

Thyroid autoimmunity and type 1 diabetes in children and adolescents: screening data from Juvenile Diabetes Tuscany Regional Centre

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Abstract. *Background and Aims:* The incidence of autoimmune thyroiditis in patients with type 1 diabetes mellitus (T1DM) is higher than in healthy population. The aim of this study is to investigate epidemiology and natural history of thyroid autoimmunity (AIT), thyroiditis diagnosis and need for therapy in paediatric patients with T1DM and to find the most suitable timing of AIT screening. *Methods:* T1DM patients (493 pts., 268 males and 225 females) treated in the Juvenile Diabetes Tuscany Regional Centre at Meyer's Children Hospital were enrolled to determine TSH, fT₄, thyroid autoantibodies levels and to undergo thyroid ultrasound. Anamnestic data about T1DM onset, AIT onset, time frame between T1DM and AIT onsets and the relationship between AIT and celiac disease (CD) were studied. *Results:* In the screened population 11.7% of patients presented with increased thyroid autoantibodies, and 63.6% of them showed positive thyroid ultrasound. AIT was significantly more frequent in females compared to males ($p < 0.01$). The mean age at AIT onset was $11,17 \pm 3,29$ years (range 4,99-20,30) and AIT onset before 12 yrs. of age was found in 54.5% of cases; 18.4% patients (all females) presented CD. The mean time between T1DM and AIT onset was $2,46 \pm 3,41$ years (range 0-13,41). The subgroup with increased thyroid autoantibodies was not statistically different from the whole population with regard to TDM1 duration and mean age at onset. *Conclusions:* AIT is frequently associated with T1DM (11.7%) regardless of age and duration of diabetes. We suggest a yearly screening for AIT after TDM1 onset, at every age. (www.actabiomedica.it)

Key words: Autoimmune thyroiditis, IDDM, type 1 diabetes, thyroiditis frequency, thyroid antibodies, celiac disease

Introduction

The relationship between type 1 diabetes mellitus (T1DM) and other autoimmune disorders is widely described in literature; particularly, the increase of thyroid autoantibodies levels (thyroid autoimmunity, AIT) is the most frequent manifestation of autoimmunity and its incidence is higher than in healthy population (10-17% vs 6%) (1-6), in which it increases with age (7). Chronic autoimmune thyroiditis is characterised by the presence of thyroid specific au-

toantibodies in serum and by different degrees of thyroid dysfunction (8). Moreover, ultrasound studies of the thyroid gland have shown that gland enlargement and typical patterns of parenchymal hypo-echogenicity are present in patients with autoimmune thyroiditis (9).

The difference between the presence of thyroid autoantibodies and a real thyroid dysfunction requiring substitutive therapy is not well documented in T1DM patients, especially in children and adolescents.

Many authors claim that, in T1DM patients, the risk of developing chronic thyroiditis seems to increase from adolescence and recommend a regular screening from 12 yrs. of age (10). In several studies thyroiditis has been associated with worse metabolic control (11); therefore, recognition of thyroid dysfunction and treatment, if needed, are important (12).

This retrospective study aims at examining data about annual screening for thyroid autoimmunity, thyroiditis onset and the need for therapy in a group of children and adolescents attending our pediatric diabetes center, in order to investigate thyroid autoimmunity epidemiology and its natural history and to find the most suitable timing for thyroid autoimmunity screening.

Subjects and methods

Between January 2006 and January 2009 we carried out a screening test for thyroid autoimmunity in pediatric and adolescent T1DM patients (493 pts., 268 males and 225 females), treated in the Juvenile Diabetes Tuscany Regional Center at Meyer's Children Hospital.

In each subject we performed thyroid function tests (TSH, fT_4) by routine assays; we also determined autoantibodies against thyroglobulin (ATA) and against microsomes (AMA) by chemiluminescence.

The normal range of TSH was 0,85-3,33 $\mu\text{g}/\text{mL}$, of fT_4 0,8-1,8 ng/mL . A titre exceeding 35 UI/mL for AMA and 40 UI/mL for ATA was considered as positive; a titre of AMA or ATA above 100 UI/mL was considered as significantly increased.

Patients with positive autoantibodies underwent a thyroid ultrasound for thyroid size and an altered echostructure was reported especially for an inhomogeneous echopattern typical of thyroiditis.

Treatment with L-thyroxine started whenever TSH was $\geq 7 \mu\text{g}/\text{mL}$.

We assessed anamnestic data about T1DM onset and AIT onset and we calculated the time between T1DM and AIT onset; moreover, the presence of AIT was related to the presence or the absence of celiac disease (CD).

Data were analyzed using "Statistica", a statistical software package, version 8.0 (Statsoft, Tulsa, OK,

USA). Data are presented as mean \pm SD for normally distributed variables. In presence of a normal distribution, significant differences were assessed with the Student's t-test. Values of $p < 0.05$ were considered as statistically significant.

Results

We analyzed 468 patients (255 males and 213 females), amounting to 94.9% of our T1DM population. The mean age at T1DM onset was $6,96 \pm 4,20$ years, the mean duration of T1DM was $5,92 \pm 4,16$ years; 40 subjects (18 males and 22 females) were affected by CD.

No significant difference was found between males and females as far as the parameters taken into consideration.

Fifty-five patients (17 males and 38 females), 11.7% of our T1DM population, were positive for thyroid autoantibodies (Figure 1).

The distribution of age of prevalence of AIT shows that AIT onset occurs before 12 yrs. of age in more than half of patients (Figure 2).

The subgroup with AIT was not statistically different from the whole population with regard to T1DM duration and mean age at onset (Table 1).

Forty-five patients underwent thyroid ultrasound; ultrasound abnormalities typical of thyroiditis were present in 35 (11 males and 24 females) out of 45 pts.(63.6%).

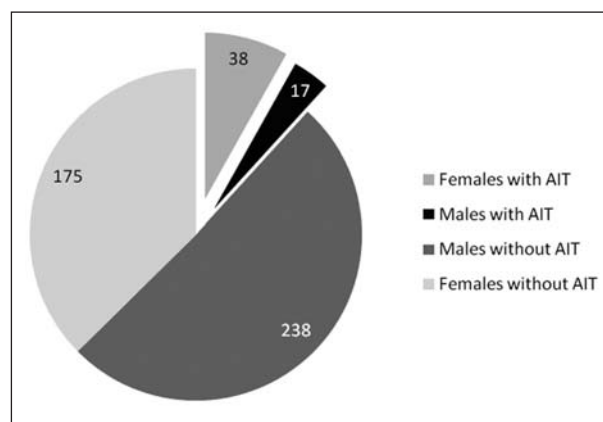


Figure 1. Patients with AIT in screened population

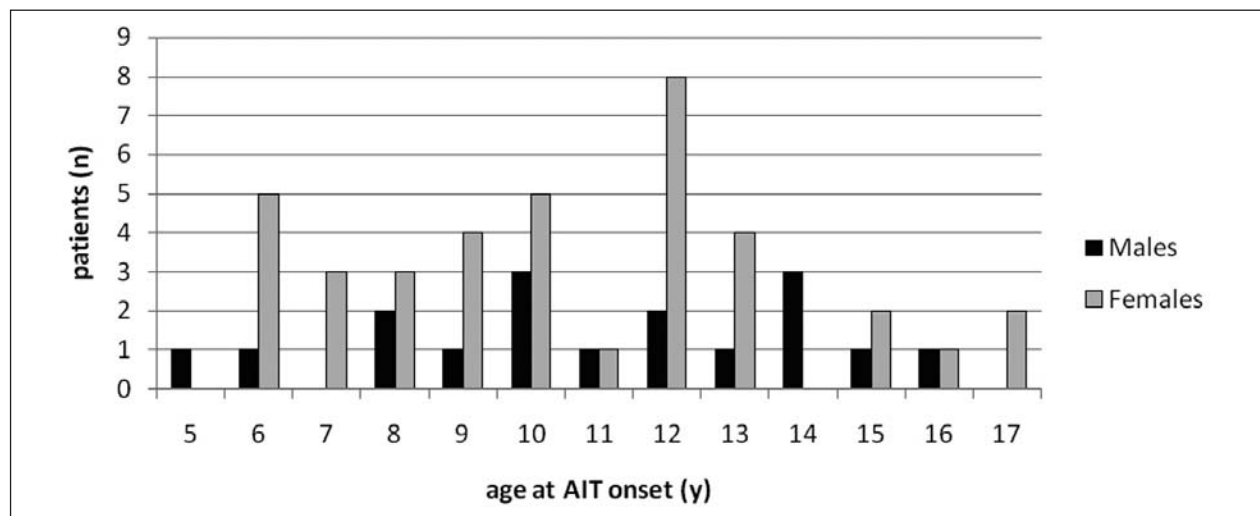


Figure 2. Age at AIT onset

Table 1. Comparison between screened population and AIT subgroup of patients. Data reported as mean \pm SD or number of cases (%)

	Screened population (n=468)	Patients with AIT (n=55)	P
Age at T1DM onset (y)	6,96 \pm 4,20	8,80 \pm 3,84	ns
Duration of T1DM (y)	5,92 \pm 4,16	7,79 \pm 5,82	ns
CD (n)	40 (8,55%)	7 (18,4%)	<0,05
Males (n)	255 (54,5%)	17 (30,9%)	<0,05
Females (n)	213 (45,5%)	38 (69,1%)	<0,05

Table 2. Characteristics of diabetic patients with AIT (n = 56). Data reported as mean \pm SD or number of cases (%)

	Males with AIT (n=17)	Females with AIT (n=38)	p
Age at T1DM onset (y)	9,60 \pm 3,97	8,44 \pm 3,78	ns
Duration of T1DM (y)	8,32 \pm 5,92	7,55 \pm 5,84	ns
Age at AITD onset (y)	11,41 \pm 3,14	11,00 \pm 3,10	ns
Interval T1DM-AITD (y)	1,81 \pm 3,06	2,56 \pm 3,16	ns
Positive ultrasound (n)	11 (65%)	24 (63,2%)	ns
L-T ₄ therapy (n)	7 (41%)	11 (28,9%)	ns
CD (n)	0	7 (18,4%)	< 0,05

Eighteen patients out of 55 (32.7%) needed treatment with L-thyroxine; the remaining 37 patients did not meet the criteria for therapy with L-thyroxine (TSH \geq 7 μ g/mL).

In the group of patients with AIT, the mean age at T1DM onset was 8,80 \pm 3,84 years (range 1,04-15,39), mean duration of T1DM was 7,79 \pm 5,82 years. The mean age at AIT onset was 11,13 \pm 3,09 years (range 5,06-17,65). The mean interval between T1DM onset and AIT onset was 2,33 \pm 3,12 years (range 0-13,17). We did not find statistically significant differences between males and females in the mean age at T1DM onset, mean age at AIT onset, and the time frame between T1DM onset and AIT onset.

CD was diagnosed in 7 patients out of 55 (18.4%), all females, while no males had CD.

Data of AIT group are shown in table 2.

There were no differences between males and females regarding the age at the beginning of L-T₄ substitution.

Discussion and conclusions

In our retrospective study we enrolled 94.9% patients treated in our center, a highly representative sample of T1DM patients aged between 1,20 and 19,98 years.

We confirm the literature stating that AIT is frequently associated with T1DM; moreover, our study confirms the higher incidence of AIT in females (13, 14).

Although in literature the risk of thyroiditis is thought to increase with age and especially in puberty (10, 15), in our sample more than half of AIT patients showed AIT onset before 12 yrs. of age, with no differences between males and females.

We suggest that the screening for AIT must be carried out yearly at every age, after T1DM onset; 18.4% of females affected by AIT showed CD, while no males showed CD; the difference is statistically significant and may indicate that presence of one autoimmune disease increase the risk of other autoimmune diseases, especially if females.

Therefore, a screening for CD should be performed even in asymptomatic patients, starting from T1DM diagnosis.

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