6.68).

Table 3 shows the distribution of patient with diabetes and patient without diabetes subjects with high, low, and euthyroid thyroid hormone levels. Total 60 patient with diabetes subjects studied, among them 10 (16.67%) were thyroid dysfunction, whereas 2 (3.33%) were sub clinical hypothyroidism, 4 (6.67%) were overt hypothyroidism, 3 (5%) were sub clinical hyperthyroidism and 1 (1.67%) was overt hyperthyroidism. The prevalence rate of thyroid dysfunction was significantly ($p < 0.05$) higher in patient with diabetes subjects 10 (16.67%) than in patient without diabetes subjects 7 (11.66%) (**Figure 4**).

Table 4 shows, serum TSH values were positively correlated with triglyceride ($r = 0.240$, $p < 0.05$) and total cholesterol ($r = 0.290$, $p < 0.020$). On the other hand, free T₄ values were inversely correlated with postprandial plasma glucose ($r = -0.259$, $p < 0.046$), total cholesterol ($r = -0.316$, $p < 0.011$) and HDL-C ($r = -0.329$, $p < 0.051$).

Table 5 shows, the total 120 subjects (patient with diabetes = 60 and patient without diabetes = 60) studied among them secondary dyslipidemia were in patient with diabetes cases 6.66% and in patient without diabetes cases 1.66%. So it was clear that the prevalence rate of secondary dyslipidemia was significantly higher in patient with diabetes subjects 5 (8.33%, $p < 0.05$) than in patient without diabetes subjects 1 (1.66%) (**Figure 5**).

4. Discussion

Diabetes mellitus is an important health problem affecting major populations worldwide. It is found that diabetic mellitus may be associated with altered thyroid functions. But this phenomenon has been observed mainly in IDDM and NIDDM patients. In Bangladesh a substantial

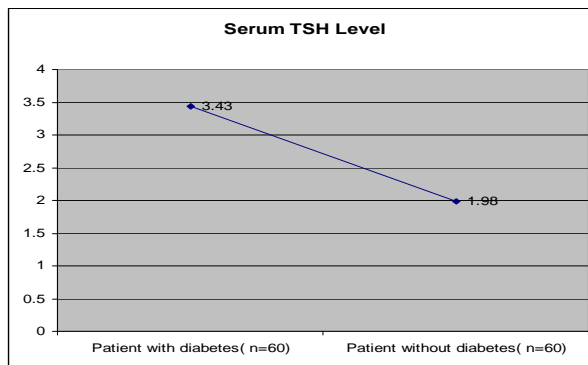


Figure 3. Comparison of thyroid dysfunction of the study subjects (patient with diabetes and patient without diabetes).

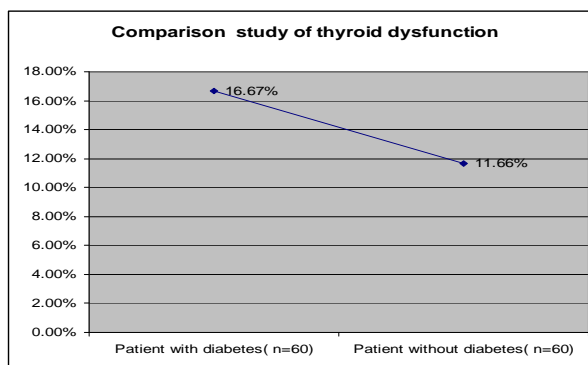


Figure 4. Comparison of thyroid dysfunction of the study subjects (patient with diabetes and patient with diabetes).

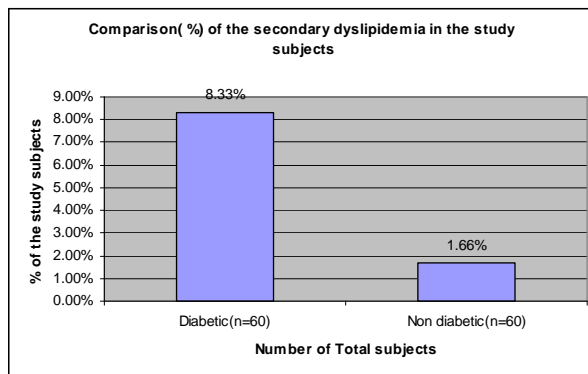


Figure 5. Comparison study of the secondary dyslipidemia of study subjects (diabetic and non diabetic).

number of young patient with diabetes do not show typical characteristics of either IDDM or NIDDM. Three studies have previously been performed at BIRDEM on thyroid functions and alteration of their thyroid function has been found. For a more conclusive comment the better indicators of thyroid dysfunction, free T₃, free T₄ are necessary. It is also important to explore the thyroid autoimmunity and morphological changes for better understanding of thyroid dysfunction in these subjects. The

Table 3. The distribution of subjects with high, low, or euthyroid thyroid hormone levels in patient without diabetes and patient with diabetes subjects.

Dysfunction	Patient without diabetes subjects (n = 60)			Patient with diabetes patients (n = 60)		
	Total	Male	Female	Total	Male	Female
Sub clinical hypothyroidism	0 (0%)	0 (0%)	0 (0%)	2 (3.33%)	0 (0%)	2 (3.33%)
Overt hypothyroidism	4 (6.66%)	3 (5%)	1 (1.66%)	4 (6.67%)	0 (0%)	4 (6.67%)*
Sub clinical hyperthyroidism	1 (1.66%)	0 (0%)	1 (1.66%)	3 (5%)	2 (3.33%)	1 (1.67%)
Overt hyperthyroidism	2 (3.33%)	2 (3.33%)	0 (0%)	1 (1.67%)	1 (1.67%)	0 (0%)
Total	7 (11.66%)	5 (8.33%)	2 (3.33%)	10 (16.67%)	3 (5%)	7 (11.67%)

n = number of individuals. The statistical significance was evaluated by Student's t-test (paired sample t test). Values are given as mean \pm SD from 60 subjects in patient without diabetes and patient with diabetes subjects. Patient without diabetes subject compared with patient with diabetes subjects, *p < 0.05, **p < 0.01, ***p < 0.001, ^{NS}Not significant).

Table 4. Correlation of serum FT₄, TSH with cholesterol, triglyceride, HDL, LDL, Fasting blood glucose, postprandial plasma glucose (PPG) and HbA1c in the study subjects (patients with diabetes individuals).

Parameter	FT ₄		TSH	
	r	p	r	p
FBS	-0.171	0.179	0.240*	0.05
PPG	-0.256*	0.046	0.130	0.359
HbA1c	0.046	0.760	0.064	0.640
Cholesterol	-0.316**	0.011	0.290*	0.020
Triglyceride	-0.229	0.06	0.246*	0.05
HDL	-0.329*	0.051	0.091	0.459
LDL	-0.190	0.138	0.205	0.101

The statistical significance was evaluated by Student's t-test (paired sample t test). Values are given as mean \pm SD from 60 subjects in patient without diabetes and patient with diabetes subjects. Patient without diabetes subject compared with patient with diabetes subjects, *p < 0.05, **p < 0.01, ***p < 0.001, ^{NS}Not significant.

Table 5. According to the distribution of subjects with high and low level of lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol and triglyceride), in patient without diabetes and patient with diabetes subjects.

Dysfunction	Study group					
	Patient without diabetes subjects (n = 60)			Patient with diabetes subjects (n = 60)		
	Total	Male	Female	Total	Male	Female
Secondary dyslipidemia	1 (1.66%)	0 (0%)	1 (1.66%)	5 (8.33%)	3 (5%)	2 (3.33%)
Total (%)	1 (1.66%)	0 (0%)	1 (1.66%)	5 (8.33%)	3 (5%)	2 (3.33%)

n = number of individuals; % = number of percentage.

presence of both high and low levels of thyroid hormones in diabetics in this study may also be due to modified TRH synthesis and release and may depend on the glycaemic status of the with diabetes studied. Glycaemic status is influenced by insulin, which is known to modulate TRH and TSH levels [23]. This finding is probably associated with the higher prevalence of obesity recorded in female patient with diabetes. In theory, treating patient

with diabetes should be simple: just prevent hyperglycemia from hypoglycemia to cause coma. In practice, it does not work that way. Glucose fluctuations occur all the time. One way to assess the mean levels is to monitor the HbA1c, which gives the average blood glucose level of the preceding 2 - 3 months. In uncontrolled or poorly controlled diabetes there is an increased glycosylation of a number of proteins, including hemoglobin and α -crys-

talline of the lenses. HbA1c was found to increase in patients with diabetes to approximately 16%, and the amount of increase was directly proportional to the fasting blood glucose level. During patient with diabetes, the excess glucose present in blood reacts with hemoglobin [24,25]. In the present study, we noticed a marked increase in HbA1c levels in diabetic patients, which could be due to excessive glycosylation of hemoglobin [26].

5. Conclusion

In Comparison of demographic characteristics of without diabetes and with diabetes subjects we found that age, BMI, Hypertension and smoking habit were significantly higher with diabetes cases than without diabetes cases. Serum TSH levels were significantly elevated with diabetes cases when compared to the without diabetes cases. With diabetes cases, increases the level of serum total cholesterol, triglyceride and LDL-cholesterol and decreases in HDL cholesterol levels were significantly higher than without diabetes cases. So, finally our findings demonstrate that detection of abnormal thyroid hormone levels in addition to other biochemical variables (lipid profile) in the early stage of diabetes will help patients improve their health and reduce their morbidity rate.

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