

# PREVALENCE OF CELIAC DISEASE IN PATIENTS WITH TURNER'S SYNDROME

H. Moayeri\* and S. H. Bahremand

Department of Pediatrics, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

---

**Abstract-** Celiac disease (CD) has been reported in association with genetic disorders such as Down's syndrome and Turner's syndrome (TS). This study was undertaken to assess the prevalence of CD among a group of patients with TS. Forty eight girls with TS and a control group composed by 48 healthy unrelated girls were screened for CD by IgA antiendomysial antibody (IgA-EMA). Total IgA of serum was measured in all of the patients and controls and EMA was measured in subjects who had normal range of IgA. Endoscopy and biopsy of duodenum was performed for EMA positive patients and pathologic evaluation was done according to Marsh's classification. Total IgA of serum in all of the subjects was in normal range. Two subjects, both with TS, were EMA positive, resulting in a prevalence of 4.1% in TS. Duodenal biopsy was performed in these patients and histologic changes of samples were classified as grade II in one and grade II b in another one. Results of this study are compatible with previous observations placing girls with TS at higher risk for CD relative to general population and justifying screening of CD in patients with TS.

*Acta Medica Iranica*, 43(4): 287-290; 2005

**Key words:** Celiac disease, IgA endomysial antibody, Turner's syndrome

---

## INTRODUCTION

Turner's syndrome (TS) is the most common chromosomal abnormality in females, affecting 1:2500 live female births. It is the result of absence of an X chromosome or the presence of a structurally abnormal X chromosome (1, 2). Celiac disease (CD), also known as gluten sensitive enteropathy, is a lifelong disorder of variable severity characterized by malabsorption and specific, though not pathognomonic, lesions of the small intestinal mucosa (3-6).

CD may present asymptotically in up to one third of cases or as an active malabsorption syndrome with a variety of different symptoms and signs may of which are not gastrointestinal (7). The pathogenesis of CD is still not completely

understood but several lines of evidence point to probable autoimmune mechanisms, triggered by an inappropriate T-cell mediated immune response against dietary gluten (3-6). During the last two decades, with the advent of reliable serologic assays to detect the disease activity, the diagnosis of CD has been greatly facilitated. Given the high sensitivity and specificity reported for these screening tools, especially for IgA antiendomysial (EMA) (8) and anti-transglutaminase antibody test (9), it is now accepted that a definitive diagnosis of CD can be based on positive serologic tests (serum IgA-EMA or t TG antibody) and a single intestinal biopsy showing the loss of normal villous structure (10-12).

CD occurs at higher rate in person with dermatitis herpetiformis, selective IgA deficiency, type I diabetes mellitus and autoimmune thyroid disease (13, 14). Genetic disorders known for their association to other autoimmune disease, such as Down's syndrome (15, 16) and Turner's syndrome (17-21) also show a high CD prevalence.

In recent years several screening studies on the prevalence of CD among patients with TS have been

---

Received: 28 Feb. 2004, Revised: 5 July 2004, Accepted: 21 Dec. 2004

**\* Corresponding Author:**

H. Moayeri, Department of Pediatrics Endocrinologist, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran  
Tel: +98 21 8004446, Fax: +98 21 8270902  
E-mail: H. Moayeri@yahoo.com

published (17-21). This study was undertaken to assess the prevalence of CD among a group of girls with TS in Pediatrics Endocrine Clinic of Tehran University of Medical Sciences.

## MATERIALS AND METHODS

### Subjects

From October 2002 to January 2004 serum samples were collected from 48 girls with TS attending the Pediatrics Endocrine Clinic of Tehran University of Medical Sciences. The age range of the study participants was 4-19 years with a mean age of  $13.1 \pm 4.2$  years. They were diagnosed as having TS on the basis of chromosomal analysis (complete or partial absence of one of the X chromosomes) and characteristic physical features.

A group of 48 healthy girls, aged 4-18 years (mean age  $12.9 \pm 3.8$  years), served as controls. The control subjects were included in the study based on the following inclusion criteria: 1) female sex, 2) normal growth and development and 3) without any known systemic disease. Patients with any symptoms compatible with CD or family history of CD were excluded.

We obtained informed consent from all subjects.

### Methods

After ruling out IgA deficiency both patients and controls were screened for CD applying the IgA-EMA, according to standard immunofluorescence technique.

To confirm the diagnosis of CD, intestinal biopsy were preformed in IgA-EMA positive patients. During the procedure, multiple duodenal biopsy samples were obtained for routine histologic analysis and pathologic evaluation was done according to Marsh's classification (12).

### Statistical analysis

All results are presented as mean  $\pm$  SD. Student *t* test was used for statistical analysis of the data. A *P* value of 5% or less was considered statistically significant.

## RESULTS

Of the total group of 48 patients with TS, two patients disclosed a positive IgA-EMA (2: 48). In the control group none had IgA-EMA. The two EMA positive patients, both with karyotype 45XO, revealed the typical aspect of celiac enteropathy in intestinal biopsy specimens supporting the diagnosis of CD. Histologic changes of samples according to Marsh's classification were grade II in one patient and grade III<sub>b</sub> in another one. The Turner's girls with CD had a median age of  $12.6 \pm 2.1$  yr at the time of screening compared with  $13.4 \pm 3.9$  yr in Turner's patients without CD. Both were asymptomatic and did not report any symptoms indicating CD at the time of screening. In patients with CD, the mean weight standard deviation score (SDS) was  $-2.9 \pm 0.63$  kg compared with  $-1.1 \pm 0.67$  kg in patients without CD ( $P < 0.05$ ). In patients with CD, the mean height SDS was  $-5.2 \pm 1.7$  cm compared to  $-3.7 \pm 1.1$  cm in patients without CD ( $P < 0.05$ ).

## DISCUSSION

The goal of this study was to test the hypothesis that girls with TS have higher prevalence of CD than normal population. More than three decades have been elapsed since the first description of CD in a patients suffering from TS (22), but the reason for the increased prevalence remains unknown. The link between CD and TS may be represented by the presence of common histocompatibility antigens, as has been suggested for the link between CD and Down's syndrome (23). The propensity of patients with TS to develop other autoimmune diseases such as autoimmune thyroiditis may be a factor of relevance. (24).

CD shows a marked geographic variation with the highest incidence in western Europe (12). It occurs with a prevalence rate of 1 to 12 per 1000 persons in the general population (12, 25, 26). In the study performed by Shahbazkhani and coworkers in apparently healthy Iranian blood donors, the prevalence of CD was reported to be 0.6% (27). The prevalence of CD among patients with TS ranges from 2.2% to 6.6 % in various reports (17-21). Gillet

*et al.* in a study on 45 TS patients found a prevalence of 2.2% of CD (20). In Ivarsson *et al.* study the prevalence of CD in 87 patients with TS was reported to be 4.6% (17). In a multicenter study on 389 patients with TS, Bonamico and colleagues demonstrated that 6.6% of TS patients had CD (18,19).

In the present study, 2 patients out of 48 girls with TS met the criteria for CD resulting in a prevalence of 4.1%. This is a relatively high prevalence of CD among patients with TS relative to general population (0.6%). The wide range of prevalences in various studies may be due to differences in ethnic groups, geographic area and population size in each report. In this study Turner's with CD had significantly lower height and weight compared with patients without CD but did not report any symptoms indicating CD at the first interview indicating patients in risk groups for CD such as type I diabetes mellitus and Turner's syndrome represent a special case and may be asymptomatic or disclose only mild or atypical features. Thus evaluation of patients with Turner's syndrome for CD regardless of symptoms is recommended. review of previously published studies and our findings to account all EMA positive patients who underwent intestinal biopsy had CD, thus showing the predictive value of EMA positivity to be as high among patients ,with TS as the general population and provides a rapid mean of identifying those patients who should be biopsied (8, 10-12, 25).

## REFERENCES

1. Ranke MB, Saenger P. Turner's syndrome. *Lancet*. 2001 Jul 28; 358(9278):309-314.
2. Elsheikh M, Dunger DB, Conway GS, Wass JA. Turner's syndrome in adulthood. *Endocr Rev*. 2002 Feb; 23(1):120-140.
3. Little Wood JM: Celiac disease in childhood. *Baillieres Clin Gastroenterol*; 9: 295-327; 1995.
4. Trier JS. Celiac sprue. *N Engl J Med*. 1991 Dec 12; 325(24):1709-1719.
5. Tighe MR, Ciclitira PJ. The implications of recent advances in coeliac disease. *Acta Paediatr*. 1993 Oct; 82(10):805-810.
6. Farrell RJ, Kelly CP. Celiac sprue. *N Engl J Med*. 2002 Jan 17; 346(3):180-188.
7. Hin H, Bird G, Fisher P, Mahy N, Jewell D. Coeliac disease in primary care: case finding study. *BMJ*. 1999 Jan 16; 318(7177):164-167.
8. Ladinsler B, Rossipal E, Pittschieler K. Endomysium antibodies in coeliac disease: an improved method. *Gut*. 1994 Jun; 35(6):776-778.
9. Amin M, Eckhardt T, Kapitza S, Fleckenstein B, Jung G, Seissler J, Weichert H, Richter T, Stern M, Mothes T. Correlation between tissue transglutaminase antibodies and endomysium antibodies as diagnostic markers of coeliac disease. *Clin Chim Acta*. 1999 Apr; 282(1-2):219-225.
10. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology*. 2001 Feb; 120(3):636-651.
11. Harewood GC, Murray JA. Diagnostic approach to a patient with suspected celiac disease: a cost analysis. *Dig Dis Sci*. 2001 Nov; 46(11):2510-2514.
12. Richard I Forrell, MD and Ciaren P. Kelly. Celiac sprue and refractory sprue. *Sleisenger and Fordtrant's Gastrointestinal and liver Disease*. 7th ed. Philadelphia: WB Saunders, 1817-1841,2002.
13. Farrell RJ, Kelly CP. Celiac sprue. *N Engl J Med*. 2002 Jan 17; 346(3):180-188.
14. Quisel A, Gill JM, Westerberg D. Guideline for diagnosis of celiac disease. *Del Med J*. 2002 May; 74(5):229-241.
15. Carlsson A, Axelsson I, Borulf S, Bredberg A, Forslund M, Lindberg B, Sjoberg K, Ivarsson SA. Prevalence of IgA-antigliadin antibodies and IgA-antiendomysium antibodies related to celiac disease in children with Down syndrome. *Pediatrics*. 1998 Feb; 101(2):272-275.
16. Jansson U, Johansson C. Down syndrome and celiac disease. *J Pediatr Gastroenterol Nutr*. 1995 Nov; 21(4):443-445.
17. Ivarsson SA, Carlsson A, Bredberg A, Alm J, Aronsson S, Gustafsson J, Hagenas L, Hager A, Kristrom B, Marcus C, Moell C, Nilsson KO, Tuvemo T, Westphal O, Albertsson-Wikland K, Aman J. Prevalence of coeliac disease in Turner syndrome. *Acta Paediatr*. 1999 Sep; 88(9):933-936.
18. Bonamico M, Pasquino AM, Mariani P, Danesi HM, Culasso F, Mazzanti L, Petri A, Bona G; Italian Society Of Pediatric Gastroenterology Hepatology (SIGEP); Italian Study Group for Turner Syndrom (ISGTS). Prevalence and clinical picture of celiac disease in Turner syndrome. *J Clin Endocrinol Metab*. 2002 Dec; 87(12):5495-5498.
19. Bonamico M, Bottaro G, Pasquino AM, Caruso-Nicoletti M, Mariani P, Gemme G, Paradiso E, Ragusa MC, Spina M. Celiac disease and Turner syndrome. *J Pediatr Gastroenterol Nutr*. 1998 May; 26(5):496-499.

## Prevalence of celiac disease in TS

20. Gillett PM, Gillett HR, Israel DM, Metzger DL, Stewart L, Chanoine JP, Freeman HJ. Increased prevalence of celiac disease in girls with Turner syndrome detected using antibodies to endomysium and tissue transglutaminase. *Can J Gastroenterol*. 2000 Dec; 14(11):915-918.
21. Ivarsson SA, Carlsson A, Bredberg A, Nilsson Ko: Coeliac disease and Turner's syndrome. *Horm Res*; 48 supp12:58; 1997.
22. Scobie BA. Co-existing coeliac and inflammatory bowel disease in a patient with Turner's syndrome. *Aust N Z J Med*. 1979 Jun; 9(3):316-317.
23. Castro M, Crino A, Papadatou B, Purpura M, Giannotti A, Ferretti F, Colistro F, Mottola L, Digilio MC, Lucidi V, et al. Down's syndrome and celiac disease: the prevalence of high IgA-antigliadin antibodies and HLA-DR and DQ antigens in trisomy 21. *J Pediatr Gastroenterol Nutr*. 1993 Apr; 16(3):265-268.
24. Ivarsson SA, Ericsson UB, Nilsson KO, Gustafsson J, Hagenas L, Hager A, Moell C, Tuvemo T, Westphal O, Albertsson-Wikland K, et al. Thyroid autoantibodies, Turner's syndrome and growth hormone therapy. *Acta Paediatr*. 1995 Jan; 84(1):63-65.
25. Bak RS. Celiac disease serology. Wraide report, A publication of Wraide Medical Laboratory 2003; 14(1).
26. Maki M, Mustalahti K, Kokkonen J, Kulmala P, Haapalahti M, Karttunen T, Ilonen J, Laurila K, Dahlbom I, Hansson T, Hopfl P, Knip M. Prevalence of Celiac disease among children in Finland. *N Engl J Med*. 2003 Jun 19; 348(25):2517-2524.
27. Shahbazkhani B, Malekzadeh R, Sotoudeh M, Moghadam KF, Farhadi M, Ansari R, Elahyfar A, Rostami K. High prevalence of coeliac disease in apparently healthy Iranian blood donors. *Eur J Gastroenterol Hepatol*. 2003 May; 15(5):475-478.