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Retrospective Study

Epidemiological, Clinical, and Histological Presentation of Celiac Disease in Northwest China

Celiac disease in Northwest China

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Abstract

BACKGROUND

Research on celiac disease (CD) in Northwest China is still in its infancy. At present, large sample data on the epidemiological, clinical, and pathological characteristics of CD are limited.

AIM

To investigate the epidemiological, clinical, and pathological characteristics of CD in northwest China.

METHODS

The clinical data of 2,884 patients with gastrointestinal (GI) symptoms were retrospectively analyzed. Total immunoglobulin A and anti-tissue transglutaminase IgA levels were examined for all patients. Gastroscopy and colonoscopy were performed in patients with positive anti-tTG IgA and deficient total IgA levels. Atrophy of the duodenal and ileal villi was examined, and histopathological examinations were performed. The modified Marsh–Oberhuber classification system was used to grade villous atrophy in the duodenum or distal ileum. Patient *H. pylori* infection status was compared in terms of clinical presentation and Marsh grade. Statistical analyses were performed using t-test or chi-square test.

RESULTS

Among the 2,884 patients, 73 were positive for serum anti-tTG IgA and 50 were diagnosed with CD. The detection rate of CD was significantly higher in Kazakhs (4.39%) than in Uygurs (2.19%), Huis (0.71%), and Hans (0.55%). The main symptoms of CD were chronic diarrhea, anorexia, anemia, fatigue, weight loss, sleep disorders, osteopenia, and osteoporosis. The body mass index of CD patients was significantly lower than that of non-CD patients. A total of 69 patients with positive serum anti-tTG IgA and two patients with deficient total IgA levels underwent GI endoscopy.

Endoscopy revealed crypt hyperplasia and/or duodenal villous atrophy, which mainly manifested as nodular mucosal atrophy, grooves, and fissures. The difference in *H. pylori* infection rates was not statistically significant between CD and non-CD patients, but was significantly different among CD patients with different Marsh grades.

CONCLUSION

Among patients with GI symptoms in northwestern China, CD mainly occurs in the Uygur and Kazakh populations. *H. pylori* infection may be associated with CD severity.

Key Words: Celiac disease; Epidemiology; Gastrointestinal symptoms; Pathology; *Helicobacter pylori* infection

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Core Tip: Celiac disease is an autoimmune disease caused by the ingestion of gluten in genetically susceptible individuals. The global prevalence of celiac disease is approximately 1.4%. An increase in celiac-specific autoantibody levels can lead to varying degrees of damage to the small intestinal mucosa and, consequently, to various gastrointestinal and systemic symptoms. This study reports the epidemiological, clinical, and pathological characteristics of celiac disease and its association with *H. pylori* infection, and aims to provide useful information for clinical diagnosis and treatment of celiac disease.

INTRODUCTION

Celiac disease (CD) is an autoimmune chronic inflammatory disorder of the small intestine caused by the ingestion of gluten in genetically susceptible individuals. Intestinal mucosal gluten reactive CD4 T cells are involved in the

pathogenesis of CD[1]. The presence of T-cells in the mucosa can cause varying degrees of damage to the small intestinal mucosa and consequently lead to a variety of gastrointestinal (GI) and systemic symptoms[2]. Typical GI manifestations include abdominal pain, abdominal distension, and diarrhea, while non-GI manifestations include anemia, osteoporosis, herpetic dermatitis, and neurological symptoms [3]. Early epidemiological studies have suggested that CD is common in Caucasian populations, mainly in Europe and North America [4, 5]. Further studies in other regions have shown similar CD prevalence rates in the Middle East, Asia, Southeast Asia, and Oceania (0.2%–1%) [6-8]. The global prevalence of CD is approximately 1.4%, which is gradually increasing [9, 10]. The prevalence of CD in hospital patients has also been investigated. A report from Brazil found that the prevalence of celiac disease was 1.9% among 1030 patients in hospitals in Brazil[11]. The detection rate of CD was 4.48% in patients with irritable bowel syndrome[12].

There is little data on the prevalence of CD in Asia, and no data has been compiled for some countries. The prevalence of CD among asymptomatic adults in Japan is 0.05%, and no studies have investigated the rates of CD In Japanese children[13]. The prevalence of CD among Indian children is approximately 1%[14]. In Central Asia, the prevalence of HLA-DQ alleles susceptible to CD is similar to the prevalence in Europe, but epidemiological and clinical studies are lacking[15]. The seropositivity of celiac disease in the Chinese population is mainly concentrated in the northern region. A meta-analysis reported that the CD seroprevalence of the general population in China was 0.27%, while the CD seroprevalence in the high-risk population was 8.34%[16]. One study screened 118 Chinese children with chronic diarrhea, and subsequently diagnosed 14 patients with CD[17]. Research on CD in China is still in its infancy, with only a few cases reported [17, 18]. However, the presence of CD susceptibility genes is not uncommon among the Chinese population, and it is believed that the actual number of CD cases in China may be much higher than the currently reported number of diagnosed cases [19].

Serum endomysium antibodies (EMA) and antibodies against tissue transglutaminase (tTG) are commonly used serological tests for celiac disease. Studies have shown that

the sensitivity and specificity of anti-tTG IgA are 92.5% and 97.9%, respectively. EMA IgA testing is less sensitive, but more specific than anti-tTG IgA, with sensitivity and specificity of 79.0% and 99.0%, respectively[20]. Anti-tTG IgA is the standard test to screen for CD, but EMA IgA is widely used to confirm the diagnosis. Human leukocyte antigen (HLA)-DQ2 and HLA-DQ8 genotyping can be used to exclude CD [21, 22]; however, they are poor diagnostic tests as not all people with these genetic variations develop CD. Duodenal mucosal biopsy findings remain the gold standard for diagnosing CD, and the characteristic changes include villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis. Therefore, specific serum antibody testing and endoscopic duodenal mucosal biopsy should be performed for patients with suspected CD [23, 24].

The clinical presentation of CD is complex and diverse. However, diagnosis and treatment of CD are relatively simple. A strict gluten-free diet (GFD) is the most effective dietary intervention for disease control, although it has some limitations. Clinical trials of other non-dietary therapies are currently in progress. However, due to the lack of understanding of the disease, identification of high-risk populations for CD remains a challenge, which leads to high rates of missed diagnoses of early stage CD, and patients commonly develop serious complications as a result.

Northwest China is a multi-ethnic region, with ethnic groups such as Hans, Uygurs, Huis, and Kazakhs. The people living in this area have similar eating habits, and wheat is the staple food crop. In addition, this region is located in Central Asia and is geographically close to Europe, where the incidence of CD is high. It is possible that genetic exchanges may have occurred between residents and travelers on the ancient Silk Road in this region. Therefore, many cases of CD may remain undiagnosed in this geographical area due to insufficient knowledge of the disease. This study explored the prevalence, clinical manifestations, and pathological characteristics of CD in Northwest China with the aim of improving clinician awareness of the disease, reducing the rates of missed diagnoses and misdiagnoses, and improving patients' quality of life.

MATERIALS AND METHODS

Patient and public involvement

This was a retrospective cross-sectional study conducted in the Department of Gastroenterology of the People's Hospital of Xinjiang Uygur Autonomous Region. The study was approved by the Hospital's Institutional Review Board (IRB) (Register number: KY2021052611). All patients who underwent gastroduodenoscopy signed procedural informed consent, and the IRB waived the requirement for informed consent for other clinical data. This study adhered to the applicable STROBE guidelines.

Inclusion and exclusion criteria

The clinical data of 3,147 patients, including adults and children, with GI symptoms such as chronic diarrhea, abdominal pain, abdominal distension, constipation, vomiting, nausea, anorexia, heartburn, acid reflux, and burping were collected from both inpatient and outpatient services between March 2016 and February 2021. All included patients agreed to be tested for CD, and all relevant clinical data were kept confidential. To investigate the incidence of ileal villous atrophy and exclude diseases other than CD, anti-tTG IgA-positive patients were further examined by gastroduodenoscopy. Colonoscopy with ileal biopsy was not mandatory for CD diagnosis. The exclusion criteria for the study were as follows: physically healthy patients without GI symptoms; patients with digestive tract tumors or a history of other cancer types; patients with a history of cholecystectomy or gastric, duodenal, colon, or small intestinal surgery, and patients with liver cirrhosis, hepatitis, or acquired immunodeficiency syndrome.

Chronic diarrhea was defined as diarrhea lasting for >4 wk or recurrent diarrhea with an intermittent period of 2–4 wk. Anemia was defined as hemoglobin (Hb) levels of <110 g/L in children aged 6 mo to 6 years, <120 g/L in children aged 6–14 years, <130 g/L in adult men, and <120 g/L in adult women. Bone mineral density was measured using dual energy X-ray absorptiometry, with T-scores of -2.5 to -1 defined as osteopenia and T-scores of ≤-2.5 defined as osteoporosis. Weight loss was defined as an unexplained reduction of >5% in the initial body weight within 6 mo. Anxiety and

depression were quantified using the Hamilton Anxiety Rating Scale and the Hamilton Depression Rating Scale, respectively. General patient information, including sex, age, race, body mass index (BMI), GI signs and symptoms, comorbidities, *Helicobacter pylori* infection status, and GI endoscopy and pathology results were collected.

Serological tests

Approximately 3–5 mL of venous blood was drawn from each patient, centrifuged to separate the serum, aliquoted, and frozen at -70 °C until required. Serum total IgA was evaluated using the immunoturbidimetric method, with levels of <0.82 g/L considered as absence of selective IgA. Anti-tTG IgA levels were measured for patients with normal total IgA using enzyme-linked immunosorbent assays, with anti-tTG IgA levels >20 CU defined as positive. Testing was conducted in accordance with kit instructions and the test kit was sourced from INOVA Diagnostics Inc., USA. Patients with positive anti-tTG IgA and total IgA deficiency underwent GI endoscopy.

Endoscopic, histological assessments and H. pylori infection

GI endoscopy was performed using an Olympus endoscope (Olympus EVIS LUCERA CV290; Tokyo, Japan). The mucosa of the duodenal bulb, descending duodenum, and terminal ileum was observed by white light endoscopy. The villous architecture was further observed by near-focus narrow-band imaging, the water immersion method, and indigo carmine staining. Pathological biopsies were performed on the duodenal bulb (two pathological tissue samples), the descending duodenum (four pathological tissue samples), and the terminal ileum (two pathological tissue samples). Two blinded pathologists made the histopathological diagnoses and graded the villous atrophy in the duodenum or distal ileum according to the modified Marsh–Oberhuber classification system[25]. Disagreements in classification and grading were resolved by consensus. CD was diagnosed when the biopsy was classified with a Marsh grade ≥2.

For the histological diagnosis of *H. pylori* infection, biopsy specimens were obtained from the antrum, corpus, and angulus of the stomach. Hematoxylin-eosin and Giemsa staining were performed as appropriate. *H. pylori* infection was considered negative if *H. pylori* was absent in all biopsy sites and was considered positive if *H. pylori* was

present in at least one biopsy site. If the histological diagnosis of *H. pylori* infection was negative, but a urea breath test returned positive results, the patient was diagnosed with *H. pylori* infection.

Statistical analysis

SPSS software (version 17.0) was used for all statistical analyses. Normally distributed continuous data were compared using the t-test and are presented as mean ± standard deviation, whereas categorical data were compared using the chi-square or Fisher's exact test and are presented as numbers and percentages. Statistical significance was set at $p < 0.05$.

Data availability

The datasets used and/or analyzed during the study are available from the corresponding author upon reasonable request.

RESULTS

Epidemiological characteristics

Of the 3,147 patients with GI symptoms such as chronic diarrhea, abdominal pain, abdominal distension, and weight loss, 2,884 met the inclusion criteria (**Figure 1**). The subjects were divided into categories according to their age. The subject's ages ranged from 2 to 96 years old, and the majority of subjects fell within the 40-59 years, and ≥60 years age groups (34.3% and 30.7%, respectively). There were 1,531 men (53.1%) and 1,353 women (46.9%). When patients were grouped by ethnicity, 1,097 (38.0%) were Hans, 1,048 (36.3%) were Uygurs, 387 (13.5%) were Kazakhs, 283 (9.8%) were Hui, and 69 (2.4%) were other ethnicities. **Table 1** summarizes the incidence of CD based on ethnic group, sex, age group, and BMI and the correlation analysis results for each variable. Among these factors, there were significant associations based on ethnicity ($P < 0.05$) or BMI ($P < 0.01$). In terms of ethnicity, CD incidence was the lowest in Hans (0.55% in Hans, 2.19% in Uygurs, 4.39% in Kazakhs, and 0.71% in Huis). Among the other ethnicities, one Mongolian and one Uzbek patient were diagnosed with CD but this was not analyzed further because of the small sample size for these ethnicities. All

participants were tested for serum total IgA and anti-tTG IgA levels. Overall, two IgA-deficient patients and 73 anti-tTG IgA-positive patients were identified. The rate of positive serum anti-tTG IgA levels was 2.53%. A total of 71 patients underwent GE: two total IgA-deficient patients and 69 anti-tTG IgA-positive patients. Pathological classification was performed according to the modified Marsh–Oberhuber classification (**Table** 2). Two patients with total IgA deficiency had Marsh grade 0. Among the 69 patients, 10 had Marsh grade 0, 9 had Marsh grade 1, and 50 had Marsh grade ≥2. Patients with Marsh grades 0 and 1 were excluded, and 50 patients with Marsh grade ≥2 were eventually diagnosed with CD. The overall CD detection rate was 1.73%.

Clinical signs and symptoms

CD was more common in patients with BMI ≤18.49 kg/m^2 (5.50%). No significant differences were noted in CD incidence when the patients were evaluated based on age or sex. The main symptoms of non-CD and CD patients were abdominal pain (50.7% and 54.0%, respectively) and abdominal distension (49.4% and 58.0%, respectively). The rates of chronic diarrhea, anorexia, anemia, fatigue, weight loss, sleep disorder, osteopenia, and osteoporosis were significantly higher in patients with CD than in those without CD. No significant differences were noted in the incidence of constipation, vomiting and/or nausea, heartburn and/or acid reflux, belching, headache and/or dizziness, anxiety and/or depression, or *H. pylori* infection between CD and non-CD patients (**Table 3**).

Histological presentation

The main endoscopic manifestations of duodenal villous atrophy in CD patients were nodular mucosal atrophy, grooves, and fissure-like lesions. Overall, 24 patients showed nodular mucosal atrophy, 29 showed grooves and fissure-like lesions, 4 showed mosaic signs, 12 showed scallop-like lesions, 9 showed wrinkle reduction or disappearance, and 15 showed multiple manifestations. Villous atrophy in the terminal ileum was observed in 10 patients with CD, whereas normal terminal ileal mucosa was observed in another 40 patients. The histological findings of CD included total villous atrophy, increased intraepithelial lymphocytes, and crypt hyperplasia.

H. pylori infection

The *H. pylori* infection rates of CD and non-CD patients were 48.0% and 57.4%, respectively, and the difference was not statistically significant. Abdominal pain was significantly more frequent in CD patients without *H. pylori* infection than in those with *H. pylori* infection. Of the patients with CD, 17 were classified as Marsh grade 2 and 33 were Marsh grade 3. The rates of *H. pylori* infection were significantly different between the different Marsh grades (P = 0.032) (**Table** 4). Further pairwise comparisons showed significant differences in the detection rate of *H. pylori* between CD patients with Marsh grades 2 and 3b (P = 0.025). Patients with *H. pylori* infection were more commonly found with Marsh grade 2 and more patients without *H. pylori* had Marsh grade 3b.

DISCUSSION

At present, there is a paucity of clinical and epidemiological data on CD in China. To the best of our knowledge, no large-sized sample data analysis on the pathological characteristics of CD patients is available in the literature to date. Additionally, there are no published reports on the relationship between CD and *H. pylori* infection. The prevalence of celiac disease is high in Europe[9, 26]. Northwest China connects Eurasia and lies on the ancient Silk Road. Historically, there may have been intermarriages between the populations of this region and those of Europe. CD susceptibility genes present in European populations may have thus been introduced into this region, leading to an increase in CD incidence. In addition to genetic susceptibility, wheat is the main food crop in this population. These factors may contribute to the high detection rate of CD in northwest China. Northwest China is a multi-ethnic region, where ethnic groups such as Hans, Uygurs, Huis, and Kazakhs live together. A previous study by Zhou *et al* found a high incidence of CD in Xinjiang and a higher detection rate of CD in Kazakhs than in Uygurs and Hans[27]. Studies have found that HLA-DQ2 and HLA-DQ8 gene carrier rates are high in Kazakhs and Uygurs[27, 28]. Genetic susceptibility may be the reason for the difference in prevalence among the different races.

In this study, 2,884 patients with GI symptoms were screened for CD according to the global guidelines of the World Gastroenterology Organization [29]. Among them, 73 were positive for anti-tTG IgA, and 50 were pathologically diagnosed with CD. CD can occur at any age, and the prevalence rate in women is 2–4 times higher than that in men [30, 31]. In line with this, our study found higher prevalence rates of CD in female patients than in male patients. The clinical manifestations of CD include delayed growth, malnutrition, chronic diarrhea, abdominal pain, and abdominal distension. Up to 17% of female patients may present with severe clinical manifestations during pregnancy or puerperium [32]. This study found that the main clinical manifestations of CD patients in Xinjiang included chronic diarrhea, severe malnutrition, osteoporosis, anemia, fatigue, and decreased BMI. BMI is an important index for evaluating and predicting CD and diarrhea is a typical symptom of CD. The immune response caused by gluten intake in susceptible populations leads to intestinal absorption dysfunction and osmotic diarrhea. In our study, 21 patients with CD-related diarrhea mainly presented with profuse watery and fatty diarrhea. Due to the lack of knowledge and limited diagnostic criteria for CD, diarrhea often becomes chronic, making the disease more difficult to control. Therefore, most patients exhibit significant weight loss, accompanied by anemia, iron and vitamin D deficiency, and other forms of malnutrition. In Britain, individuals with suspected CD were screened to avoid complications associated with delayed CD diagnosis [24]. Therefore, CD screening should be performed in patients with GI symptoms in China, especially those with anorexia and significant weight loss. Most new celiac disease patients in Europe present with extra intestinal manifestations and are missed because they are not tested for CD [33]. The European Society for Paediatric Gastroenterology Hepatology and Nutrition, suggests that the relatives of patients with CD or other autoimmune diseases should also be screened for the same conditions. Mass screening for celiac disease is not currently recommended[3]. At present, there are no relevant guidelines for celiac disease in the Chinese population; however, a similar strategy to that followed in Europe could be adopted.

CD is caused by gluten in susceptible subjects, and its etiology is not fully understood. With the increasing prevalence of CD, people have begun to consider environmental risk factors that may trigger autoimmunity in the small intestine[34]. *H. pylori* is one of the most common chronic bacterial infections worldwide, and can cause severe gastroduodenal diseases [35]. Both *H. pylori* infection and CD involve systemic humoral and local immune inflammatory responses. Chronic gastric infection that can induce duodenal ulcers and affect the systemic immune response may trigger autoimmunity in the small intestine[36]. Whether *H. pylori* infection can prevent or induce CD remains a hot topic. Epidemiological studies have been conducted on the association between *H. pylori* infection and CD. However, these studies have reported conflicting results[37-39]. The variability of the results may be due to the different prevalence of *H. pylori* infection in different populations and the identification of patients who have not yet demonstrated clinically significant CD. There are no reports on the relationship between celiac disease and *H. pylori* infection in the population of Northwest China.

We evaluated the relationship between *H. pylori* infection and CD and found that *H. pylori*-positive CD patients demonstrated more severe mucosal damage than *H. pylori*-negative CD patients (Marsh grades 2 and 3) (P = 0.018). This is similar to the findings of Gungor *et al* [40]. However, it has been reported that in people without CD, *H. pylori* infection itself can cause duodenal mucosal damage[41]. In a study by Konturek *et al*, the prevalence of *H. pylori* infection was higher in CD patients than in controls [42]. Previous studies have shown that *H. pylori* infection can prevent the development of CD [43, 44]. This association may be related to the genetic factors of CD and/or *H. pylori*, the virulence of *H. pylori*, and the immunopathology involved. In addition to altering the acidity and content of gastric juice, *H. pylori* directly interacts with the immune system and increases intestinal permeability [45].

In CD patients, biopsy usually shows villous atrophy, crypt hyperplasia, and inflammation. However, some serologically positive individuals can have normal intestinal mucosa, but many of these patients later develop CD, which is sometimes termed “latent CD” [46]. In these atypical cases, more than 95% of anti-tTG IgA-positive

patients may be sensitive to glutenin [47]. Our study found that the grades of five patients who presented with Marsh grade 1 in 2016–2019 improved to Marsh grade 0 by gastroscopy after following a GFD for at least half a year. Therefore, we speculate that early initiation of a GFD can improve the condition of patients with anti-tTG IgA-positive "latent CD." The healing rates of patients often differ significantly, and the older the patient at the time of the first diagnosis, the slower the intestinal healing process and the higher the possibility of non-reactive CD. There is no relevant research on "latent CD" in China, and more extensive screening and follow-up are necessary. Early diagnosis of CD can reduce the long-term and persistent damage caused by gluten to the intestinal tract and the whole body, thus resulting in better patient prognosis. Common causes of CD-related deaths are intestinal non-Hodgkin's lymphoma and small bowel cancers [48]. Refractory CD (RCD) is a major cause of poor prognosis. RCD can be divided into types I (RCD I) and II (RCD II). The phenotype of intraepithelial lymphocytes (IELs) is abnormal in RCD II patients and normal in RCD I patients. Approximately 50%–60% of RCD II patients develop EATL within 5 years after diagnosis[49]. Both are (pre)malignant complications of CD. Patients with RCD II and EATL are often associated with more severe malnutrition due to intestinal malabsorption and hypermetabolism[50]. No patients with RCD or EATL were found in this study, but Marsh grades were positively correlated with patient age. Therefore, CD patients who have significant weight loss or are elderly should be screened for CD GI endoscopy.

Study limitations

To the best of our knowledge, this is the first study to comprehensively analyze the clinical and pathological characteristics of Chinese CD patients and evaluate the association of CD with *H. pylori* infection. Our study not only bridges the gap in relevant research in the Chinese population, but also provides reference values for the diagnosis and treatment of CD. However, this study had several limitations. The subjects were patients with GI symptoms in the hospital, which may have resulted in selection bias. HLA-DQ2 or HLA-DQ8 genotypes were not identified in our study;

therefore, further research on the relationship between these genotypes and the pathological types of CD is warranted.

CONCLUSION

Among people with GI symptoms in Northwest China, the prevalence of CD is higher in the Uygur and Kazak populations. Physicians should be aware of the risk of CD in the regional population. *H. pylori* infection may be related to the severity of CD, which warrants further study.

ARTICLE HIGHLIGHTS

Research background

Research on celiac disease (CD) in Northwest China is still in its infancy. At present, large sample data on the epidemiological, clinical, and pathological characteristics of CD are limited.

Research motivation

This study reports the epidemiological, clinical, and pathological characteristics of celiac disease and its association with *H. pylori* infection, and aims to provide useful information for clinical diagnosis and treatment of CD.

Research objectives

To investigate the epidemiological, clinical, and pathological characteristics of CD in northwest China.

Research methods

The clinical data of 2,884 patients with gastrointestinal (GI) symptoms were retrospectively analyzed. Total immunoglobulin A and anti-tissue transglutaminase IgA levels were examined for all patients. Gastroscopy and colonoscopy were performed in patients with positive anti-tTG IgA and deficient total IgA levels. Atrophy

of the duodenal and ileal villi was examined, and histopathological examinations were performed. The modified Marsh–Oberhuber classification system was used to grade villous atrophy in the duodenum or distal ileum. Patient *H. pylori* infection status was compared in terms of clinical presentation and Marsh grade. Statistical analyses were performed using t-test or chi-square test.

Research results

The detection rate of CD was significantly higher in Kazakhs (4.39%) than in Uygurs (2.19%), Huis (0.71%), and Hans (0.55%). The main symptoms of CD were chronic diarrhea, anorexia, anemia, fatigue, weight loss, sleep disorders, osteopenia, and osteoporosis. The BMI of CD patients was significantly lower than that of non-CD patients. Endoscopy revealed crypt hyperplasia and/or duodenal villous atrophy, which mainly manifested as nodular mucosal atrophy, grooves, and fissures. The difference in *H. pylori* infection rates was not statistically significant between CD and non-CD patients, but was significantly different among CD patients with different Marsh grades. Patients with *H. pylori* infection were more commonly found with Marsh grade 2 and more patients without *H. pylori* had Marsh grade 3b.

Research conclusions

Among people with GI symptoms in Northwest China, the prevalence of CD is higher in the Uygur and Kazak populations. Physicians should be aware of the risk of CD in the regional population. *H. pylori* infection may be related to the severity of CD, which warrants further study.

Research perspectives

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