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The authors have nothing to disclose

Analysis of zinc transporter ZnT8 autoantibodies in children and adolescents with autoimmune thyroid diseases

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Objectives

Recent studies have revealed the presence of zinc and the expression of zinc transporter (ZnT) family members in most endocrine cell types. Moreover it was demonstrated that ZnT family plays an important role in the synthesis and secretion of many hormones. ZnT8 Ab (zinc transporter-8 autoantibodies) next to GAD Ab (glutamic acid decarboxylase antibodies), IAA (insulin autoantibodies) and IA-2 Ab (islet antigen-2 antibodies) have been described as markers of autoimmune process in patients with type 1 diabetes mellitus.

Since autoimmune disorders are known to be the pathophysiological factor in development of type 1 diabetes mellitus as well as thyroid diseases, we wanted to estimate in our study, the prevalence of ZnT8 Ab in patients with autoimmune thyroid diseases (AITDs).

Materials and Methods

The study was performed in the group consisting of 14 Graves' disease patients (mean age, 13.3± 5.7), 13 Hashimoto's thyroiditis patients (mean age, 16.5±2.3) and 83 with DT 1 (mean age, 14±4.7).They were hospitalised in endocrine outpatient clinic.

FIRS Laboratories, RSR Ltd based at Parc Ty Glas, Llanishen, Cardiff CF14 5DU, UK:

-GAD65 Ab was measured by ELISA using kits from RSR Ltd (Cardiff, UK) and values of GAD65 Ab of ≥5.0 WHO units/mL (National Institute for Biological Standards and Control; NIBSC 97/550) were considered positive.

-IA-2 Ab was measured using an immunoprecipitation assay (IPA) based on 125I-labelled IA-2 (kits from RSR Ltd). IA-2 Ab levels >1 WHO units/mL were considered positive.

-Insulin Ab were measured using immunoprecipitation assay with>0.4 U/mL value considered positive (RSR Ltd, UK)

-Autoantibodies to ZnT8 were measured by ELISA using kits from RSR Ltd and values of ZnT8Ab of ≥15 units/mL were positive.

In the Islet Autoantibody Standardization Program 2012 (IASP 2012), the GAD65 Ab ELISA showed 74% sensitivity and 99% specificity, IA-2 Ab IPA 74% sensitivity and 98% specificity and ZnT8 Ab ELISA 72% sensitivity and 99% specificity.

- 21OH Ab were measured with immunofluorescence method with value >1 U/ml considered positive (RSR Ltd, UK)

Children's University Hospital Laboratory:

- Antithyroid antibodies (anti-TPO >34 Iu/ml, anti-TG >115 Iu/ml, anti-TRAb >1.7 IU/ml) electrochemiluminescence method (Roche Diagnostics, Poland)

-tissue transglutaminase antibodies, t-TGA (immunoenzymatic method, >10 Iu/ml)

Prevalence of positive antibodies were then analysed according to:

-Gender (boys/girls)

-Patient age (up to 5 yrs, between 5 and 10 yrs, and above 10 yrs)

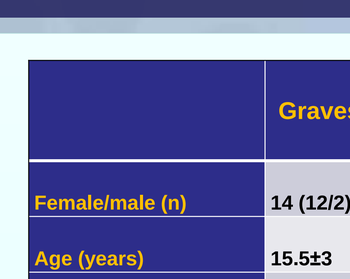
-Disease duration ((up to 5 yrs, between 5 and 10 yrs, and above 10 yrs)

-HbA1c value (<7.5% and > 7.5%)

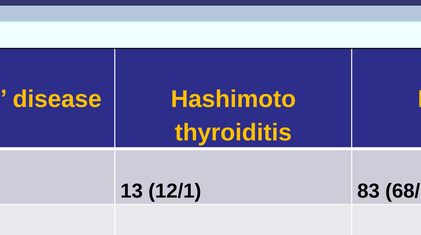
Figures and tables

	Graves' disease	Hashimoto thyroiditis	DT1	*p, **p
Female/male (n)	14 (12/2)	13 (12/1)	83 (68/15)	
Age (years)	15.5±3	15.2±4.2	14.3±3	NS, NS
Weight(kg)	55.19±2.39	58±5.28	56.2±7.8	NS, NS
Height (cm)	160.3±3.69	156.6±4.3	158±8	NS, NS
fT4 (ng/dl)	14.18±2.7	1.8±0.63	1.2±0.46	*p<0.001, NS
fT3 (ng/dl)	12.19±2.27	3.08±0.5	3.2±0.38	*p<0.001, NS
TSH (µU/ml)	1.37±1.1	9.87±4.37	3.04±0.72	p<0.01, p<0.025
TRAb (U/l)	12.5±4.2	0.5±0.31	0.4±0.22	*p<0.001, NS
anti-TGAb (IU/mL)	447.6±96.5	620.98±240.34	98.6±40.6	*p<0.01, **p<0.001
anti-TPOAb (IU/mL)	332.4±68.7	482.2±62.43	56±32.3	*p<0.01, **p<0.001
treatment	Methimazole	L-thyroxine	Insuline	

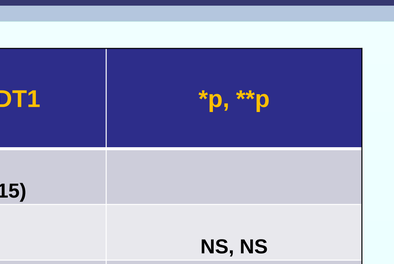
Prevelance of diabetic antidobodies



IA-2 antibodies

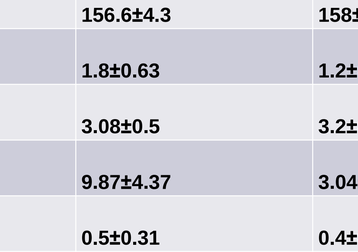


TPO antibodies

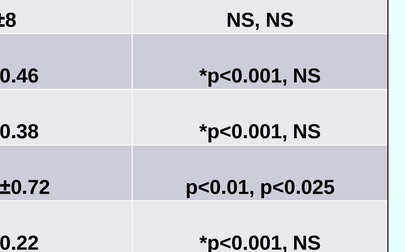


GAD 65 antibodies

ZnT8 antibodies



ATG antibodies



Prevelance of antidobodies in diabetic patients

Results

In our study we observed the presence of ZnT8 Ab in 1 patient (7.14%) in the case of Graves' disease patients while 1 patient (7.14%) in this group was positive for GAD Ab. In the case of Hashimoto's thyroiditis 3 patients (23%) were positive for ZnT8Ab. One of ZnT8 Ab positive HT patients had additionally positive GAD Ab, IA-2 Ab, IAA. In patients with DT1 we identified positive ZnT8 Ab (65,06%), GAD Ab (57,83%) and IA2 (49,4%) antibodies.

Autoantibodies results in examined patients	Graves'patients	Hashimoto's thyroiditis	DT 1
anti-TRAb	100%	-	-
aTPO Abs	78%	86%	22%
aATG Abs	54%	75%	18%
GAD Abs	7.14%	7.69%	57.83%
IA-2 Abs	-	7.69%	49.4%
Ins Abs	-	7.69%	+
ZnT8 Abs	7.14%	23%	65.06%
tTGA Abs	-	-	9.8%
21OH Abs	-	7.69%	2.4%

Conclusions

1. Our results may suggest that the presence of ZnT8 antibodies might not only be a marker of type 1 diabetes mellitus but also can be associated with other autoimmune diseases especially Hashimoto's thyroiditis.

2. The prevalence of positive antibodies in children with diabetes type 1 is higher than the prevalence already clinically recognised autoimmue diseases.

3. The prevalence of antibodies increases with patients age and diabetes duration, is higher in girls, and in patients with poor metabolic control.

4. Taking into consideration the fact that diabetes mellitus type 1 is the risk factor to coincidence another autoimmune disease, screening which uses autoantibodies is a proper action. It can result in separating groups with a higher risk of other autoimmune diseases, monitoring them, and finally early detecting and treating. All this can prevent further complications.