

# Frequency of patients with Abnormal Celiac Serological Marker (Anti-Tissue Transglutaminase IgA) in newly Diagnosed Cases of Diabetes Mellitus-I without Gastrointestinal Tract Symptoms

SAJID MUSTAFA<sup>1</sup>, MUHAMMAD ALI RABBANI<sup>2</sup>, M HASSAM REHIM<sup>3</sup>

## ABSTRACT

**Aim:** To determine the frequency of patients with abnormal celiac serological marker (anti-tissue transglutaminase IgA) in newly diagnosed cases of type I diabetes mellitus without gastrointestinal tract symptoms.

**Methods:** This cross sectional study was conducted at Department of Pediatric Medicine, Sahiwal Medical College, Sahiwal from September 2015 to August 2016. Total 100 newly diagnosed cases at the time of admission in this unit with Type I diabetes mellitus without GIT symptoms (loose motions with or without vomiting), either male or female having age from 6-16 years were selected.

**Results:** Mean age of the children was 10.66±3.55. Out of 100 diabetic children, abnormal celiac serological marker was found in 20 (20%) children. Abnormal celiac serological marker was noted in 12(20.34%) children and 8(19.51%) children respectively in age group 6-11 year and 12-16 years. Abnormal celiac serological marker was found in 8 (21.62%) male and 12(19.05%) female children.

**Conclusion:** Results of this study showed a high percentage of abnormal celiac serological marker. Insignificant association of abnormal celiac serological marker with age, gender and family history of diabetes mellitus was noted.

**Keywords:** Diabetes mellitus, celiac disease, anti tissue transglutaminase orogastroduodenal biopsy

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## INTRODUCTION

Celiac disease (CD) is a chronic, immunologically determined form of enteropathy affecting the small intestine in genetically predisposed children and adults in response to ingestion of gluten-containing foods.<sup>1</sup> Celiac disease is one of the most frequent autoimmune disorders occurring in Type 1 diabetes mellitus (T1DM). The prevalence of CD in T1DM varies from 3 to 16%<sup>2,3</sup>.

The both conditions are strongly linked to the HLA system, in particular the haplotypes A1, B8, DR3 and DQ2.<sup>4</sup> Moreover celiac disease is believed to have an adverse effect on T1DM, particularly with regards to glycemic control. In addition, coexistence of CD is associated with significant increased risk of diabetic associated morbidity and mortality<sup>5</sup>. The clinical presentation of CD in T1DM is symptomless in approximately half of cases. So serological screening for CD should be performed in all T1DM patients by means of antibodies at the time of diagnosis of T1DM<sup>3</sup> and the diagnosis should be confirmed by duodenal biopsy in cases of abnormal serological screening.<sup>1</sup> There are number of antibodies like anti-endomysium IgA antibody, anti-

tissue transglutaminase IgA antibody, anti-tissue transglutaminase IgG antibody (anti tTG), anti-gliadin IgA and IgG and anti-reticulin IgA which may be elevated in celiac disease<sup>6</sup> but the best for screening CD in T1DM is anti-tissue transglutaminase IgA<sup>7,8</sup>.

Both T1DM and CD are common in Pakistan but the exact incidence is unknown<sup>9,10</sup>. Moreover the frequency of CD in T1DM varies from study to study internationally but no Pakistani data is available both nationally and locally. This study is design to generate local data, as no local data is available. If frequency is found to be high than strategy could be made to screen all newly diagnose cases of Type-I diabetes mellitus for celiac disease.

## MATERIAL AND METHODS

This cross sectional study was conducted at Department of Pediatric Medicine Sahiwal Medical College, Sahiwal from September 2015 to August 2016. Total 100 newly diagnosed cases at the time of admission in this unit with Type I diabetes mellitus without GIT symptoms (loose motions with or without vomiting), either male or female having age from 6-16 years were selected for this study.

All patients with type-I diabetes mellitus having gastrointestinal symptoms (loose motions with or without vomiting), parents/guardians unwilling to be included for the study, IgA deficient cases confirmed

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<sup>1</sup>Assistant Professor Pediatrics, Sahiwal Medical College, Sahiwal

<sup>2</sup>Nishtar Medical College and Hospital, Multan

<sup>3</sup>Assistant Professor Community Medicine, Sahiwal Medical College, Sahiwal

Correspondence to Dr. Sajid Mustafa,

Email: drsajidmustafa@yahoo.com Cell: 03008366088

by measuring total serum IgA level were excluded from the study.

**OPERATIONAL DEFINITION**

**Abnormal celiac serological marker:** Patients will be labeled as abnormal celiac serological marker if anti-tissue transglutaminase IgA is  $\geq 18\text{u/ml}^8$ . Fasting plasma glucose  $\geq 126\text{mg/dL}$  on more than one occasion with interval of more than 24 hours apart.

After selecting patients, history was taken and examination was done of each case. Five ml blood sample was taken from every patient and sent to laboratory. The quantitative determination of anti-tissue transglutaminase IgA was done by indirect chemiluminescence immunoassay. Findings were entered on pre-designed proforma along with demographic profile of the patients. Patients were labeled as abnormal celiac serological marker if anti-tissue transglutaminase IgA is  $\geq 18\text{u/ml}$

Data was entered on computer software SPSS version 16. The quantitative variables of the study i.e., age, was presented as mean and standard deviation. The frequency of abnormal celiac serological marker (anti-tissue transglutaminase IgA), gender, any family history of celiac disease were calculated.

Stratification was performed to control effect modifier like age, gender, any family history of celiac disease. The Chi square test was applied to see the effect of age, gender, any family history of celiac disease on outcome variable i.e., abnormal celiac serological marker (anti-tissue transglutaminase IgA). P value  $<0.05$  was taken as significant.

**RESULTS**

Total 100 newly diagnosed diabetic children were selected in this study. Mean age of the children was  $10.66 \pm 3.55$ . Out of 100 diabetic children, abnormal celiac serological marker was found in 20(20%) children (Fig.1). Selected children were divided into two age groups i.e., age group 6-11 years and age group 12-16 years. Out of 59(59%) children of age group 6-11 years, abnormal celiac serological marker were noted in 12(20.34%) children. Out of 41(41%) children of age group 12-16 years, abnormal celiac serological marker were noted in 8(19.51%) children. But statistically insignificant association between abnormal celiac serological marker and age was noted with p value 1.00 (Table 1).

Male children were 37(37%) and female children were 63(63%). Abnormal celiac serological marker was found in 8(21.62%) male children and 12(19.05%) female children. Insignificant association between abnormal celiac serological marker and gender was noted with p value 0.474 (Table 2).

Total 12(12%) children were found with family history of diabetes mellitus and 88 (88%) children were without family history of diabetes mellitus. Insignificant association of abnormal celiac serological marker with family history of diabetes mellitus was noted with p value 0.60 (Table 3).

Fig. 1: Frequency of abnormal celiac serological marker

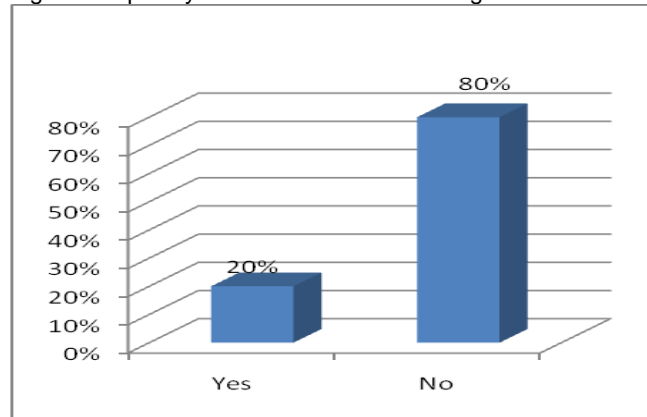


Table 1: Relation of abnormal celiac serological marker with age

Age group	Abnormal Celiac Serological Marker		Total
	Yes	No	
6-11	12(20.34%)	47(79.66%)	59(59%)
12-16	8(19.51%)	33(80.49%)	41(41%)
Total	20(20%)	80(80%)	100

P value: 1.00

Table 2: Relation of abnormal celiac serological marker with gender

Gender	Abnormal Celiac Serological Marker		Total
	Yes	No	
Male	8(21.62%)	29(78.38%)	37(37%)
Female	12(19.05%)	51(80.95%)	63(63%)
Total	20(20%)	80(80%)	100

P value: 0.474

Table 3: Relation of abnormal celiac serological marker with family H/O DM

Gender	Abnormal Celiac Serological Marker		Total
	Yes	No	
Yes	5(41.67%)	7(58.33%)	12(12%)
No	15(17.05%)	73(82.95%)	88(88%)
Total	20(20%)	80(80%)	100

P value: 0.60

**DISCUSSION**

Celiac disease (CD), a common cause of chronic malabsorption in children is characterized by mucosal damage of the small intestine due to hypersensitivity to gluten containing food. Clinically, the disease ranges from silent asymptomatic to active full blown picture, it has been reported that celiac disease is more common among patients with type 1 diabetes mellitus (DM) than among the general population<sup>11</sup>.

The gold standard for the diagnosis of (CD) is duodenal biopsy, however screening for celiac disease has been recommended for specific risk factors; the anti-endomysium IgA antibody and anti-tissue transglutaminase IgA antibody (anti tTG) tests are highly sensitive and specific in identifying individuals with celiac disease.<sup>12</sup> The antiendomysium IgA antibody test is an immunofluorescent technique and is relatively expensive; interpretation is operator dependent and Prone to errors so that it has largely been replaced by anti-tissue transglutaminase IgA antibody tests, which are simpler to perform and have similar sensitivity and specificity. Anti-gliadin IgA and IgG and anti-reticulon IgA antibody tests are no longer recommended tests due to lack of specificity<sup>13</sup>.

The objective of present study was determine the frequency of patients with abnormal celiac serological marker (anti-tissue transglutaminase IgA) in newly diagnosed cases of type I diabetes mellitus without gastrointestinal tract symptoms. In present study abnormal celiac serological marker was noted in 20% children. In one study by Honar et al frequency of abnormal celiac serological marker was reported as 14.4%<sup>8</sup>. Abduljabbar et al<sup>14</sup> reported frequency of abnormal celiac serological marker as 8.6% in type I diabetic children.

Sharifi et al<sup>15</sup> found abnormal celiac serological marker in only 8% type I diabetics. A recent study conducted in UK, of total 113 children and adolescents with T1DM, 6.2% were found with abnormal celiac serological marker<sup>16</sup>. About 12.3% Danish children were found with abnormal celiac serological marker<sup>17</sup>. The prevalence of CD in Libya and Algeria was 21.3% and 16.3% respectively<sup>18-19</sup>. In the Middle-East countries, positive serology tests for CD was detected in 20.9% of Saudi children with T1DM<sup>20</sup>. The prevalence detected in our diabetic population was much higher than other different of the world. This difference may due to differences in genetics and the environment.

## CONCLUSION

Results of this study showed a high percentage of abnormal celiac serological marker. Insignificant association of abnormal celiac serological marker with age, gender and family history of diabetes mellitus was noted.

## REFERENCES

1. Guandalini S, Assiri A. Celiac disease: a review. *JAMA Pediatr* 2014;168(3):272-8.

2. Sapone A, Bai JC, Ciacci C, Dolinsek J, Green PH, et al. Spectrum of gluten-related disorders: consensus on new nomenclature and classification. *BMC Med* 2012;10:13.
3. Volta U, Tovoli F, Caio G. Clinical and immunological features of celiac disease in patients with Type 1 diabetes mellitus. *Expert Rev Gastroenterol Hepatol* 2011;5(4):479-87.
4. Sollid LM, Thorsby E. HLA susceptibility genes in celiac disease: genetic mapping and role in pathogenesis. *Gastroenterology* 1993;105(3):910-22.
5. Akirov A, Pinhas-Hamiel O. Co-occurrence of type 1 diabetes mellitus and celiac disease. *World J Diabetes* 2015;6(5):707.
6. Lohi S, Mustalahti K, Kaukinen K. Increasing prevalence of coeliac disease over time. *Aliment Pharmacol Ther* 2007;26:1217-25.
7. Gabriel S, Mihaela I, Angela B, Mariana A, Doru D. Prevalence of IgA antitissue transglutaminase antibodies in children with type 1 diabetes mellitus. *J Clin Lab Anal* 2011;25(3):156-61.
8. Honar N, Karamizadeh Z, Saki F. Prevalence of celiac disease in patients with type 1 diabetes mellitus in the south of Iran. *Turk J Gastroenterol* 2013;24(2):122-6.
9. Hakeem R, Fawwad A. Diabetes in Pakistan: epidemiology, Determinants and prevention. *J Diabetol* 2010;3(4):1-13.
10. Ramakrishna BS. Celiac disease: can we avert the impending epidemic in India? *Indian J Med Res* 2011;133:5-8.
11. Elli L, Branchi F, Tomba C, Villalta D, Norsa L, Ferretti F, et al. Diagnosis of gluten related disorders: Celiac disease, wheat allergy and non-celiac gluten sensitivity. *World J Gastroenterol*. 2015 Jun 21;21(23):7110-9.
12. Lebowl B, Rubio-Tapia A, Guandalini S, Newland C, Assiri A. Diagnosis of Celiac Disease. *Gastrointest Endosc Clin N Am*. 2012 Oct;22(4):661-77.
13. Nandiwada SL, Tebo AE. Testing for Antireticulin Antibodies in Patients with Celiac Disease Is Obsolete: a Review of Recommendations for Serologic Screening and the Literature. *Clin Vaccine Immunol*. 2013 Apr;20(4):447-51.
14. Abduljabbar HA, Matloub HY, Yassin BAG. Prevalence of Celiac Disease in type 1 Diabetes Mellitus in children and adolescents attending Children Welfare Teaching Hospital. [cited 2016 June 18]; Available from: <http://www.repository.uobaghdad.edu.iq/uploads/magazines/collection/20of%20medicine/2012/Volume%2054%20Issue%201/55118.pdf>
15. Sharifi N, Khoshbaten M, Aliasgarzade A, Bahrami A. Celiac disease in patients with type-1 diabetes mellitus screened by tissue transglutaminase antibodies in northwest of Iran. *Int J Diabetes Dev Ctries*. 2008;28(3):95-9.
16. Goh C, Banerjee K. Prevalence of coeliac disease in children and adolescents with type 1 diabetes mellitus in a clinic based population. *Postgrad Med J*. 2007 Feb;83(976):132-6.
17. Hansen D, Brock-Jacobsen B, Lund E, Bjorn C, Hansen LP, Nielsen C, et al. Clinical benefit of a gluten-free diet in type 1 diabetic children with screening detected celiac disease. *Diabetes Care*. 2006;29:2452-6
18. Ashabani A, Abushafa U, Abusrewil S, Abdelazez M, Tuckova L, Tlaskalova-Hogenova H. The prevalence of celiac disease in Libyan children with type 1 diabetes mellitus. *Diabetes Metab Res Rev*. 2003;19:69-75.
19. Boudraa G, Hachelaf W, Benbouabdellah M, Belkadi M, Benmansour FL, Touhami M. Prevalence of celiac disease in children and their first-degree relatives in West Algeria: Screening with serological markers. *Acta Paediatr*. 1996;412:58-60.
20. Saadah OI, Al Agha AE, Albokhari SM, Almoghales JA. Prevalence of celiac disease in Saudi children with type 1 diabetes mellitus. *J Pediatr Gastroenol Nutr*. 2004;39:S211.