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Short Communication

Paediatrics Section

Prevalence of Beta-Cell, Thyroid and Celiac Autoimmunity in North Indian Children with Recent Onset Type 1 Diabetes (T1D)

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ABSTRACT

There is wide variation in the prevalence of pancreatic and other major autoantibodies in different patient populations of Type 1 diabetes (T1D) across continents and even within countries. The data on frequency of associated autoimmunity Indian children with T1D is limited. A retrospective record review of 310 children aged 7.28±3.3 y (range 0.7-15 y) with recently diagnosed T1D attending our Pediatric Diabetes Clinic between April 2004 to September 2014, showed positivity for anti-GAD65, anti-IA2b, anti-TPO and anti-tTGA of 50% (64/128), 16% (12/72), 18.7% (23/123) and 22% (47/212) respectively. The male:female ratio in patients with anti-GAD, anti-TPO and anti-tTG positivity was 1.3, 0.7 and 0.6 respectively. In conclusion, our patient cohort exhibited a moderate prevalence of anti-GAD 65, low prevalence of anti-TPO and high prevalence of anti-tTGA autoantibodies as compared to previous reports. Male preponderance was noted in children with GAD65 positivity.

Keywords: Autoantibodies, Children, Glutamic acid decarboxylase 65, Type 1 diabetes, Thyroid peroxidase, Tissue transglutaminase

INTRODUCTION

T1D results from a complex interplay of genetic, immunological and environmental factors [1]. Although the disease is characterized by β cell destruction and presence of pancreatic autoantibodies, the autoimmune attack may involve other organs particularly thyroid, gut, adrenals and gastric parietal cells [1]. The presence of autoimmunity of other organs in patients with T1D influences the disease prognosis and screening for associated autoimmunity is therefore recommended [2]. Majority of the data on prevalence of autoimmunity in T1D has emerged from the developed countries. There is however wide variation in the frequencies of various autoantibodies in different populations of the world [3]. The prevalence of pancreatic autoantibodies is much lower in India as compared to other populations and has been considered to result from etiologic heterogeneity of T1D [3-8]. Majority of the patients of T1D are therefore labeled as Type 1B in India [9]. A higher prevalence of thyroid autoimmunity has also been noted in Indian patients as compared to other regions [2,10]. The prevalence of celiac autoimmunity in T1D, however appears to be similar to other reports [11,12]. In a recently published data from India, more than 50% of patients with T1D were noted to have associated clinical autoimmune disease, indirect evidence that autoantibodies are present in majority of patients [13]. The data on the frequency of various major associated autoantibodies in Indian children with T1D is limited. We thus aimed to conduct the present study in our large follow up cohort of children with T1D to determine the frequency of beta-cell, thyroid and celiac autoimmunity.

MATERIALS AND METHODS

The retrospective record review of patients on follow up in Pediatric Diabetes Clinic of our hospital between April 2004 to September 2014 was performed. The diagnosis of diabetes was based on the ISPAD (The International Society for Pediatric and Adolescent Diabetes) criteria first published in 2000 and revised in 2009 [14]. Children aged <15 y with short history of osmotic symptoms, initial ketonuria, low C-peptide levels and absolute insulin dependence for maintaining normoglycemia, and who had their autoantibodies estimated within six months of diagnosis were included. Children with T2D, monogenic and secondary diabetes were excluded.

Autoantibodies to glutamic acid decarboxylase 65 (anti-GAD65), tyrosine phosphatase (IA-2b) and tissue transglutaminase IgA (anti-tTGA) were measured by enzyme immunoassay (ELISA) kits (Aeskulisa, Germany and Phadia, USA). The tests were performed as per manufacturers' instructions. Anti-thyroid peroxidase (anti-TPO) antibodies were measured by using electrochemiluminiscence kits (Roche Diagnostics, Germany). Cut offs values were calculated by receiver operating curves and concentrations of >25 IU/ml for anti-GAD-65, >20 U/mL for ICA512, >34.0 U/l for anti-TPO and >8 U/mL for anti-tTG were considered positive.

RESULTS

Of the 548 children with T1D registered in the clinic during the study period, 310 were found eligible; 181 (58%) were boys. The mean age was 7.28±3.3 y (range 0.7-15 y). Anti-GAD65 and anti-IA2 antibodies were positive in 64 (50%) of 128 and 12 (16%) of the 72 patients tested, respectively; the combined positivity was 54%. Anti-TPO antibodies were positive in 23 (18.7%) of the 123 patients. Anti-tTGA antibodies were positive in 47 (22%) of the 212 patients tested. The male: female ratio in patients with anti-GAD, anti-TPO and anti-tTG positivity was 1.3, 0.7 and 0.6 respectively.

DISCUSSION

The presence of associated autoimmunity in T1D may result from a common genetic background (HLA antigens) as well as a defective immunoregulation or a poor ability to develop tolerance to autoantigens [1]. Timely additional work-up and intervention in cases of antibody positivity can improve clinical course of the disease [2]. The prevalence of beta-cell autoantibodies in our patients was higher as compared to data from other Indian centers [4-7] but lower than studies from West and South India [8,15] as well

as from European countries [3,15]. The reasons for the worldwide differences in frequencies of various autoantibodies amongst patient populations of T1D are poorly understood. Timing of estimation from disease onset, differences in laboratory assays and threshold limits, patient recruitment procedures and small patient numbers have been cited as the potential causes for differences in the prevalence of pancreatic autoantibodies [8]. The higher prevalence in our study and the previous Indian studies could be due to the inclusion of patients with a recent onset of disease [8]. Frequency of pancreatic autoantibodies decreases with disease duration [16]. Conversely, thyroid autoimmunity is detected in about 29% of patients during first year of onset of T1D but its prevalence increases with disease duration [2,17]. The lower frequency in our study is similar to previous observations on an Indian cohort which exhibited anti-TPO prevalence of 25% in patients with disease duration of <2 y and 100% in those having disease for >6 y [10]. The higher prevalence of celiac autoantibodies in our patients as compared to previous studies may be explained by regional variations [11.12]. The female preponderance of anti-TPO and anti-tTGA positivity in our patients is similar to previous observations [18,19]. However, the observed sex ratio in GAD 65 positive patients was different from the previous reports [8]. We did not test for anti-adrenal and anti-parietal cell antibodies as their prevalence is too low in children with T1D to be cost-effective [18].

CONCLUSION

In conclusion, children with recently diagnosed T1D showed a moderate prevalence of anti-GAD65, low prevalence of anti-TPO and high prevalence of anti-tTGA autoantibodies. Male preponderance was noted in children with GAD65 positivity.

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