Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2015; 3(8D):2994-2997 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Research Article

Prevalence of Anti-Tissue Transglutaminase IgA in Type 1 Diabetes Mellitus Patients Attending Al-Dewanyia Teaching hospital

Rateb F. Abo Khadher[1], Ibrahim Abdulmajeed Altamemi[2]
[1]Al-dewanyia Teaching Hospital (Immunology Unit), Iraq
[2]Department of Microbiology, College of Medicine, Al-Qadisyia University, Iraq

***Corresponding author**
Ibrahim Abdulmajeed Altamemi
Email: Ibrahim.altamemi@gmail.com

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 1diabetes. A total of 80patients with type 1 diabetes attending Dewanyia Teaching Hospital; 35 boys, 45 girls with mean age of 10.3 year± 3.7 and mean duration of diabetes3.5years ±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 about8.6%. The classical presentation of the disease was lacking in mostpatients, 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

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. Theanti-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 biopsied[4, 5].The prevalence of celiac disease in children with type 1 diabetes mellitus ranges between 1.3 to12%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 silentceliac 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 type1 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 transglutaminaseIgA antibody among patients with type one DM attending the Dewanyia teachinghospital.

PATIENTS AND METHODS

A total of 80 patients, 35 males and 45 females with type1 diabetes mellitus attending the department of diabetes and endocrinology in Al- Dewanyia teaching Hospital were included in this study over a period of one year (June2013 -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 ofDM, 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) (Table1). 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 nostatistically significant association in patients with anti- tissue transglutaminase and as shown in (Table 3).

Table 1: distribution of study groupby 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) Means± SD*	1-16 9.9 ± 3.8	3.5-18 10.6± 3.5	1–18 10.3 ± 3.6
Duration of DM (in year)**	3.6 ± 2.7	3.3 ± 2.4	3.5 ± 2.5
Anti-tTGIgA*** Positive Negative	 4.0 (32%) 31 (46.5 %)	 9.0 (68 %) 36 (53.5 %)	 13 (16.5 %) 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 withAnti-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 Groupaccording 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 IgAin type 1 DM to be 8.6 % thisresult 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%), andCerutti 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 wasreached 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 type1DM in these children essential [25], other studies noticed a decline in linear growth in patients with type1 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 reflects the possibility of loss of antigenic simulation 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 tomaintain 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.

REFERENCES

1. Hill ID, Drks MH, Liptak GS, Colletti RB, Fasano A, Guandalini S et al.; North American society For paediatric Gastroenterology. Hepatology and nutrition. Guideline for the diagnosis andtreatment of celiac disease in children: recommendation of North American Society for paediatric gastroentrolog. Hepatology and nutrition. J Ped. Gastroenterol Nutr, pediatr Gastroenterol Nutr., 2005; 40; 1-19.
2. Catassi C Fabiami E; The spectrum of celiac disease in children. Baillieres Clin Gastroenterrol., 1997; 11:487.
3. Koletzko S, Burgin Wolff A, Koletzko B, Knapp M, Burger W, Gruneklee D et al.; Prevalence ofceliacdisease in diabetic children andadolescents. Amulticentre study. Eur J Pediatr, 1988; 148:113-117.
4. Gronin, Shanahon F; Insulin dependent diabetes mellitus and celiac disease. Diab Med,2001; 18: 169–177.
5. Brnski D, Troncone R; Celiac disease In: Behrman RE, KliegmanRM, JensonHB; Nelson Textbook of Pediatrics),19th ed. Pheladelpha ,WB Saunders,2011; 1308-1311.
6. Cacciari E, Salardi S, Volta U, Biasco G, Patersotti S, Mantovani W et al.; Prevalence and characteristics of celiac disease in type 1 diabetes mellitus. Acta Pediatr Scand, 1987; 76:671-2.
7. De Vitis I, Ghirlanda G; Prevalence of coeliac disease in type 1 diabetes. A multicenter study. Acta Paediatr, 1996; 412: (Suppl) 56-57.
8. Lite, Jordan; Diabetes and celiac disease: Agenetic connection. 2008, from: www.scientificamerican.com/.../post.cfm.
9. Smyth DJ, Plagnol V, Walker NM, Cooper JD, Downes K, Yang JHM et al.; Shared and Distinct Genetic variants in type1diabetes and celiac disease. NEJM, 2008; 10:2767-2777.
10. Khoshoo V, Bhan MK, Jain R, Philipsad, Walker Smith JA, Unsworth DJ et al.; Celiac disease as a cause of protracted diarrhoea in Indian children Lancet, 1998; 1:126-7.
11. Park YS , park HW , Kim J8, Kim DS and et al.; "Measurement of anti-GAD 65 auto antibodiesin potential with type 1 Diabetes mellitus with /without autoimmune Thyroid diseases" ,Endocrinology Metabolism, 2000; 15 (2) : 190 - 203.
12. Michael J, Foweler MD; Diagnosis, classification and lifestyle treatment of diabetes, Clinical diabetes, 2010; 28 (2): 79-86.Prevalence of Celiac Disease in type 1 Diabetes Mellitus in children Hana A; Abduljabbaradolescents attending Children Welfare Teaching Hospital J Fac Med Baghdad,2012; 32(54).

13. World Health Organization; Group Report of diabetes mellitus technical report, series no.727.World Health Organization Geneva, 1985.
14. Marsh MN, Gluten; major histocompatibility complex, and the small intestine. A molecular andimmunological approach to the spectrum of gluten sensitivity (celiac sprue). Gastroenterology, 1992; 102(1):330-54.
15. Husby S, KoletzkoS, KorponaySzabo IR, MearinML, Phillips A, Shamir R, TronconeR, GiersiepenK, BranskiD, CatassiC, LelgemanM, Maki M, Ribes-Koninckx C, Ventura A, Zimmer KP; forthe ESPGHAN Working Group on Celiac Disease Diagnosis, on behalf of the ESPGHAN Gastroenterology Committee. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the Diagnosis of Celiac Disease. J Pediatr Gastroenterol Nutr., 2012; 54(1):136-60.
16. EI SaadanyS, Farrag W, Saleh MA, Esmail SA, Menessy A, Hamouda H; Prevalence of celiac disease in Egyptian children and adolescents with Diabetes Mellitus: a clinical, biochemical &histopathologicalstudy.20August 2008.
17. Moayeri H, Bahremand SH; Prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus. Medical Journal of the Islamic Republic of Iran, 2004; 18(1):39-43.
18. Kakleas K, Karayianni C, Critselis E, Papathanasiou A, Petrou V, Fotinou A, Karavanaki K; The prevalence and risk factors for celiac disease among children and adolescents with T1DM 9August. Diabetic Research clinical Practice, 2010; 99(2):202-208.
19. Jacob A, Kumar SPS; Celiac disease inpatients with type 1diabetes screened by tissue transglutaminase antibodies in southern Kerala, India. The Internal Journal of Nutrition and Wellness, 2009; 8 (2).
20. Cerruti F, Bruno G, Chiarelli F, Lorini R, Meschi F, Saccetti; Younger age at onset and sexpredict celiac disease in children and adolescents with type 1 diabetes. Diabetescare,2004;27(6):1294-8
21. Kordonouri O, Dietrich W, Becker M, Muller C; Antibodies to tissue transglutaminase predict latent celiac disease in children with diabetes mellitus. Diab Res Clin Pract., 1999; 44:S6.
22. Patwari AK, Anand VK, Kapur G, Narayan S; Clinical and nutritional profile of children with celiac disease. Indian Pediatr., 2003; 40:337 –342.
23. Ventura A, Neri E, Vghi C; Glutin –dependent diabetes- related and thyriod- related autoanti bodies in patients with celiac disease. JPediatr., 2000; 137:263-265.
24. Schober E, Bittmann B, Huppe A, Jagar A; Screening by anti-endomysium antibody for celiacdisease in diabetic children and adolescents withtype1 diabetes. diabetic research clinicalpractice2010.
25. Saukkonen T, Savilahti E, Reijonen H, IIonen J, Tuomilrhto-Wolf E, Akerblom HK; Celiac disease: frequent occurrence after clinical onset of insulin dependent diabetes mellitus. Childhood diabetes in Finland Study Group. Diabet Med, 1996; 13:464-9.
26. Shihab SM, attiaNand AL-Ashwal A; Prevalence and characteristics of celiac disease ininsulin dependent diabetes mellitus in Saudi Arabia. Saudi JGastroenterol, 2003; 9:110.
27. Bird G, Ahmed M, Rossk MG; Coeliac disease in children and adolescents with IDDM: Clinical characteristics and response to gluten free diet. Diad Med., 1998; 15:38.
28. Rubin RR, Peyrot M; Quality of life anddiabetes; Diabetes Metab Res Rev., 1999; 15:205–218.
29. Jacobson AM,De Groot M, Samson JA; Theevaluation of two measures of quality of life inpatients with type 1 and type2 diabetes. Diabetes Care, 1994; 17:267-274.