A COMPARATIVE STUDY OF THYROID HORMONE LEVELS IN DIABETIC AND NON-DIABETIC PATIENTS

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Abstract. Diabetic patients have a higher prevalence of thyroid disorders than the general population, this may influence diabetic management. In this study, we investigated thyroid hormone levels in uncontrolled diabetic patients. This comparative study was conducted at the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM). Fifty-two diabetic patients were consecutively selected from diabetic patients attending the out-patient department of BIRDEM. Fifty control subjects were selected from non-diabetic patients who attended the out-patient department of BIRDEM for routine check-ups as advised by their attending physicians. The subjects in both groups were above 30 years of age. The concentration of thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and thyroxine (FT4) were evaluated using a Microparticle Enzyme Immunoassay (MEIA) procedure. Patients with type 2 diabetes had significantly lower serum FT3 levels (p=0.000) compared to the control groups. There were no significant differences observed in serum FT4 (p=0.339) and TSH (p=0.216) levels between the control and study subjects. All the diabetic patients had high fasting blood glucose levels (12.15±2.12). We conclude that FT3 levels were altered in these study patients with uncontrolled diabetes.

INTRODUCTION

Thyroid disease is common in the general population and the prevalence increases with age (Hegedus *et al,* 1983). Hypothyroidism is the most common thyroid disorder in the adult population, especially in older women. It is usually autoimmune in origin, presenting as either primary atrophic hypothyroidism or Hashimoto's thyroiditis (Kamel, 1999).

In types 1 and 2 diabetes, the metabolism of foodstuff is altered (Briscoe *et al,* 2006). Lack of insulin or insulin resistance prevents the efficient uptake and utilization of glucose by most cells of the body, except those of the brain. As a result, blood glucose concentration increases, cell utilization of glucose decreases and utilization of fats and proteins increases (Briscoe *et al,* 2006; Guyton and Hall, 2006).

Diabetes patients have a higher prevalence of thyroid disorders than the normal population (Wu, 2000). Thyroid disease is found in both types 1 and 2 diabetes. People with type 1 diabetes and underlying autoimmune disease may have associated thyroid disease (Johnson, 2006). Since thyroid hormones regulate metabolism and diabetes can alter metabolism of foodstuff, the metabolism of the organism may be further affected by the combination of thyroid disease and diabetes (Bernal and Refeloff, 1977; Notarbartolo

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et al, 1983; Wu, 2000). The association between thyroid dysfunction and poor glycemic control in diabetic patients is not known. We carried out this study in order to evaluate the magnitude of the problem of thyroid dysfunction in diabetic patients.

MATERIALS AND METHODS

This study was conducted at the out-patient department of Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders (BIRDEM). Fifty-two patients with uncontrolled type 2 diabetes were chosen consecutively and included in this study. All patients in the study were between 40 and 50 years of age. All had high fasting blood sugar levels. The patients were receiving either oral hypoglycemic agents or insulin according to the severity of the disease. Fifty age matched non-diabetic subjects who came in the hospital for routine check-ups as advised by their attending physicians were included as controls in this study. The controls were not taking any drugs. The study was carried out from May 2006 to June 2007.

Most study subjects came from Dhaka District and attended the out-patient department (OPD) of BIRDEM. The study was approved by the Ethics Committee of BIRDEM. Informed verbal consent was obtained from each study subject before being enrolled in the study. Blood samples were collected from the patients and sent to the biochemical laboratory of BIRDEM for analysis. A standard medical history was obtained from each subject and a physical examination was performed by an on duty nurse. The TSH, FT3 and FT4 levels for the preserved serum samples were measured using the Abbott AxSYM System (Abbott AxSYM, Abbott Laboratories Diagnostics Division, IL). Blood glucose levels were also measured.

Statistical analysis

Data were analyzed using SPSS for windows version 10 (SPSS, Chicago, IL). Demographic data, such as age, body weight, and BMI, were compared using the Student's *t*-test; categorical variables, such as sex, were compared using the chi-square test. The thyroid hormone levels (TSH, FT3, FT4) were compared using the Student's *t*-test.

RESULTS

Of the total of 102 subjects who participated in the study, 52 were patients and 50 were controls. Baseline characteristics are shown in Table 1. All the characteristics, such as age and sex, were comparable between the groups (study subjects and controls) except for height and weight. The reason for the differences in heights and weights cannot be explained.

The different hormone levels are presented in Table 2. The mean serum levels for FT4 and TSH were similar between the two groups. However, the average FT3 level was significantly lower in the patient group than in the control group (p=0.000). The mean serum ratio of FT3/FT4 was significantly lower in the patient group than in the control group (p=0.000).

DISCUSSION

The results of this study show that the mean serum FT3 in patients was significantly lower than controls (1.48 pmol/l). However, the FT4 and TSH levels were not significantly different between the patient and control group, which indicates euthyroidism in the diabetic patients.

Altered thyroid hormone levels have been previously reported in insulin-requiring diabetic patients before and after treatment (Saunders *et al,* 1978) where mean plasma T4 and T3 levels were significantly different between untreated diabetics and normal control subjects. Following insulin treatment, T3 and T4 levels

rose in these patients. In our study non-insulin dependent diabetic patients had lower serum T3 levels but normal T4 and TSH levels. Diabetic control was not assessed by the percentage of glycosylated hemoglobin (HbA1c) in our study, therefore we could not show any correlation between diabetes control and thyroid hormones levels. However, our patients had high fasting glucose levels, which indicates poor glycemic control in these subjects. The measurement of thyroid antibodies and glycosylated hemoglobin levels would have been helpful in interpreting the results but this could not be done for this study.

Although we could not measure the reverse T3 (rT3) level, previous reports have shown that rT3 and FT3 levels may be altered by other conditions (Eftekhari *et al,* 2006; Zoccali *et al,* 2006; Pinelli *et al,* 2007). A study by Saunders *et al* (1978) also showed a significantly higher T4:T3 ratio in patients when compared with normal controls. Our study also showed a significantly different T3:T4 ratio between patients and controls.

Another study showed that in both diabetic groups (IDDM and NIDDM) T3 levels may be lower, with a corresponding rise in the rT3 level and a normal T4 level, which may be related to the uncontrolled diabetic conditions found in our diabetic patients (Schlienger *et al,* 1982). Our study corroborates the findings of Schlienger *et al* (1982) who showed a significant decrease in T3 levels in NIDDM patients. Our study patients had poor diabetic control as evidenced by high random blood glucose levels.

Table 1
Baseline characteristics of study subjects.

Baseline characteristics	Control	Patients	p-value
Age (years)	45.50±3.14	43.19±8.87	0.085
Sex: Male	40	18	
Female	10	34	
Height (cm)	163.88±8.64	154.96±8.43	0.000
Weight (kg)	58.86±8.97	51.71±12.90	0.002
BMI (kg/m^2)	21.90±2.73	21.57±5.08	0.677
FBG (mmol/l)	5.31±0.44	12.15±2.12	0.000

FBG=fasting blood glucose; All values are in mean ± SD

Table 2
Comparison of hormone levels between patient and control groups.

Variable	Patients (*N*=52)	Controls (*N*=50)	p-value
TSH (µlU/ml)	1.7 ± 1.12	1.47 ± 0.78	0.216
FT3 (pmol/l)	1.48 ± 0.41	2.77 ± 0.76	0.000
FT4 (pmol/l)	13.67 ± 2.98	13.14 ± 2.54	0.339
Ratio FT3/FT4	0.11 ± 3.9	0.22 ±7.9	0.000

Normal range for FT4 is 9.14-23.81 pmol/l, FT3 is 2.23-6.43 pmol/l, TSH is 0.47-4.64 µlU/ml; All values are in mean ± SD

We conclude that alteration of thyroid hormones is a common feature in uncontrolled diabetic patients. Glycemic control is important for the management of diabetes. Further study is needed to compare thyroid hormone levels and thyroid antibodies in controlled and uncontrolled diabetic patients. Glycosylated hemoglobin levels would need to be measured to evaluate the level of control of diabetes. A reverse T3 level should also be determined to further evaluate the degree of thyroid abnormalities in the study and control groups.

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REFERENCES

Bernal J, Refetoff S. The action of thyroid hormone. *Clin Endocrinol* 1977; 6: 227-49.

Briscoe VJ, Davis SN. Hypoglycemia in type 1 and type 2 diabetes: physiology, pathophysiology, and management. *Clin Diabetes* 2006; 24: 115-21.

Eftekhari MH, Keshavarz SA, Jalali M, Elguero E, Eshraghian MR, Simondon KB. The relationship between iron status and thyroid hormone concentration in iron-deficient adolescent Iranian girls. *Asia Pac J Clin Nutr* 2006; 15: 50-5.

Guyton AC, Hall JE. Textbook of medical physiology. 11th ed. New Delhi: Elsevier, 2006: 972-7.

Hegedus L, Perrild H, Poulsen LR, *et al*. The determination of thyroid volume by ultrasound and its relationship to body weight, age, and sex in normal subjects. *J Clin Endocrinol Metab* 1983; 56: 260-3.

Johnson JL. Diabetes control in thyroid disease. *Diabetes Spect* 2006; 19: 148-53.

Kamel HK. Hypothyroidism in the elderly. *Clin Geriatr* 1999; 7: 1070-389.

Notarbartolo A, Rini G, Licata G, *et al*. Correlation between different degree and duration of metabolic control and thyroid hormone levels in type 1 and type 2 diabetics. *Acta Diabetol* 1983; 20: 341-6.

Pinelli M, Bindi M, Cassetti G, *et al*. Relationship between low T3 syndrome and NT-proBNP levels in non-cardiac patients. *Acta Cardiol* 2007; 62: 19-24.

Saunders J, Hall SHE, Sonksen PH. Thyroid hormones in insulin requiring diabetes before and after treatment. *Diabetologia* 1978; 15: 29-32.

Schlienger JL, Anceau A, Ghabrier G, North ML, Stephan F. Effect of diabetic control on the level of circulating thyroid hormones. *Diabetologia* 1982; 22: 486-8.

Wu P. Thyroid disease and diabetes. *Clin Diabetes* 2000; 18: 38.

Zoccali C, Benedetto F, Mallamaci F, *et al*. Low triiodothyronine and cardiomyopathy in patients with end-stage renal disease. *J Hypertens* 2006; 24: 2039-46.