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Original Article

Epidemiological investigation, extraesophageal symptoms and risk factors of gastroesophageal reflux disease in Kashgar, Xinjiang, China

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Abstract: Objective: To explore the incidence, distribution characteristics and related symptoms of gastroesophageal reflux disease (GERD) as well as its related risk factors in Kashgar, Xinjiang. Methods: From March 2020 to October 2020, a questionnaire survey was conducted among 5,080 permanent residents aged 18-80 years in Kashgar using cluster sampling and stratified sampling methods. The content included basic information, accompanying symptoms and diseases, living, customs and eating habits, and Gastroesophageal Reflux Disease Questionnaire score, *etc*. Results: The prevalence of GERD in Kashgar was 23.4% (1187/5080), and the proportions of patients with reflux symptoms lasting 1 day, 2-3 days and 4-7 days within a week were 12.5%, 6.4% and 4.4%, respectively. The proportion of patients showing symptoms in the GERD group was significantly higher than that in the non-GERD group ($P<0.05$). The proportion of people who are overweight or obese, take alcohol drink, eat, constipate, or take various chronic disease drugs in the GERD group is higher than that in the non-GERD group. The proportion of people in the GERD group who often eat sweet foods, pickled products, roasted products, spicy foods and meat, or drink coffee, acidic beverages, and cold drinks was higher than that in the non-GERD ($P<0.05$). The proportion of people in the GERD group who regularly consume fish, milk, eggs, vegetables, and fruits was significantly lower than that in non-GERD group ($P<0.05$). Logistic regression analysis found that Uyghur nationality (for the Han nationality), age (for the 30-39 years group), drinking, overeat, constipation, and frequent medication were risk factors ($P<0.05$, OR>1). Multivariate logistic regression analysis found that sweets, baked products, cold drinks, and spicy foods were independent risk factors ($P<0.05$, OR>1). Eggs and vegetables were protective factors ($P<0.05$, OR<1). Conclusion: The high incidence of GRED in Kashgar, Xinjiang may be related to the local living environment, and life and eating habits.

Keywords: Gastroesophageal reflux disease, Kashgar area, epidemiological research, risk factors

Introduction

Gastroesophageal reflux disease (GERD) refers to the symptoms of acid reflux, heartburn, etc. caused by the regurgitation of gastroduodenal contents to the esophagus, as well as extraesophageal diseases caused by regurgitation to the throat and even the lungs, such as asthma, chronic cough, idiopathic pulmonary fibrosis, hoarseness, pharyngitis and dental erosion [1]. GERD is not only a group of digestive diseases, but also chronic diseases related to asthma, obstructive sleep apnea syndrome, otitis media, chronic pharyngitis, depression, and anxiety, which seriously affect people's physical and mental health; however, the public and even medical personnel paid little attention to it [2, 3].

The prevalence of GERD is about 18.1-27.8% in North America, 8.8-25.9% in Europe, 2.5-7.8% in East Asia, 8.7-33.1% in the Middle East, and

11.6% in Australia [4]. An investigation of the 37,442 cases of Chinese adults showed that the incidence of GERD in adults in China was up to 19.89% [5]. A study in 2012 reported that the incidence of GERD was 35% in Uygur population and 26% in Han population, respectively, in Urumqi, Xinjiang [6]. Numerous studies have shown that there are significant differences in the prevalence of GERD and its risk factors in different regions, occupations, ages, body mass index (BMI), diets, and living habits, and there is an upward trend [7-9].

Materials and methods

From March 2020 to October 2020, a survey was conducted in permanent residents aged 18-80 years in Kashgar, including 2927 (57.6%) females and 2153 males (42.4%) with 4865 Uyghurs (95.7%) and 215 Hans (4.3%). The average age was 43.2±15.4 years. Patients with malignant tumors, failure to cooperate in completing the investigation due to residents' educational level, language and mental retardation, etc., and patients with heart failure and malignant tumors were excluded. This study was approved by the First People's Hospital of Kashgar Prefecture (No. [2020] Quick Review (85)), and all subjects signed informed consent before participating in the survey.

Sampling methods: Through cluster sampling and stratified sampling methods, 4 counties/cities (except Ta County) in Kashgar Prefecture were randomly selected as the survey area, and were divided into two groups (two cites/countries in each group).

Method

Gastroesophageal Reflux Disease Questionnaire (GERD-Q) survey method [10]: the paper version of the GERD-Q score sheet and the electronic version of the questionnaire star QR code were used. The GERD-Q included 6 scoring items: (1) the frequency of a burning sensation (heartburn) behind the sternum; (2) the frequency of the stomach contents moving upwards to the throat or mouth (regurgitation); (3) the frequency of pain in the center of the upper stomach; (4) the frequency of nausea; (5) the frequency of difficulty in getting a good night's sleep because of heartburn and/or regurgitation; (6) self-use of additional medicines for heartburn and/or regurgitation.

In above 6 items, 4 of which assess symptoms and situations considered positive predictors for GERD diagnosis: heartburn, regurgitations, disorders related to sleep and use of over-the-counter drugs. Other 2 items assess symptoms considered negative predictors for reflux, such as nausea and epigastric pain. Patients answered each question about symptom frequency during last week using a Likert like scale from 0 to 3 for positive predictors and 3 to 0 for negative predictors. The total score of 6 items ≥8 points indicated the occurrence of GERD; the total score of (5) and (6) n3 points indicated that GERD had an impact on the quality of life.

Survey content of risk factors for GERD

(1) General information: gender, age, ethnicity, occupation, marital status, and body mass index. (2) Living habits: regular work and rest, over-saturated diet, mental stress, workload, smoking, and drinking. (3) Eating habits: sweets, preserved foods, roasted foods, spicy foods, coffee, acid beverages, cold drinks, strong teas, meats, cooked foods of animal offal, soy products, fish, eggs, milk, vegetables, salty food, and fruits. (4) Related symptoms: heartburn, chronic cough, regurgitation, acid reflux, chest pain, abdominal distension, nausea, vomiting, loss of appetite, back pain, and dysuria. (5) Medication history: weight loss pills, contraceptives, stomach medicine, high blood pressure, diabetes, analgesics, *etc*.

Training and assessment of investigators

Family doctors in the surveyed area and medical staff from the community and township hospitals were employed as investigators in this survey. Prior to the survey, uniform training and assessment were conducted, and only those passed the assessment were included in the survey team. The survey was carried out under regular supervision and regular inspections.

Statistical analysis

SPSS25.0 statistical software was used to analyze the survey results. Because of the large sample size, two independent sample t test or analysis of variance was used for the comparison of measurement data, the chi-square test was used for the comparison of count data, and nonparametric test was used for the com-

parison of rank data. Logistic regression analysis was performed for multivariate analysis. The *P* values were bilateral probability, and the test level was 0.05.

Results

The prevalence of GERD among the 5,080 subjects was 23.4%, among which the prevalence in Uyghurs was 23.8%, and in Hans was 16.8%. The prevalence of GERD in Uyghurs was significantly higher than that in Hans (*P*=0.01). The prevalence of GERD in different age groups was also significantly different with the lowest (19.9%) in population of 30-39 years old and the highest (28.6%) in population of 50-59 years old (*P*<0.001). The prevalence of GERD was also statistically different in population with different occupations. The prevalence of gastroesophageal reflux is the highest among civil servants and police with the rate of 37.6% and 28.6% respectively, showing significant difference between these two groups of people (χ^2=69.58, P<0.001). In addition, the prevalence of GERD in obese people was 25.7%, which was significantly higher than that of slim, normal or overweight people (*P*=0.02). Moreover, the prevalence of GERD in the population who regularly overate, had constipation and took drugs was significantly higher than that in the population who did not regularly overeat, had no constipation and did not take drugs (*P*<0.001) (**Table 1**).

Comparison of extra-esophageal manifestations

GERD group had more extra-esophageal symptoms. The results of this study showed that the incidences of asthma, chronic cough, dental caries, chronic obstructive pulmonary disease (COPD), otitis media, atrial fibrillation, interstitial pneumonia, loss of appetite, chronic chest pain, abdominal distension and other diseases or symptoms were significantly higher in the GERD group than those in the non-GERD group (all *P*<0.05). In addition, the incidences of gastroduodenal ulcer or inflammation, anxiety disorder, and chronic viral hepatitis in the GERD group were also significantly higher than those in the non-GERD group (all *P*<0.05) (**Table 2**).

Distribution of GERD among residents with different dietary habits

In the GERD group, the proportion of people who often eat sweets, preserved foods, roasted foods, spicy foods, coffee, acidic beverages, cold drinks, meat, and fish was significantly higher than that in the non-GERD group (P< 0.05). In the GERD group, the proportion of people who regularly consume fish, milk, eggs, vegetables, and fruits was significantly lower than that in non-GERD group (P<0.05). There was no significant difference in the proportion of people who regularly consume strong tea, animal offal, soy products, and salty food between the two groups (P≥0.05). See **Table 3**.

Analysis of multiple risk factors of GERD residents with different features

Characteristics of residents surveyed were grouped, and it was found in Logistic regression that Uighur nationality, age (30-39 years), alcohol consumption, satiation, constipation, and regular medication were risk factors (*P*< 0.05, OR>1). The Han nationality was a protective factor for GERD (*P*<0.05, OR=0.52), as shown in **Figure 1**.

Analysis of multiple risk factors of residents with different eating habits

Multivariate Logistic regression analysis found that sweets, baked products, cold drinks, and spicy foods were independent risk factors (*P*<0.05, OR>1). Eggs and vegetables were protective factors (*P*<0.05, OR<1), as shown in **Figure 2**.

Discussion

This study was conducted on an epidemiological survey of 5,080 residents in Kashgar Prefecture through the GERD-Q score sheet random stratified sampling method to study the prevalence of GERD, living and eating habits as well as risk factors in Kashgar Prefecture. The results of this study showed that the prevalence of GERD in the Kashgar Prefecture of Xinjiang was 23.4%, which was higher than the average prevalence of 12.89-19.8% reported in a previous Chinese literature [7], and was higher than that of some European and American countries [4]. The reason may be related to the geographical environment of the region and its more unique living and eating habits.

There was no significant difference in the distribution of GERD among different genders, but the prevalence of GERD was different among different ethnic group. For example, the prevalence of GERD in Uyghur population was higher

Table 1. Comparison of distribution of GERD among residents with different characteristics

Feature	Number of people surveyed (cases)	Number of GERD-affected population (cases)	Number of GERD-unaffected population (cases)	Prevalence rate (%)	χ^2/Z	*P* value
Gender						
Male	2153	479	1674	22.2	2.60	0.11
Female	2927	708	2219	24.1		
Nationality						
Uighur	4789	1138	3651	23.8	7.35[a]	0.01
Han	291	49	242	16.8		
Age group (years old)						
18-29	1080	227	853	21.1	37.40	<0.001
30-39	1367	272	1095	19.9		
40-49	875	191	684	21.8		
50-59	884	253	631	28.6		
>60	874	244	630	27.9		
Occupation						
Medical staff	463	110	353	23.8	69.58[a]	<0.001
Teacher	112	27	85	24.1		
Farmer	3545	821	2724	23.1		
Individual business	321	45	276	14.0		
Policemen	42	12	30	28.6		
Civil servants	340	128	212	37.6		
Students	90	7	83	7.8		
Catering industry	31	5	26	16.1		
Other	136	32	104	23.5		
BMI						
Low	163	24	139	14.7	-2.30	0.02
Normal	2046	460	1586	22.5		
Overweight	1755	416	1339	23.7		
Obesity	1116	287	829	25.7		
Smoking						
Yes	570	126	444	22.1	0.57	0.45
No	4510	1061	3449	23.5		
Drinking						
Yes	291	190	101	34.7	22.18	<0.001
No	4789	997	3703	22.7		
Mental state						
High pressure	1762	461	1201	31.8	2.05	0.36
Tension	1728	421	1184	31.5		
Easy to get angry	1590	205	1118	29.7		
Overeat						
Yes	1301	380	921	29.2	33.34	<0.001
No	3779	807	2972	21.4		
Constipation						
Yes	396	121	275	30.6	12.40	<0.001
No	4684	1066	3618	22.8		
Abdominal surgery						
Yes	301	80	221	26.6	1.84[a]	0.18
No	4779	1107	3672	23.2		
Regular medication						
Yes	686	208	478	30.3		<0.001
No	4394	979	3415	22.3	21.42[a]	

a, The expected value of 0 cells (0.0%) is less than 5.

Table 2. Comparison of extraesophageal symptoms between GERD group and non-GERD group

Extraesophageal symptoms	GERD group (n=1187)		Non-GERD group (n=3893)		Total	χ^2	*P*
	n	%	n	%			
Asthma	37	3.1	35	0.9	72	31.98[a]	<0.001
Chronic cough	86	7.2	99	2.5	185	57.21[a]	<0.001
Mouth ulcers	17	1.4	39	1.9	56	1.54[a]	0.22
Gastroduodenal inflammation/ulcer	87	7.4	92	2.4	179	67.78[a]	<0.001
Snore	122	10.3	186	4.8	308	48.21[a]	<0.001
Viral hepatitis liver disease	22	1.9	34	0.9	56	8.00[a]	0.01
Caries	121	10.2	298	7.7	419	7.70[a]	0.01
COPD	6	0.5	6	0.2	12	4.76[a]	0.03
Otitis media	19	1.6	28	0.7	47	7.69[a]	0.01
Pulmonary fibrosis	3	0.3	8	0.2	11	0.93[a]	0.76
Depression	11	0.9	18	0.5	29	3.45[a]	0.06
Anxiety	24	2	30	0.8	54	13.52[a]	<0.001
Atrial fibrillation	10	0.8	5	0.1	15	15.74[a]	<0.001
Interstitial pneumonia	48	4	65	1.7	113	23.82[a]	<0.001
Decreased appetite	108	9.1	120	3.1	228	76.67[a]	<0.001
Chest pain	38	3.2	29	0.7	67	42.12[a]	<0.001
Bloating	155	13.0	240	6.2	295	60.13[a]	<0.001
Backache	226	19	245	6.3	471	175.39[a]	<0.001

a, The expected value of 0 cells (0.0%) is less than 5.

Table 3. Comparison of GERD distribution among residents with different eating habits

dietary habits	Number of people exposed	No. of GERD cases	Incidence (%)	No. of Non-exposed cases	No. of GERD cases	Incidence (%)	χ^2	*P*
Sweets	2080	527	25.3	3000	660	22.0	7.64[a]	0.01
Pickled food	348	161	46.3	4732	1026	21.7	109.40[a]	<0.001
Grilled food	1551	414	26.7	3529	773	21.9	13.80[a]	<0.001
Spicy food	1033	281	27.2	4047	906	22.4	10.66[a]	<0.001
coffee	582	157	27.9	4498	1030	22.9	4.78[a]	0.03
Acid drink	676	187	27.7	4404	1000	22.7	8.04[a]	0.01
cold drink	3723	916	24.6	1357	271	20.0	11.92[a]	0.00
Strong tea	715	187	22.9	1893	629	24.9	0.44[a]	0.51
meat	1517	440	29.0	2816	747	21.0	38.40[a]	<0.001
animal organs	1060	261	24.6	3094	926	23.0	1.81[a]	0.28
Soy products	1068	242	22.7	3067	945	23.6	0.38[a]	0.54
Fishes	2293	495	21.3	2786	692	24.8	7.42[a]	0.01
Eggs	3057	587	19.2	2023	600	29.7	74.34[a]	<0.001
Milk	2113	435	20.6	2967	752	25.3	15.61[a]	<0.001
vegetable	3824	776	20.3	1256	411	32.7	81.58[a]	<0.001
fruit	3884	841	21.7	1196	346	28.9	27.04[a]	<0.001
Salty food	632	159	25.2	4448	1028	23.1	1.30[a]	0.26

a, The expected value of 0 cells (0.0%) is less than 5.

than that of Han population. Some scholars have reported that the prevalence of GERD in females is higher than that in males, which is inconsistent with the results of this study. The prevalence for males and females may differ by region and ethnic group [11]. Niu et al. [6] reported that the prevalence of GERD in Urumqi and Han populations in Urumqi, Xinjiang was 35% and 28%, respectively, which was higher than the results of this study. The reason may be that the number of patients in the hospital was mainly small, so the prevalence may be

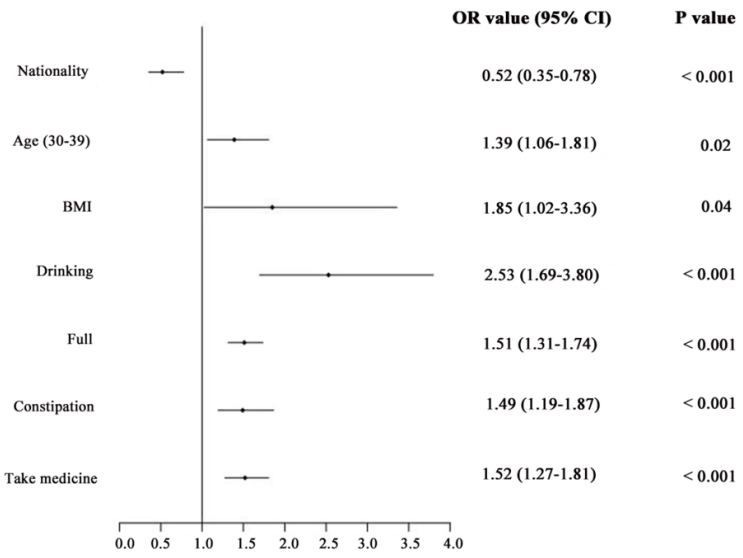

Figure 1. Logistic regression analysis of different residents' characteristics in GERD.

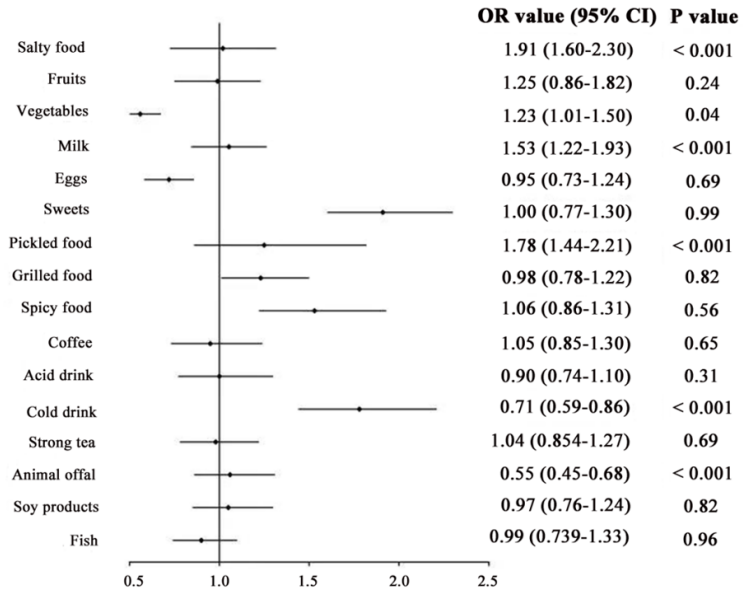

Figure 2. Logistic regression analysis of risk factors for GERD eating habits.

higher than this study, but the prevalence of Uyghur population was higher than that of Han population, and the findings were consistent with the results of this study.

This study exhibited significant differences in the prevalence of GERD among people with different age, occupations, BMI, and diet and bowl movement status. The prevalence of GERD in different age groups also varies a lot. Among them, the prevalence of GERD in people aged 50-59 years was the highest (28.6%), which was significantly higher than other age groups. The logistic regression results also showed that age was a risk factor for GERD. Jemilohun et al. [12] and Kariri et al. [13] reported that the prevalence of GERD increased with age, and age was one of the risk factors for GERD, similar to the results of this study. Minatsuki et al. [14] grouped people into different age groups similar to the method of this study, and the results suggested that the prevalence in 50-54 and 55-55 age groups were 19.2% and 19.7%, respectively, which were significantly higher than other age groups, similar to the results of this study. The distribution of GERD was different in different occupations. The results of epidemiological studies by Farjam et al. [15] and Karimian et al. [16] showed that the prevalence of GERD in administrative staff and medical staff was significantly higher than that in other occupations. The occupational characteristics of this study showed that civil servant and police personnel had the highest incidence, followed by medical staff, which is similar to the above research. The reasons may be closely related to work and rest habits, work stress and irregular eating habits. Obesity is a recognized risk factor for GERD. The results of this study showed that the prevalence of GERD increased significantly with the increase of BMI. Multiple studies have reported that the prevalence of GERD increases significantly with the increase of BMI or abdominal circumference, regardless of different geographic environments or ethnicity, and obesity is listed as an independent risk factor [2].

In addition, the prevalence of GERD in people who overeat, consume alcohol, constipate or take medication, was significantly higher than

people who do not. After analyzing the single-factor risk factors of the above residents, it was found that the prevalence of GERD in population with obese, high blood pressure or coronary heart disease, and those who overate, consumed alcohol, constipate and take medication regularly was significantly higher than those without. Nwokediuko et al. [9] reported that oral herbal medicines or analgesics were risk factors for GERD. Hu et al. [17] reported that constipation and satiety were risk factors for GERD. The results of the above studies were similar to this study. Gong et al. [5] reported that weight, alcohol consumption, and smoking were risk factors, but the results of this study showed that smoking was not significantly related to GERD. Some studies have shown that most patients with GERD have chronic diseases such as hypertension, diabetes, and hyperlipidemia [18]. Bor et al. [19] reported that the prevalence of GERD among people who consumed alcohol and cigarette was significantly higher than that of other people, and the prevalence increased significantly with the increase of age and weight. In short, combined with the results of this study and many other studies, bad living habits are the main pathogenic factor of GERD. Adjusting lifestyle habits, weight control, early detection, early treatment of chronic diseases such as hypertension and diabetes can effectively reduce the prevalence of GERD.

Some scholars have reported that GERD is related to poor eating habits [5]. This study suggested that the prevalence of GERD was significantly higher in the people with dietary habits preferring sweets, preserved foods, roasted foods, spicy foods, coffee, acid beverages, cold drinks, and meats. The prevalence of GERD in people who consumed more vegetables, fruits, eggs, and fish was lower than those who consumed more alcohol and overate. Multivariate Logistic regression analysis showed that sweets, baked products, and spicy foods were independent risk factors, and vegetables and eggs were protective factors. From the perspective of eating habits, several studies have shown that sweets, spicy foods, coffee or tea, meat or high-fat foods are listed as the main risk factors for GERD, which are similar to the results of this study [20]. It has been reported that vegetables and fruits can significantly reduce the prevalence of GERD, which is similar to the results of this study [5]. However, the ingestion of eggs and fish is also a risk factor for GERD. On the contrary, the results of this study suggested that it was a protective factor. The results of the study were contradictory, and more in-depth research is needed in the future [5]. Studies have shown that fruits, vegetables, and high-fiber foods are related to the low prevalence of GERD, which is similar to the results of this study [21]. Scholars such as Halawani and Banoon [22] have reported that tomatoes or tomato products, acid beverages, salty foods, and various pain medications are risk factors for GERD. Yao et al. [23] also reported that bad eating habits preferring satiety, sweets, spicy foods, high-fat foods, and alcohol are risk factors for GERD, which is similar to the results of this study.

The Uyghurs account for 92.56% of the total population in this region. Their main food is mainly lamb and pasta. The residents tend to consume less vegetables, but more fruits, roasted products, strong tea, etc., and even overeat. Eating habits such as short interval between bedtimes may increase the prevalence of GERD in this region.

This study has certain limitations. It was conducted by using the GERD-Q scale to diagnose GERD with symptoms, and did not use objective examination indicators such as gastroscopy, contrast-enhanced ultrasound, or esophageal acid test, and the above could not be achieved through extensive epidemiological screening. The survey results were affected by factors influencing the investigator or the respondent, which may cause misclassification of diseases and/or symptoms, reduce the accuracy of the research, and it is difficult for cross-sectional studies to determine the causal sequence of exposure and disease. Therefore, finding a simple, cheap, and objective examination method is a new research direction for the diagnosis, treatment and follow-up of GERD in the future.

In summary, GERD is a group of diseases with heartburn sensation and regurgitation predominantly, including many extraesophageal symptoms. The incidence of GERD in Kashgar, Xinjiang is higher than that in other regions. The reason may be related to the living environment, and unique living and eating habits in this region. Adjusting bad eating and living hab-

its and improving the awareness of GERD are beneficial to the physical and mental health of the local residents.

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Disclosure of conflict of interest

None.

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