



PREVALENCE OF THYROID-ANTIBODIES AND SUBCLINICAL THYROID FAILURE IN FIRST-DEGREE RELATIVES OF TYPE 1 DIABETIC PATIENTS

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Objective:

Type I diabetes mellitus results from autoimmune destruction of pancreatic β -cells and is frequently associated with organ-specific autoimmune diseases, including autoimmune thyroid disease.

The aim of the present study was to determine the significance of **Thyroid-Abs** as well as the **TSH- levels** in first-degree relatives of type 1 diabetic patients who are at risk for diabetes (islet autoantibody positivity). Thus, to evaluate the predictive value of these markers for impaired thyroid function in these subjects

Materials and methods:

In this study, 425 first-degree relatives of patients with type 1 diabetes mellitus (mean age 29.2 ± 14.4 yrs) were examined. All of these subjects participated in the Giessen - Bad Oeynhausen Family Study. The distribution of the relatives was:

siblings/offsprings 199 (**group A**) and **parents** 226 (**group B**). In all cases, serum obtained at study entry was analyzed for **ICA**, **IA-2ic**, **GAD 65 Abs**, **thyroid (TG/TPO) antibodies** as well as for **TSH-levels basal**.

Antibody status of these subjects is shown in **Table 1**.

Table 1: Antibody (Ab) characteristics of the study population (n=425). Data are given as absolute numbers and percentage.

Study Population (n=425)	Number of Subjects (%)
• ICA pos.	28 (6.6)
• IA-2ic pos.	29 (6.8)
• GAD65 Ab pos.	18 (4.2)
• Thyroid Ab pos. (total) (TG and TPO)	50 (11.8)
• Thyroid Ab pos. (Group A)	24 (12.1)
• Thyroid Ab pos. (Group B)	26 (11.5)

Islet cell antibodies: Islet cell antibodies (ICA) were determined by indirect immunofluorescence technique using cryostat sections of human pancreas as substrate. This assay is regularly tested in the IDW proficiency workshop series on standardization of the ICA assay. Titres have been converted to Juvenile Diabetes Foundation (JDF) units using a JDF standard reference serum. The detection limit of the assay is 5JDF units.

GAD 65 antibody assay: GAD 65 antibodies were detected in a radioligand GAD 65 assay using as tracer recombinant, in vitro translated, human [35S]- methionin-labelled GAD 65. The cut-off index level for GAD 65 antibody positivity was determined from 150 healthy control subjects. Sera with GAD 65 antibody index values above the mean index plus three times the standard deviation were regarded as positive. This assay has been evaluated in the first IDW proficiency workshop on GADA, all samples were tested in duplicate.

IA-2ic antibody assay: Autoantibodies to the intracytoplasmic domain of IA-2 (anti-IA-2ic) were determined using radiolabelled recombinant antigens in a 96-well assay format. Recombinant autoantigens were produced by coupled in vitro transcription and translation of human IA-2ic cDNA. To achieve high specificity the cut off for antibody positivity was set at mean + 4 SD of antibody levels in 100 normal controls. In the combined IDW autoantibody workshop this assay had a diagnostic sensitivity of 73% and a specificity of 96% for type I diabetes. [Dr. J. Seissler, Leipzig]

TSH assay: TSH-levels were determined by an automated chemoluminescent system using a commercially available, ultra sensitive TSH assay (ACS: 180, Chiron Diagnostics, Fernwald, Germany).

Thyroid autoantibodies were determined with a commercially available enzyme-linked immunosorbent assay, using recombinant human TG or TPO as substrate. Standardization was carried out against the WHO Standard NIBSC 66/387.

Statistical analysis

Correlations were calculated according to Spearman rank correlation coefficient. Two sample analysis according to t-test was applied to compare TSH-levels between groups. Kolmogorov-Smirnov test was applied to examine the normality of the data. A p value of less than 0.05 was considered to be significant.

Results:

- In **group A**, a positive correlation ($r=0.45$, $p<0.001$) was observed between TPO-Abs and TSH-levels, i.e higher TSH-levels were observed in subjects with TPO-positivity in comparison to those tested negative for TPO-Abs (**Figure 1**)
- In **contrast**, no significant correlation was observed regarding the **group B** (**Figure 2**)
- In **group A**, a significant positive correlation was seen between IA-2ic and TPO-Ab positivity ($r=0.31$, $p<0.001$) (**Figure 3**)

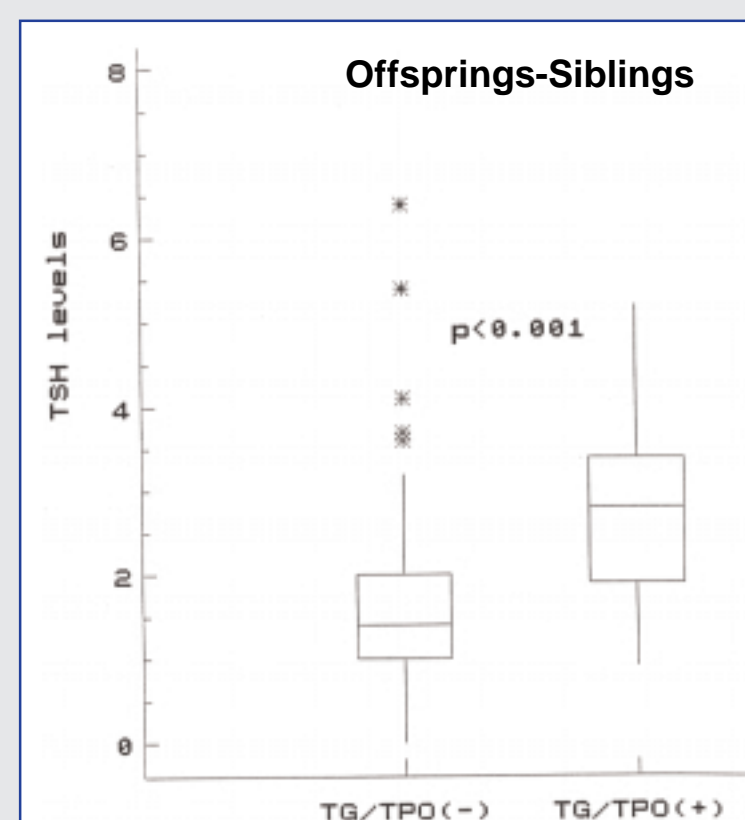


Figure 1

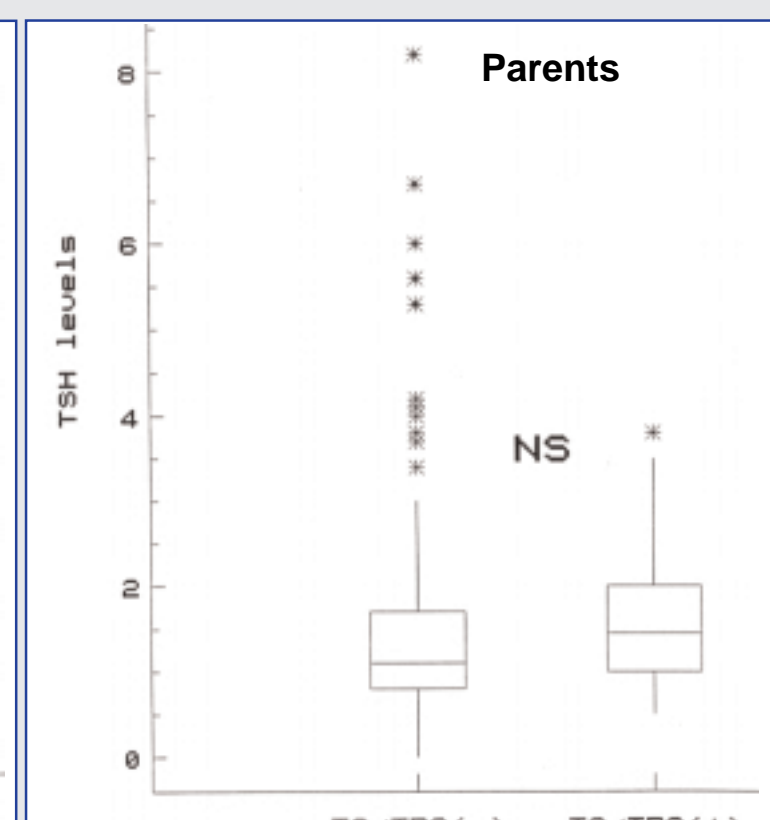


Figure 2

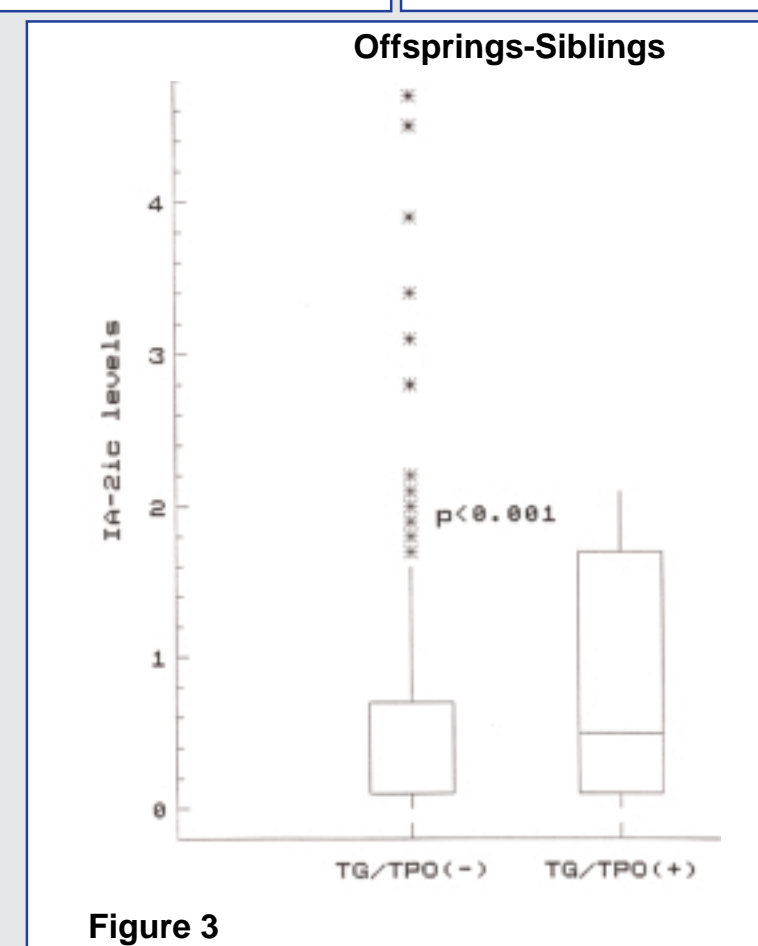


Figure 3

Conclusions:

Our observations indicate that screening for thyroid-autoimmunity is highly recommended in first-degree relatives of type 1 diabetic patients, particularly siblings and offsprings, who are at risk for developing type I diabetes (islet-autoantibody positivity).