

# Prevalence of celiac disease in healthy Iranian school children

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**BACKGROUND AND OBJECTIVES:** Other than its classic presentation, celiac disease can be completely asymptomatic in a proportion of the general population. Subjects with silent celiac disease are at risk of potential complications of the disease, which indicates the importance of early diagnosis. In this study we investigated the prevalence of silent celiac disease in healthy children in our area.

**DESIGN AND SETTING:** Cross-sectional screening of healthy children in Shiraz city.

**SUBJECTS AND METHODS:** Fifteen hundred school children, 6 to 12 years of age in Shiraz (Southern Iran) were screened for celiac disease through serological testing of their serum anti-tissue transglutaminase immunoglobulin A antibodies. A small intestinal biopsy was performed for children with positive serology tests and pathologic reports were given according to the modified Marsh criteria.

**RESULTS:** Of the total students included, with a mean (SD) age of 9.5 (1.3) years, 30 subjects had positive anti-tissue transglutaminase immunoglobulin A antibodies, resulting in a total seropositivity of 2%. The prevalence of biopsy proven celiac disease (silent celiac) was 0.6%.

**CONCLUSION:** As in many other regions worldwide, this study estimated a relatively high prevalence of silent celiac disease in children in our area, citing the disease as an important health problem in our region.

Occurring most often in the white population, celiac disease (CD), also called gluten sensitive enteropathy, is an autoimmune disease that causes a nutritional malabsorption in the small intestine.<sup>1</sup> The etiology of the disease implicated up to now are genetic predispositions and exposure to wheat and other gluten-containing cereals.<sup>2</sup> Its characteristic sign and symptoms such as diarrhea and weight loss were first described by Samuel Gee in 1888.<sup>3</sup> Years later a few studies described asymptomatic or silent CD, discovered in first-degree relatives of patients with CD.<sup>4,5</sup> Patients with untreated CD are at risk of complications such as lymphoma,<sup>6,7</sup> osteopenia,<sup>8,9</sup> and infertility.<sup>10</sup> Also there is an association between CD and autoimmune disorders, for example diabetes mellitus type 1;<sup>11,12</sup> which raises the importance of early diagnosis and treatment of the disease, especially in subjects with the silent form of the illness. At the present time determination of serum anti-tissue transglutaminase immunoglobulin A antibodies (tTGA) by ELISA seems to be the most sensitive and specific test for diagnosis

of CD.<sup>13</sup> However, it is important to keep in mind that intestinal biopsy is still an essential criterion for final diagnosis of the disease.<sup>14</sup> Considering the fact that wheat is a major staple food in our area at southern Iran, we designed this study to investigate the prevalence of silent CD in healthy school-aged children in our region.

## SUBJECTS AND METHODS

This study was carried out in Shiraz city, capital of Fars province. Sample size was estimated as 1521 subjects using the standard formula with  $P=.01$ ,  $Z=1.96$  and  $d=0.005$ . A total of 1910 primary school children were selected from schools in Shiraz city through multistage random sampling. Education departments of Shiraz city consist of four areas. At first stage 4 schools were randomly selected from each educational area, then by random sampling from each school 4 classes were selected. Finally, 64 classes were included and all students of these classes were involved in this study. Since the average number of students in primary school classes is 30, the total number was 1910. Of these, parents of

1500 children agreed to enter their children to the study.

A questionnaire was completed for each student, which contained the patients' age, sex, weight, and height. Also, the subjects were asked about any gastrointestinal complaints (eg, diarrhea, abdominal pain, anorexia) and any possible positive family history of CD in their first-degree relatives. A 5 mL venous blood sample was obtained from each student, and stored at  $-20^{\circ}\text{C}$  before testing. Screening for CD was done through measuring the tTGA blood level by using a previously available kit (AESKU REF 3503, Germany), therefore a positive tTGA was regarded as above 12 units per milliliters according to the users manual. A total immunoglobulin A (IgA) level was also measured for each patient. In case of IgA deficiency in any patient, serum anti-tissue transglutaminase immunoglobulin G antibody levels were checked. Parents of children with a positive serology test were notified of the possibility of the disease and finally a small intestinal biopsy was performed for confirmation of the disease. Samples were reviewed by a pathologist blinded to the serology results and reported according to the Modified Marsh Criteria.<sup>1</sup> Informed consent was obtained from all students' parents. This study was also approved by Shiraz University of Medical Sciences Institutional Review Board. Finally, statistical analyses were carried out by using the Statistical Package for the Social Sciences (SPSS) version 15.0.

## RESULTS

We screened 1500 healthy school children with a mean (SD) age of 9.5 (1.3) years (range 6-12 years), for CD. There were 825 (55%) males and 675 (45%) females, with a male to female ratio 1.2:1. None of the students had complaints related to the gastrointestinal tract or a positive family history of CD. Tests revealed no IgA deficiency in our subjects. Of the total students included, 30 had a positive tTGA level, resulting in a total seropositivity of 2%. The mean (SD) age of the 30 seropositive patients was 9.6 (2.5) years, which included 16 (53.3%) girls and 14 (46.7%) boys.

According to the patients' weight and height the mean body mass index (BMI) was 17.16 (2.33)  $\text{kg}/\text{m}^2$  in the seropositive group and 17.34 (1.93)  $\text{kg}/\text{m}^2$  in the rest of subjects which difference was not significant statistically. There was no statistically significant relationship between the patient's BMI and total tTGA level.

Parents of all 30 subjects with a positive serology agreed to further investigation. Biopsy of the small intestine revealed abnormal pathology suggesting CD in 9 patients (5 girls and 4 boys), of which 6 had enteropathy of type II according to Marsh Criteria and 3 were reported as type III.

Twenty-one seropositive students (1.4%) with a normal duodenal pathology were considered as potentially having CD and were recommended for regular follow-ups, due to possibility of a CD in future. Meanwhile all subjects with a confirmed diagnosis of CD through biopsy were placed on a gluten-free diet.

Therefore, in this population study we estimated the prevalence of CD based on tTGA screening test as 1:50, whereas the prevalence of biopsy-proven CD (silent celiac) was 1:167.

## DISCUSSION

Until a few years ago, CD was thought to be a disease that exclusively affected people of the European origin. However, with the application of modern serologic screening tests, many recent studies worldwide have shown that the prevalence of CD is not only low, but somewhat similar to the Western countries.<sup>15</sup> Studies from several countries worldwide suggest that CD affects up to 1% of the adult population based on serologic tests.<sup>5</sup>

Many studies worldwide have reported the prevalence of silent CD in healthy children of their populations. In 2003 Fasano et al estimated the prevalence of asymptomatic CD as 1:133 in children and adults were not at risk for CD living in the United States.<sup>16</sup> His report concurred with those of the European countries such as Switzerland (1:132), Finland (1:99), Italy (1:210), and Hungary (1:85).<sup>17-20</sup> Through an epidemiologic study on healthy school children in India, Sood A et al revealed a prevalence of 1:310 for CD, comparable to the reports from Western countries.<sup>21</sup>

Serologic screening studies, including confirmation by duodenal biopsies, on low-risk children from different regions of the Middle East such as Turkey, Egypt and Tunisia have shown prevalence rates of 1:213, 1:188 and 1:156 respectively.<sup>22-24</sup> Data on the prevalence of CD in the healthy low-risk population of Iranian children has been published. Previous research on the healthy adult population from different geographic regions of Iran, have reported prevalence rates of 1:104-1:180 considering silent CD.<sup>25-27</sup> Originally in this study we have estimated the prevalence of asymptomatic CD based on small intestinal biopsy, in healthy low-risk school children in Shiraz (Southern Iran) to be 1:167, which is almost similar to that stated elsewhere.

We found a significantly higher prevalence of CD (1:50) according to serology testing alone. This finding necessitates the importance of duodenal biopsy for confirmation of the disease, albeit the high sensitivity and specificity of tTGA measurements.<sup>13</sup> We waited

so that all blood samples would be collected from the 1500 patients, prior to performing the desired tests, so although all samples were stored at  $-20^{\circ}\text{C}$ , there was a time gap between the point of sampling and that of testing. Thus, the latter explanations could raise the possibility of false positive results in our study.

Regardless, the study findings suggest that silent CD is highly prevalent in our area, citing the dis-

ease as an important health problem in our country. Therefore, physicians in our geographic region should be well aware of this dilemma, knowing the fact that early diagnosis and thus treatment of the disease might prevent potential complications. We also recommend larger epidemiological studies on the prevalence of the disease in Iran, based on both serologic testing and confirmation through intestinal biopsy.

## REFERENCES

- 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;102:330-54.
- Rossi M, Bot A. Celiac disease: progress towards diagnosis and definition of pathogenic mechanisms. *Int Rev Immunol*. 2011;30:183-4.
- Gee S, Herter CA, Dicke WK. On the coeliac affection. *St Barth Hosp Rep*. 1888;24:17-20.
- Stokes PL, Ferguson R, Holmes GK, Cooke WT. Familial aspects of coeliac disease. *Q J Med*. 1976;45:567-82.
- Vitoria JC, Arrieta A, Astigarraga I, García-Masdevall D, Rodríguez-Soriano J. Use of serological markers as a screening test in family members of patients with celiac disease. *J Pediatr Gastroenterol Nutr*. 1994;19:304-9.
- Freeman HJ, Chiu BK. Multifocal small bowel lymphoma and latent celiac sprue. *Gastroenterology*. 1986;90:1992-7.
- Holmes GK, Prior P, Lane MR, Pope D, Allan RN. Malignancy in coeliac disease--effect of a gluten free diet. *Gut*. 1989;30:333-8.
- Corazza GR, Di Sario A, Cecchetti L, Tarozzi C, Corrao G, Bernardi M, et al. Bone mass and metabolism in patients with celiac disease. *Gastroenterology*. 1995;109:122-8.
- Mustalahti K, Collin P, Sievänen H, Salmi J, Mäki M. Osteopenia in patients with clinically silent coeliac disease warrants screening. *Lancet*. 1999;354:744-5.
- Meloni GF, Dessole S, Vargiu N, Tomasi PA, Musumeci S. The prevalence of coeliac disease in infertility. *Hum Reprod*. 1999;14:2759-61.
- Fisher AH, Lomasky SJ, Fisher MJ, Oppenheim YL. Celiac disease and the endocrinologist: a diagnostic opportunity. *Endocr Pract*. 2008;14:381-8.
- Gillett PM, Gillett HR, Israel DM, Metzger DL, Stewart L, Chanoine JP, et al. High prevalence of celiac disease in patients with type 1 diabetes detected by antibodies to endomysium and tissue transglutaminase. *Can J Gastroenterol*. 2001;15:297-301.
- Vitoria JC, Arrieta A, Ortiz L, Ayesta A. Antibodies to human tissue transglutaminase for the diagnosis of celiac disease. *J Pediatr Gastroenterol Nutr*. 2001;33:349-50.
- Revised criteria for diagnosis of coeliac disease. Report of Working Group of European Society of Paediatric Gastroenterology and Nutrition. *Arch Dis Child*. 1990;65:909-11.
- Cataldo F, Montalto G. Celiac disease in the developing countries: a new and challenging public health problem. *World J Gastroenterol*. 2007;13:2153-9.
- Fasano A, Berti I, Gerarduzzi T, Not T, Colletti RB, Drago S, et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. *Arch Intern Med*. 2003;163:286-92.
- Rutz R, Ritzler E, Fierz W, Herzog D. Prevalence of asymptomatic celiac disease in adolescents of eastern Switzerland. *Swiss Med Wkly*. 2002;132:43-7.
- Catassi C, Fabiani E, Rättsch IM, Coppa GV, Giorgi PL, Pierdomenico R, et al. The coeliac iceberg in Italy. A multicentre antigliadin antibodies screening for coeliac disease in school-age subjects. *Acta Paediatr Suppl*. 1996;412:29-35.
- Mäki M, Mustalahti K, Kokkonen J, Kulmala P, Haapalahti M, Karttunen T, et al. Prevalence of Celiac disease among children in Finland. *N Engl J Med*. 2003;348:2517-24.
- Korponay-Szabó IR, Kovács JB, Czinner A, Gorácz G, Vámos A, Szabó T. High prevalence of silent celiac disease in preschool children screened with IgA/IgG antiendomysium antibodies. *J Pediatr Gastroenterol Nutr*. 1999;28:26-30.
- Sood A, Midha V, Sood N, Avasthi G, Sehgal A. Prevalence of celiac disease among school children in Punjab, North India. *J Gastroenterol Hepatol*. 2006 Oct;21:1622-5.
- Dalgic B, Sari S, Basturk B, Ensari A, Egirtas O, Bukulmez A, et al. Prevalence of celiac disease in healthy Turkish school children. *Am J Gastroenterol*. 2011;106:1512-7.
- Abu-Zekry M, Kryszak D, Diab M, Catassi C, Fasano A. Prevalence of celiac disease in Egyptian children disputes the east-west agriculture-dependent spread of the disease. *J Pediatr Gastroenterol Nutr*. 2008;47:136-40.
- Ben Hariz M, Kallel-Sellami M, Kallel L, Lahmer A, Halioui S, Bouraoui S, et al. Prevalence of celiac disease in Tunisia: mass-screening study in schoolchildren. *Eur J Gastroenterol Hepatol*. 2007;19:687-94.
- Shahbakhani B, Malekzadeh R, Sotoudeh M, Moghadam KF, Farhadi M, Ansari R, et al. High prevalence of coeliac disease in apparently healthy Iranian blood donors. *Eur J Gastroenterol Hepatol*. 2003;15:475-8.
- Akbari MR, Mohammadkhani A, Fakheri H, Javad Zahedi M, Shahbakhani B, Nouraei M, et al. Screening of the adult population in Iran for coeliac disease: comparison of the tissue-transglutaminase antibody and anti-endomysial antibody tests. *Eur J Gastroenterol Hepatol*. 2006;18:1181-6.
- Saberi-Firouzi M, Omrani GR, Nejabat M, Mehrabani D, Khademolhosseini F. Prevalence of celiac disease in Shiraz, southern Iran. *Saudi J Gastroenterol*. 2008;14:135-8.