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CELIAC DISEASE ASSOCIATED WITH TYPE 1 DIABETES MELLITUS IN CHILDREN AND ADOLESCENTS

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ABSTRACT

Type 1 diabetes mellitus is the most common endocrinopathy. A retrospective, hospital-based study during the period January 1995 and December 2012 was conducted on a cohort of 305 Saudi children and adolescents, 163 (53.4%), were females and 142 (46.6%) males. Sixty-two (20.3%) patients were referred to a pediatric gastroenterologist, 26 (8.5%) patients, were proved to have CD. Further, 36 (11.8%) patients were considered potential CD. In conclusion, the prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus in this study is considered to be among the highest reported, (20.3%). A specialized follow-up and dietary counselling are essential in the management of patient's affected by both type 1 diabetes and CD.

KEYWORDS: Children, adolescents, celiac disease, Type 1 diabetes mellitus, prevalence, Saudi Arabia.

INTRODUCTION

Autoimmune diseases occur when an individual develops an immune targeted against specific organ or number of organs. Genetic susceptibility and environmental factors are the main responsible of the development of the autoimmune process leading to a clinically evident disease.[1]

Type 1 diabetes mellitus is the most common endocrinopathy, to have clinical onset in childhood and adolescents, with rising incidence.[2,3] The majority of organ-specific autoimmune disease characterized by an initial infiltration by lymphocytes and macrophages, of the organ, with impaired activity of the organ followed by atrophy. This progressive autoimmune process takes time and is T-cell mediated. Antibodies against specific antigens of the involved gland are delectable in the blood before the clinical onset of the specific disease, so they represent a risk marker and their screening and follow-up allow precocious diagnosis and treatment of autoimmune-related disease in genetically susceptible individuals.[4]

Genetic factor and autoimmunity are closely related since the developmental maturation of T-cells occurs through an interaction between HLA antigen and T-cell receptor. In genetically susceptible individuals, disease-prone HLA molecules are ineffective at bonding and presenting peptides from tissue-specific antigens, therefore auto-reactive T cells can survive and trigger a poorly regulated immune response thereafter.[5]

The frequency of organ specific autoimmunity in patients with type 1 diabetes mellitus might be due to multiple immunologic abnormalities, i.e., an imbalance in B and T lymphocytes, or a tendency to reach against specific antigens, or poor ability to develop immune tolerance.

Celiac disease (CD) prevalence is higher in patients with type 1 DM as compared to general population is universally accepted. After autoimmune thyroiditis, the second most commonly reported autoimmune disease in type 1 DM is celiac disease. Published data on the prevalence of CD in type 1 DM in Saudi Arabia, indicated a prevalence ranging from 4.9% and 11.1%, in two limited hospital-based studies from Riyadh and Jeddah.[6,7]

The mean prevalence of coeliac disease in type 1 diabetes mellitus is about 8% with extremely variable range (from 1% in Finland[8-10] up to 11% in Italy[11]), almost 10-20 fold higher than observed in general pediatric population. The prevalence of CD has significantly increased over the last decade, probably due to changes in environmental factors, namely, eating habits and viral infections.[12]

The mean objective of this study was to determine the prevalence of CD in a cohort of 305 children and adolescents with type 1 DM.

MATERIALS AND METHODS

This is a retrospective hospital-based study included children and adolescents with type 1 diabetes mellitus who were diagnosed with celiac disease between the period January 1995 and December 2012.

Initially, all patients were screened serologically (Anti-gliadin antibody (AGA), anti-endomysial antibody (EMA), anti-tissue transglutaminase antibody (tTG). Serological tests are automated, except, EMA test, which is operator-dependent. Also, Immunoglobulin A is measured at the same time. Positive patients were referred for upper endoscopy where multiple biopsy specimen where taken. The severity of small bowel mucosal damage was reviewed by an experienced gastrointestinal pathologist, and graded according to the Marsh Classification from I to III.[13] The diagnosis of CD, is based on the revised criteria for the diagnosis of celiac disease.[14]

RESULTS

The cohort includes 305 Saudi children and adolescents, 163 (53.4%) were females and 142 (46.6%) males. The age ranged between 0.6 to 16 years with a mean age of 9.5 years. The duration of diabetes was ranging between 1 and 13 years, with a mean of 7.5 years.

Sixty-two (20.3%) patients were referred to a pediatric gastroenterologist to perform upper gastrointestinal endoscopy and biopsy either because of gastrointestinal symptoms such as abdominal pain or diarrhea or due to any positive screening test. In twenty-six (8.5%) patients, 17 were females and 9 males with an age range of 7-16 years, (mean 11.5), and the duration of diabetes was 1.5-11.5 years (mean 5).

DISCUSSION

Celiac disease is an immune-mediated disorders resulting from a permanent gluten intolerance trigged by the ingestion of the gliadin fraction of wheat gluten and similar alcohol soluble proteins named prolamine of barley and rye. Gluten intolerance exerts a chronic inflammatory lesion characterized by flattened villi of the small bowel mucosa and sub-mucosa, with a diverse clinical heterogenecity ranging from asymptomatic to severe disease in genetically susceptible individual.[15,16] The association of type 1 diabetes mellitus and celiac disease is well known, and with rising incidence. Since both disorders have an increase frequency of human leukocyte antigen HLA-DR3 and other HLA number.[17,18,19] Once considered a rare disease in childhood. Celiac disease is now known to be a very common condition, even if it remains widely unrecognized and underdiagnosed worldwide both in children and adults.[20-24]

Type 1 diabetes mellitus is the most common endocrinopathy to have clinical onset in childhood and adolescents, with varied pathogenesis, clinical appearance and outcome and seriously affects patients and families life. A combination of genetic, environmental and immunological factors exerts to a T-cell mediated autoimmune process targeted against insulin-producing β-cells in the pancreatic islet of Langerlans. The incidence of type 1 diabetes is increasing world-wide and may double the burden of the disease in the youngest children by 2020. Large collaborative studies demonstrated an increase in the incidence of type 1 diabetes mellitus over the last decades.[3] In particular, Type 1 DM is common among Saudi children and adolescents as Al Herbish et al[25] reported a high prevalence of 109.5 per 100,000 populations in children and adolescents in Saudi Arabia. Availability of new very sensitive and specific serological markers (initially anti-gliadin and anti-reticulin antibodies and thereafter anti-endomysial and anti-transglutaminase antibodies), allowed more efficient screening. Therefore, the prevalence of celiac disease was dramatically increased. Celiac disease is associated with circulating antibodies against gliadin and endomysial tyrosine. Anti-endomysial antibodies showed higher specificity and sensitivity than anti-gliadin antibodies and represent a useful means for screening procedures. Anti-reticulin antibodies screening showed less sensitivity and it has been replaced by anti-endomysial antibodies. The transglutaminase enzyme was found to be the auto-antigen for anti-endomysial antibodies. Both anti-endomysial and anti-transglutaminase antibodies belong to the IgA class.[15] Positivity for disease-related antibodies allow identification of patients with suspected celiac disease who must undergo intestinal biopsy. IgA transglutaminase antibodies show the highest sensitivity and allow to identify 98% of patients with celiac diseases while their specificity is lower, especially at a low titer, IgA anti-endomysial antibodies show lower sensitivity (98%) but higher specificity. Fluctuating positivity for anti-endomysial antibodies at a low titer can be detected at time of diabetes clinical onset and in absence of signs or symptoms related to celiac disease only periodical screening is recommended.[12]

Total IgA screening is essential before celiac screening.[26] It has been reported that serological screening for CD allows diagnosing 1% of patients with CD. The frequency of diagnosis increases to 85% when screening is performed in the next 5 years after diabetes diagnosis, as the case in our study group.[10,27,28,29] It has been reported that up to 85% of cases of CD is diagnosed 2-5 years after type 1 diabetes clinical onset. Markers of CD can appear within 10 years, so it is recommended to perform screening yearly for the first 5 years after diabetes diagnosis, and every 2 years in the following 6 years.[30]

Celiac disease has a wide spectrum from asymptomatic to severe disease. Potential celiac disease with positive antibodies but normal mucosa is a well-known entity, however, the finding of histological picture of villous atrophy with increased number of intraepithelial lymphocytes makes sure diagnosis of celiac disease irrespective of serological markers results. The marsh criteria are commonly used for histological staging.[1,13,14]

The prevalence of celiac disease in our cohort of 305 patients is 8.5% as diagnosed by biopsy is compatible to that reported worldwide and that from Saudi Arabia.[6,7,11,31] However, further 11.8% are considered as potential celiac disease as they have positive antibodies.

In conclusion, the prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus in this study, is considered to be among the highest reported (20.3%). Twenty-six (8.5%) patients with diagnosed CD and further 36 (11.8%) patients were considered potential for CD. A specialized follow-up and dietary counselling are essential in the management of patients affected by both type 1 diabetes mellitus and CD.

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