PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN SIBLINGS OF PATIENTS WITH TYPE 1 DIABETES

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INTRODUCTION

Destruction of the insulin-secreting beta cells is an immunologically mediated disorder responsible for type 1 diabetes (IDDM). The pathogenesis looks similar to other autoimmune diseases often associated with IDDM. In particular, a higher prevalence of clinical hypo and hyperthyroidism as well as subclinical hypothyroidism (SCH) has been reported in IDDM. The purposes of the present work were, firstly, to study the prevalence of SCH in siblings of patients with IDDM, and secondly, to compare it with that observed in IDDM patients and controls.

PATIENTS AND METHODS

In order to evaluate the presence of SCH in siblings of IDDM patients not previously suspected of having thyroid disease, TSH levels before and following the administration of TRH and thyroid peroxidase (TPO-Ab) and thyroglobulin (TGB-Ab) antibodies were determined in 42 IDDM patients, 64 non diabetic siblings and 70 controls (Table 1).

TABLE 1

Demographic characteristics of IDDM patients, non-diabetic siblings and controls

GROUPS	IDDM	NON DIABETIC SIBLINGS	CONTROLS
n	42	64	70
Sex			
Male	17	30	29
Female	25	34	41
Age (years)			
X +/- D.S.	24+/-7	29+/-10	27+/-9

TSH was measured by a specific RIA and thyroid antibodies by hemoaglutination. Abnormal levels of TSH were considered those above 5 and 25 uU/ml at 0 and 25 minutes following the I.V. administration of 200 ugs of TRH, respectively. TPO - Ab and TGB-Ab were taken as positive with titers > 1/100.

The presence of an enlarged thyroid was evaluated clinically by palpation of the neck.

The differences among the groups were examined using X 's test. Odds Ratio were calculated both for IDDM patients and non-diabetic siblings in comparison to the controls.

RESULTS

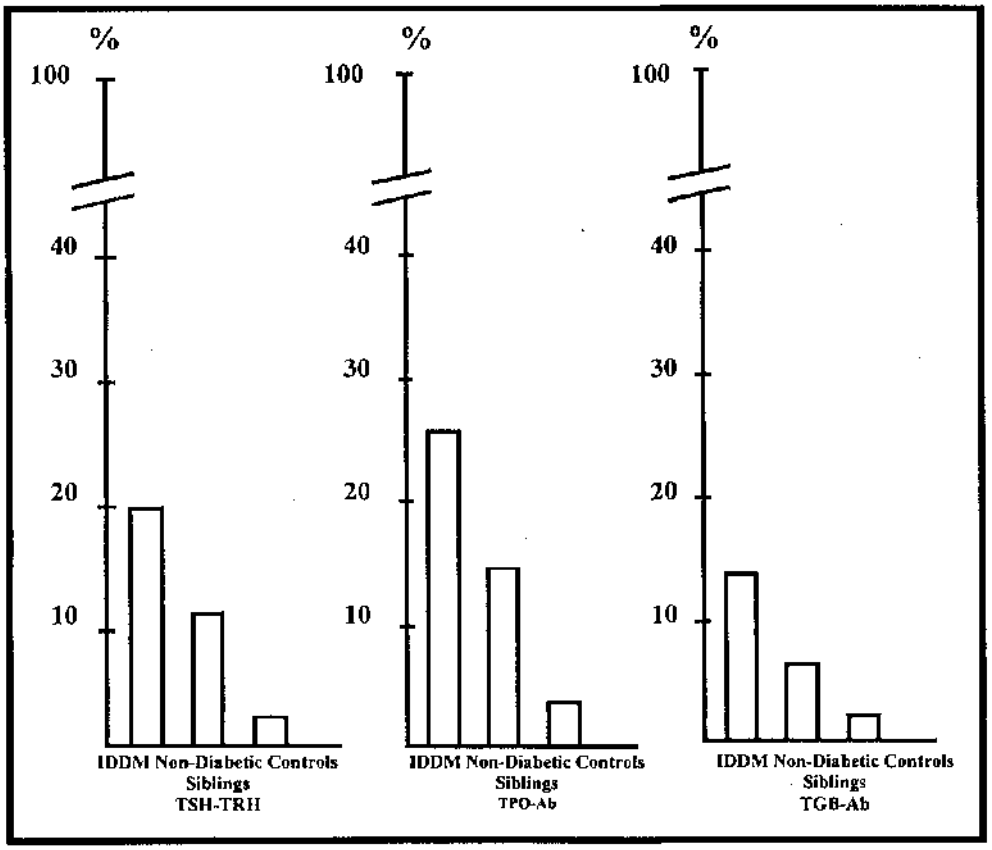
The prevalence of increased TSH-TRH and positive thyroid antibodies in the three groups are described in Table 2 and depicted in Fig.l.

TABLE 2

Elevated TSH-TRH and positive TPO-Ab and TGB-Ab in IDDM Patients, Non-Diabetic Siblings and Controls

GROUPS	IDDM		NON-DIABETIC SIBLINGS		CONTROLS	
Variables	%	n	%	n	%	n
TSH-TRH	19.0	8	10.9	7	2.8	2
TPO-Ab	26.1	11	14.0	9	4.2	3
TGB-Ab	14.2	6	6.2	4	2.8	2

FIGURE 1
Elevated TSH-TRH and positive TPO-Ab and TGB-Ab
in IDDM Patients, Non Diabetic Siblings and Controls



A significant difference was found for both TSH-TRH and TPO-Ab. Although there was a higher frequency of abnormal values for TGB-Ab in both IDDM patients and non-diabetic siblings, the difference was not found to be statistically significant.

The values of X^2 test and the level of significance are presented in Table 3.

TABLE 3

Evaluation of differences among groups

VARIABLES	X^2	p
TSH-TRH	8.08	< 0.05
TPO-Ab	15.87	< 0.01
TGB-Ab	5.41	> 0.05

The Odds of having abnormal results for IDDM patients and the non-diabetic siblings in comparison to the controls are presented in Table 4.

TABLE 4

Odds Ratio for IDDM Patients and Controls and for Non-Diabetic Siblings and Controls.

VARIABLES	IDDM/CONTROLS	NON DIABETIC SIBLINGS/ CONTROLS
TSH-TRH	8.00	4.18
TPO-Ab	7.92	3.65
TGB-Ab	5.66	2.26

The Odds of having thyroid autoimmunity with SCH were greater in the IDDM patients and in the non-diabetic siblings than in the controls.

The presence of goiter in the three groups is shown in Table 5. A significant difference was found among them ($X^2 = 9.84$, $p < 0.01$).

TABLE 5

Presence of goiter in IDDM patients Non-Diabetic Siblings and Controls

GROUPS	%	n
IDDM PATIENTS	14.2	10
NON DIABETIC SIBLINGS	7.8	5
CONTROLS	5.6	4

DISCUSSION

Different observations performed during the last two decades support the existence of a strong association of thyroid autoimmune disease, either Hashimoto thyroiditis or Graves - Basedow disease, with IDDM.

The increased prevalence of thyroid antibodies and SCH in patients with IDDM suggests the existence of a tendency to react strongly against certain antigens, or to a genetically poor ability to acquire tolerance to autoantigens, or perhaps to some common antigen shared in the tissues prone to autoimmune disease.

The results obtained in this study tend to demonstrate the existence of a higher prevalence of autoimmune SCH not only in IDDM patients, but also in their non-diabetic siblings.

Irvine and coworkers reported for the first time that both atrophic gastritis and thyroid autoimmune disease are more frequent in first degree relatives of IDDM patients.

The practical conclusion of these observations lies in the need to evaluate periodically following the diagnosis of IDDM the existence of autoimmune SCH, not only in the probands, but also in the first-degree relatives. The evaluation may start with the study of thyroid antibodies, mainly TPO-Ab; when positive, a TSH-TRH test should be performed.

One could argue that an experienced clinician will recognize the onset of thyroid disease in an IDDM patient or in a relative; however, the onset of the disease may be insidious and easily overlooked unless specifically and routinely tested for, even more so in a high risk population.

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