The Relation between Type One Diabetes Mellitus and Occurrence of Celiac Disease in Patients with in Babylon Teaching Hospital for Maternity and Children

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Abstract

Although the association between type 1 diabetes mellitus and celiac disease is well known, the presenting features and clinical characteristics of the two diseases, when they coexist, are less well documented so the study aimed to Estimate the incidence of celiac disease among patients attended to diabetic clinic in the Babylon maternity and pediatric teaching hospital. Include retrospective study involves patients with T1DM attending the pediatric diabetic clinic in the Babylon maternity and pediatric teaching hospital, were screened for celiac disease by serological testing for celiac antibodies (tissue transglutaminase). Control group without diabetes mellitus were also been evaluated. The control group are those who were admitted to the hospital for other diseases like gastroenteritis or chest infection, have no past medical history or chronic illnesses, and have no diabetes mellitus neither symptoms nor abnormal blood investigation results. Of the 50 patients with T1DM and 50 without diabetes mellitus, 3 patients (6%) of the study group tested were antibody positive. Celiac disease presented atypically in the majority of cases with an unpredictable interval between diagnosis of diabetes and celiac disease presentation. In this study, we found that patients with classical symptoms of celiac disease, (diarrhea, anorexia, abdominal distension, foul smelling stool, short stature, unexplained hypochromic anemia), may have negative screening for celiac disease, while those with positive screening test, were asymtomatic.

Keywords: *Diabetes mellitus, celiac disease, patients, maternity, children*

Introduction

Celiac disease is an immune-mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals and characterized by the presence of a variable combination of gluten-dependent clinical manifestations, celiac disease–specific antibodies, HLA-DQ2 or DQ8 haplotypes, and enteropathy [(1)]. HLA DQ2/DQ8 was present in 98,4% of celiac patients [(2)]. Celiac disease and T1DM have common autoimmune origins. Both are associated with the major histocompatibility complex class II antigen DQ2 encoded by the alleles, HLA typing may be useful in patients who are already on a gluten-free diet without having achieved a firm diagnosis. Those without HLA DQ2 or DQ8 are very unlikely to have celiac disease(3). Recent work has also revealed 7 shared non-HLA loci associated with CD and T1DM including RGS1 on chromosome 1q31, IL18 RAP on chromosome 2q12, TAGAP on chromosome 6q25, PTPN2 on chromosome 18p11, CTLA4 on chromosome 2q33, SH2B3 on chromosome 12q24, and a32-bp insertion-deletion variant on chromosome 3p21 [(3)]. This shared genetic basis is strongly suggestive of a common etiology for both conditions [(3)] The prevalence of celiac disease based on serologic test results is 1.4% and based on biopsy results is 0.7%. The prevalence of celiac disease varies with sex, age, and location.[(4)] While the prevalence of CD in IDDM has been reported to be 5–7 times greater than the general population with increased prevalence rates among most ethnic groups [(5)]. Clinical Spectrum of Celiac Disease SYMPTOMATIC:Frank malabsorption symptoms and signs (e.g., chronic diarrhea, failure to

thrive, weight loss) Extraintestinal symptoms and signs (e.g., anemia, fatigue, hypertransaminasemia, neurologic disorders, shortstature, dental enamel defects,arthralgia, aphthous stomatitis) SILENT:No apparent symptoms in spite of histologic evidence of villous atrophy In most cases identified by serologic screening in at-risk groups LATENT:Subjects who have a normal intestinal histology, but at some other time have shown a gluten-dependent enteropathy POTENTIAL:Subjects with positive celiac disease serology but without evidence of altered intestinal histology. Patients may or may not have symptoms and signs of disease and may or may not develop a gluten-dependent enteropathy later [(1)] (. Typical form of celiac disease presents with GI symptoms that characteristically appear at age 9-24 months, as chronic diarrhea, anorexia, abdominal distension, abdominal pain, poor weight gain or weight loss, and vomiting. Severe malnutrition can occur if the diagnosis is delayed. Behavioral changes are common and include irritability and an introverted attitude.GI symptoms in older children are typically less evident and include nausea, recurrent abdominal pain, bloating, constipation, and intermittent diarrhea [(6)]. In teenagers and young adults, anemia is the most common form of presentation. The classical presentation of CD can occur in T1DM patients, but many patients with CD and T1DM are either asymptomatic (silent CD) or present with only mild symptoms [(7)]. The diagnosis of CD is based on a combination of symptoms, antibodies, HLA status, and duodenal histology. The introduction of serologic testing has facilitated screening populations at risk for CD, including conditions such as T1DM as well as down and turner syndromes [(8)]. Serologic testing has also led to a rise in the rates of diagnosis of CD and altered the clinical pattern of CD presentation(9). As a general rule, testing should begin with serologic evaluation, the most sensitive and specific tests are IgA anti-tissue transglutaminase and IgA endomysial antibody, which have equivalent diagnostic accuracy (sensitivity 87 percent, specificity 95 percent) [(10)]. Biopsy remains the gold standard of diagnosis, Patients with a positive IgA endomysial or transglutaminase antibody test should undergo a small bowel biopsy, multiple biopsies should be obtained in the second and third portion of the duodenum(1). The duodenal mucosa may appear atrophic with loss of folds, contain visible fissures, have a nodular appearance or the folds may be scalloped, but such findings are not universally present in this disorder [(11)].

Aims of the Study

1- To estimate the incidence of celiac disease among children with T1DM. 2- To study the presentation of celiac disease among children with T1DM in terms of its time of onset and prognosis.

Patients and Methods

Patients and methods Retrospective study of two groups of patients, the first group (A) which includes 50 patients (27 male and 23 female), aged 2-12 years with the mean age of 7 years, classified as preschool age, school age, and adolescents, known cases of T1DM who were currently attending the Babylon maternity and pediatric teaching hospital in Babel from 17th of Oct. 2018 to 17th of June 2019, all those patients with T1DM have been screened for celiac antibodies (tissue transglutaminase) at time of diagnosis. The tissue transglutaminase antibody was measured by a specialist doctor with using Aeskulisa kits of Germany manufacture. The test is considered negative if the level of antibodies is less than 12 IU, equivocal between 12-18 IU, and positive if more than 18 IU. Patients with a positive celiac screen were recommended for an endoscopic gastroduodenojejunal biopsy to prove the diagnosis. Biopsies were examined histologically by expert histopathology doctor and the diagnosis of celiac disease was based on the characteristic findings of subtotal or total villous atrophy, crypt hyperplasia and intraepithelial lymphocyte proliferation in the biopsy. The mean height was measured for patients with positive serologic test in group (A) and compared with those who are celiac screen negative in the same group, to see if there is a significant difference in stature between these two groups. The mean weight was also measured for diabetic patients with celiac positive and compared with the patients with celiac screen negative matched for age and sex in the same group. Growth charts were used for both groups and the results were compared to

see if there is a significant difference or not. Levels of glycemic control were analyzed by comparing patients HbA1c in the study group (diabetic patients with celiac screen positive), with other subjects, (children who had diabetes mellitus without celiac disease), included in the study and who were ages and sex matched. Normally, it is less than 6, level between 6-8, is good metabolic control, 8-10, is fair metabolic control, and more than 10 is considered poor metabolic control. The second group (B), a control group, includes 50 non diabetic patients, (27 male and 23 female), aged 2-12 years with the mean age of 7 years. Those patients have been admitted to the hospital for other diseases such as gastroenteritis or chest infection. Blood sample was taken from them for screening of tissue transglutaminase antibody, and measurement of HbA1c, and compared with the patients of group (A). The mean height, weight of control group was also measured for comparison with a case study group. Full history and specific questions containing GI symtoms like abdominal pain, distention, weight loss ,offensive smelling stool and recurrent hypoglycemia had been taken. Statistical method used is p value according to SPSS version 13. When the p value is less than 0.05, it considered significant, if less than 0.001, it is highly significant, and if it is more than 0.05, it is not significant.

Results

Table (1): incidence of celiac disease in patients and control

Title	Celiac +ve	Celiac –ve	Total
Patients	3	47	50
Control	0	50	50

Only 6% (3 patients) have celiac disease, compared with 0.0% of control group, and it is not statistically significant. P value= 0.242

Table (2): Age distribution of patients and control group

AGE (years)	patients (A)					control (B)					p-value
	Celiac positive		Celiac negative		Total	Celiac positive		Celiac negative		Total	
	Count	percentage	Count	percentage	Count	Count	percentage	Count	percentage	Count	
<6	1	0.02	14	0.28	15	0	0	15	0.30	15	0.748
≥6-<11	2	0.04	26	0.52	28	0	0	28	0.46	28	0.527
≥11	0	0	7	0.14	7	0	0	7	0.14	7	0.913
Total	3	0.06	47	0.94	50	0	0	50	1.0	50	0.242

Age of the patients is not statistically significant in development of celiac disease.

Table (3): distribution of patients according to gender

sex	patients (A)					Control (B)					
	Celiac positive		Celiac negative		Total	Celiac positive		Celiac negative		Total	p-value
	Count	Percentage	Count	percentage	Count	Count	Percentage	Count	percentage	Count	
Male	1	0.02	26	0.52	27	0	0	27	0.54	27	0.533
Female	2	0.04	21	0.42	23	0	0	23	0.46	23	0.412
Total	3	0.06	47	0.94	50	0	0	50	1.0	50	0.297

There was no statistical significance to get celiac disease regarding gender of the patients.

Table (4): classification of positive cases according to age, serology, and biopsy results

Subject no.	Age (yrs.)	Antibodies +ve	Biopsy result
1	5.5	TTG	+VE
2	7	TTG	+VE
3	11	TTG	-VE

Two third of patients with positive antibodies, getting positive biopsy results.

Table (5): interval between diagnosis of type1 diabetes mellitus and detection of celiac antibodies

Patient	Interval (months)
Patient 1	6
Patient 2	13
Patient 3	16

All of the positive celiac patients, getting their diagnosis in the 1st two years from the onset of T1DM.

Table (6): gastrointestinal symptoms in patients with T1DM as having celiac antibodies+ve test

Patient	Sex	Age(yrs.)	Gastrointestinal symptoms
1	Male	5.5	None.
2	Female	7	Abdominal pain.
3	Female	11	Abdominal pain, weight loss, abdominal distension, offensive smelling stool.

There was no classical presentation of celiac disease in diabetic patients.

Discussion

The result of our study shows that only 3 patients (6%) have celiac disease, compared with no patient (0.0%) have celiac disease in control group. This result is nearly equal to other studies performed in Saudi Arabia[12]. This means that incidence of celiac disease is increased in patients with T1DM because of both celiac disease and T1DM have common autoimmune origins[13]. Both are associated with the major histocompatibility complex class II antigen DQ2 encoded by the alleles, HLA typing may be useful in patients who are already on a gluten-free diet without having achieved a firm diagnosis[14].

The age between 7-11 years is the commonest age to develop celiac disease in our study, which was statistically not significant when compared with control group. Unlike other study performed in Kanada, which shows a significant difference between patients and control[15. Possibly, because of small number of the patients and control groups in this study.

We have different presentations of celiac disease, in our study, signs and symptoms does not correlate with positive results, this agree with study performed in sample of turkish childreen by Ertekin V. etal[16]. This means that a diagnosis of celiac disease cannot be based on signs and symptoms alone without serological tests or a definitive small bowel biopsy[17, beacause the vast majority of patients with CD and T1DM have asymptomatic or subclinical CD with some vague gastrointestinal symotoms which means that the CD may remain asymptomatic[18].

Screening allows us to detect the atypical and asymptomatic presentations of celiac disease which may be beneficial in that the risk of potential complications can be reduced by early treatment[19].

In patients with positive cealiac disease and T1DM, the mean weight, height, are affected (<3rd centile), compared with patients who have T1DM alone, this is statistically significant, and indicate that celiac disease has a additional risk factor to cause growth failure[20]. This point has been inadequately described in previous studies. Some report short stature with no differences in weight[21], whereas others have shown no differences in height or weight[22]. Both these features may be consistent with the effects of villous atrophy secondary to celiac disease and subsequent carbohydrate malabsorption[23]. This may be further evidence of a possible common immunopathology in genetically susceptible individuals, however, the pathogenetic mechanisms remain unexplained[23].

The mean level of HbA1c is 11.5 for diabetic patients with positive celiac serology, compared with 9.53 for patients with T1DM alone, this mean that patients having celiac disease and T1DM may have poorer glycaemic control than patients with T1DM

alone. This result is nearly equal to other studies performed in Finland[24]. The reason for this may be that patients with co-existing celiac disease will result in decrease of pancreatic secretions[24]. In addition, the large proportion of asymptomatic cases mean that the intestinal mucosa has not been damaged sufficiently to cause symptoms of malabsorption[25, but in our study, this difference was not statistically significant . Possibly, because of the small number of the positive cases.

Conclusions

1-Six percent of T1DM associated with celiac disease, and its occurance associated with increase malabsorption and growth failure.

2-Results of our study show different presentations of celiac disease, investigations include celiac antibodies and biopsy are manditory for the diagnosis of celiac disease.

Recommendations

1-All patients with T1DM need screening investigations for celiac disease, and development of celiac antibodies may be negative in patients with T1DM at presentation, so follow up is very important.

2-Those patients with positive celiac antibodies need to be reffered to a gastroenterologist for small intestinal biopsy to confirm the diagnosis.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: "All experimental protocols were approved under the Babylon Teaching hospital for maternity and children and carried out in accordance with approved guidelines".

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