

Evaluation of Thyroid Autoantibodies in Type 2 Diabetes

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ABSTRACT

OBJECTIVE: Diabetes mellitus and thyroid disease are the two common endocrinopathies seen in adult population. Studies to evaluate thyroid disorders in patients with type 2 diabetes are lacking. The aim of this study was to compare prevalence of thyroid dysfunction and autoimmunity in type 2 diabetic patients with age and sex matched non-diabetic control group.

MATERIAL AND METHODS: Among patients referred to Yazd Diabetes Research Center, 2797 type 2 diabetic patients were recruited. Clinical examination were carried out and samples for thyroid function test were obtained including thyroxin (T4), triiodothyronine (T3), Thyroid Stimulating Hormone (TSH), T3 Resin Uptake (T3RU), thyroid peroxidase antibodies (TPO-Ab) and thyroglobulin antibodies (TG-Ab). They were compared with 4844 non-diabetic, age and sex matched control subjects.

RESULTS: Our findings showed that the levels of thyroid hormone were not significantly different from levels in non-diabetic controls ($P < 0.05$). Positive TPO antibody was found in 1032 type 2 diabetic patients (36.9%) versus 1802 (37.2%) in control group ($P = 0.8$). Positive both thyroid antibodies, TPO antibody and TG antibody were found in 314 diabetic patients; (11.2%) versus 516 (10.8%) in controls ($P = 0.54$).

CONCLUSION: Our findings indicate that the frequency of thyroid autoimmunity is not significantly higher in type 2 diabetic patients than in non-diabetic control group.

KEY WORDS: Type 2 diabetes mellitus, Thyroid peroxidase antibodies, Thyroglobulin antibodies (TG-Ab).

INTRODUCTION

Diabetic patients have a higher prevalence of thyroid disorders compared with the general population because patients with one organ-specific autoimmune disease are at risk of developing other autoimmune disorders (1,2). A number of reports have also indicated a higher than normal prevalence of thyroid disorders in type 2 diabetic patients, with hypothyroidism being the most common disorder (3). Moreover, type 2 diabetes is a common disorder recognized as a major health problem in Iran. It is estimated that more than 1.5 million people are affected by diabetes in

this area (4). The presence of thyroid dysfunction may affect diabetes control (2). Hyperthyroidism is typically associated with worsening glycemic control and increased insulin requirements. There is underlying increased hepatic gluconeogenesis, rapid gastrointestinal glucose absorption, and probably increased insulin resistance. Indeed, thyrotoxicosis may unmask latent diabetes (2). More importantly, hypothyroidism is accompanied by a variety of abnormalities in plasma lipid metabolism, including elevated triglyceride and Low-Density Lipoprotein (LDL) cholesterol concentrations (5). The aim of this study was

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to compare prevalence of thyroid dysfunction and autoimmunity in type 2 diabetic patients with age and sex matched control group.

MATERIAL AND METHODS

In this study the subjects consisted of 2797 patients with type 2 diabetes including 1879 females and 918 males, who referred to the diabetic clinic of Yazd Diabetes Research Center. The criteria for eligibility included type 2 diabetes (according to ADA 2004), fasting blood sugar of 126 mg/dl at more than one occasion, random blood sugar of 200 mg/dl or taking hypoglycemic drugs or insulin, or physical exercise therapy for diabetes, not having any episodes of ketosis in the past (6), absence of severe diabetes complications, hypercholesterolemia or medical conditions that can affect thyroid function. Subjects with secondary diabetes and those on medication affecting thyroid function were excluded. Blood specimens from 4844 age and sex matched non-diabetic volunteers without history of diabetes mellitus, whose FBS was less than 126 mg/dl on two occasions, were control group. The University Ethics Committee approval was obtained prior to study enrollment. Informed consent was obtained in all subjects. Clinical data of all patients included sex, age at onset of diabetes, duration of diabetes and thyroid diseases, as well as a history of thyroid dysfunction were obtained by reviewing the medical records and direct patient interview.

Laboratory assessment: Sera were obtained from all patients for the measurement of thyroglobulin antibodies (TG-Ab) and thyroid peroxidase antibodies (TPO-Ab). TG-Ab and TPO-Ab were measured by enzyme-linked immunosorbent assay (ELISA) method (Radin Co., Italy).

Hypothyroidism was defined as showing TSH more than 10 mU/l or if the patient had been on thyroxine therapy on the basis of raised TSH values. Subclinical hypothyroidism was defined as a normal free T4 in association with a raised TSH (3-10 mU/l) in subjects not on thyroxin therapy.

Statistical analysis: Statistical analysis was performed using SPSS 13 for Windows. Data

were presented as mean \pm SD. Two unrelated samples were compared by student T-test. Variation of grouped data was assessed by two-way analysis of variance. A significant level of $P < 0.05$ was used for univariate test. Logistic regression analysis was carried out to identify independent association of thyroid dysfunction, anti TPO Ab and anti TG-Ab.

RESULTS

Table 1 shows that the levels of thyroid hormone were not significantly different from levels in non-diabetic controls ($P < 0.05$).

Table 2 shows that the levels of T4, T3 and TSH varied significantly with age in non-diabetic controls ($P = 0.03, 0.02, 0.02$), respectively. There was no such variation in diabetic patients ($P < 0.05$). Positive TPO antibody was found in 1032 type 2 diabetic patients (36.9%) versus 1802 (37.2%) in control group ($P = 0.8$). Positive both thyroid antibodies TPO antibody and TG antibody were found in 314 diabetic patients (11.2%) versus 516 (10.8%) in controls ($P = 0.54$). 15.1% of type 2 diabetic patients were found to have thyroid dysfunction, 190 (15.1%) were positive for TPO antibody and TG antibody, while of 14.6% of the subjects, who were found to have thyroid dysfunction in control subjects, had positive TPO and TG antibodies ($P = 0.65$).

The frequency of TPO-Ab positivity (>34 IU/ml) was 45.8% in diabetic group and 45.3% in non-diabetic controls. No significant difference was observed between diabetic and control groups at any of the two cutoffs used for TPO-Ab positivity (34 or 100 IU/ml) (34.2 vs. 36.3, 57.4 vs. 55.9), respectively.

The logistic regression of thyroid dysfunction on TPO status (positive versus negative) was significant (likelihood ratio $\chi^2 = 432.43$ [$P = 0.0001$]). Diabetic patients who were TPO positive were 5.3 times as likely to develop thyroid dysfunction (95% CI 4.48-6.27) and it was 4.8 (95% CI: 4.2-5.42) in non-diabetic controls.

Across the groups, the majority of patients with thyroid dysfunction had coexistent TPO-Ab (56.4 TPO positive vs. 43.6% TPO negative [$P=0.0001$]). No significant difference was observed of TPO-Ab positivity and thyroid dysfunction at any of the cutoffs (34 or

100 IU/ml) between diabetic and control group ($P = 0.79$ and 0.69 , respectively).

The frequency of TPO-Ab positive was slightly higher in patients with diabetes who

had thyroid dysfunction compared with those with no diabetes, but it was not significant at 5% level (Figure 1)

Table 1- Comparison of thyroid hormones in diabetic and non-diabetic subjects

Test	Diabetic (n = 2797)	Non-diabetic (n = 4844)	P value*
T3	154.16 ± 68.72	155.38 ± 70.59	0.27
T4	8.4 ± 3.66	8.44 ± 3.76	0.28
TSH	7.45 ± 15.11	7.71 ± 15.74	0.25
T3RU	29.21 ± 4.41	29.28 ± 4.55	0.15

*Independent sample T-test

Table 2- Comparison of thyroid hormones of diabetic and non-diabetic control subjects at different age intervals

Age (years)	Diabetic subjects			Non-diabetic subjects		
	TSH	T3	T4	TSH	T3	T4
≤35	7.89 ± 13.25	140.76 ± 48.85	8.81 ± 3.64	4.58 ± 9.06	168.79 ± 87.05	9.4 ± 3.91
35-45	7.12 ± 14.16	151.35 ± 63.16	8.32 ± 3.47	8.52 ± 16.66	151.61 ± 66.19	8.37 ± 3.77
45-55	7.7 ± 16.33	155.02 ± 71.12	8.37 ± 3.72	7.86 ± 16.36	156.56 ± 72.37	8.42 ± 3.83
55-65	7.13 ± 13.41	155.03 ± 68.48	8.49 ± 3.67	6.9 ± 14	157.53 ± 71.83	8.54 ± 3.6
>65	7.02 ± 13.78	156.6 ± 70.5	8.52 ± 3.68	7.99 ± 16.93	150.06 ± 4.7	8.14 ± 3.57
P value	0.8	0.4	0.7	0.02	0.02	0.03

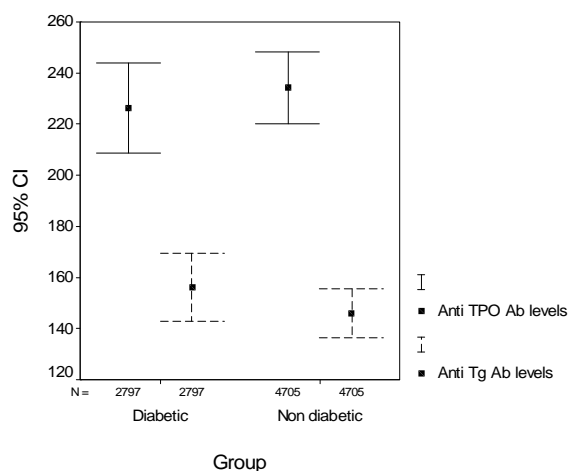


Figure 1- Anti TPO and TG Ab levels in diabetic and non-diabetic control subjects.

DISCUSSION

Thyroid disease is reported to occur rather commonly in both type 1 and type 2 diabetes, with a prevalence of 10-15%. Women are more frequent affected than men and hypothyroidism is more common than thyrotoxicosis (7). This pattern was seen in our study. Our results showed strong associations of thyroid dysfunction with auto antibodies, especially in patients with anti-TPO positive,

which are in accordance with several previous studies (1,8,10 and 11).

The results of the current study indicate that frequency of TPO-Ab positivity in male and female diabetic patients were comparable to non-diabetic control subjects, as confirmed in separate studies by Radaideh et al. (9) and Gonzalez et al. (12), while other case-control studies have reported high prevalence of auto antibodies in type 2 diabetic patients compared with control group (8,13). Akbar et al. studied 100 type 2 diabetics and 100 age and sex-matched controls. Thyroid autoimmunity was detected in 10% diabetics versus 5% controls (8). In Yasmin study anti-TPO antibodies in type 2 diabetics was 42.3% whereas it was 12% in control group (13).

Our study showed significant variation in frequency of thyroid dysfunction in different age groups in both diabetic and non-diabetic controls. The prevalence of thyroid dysfunction was highest between the ages of 45-55 years with another spike between 56-65 years. Nevertheless in Babu's Study most of patients were concentrated between 30-49 years and subsequently 60-69 years (14). So general screening of thyroid dysfunction

should be done earlier (below 50 years of age) in our population, than recommended in other populations (15).

CONCLUSION

The results of the present study indicate that the frequency of thyroid autoimmunity is not

significantly higher in type 2 diabetic patients than in non-diabetic control group.

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