

**Research Article****Prevalence of Anti-Tissue Transglutaminase IgA in Type 1 Diabetes Mellitus Patients Attending Al-Dewanyia Teaching hospital**Rateb F. Abo Khadher<sup>1</sup>, Ibrahim Abdulmajeed Altamemi<sup>2</sup><sup>1</sup>Al-dewanyia Teaching Hospital (Immunology Unit), Iraq<sup>2</sup>Department of Microbiology, College of Medicine, Al-Qadisiya University, Iraq**\*Corresponding author**

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**Abstract:** It has been shown that there was an association between celiac disease and type 1 diabetes mellitus due to shared immunological background, periodic serological screening is necessary for early diagnosis of celiac disease due to this relation. Thus, the objective is to study the prevalence of anti-tissue transglutaminase antibody IgA in patients with type 1 diabetes. A total of 80 patients with type 1 diabetes attending Dewanyia Teaching Hospital; 35 boys, 45 girls with mean age of 10.3 year  $\pm$  3.7 and mean duration of diabetes 3.5 years  $\pm$  2.5, from June 2013 - June 2014 were screened for anti-tissue transglutaminase IgA. The present study found that the Anti-tissue transglutaminase antibody was positive in 13 patients, more in girls (68%), making the prevalence of celiac disease about 8.6%. The classical presentation of the disease was lacking in most patients, but they presented with short stature which was below the third percentile in 79% of patient with celiac disease. In most cases Celiac disease was diagnosed within the first year of diabetes diagnosis. Thus, we concluded that Annual autoantibody screening is recommended, for early diagnosis and management of patients with diabetes type 1.

**Keywords:** Diabetes mellitus, celiac disease, anti-tissue transglutaminase antibody, celiac risk factor, anti-glutamic acid decarboxylase, DM leading celiac disease

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**INTRODUCTION**

Celiac disease (CD) is a common inflammatory disease in children it is characterized by damaging the mucosa of the small intestine due to hypersensitivity to wheat gliadin [1, 2]. Clinically, the disease ranges from silent asymptomatic to active full blown picture (2), it has been reported that celiac disease is more common among patients with type 1 diabetes mellitus (DM) than among the general population [3, 4]. The gold standard for the diagnosis of (CD) is total villous atrophy [1, 5, 15], however screening for celiac disease has been recommended for specific risk factors [4, 5]; the standard serological tests for celiac disease are IgA endomysial antibodies. The anti-endomysium IgA antibody test is an immunofluorescent technique and is relatively expensive (monkey oesophagus sections or human umbilical vein); 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. The anti-endomysium IgA and anti-tissue transglutaminase IgA antibody test can be falsely negative with IgA deficiency, which is associated with an increased incidence of celiac disease but serological tests are now recognized to have high

sensitivity and specificity, and many patients, particularly children, will not be biopsied [4, 5]. The prevalence of celiac disease in children with type 1 diabetes mellitus ranges between 1.3 to 12% worldwide and may contain high population of clinically asymptomatic and atypical cases [4, 6, 7]. The association between type 1 diabetes mellitus and celiac disease was suggested to be due to sharing by seven chromosome regions between the two diseases and having the same mechanism of autoimmunity related tissue damage and dietary antigen intolerance [8, 9]. The terms latent and silent celiac disease are used to refer to patients who have inherited the genes that predispose them to celiac disease but have not yet developed the symptoms or signs of celiac disease. Latent celiac disease refers specifically to patients who have abnormal antibody blood tests for celiac disease but who have normal small intestines and no signs or symptoms of celiac disease [10]. Silent celiac disease refers to patients who have abnormal antibody blood tests for celiac disease as well as histopathological abnormality in the small intestine but have no symptoms or signs of celiac disease [10]. An anti-glutamic acid decarboxylase (Anti GAD) auto antibody is recognized as one of the major serological markers

for type 1 diabetes and has been reported to be higher in type 1 diabetes patients [11]. Positivity varies based on age, duration of diabetes and ethnicity [12]. This study was undertaken to estimate the prevalence of anti-tissue transglutaminase IgA antibody among patients with type one DM attending the Dewanya teaching hospital.

**PATIENTS AND METHODS**

A total of 80 patients, 35 males and 45 females with type 1 diabetes mellitus attending the department of diabetes and endocrinology in Al- Dewanya teaching Hospital were included in this study over a period of one year (June 2013 - June 2014). Diagnosis of type 1 DM was made according to WHO criteria [13]. Full history and complete physical examination were performed for all patients. Patients' records were reviewed for registering information including age of onset of DM, duration of the disease, date of presentation of gastrointestinal symptoms suggestive of celiac disease like diarrhea, abdominal distension, loss of weight or failure to gain weight, anorexia, constipation and stunted growth. Anti-tissue transglutaminase (anti tTG) IgA class, anti-glutamic

acid decarboxylase (Anti GAD) antibodies by Elisa were done for the patients.

**RESULT**

A total of 80 patients with type I Diabetes Mellitus were included in the study, 35 (44.1%) males and 45 (55.9%) females. The age ranges from (1-18) years with a mean of 10.3 years ± 3.6 SD, and mean duration of diabetes 3.5±2.5, with no statistical difference between boys and girls (Table 1). Anti-tissue transglutaminase antibody test Results showed that only 13 patients (32% boys & 68% girls) were positive compared to 77 patients with negative results (46.5% boys & 53.5% girls), yet the association were statistically not significant and antibodies gradually disappear with gluten avoidance and reappear with on gluten challenge. ( $\chi^2 = 1.8$ ,  $df = 1$ ,  $p$  value > 0.05) (Table 1). Table (2) showed the distribution of our data according to age, gender, and duration of diabetes both in patient with and without anti-tissue transglutaminase. Regarding anti GAD test, there was no statistically significant association in patients with anti-tissue transglutaminase and as shown in (Table 3).

**Table 1: distribution of study group by Age, Gender, duration of D.M and anti-tissue transglutaminase IgA result**

Variables	Males	Females	Total
Patients No. %	35 (44.1%)	45 (59.9 %)	80 (100%)
Age (in years )	1-16	3.5-18	1-18
Means ± SD*	9.9 ± 3.8	10.6 ± 3.5	10.3 ± 3.6
Duration of DM (in year)**	3.6 ± 2.7	3.3 ± 2.4	3.5 ± 2.5
Anti-tTG IgA***			
Positive	4.0 (32%)	9.0 (68 %)	13 (16.5 %)
Negative	31 (46.5 %)	36 (53.5 %)	67 (83.5 %)

\*Difference is statistically not significant (T test,  $p$  value > 0.05)

\*\*Difference is statistically not significant (T test,  $p$  value > 0.05)

\*\*\* The association is statistically not significant ( $\chi^2 = 1.8$ ,  $df = 1$ ,  $p$  value > 0.05)

**Table 2: Distribution of the Study Group by Age, Duration of DM (in years) and Presence of Anti-tTG IgA**

Variables	DM with Anti-tTG IgA +ve	DM with anti-tTG IgA -ve	Total
Age (in Years) Mean ± Sd*	8-15 10.3 ± 2.4	1-18 10.3 ± 3.8	1 – 18 10.3 ± 3.6
Duration of DM (in year)**	3.3 ± 2.4	3.5 ± 2.6	3.4 ± 2.5

\* Difference is statistically not significant (T test,  $df = 150$ ,  $p$  value > 0.05)

\*\* Difference is statistically not significant (T test,  $df = 150$ ,  $p$  value > 0.05)

**Table (3) Distribution of the Study Group according to Anti GAD test Results\***

Anti-GAD test	DM without Anti-tissue TG IgA		DM with anti-tissue TG IgA	
	No.	%	No.	%
Positive	17	23	3.0	46.2
Negative	56	77	4.0	53.8
Total	73	100	7.0	100

\* The association is statistically not significant ( $\chi^2 = 3.4$ ,  $df = 1$ ,  $p$  value > 0.05)

## DISCUSSION

The current study showed that the prevalence of anti-tissue transglutaminase IgA in type 1 DM to be 8.6 % this result was lower than what was found by El-Saadany *et al.* in Egypt (11.2%) [16]. While it is higher than what was found in Iran (6.2%) [17], and nearly the same prevalence was found by many other researchers from Greece (8.6%) [18], Kerala-India (8%) [19], Canada (7.7%), and Cerutti study (6.8%) [20]. Very low prevalence rates were found in Germany (1.4%) [21], US [22] and Scotland (5.8%) [23]. There was no significant difference in anti-tTG IgA Ab test results between boys and girls, although out of 13 patients, they were tested positive, girls were higher (68%) than boys (32%) same conclusion was reached by the Kostas *et al.* [18] and Cerutti *et al.* study [20] while in the Egyptian study the girls: boys ratio was nearly equal [24]. The age of the onset of DM was nearly the same in both groups (with or without anti-tTG), and most of those who suffered from celiac disease developed the disease after short period of having DM, same results were reached by other worker as in the Kostas *et al.* study [18] and disagreed with that of Jacob & Kumar study [19] and Cerutti study [20] in which diabetic children with celiac disease developed DM at a significantly younger age than those without celiac. Patients with positive serology need close follow up to elicit early diagnosis of CD. Presentation of CD like abdominal distension flatulence, anorexia and steatorrhea or constipation is not considered a clear evident any more making periodic screening for CD especially within the first five years after diagnosing type 1 DM in these children essential [25], other studies noticed a decline in linear growth in patients with type 1 DM and CD with a frequency ranging from 30% to 96% [26, 27], this emphasized that all diabetic children specially having stunted growth should be screened for CD, although there are other causes for stunted growth [2, 5]. The anti-GAD positivity, there was no statistically significant association among diabetic patients with and without anti-tTG IgA, same conclusion was reached by Kostas *et al.* [18], this might reflect the possibility of loss of antigenic stimulation due to cell depletion by time. Despite attempts to make screening convenient and free, many diabetic patients were apprehensive about CD testing. For patients and families, diabetes is a challenging condition that requires daily effort to balance meals, activity, and insulin administration to maintain adequate metabolic control. The effect of an additional chronic disease, such as CD, may substantially affect the quality of life in diabetic patients. Unfortunately, we are not aware of studies that address the psychosocial effect of CD screening in asymptomatic diabetic patients [28, 29].

## CONCLUSION

Children with type 1 diabetes should be screened annually for celiac disease.

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