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Association of Serum Anti-TTG Levels with Serum Anti-TPO Levels in Paediatric Population

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Abstract Original Research Article

Background: There have been several autoimmune disorders which are reported to coexist with other organ-specific autoantibodies. Aim: The aim of the present study was to evaluate the presence of anti-TPO antibodies in children of age group 5-18 years who have positive levels of tissue transglutaminase anti-TTG antibodies, which may indicate high risk for developing thyroiditis in future. ***Material & Method:*** Samples of 20 children who have been tested positive with anti-TTG antibodies were simultaneously tested for anti-TPO antibodies. Equal number of age and sex matched controls of samples that were tested negative for anti-TTG antibodies, acted as controls to form a case control study. The observed values were expressed as Mean ± SD. The significance of mean difference between patients and controls groups was compared by using Student's t test and distribution of probability (p). ***Result:*** A total of 40 subjects (20 cases and 20 controls) were included in this study. Subclinical Hypothyroidism was present in 40 % cases compared to only 5% in controls (P<0.001). Anti-TPO antibodies were present in 20% subjects among cases compared to 5per cent (P=0.001) in controls, respectively. Levels of anti-TPO antibodies increased with increasing titre of anti-TTG antibody. ***Conclusion:*** The findings of present case control study showed high positivity of anti-TPO antibodies among subjects with positive anti TTG antibodies. It is, therefore, important to have high index of suspicion for autoimmune thyroiditis in patients with high suspicion of celiac disease found by positive anti- TTG antibodies in serum.

Keywords: Thyroiditis, celiac disease, anti-TTG antibody, anti-TPO antibody.

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INTRODUCTION

It is well known that tolerance to self-antigen is acquired by removal of autoreactive T-cells in body [1]. But breakdown of this tolerance can lead to T cell activation cells and hence autoimmunity. Many mechanisms have been postulated to explain autoimmunity, to name a few are, genetic susceptibility, release of sequestrated self-antigen by infection or molecular mimicry [2]. The presence of auto-antibodies in serum, have very strong predictive value in cases with organ-specific autoimmune disorders, which have a long preclinical phase, before the disease finally develops [3]. In patients with type 1 diabetes mellitus (T1DM), many studies exist for measurement of thyroid and gut autoimmunity [4]. However, no such recommendations exist for patients with celiac disease and that too in children and adoloscents.

In view of limited reports showing association between thyroid autoimmunity and celiac disease, especially in children and adolescents [5-11]. We undertook this study to evaluate presence of thyroid autoimmunity in patients with positive tissue transglutaminase (TTG) antibodies.

MATERIAL AND METHODS

The present study was carried out in Department of Biochemistry at Super Speciality Paediatric Hospital and Post graduate Teaching Institute, Noida, between June 2018 to December 2018. A total number of 40 samples of children between age group 5-15 years, whose sample tested positive for Anti-TTG antibodies were tested simultaneously for Anti-TPO antiobodies, the samples were then stored at -20 celsius for further evaluation.

Exclusion criteria included subjects with known systemic disorders or medications. Children (n=20) who were found to be positive for anti-tissue transglutaminase (anti-TTG) antibodies (>30 IU/ml)

were enrolled as patient group subjects. Equal number of age and sex matched anti-TTG antibody negative controls (n=20) were selected from the same cohort for paired case-control study. Serum samples of cases and controls were analysed for thyroid function test (FT3, FT4, and TSH) and anti-TPO antibodies. The study protocol was excluded from the Ethics Committee of the institute as patients directly were not involved in this study and the samples which came for routine diagnosis of anti TTG antibodies, were tested and the same sample was re tested for anti-TPO antibodies.

Thyroid function tests were performed by immunoassay using Vidas immuno autoananalyser and normal ranges for FT3, FT4 and TSH were 2.8-7.1 pmol/l, 12.0-22.0 pmol/l, and 0.27-4.20 mIU/l, respectively. Subjects with TSH >4.5 mIU/l were defined either as subclinical hypothyroidism if FT4 was normal or overt hypothyroidism if FT4 was low. Anti-TPO antibodies were measured by using immunoasay using Vidas auto immuno analyser with normal range from 0.0- 35 IU/l. Anti-TTG antibodies were measured by enzyme immunoassay (ELISA) kit supplied by BioRad as per the manufacturer's protocol. Anti- TTG antibody levels of >30 IU/ml were considered positive.

STATISTICAL ANALYSIS

The data collected from patients and control were entered separately in Microsoft Excel sheet of windows 2007 and values were expressed as Mean ± SD. The significance of mean difference between groups was compared by using Student's t-test and distribution of probability (P).

RESULT

Mean age, thyroid function tests and anti-TPO levels among cases and controls group subjects are representated in table 1. Our study found out that Subclinical Hypothyroidism was present in 40 per cent (8) cases when compared to 5 per cent (1) in controls (P<0.001). Overt hypothyroidism was present in 10 per cent (n=2) of cases and none in controls. FT4 and FT3 levels were significantly lower and TSH levels were significantly higher in cases than in controls. The levels of anti-TPO antibodies were significantly higher in cases when compared to controls (p<0.001).

Table-1: Mean age, Thyroid profile and anti TPO antibodies in study group subjects (Mean ± SD)

S. No.	Parameters	Patient group (n=20)	Control group (n=20)
1	Age (years)	11.30 ± 2.4	13.5 ± 2.75
2	Serum TSH (mIU/ml)	5.68 ± 1.2	2.86 ± 0.85
3	Free T4 (pmol/L)	17.75 ± 3.50	22.05 ± 3.84
4	Free T3 (pmol/L)	4.20 ± 1.32	4.79 ± 1.48
5	Anti-TPO antibodies (IU/ml)	41.0 ± 7.4	6.5 ± 2.32

Where,
*p<0.1: Non-significant
** p<0.05: Significant;
*** p<0.001: Highly Significant;

DISCUSSION

The presence of anti-TPO antibody was significantly higher among cases than in controls. Till now, there are limited reports on an increasing prevalence of autoimmune thyroid disorders in patients with celiac disease. A few reports on high occurrence of anti-TTG antibody in children with autoimmune thyroiditis are available. There are two reports available from outside India, where anti-TTG antibodies have been observed in 7.9 and 7.8 per cent respectively children with autoimmune thyroid disease [11, 12]. Also, in patients having celiac disease, anti-TPO antibody and autoimmune thyroiditis have been reported to range from 10.5-14.6 percent [5, 13]. In one study reported from Northern India, the level of anti-TTG antibodies were reported in 10.6 per cent suspected cases of celiac disease through a structured questionnaire in 3-17 yr old children [14].

It is been proposed that celiac disease could have a role in the development of thyroid autoimmunity [15]. The present study showed a positive relation between anti-TTG antibody and anti-TPO antibodies. However one study from outside India, Jiskra *et al*. did not show any significant relation between anti-TPO and anti-TTG-antibodies [16].

CONCLUSION

In conclusion, our study showed high anti-TPO positivity among subjects with high anti TTG antibodies. It is, therefore, important to have high clinical index of suspicion for autoimmune thyroiditis

in patients with positive suspicion of celiac disease. However, small sample size, non-inclusion of histological evaluation of intestinal biopsy to confirm diagnosis of celiac disease and absence long term follow up of anti-TTG antibody positive patients were the limitations of present study which needs more in-depth study in future.

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