Research Article

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The Prevalence Of Celiac Disease in Saudi Patients with Type 1 Diabetes Mellitus: Cross Sectional Study

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Abstract

Objectives: *The relationship between type I diabetes mellitus (T1DM) and celiac disease (CD) has been known. The prevalence of CD in the Kingdom of Saudi Arabia (KSA) has not been determined. We examined the prevalence of celiac CD in patients in the Kingdom of Saudi Arabia with T1DM.*

Methods: *A cross-sectional study for 218 patients with T1DM at the diabetic clinic of King Fahd Armed Force Hospital in Jeddah, KSA between January 2008 and June 2009. Anti-tissue transglutaminase antibodies (Anti-TTG) was done in all patients. Duodenal biopsy were performed for patients with positive serology for Anti-TTG antibodies.*

Results: *There were 69 males and 54 females who ranged in age from 12-50 years (mean ± SD 21.3 ± 7.2). The age at onset of type I diabetes mellitus was 13.8 ± 7.1 and the duration of type I diabetes mellitus was between 1 and 28 years (7.6 ± 5.7). Elevated Anti-TTG levels were found in the sera of 16 (7.3%) of 218 diabetic patients in our clinic. The gender ratio of the Anti-TTG positive is 1 male: 3 female. All None had any gastrointestinal symptoms. 12 of the 16 subjects had duodonal biopsies and 8 (3.7%) biopsies showed total villous atrophy, 2 (0.8%) subtotal villous atrophy and 2 (0.8 %) chronic duodonitis , biopsy was not carried out in the other 4 subjects.*

Conclusion: *The maximum prevalence of celiac disease in our population was 7.3% based on immunological marker and the minimum was 4.6% based on antibodies and biopsy results.*

Keywords: Prevalence, Celiac disease, Type 1 Diabetes Mellitus.

Introduction

T1DM is known to be associated with other autoimmune conditions such as the celiac disease which may complicate the management of the disease [1-3]. Celiac disease is a chronic systemic autoimmune disorder aggravated by an ingestion of gluten, which is a protein found in wheat, rye and barely [4]. T1DM and CD both are associated with human leucocyte antigen(HLA) class II molecules, and presence of DQ8 and DQ2 have the major genetic association with T1DM and CD [5]. Although the genotyping test for CD has a strong negative predictive value to exclude CD but

still not recommended being a routine test for diagnosis. However HLA association was found to be present in general population and it is expensive and not available in every institute [6]. Studies done on different populations showed that CD occur in patient with T1DM varies from 4.4 to 11.1% [7]. Few studies from Saudi Arabia showed the prevalence varies from 4.9 to11.3% [8-10]. The aim of this study was to determine the prevalence of CD in patients with T1DM in a western region of Saudi Arabia and to evaluate the clinical profile of such patients.

Methods

The subject population included 218 patients with T1DM that were followed in the Diabetes Clinic at King Fahd Armed Force Hospital in Jeddah, Saudi Arabia in 2008 and 2009. We included patient's ≥12 years of age with the diagnosis of T1DM and demographic data of patient's characteristics were obtained. Anthropometric measures and nutritional data were obtained to compare between celiac and non-celiac patients, height, weight, Body mass index (BMI) was calculated using the formula of body weight in kilograms/height in meters squared, albumin, 25 hydroxyvitamin vitamin-D, calcium, hemoglobin and parathyroid hormone. Blood for determination of Anti-TTG antibodies were obtained during routine clinic visits and antibody positive patients were encouraged to undergo duodonal biopsy to confirm the diagnosis. Anti-TTG (IgA) samples were analyzed using Fluorescent Enzyme Immunoassay method (FEIA) and values more than 7U/ml is considered positive. Duodonal biopsy specimens were obtained and examined histological by the local pathologist at King Fahd Armed Force Hospital. The study was approved by Hospital Research and Ethical Committee.

Statistical Analysis

Univariate analysis of demography and clinical laboratory endpoints were accomplished using the unpaired t-test. Chi-square (X^2) test was used for categorical data comparison. Statistical analyzes were performed using SPSS Version 23.0. P values were based on two-sided tests and considered significant when P value <0.05.

Results

There were 69 males and 54 females who ranged in age from 12-50 years (mean ± SD 21.3 ± 7.2). The age at onset of type I diabetes mellitus was 13.8 ± 7.1 and the duration of type I diabetes mellitus was between 1 and 28 years (7.6 ± 5.7). Elevated Anti-TTG levels were found in the sera of 16 (7.3%) of 218 diabetic patients in our clinic. Clinical description and test results in the 4 males and 12 females are shown in Table 1. The gender ratio of the Anti-TTG positive is 1 male: 3 female. All None had any gastrointestinal symptoms. 12 of the 16 subjects had duodonal biopsies and 8 (3.7%) biopsies showed total villous atrophy, 2 (0.8%) subtotal villous atrophy and 2 (0.8 %) chronic duodonitis , biopsy was not carried out in the other 4 subjects as shown in table 2.

Patients	Age (years)	Gender	Diabetes duration (years)	Age at diagnosis of diabetes (years)	Anti-TTG (20 U/ml)	Histopathology of the duodonal biopsy
1	31.5	F	1	30.5	430	Total villous atrophy
2	15.5	F	1	14.5	7	Total villous atrophy
3	15.5	F	12	3.5	78	Total villous atrophy
4	31	F	9	22	1200	Total villous atrophy
5	14.5	M	7	7.5	28	Subtotal villous atrophy
6	13	M	1	12	19	Not done
7	34	F	28	6	420	Total villous atrophy
8	14	M	8	6	112	Chronic dudonitis
9	26	F	23	3	1200	Total villous atrophy
10	22	M	20	2	13	Chronic dudonitis
11	14	F	1	13	13	Not done
12	22	M	4	18	300	Total villous atrophy
13	23	F	1	22	710	Total villous atrophy
14	13	F	4	9	1200	Subtotal villous atrophy
15	26	F	9	17	7	Not done
16	24	F	6	18	65	Not done

Table 1: Clinical and histopthological profiles of patients with diabetes mellitus type1 and celiac disease.

Characteristics		Celiac disease		P value
		Yes (n=16)	No (n=202)	
Gender	Male (%)	4 (25)	87 (43.1)	0.2
	Female (%)	12 (75)	115 (56.9)	
Age (years)		22.2 ± 7.7	21.2 ± 7.2	0.6

HbA1c	10.2 ± 3.3	9.4 ± 2.2	0.2
Diabetes duration (years)	8.9 ± 8.7	7.5 ± 5.4	0.3
Weight (kg)	51.8 ± 17.1	61.4 ± 16.2	0.03
Height (cm)	154.3 ± 8.5	160.1 ± 10.0	0.01
Body mass index (kg/m^2)	21.6 ± 6.2	23.5 ± 5.3	0.2
25-hydroxyvitamin D (nmol/l)	23.1 ± 9.1	25.7 ± 11.2	0.4
Hemogobin (gm/dl)	12.2 ± 1.7	13.3 ± 1.6	0.009
Calcium (mmol/l)	2.3 ± 0.2	2.3 ± 0.2	0.2
Albumin (gm/l)	42.7 ± 3.3	43.3 ± 4.8	0.6
Alkaline phosphotase	165.0 ± 125.4	133.0 ± 96.3	0.2
24-hours Urine calcium (mmol)	3.3 ± 6.7	2.4 ± 1.9	0.2
Parathyroid hormone (pmol/l)	11.7 ± 11.8	5.4 ± 3.0	<0.001

Table 2: Comparison of Type 1 diabetes patients with and without celiac disease; Data are numbers, percentage and mean (± SD).

Discussion

Type I diabetes and CD are parts of polyglandular autoimmune disease, Type II cluster that includes thyroid, adrenal and other autoimmune disease. The association between type I diabetes mellitus and CD is not surprising, since both conditions have an increase frequency of human leukocyte antigen (HLA)-DR3 and other HLA number. Although CD occasionally precedes the onset, type I diabetes mellitus is diagnosed before CD in the great majority of patients. The prevalence of CD in T1DM considered to be high. It was found to be 5-7 times more prevalent in T1DM compared to non-diabetic patients [11,12]. With estimated prevalence of 4.4% to 11.1% in different populations [3,7]. In our study, we investigated a total of 218 adults with T1DM at a large center in Saudi Arabia, we found a prevalence of celiac disease in this group of patients is 7.3%. Although Anti-TTG antibodies are very sensitive markers for the presence of clinical CD, it is possible that some patients were antibody positive, without having frank disease. These patients could have latent diseases and need to be closely followed up. The maximum prevalence of CD in our population was 7.3%, based on immunologic findings and the minimum prevalence was 4.6%, based on antibody and biopsy results. Our prevalence of celiac disease in patients with T1DM are within the same range reported from studies in Saudi Arabia, 4.8% - 11.3% [8-10]. The prevalence reported from arab regions were within our range, Eygpt (11.2) (5.4), Libya (11%), Tunisia (5.3%) and Algeria (16.4%) [12-16].

The current recommendations for screening subjects with T1DM are to obtain autoantibodies for CD at diagnosis of diabetes and every two years thereafter or if symptomatic. The subjects with positive tTG should undergo small bowel biopsy to confirm the diagnosis [17]. Many studies have been done with the aim of identifying serological screening methods with appropriate diagnostic accuracy that could be an alternative to small intestine biopsy for the diagnosis of CD [24-26]. The diagnosis of CD involves several serological tests, anti-gliadin antibodies (AGA) have been used as a first step recognizing celiac autoimmunity, but currently it was replaced by the new effective and superior serology such as endomysial antibodies (EMA), tissue transglutaminase (TTG) antibodies [18.] The EMA and anti-TTG are highly sensitive and specific in detecting individuals with celiac disease [19,20]. Although the specificity of EMA is high enough but inadequate sensitivity resulted in some false negative values, in addition to that the test is high cost, complex, and handler-dependent [6,21-23]. Anti- TTG is the preferred first serological test to identify cases of CD because of its high sensitivity and accuracy [22]. The Presence of CD in T1DM patients is considered to be an additional chronic disease affect the clinical management of such cases such as predisposition to nutritional deficiencies and metabolic bone disease in most of cases.

CD affects growth parameters (short stature, weight loss) and glycemic index. We found that patients with celiac disease were significantly shorter and underweight and there was no significant difference in the celiac patients for the higher HbA1C.

The study was limited by the absence of control group of patients. Sample size may be another factor and the study reflects a single center region. The estimation of the prevalence of CD might be underestimated as we used only IgA anti-TTG, and IgA deficiency was not investigated.

We conclude that the maximum prevalence of celiac disease in our population was 7.3% based on immunological marker and the minimum was 4.6% based on antibodies and biopsy results. our data supports the importance of regular screening for CD in all patients with T1DM.

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