# Frequency of Diabetes and Thyroid Autoantibodies in Patients with Type 1 Diabetes and Their Siblings

Ka Young Oh, Yun Hee Kim, Eun Mi Yang, and Chan Jong Kim
Department of Pediatrics, Chonnam National University Medical School & Hospital, Gwangju, Republic of Korea

## Abstract

This study aim to investigate the frequency of autoimmune thyroid and diabetes anitbodies in patients of type 1 diabetes mellitus and their siblings. TPOAb and TGAb were significantly different between probands and control subjects (p=0.002 and p=0.018, respectively). The rates of TPOAb and TGAb positivity in siblings were higher than those of controls, but there was no significant difference between two groups. Thyroid autoimmunity (TA) was significantly different among groups (p=0.004). Siblings of TA-positive probands revealed a greater prevalence of thyroid autoantibodies than did the control subjects (p=0.022), whereas siblings of TA-negative probands did not show such an increase over controls. The prevalence of pancreatic and thyroid antibodies positivity in probands was statistically significant compared to siblings and controls. Siblings of TA-positive probands revealed a greater prevalence of thyroid autoantibodies than did the control subjects. So the screening for TA in siblings, particularly siblings of TA-positive probands, is as important as in probands.

## Background

Type 1 diabetes mellitus (T1DM) is generally thought to be caused by an immune-associated, if not directly immune-mediated, destruction of insulin-producing pancreatic β cells. Most patients with T1DM have one or more of the following autoantibodies at disease onset: insulin autoantibodies (IAA), glutamic acid decarboxylase (GADA), and islet cell antibody (ICA). T1DM patients are at an increased risk for additional autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, Addison's disease, and celiac disease.[3] The most common autoimmune disease associated with T1DM is autoimmune thyroid disease (AIT). The frequency of positive thyroid antibodies in children with T1DM has been reported in ~50% in different countries, varying with age, sex, and ethnicity. Thyroid diseases occurred within 3 to 4 years from the half of the thyroid antibody positive groups. It is suggested that TIDM and autoimmune thyroiditis are based on a common genetic origin, since they have similar pathogenicity and frequently occur simultaneously in the same individual and/or the same family. The risk for this autoimmune disease is known to be increased in first-degree relatives of patients with T1DM, and 8% of first-degree relatives have AIT.

To our knowledge, the statue of autoantiboides for pancreas and thyroid in Korean children with T1DM and their siblings have not been studied extensively. Therefore, in the present study, we aim to investigate the frequency of autoimmune thyroid and diabetes anitbodies in patients of T1DM, their siblings and healthy controls.

## Methods

The patients consisted of 31 children and adolescents with T1DM. Forty siblings of T1DM patients were recruited. The 40 healthy controls with no family history of autoimmune disease were selected from the same ethnic population and were matched with the siblings for age and sex. Screening for AIT was performed using measurements of FT4, TSH, TPOAb, TGAb, TSHRAb. The presence of AIT was determined by the following criteria: TSH levels outside the assay reference plus positive thyroid antibodies. The one-way ANOVA test was performed to compare continuous variables. The chi-square test or Fisher's exact probability test depending on the number of the cases was used to compare frequencies of autoimmune diseases among the groups. Outcomes included pancreatic antibody positivity and TA. The p value of less than 0.05 was considered statistically significant.

## Results

Thirty one T1DM patients were enrolled in our study, 13 were boys (41.9%) and 18 (58.1%) were girls. Twenty five T1DM patients (80.6%) were positive for GADA, 11 (35.5%) for IAA, and 2 (6.5%) for IAA, respectively. Only one sibling showed GADA positivity (2.5%), and all siblings of probands revealed negative for IAA and ICA. Of control groups, two subjects (5%) had GADA positivity, but none had positivity for IAA and ICA. So the frequency of GADA and IAA positivity was significantly higher in probands compared to siblings and controls (p<0.001). All pancreatic autoantibodies were not significantly different between siblings and controls. The positivity of TPOAb, TGAb, and TSHRAb was 22.6%, 22.6%, and 0% in patients with T1DM, respectively. In their siblings, the rates of TPOAb, TGAb and TSHRAb positivity were 7.5%, 10.0% and 2.5%, respectively. Only one control subject showed TGAb positivity and others were all negative for thyroid autoantibodies. TPOAb and TGAb were significantly different among groups (p=0.002 and 0.026, respectively), also TA was significantly different among groups (p=0.004). Our data showed higher prevalence of thyroid autoantibodies in sibling groups (15%) than that of control subjects (2.5%), but the difference was not significant (p=0.108). We evaluated both TSH and FT4 levels as well as clinical examination. AIT was detected in 2 of 31 probands (6.5%). One of 40 siblings (2.5%) showed clinical and biochemical evidence of hyperthyroidism and treated with methimazole. Siblings of TA-positive probands revealed a greater prevalence of thyroid autoantibodies than did the control subjects (p=0.022), whereas siblings of TA-negative probands did not show such an increase over controls.

## Discussion

Positivity of antibodies in Japanese T1DM patients are 60–70% for GADA, 45–50% for IAA, and 60–65% for IA-2 autoantibodies at disease onset. Our results indicated that GADA, IAA and ICA were positive in 80.6%, 35.5% and 6.5% of Korean patients with T1DM. Many studies have shown that siblings of patients with T1DM place at increased risk of diabetes-related autoimmunity. Our study revealed that the only 1 of 40 (2.5%) siblings had GADA positivity and two subjects (5%) of control groups had GADA positivity. Asian studies have reported an AIT prevalence of 21.8% in a Taiwanese population and 18% in a Japanese population. In our study, TPOAb and TGAb were positive in 22.6% and 22.6 % of Korean patients with T1DM, respectively. The overall prevalence of TA was 29.0% in T1DM patients, which was similar to the findings in other studies. In our study, the prevalence of TPOAb, TGAb and TSHRAb positivity in siblings of probands was 7.5%, 10.0%, and 2.5%, respectively. Our data showed higher prevalence of thyroid autoantibodies in sibling groups (15%) than that of control subjects (2.5%). Siblings of TA-positive probands revealed significantly increased prevalence of thyroid autoantibodies than did the control subjects (p=0.022), whereas siblings of TA-negative probands did not show such an increase over controls. One sibling of TA-positive proband revealed Graves' disease and treated with methimazole. The present study reports on the prevalence of pancreas and thyroid autoantibody positivity in Korean patients with T1DM, their siblings and healthy control subjects. This study is the first one regarding the prevalence of TA and pancreatic autoantibody in Korean children and adolescents with T1DM, their siblings and healthy control subjects. It is noteworthy that 6.5% of our TIDM patients already had AIT at screening and one sibling showed Graves' disease.

## Conclusion

The prevalence of pancreatic and thyroid antibodies positivity in probands was statistically significant compared to siblings and controls. And siblings of TA-positive probands showed a statistically significant prevalence of thyroid autoantibodies than control subjects. So the screening for TA in siblings, particularly siblings of TA-positive probands, is as important as in probands.

## References

1. Barker JM. *Clinical review: Type 1 diabetes-associated autoimmunity: natural history, genetic associations, and screening. J Clin Endocrinol Metab 2006;91:1210-7.*
2. Kordonouri O, Klinghammer A, Lang EB, Gruters-Kieslich A, Grabert M, Holl RW. *Thyroid autoimmunity in children and adolescents with type 1 diabetes: a multicenter survey. Diabetes Care 2002; 25: 1346-50.*

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Chan Jong
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