

Presence of Celiac Disease in Type 1 Diabetic Patients Presenting at Jinnah Hospital, Lahore

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Abstract

Background: Celiac disease (CD) is an auto-immune disease that usually occurs in genetically susceptible persons and is activated by gluten components of wheat. Type 1 diabetes is associated with CD with a prevalence rate of 4–6% but there is a lack of data on its prevalence in Pakistan.

Objective: The objective of this study is to evaluate the frequency of CD in patients having Type 1 diabetes presenting in Diabetic center (JAIDE) Jinnah Hospital Lahore and to observe its various clinical characteristics.

Methodology: In this cross sectional study, 68 patients following up for treatment of type 1 diabetes mellitus undergoing insulin therapy were selected. This study was conducted from July 2013 to January 2014 at JAIDE (Jinnah Allama Iqbal Institute of Diabetes and Endocrinology), Lahore. IgA anti tissue transglutaminase assay was used for screening of CD. Gluten free diet was advised in patients who turned out to be positive for CD. Patients were having the mean age of 15.8 ± 5.7 years. Positive antibodies were found in 8.8% patients having 33.3% males and 66.7% females with CD and 91.2% patients had no antibodies. In most of the cases, CD was silent and diagnosis of diabetes and CD was also unpredictable.

Conclusion: It is concluded that CD is very high in type 1 diabetic patients. Hence, screening for CD in type 1 diabetic patients should be done in order to have a better glycemic control and to prevent its long term complications.

Key Words: Type 1 DM, celiac disease, IgA anti tissue transglutaminase assay

Introduction

Genetically susceptible persons develop Celiac disease (CD) and multiple factors are involved in its

causation, basic underlined pathology involves autoimmunity. CD is stimulated by a various environmental factors and among the related factors, gluten prolamins are the major risks resulting in generation of anti-tissue transglutaminase which act as auto-antigen. CD target is small intestine, resulting inflattening of small intestinal mucosa over a period of time. Wheat, rye, and barley contain gluten and are hazardous for patients with CD especially having type 1 diabetes⁽¹⁾.

CD is a spectrum ranging from no clinical sign and symptoms to full blown malabsorption syndrome leading to weight loss diarrhea, micro nutrient

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depletion, hampering the quality of life. Relatives of CD have been recognized of Having the same problem even if asymptomatic⁽²⁾.

IgA anti tissue transglutaminase assay and IgA endomysial antibody is at present most sensitive and specific non-invasive test. These antibodies assays are 90% sensitive and >95% specific for making the diagnosis of celiac disease. CD can be excluded with appreciable reliability when this serological test turns out to be negative. IgA levels should be done if serological test turns out to be negative because underlying IgA deficiency can mask the diagnosis of CD. Gold standard test for diagnosis of CD is endoscopic biopsy of proximal small gut i.e. distal duodenum and proximal jejunum.^(3,4)

As a result of auto-immunity pancreatic beta-cells are destroyed by auto-antigens as a result of which there is lack of insulin and inevitably resulting in hyperglycemia and glycosuria. The clinical features include polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger), and weight loss.⁽⁵⁾

The genetic determinants of type 1 diabetes include single nucleotide polymorphism of class 2 human leukocyte antigen genes encoding DR and DQ. About 95% of patients with type 1 DM have either HLA-DR3 or HLA-DR4. HLA-DQs are also considered particular markers of type 1 DM susceptibility⁽⁶⁾. There are strong evidences regarding mimicry in genetic and environmental risk factors of type 1 diabetes and CD⁽⁶⁾.

Since late 1960s, CD has been associated with type 1 diabetes and nowadays has become clear that there is strong association of type 1 DM and CD. Four to Six percent prevalence in Type 1 DM has been shown⁽⁷⁾. Nowadays CD has been recognized as a spectrum with much more variability and a full blown disease just representing a small portion of total diseased population⁽⁸⁾. CD patient are more prone to develop type 1 diabetes if persistently exposed to gluten⁽⁹⁾.

The latest guidelines recommend screening of CD in type 1 diabetic patients yearly even if asymp-

tomatic⁽¹⁰⁾.

Early testing for anti-tissue transglutaminase antibodies may decrease the risk of glycemic variability and hypoglycemia in patient with type 1 diabetes owing to the early diagnosis making it feasible to carefully monitor the insulin needs and keeping the blood glucose levels within range after initiating insulin in these patients⁽¹¹⁾.

The previous studies done on type 1 diabetic patients do not reveal any information about the frequency of CD in our local population so in order to add the knowledge about type 1 diabetes and to devise a plan to do screening test for type 1 diabetic patients earlier in our population as well, we have designed this study which will help not only patients but the diabetes managing personals also.

Methods

In this observational cross-sectional study, a total of 68 patients were selected by using the formula

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where, P = prevalence 4-6%; z= 1.96; d= 5%; by taking average 5%, sample size came out to be approximately 68-70. Selection was based upon non probability purposive sampling and 68 patients with T1DM of any age, both males and females were selected. As per protocol, consent was taken after explanation of study agenda. The study was conducted for a period of six months from July 2013 onwards at JAIDE Lahore. Ethical committee granted permission for this research as per standard protocol.

Complete clinical assessment on basis of history and examination was done for all patients. Complete history about the duration and onset of diabetes was taken. Patients with other malabsorptive disorders on basis of history and previous records were excluded from the study and were tested for anti-tissue transglutaminase. Those patients who turned out to be having CD were advised gluten free diet.

Serological test i.e. IgA anti tissue transglutaminase, was done by ELISA method.

Analysis of data collected was done through SPSS versions 16.

Results

Our study represents the average age of patients as (mean $\pm$ SD) 15.8 $\pm$ 5.7 years. The age ranges were 6-10 years including 5 (7.4%) patients, 11-15 years including 31 (45.6%) patients and 16-20 years including 32 (47.0%) patients, amongst which 40 (58.8%) were males and 28 (41.2%) were females. Relating to the frequency of CD in patients, 6 (8.8%) had positive serology resulting from high anti-TTG titers while 62 (91.2%) had negative serology for CD by having anti-TTG titers within normal range. (Table 1).

Table 1: Distribution of patients by frequency of celiac disease (n=68)

Celiac disease	No. of patients	Percentage
Yes	6	8.8
No	62	91.2
Total	68	100.0

Patients with positive serology are categorized as 2 (33.3%) males and 4 (66.7%) females, according to GI symptoms as shown in Table 2.

Table 2: Distribution of patients by GI symptoms in celiac disease (n=6)

GI symptoms	No. of patients	Frequency
Abdomen pain	1	16.7
Diarrhea	1	16.7
Abdomen pain and diarrhea	1	16.7
Abdomen pain and constipation	1	16.7
No symptom	2	33.3
Total	6	100.0

The average range of anti-TTG titer (anti-transglutaminase antibodies) was 129.9 $\pm$ 21.3. The anti TTG titer range of <20 includes 1 (16.7%) patient, 20-100 includes 4 (66.7%) patients and

>100 includes 1 (16.7%) patients.

Table 3 shows clinical and serological data of positive serology patients.

Table 3: Clinical and serological data of 6 Patients (n=6)

Age	Sex	GI symptoms	Age of onset of T1DM	Age at diagnosis of CD	Anti TTG Titer
17	Male	Abdomen pain	10	17	556
19	Female	Diarrhea	07	19	28.1
20	Male	Asymptomatic	05	20	21.87
14	Female	Abdomen pain & diarrhea	02	14	67.00
14.5	Female	Asymptomatic	06	14.5	88.30
08	Female	Abdomen pain & constipation	03	08	18.60

Discussion

The present study shows rate of recurrence of CD as 8.8%. Though this recurrence is not well illustrated in Pakistan, but relating to 0.6%-1% prevalence of CD in general population of developing countries, it shows that Pakistani population prevail CD 8-14 times more frequently than what can be predicted for general population.

ADA (American Diabetes Association) recommends regular screening of type 1 diabetic patients with CD shortly after diagnosis⁽¹²⁾ and it can be proved by the fact that these antibodies can appear in any patient at any age and time of life^(13,14).

1-10% prevalence of CD in children with T1DM is shown worldwide^(15,16), excluding Argentina and Algeria, where prevalence rates were 13.9%⁽¹⁷⁾ and 16.4%⁽¹⁸⁾ correspondingly. Our study is first time reporting the frequency of CD in Pakistan, which is related to the genetic, life style, nutritional and environmental factors.

Controversies exist regarding diagnosis and treatment of subclinical CD however risk of developing complications like gastrointestinal tumors,

particularly small intestine tumors, persists in asymptomatic T1DM⁽¹⁹⁾. Use of gluten free diet can reduce this malignancy risk and this risk becomes equal to that of the general population if strict consumption of gluten free diet is followed for five years⁽²⁰⁾.

Our study represents the mean age of the patients as 15.8±5.7 years with 58.8% males and 41.2% females. 8.8% patients had positive antibodies for CD. Our results are comparable with Al-Hussaini et al study⁽¹⁷⁾ in which 11.3% patients had positive serology for it.

In our study, among patients with high anti-TTG antibodies, there were 2 (33.3%) male and 4 (66.7%) female patients amongst which 66.7% patients had GI symptoms comparable to the study of Al-Hussaini et al.,⁽¹⁷⁾ where 41.6% patients had gastrointestinal symptoms like abdominal pain, diarrhea and constipation.

The average range of anti-TTG antibodies was 129.9±21.3. The anti TTG titer range of <20 and >100 includes 1 (16.7%) patients while 4 (66.7%) patients are included in anti TTG titer range of 20-100.

In literature, most studies have proved the positive correlation of villous atrophy with high anti-transglutaminase antibodies. Particularly if antibody titers are 3 times above the normal limit then sensitivity and specificity for diagnosis of CD was 100% and 99% respectively⁽¹⁷⁾.

Larger studies in order to determine the effect of dietary modifications in CD in overall growth and glycemic control are required.

Conclusion

CD is a significant finding in patient with T1DM in our population and CD if present in diabetic patient can affect the glycemic control adversely so in order to have best glycemic control in T1DM, CD should be kept in mind while treating a patient with T1DM. Hence all medical and educator staff concerned in management of T1DM should know the relation of T1DM and CD so the benefit of gluten free diet can be given to the patients in order

to prevent the immediate and long term complications of CD as well as to have a better glycemic profile in T1DM patients.

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