Prevalence of Celiac Disease Autoimmunity Among Adolescents and Young Adults in China

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BACKGROUND & AIMS: **In China, epidemiologic information on celiac disease autoimmunity is scarce and fragmented. We investigated the prevalence of celiac disease autoimmunity in the general Chinese population.**

METHODS: **In a cross-sectional prospective study, 19,778 undiagnosed Chinese adolescents and young adults (age, 16–25 y) were recruited from consecutive new students who underwent routine physical examinations at 2 universities in Jiangxi, China, from September 2010 through October 2013; the students were from 27 geographic regions in China. All subjects were tested for serum IgG, IgG against deamidated gliadin peptides (IgG anti-DGP), and IgA anti–tissue transglutaminase antibodies (IgA anti-tTG). We also analyzed HLA genotypes in subgroups of participants with different results from tests for serum markers of celiac disease.**

RESULTS: **A total of 434 students (2.19%) tested positive for serum markers for celiac disease (95% confidence interval [CI], 1.99%–2.41%), 0.36% of the students tested positive for anti-tTG IgA (95% CI, 0.28%–0.46%), and 1.88% tested positive for anti-DGP IgG (95% CI, 1.70%–2.09%). The prevalence of celiac disease autoimmunity (positive results in assays for anti-tTG IgA and anti-DGP-IgG) was 0.06% (95% CI, 0.03%–0.10%). Celiac disease autoimmunity was associated with the consumption of wheat and female sex. The prevalence in the Shandong province in north China, where wheat is a staple in the diet, was 0.76% (95% CI, 0.21%–1.95%). The frequencies of the HLA-DQ2/-DQ8 genotypes associated with celiac disease were higher in subjects with celiac disease autoimmunity, based on detection of both serum markers, than in subjects with positive results from a single test ($P < .01$). All subjects with positive results from both assays carried the HLA-DQ2 genotype.**

CONCLUSIONS: **Approximately 2% of adolescents or young adults in China had positive results from assays for serum markers for celiac disease. The prevalence of celiac disease autoimmunity in the Shandong province in north China, where wheat is a staple in the diet, was 0.76%.**

Keywords: Tissue Transglutaminase Antibody; Anti–Deamidated Gliadin Peptide; HLA Class II; Gene.

Celiac disease (CD) is a chronic small intestinal immune-mediated enteropathy elicited in genetically predisposed individuals by consumption of foods containing gluten-containing grains (ie, wheat, barley, and rye) or ingredients generated from these grains.[1,2] Gluten antigens are presented by HLA-DQ2 and -DQ8, then activate autoreactive T lymphocytes, leading to immune responses in intestinal mucosa.[3]

In past reports, CD showed obvious racial and geographic differences, common in populations of European descent.[4] In fact, the worldwide distribution of the major CD-predisposing genes (HLA-DQ2 and -DQ8), the rapid worldwide increase of the Western diet (ie, wheat consumption), and the population migratory flows may have led to the global increase of CD.[4] A great number of epidemiologic data have shown that CD is already a widespread problem of public health.[4] In China, CD once

Abbreviations used in this paper: BMI, body mass index; CD, celiac disease; CI, confidence interval; DGP, deamidated gliadin peptide; tTG, tissue transglutaminase.

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2017.04.025

was considered to be rare. However, our previous study strongly suggested that undiagnosed celiac disease should be more common in China than earlier recognized.[2] In that study we analyzed the predisposing HLA gene frequencies and wheat consumption in the Chinese population, from which the occurrence of CD appeared. We hypothesized a sharp increase of CD in China with the rapidly increasing exposure to gluten as a result of the present change of dietary habits in southern and northern China with the widespread Western dietary patterns in modern China.[2]

At present, epidemiologic CD data are scarce in China; only a few studies have performed screening for CD in high-risk groups. The prevalence of CD in adult patients and pediatric patients with chronic diarrhea was 6.5% and 11.9%, respectively,[5,6] and the prevalence of CD autoimmunity in patients with diarrhea-predominant irritable bowel syndrome,[7] insulin-dependent diabetes mellitus, or autoimmune thyroid disease[8] was 1.77% and 22%, respectively, but the prevalence of CD autoimmunity in the general Chinese population was unknown. In this work, we performed mass screening in Chinese adolescents and young adults (age, 16–25 y) on the occurrence of serum IgG antibody against deamidated gliadin peptides (anti-DGP IgG) and of IgA antibodies against tissue transglutaminase (anti-tTG IgA), 2 serum markers of CD, to acquire the prevalence of CD autoimmunity in China. In addition, the CD-predisposing HLA genes were determined in representative numbers of participants with different test results of CD serum markers to define the association of HLA genes and serum markers of CD.

Methods

Subjects and Information Collection

In this study, 21,517 adolescents and young adults were recruited consecutively from new students who underwent routine physical examinations at the School Hospital of Nanchang University and Nanchang Hangkong University (Jiangxi, China) between September 2010 and October 2013. The percentage of recruited students from the routine physical examination program was 70.11%. A 5-mL blood sample was collected from all subjects. After centrifugation at 2130 × g for 5 minutes, serum samples and blood clot samples were obtained and stored at -80°C until use. All physical examination records were collected and investigated, which involved general information (eg, age, sex, nationality, native place, place of residence, and so forth), medical history, physical examination, and physician assessment. The physical examinations included ophthalmology and otorhinolaryngology, surgical (including height, weight, and so forth), medical, radiograph, and blood examination. Blood examination included routine blood tests, and liver and kidney function tests. Body mass index (BMI) was calculated by weight/height^2 (kg/m^2). BMI values less than 18.5 kg/m^2, between 18.5 and 23.9 kg/m^2, between 24 and 27.9 kg/m^2, and greater than 28 kg/m^2 are considered underweight, normal, overweight, and obese, respectively.[9]

Considering that the difference between native place and place of residence can effect dietary habits of individuals during different period of their life, 1636 subjects whose native place were different from place of residence were excluded from the study. In addition, 103 hemolytic samples were eliminated in subsequent serum CD marker tests. Finally, 19,778 adolescents and young adults (13,322 males, 6456 females; age, 18.8 ± 1.1 y) were included in the study. Subjects were from 27 geographic regions in China; and all subjects were Chinese. There were 19,094 subjects of Han nationality, and 684 subjects originated from ethnic minorities. According to medical history, none of the recruited subjects had been diagnosed previously with CD. This study was approved by the ethics committee of the Second Affiliated Hospital of Nanchang University (no. [2010] 041), and all subjects provided informed consent before participation.

Combined Anti–Deamidated Gliadin Peptide IgG and Anti–Tissue Transglutaminase IgA assay

The anti-DGP–IgG level was measured by using the commercial Wieslab Celiac hs Screen Enzyme-Linked Immunosorbent Assay kit (Euro Diagnostica AB, Malmö, Sweden) in which the specific antibody was raised against a unique synthetic deamidated gliadin peptide containing a well-defined T-cell stimulatory toxic epitope related to CD. The Wieslab Celiac hs Screen test with a cut-off value (>3 U/mL) possessed high sensitivity but low specificity, and a higher cut-off value (>5 U/mL) increased the specificity without a significant loss in sensitivity.[10] Accordingly, 5 U/mL was regarded as the cut-off limit of normality. The anti-tTG IgA was tested with a commercial Quanta Lite TM h-tTG IgA Enzyme-Linked Immunosorbent Assay kit (Inova Diagnostics, San Diego, CA), in which the purified human erythrocyte tTG was used to capture and measure anti-tTG IgA. According to the recommendations of the manufacturer, anti-tTG–IgA antibody levels of less than 20 U were regarded as negative, 20 to 30 U as weak positive, and greater than 30 U as moderate to strong positive. The anti-DGP–IgG test was applied preceding the IgA anti-tTG test in the present study because the IgG test can prevent missing IgA-deficient individuals.

All positive and border test results were repeated. In samples with positive anti-DGP IgG and negative anti-tTG IgA, the total amount of serum IgA was quantified by rate nephelometry on an Immage 800 immunochemistry system (Beckman Coulter, Inc, CA) to rule out IgA deficiency.

Celiac Disease Autoimmunity

Celiac disease autoimmunity was defined as being positive for both anti-DGP IgG and anti-tTG IgA.