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THE FREQUENCY OF ANTI-CELIAC AUTOANTIBODIES AMONG CHILDREN WITH DIABETES MELLITUS REFERRED TO AHVAZ ABUZAR CHILDREN'S HOSPITAL

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Abstract

Background and Objective: Celiac disease (CD) is a chronic enteropathy caused by hypersensitivity to gluten. Most studies have shown more prevalence of CD is in the patients with diabetes type 1 (DM1). The prevalence of CD among DM1 children is unknown in our area. The aim of this study is to investigate the prevalence of celiac disease in diabetic children in Ahwaz.

Materials and Methods: This was a cross-sectional study conducted on 226 children with type I diabetes mellitus referring to Abuzar children's Hospital (endocrine department and clinic) from 2009 to 2011. The serum levels of Anti-tTG and IgA were measured respectively by immunometric Enzyme Immunoassay and immunotorbidimetric.

Findings: 28 of 226 patients (12.4%) with type I diabetes mellitus were positive for celiac (cut off $\geq$ 20 U/ml). 21 of seropositive patients were female (75%) and 7 (25%) were male. Prevalence was calculated respectively 18.4% and 6.2% in female and male.

Conclusion: Celiac disease in childhood diabetes (DM1) is common. Screening of celiac disease with serologic tests and confirming by biopsy is necessary, while early diagnosis can prevent diseases complications.

Keywords: Type I diabetes, Celiac disease, Screening.

Introduction

Type I diabetes which was called insulin-dependent mellitus diabetes or juvenile diabetes before is a common chronic metabolic disorder which it shows itself with the increase in blood sugar due to the reduction or absence of endogenous insulin. This reduction or absence of endogenous insulin happens due to loss of β cells in the islets of Langerhans of the pancreas due to an autoimmune process in the T lymphocytes (1). This type of diabetes often starts in childhood (the

average age of its onset is 7-15 years old), but may be arise at any age (1). Type I diabetes is associated with some other autoimmune diseases including thyroiditis, celiac disease, multiple sclerosis and Wilson's disease (1), so that the prevalence of celiac disease is more common than normal society in patients with type I diabetes (1-3).

Celiac disease which is also known as gluten sensitive enteropathy is a stable intestinal intolerance to gliadin in wheat and proteins dependent to it which causes the creation of mucosal lesions in the intestines of people who have its genetic predisposition (2). In this digestive disease, the small intestine villi hurt and the absorption of food is impaired. If patients with celiac disease consume a protein of gluten category which is available in some cereals such as wheat, barley, rye and sometimes oat, they are experiencing symptoms of intolerance. Apparently the login of gluten to the cells of intestinal villi causes immunity system response. The created inflammatory reaction causes villous atrophy and the decreasing of intestinal enzyme activity. Because much of nutrient absorption in the intestine will be done in the intestinal villi, the destruction of the villi causes malabsorption (9). The accompaniment of celiac disease with type I diabetes can lead to outbreak some complications related to celiac disease such as malnutrition, lagging growth, anemia, bone problems, irritability and lack of proper focus of these patients (2, 10). Also as regards patients with type I diabetes are at the age of growth and development, these complications can cause the creation of irreparable lesions in them. Anti-gliadin antibodies and anti-EMA antibodies are available in people with celiac disease. Lately in this disease has been used Tissue Transglutaminase antibodies to identify for more specific (2, 11, 12). 6% of patients with type I diabetes have positive anti-EMA (3). In various studies has been done antibodies against tissue transglutaminase has been variable from 8 to 11% in patients with type I diabetes (13, 14).

About the prevalence of celiac in Iran, more studies have been based on the measurement of autoantibodies of celiac in the adult population. In separate studies which was done in Tehran (15), Gonbad-e Qabus (16), Khuzestan (17) and Sari (18) in the general population, the prevalence of Anti tTG is reported about 1%. Considering that so far a few studies have been done in Iran and more studies were related to adult age groups and that the incidence of celiac is not specified in the children with type I diabetes of Khuzestan province, we decided to examine the incidence of celiac auto antibodies in children with type I diabetes in the south of the country by projecting a study. This study after doing provides this possibility to confirm the diagnosis of celiac disease after identifying the seropositive children by endoscopy and biopsy of the intestine and with on time treatment of celiac disease which is indeed gluten-free diet not

only we treat malabsorption and signs and symptoms associated with it including growth disorder, short stature, anemia, bone problems and so on, but also we prevent from creating a serious complication of celiac which is intestinal lymphoma and other forms of colon cancer specially adenocarcinoma of the small intestine.

Materials and Method

This study is a cross-sectional study which was conducted in the department of endocrinology Abuzar hospital in Ahwaz (Iran) between the 2004-2006 years. The studied statistical society was included diabetics referred to the mentioned department of endocrinology hospital with criteria of catching diabetes, younger than 15 years old, the consent of the patient or parent to participate in the study. As well as patients went out of study with criteria of unable to perform the relevant tests and serum IgA level lower than normal.

The method was in this case that all known previously patients who were recalled all patients of 1 to 15 years old with diabetes referred to endocrinology clinic of Abuzar hospital or hospitalized in the department of endocrinology of Abuzar hospital in the interval of October 2004 till October 2006 which their diabetes was proof in one of 3 ways 1) fasting glucose more than 126, 2) random sugar more than 200 in the presence of diabetes symptoms like polyuria, polydipsia and weight loss and 3) referred with DKA symptoms in the presence of laboratory evidences, serum sample was taken to measure the level of anti tTG-IgA and the level of IgA serum (Immunoturbidometric method). The immunometric Enzyme Immunoassay method is for quantitative detection of autoantibodies of IgA against tissue transglutaminase. The maximum normal amount is considered 10 u/ml. The used kit is German ORGENEC Diagnostic GmbH. The available kit identifies dedicated IgA antibodies. The sensitivity of this test is more than 90% based on majority of reports (19). Finally, the obtained information is registered in SPSS18 software was analyzed by t student ANOVA test, chi-square test and Fisher's exact test.

Results

In this study were studied 227 patients 1-15 years old with diabetes which one person was removed of study due to lower than normal level of serum IgA [a 9-year-old girl with the serum IgA 42 mg per deciliter (normal= 51-297). The average age of studied patients was 3.2 ±7.7 years old and the minimum and maximum observed age was respectively 1 and 15 years old. Also 41 people (18.1%) have age under 5 years old, 115 people (50.9%) are in the age range of 5-10 years old and 70 people (31%) are in the age range of 10-15 years old (figure 1). As well as the average age in less than

5 years old group was 1.1 ± 3, in the age group of 5-10 years old was 1.4 ±7.2 and in the age group of 10 years old and above was 1.3 ±11.4. 112 (49.6%) of studied patients were boy and 114 (50.4%) of them were girl. The average age of boys and girls under study was respectively 3.4 ± 7.7 and 3 ±7.7 years old and according to the T test the average age of boys and girls had not significant difference (p= 0.97).

In this study to avoid false positive answers was considered positive Anti tTG< 20 u/ml (9), so that in 28 (12.4%) of patients under study was positive and in 200 (87.6%) of them was negative. Among positive patients in terms of Anti tTG, the least was 22 and the most was 775. The average of Anti TTG in the positive patients was 131 ± 202.18 in terms of this antibody (values above 20). The average age of positive test patients was 3.1 ±7.7 and the average age of negative test patients was 3.2 ±7.8 years old, but according to T test was not observed a significant difference between two groups (p= 0.08). It is noteworthy that in the group of children lower than 5 years old 8 (19.5%), in the 5-10 years old group, 13 (11.3%) in the 10-15 years old group, 7 (10%) had positive test result and according to the chi-square test, there had not a significant difference between 3 groups (p= 0.3) (table 1).

The average positive Anti TTG serum level in the children under 5 years old (9) was 37 ± 65.86, in the children 5-10 years old (14) was 192.86 ± 274 and in children 10-15 years old (5) was 33 ±80.88 and according to the unilateral variance analysis test, Anti TTG level difference had not a significant difference in terms of age group of patients (p= 0.28). The Anti TTG result test was positive in 7 girls and 21 boys (25% versus 75%). Anti tTG frequency was calculated respectively 6.2% and 18.4% in the population pf boys and girls. And according to the chi-k test, the mentioned test result in girls and boys had a significant difference (p= 0.005). Anti TTG average level in boys was 35.02 ± 70.06 and in girls was 152.7 ±229.57 and according to T test the difference between the two sexes was not significant (p= 0.35).

Discussion

The overall goal of this study was to investigate the frequency of celiac autoantibodies in children with type I diabetes referred to Abuzar hospital of Ahwaz. In this study were examined the patients who had known catching to type I diabetes and according to the hypothesis of this study supposed the prevalence of celiac disease in these patients be higher than normal society. In this study, the prevalence of positive Anti-tTG IgA antibody among the children with diabetes was 12.4%. Which is in a one direction with the results of a similar study by Kakleas and et al based on 8.6%

prevalence (9), the study of Gabriel and et al based on 9.2% prevalence (14), the study of Bhadada and et al based on

11.1% prevalence (13) and the study of Saadah and et al based on 21.2% prevalence (20).

In our study positive Anti-tTG IgA antibody in females is 18.4% and in males is 6.2% which this difference is

significant statistically. It is necessary to mention that in the previous similar studies, the prevalence in gender is not

specified separately. As well as the frequency of positive Anti-tTG IgA antibody had not a significant difference in the

different age groups statistically. This in the way that in the study of Kakleas and et al the presence of this antibody had
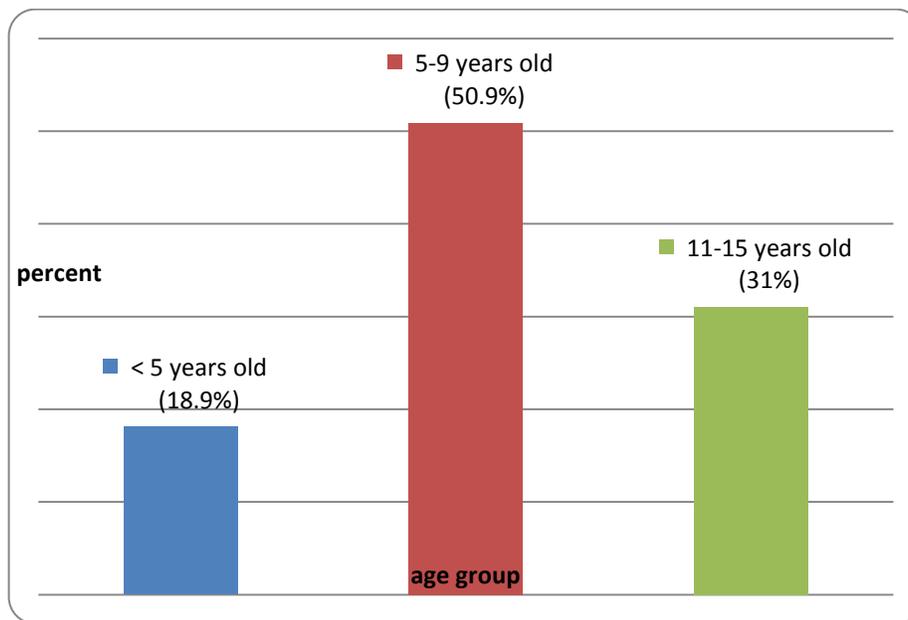
more accompaniment with a lower age (9).

Figure-1. The frequency percentage of age group of patients under study.

Table-1. The frequency distribution of the result of anti TTG test in terms of patients' age.

Age group Test result	Lower than 5 years old		5-10 years old		11-15 years old	
	Number	Percentage	Number	Percentage	Number	Percentage
Positive	8	19.5	13	11.3	7	10
Negative	33	80.5	102	88.7	63	90
Total	41	100	115	100	70	100

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