

Original Article

Risk factors of inflammatory bowel disease in the North-Western Chinese population

*Yahong Li**, *Shengjun Wu***, *Jie Liang****, *Xia Zhu*****, *Xin Zhang******,
*Kaichun Wu******, *Danmin Miao ******

Abstract

BACKGROUND: The aim of study was to screen the risk factors of inflammatory bowel disease (IBD) in north-western Chinese population by case investigation.

METHODS: 72 determined IBD patients and 72 paired healthy subjects were surveyed with an organized inventory comprising of relevant items to IBD. Cox regression method was used to screen the statistically significant risk factors for IBD.

RESULTS: Cox regression indicated the statistical significance in stress, milk and fried food over the other postulated risk factors for IBD in the north-western Chinese population.

CONCLUSIONS: Stress, milk and fried food are the potential risk factors for IBD in the north-western Chinese population.

KEY WORDS: Inflammatory bowel disease, north-western Chinese population, risk factors.

JRMS 2007; 12(3): 112-116

Since World War II, the incidence of inflammatory bowel disease (IBD) has been increased by approximately 6/100,000 for Crohn's disease (CD) and 15 to 20/100,000 for ulcerative colitis (UC). A marked rise in the twenty to forty years age group is observed for the both entities¹. IBD was once an uncommon gastrointestinal problem in Asia. However, there have been many reports demonstrating a

recent growing incidence of these diseases in this continent². In China, in the latest decade, more than 20,000 UC cases have been reported³. The ulcerations occur primarily in the small and large intestines. But, they may appear anywhere in the digestive tract from the mouth to the anus. Although the common symptoms of CD are mostly abdominal pain (which often occurs in the lower right area) and diarrhea,

*Co-first Author, Attending Physician of Gastroenterology, PLA 323 Hospital, Datong, China.

**Co-first Author, Teaching Assistant of Psychology, Department of Psychology, Faculty of Aerospace Medicine, Fourth Military Medical University, Xi'an, China.

***Clinical Resident of Gastroenterology, State Key Laboratory of Cancer Biology, XiJing Hospital, Fourth Military Medical University, Xi'an, China.

****Associate Professor of Psychology, Department of Psychology, Faculty of Aerospace Medicine, Fourth Military Medical University, Xi'an, China.

*****Attending Physician of Gastroenterology, Central Hospital of Xi'an, China.

*****Professor of Gastroenterology, State Key Laboratory of Cancer Biology, XiJing Hospital, Fourth Military Medical University, Xi'an, China. e-mail: kaicwu@fmmu.edu.cn (Corresponding Author)

*****Professor of Psychology, Department of Psychology, Faculty of Aerospace Medicine, Fourth Military Medical University, Xi'an, China. e-mail: psych@fmmu.edu.cn (Corresponding Author)

rectal bleeding, weight loss and fever may also appear. The causes of the ulcerations have not been yet identified but, the genetic factors which induce the continued abnormal activation of the immune system and also the environmental factors which trigger IBD have been suggested ^{4,5}. Leong RW et al studied the epidemiology and the phenotype of CD in the Chinese Hong Kong population. He indicated that the increased incidence of CD in the Chinese Hong Kong population holds a notable epidemiological and phenotypic difference from the Caucasian CD. These differences include the lack of familial clustering, male predominance, and higher proportion of upper gastrointestinal tract involvement and lower frequency of isolated terminal ileal disease ⁶. The epidemiology of IBD in the north-western Chinese population remains unclear. To clarify the epidemiology and the possible risk factors of IBD in the north-western Chinese population, this population-based cohort of newly diagnosed cases was done.

Methods

Patients

Between September 2004 to July 2005 all patients with the diagnosis of IBD at the XiJing Hospital (Xi'an, China) were included in this study. The diagnosis of IBD was based on the clinical, endoscopic, radiological and histological features according to national modified agreed criteria (Chengdu, Sichuan, 2000). 72 patients (44 male and 28 female) between the ages of 20 to 65 with the mean age of 46.6, were included in this study. From the total number of the cases, 65 patients had UC and 7 patients had CD. The subjects were compared with the same number of population who aged 15-65 years in the same residential quarter (the patients' neighbors) and did not suffer from the digestive system disease. Care was taken to exclude, by microscopy and culture of stool samples, infective causes of colitis. Patients with microscopic colitis were also excluded. Those under 15 or over 65 years old or subjects who lived relatively far were carefully excluded from the control population.

Clinical characteristics

For all patients, clinical characteristics at the initial presentation were obtained by the review of the medical notes, X-rays, endoscopic and histological reports. The extent of disease at diagnosis was defined macroscopically by the proximal limit of inflammation at colonoscopy (carried out in 95% of patients) and was divided into mild, moderate and severe categories. There were 13 mild, 44 moderate and 15 severe patients all together.

Questionnaire

The questionnaire was specifically made according to the recommended items in the National IBD Patients Case Control Research Project (protocol). It included 14 items such as genetic factors (whether one of the parents had the IBD medical history), infective enteropathy, eating habits (drinking, hydroposia, vegetarian diet or carnivorous), economic status, family sanitation conditions, smoking (calculated by one), drinking milk (calculated by ml), eating fried food (converted to the numbers of deep-fried twisted dough sticks) and eating hot food. 60 patients filled out the questionnaire in our department with the guidance of the investigator. 12 patients completed the questionnaire at home and hand delivered or mailed it to us.

Statistical analysis

Data were analyzed by Cox regression method in SPSS 11.0 software to select the significant risk factors with IBD in the north-western Chinese population. Differences were considered significant when $P < 0.05$.

Results

From September 2004 to July 2005, 72 new IBD patients were diagnosed at the XiJing Hospital. Of these patients, 65 (90.3%) had UC and 7 (9.7%) had CD; i.e. the hospital incidence of UC in the north-western China is nine times that of CD but, it is difficult to determine the true population incidence of IBD from the observed data as an accurate denominator for this calculation is not available. In another word, the size of the population served exclu-

sively by our hospital cannot be defined by geographical boundaries as patients may choose to seek help from different hospitals.

Gender

The male-female ratio was 1.6:1 for IBD patients.

Age at diagnosis

The ages at diagnosis of UC and CD patients were from 20 to 65 years with the mean age of 46.6 years. Most of the patients were clustered on the 3rd and 6th decades of their lives.

Risk factors related to IBD

Among the 14 items in the questionnaire, stress, drinking milk and eating fried food were shown to be significantly related to IBD in the north-western Chinese population as indicated in table 1. Stress and eating fried food manifested as more statically significant.

Table 1. Risk Factors of IBD in north-western population of China.

Risk Factors	P Value
Stress	0.000
Milk	0.012
Fried Food	0.000

Discussion

IBD is a kind of enter-inflammatory disease with unclear causes which might be caused by the inherent IBD, hereditary susceptibility, environmental factors, micro-organism antigen, or abnormal immunological reactions. Its underlying mechanism is related to a polygenic inheritance but this disease also shows genetic heterogeneities. Patients may experience similar symptoms with totally different hereditary basis. Ahmed FE et al ⁷ recently studied the transgenic or knockout mice and found that some immunologic agents like interleukin-10 (-/-), T-cell receptor alpha (-/-), Galphai (-/-) and N-cadherin (-/-), develop colitis-like inflammation similar to that of humans. Though we are not sure about the etiological factors, it's still helpful to select some risk factors in the population to enhance our recognition and prevention of IBD. Our study on IBD patients

of the north-western of China showed some characteristics: 1) Most IBD patients in our study were in the 3rd or 6th decades of life. It may be caused by different risk factors in the two different age groups. Patients in their 3rd decades of lives might fall in IBD because of the strong immunological function in their gastrointestinal tract which produces excessive immunological response to antigenic stimulation. While the old ones might have IBD because of the long time exposures to certain environmental risk factors. 2) The gender ration of the IBD patients in our study was 1.6:1. This ratio was different from the general morbidity of IBD which was more severe in female than in male. Some other reports also showed the same pattern ⁸. The reason may lie in the limit of samples in our research. 3) Distribution of severity of IBD was different in different age groups. In our study, the patients in their thirties showed severe symptoms, while the much older patients (those in their sixties) showed either light or severe IBD. 4) The incidence of IBD in our research included 90.3% UC and only 9.7% CD which was similar with the general population studies and was in accordance with studies in other places of China. Findings of the questionnaire analysis indicated three risk factors which were significantly related to IBD. Stress was one of the risk factors which is the same with other observations ^{9,10}. Because of the acceleration of modern life and more complicated population relationships, people will suffer more stress. This may be one of the reasons that the incidence of IBD is increasing every year. It was previously found that the functional enteropathy was related to the psycho-mental factors ¹¹. Physical and mental diseases have been hot investigative targets for both the psychological and clinical medicine. The interaction between them is through the neuroendocrine system. Our human body will be in a kind of excitable status when we have stress. Then, the hypothalamic-pituitary-adrenal axis (HPAA) will be over activated and will secret more adrenal cortex hormone (ACH), luteotropin (PRL) and glucagons (GN). Thus, it causes the abnormal immunological

function in the local gastrointestinal tract. Similar psychological diseases and somatization phenomena have been widely found in clinic nowadays^{12,13}.

The second risk factor was fried food which is becoming more and more popular in our daily lives. With the accumulation of fried food, people may be easily fall in IBD¹⁴. Like the deep-fried twisted dough sticks, which are mostly fried again and again in a high temperature with the same oil, some toxic materials accumulated during the repeated overheated fried oil, will cause food poisoning or a potential harm. For example, the lipid peroxidation is the key factor in producing atherosclerosis; hydroxide radical peroxidase and its secondary products (polymerizer) will cause mutation. Experts in National CDC Nutrition and Food Hygiene Institute proved that over-used oil will produce polycyclic aromatic hydrocarbons, which contain acrylamides and

damages DNA and also induce colon carcinoma¹⁵. The third risk factor was milk. As the main protein in milk, casein will cause a series of allergic symptoms reflected in gastrointestinal tract, both in children and adults^{16,17}. Another protein, bovine serum albumin (BSA) causes allergy and is a cause of type I diabetes mellitus (IDDM) as well. In Karjalainen's report nearly 100% of newly diagnosed IDDM patients had higher BSA IgG antibody¹⁸. Taken together, in our study, we found that stress, fried food and milk were the possible risk factors of IBD in the north-western population and were all related to people's modern lives. To avoid such risk factors, it may be helpful to encourage people to lead a healthier life and therefore to prevent IBD.

Acknowledgements

This study was supported in part by the grants from the Chinese National Foundation of National Sciences (30572134).

References

1. Ekblom A. **The epidemiology of IBD: a lot of data but little knowledge. How shall we proceed?** *Inflamm Bowel Dis* 2004; 10 Suppl 1:S32-S34.
2. Rerknimitr R, Chalapipat O, Kongkam P, Mb PK. **Clinical characteristics of inflammatory bowel disease in Thailand: a 16 years review.** *J Med Assoc Thai* 2005; 88 Suppl 4:S129-S133.
3. Zheng JJ. **Clinical aspects of ulcerative colitis in mainland China.** *Chin J Dig Dis* 2006; 7(2):71-75.
4. Oostenbrug LE, van Dullemen HM, te Meerman GJ, Jansen PL. **IBD and genetics: new developments.** *Scand J Gastroenterol Suppl* 2003;(239):63-68.
5. Esters N, Pierik M, van Steen K, Vermeire S, Claessens G, Joossens S et al. **Transmission of CARD15 (NOD2) variants within families of patients with inflammatory bowel disease.** *Am J Gastroenterol* 2004; 99(2):299-305.
6. Leong RW, Lau JY, Sung JJ. **The epidemiology and phenotype of Crohn's disease in the Chinese population.** *Inflamm Bowel Dis* 2004; 10(5):646-651.
7. Ahmed FE. **Role of genes, the environment and their interactions in the etiology of inflammatory bowel diseases.** *Expert Rev Mol Diagn* 2006; 6(3):345-363.
8. Cao Q, Si JM, Gao M, Zhou G, Hu WL, Li JH. **Clinical presentation of inflammatory bowel disease: a hospital based retrospective study of 379 patients in eastern China.** *Chin Med J (Engl)* 2005; 118(9):747-752.
9. Kim SC, Ferry GD. **Inflammatory bowel diseases in pediatric and adolescent patients: clinical, therapeutic, and psychosocial considerations.** *Gastroenterology* 2004; 126(6):1550-1560.
10. Mackner LM, Sisson DP, Crandall WV. **Review: psychosocial issues in pediatric inflammatory bowel disease.** *J Pediatr Psychol* 2004; 29(4):243-257.
11. Wang L, Xia X, Jiang S. **Psychological analysis of functional gastroenteropathy.** *Railway Medical Journal* 2002; 30(1):31-32.
12. Andersen MO, Andersen GR, Thomsen K, Christensen SB. **Early weaning might reduce the psychological strain of Boston bracing: a study of 136 patients with adolescent idiopathic scoliosis at 3.5 years after termination of brace treatment.** *J Pediatr Orthop B* 2002; 11(2):96-99.
13. Olafsson Y, Saraste H, Al Dabbagh Z. **Brace treatment in neuromuscular spine deformity.** *J Pediatr Orthop* 1999; 19(3):376-379.
14. Persson PG, Ahlborn A, Hellers G. **Diet and inflammatory bowel disease: a case-control study.** *Epidemiology* 1992; 3(1):47-52.

15. Wang A. **New carcinogen in fried starch food: acrylamide.** *Environment and Occupation Medicine* 2002; 19(6):347.
16. Levy FS, Bircher AJ, Gebbers JO. **Adult onset of cow's milk protein allergy with small-intestinal mucosal IgE mast cells.** *Allergy* 1996; 51(6):417-420.
17. Iacono G, Carroccio A, Cavataio F, Montalto G, Kazmierska I, Lorello D et al. **Gastroesophageal reflux and cow's milk allergy in infants: a prospective study.** *J Allergy Clin Immunol* 1996; 97(3):822-827.
18. Karjalainen J, Saukkonen T, Savilahti E, Dosch HM. **Disease-associated anti-bovine serum albumin antibodies in type 1 (insulin-dependent) diabetes mellitus are detected by particle concentration fluoroimmunoassay, and not by enzyme linked immunoassay.** *Diabetologia* 1992; 35(10):985-990.