PO Box 2345, Beijing 100023, China
www.wjgnet.com
wjg@wjgnet.com

World J Gastroenterol 2007 March 14; 13(10): 1599-1601
World Journal of Gastroenterology ISSN 1007-9327

RAPID COMMUNICATION

Prevalence of coeliac disease in patients with autoimmune thyroiditis in a Turkish population

Sefa Guliter, Fahri Yakaryilmaz, Zubeyde Ozkurt, Reyhan Ersoy, Derya Ucardag, Osman Caglayan, Pınar Atasoy

Sefa Guliter, Fahri Yakaryilmaz, Section of Gastroenterology, Department of Internal Medicine, Kirikkale University Faculty of Medicine, Kirikkale, Turkey
Zubeyde Ozkurt, Department of Internal Medicine, Gazi University Faculty of Medicine, Turkey
Reyhan Ersoy, Department of Endocrinology, Ankara Ataturk Education Hospital, Ministry of Health, Ankara, Turkey
Derya Ucardag, Department of Internal Medicine, Kirikkale University Faculty of Medicine, Kirikkale, Turkey
Osman Caglayan, Department of Biochemistry, Kirikkale University Faculty of Medicine, Kirikkale, Turkey
Pınar Atasoy, Department of Pathology, Kirikkale University Faculty of Medicine, Kirikkale, Turkey
Correspondence to: Dr. Sefa Guliter, MD, Department of Internal Medicine, Kirikkale University Faculty of Medicine, Emek Mah 78 Sokak 3/8, Ankara, 06510, Turkey. sguliter@yahoo.com
Telephone: +90-312-2225621 Fax: +90-318-2244697
Received: 2006-12-13 Accepted: 2007-02-09

Abstract

AIM: To investigate the prevalence of coeliac disease in a series of Turkish patients with autoimmune thyroiditis.

METHODS: Sera from 136 consecutive patients with newly diagnosed autoimmune thyroiditis and 119 healthy blood donors were tested for IgA tissue transglutaminase antibody with enzyme-linked immunosorbent assay. Endoscopic mucosal biopsy from the second part of duodenum was performed in patients with positive antibody test.

RESULTS: Eight patients (5.9%) and one control subject (0.8%) were positive for IgA tissue transglutaminase antibody (OR: 7.38, 95% CI: 0.91-59.85, P = 0.04). Six patients and one control agreed to take biopsies. Histopathological examination revealed changes classified as Marsh Ⅲa in one, Marsh Ⅱ in one, Marsh Ⅰ in two, and Marsh 0 in two patients with autoimmune throiditis, and Marsh Ⅰ in one blood donor.

CONCLUSION: Turkish patients with autoimmune thyroiditis have an increased risk of coeliac disease and serological screening may be useful for early detection of coeliac disease in these patients. Our findings need to be confirmed in a larger series of patients.

Key words: Coeliac disease; Autoimmune thyroiditis; Tissue transglutaminase

Guliter S, Yakaryilmaz F, Ozkurt Z, Ersoy R, Ucardag D, Caglayan O, Atasoy P. Prevalence of coeliac disease in patients with autoimmune thyroiditis in a Turkish population. *World J Gastroenterol* 2007; 13(10): 1599-1601

http://www.wjgnet.com/1007-9327/13/1599.asp

INTRODUCTION

Coeliac disease (CD) is characterized by malabsorbsion of nutrients, chronic inflammation and damage of the small intestinal mucosa caused by the ingestion of gliadin fraction of wheat gluten and similar alcohol-soluble proteins of barley and rye in genetically susceptible subjects[1]. While the elimination of gluten from the patient's diet results in clinical and complete histological recovery, reintroduction of gluten leads to relapse[1,2].

The clinical presentation of CD is extremely heterogeneous. Typical symptoms include chronic diarrhea and abdominal distension[2,3]. However, only few patients with CD show clinical malabsorption, while most patients have subtle symptoms, if any[1]. Therefore, the disease is clearly underdiagnosed[3]. Diagnostic tests of anti-endomysial antibodies (EMA) and the anti-tissue transglutaminase (tTG) for CD with a sensitivity and specificity of over 95% were recently introduced[3-5]. The prevalence of CD has changed over the past 30-40 years with the availability of new sensitive serologic tests which have increased the possibility of the diagnosis of subclinical cases[1]. Screening studies show a high prevalence of CD (between 1/80-1/300) among both healthy children and adults in European countries[6,7].

It is known that CD is associated with some autoimmune disorders, especially type- I diabetes mellitus, autoimmune thyroid diseases, collagen disorders, Addison's disease, pernicious anaemia, alopecia and autoimmune hepatitis[8-10]. Among adult patients with autoimmune thyroiditis, the prevalence of CD has been reported to be 3.3-4.8 times more than in the general population[11-14]. In contrast, a study reported a CD prevalence of 0% in patients with autoimmune thyroiditis[15].

To our knowledge, there is no study in Turkey about prevalence of CD in patients with autoimmune thyroiditis. The aim of this study was to define the prevalence of CD in a series of Turkish patients with autoimmune thyroiditis.

MATERIALS AND METHODS

Between January and September 2006, 136 consecutive patients aged between 17 and 65 years (mean age 43.1 ± 10.5), including 118 female (86.8%) and 18 males (13.2%) with newly diagnosed autoimmune thyroiditis (AT) and 119 healthy blood donors aged between 18-64 years (mean age 41.5 ± 10.1), including 109 female (91.6%) and 10 males (8.4%) as control group, were included into the study. The diagnosis of AT was made based on clinical and biochemical findings, including positive titres of anti-thyroid peroxidase antibody and/or anti-thyroglobulin antibodies, and a positive ultrasound scan defined by either diffuse marked hypoechogenicity or a focal non-homogeneous pattern with hypoechogeneous areas. None of the patients had other autoimmune diseases such as Addison's disease, vitiligo, and diabetes mellitus.

Antibody test

Sera from patients with AT and controls were stored at -70℃. IgA anti-tTG assays were carried out by enzyme-linked immunosorbent assay (ELISA), (Aida Gmbh, Germany). Cut-off values were 15 IU/mL set by the manufacturer. In all subjects who were positive for IgA anti-tTG serum iron, ferritin, folate and vitamin B12 levels were assayed, and endoscopic mucosal biopsy was performed from the second part of duodenum in patients who agreed to the procedure. Samples of duodenal mucosa were graded according to the modified Marsh classification[16,17].

The study protocol was approved by the ethics committee of the Kirikkale University Hospital.

Statistical analysis

Fisher's exact test was used to compare CD prevalence and gender differences between the two groups. The comparison of mean ages between the two groups was done with Student's *t* test. The statistical analyses were performed using a statistical program for PC (SPSS 11.0 for Windows, SPSS Inc., IL, USA). *P* values of less than 0.05 were considered statistically significant.

RESULTS

The age and gender were similar in both groups ($P = 0.21$ and $P = 0.32$, respectively). Clinical, serologic and histological features of the patients with AT are shown in Table 1.

IgA anti-tTG antibody was found to be positive in 8 (7 female) patients (5.9%) with AT (Table 1) and in one female blood donor (0.8%) (OR: 7.38, 95% CI: 0.91-59.85, $P = 0.04$).

Six patients (5 female and 1 male) and one control subject agreed to endoscopy and duodenal biopsy. Four patients (3 female and 1 male) and one control subject had histological findings of CD, and two patients with AT had normal duodenal histology. Histopathological examination revealed changes classified as Marsh IIIa in one, Marsh II in one, Marsh I in two patients with AT, and Marsh I in one blood donor.

Among the 8 patients who were positive in antibody tests, one patient (case 7), a 61 years old female with histological CD as Marsh IIIa, had iron-deficiency anemia and osteopenia, and one patient (case 8), a 40 years old female with histological CD as Marsh II, had iron-deficiency, but no anemia (Table 1). The other 6 patients with AT and one control subject who had positive antibody test did not have any symptoms, signs or laboratory findings of malabsorbtion. All subjects with histologically proven CD were prescribed gluten-free diet.

Table 1 Clinical, antibody and histological features of 8 autoimmune throiditis patients with positive IgA anti-tTG test

Patient	Gender	Age (yr)	Anti-tTG IgA (> 15 IU/mL)	Duodenal biopsy	BMI (kg/m^2)	Malabsorption
1	F	31	79.6	Not performed	26.0	Absent
2	F	56	55.1	0	29.9	Absent
3	F	18	57.8	0	22.3	Absent
4	F	34	26.2	I	23.7	Absent
5	F	44	17.9	Not performed	35.3	Absent
6	M	35	43.4	I	27.6	Absent
7	F	61	39.1	IIIa	24.0	Present
8	F	40	27.9	II	30.1	Present

BMI: body mass index. Modified Marsh classification: IIIa = mild atrophy, II = intraepithelial lymphocytosis + crypt hyperplasia, I = intraepithelial lymphocytosis (> 40/100 epithelial cells).

DISCUSSION

The association between coeliac disease and autoimmune thyroiditis has been previously reported. An increased prevalence of coeliac disease has been found in patients with AT and Graves' disease[11-14]. Moreover, it has been demonstrated that many coeliacs are prone to autoimmune thyroid dysfunction[18,19]. This association could be related to a common genetic background (HLA-DQ2 and HLA-DQ8).

Serologic tests developed in the past decade provide a non-invasive tool to screen both individuals at risk for the disease and general population. IgA anti-tTG assays by ELISA are highly sensitive (90%-98%) and specific (94-97) for diagnosis of coeliac disease. It is now widely available, less costly, and easier to perform than the immunofluorescence assay used to detect IgA EMA[2].

Screening studies show a high prevalence (between 1/80-1/300) of CD among both healthy children and adults in European countries[6,7]. The prevalence of coeliac disease in 2000 healthy blood donors has recently been found to be 1.3% (1/77) in Turkey[20]. This study shows that the prevalence of CD in the Turkish population is relatively high in comparison to Western world.

In our study, the prevalence of positive IgA anti-tTG test in patients with AT was significantly higher than the controls (5.9% *vs* 0.8%). Additionally, in our study, the prevalence rate of CD in patients with AT was higher than in the previous studies (mean value 3.7%)[11-14]. This might be associated with the higher prevalence rate of CD in Turkish population.

In the literature, there are some studies with different results. Ravaglia *et al*[21] reported that only the patients

aged 65 and older with AT had an increased risk of CD. In our study, the risk increased in patients under 66 years of age. In contrary to our findings, in a recent study from Italy, CD prevalence was reported as 0% in patients with autoimmune thyroiditis[15]. Racial and regional differences may explain these opposing findings.

It is of great importance to identify early CD in patients with AT, since a strict adherence to a gluten-free diet not only helps prevent the severe complications of untreated gluten-sensitive enteropathy such as ulcerative jejunoileitis, intestinal lymphoma and neoplasm[22], but also helps improve the associated autoimmune disease[12].

This is the first study conducted about association of CD with AT in a Turkish population. The relatively small sample size may be a limitation for our study. Studies with larger populations would bring more accurate results.

In conclusion, this study suggests that Turkish patients with AT have an increased risk of CD. Serological screening may be useful for early detection of CD in these patients. However, our findings need to be confirmed in a larger series of patients.

REFERENCES

1 **Fasano A**, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology* 2001; **120**: 636-651

2 **Farrel RJ**, Kelly CP. Celiac sprue and refrectory sprue. In: Feldman M, Friedman LS, Sleisenger MH, editors. Sleisenger&Fordtran's Gastrointestinal and Liver Disease Pathophysiology/Diagnosis/Management. Philadelphia: Elsevier Science, 2002: 1818-1841

3 **Farrell RJ**, Kelly CP. Celiac sprue. *N Engl J Med* 2002; **346**: 180-188

4 **Koop I**, Ilchmann R, Izzi L, Adragna A, Koop H, Barthelmes H. Detection of autoantibodies against tissue transglutaminase in patients with celiac disease and dermatitis herpetiformis. *Am J Gastroenterol* 2000; **95**: 2009-2014

5 **Gillett HR**, Freeman HJ. Serological testing in screening for adult celiac disease. *Can J Gastroenterol* 1999; **13**: 265-269

6 **Catassi C**, Rätsch IM, Fabiani E, Ricci S, Bordicchia F, Pierdomenico R, Giorgi PL. High prevalence of undiagnosed coeliac disease in 5280 Italian students screened by antigliadin antibodies. *Acta Paediatr* 1995; **84**: 672-676

7 **Mäki M**, Mustalahti K, Kokkonen J, Kulmala P, Haapalahti M, Karttunen T, Ilonen J, Laurila K, Dahlbom I, Hansson T, Höpfl P, Knip M. Prevalence of Celiac disease among children in Finland. *N Engl J Med* 2003; **348**: 2517-2524

8 **Collin P**, Reunala T, Pukkala E, Laippala P, Keyriläinen O, Pasternack A. Coeliac disease--associated disorders and survival. *Gut* 1994; **35**: 1215-1218

9 **Cronin CC**, Shanahan F. Insulin-dependent diabetes mellitus and coeliac disease. *Lancet* 1997; **349**: 1096-1097

10 **Volta U**, De Franceschi L, Molinaro N, Cassani F, Muratori L, Lenzi M, Bianchi FB, Czaja AJ. Frequency and significance of anti-gliadin and anti-endomysial antibodies in autoimmune hepatitis. *Dig Dis Sci* 1998; **43**: 2190-2195

11 **Collin P**, Salmi J, Hällström O, Reunala T, Pasternack A. Autoimmune thyroid disorders and coeliac disease. *Eur J Endocrinol* 1994; **130**: 137-140

12 **Valentino R**, Savastano S, Tommaselli AP, Dorato M, Scarpitta MT, Gigante M, Micillo M, Paparo F, Petrone E, Lombardi G, Troncone R. Prevalence of coeliac disease in patients with thyroid autoimmunity. *Horm Res* 1999; **51**: 124-127

13 **Berti I**, Trevisiol C, Tommasini A, Città A, Neri E, Geatti O, Giammarini A, Ventura A, Not T. Usefulness of screening program for celiac disease in autoimmune thyroiditis. *Dig Dis Sci* 2000; **45**: 403-406

14 **Volta U**, Ravaglia G, Granito A, Forti P, Maioli F, Petrolini N, Zoli M, Bianchi FB. Coeliac disease in patients with autoimmune thyroiditis. *Digestion* 2001; **64**: 61-65

15 **Fanciulli G**, Tomasi PA, Caucci F, Lai E, Sanciu F, Delitala G. Screening for celiac disease in patients with autoimmune thyroid disease: from research studies to daily clinical practice. *Ann Ital Med Int* 2005; **20**: 39-44

16 **Oberhuber G**, Granditsch G, Vogelsang H. The histopathology of coeliac disease: time for a standardized report scheme for pathologists. *Eur J Gastroenterol Hepatol* 1999; **11**: 1185-1194

17 **Marsh MN**. Gluten, major histocompatibility complex, and the small intestine. A molecular and immunobiologic approach to the spectrum of gluten sensitivity ('celiac sprue'). *Gastroenterology* 1992; **102**: 330-354

18 **Volta U**, De Franceschi L, Molinaro N, Tetta C, Bianchi FB. Organ-specific autoantibodies in coeliac disease: do they represent an epiphenomenon or the expression of associated autoimmune disorders? *Ital J Gastroenterol Hepatol* 1997; **29**: 18-21

19 **da Silva Kotze LM**, Nisihara RM, da Rosa Utiyama SR, Piovezan GC, Kotze LR. Thyroid disorders in Brazilian patients with celiac disease. *J Clin Gastroenterol* 2006; **40**: 33-36

20 **Tatar G**, Elsurer R, Simsek H, Balaban YH, Hascelik G, Ozcebe OI, Buyukasik Y, Sokmensuer C. Screening of tissue transglutaminase antibody in healthy blood donors for celiac disease screening in the Turkish population. *Dig Dis Sci* 2004; **49**: 1479-1484

21 **Ravaglia G**, Forti P, Maioli F, Volta U, Arnone G, Pantieri G, Talerico T, Muscari A, Zoli M. Increased prevalence of coeliac disease in autoimmune thyroiditis is restricted to aged patients. *Exp Gerontol* 2003; **38**: 589-595

22 **Murray JA**. The widening spectrum of celiac disease. *Am J Clin Nutr* 1999; **69**: 354-365

S- Editor Liu Y **L- Editor** Ma JY **E- Editor** Chin GJ