

RAPID COMMUNICATION

Risk factors of gastroesophageal reflux disease in Shiraz, southern Iran

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Abstract

AIM: To determine the prevalence and symptoms of gastroesophageal reflux disease (GERD) in a healthy general population in relation to demographic, lifestyle and health-seeking behaviors in Shiraz, southern Iran.

METHODS: A total of 1978 subjects aged > 35 years who referred to Gastroenterohepatology Research Center and who completed a questionnaire consisting of 27 questions for GERD in relation to demographic, lifestyle and health-seeking behaviors were included in this study for a period of five months. The validity and reliability of the questionnaire were determined.

RESULTS: The prevalence of GERD was 15.4%, which was higher in females (17.3%), in rural areas (19.8%), and in illiterate subjects (21.5%) and those with a mean age of 50.25 years. The prevalence was significantly lower in subjects having fried food (14.8%), and fruit and vegetables (14.6%). More symptoms were noticed in subjects consuming pickles (22.1%), taking aspirin (21%) and in subjects with psychological distresses (27.2%) and headaches (22%). The correlation was statistically significant between GERD and halitosis (18.3%), dyspepsia (30.6%), anxiety (19.5%), nightmares (23.9%) and restlessness (18.5%). Their health seeking behavior showed that there was a significant restriction of diet (20%), consumption of herbal medicine (19%), using over-the-counter drugs (29.9%) and consulting with physicians (24.8%). Presence of GERD symptoms was also significantly related to a previous family history of the disease (22.3%).

CONCLUSION: GERD is more common in females, rural and illiterate subjects and correlated with consumption of pickles, occurrence of headache, psychological distress, dyspepsia, halitosis, anxiety, nightmare and restlessness, and a family history of GERD and aspirin intake, but the correlation was negative with consumption of fat and fiber intake.

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Key words: Reflux; Risk factors; Prevalence; Southern Iran

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INTRODUCTION

Symptoms of gastroesophageal reflux disease (GERD) represent one of the most frequent health problems in the western world^[1]. Approximately 10% of the American population suffer from daily heartburn and about one third have periodic symptoms^[2]. Based on the population studied, the prevalence of the primary GERD symptoms, heartburn (a burning feeling behind the breast bone) or acid regurgitation (an acid taste in the mouth) varies between 9% and 42%^[3]. The relationship between GERD and lifestyle habits, e.g, cigarette smoking, alcohol and coffee consumption, ingestion of medications such as aspirin and non-steroidal anti-inflammatory drugs (NSAIDs), and diet has not been firmly established, and inconsistent results have been obtained from population-based studies^[1,4-8].

As there are few population-based data on GERD in Asia^[9-12], this study was performed for the first time in Shiraz, southern Iran with the aim of determining the prevalence of GERD symptoms and describing the demographic, lifestyle and health-seeking behaviors associated with GERD.

MATERIALS AND METHODS

Materials

This study was carried out in a group of GERD patients.

Table 1 Frequency of GERD symptoms and their correlation with different characteristics of subjects in Shiraz, Southern Iran (*n* = 1978)

Characteristics		GERD Symptoms (%)		<i>P</i> value
		Present	Absent	
Gender	Male	12.3	87.7	0.003
	Female	17.3	82.7	
Habitat	Urban	13	87	0.001
	Rural	19.8	80.2	
Education	Illiterate	21.5	78.5	< 0.001
	Primary school	16.1	83.9	
	High school	13.6	86.4	
Physical activity	University	12.3	87.7	0.373
	No	14.8	85.2	
Psychological distress	Yes	16.3	83.7	0.003
	No	14.9	85.1	
Recurrent headache	Yes	27.2	72.8	0.009
	No	14.7	85.3	
Past GI disease history	Yes	22	78	< 0.001
	No	13.3	86.7	
	Thin	22.3	77.7	
Body mass index	Thin	10.5	89.5	0.065
	Normal	15.7	84.3	
	Overweight	13.4	86.6	
Age (mean) (yr)	Obese	18.8	81.2	0.547
		50.25	49.83	

GERD: Gastroesophageal reflux disease.

Methods

In a population-based study, 3600 subjects were selected by cluster random sampling method based on postal code division of Shiraz, southern Iran into 17 districts. After clarifying the research project for each subject, he/she received an invitation letter to refer to Mottahari Digestive Clinic of Gastroenterohepatology Research Center affiliated to Shiraz University of Medical Sciences. The project was approved by the Ethics Committee of the university and a written consent was obtained from each patient participating in the study. The study was undertaken for a period of five months from April to September 2004 while 1978 subjects completed the questionnaire. The included subjects were aged > 35 years, of both genders, and from both urban and rural areas. A team of interviewers who had received an intense training completed the questionnaire consisting of 27 questions categorized into three sections of demographic, lifestyle and symptoms of GERD (Appendix 1). A gastroenterologist completed the clinical questions of the questionnaire in the clinic. The reliability and validity of the questionnaire were determined by requesting 100 subjects to be interviewed at our clinic by the same trained interviewers and a gastroenterologist for completion of the questionnaire, respectively. Heartburn was defined as a burning feeling in epigastric area that rises through the chest in substernal area and acid regurgitation as liquid coming back into the mouth leaving a bitter or sour taste. A subject was defined to suffer from GERD when he/she reported heartburn and/or acid regurgitation in the preceding year with a frequency of at least three times a week irrespective of its severity or duration. Sociodemographic variables included age, gender, habitat, marital status, educational level, biological characteristics, such as BMI [weight in kg in the fasting state divided by the

square of the height in meters, resulting in five categories of thin (< 18 kg/m²), normal (18-24.9 kg/m²), overweight (25-29.9 kg/m²), obese (30-40 kg/m²) and very obese (> 40 kg/m²), lifestyle such as physical activity (at least 30 min/week or sufficient to produce adequate sweating), dietary habits, cigarette smoking, alcohol, coffee and tea consumption and the use of aspirin and NSAIDs. Rural and urban habitats were defined by the size of the residence area (under 30 000 inhabitants vs 30 000 inhabitants or more). Dyspepsia was defined as epigastric or upper abdominal symptoms (pain or discomfort) in the past year. Information was put directly into a computer database under supervision of a professional biostatistician.

Statistical analysis

Statistical analysis was performed using the SPSS computer software package (Version 11.5, Chicago, IL). A *P* value of 0.05 or less was considered to be statistically significant and all reported *P* values were two sided using Chi-square tests.

RESULTS

Among 3600 visited households, the interview questionnaire was completed in 1978 subjects (response rate, 54.9%; mean age, 49.90 ± 11.14 years). Among the subjects, 29.4% were male, 56.6 % lived in urban and 43.4% in rural regions; 39.7%, 29.7%, 17.2% and 13.5% of the subjects were respectively in 35-44, 45-54, 55-64 and > 65 years age groups; 25.6%, 32.3%, 14.5% and 27.6% of the participants were illiterate, or with primary, high school and university educational levels, respectively. The reliability and validity of the questionnaire were 82% and 70%, respectively.

The prevalence rate of GERD was 15.4% (304 subjects, GERD occurring at least 3 times per week). Table 1 shows the prevalence rates of GERD in relation to demographic data, revealing that the prevalence was higher in females (17.3%, *P* = 0.003), in rural areas (19.8%, *P* = 0.001), and in illiterate subjects (21.5%, *P* = 0.001). In subjects with GERD, a higher prevalence of psychological distress (27.2%, *P* = 0.003) and headaches (22%, *P* = 0.009) was observed.

Table 2 demonstrates the frequency of GERD symptoms in relation to dietary, smoking and drinking habits and medication of the participants. The results indicated a lower prevalence in subjects having fried food (14.8%, *P* = 0.005), and a higher prevalence among those consuming pickles (22.1%, *P* = 0.001). There was no association between GERD symptoms and drinking spirits (*P* = 0.095) or water (*P* = 0.063) with meals, salt intake (*P* = 0.458) and physical activity (*P* = 0.373). The correlation between GERD symptoms and subjects being a current or former cigarette smoker (10.8%, *P* = 0.055) or water pipe smoker (18.7%, *P* = 0.096) was not significant either.

The prevalence of GERD was lower in subjects with more fruits and vegetables intake (14.6%, *P* = 0.001) and those drinking tea (14.9%, *P* = 0.465) and coffee (12.9%, *P* = 0.701), but was higher among those drinking alcohol (15.6%, *P* = 0.205) but the difference was significant from those with consumption of fruits and vegetables.

Table 2 Prevalence of GERD in relation to lifestyle of subjects in Shiraz, southern Iran (*n* = 1978)

Life style and dietary habits		GERD symptoms (%)		P value
		Present	Absent	
Pickle	Yes	22.1	77.9	< 0.001
	No	12.8	87.2	
Salt	No	15	85	0.458
	Yes	16.3	83.7	
Fried food	No	24	76	0.005
	Yes	14.8	85.2	
Fast food	No	15.7	84.3	0.518
	Yes	14.5	85.5	
Fiber (fruit and vegetables)	No	30.2	69.8	< 0.001
	Yes	14.6	85.4	
Cigarette	No	15.9	84.1	0.055
	Yes	10.8	89.2	
Water pipe	No	14.8	85.2	0.096
	Yes	18.7	81.3	
Tea	No	16.1	83.9	0.465
	Yes	14.9	85.1	
Coffee	No	15.4	84.6	0.701
	Yes	12.9	87.1	
Spirit with meal	No	16.7	83.3	0.095
	Yes	14	86	
Water with meal	No	17.6	82.4	0.063
	Yes	14.3	85.7	
Alcohol	No	9.7	90.3	0.205
	Yes	15.6	84.4	
Feeding duration (min)	< 10	16.5	83.5	0.519
	10-20	14.5	85.5	
	> 20	16.1	83.9	
Aspirin	No	14.7	85.3	0.02
	Yes	21	79	
NSAIDs	No	14.5	85.5	0.067
	Yes	17.9	82.1	

GERD: Gastroesophageal reflux disease; NSAIDs: Non-steroidal anti-inflammatory drugs.

We noticed more symptoms in subjects taking NSAIDs (17.9%, *P* = 0.067), and aspirin (21%, *P* = 0.020) (Table 2), but the difference was only significant for aspirin. Subjects with GERD symptoms are restricting their diets (20%, *P* = 0.001), taking herbal medicine (19.0%, *P* = 0.001), using the over-the-counter (OTC) drugs (29.9%, *P* = 0.001) and consulting with physicians (24.8%, *P* = 0.001). In subjects consuming medication advised by their friends, the difference was not statistically significant (23.5%, *P* = 0.058). Subjects with GERD had a significantly higher occurrence of halitosis (18.3%; *P* = 0.024), dyspepsia (30.6%; *P* = 0.001), anxiety (19.5%; *P* = 0.001), nightmare (23.9%; *P* = 0.001) and restlessness (18.5%; *P* = 0.001) (Table 3). There was an association between GERD symptoms and a family history of the disease (22.3%; *P* = 0.001) (Table 1).

DISCUSSION

It has been estimated that the digestive disease with the highest annual direct cost in the USA is GERD (about US\$ 9.3 billion)^[13]. Furthermore GERD patients have reported decrements in the health-related quality of life when compared with the general population^[14,15]. Among western patients, heartburn and acid regurgitation are known to be specific for GERD^[16].

Table 3 Health-seeking behavior of subjects with GERD Symptoms in Shiraz, Southern Iran (*n* = 1978)

Health-seeking behavior and associated symptoms		GERD Symptoms (%)		P value
		Present	Absent	
Restricting diet	No	12.9	87.1	< 0.001
	Yes	20	80	
Herbal medicine intake	No	13.2	86.8	0.001
	Yes	19	81	
Medication advised by friends	No	15.1	84.9	0.058
	Yes	23.5	76.5	
Over-the-counter drugs	No	12.2	87.8	< 0.001
	Yes	29.9	70.1	
Visiting physician	No	10.5	89.5	< 0.001
	Yes	24.8	75.2	
Halitosis	No	14.2	85.8	0.024
	Yes	18.3	81.7	
Dyspepsia	No	8.9	91.1	< 0.001
	Yes	30.6	69.4	
Anxiety	No	9.5	90.5	< 0.001
	Yes	19.5	80.5	
Nightmare	No	12.1	87.9	< 0.001
	Yes	23.9	76.1	
Restlessness	No	10.2	89.8	< 0.001
	Yes	18.5	81.5	

In our population-based study, the prevalence of GERD was 15.4% defined as heartburn and/or acid regurgitation at least three times per week. In a population-based study, Khoshbaten^[17] reported a prevalence of 2.7% for GERD as heartburn occurring at least thrice in recent two weeks in Tabriz, northwestern Iran. This difference may be due to his different case definition in the questionnaire. In a sample of general population in Germany, 18% of subjects suffered from GERD^[18]. Wong *et al*^[15] in a study by telephone contact reported a prevalence of 29.8% in a Chinese population. A study by telephone calls in a Spanish population showed a prevalence rate of 25.2%-34.7%^[19]. A monthly prevalence of 1.6% was reported in Singapore^[9]. Hu *et al*^[20] demonstrated that only 5% of a Chinese population had GERD. In a large study of Taiwanese patients, 17% had at least one of three reflux symptoms daily^[21]. Several factors that may influence the prevalence of GERD have been identified, including genetic factors and differences in body mass index and lifestyle^[22-25]. Geographical differences in GERD prevalence are difficult to interpret due to the different case definitions and questionnaires used^[14,26].

As shown in Table 1, the GERD prevalence was higher in females, rural areas, and illiterate subjects and those with a mean age of 50.25 years. Wong *et al*^[11], Diaz-Rubio *et al*^[12] and Mahadeva *et al*^[19] also reported a higher prevalence of GERD in females. Some studies have not demonstrated a relationship between gender and GERD^[10,27]. In relation to habitat, Diaz-Rubio *et al*^[9] showed that GERD prevalence was higher in rural areas and in relation to educational level, a higher prevalence in illiterate subjects similar to our study. The relationship between a lower educational level and the frequency of GERD was described previously, which probably reflects the action of certain unhealthy lifestyle habits, or less ability to modify such habits^[7,19].

In relation to life style, smoking and alcohol have often been cited as risk factors for GERD, although findings of

studies on this matter have been inconsistent^[3,27,28,29]. According to Nocon *et al.*^[18], smoking was a risk factor for GERD, which was associated with reflux symptoms and was dose-dependent. Nilsson *et al.*^[3], reported that smoking and salt were risk factors for reflux symptoms. Our results showed no correlation between GERD and smoking.

In our study, we found no effect of alcohol, tea, coffee and spirits on GERD symptoms. In a population-based study, Nilsson *et al.*^[3] did not notice any effect for these risk factors. No relationship in Nocon *et al.*'s^[18] study was found between the intake of alcohol and reflux symptoms. Wong *et al.*^[11] and Mahadeva *et al.*^[12] indicated the increase of GERD prevalence due to consumption of alcohol, which is not consistent with our results. Drinks such as tea and coffee have also been reported to be linked to GERD but this is controversial. Although tea has been shown to increase gastric acid secretion, it does not appear to contribute to GERD^[22]. Wendle *et al.*^[30] showed that coffee increases GERD and the irritant effect of coffee was correlated to the caffeine content, but this has also been disputed. Chang *et al.*^[21] found no link between coffee or tea consumption and the incidence of GERD. Diaz-Rubio *et al.*^[19] also noticed that occurrence of GERD was inversely associated with coffee consumption. There was also no effect of tea or coffee on GERD symptoms in Nocon *et al.*'s^[18] study. The inverse relationship with coffee, tea or alcohol consumption should not be interpreted as a protective role for these beverages. Restriction in drinking of tea, coffee and alcohol may arise from the suggestions of their friends, even in our country, where alcohol consumption is not legally allowed. The role of coffee as a promoter of gastroesophageal reflux disease^[30] is also consistent, suggesting that the avoidance of coffee is a sound recommendation for GERD sufferers. In relation to fiber intake, El-Serag *et al.*^[5] and Nocon *et al.*^[18] reported that consumption of fruits were associated with GERD symptoms and found a protective effect of dietary fiber, which was similar to our results. In relation to dietary fat, El-Serag *et al.*^[5] found an increased risk of GERD in subjects with a high intake of dietary fat. The data of Nocon *et al.*^[18] also showed that subjects with reflux symptoms tend to have a diet richer in fat. It has been shown that dietary fat can increase the transient lower esophageal sphincter relaxation^[31], possibly *via* release of cholecystokinin^[32]. Therefore, the lower fat content in a population may explain, in part, the lower prevalence of GERD.

In relation to consumption of spirits, we found no association between reflux symptoms and consumption of spirits. These results were different from Nocon *et al.*^[18]. With regard to physical exercise, there are conflicting results^[29]. According to Nocon *et al.*^[18], subjects with GERD were less active physically, but our data did not confirm these results. Some studies have observed an association between the use of aspirin or NSAIDs and the presence of GERD^[19,33] and use of NSAIDs is a risk factor for erosive esophagitis^[5,15,34], whereas others have not^[27,35]. A higher consumption of NSAIDs and aspirin were visible in subjects of our study with GERD symptoms but was only statistically significant for aspirin. In relation to medical care utilization, the results vary among countries from 16% to 56%. A study from Singapore found that 40% of

GERD sufferers used OTC drugs or visited a physician for GERD symptoms^[9]. This is in contrast with a study in Minnesota, USA, in which only 5.4% of GERD sufferers visited physicians^[27]. In the study of Wong *et al.*^[15], 48% of subjects with GERD had received treatment, 6% had taken OTC medication, and 35% had visited physicians. In our study, in relation to health seeking behavior, there were significant differences between GERD symptoms and restricting diets, consumption of herbal medicine, using OTC drugs and visiting a physician. Caution should be taken when applying the data to countries in which medical care is available on a fee-for-service basis. Patients usually associate certain nutritional habits with the occurrence of reflux symptoms, and the avoidance of certain food is often cited as a therapeutic measure^[1,7,8]. Nevertheless, the causal role of particular food in the etiology of GERD is still unclear. A family history of reflux symptoms was reported as a risk factor for GERD^[36]. GERD in the sufferer's spouse or a direct family member was reported to be associated with the presence of GERD^[19]. These results were identical to our data. In relation to BMI, although most studies have confirmed the association between BMI and GERD symptoms, the results to date have remained inconsistent. Risk factors for GERD in the West have been shown to include a high BMI^[27]. Similar to our study, a cohort study from New Zealand, also found no association between BMI and reflux symptoms^[37]. In contrast, the large population-based HUNT 2 study reported an association between BMI and reflux symptoms. Nocon *et al.*^[18] reported similar results while being overweight or obese was significantly associated with GERD symptoms. Hampel *et al.*^[38] also found a significant association between obesity and GERD symptoms. The association between obesity and the prevalence and severity of GERD was confirmed by several other authors^[5,39].

Our study showed that halitosis, headaches, psychological distress, anxiety, nightmares and restlessness were common in GERD subjects. The importance of psychological distress was also suggested by others^[8,19,40]. Some population surveys conducted in western countries have suggested that patients with GERD have a higher level of stress and anxiety^[14,40,41]. Wong *et al.*^[15] showed that psychological morbidity may play an important role in health care-seeking behavior, and co-existing depression and anxiety may act as a catalyst for a patient to seek medical care, rather than as a cause of symptoms. Lower levels of psychological well-being were observed in subjects with GERD^[42]. The important strength of our study was its large sample of subjects in a healthy population, which is representative of the adult population in our country between the ages of 35-75 years.

In conclusion, the prevalence of GERD (15.4%) was significantly higher in females, rural and illiterate subjects. An inverse correlation was seen between GERD and consumption of fat and fiber intake. A correlation was noticed between GERD and pickle consumption, occurrence of headache, psychological distress, dyspepsia, halitosis, anxiety, nightmare and restlessness and a previous family history of GERD. The association between GERD and aspirin was also significant. Future longitudinal studies and follow-ups are needed to clarify other possible risk factors and associations with GERD.

COMMENTS

Background

Symptoms of gastroesophageal reflux disease (GERD) represent one of the most frequent health problems in the western world. When compared with the general population, GERD patients have reported decrements in the health-related quality of life. Based on the population studied, the prevalence of the primary GERD symptoms, heartburn or acid regurgitation varies between 9% and 42%. The relationship between GERD and lifestyle habits, e.g., cigarette smoking, alcohol and coffee consumption, ingestion of medications such as aspirin and non-steroidal anti-inflammatory drugs (NSAIDs), and diet has not been firmly established, and inconsistent results have been obtained by population-based studies.

Research frontiers

The study was performed to determine the relationship between GERD and demographic factors, lifestyle habits, family history, health-seeking behaviors and other GI symptoms. How GERD might affect quality of life awaits further studies.

Innovations and breakthroughs

Many other studies on GERD were conducted by telephone surveys or in the form of questionnaires. In our study, however, subjects were interviewed face-to-face by a team of trained interviewers using a questionnaire for which validity and reliability had been determined. Both rural and urban inhabitants participated in this study, making possible a comparison of these two populations in regards to GERD. In our population-based study, the prevalence of GERD was 15.4%, which is higher than that reported by some other studies in Iran. Obesity, consumption of spirits and smoking have been suggested as the most important lifestyle risk factors for GERD symptoms, but we found no association between reflux symptoms and consumption of spirits, smoking or BMI.

Applications

The findings of this study are helpful to both the clinicians in handling GERD patients and patients in primary and secondary healthcare.

Terminology

Heartburn is defined as a burning pain or discomfort behind the breast bone. Acid regurgitation is referred to liquid coming back into the mouth leaving a bitter or sour taste. GERD, in this study, is considered as heartburn and/or acid regurgitation occurring at least three times per week.

Peer review

This is an extensive cross sectional study performed in Iran and gives attention to the contributing factors and demographics of GERD in the country of the authors.

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Appendix 1

Questionnaire

Gastroenterohepatology Research Center, Shiraz University of Medical Sciences

Frequency and associated factors of digestive and hepatic disorders in subjects aged ≥ 35 yr in Shiraz, Southern Iran

Questionnaire No:

Sex Female Male

Ageyears

Marital status Single Married Widow Divorced

Habitat Urban Rural

Family size

Education Illiterate Primary Middle High school University

Occupation

Past medical history Headache Psychological distress Hyperlipidemia

Physical activityTimes per week

Family history of gastrointestinal diseases Yes No If Yes : Specify the disease

Number of meals/day Breakfast Lunch Dinner More

Duration of serving each mealmin

Pickles consumption with meal? Yes No

Salt consumption with meal? Yes No

Having fast food? Yes No

If yes, how many/week?

Having fried foods? Yes No

Any smoking? Yes (Cigarette Water pipe No

If yes/dayyear

Type of analgesics regularly used? NSAIDs Aspirin

Having fibers (fruits,vegetables) Yes No

Type and time of drinks? Tea, after meal Water, with or after meal Coffee, after meal

Spirit, with or after meal

Yes, usually Yes, occasionally Never

Yes No

Alcohol drinking? Yes No

Any history of Gastroesophageal reflux (Heartburn or acid regurgitation) during last year? Diet restriction Herbal medicine Using medicine suggested by friends

Any upper abdominal discomfort or dyspepsia? Over-the-counter drugs Visiting a physician

Health care-seeking behavior? Anxiety Nightmares Restlessness Halitosis

Any complaints of:

Name and Signature of interviewer