

Research Article

Frequency of patients with abnormal celiac serological marker (anti-tissue transglutaminase IgA) in newly diagnosed cases of diabetes mellitus-I without gastrointestinal tract symptoms.

**¹Muhammad Uzair, ²Hira Shahid
and ³Noor ul Ain Fatima**

¹Assistant Professor, Department of Pediatrics, Children Hospital, Lahore

²Ex-House Officer, Bahawal Victoria Hospital, Bahawalpur

³Ex-house Officer, Sir Gangaram Hospital, Lahore

[Received: 02/12/2018; Accepted: 20/12/2018; Published: 21/12/2018]

ABSTRACT

Objective: 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.

Material and methods: This cross sectional study was conducted at Children Hospital, Lahore from July 2017 to December 2017 over the period of 6 months. Total 90 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 1-16 years were selected. Blood sample was taken of every patients and send to laboratory for anti-tissue transglutaminase IgA analysis.

Results: Mean age of the patients was 8.39 ± 4.84 years. Total 22 (24%) patients found with abnormal celiac serological marker. Abnormal celiac serological marker was found in 16 (32%) patients and 6 (15%) patients respectively in age group 1-8 years and 9-16 years. Statistically insignificant association between abnormal celiac serological marker and age groups was noted with p value 0.085. Significantly higher rate of abnormal celiac serological marker was noted in male patients as compared to female patients with p value 0.045.

Conclusion: Results of present study showed a higher number of abnormal celiac serological marker. Most of the patients were adolescents and insignificant association between age group and abnormal celiac serological marker was noted. Most of the male patients found with abnormal celiac serological marker as compared to female patients.

Keywords: celiac serological marker, diabetes mellitus-I and gastrointestinal tract symptoms.

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.¹ 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%.^{2,3} The both conditions are strongly linked to the HLA system, in particular the haplotypes A1, B8, DR3 and DQ2.⁴ 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.⁵ 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 T1DM³ and the diagnosis should be confirmed by duodenal biopsy in cases of abnormal serological screening.¹ 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 disease⁶ but the best for screening CD in T1DM is anti-tissue transglutaminase IgA.⁷

Honar et al 2013⁸ showed that 14.4% diabetic children were having a high titer of anti-tissue transglutaminase immunoglobulin A ($\geq 18\text{u/ml}$), out of which biopsy confirmed CD in 33% cases.

Both T1DM and CD are common in Pakistan but the exact incidence is unknown.^{9,10} Moreover the incidence of CD in T1DM varies from study to study internationally but no Pakistani data is available both nationally and locally. So this study is planned to know the abnormal celiac serological marker (anti-tissue transglutaminase IgA) in T1DM.

OPERATIONAL DEFINITION

Abnormal celiac serological marker:

Patients was labeled as abnormal celiac serological marker if anti-tissue transglutaminase IgA is $\geq 18\text{u/ml}$.⁸

Type-I diabetes mellitus:

Defined as fasting plasma glucose $\geq 126\text{ mg/dL}$ on more than one occasion with interval of more than 24 hours apart.

MATERIAL AND METHODS

This cross sectional study was conducted at Children Hospital, Lahore from July 2017 to December 2017 over the period of 6 months. Total 90 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 1-16 years were selected. 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 by measuring total serum IgA level were excluded from the study.

The study was approved by local ethical committee. The verbal informed consent was taken from patient parents and guardians if parents are not accompanying the patients.

The history was taken and examination was done of each case to get required data. 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. Data was collected through predesigned Performa along with demographic profile of the patients.

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) and gender was calculated.

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

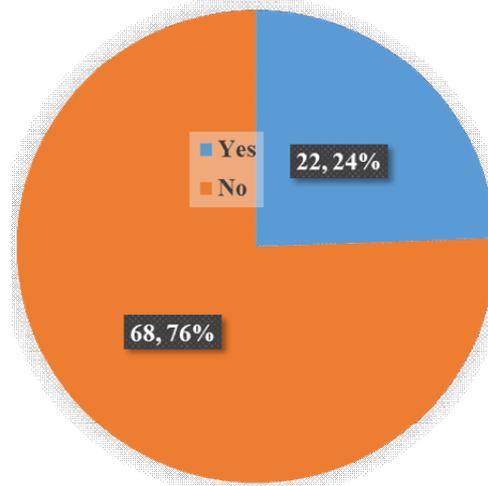
RESULTS

Total 90 newly diagnosed cases of type I diabetes mellitus without gastrointestinal tract symptoms were selected for present study. Mean age of the patients was 8.39 ± 4.84 years. Total 22 (24%) patients found with abnormal celiac serological marker. (Fig. 1)

Minimum age of the patients was 1 year and maximum age was 16 years. Patients were divided into two age groups i.e. age group 1-8 years and age group 9-16 years. Total 50

(55.56%) patients belonged to age group 1-8 years and 40 (44.44%) patients belonged to age group 9-16 years. Abnormal celiac serological marker was found in 16 (32%) patients and 6 (15%) patients respectively in age group 1-8 years and 9-16 years. Statistically insignificant association between abnormal celiac serological marker and age groups was noted with p value 0.085. (Table 1)

Fig. 1: frequency of abnormal celiac serological marker



Total 57 (63.33%) patients were male and 33 (36.67%) patients were female. Abnormal celiac serological marker was seen in 18 (31.58%) male patients and in 4 (12.12%) female patients. Significantly higher abnormal celiac serological marker was noted in male patients as compared to female patients with p value 0.045. (Table 2)

Table 1: Stratification for age

Age group	Celiac Disease		Total	P value
	Yes	No		
1-8	16 (32)	34 (68)	50 (55.56)	0.085
9-16	6 (15)	34 (85)	40 (44.44)	
Total	22 (25)	68 (75)	90	

Table 2: Stratification for gender

Gender	Celiac Disease		Total	P value
	Yes	No		
Male	18 (31.58)	39 (68.42)	57 (63.33)	0.045
Female	4 (12.12)	29 (87.88)	33 (36.67)	
Total	22 (25)	68 (75)	90	

DISCUSSION

Celiac disease is a chronic disease of the gastrointestinal system, in which characteristic atrophy of the small intestinal mucosa occurs in genetically predisposed people in response to the presence of gluten in food.¹¹ It is a continuous intolerance of gluten, gliadin and responsive prolamins that are present in wheat, rye and barley. The major characteristic of the disease is intestinal damage due to an immune defect (autoimmune disease) that occurs in people with a genetic background.¹²

Celiac disease is a chronic disease of the proximal segment of the small intestine.¹³ The most important characteristics of celiac disease are: permanent intolerance of gluten (a constituent of some cereals); typical mucosal findings in jejunal biopsy specimen; Diabetologia Croatica typical presentation (malabsorption); and subsequent improvement on a gluten-free diet with complete histologic and clinical remission, and recurrence of the disease when the diet is broken.¹⁴ The disease can clinically manifest at any age, most

commonly in the first few years of life, a few months of introducing gluten in diet.

The purpose of present study was 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.

Mean age of the patients was 8.39 ± 4.84 years. Total 22 (24%) patients found with abnormal celiac serological marker. A study by Honar et al 2013⁸ showing that 14.4% diabetic children were having a high titer of anti-tissue transglutaminase immunoglobulin A (≥ 18 u/ml) which were lower than our findings. In another study by Abduljabbar et al,¹⁵ total 152 patients with type I Diabetes Mellitus were selected, celiac disease was found in 16.5% patients, 67(44.1%) males and 85(55.9%) females. The age ranges from (1-18) years with a mean of 10.3 years \pm 3.6 SD with no statistical difference between boys and girls. Results of this study are also not in agreement with our findings. In our study total 57 (63.33%) patients were male and 33 (36.67%) patients were female. Abnormal celiac serological marker was seen in 18 (31.58%) male patients and in 4 (12.12%) female patients. Significantly higher abnormal celiac serological marker was noted in male patients as compared to female patients with p value 0.045.

Nowier et al¹⁶ reported prevalence of celiac disease as 5.48% out of 73 patients of type-I DM. In this study mean age of the patients was 9.18 ± 4.09 years. In same study male patients were 35.62% and female patients were 64.38%.

In a study by Goh et al,¹⁷ of the 113 patients with T1DM, 7 (6.2%) tested antibody positive. The prevalence of celiac disease in high risk populations is up to 20 % in first degree relatives, 3–6 % with type 1 DM.¹⁸ The relatively high prevalence rate supports the practice of screening patients with Type 1DM for celiac disease.

The overall prevalence of CD in patients of all ages with type 1 diabetes with similar rates for pediatric and adult groups in the community-based study was 7.0%.¹⁹ Comparable North American studies have focused on selected

patients seen at referral centers and observed a prevalence of CD in type 1 diabetes that ranged from 1.4 % to 5.1 % in pediatric patients and from 3.5 % to 6.0 % in adults.^{20,21} Two European studies had evaluated a combined pediatric and adult type 1 diabetic cohort and observed a biopsy proven prevalence of CD of 3.6 % and 5.7 %, respectively.^{20,22}

CONCLUSION

Results of present study showed a higher number of abnormal celiac serological marker. Most of the patients were adolescents and insignificant association between age group and abnormal celiac serological marker was noted. Most of the male patients found with abnormal celiac serological marker as compared to female patients.

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, Hadjivassiliou M, 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):707-14.
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. Gujral N, Freeman HJ, Thomson AB. Celiac disease: prevalence, diagnosis, pathogenesis and treatment. *World journal of gastroenterology: WJG.* 2012 Nov 14;18(42):6036.
 12. Barker JM, Liu E. Celiac disease: pathophysiology, clinical manifestations, and associated autoimmune conditions. *Advances in pediatrics.* 2008 Sep 1;55(1):349-65.
 13. Murray JA, Rashtak S, Rubio-Tapia A. Celiac disease: Diagnosis of celiac disease in pediatric patients. *Nature Reviews Gastroenterology & Hepatology.* 2009 May;6(5):260.
 14. Kolaèek S. Celiakija. In: Vuceliæ B et al., eds. *Gastroenterologija i hepatologija.* Zagreb: Medicinska naklada, 2001:561-573.
 15. Abduljabbar HA, Matloub HY. Prevalence of Celiac Disease in type 1 Diabetes Mellitus in children and adolescents attending Children Welfare Teaching Hospital. *J Fac Med Baghdad.* 2012;5.
 16. Nowier SR, Eldeen NS, Farid MM, Rasol HAA, Mekhemer SM. Prevalence of celiac disease among type 1 diabetic Egyptian patients and the association with autoimmune thyroid disease. *Bratisl Lek Listy.* :5.
 17. Goh C, Banerjee K. Prevalence of coeliac disease in children and adolescents with type 1 diabetes mellitus in a clinic based population. *Postgraduate medical journal.* 2007 Feb 1;83(976):132-6.
 18. Karinen Hannele. Genetics and family aspects of coeliac disease. Kuopio University Publications D. Medical Sciences, 2008; 423, 110 p.
 19. Maquart FX, Gillery P, Bernar JF et al. A method for specific-ly measuring hemoglobin A1c with disposable commercial ion exchan-ge column. *Clin Chem Acta* 1980; 108: 329—332.
 20. Aktay AN, Lee PC, Kumar V et al. The prevalence and clinical characteristics of celiac disease in juvenile diabetes in Wisconsin. *J Pediatr Gastroenterol Nutr* 2001; 33: 462—465.
 21. Hansen D, Bennedbaek FN, Hansen LK et al. High prevalence of coeliac disease in Danish children with type I diabetes mellitus. *Acta Paediatr* 2001; 90: 1238—1243.
 22. Lindstedt G, Berg G, Jansson S et al. Clinical use of laboratory thyroid tests and investigations. *J Int Fed Clin Chem* 1994; 6: 136—141.