Original Article

Prevalence of Occult Celiac Disease in Healthy Iranian School Age Children

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Abstract

Background: Several studies have shown the prevalence of celiac disease (CD) to be around 1% in Iran, which is similar to the worldwide prevalence. There is scant information on occult CD in apparently healthy school age children. This study, as the first such study in Iran, aims to determine the prevalence of occult CD in healthy Iranian school age children.

Methods: In this cross-sectional study, we screened healthy school age children for CD by serum IgA and IgA anti-tissue transglutaminase antibody (tTG) levels. Measurement of these antibodies was by enzyme linked immunosorbent assay. A recheck of positive tTG tests was performed and patients who tested positive underwent endoscopic duodenal biopsies. The biopsy samples were scored according to the Marsh classification by an experienced pathologist.

Results: A total of 634 children (314 males, 320 females; mean age: 12.8 years) were included in the study. All children and/or their parents completed a questionnaire and children underwent an initial physical examination to determine study eligibility. Positive serum tTG was noted in 3 (0.5%; 2 females) out of 634 patients. Duodenal biopsies were consistent with CD in these 3 subjects. The mean age of patients with CD was 14.3 years (range: 12–17 years). The female to male ratio was 2:1. These cases had no signs and symptoms, but a gluten-free diet was recommended according to pathologic changes in their small bowels and results of the tTG test.

Conclusion: The prevalence of occult CD in these children is 0.5%, which is half of the prevalence of CD in Iranian adults. The anti-tTG concentration at initial serological CD screening is highly informative in determining occult cases of CD. The question is whether all non-symptomatic cases should be treated with a gluten-free diet or not.

Keywords: Celiac disease, children, Iran, serological screening

Cite the article as: Farahmand F, Mir-Nasseri MM, Shahraki T, Yourdkhani F, Ghotb S, Modaresi V, Khatami GR. Prevalence of Occult Celiac Disease in Healthy Iranian School Age Children. *Arch Iran Med*. 2012; **15(6):** 342 – 345.

Introduction

Several studies have shown the prevalence of celiac disease (CD) to be around 1% in Iran, which is similar to the worldwide prevalence.[1] CD, a rare disease in European children in the 1970s, is now a global occurrence, although most cases are undiagnosed.[2] Several studies have established an association of CD with functional dyspepsia,[3] viral and autoimmune hepatitis,[4,5] gastrointestinal (GI) symptoms,[6] recurrent aphthous stomatitis,[7] type 1 diabetes mellitus,[8–10] iron deficiency anemia of obscure origin,[11] children with idiopathic short stature,[12–14] chronic diarrhea,[15,16] and irritable bowel syndrome.[17]

Screening studies in children have reported a prevalence from 3 to 14 per 1000,[18–24] with an exception of 56 per 1000 among Saharawi children in Algeria.[25] However, population characteristics and screening methods vary amongst studies.[26,27]

This immune-mediated enteropathy is a lifelong condition induced by dietary gluten in genetically susceptible individuals. In addition to genetic factors, environmental factors also affect the timing, age, and feature of presentation.

With the advent of highly sensitive serological markers, several epidemiological studies have shown a prevalence in the range of 1% of the adult populations tested.[28,29] Probably less than 10% of those affected are diagnosed.[30] CD has an impressive list of associated disorders, which appears to be ever growing. Clinical presentation of CD has also changed over time, with many affected individuals being asymptomatic and identified by targeted screening.[31]

Symptoms and clinical signs of CD are diverse and vary depending on age at diagnosis and duration. The spectrum of clinical presentation has been broadly attributed to an increased awareness of atypical and subclinical cases.[32,33] It has been estimated that up to two thirds of children with CD may be diagnosed as clinically silent,[22] which would make screening an important tool to detect cases with asymptomatic variants. The rate of undiagnosed CD is much higher in Middle Eastern countries.[34,35] Untreated CD confers an increased risk for long-term complications such as osteoporosis[36] and intestinal malignancies.[37] Therefore early detection of clinically silent cases is warranted.

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Accepted for publication: 21 February 2012

Table 1. Information of participating subjects.

	Number (%)
History of CD in first degree family members	2 (0.1%)
Aphthos ulcer	367 (13%)
GI bleeding	163 (5.8%)
Epistaxis	264 (9.3%)
Epilepsy	151 (5.3%)
Skin lesions	113 (4%)
Abdominal pain	765 (27%)
Ecchymosis	24 (0.9%)
Defecation pattern	
Bowel movement (1–3/day)	2478 (87.6%)
Bowel movement (> 3/day)	192 (6.8%)
Bowel movement (1 every other day)	125 (4.4%)
Bowel movement (< 3/week)	19 (0.7%)
Abdominal pain (1/week)	148 (5.2%)
Abdominal pain (1/month)	608 (21.5%)
History of diseases in subjects	
Celiac disease (CD)	2 (0.1%)
Thyroid dysfunction	3 (1.3%)
Diabetes mellitus	2 (0.9%)
Liver disease	2 (0.9%)
Past medical history	
Diarrhea	197 (7%)
Bloody diarrhea	26 (0.9%)
Cow's milk allergy	248 (8.8%)
Limb deformity	12 (0.4%)
History of other disease	226 (7.8%)

The present study aims to estimate the proportion of undiagnosed CD (occult celiac) in a cohort of healthy students in Iran. We consider CD as a common disorder that should be screened during school age period.

Materials and Methods

A cross-sectional study was performed over 2 years (June 9, 2006 to August 25, 2008) by the Children's Gastrointestinal Unit of the Digestive Disease Research Center, Tehran University of Medical Sciences, Tehran, Iran. The Ethics Committee of Tehran University of Medical Sciences approved this study.

This study was undertaken in 5 sites of Tehran (north, south, west, east, and city center) and each site included 600 cases. One area was randomly chosen from each site. In each site, 2 girls and 2 boys schools were randomly chosen from each level of education (elementary, intermediate, and high school).

The randomly selected children (and their parents) from all 3 educational levels were invited to the study center. Children and/or parents were asked to complete a designed questionnaire. Excluded from the study were those with known cases of chronic disease, short stature or inappropriate weight for age. Eligible subjects were invited to participate in the study.

Out of 2898 children, 634 subjects consented to be evaluated for CD. Written informed consents were obtained from the subjects, their parents, or both. Serum IgA and IgA anti-tissue transglutaminase antibody (tTG) were measured by a commercial ELISA assay with quality control. tTG IgA antibodies above 20 U/mL were considered positive. In positive subjects based on tTG, upper gastrointestinal endoscopies were performed by a pediatric gastroenterologist at the Department of Pediatrics, Children's Medical Center Hospital. During the procedure, multiple duodenal-biopsy samples were obtained for histological analysis. An experienced pathologist reviewed the specimens and reported the results according to the Marsh classification.[38,39] We checked HLA in tTG-positive subjects.

Results

There were 2898 schoolchildren who completed questionnaires (Table 1). Subjects consisted of 1433 females (49.5%) and 1463 males (50.5%), with a mean age of 12.8 years. Of these, 964 (34%) attended elementary school, 985 (33.8%) were in intermediate school, and 979 (31%) attended high school.

Blood tests for serum total IgA and IgA tTG were taken from 634 cases (21.9%), ages 7 to 18 years, on a specified day. There were no subjects with IgA deficiency. According to BMI, 243 (46.6%) children had a BMI < 18.5, 220 (42.2%) between 18.5–24.9, 42 (8.1%) between 25–29.9, and 16 (3.1%) were ≥ 30. Three cases out of 634 (0.5%) had high titers of tTG IgA antibody. For these 3 cases, tTG IgA antibody levels were rechecked for confirmation of positivity. Other laboratory tests, including hematocrit levels, were normal. Two cases had pathological changes according to Marsh 2 criteria and one was Marsh 3. Their HLA tests were positive for HLADQ2 and HLAD28.

Children who received biopsy-proven diagnoses of CD had normal BMI (18.5–24.9), with no reports of abdominal pain or abnormal bowel movements. A gluten-free diet was started for these newly diagnosed cases of CD. These patients are currently being followed.

Discussion

This study showed that the prevalence of occult CD was at least 0.5%, with 3 out of 634 cases diagnosed among normal school age children in Tehran. This prevalence was relatively lower than the background population prevalence in healthy blood donors (0.6%) in Iran.[40] The reason for this low prevalence of CD in children was expected as the incidence of CD increases with age. Another possible explanation was that in our study, only 21.9% of our selected samples consented to give blood. According to our findings, the use of a simple, noninvasive serologic test in normal school age children not previously diagnosed with CD led to the determina-

tion of biopsy-proven CD disease with a prevalence of 0.5%. This result approximated the prevalence in surrounding countries. A similar study from Turkey was designed to investigate the prevalence of CD in apparently healthy Turkish school children. The detection of children with occult CD revealed a high prevalence of biopsy-proven CD (0.6%, 1:158) in subjects.[41]

Research from other countries has shown a range in the proportion of CD in the normal population from 1:100 to 1:300. Since approximately 50% of children are asymptomatic, some experts have suggested celiac screening for all adults[42] and children.[43] Recently, one published study has reported an overall prevalence of CD among Europeans at approximately 1%. This report included both the highest prevalence in Finland 2.4% (2.0%–2.8%) and the lowest in Germany at 0.3% (0.1%–0.4%).[44]

The prevalence of atypical symptoms has increased in the past decade, particularly in the past 5 years, when over half of the children with CD had atypical presentations. This has resulted in an older median age at diagnosis, since children who presented with typical symptoms were younger, with a median age at diagnosis that was similar over a 20-year period.[45]

We found the prevalence of CD to be 0.5% in healthy Iranian children, which is relatively high in proportion to other areas. One explanation for the high prevalence of CD in our study might be related to the high genetic risk of CD in this population. Another reason may be due to the high consumption of wheat in the Iranian diet. Some studies indicate that plant foods are the major components of the Iranian diet, and Iranians rank as one of the top wheat-consuming populations in the world with a per capita consumption of up to 160 kg/year.[1] A characteristic of the Iranian diet is the primary dependence on bread, followed by rice as major energy sources.

Although this study population is not representative of the Iranian children as a whole; the true prevalence of CD may likely be even higher than this report. According to our findings, the prevalence of biopsy-proven CD is high and justifies necessitation of screening methods among apparently healthy school children in Iran.

In our study, the prevalence of CD (with serologic and histopathologic markers) in healthy-appearing school age children is 0.5%, and comparable to the prevalence rates in children reported from many other areas. As occult CD among school age children is not an uncommon disorder and anti-tTG concentrations seem to be highly informative in detection of occult cases of CD, screening of school age children by anti-tTG may be justifiable. Detection of CD in its early stages may reduce the risk of further disease complications by initiation of gluten-free diets in these children.

Conflicts of interest

The authors report no conflicts of interest.

Acknowledgments

This study was supported by funds from Digestive Disease Research Center (DDRC) and the Iranian Society of Gastroenterology and Hepatology. We would like to thank Professor R. Malekzadeh for reading the manuscript and offering helpful comments.

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