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Prevalence and Correlates of Gastroesophageal Reflux Disease in Southern Iran: Pars Cohort Study

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ABSTRACT

BACKGROUND

Prevalence of gastroesophageal reflux disease (GERD) is increasing worldwide. We aimed to estimate the prevalence of GERD in Pars Cohort Study (PCS) and to find its correlates.

METHODS

We used the baseline data from PCS. PCS was conducted in the district of Valashahr in Fars province in southern Iran from 2012 to 2014. 9264 inhabitants who were 40-75 years old, and agreed to participate were enrolled. Data were collected by a structured questionnaire and simple physical examination of all participants.

RESULTS

Generally, 58.50% (95% CI 57.49 - 59.51) of the participants had GERD and 25.10% (95% CI 24.22 - 25.99) experienced it at least weekly. Approximately, 32.0%, 52.0%, and 24.4% of the participants reported heart burn sensation, regurgitation, and both symptoms, respectively. Being female (OR: 1.45, 95% CI 1.27 - 1.65), being older (OR: 1.20, 95% CI 1.06 - 1.36), being divorced/widowed/separated (OR: 1.38, 95% CI 1.01 - 1.91), and lower education (OR: 1.43, 95% CI 1.02 - 2.03) were associated with frequent GERD.

CONCLUSION

GERD is common in PCS and its prevalence is close to that in western countries. Being female, higher age, being divorced/widowed/separated, lower education, history of hypertension, anxiety, insomnia, and non-cigarette tobacco smoking were associated with frequent GERD. We are going to investigate the causal relationship between these risk factors and GERD in the next stages of PCS.

KEYWORDS:
Epidemiology; Gastroesophageal reflux; Heartburn; Regurgitation; Pars cohort study; Iran.

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INTRODUCTION

Gastroesophageal reflux disease (GERD) has been increasing across the world in the past decades.[1-3] It is especially common in western countries,[1,4,5] and is the most frequent diagnosis in patients with gastrointestinal problems. Age, sex, life style, medication, pregnancy, and geographic variation have been shown to be associated with GERD.[6-9]

The prevalence of GERD is low in East Asia, but it is more prevalent in the Middle East, where the prevalence is similar to many western countries. About 18.1 - 27.8% in North America, 23.0% in South America, 8.8 - 25.9% in Europe, 11.6% in Australia, 2.5 - 7.8% in East Asia, and 8.7 - 33.1% in the Mid-

dle East experience GERD symptoms.[2,4,8,10-14] Delavari and colleagues found that the prevalence of GERD in Iran is 21.2 %.[11] A study on the Qashqai migrating nomads of Fars province revealed that 33.1% of them had at least weekly GERD symptoms.[15] This showed a higher prevalence of GERD compared with other studies in Iran, which may not be the representative of the whole country.[12,13,15] These differences may be due to different definitions of GERD and lack of a gold standard test for diagnosing it. Most of previous studies have considered heartburn and/or regurgitation in participants as GERD.[12,14,16-23]

Burning sensation (heartburn) and regurgitation of gastro-duodenal contents into the esophagus are the typical symptoms of GERD.[3,4,7,9,24] However, its atypical symptoms are cough, asthma, chest pain, and hoarseness.[3,9,25-27] GERD has also several serious complications such as esophageal ulcer, stricture, Barrett's esophagus, and esophageal adenocarcinoma.[2,6,10] Both of its symptoms and complications affect the patients' quality of life.[4,28]

Due to different reports of epidemiological studies, increase in the trend of GERD, and lack of a large study in the south of Iran, we aimed to determine the prevalence and associated risk factors of this disease, using a cross-sectional analysis of the data obtained during Pars Cohort Study (PCS).

MATERIALS AND METHODS

Subjects

PCS has been designed as a prospective study of the burden and risk factors for non-communicable diseases in Fars province in southern Iran. The site of this study is Valashahr District with 40000 residents. The inhabitants of the region consist of a variety of ethnicities including Fars, Turk, and others. All 9721inhabitants aged between 40 - 75 years were invited, but those who were unwilling to participate or those who were a temporary resident were excluded. Finally, 9264 participants were enrolled in this study from 2012 to 2014. Details of the study design have been published earlier.[29]

Ethics Statement

The study protocol was approved by the Ethics Committees of Tehran University of Medical Sciences and Shiraz University of Medical Sciences. The purpose and the method of the study were explained to the participants if they were illiterate. The participants were invited to visit the center and participate in the study if they agreed. Informed consents were signed by the participants.

Measurement of variables and definitions

We used baseline PCS data in our cross-sectional study. Data were collected through a structured questionnaire and simple physical examination. The data on demographic characteristics, lifestyle factors, disease history, family history, medication history, smoking, and the abuse of opium and alcohol were collected. The participants were asked about GERD symptoms including heartburn (a burning sensation behind the sternum) and regurgitation (regurgitation of gastroduodenal contents into the esophagus) over the past year and severity and frequency of these symptoms. The frequency of the symptoms was categorized into: one to 10 times per year, once a month, two or three times a month, weekly, and daily. GERD was defined as at least one participant's recall of heartburn and/or regurgitation during the past 12 months and frequent GERD was having at least weekly symptoms. The severity of the symptoms was recorded as mild, moderate, severe, and very severe. Mild means that participants do not feel GERD symptoms if they do not think about it. Moderate means symptoms not interfering with daily work. Severe symptom means that it interferes with daily work, and very severe symptom means it affects the life and bothers the participants.

Height and weight were measured by a trained health worker according to a standard protocol. Body mass index (BMI) was calculated as weight in kilograms divided by squared height in meters. BMI was classified using the WHO classification as underweight (lower than 18.5), normal (18.5 - 24.9), overweight (25 - 29.9), and obese (30 or more). The waist circumference more than 102 centimeters for men and 88 centimeters for (non-pregnant) women and also waist to hip ratio above 0.90 for men and 0.85 for women were considered as central adiposity.[30,31]

Positive opium abuse (teriak, heroin, sukhteh, and shireh), non-cigarette tobacco (hookah, nass, and pipe), and cigarette were defined as at least once per week for the past six months, and positive alcohol use was defined as drinking once per month for the past six months.

Table 1: Frequency and severity of heart burn sensation and regurgitation in participants of Pars Cohort Study in the last 12 months (n=9264)

Symptom	Frequency					Severity				
	1-10/year	1/month	2-3/month	Weekly	Daily	Mild	Moderate	Severe	Very severe	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Heartburn sensation	449 (15.2)	595 (20.1)	752 (25.4)	749 (25.3)	411 (13.9)	362 (12.2)	1496 (50.6)	541 (18.3)	555 (18.8)	2959 (31.9)
Regurgitation	874 (18.5)	882 (18.7)	1163 (24.6)	1209 (25.6)	587 (12.4)	425 (9.0)	2303 (48.8)	910 (19.3)	1072 (22.7)	4723 (51.0)

Numbers may not add together to the total numbers due to a few missing data.

Statistical analysis

Data were cleaned and described by mean, standard deviation, frequency, and percentage. Univariate analyses were done applying Chi-square or Mann-Whitney U tests.

Variable selection was done according to univariate *P* value of 0.1. A multivariable logistic regression model was fitted to get adjusted odds ratios and 95% confidence intervals for variables in relation to the GERD. A backward elimination approach was applied. *P* value less than 0.05 was considered as statistically significant. Data analyses were done using SPSS software, version 21 (SPSS Inc., Chicago, IL, USA).

RESULTS

Of the participants in PCS, 4276 (46.2%) were male and 4988 (53.8%) were female. Mean age of the participants was 52.6 ± 9.7 years. Almost 32% (n = 2959) reported heartburn sensation and approximately 39.2% (n = 1160) sensed heartburn weekly or daily (table 1). But regurgitation was the most frequent symptom as about half of them (n = 4723) had regurgitation and 38% (n = 1796) reported this symptom as weekly or daily. Almost 2262 (24.4%) participants had reported both symptoms (table 1).

Overall, 5420 (58.50%, 95% CI: 57.49 - 59.51) participants had heartburn sensation and/or regurgitation, but 2325 (25.10%, 95% CI: 24.22 - 25.99) participants had frequent GERD (weekly or more frequently). Also 218 (2.3%) participants reported current use of some medications (proton pump inhibitors, H_2 receptor blockers, and antacids). However, as they had neither heartburn sensation nor regurgitation, they were not considered as GERD positive cases.

The mean age of the participants with and without GERD were 52.95 ± 9.77 and 52.21 ± 9.56 years, respectively ($P < 0.001$). GERD was significantly more prevalent in women compared with men (58.90% vs. 41.10%, $p < 0.001$).

According to univariate analysis there was a positive association between GERD and frequent GERD with being female; having higher age, higher BMI, higher waist to hip ratio, higher waist circumference, having low educational level, being divorced/widowed/separated, cigarette smoking, and using non-cigarette tobacco.

We found that being female, older ages, and having low educational level had a positive association with severe symptom sensation.

Having both symptoms (heartburn and regurgitation) was significantly associated with severity and frequency of symptoms.

Older ages, lower educational level, non-cigarette tobacco smoking, and opium consumption were significantly associated with frequent GERD in men. Also, older ages, higher BMI, abdominal obesity, being divorced/widowed/separated, lower educational level, and non-cigarette tobacco smoking were significantly associated with the presence of frequent GERD in women (table 2).

Positive history of underlying diseases including hypertension, anxiety, depression, and insomnia were significantly correlated with GERD, and frequent GERD. Diabetes mellitus had an association with GERD (table 3).

Sex, age, marital status, educational level, waist to hip ratio, hypertension, anxiety, depression, insomnia, cigarette smoking, and non-cigarette tobacco use were entered into the multivariable model. Older ages (OR 1.20, 95% CI 1.058 - 1.36), female sex (OR 1.45, 95% CI 1.27 - 1.65), divorce/widow/separation (OR 1.38, 95%

Table 2: **Sex-stratified comparison of demographic, anthropometric, and lifestyle characteristics between the studied population with GERD and frequent GERD**

Characteristics	Men (n = 4276)					Women (n = 4988)				
	All	GERD (N=2230)	*P*	Frequent GERD (N=843)	*P*	All	GERD (N= 3190)	*P*	Frequent GERD (N=1482)	*P*
	N (%)	N (%)		N (%)		N (%)	N (%)		N (%)	
Age*	52.73± 9.91	52.69 ± 10.03	0.534‡	53.54 ± 10.27	0.015‡	52.57± 9.49	53.13 ± 9.57	< 0.001‡	53.75± 9.95	< 0.001‡
BMI*			0.434•		0.521•			.012•		0.016•
Lower and Normal weight	2442 (57.4)	1252 (56.4)		497 (59)		1661 (33.5)	1017 (32)		458 (31.1)	
Over weight	1428 (33.6)	759 (34.2)		269 (31.9)		2012 (40.5)	1326 (41.8)		640 (43.5)	
Obese	386 (9)	207 (9.3)		76 (9)		1289 (26)	831 (26.2)		373 (25.4)	
Waist circumference*			0.962†		0.404†			0.001†		0.001†
Normal	3772 (88.2)	1966 (88.2)		751 (89.1)		1714 (34.4)	1045 (32.8)		459 (31)	
At risk	504 (11.8)	264 (11.8)		92 (10.9)		3274 (65.6)	2145 (67.2)		1023 (69)	
Waist to hip ratio*			0.025†		0.802†			0.016†		< 0.001†
Normal	1294 (30.4)	641 (28.9)		259 (30.8)		548 (11)	325 (10.2)		126 (8.6)	
At risk	2964 (69.6)	1577 (71.1)		583 (69.2)		4414 (89)	2849 (89.8)		1345 (91.4)	
Ethnicity			0.580†		0.069†			0.061†		0.491†
Fars	2368 (55.4)	1244 (55.8)		443 (52.6)		2849 (57.1)	1854 (58.1)		835 (56.3)	
Turk/others	1908 (44.6)	986 (44.2)		400 (47.4)		2139 (42.9)	1336 (41.9)		647 (43.7)	
Marital status			0.302•		0.185•			0.001•		< 0.001•
Single	50 (1.2)	27 (1.2)		15 (1.8)		247 (5)	142 (4.5)		53 (3.6)	
Married	4174 (97.6)	2171 (97.4)		818 (97)		4038 (81)	2559 (80.2)		1165 (78.6)	
divorced/ widowed/ separated	51 (1.2)	32 (1.4)		10 (1.2)		701 (14.1)	488 (15.3)		264 (17.8)	
Educational level			0.001•		0.001•			0.014•		0.008•
Illiterate	1336 (31.3)	678 (30.5)		307 (36.5)		3202 (64.2)	2083 (65.3)		997 (67.3)	
≤High school diploma	2673 (62.6)	601 (27)		494 (58.7)		1765 (35.4)	971 (30.5)		481 (32.5)	
University	263 (6.2)	463 (20.8)		41 (4.9)		18 (0.4)	96 (3)		3 (.2)	
Cigarette Smoking (ever)			0.165†		0.081†			0.119†		0.999†
Yes	1873 (43.8)	1000 (44.8)		392 (46.5)		45 (0.9)	34 (1.1)		13 (.9)	
No	2403 (56.2)	1230 (55.2)		451 (53.5)		4943 (99.1)	3156 (98.9)		1469 (99.1)	
Use of Non-cigarette tobacco(ever)			0.349†		0.004†			0.023†		0.002†
Yes	1231 (28.8)	649 (29.1)		277 (32.9)		2306 (46.3)	1514 (47.5)		735 (49.7)	
No	3038 (71.2)	1580 (70.9)		566 (67.1)		2672 (53.7)	1671 (52.5)		743 (50.3)	

Characteristics	Men (n = 4276)					Women (n = 4988)				
	All	GERD (N=2230)	*P*	Frequent GERD (N=843)	*P*	All	GERD (N= 3190)	*P*	Frequent GERD (N=1482)	*P*
	N (%)	N (%)		N (%)		N (%)	N (%)		N (%)	
Opium abuse (ever)			0.069†		< 0.001†			0.999†		0.336†
Yes	742 (17.4)	410 (18.4)		195 (23.1)		32 (0.6)	21 (.7)		12 (.8)	
No	3534 (82.6)	1820 (81.6)		648 (76.9)		4956 (99.4)	3169 (99.3)		1470 (99.2)	
Use of alcohol (ever)			0.205†		0.319†			0.570†		0.690†
Yes	166 (3.9)	95 (4.3)		38 (4.5)		30 (0.6)	21 (0.7)		10 (.7)	
No	4110 (96.1)	2135 (95.7)		805 (95.5)		4958 (99.4)	3169 (99.3)		1472 (99.3)	

Numbers may not add together to the total numbers due to missing data. GERD: gastroesophageal reflux disease; BMI: body mass index. * For age, the values are (mean ± standard deviation) years and *P* was calculated by Mann-Whitney U test. * Frequent GERD means having at least weekly symptoms. BMI < 18.5 is underweight, from 18.5 to 24.9 is normal weight, from 25 to 29.9 is overweight, and ≥ 30 is obesity. Waist circumference > 102 centimeters for men and > 88 centimeters for women and also waist to hip ratio > 0.90 for men and > 0.85 for women are at risk. *P* was calculated by: ‡Mann-Whitney U test, •X^2 test and †fisher exact test.

Table 3: Comparison of the history of underlying diseases between the participants with and without GERD and frequent GERD

History of underlying diseases	All GERD (N = 5420)	No GERD (N = 3844)	*P*†	Frequent* GERD (N = 2325)	No Frequent GERD (N = 6939)	*P*†
	N (%)	N (%)		N (%)	N (%)	
Hypertension			< 0.001			<0.001
Yes	996 (18.4)	517 (13.4)		478 (20.6)	1035 (14.9)	
No	4424 (81.6)	3327 (86.6)		1847 (79.4)	5904 (85.1)	
Diabetes mellitus			0.007			0.151
Yes	549 (10.1)	325 (8.5)		237 (10.2)	637 (9.2)	
No	4871 (89.9)	3519 (91.5)		2088 (89.8)	6302 (90.8)	
Anxiety			< 0.001			< 0.001
Yes	1980 (36.5)	764 (19.9)		850 (36.6)	1894 (27.3)	
No	3440 (63.5)	3074 (80.1)		1475 (63.4)	5045 (72.7)	
Depression			< 0.001			< 0.001
Yes	1291 (23.8)	504 (13.1)		566 (24.3)	1229 (17.7)	
No	4129 (76.2)	3340 (86.9)		1759 (75.7)	5710 (82.3)	
Insomnia			< 0.001			< 0.001
Yes	1260 (23.2)	535 (13.9)		596 (25.6)	1199 (17.3)	
No	4160 (76.8)	3309 (86.1)		1729 (74.4)	5740 (82.7)	

Numbers may not add together to the total numbers due to missing data. GERD: gastroesophageal reflux disease. * Frequent GERD means having at least weekly symptoms. †*P* was calculated by: fisher exact test.

CI 1.01 - 1.91), and non-cigarette tobacco smoking (OR 1.14, 95% CI 1.03 - 1.26) had correlation with frequent GERD. Also, the participants with history of hypertension (OR 1.16, 95% CI 1.02 - 1.33), anxiety (OR 1.24, 95% CI 1.11 - 1.40), and insomnia (OR 1.36, 95% CI 1.21 - 1.54) were more likely to have frequent GERD (table 4).

DISCUSSION

In this study, 25.1% of 40 - 75 years old participants had GERD symptoms weekly or more frequently. We also showed that 58.5% of all the participants had experienced GERD symptoms at least once in the last 12 months. There were strong associations between frequent GERD and fe-

Table 4: Association of covariates with frequent GERD

Variables	Frequent* GERD (N=2325)	No Frequent GERD (N=6939)	OR (95% CI)	
	N (%)	N (%)	Unadjusted	Adjusted
Age*				
40-60 years	610 (26.2)	1390 (20)	Reference	Reference
61+	1715 (73.8)	5549 (80)	1.42 (1.27 - 1.58)	1.20 (1.06 - 1.36)
Sex				
Male	843 (36.3)	3433 (49.5)	Reference	Reference
Female	1482 (63.7)	3506 (50.5)	1.72 (1.56 - 1.89)	1.45 (1.27 - 1.65)
Marital status				
Single	68 (2.9)	229 (3.3)	Reference	Reference
Married	1983 (85.3)	6229 (89.9)	1.07 (.81 - 1.41)	1.12 (.84 - 1.48)
Divorced/ widowed/ separated	274 (11.8)	478 (6.9)	1.93 (1.42 - 2.63)	1.38 (1.01 - 1.91)
Educational level				
Illiterate	1304 (56.1)	3234 (46.6)	2.17 (1.56 - 3.01)	1.43 (1.02 - 2.03)
≤ High school diploma	975 (42)	3463 (49.9)	1.51 (1.09 - 2.11)	1.29 (.92 - 1.81)
University	44 (1.9)	237 (3.4)	Reference	Reference
Waist to hip ratio*				
Normal	385 (16.6)	1457 (21.1)	Reference	Reference
At risk	1928 (83.4)	5448 (78.9)	1.34 (1.18 - 1.52)	1.12 (.98 - 1.28)
Hypertension				
Yes	478 (20.6)	1035 (14.9)	1.48 (1.31 - 1.66)	1.16 (1.02 - 1.33)
No	1847 (79.4)	5904 (85.1)	Reference	Reference
Anxiety				
Yes	850 (36.6)	1894 (27.3)	1.53 (1.39 - 1.69)	1.24 (1.11 - 1.40)
No	1475 (63.4)	5045 (72.7)	Reference	Reference
Depression				
Yes	566 (24.3)	1229 (17.7)	1.49 (1.33 - 1.67)	1.08 (.95 - 1.24)
No	1759 (75.7)	5710 (82.3)	Reference	Reference
Insomnia				
Yes	596 (25.6)	1199 (17.3)	1.65 (1.47 - 1.85)	1.36 (1.21 - 1.54)
No	1729 (74.4)	5740 (82.7)	Reference	Reference
Cigarette Smoking (ever)				
Yes	405 (17.4)	1513 (21.8)	.76 (.67 - 85)	1.13 (.97 - 1.30)
No	1920 (82.6)	5426 (78.2)	Reference	Reference
Usage of Non-cigarette tobacco (ever)				
Yes	1012 (43.6)	2525 (36.5)	1.35 (1.22 - 1.48)	1.14 (1.03 - 1.26)
No	1309 (56.4)	4401 (63.5)	Reference	Reference

* Frequent GERD means having at least weekly symptoms. GERD: gastroesophageal reflux disease. * For age, the values are (mean ± standard deviation) years and *P* was calculated by Mann-Whitney U test. * Waist to hip ratio > 0.90 for men and > 0.85 for women are at risk.

male sex, and positive history of anxiety and insomnia.

The prevalence of frequent GERD in our study was close to that in western countries and Iran, but it was higher than East Asia.[9,28,32] It may be due to more westernized lifestyle in the target population.[33,34]

In our study, about 32% of the participants reported heartburn sensation and 51% of them had regurgitation. Almost 24.4% of the participants had reported both

symptoms. Consistent with previous studies, regurgitation was more common than heartburn in this study.[1,2,10,27,35,36] Our data also showed that about half of the participants had moderate GERD symptoms similar to some of previous studies.[10,16]

In our study, older ages had an association with frequent GERD and sensing severe symptoms. This finding is consistent with some previous reports.[9,12,13] This relationship may be due to the decrease in defense mechanisms against reflux i.e. the decrease in pressure of the lower esophageal sphincter. However, there are controversies regarding the association between increased age and frequent GERD as some studies have shown an increase in the incidence of GERD by increasing age up to 60 - 69 years and then a decrease.[12,13,16,18]

Unlike most of previous studies, our findings showed that male sex was a protective factor for the presence and severity of GERD symptoms.[3,9,16,18,28,37] Higher prevalence among women may be due to higher prevalence of obesity in women compared with men.[37-39] It also may be due to the effects of female sex hormones on the lower esophageal sphincter.[37,39,40]

Among the participants with abdominal obesity, GERD and frequent GERD were more common. Many studies reported a significant association between GERD and abdominal obesity. It is probably because of hiatal hernia and increase in intra-abdominal pressure among patients with central obesity. In addition to central obesity, previous studies have shown that BMI and weight cycling could be associated with GERD.[3,9,28,37,40-42]

We found that frequency and severity of GERD were associated with marital status because frequent GERD was more common among divorced/widowed/separated participants compared with singles and married ones (OR 1.38, 95% CI 1.01 - 1.91). It maybe resulted from a higher prevalence of depression and anxiety among divorced/widowed/separated participants. It may also be also due to considerable changes in dietary pattern.[32,43-45]

Consistent with the findings of some previous studies like those conducted in Albania, India, and Iran, the frequency and severity of GERD symptoms in participants with lower educational level was significantly higher than those with higher educational level.[8,16,28,46]

In both men and women, non-cigarette tobacco smoking had an association with GERD (OR 1.14, 95% CI 1.03 - 1.26). There is also some evidence (reduce the LES pressure and salivary secretion of bicarbonates) showing that non-cigarette tobacco use is correlated with GERD presence, but some other studies did not show such a relationship.[8,28,38,45-47]

In contrast to some studies, we found that there was an association between opium consumption and GERD.[8,16,28,46] Despite this, after sex stratification, opium had only an association with frequent GERD in men.

Sharma and colleagues showed a positive relationship between hypertension and GERD.[48] In our study, we found that having a positive history of hypertension was related to GERD, frequent GERD, and having severe GERD symptoms.

In this study, having a history of diabetes mellitus (DM) had a significant association with GERD in univariate analysis, although this association was not confirmed in multivariable analysis. One study in the United States has shown that approximately 41% of the patients with diabetes had GERD symptoms.[49,50] Also, a meta-analysis has indicated the higher prevalence of GERD in patients with DM than general population. Association of obesity and metabolic syndrome could be considered as a potential justification for the relationship between GERD symptoms and type II DM. Peripheral neuropathy as a consequence of type II DM may be another reason for this relationship.[42,50-56]

Previous studies showed bidirectional association between GERD and psychological problems such as anxiety, depression, sleep disturbance, and insomnia.[32,57-59] In our results, positive history of anxiety (OR 1.24, 95% CI 1.11 - 1.40) and insomnia (OR 1.36, 95% CI 1.21 - 1.54) were significantly associated with GERD and frequent GERD.

Strengths and Limitations of the Study

The strengths of this study are large sample size, and availability of many lifestyle factors, some of which have not been previously studied.

We also cross-validated the specificity of our prevalence estimate, considering the current use of medications, which could result in GERD symptom relief for cases who did not have heartburn sensation or regurgitation symptoms. As less than 2.3% of the participants reported the use of interested medications, our estimated prevalence may be a little increased if these cases considered as GERD positive.

The main limitation of this study is the cross-sectional nature of the study, which may not be able to determine the causal relationship between exposures and outcomes. Therefore, we should be cautious in the interpretation of the results. Also, we studied the data of a cohort on 40 - 75 years old people, so we cannot generalize the results to all population.

In conclusion, one out of four middle aged people in rural population suffer from GERD. We found that some factors such as female sex, higher age, higher BMI, having abdominal obesity, being divorced/widowed/separated, having low educational level, using non-cigarette tobacco, and history of hypertension, anxiety, and insomnia are associated with prevalent GERD.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

1. Pourshams A, Rahmani A, Hatami K. Gastroesophageal reflux disease in Iran. *Govaresh* 2005;**10**:48-53.
2. Somi MH, Farhang S, Mirinezhad K, Jazayeri E, Nasseri-Moghaddam S, Moayeri S, et al. Prevalence and precipitating factors of gastroesophageal reflux disease in a young population of Tabriz, Northwest of Iran. *Saudi Med J* 2006;**27**:1878-81.
3. Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management: Saunders/Elsevier; 2015.
4. Badillo R, Francis D. Diagnosis and treatment of gastroesophageal reflux disease. *World J Gastrointest Pharmacol Ther* 2014;**5**:105-12. doi: 10.4292/wjgpt.v5.i3.105.
5. Tan VP, Wong BC, Wong WM, Leung WK, Tong D, Yuen MF, et al. Gastroesophageal Reflux Disease: Cross-Sectional Study Demonstrating Rising Prevalence in a Chinese Population. *J Clin Gastroenterol* 2016;**50**:e1-7. doi: 10.1097/MCG.0000000000000304.
6. Islami F, Pourshams A, Nasseri-Moghaddam S, Khademi H, Poutschi H, Khoshnia M, et al. Gastroesophageal Reflux Disease and overall and Cause-specific Mortality: A Prospective Study of 50000 Individuals. *Middle East J Dig Dis* 2014;**6**:65. doi: 10.1016/S0016-5085(14)63119-X.
7. Sepanlou S, Khademi H, Abdollahzadeh N, Noori F, Malekzadeh F, Malekzadeh R. Time Trends of Gastro-esophageal Reflux Disease (GERD) and Peptic Ulcer Disease (PUD) in Iran. *Middle East J Dig Dis* 2010;**2**:78-83.
8. Islami F, Nasseri-Moghaddam S, Pourshams A, Poustchi H, Semnani S, Kamangar F, et al. Determinants of gastroesophageal reflux disease, including hookah smoking and opium use- a cross-sectional analysis of 50,000 individuals. *PLoS One* 2014;**9**:e89256. doi: 10.1371/journal.pone.0089256.
9. Podolsky DK, Camilleri M, Fitz JG, Kalloo AN, Shanahan F, Wang TC. Yamada's Textbook of Gastroenterology, 2 Volume Set: *Wiley* 2015.
10. Nouraie M, Razjouyan H, Assady M, Malekzadeh R, Nasseri-Moghaddam S. Epidemiology of gastroesophageal reflux symptoms in Tehran, Iran: a population-based telephone survey. *Arch Iran Med* 2007;**10**:289-94. doi: 07103/AIM.003.
11. Delavari A, Moradi G, Birjandi F, Elahi E, Saberifiroozi M. The Prevalence of Gastroesophageal Reflux Disease (GERD) in the Islamic Republic of Iran: A Systematic Review. *Middle East J Dig Dis* 2012;**4**:5-15.
12. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2014;**63**:871-80. doi: 10.1136/gutjnl-2012-304269.
13. Boeckxstaens G, El-Serag HB, Smout AJ, Kahrilas PJ. *Symptomatic reflux disease*:1185-93. doi:10.1136/gutjnl-2013-306393.
14. Nouraie M, Radmard AR, Zaer-Rezaii H, Razjouyan H, Nasseri-Moghaddam S, Malekzadeh R. Hygiene could affect GERD prevalence independently: a population-based study in Tehran. *Am J Gastroenterol* 2007;**102**:1353-60. doi: 10.1111/j.1572-0241.2007.01208.x.
15. Masoumi SJ, Khademolhosseini F, Mehrabani D, Moradi F, Mostaghni AA, Zare N, et al. Correlation of quality of life with gastroesophageal reflux disease amongst Qashqai nomads in Iran. *Arch Iran Med* 2012;**15**:747-50. doi: 0121512/AIM.005.
16. Nasseri-Moghaddam S, Mofid A, Ghotbi MH, Razjouyan H, Nouraie M, Ramard AR, et al. Epidemiological study of gastro-oesophageal reflux disease: reflux in spouse as a risk factor. *Aliment Pharmacol Ther* 2008;**28**:144-53. doi: 10.1111/j.1365-2036.2008.03708.x.
17. Wong BC, Kinoshita Y. Systematic review on epidemiology of gastroesophageal reflux disease in Asia. *Clin Gastroenterol Hepatol* 2006;**4**:398-407. doi: 10.1016/j.cgh.2005.10.011.
18. Bor S, Lazebnik L, Kitapcioglu G, Manannikof I, Vasiliev Y. Prevalence of gastroesophageal reflux disease in Moscow. *Dis Esophagus* 2016:159-65. doi: 10.1111/dote.12310.
19. Jung HK. Epidemiology of gastroesophageal reflux disease in Asia: a systematic review. *J Neurogastroenterol*

Motil 2011;**17**:14-27. doi: 10.5056/jnm.2011.17.1.14.

20. Wang R, Yan X, Ma X-Q, Cao Y, Wallander MA, Johansson S, et al. Burden of gastroesophageal reflux disease in Shanghai, China. *Dig Liver Dis* 2009;**41**:110-5. doi: 10.1016/j.dld.2008.06.014.
21. Wong W, Lai K, Lam K, Hui W, Hu W, Lam C, et al. Prevalence, clinical spectrum and health care utilization of gastro-oesophageal reflux disease in a Chinese population: a population-based study. *Aliment Pharmacol Ther* 2003;**18**:595-604. doi: 10.1046/j.1365-2036.2003.01737.x.
22. Cho YS, Choi MG, Jeong JJ, Chung WC, Lee IS, Kim SW, et al. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Asansi, Korea. *Am J Gastroenterol* 2005;**100**:747-53. doi: 10.1111/j.1572-0241.2005.41245.x.
23. Kahrilas PJ. Diagnosis of symptomatic gastroesophageal reflux disease. *Am J Gastroenterol* 2003;**98**:S15-23. doi:10.1016/S0002-9270(03)00011-X.
24. Nasseri-Moghaddam S, Malekzadeh R, Sotoudeh M, Tavangar M, Azimi K, Sohrabpour AA, et al. Lower esophagus in dyspeptic Iranian patients: a prospective study. *J Gastroenterol Hepatol* 2003;**18**:315-21. doi: 10.1046/j.1440-1746.2003.02969.x.
25. Manterola C, Munoz S, Grande L, Bustos L. Initial validation of a questionnaire for detecting gastroesophageal reflux disease in epidemiological settings. *J Clin Epidemiol* 2002;**55**:1041-5. doi:10.1016/S0895-4356(02)00454-7.
26. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol* 2013;**108**:308-28; quiz 29. doi: 10.1038/ajg.2012.444.
27. Bor S, Mandiracioglu A, Kitapcioglu G, Caymaz-Bor C, Gilbert RJ. Gastroesophageal reflux disease in a low-income region in Turkey. *Am J Gastroenterol* 2005;**100**:759-65. doi: 10.1111/j.1572-0241.2005.41065.x.
28. Wang HY, Leena KB, Plymoth A, Hergens MP, Yin L, Shenoy KT, et al. Prevalence of gastro-esophageal reflux disease and its risk factors in a community-based population in southern India. *BMC Gastroenterol* 2016;**16**:36. doi: 10.1186/s12876-016-0452-1.
29. Gandomkar A, Poustchi H, Moini M, Moghadami M, Imanieh H, Fattahi MR, et al. Pars cohort study of noncommunicable diseases in Iran: protocol and preliminary results. *Int J Public Health* 2017;**62**:397-406. doi: 10.1007/s00038-016-0848-2.
30. Obesity: preventing and managing the global epidemic: Report of a WHO consultation.*World Health Organ Tech Rep Ser* 2000;**894**:i-xii, 1-253.
31. Consultation WE. Waist circumference and waist-hip ratio. Report of a WHO Expert Consultation Geneva: World Health Organization. 2008:8-11.
32. Aletaha N, Pourshams A, Nouraie S, Malekzadeh R. The Role of Psychosocial Disorders in Gastroesophageal Reflux Disease. *Govaresh* 2007;**12**:92-7.
33. Ahmadi B, Alimohammadian M, Yaseri M, Majidi A, Boreiri M, Islami F, et al. Multimorbidity: Epidemiology and Risk Factors in the Golestan Cohort Study, Iran: A Cross-Sectional Analysis. *Medicine (Baltimore)*. 2016;**95**:e2756. doi: 10.1097/MD.0000000000002756.
34. Rafiemanesh H, Maleki F, Mohammadian-Hafshejani A, Salemi M, Salehiniya H. The Trend in Histological Changes and the Incidence of Esophagus Cancer in Iran (2003-2008). *Int J Prev Med* 2016;**7**:31. doi: 10.4103/2008-7802.175990.
35. Delaney BC. Review article: prevalence and epidemiology of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2004;**20 Suppl 8**:2-4. doi: 10.1111/j.1365-2036.2004.02219.x.
36. Wang JH, Luo JY, Dong L, Gong J, Tong M. Epidemiology of gastroesophageal reflux disease: a general population-based study in Xi'an of Northwest China. *World J Gastroenterol* 2004;**10**:1647-51. doi:10.3748/wjg.v10.i11.1647.
37. Chen Z, Thompson SK, Jamieson GG, Devitt PG, Watson DI. Effect of sex on symptoms associated with gastroesophageal reflux. *Arch Surg* 2011;**146**:1164-9. doi: 10.1001/archsurg.2011.248.
38. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Lifestyle related risk factors in the aetiology of gastro-oesophageal reflux. *Gut* 2004;**53**:1730-5. doi: 10.1136/gut.2004.043265.
39. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med* 2005;**143**:199-211. doi: 10.7326/0003-4819-143-3-200508020-00006.
40. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Obesity and estrogen as risk factors for gastroesophageal reflux symptoms. *JAMA* 2003;**290**:66-72. doi:10.1001/jama.290.1.66.
41. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo Jr CA. Body-mass index and symptoms of gastroesophageal reflux in women. *N Engl J Med* 2006;**354**:2340-8 doi: 10.1056/NEJMoa054391.
42. Sun XM, Tan JC, Zhu Y, Lin L. Association between diabetes mellitus and gastroesophageal reflux disease: A meta-analysis. *World J Gastroenterol* 2015;**21**:3085-92. doi: 10.3748/wjg.v21.i10.3085.
43. Chen M, Xiong L, Chen H, Xu A, He L, Hu P. Prevalence, risk factors and impact of gastroesophageal reflux disease symptoms: a population-based study in South China. *Scand J Gastroenterol* 2005;**40**:759-67. doi: 10.1080/00365520510015610.
44. Lee S, Cho E, Grodstein F, Kawachi I, Hu FB, Colditz GA. Effects of marital transitions on changes in dietary and other health behaviours in US women. *Int J Epidemiol* 2005;**34**:69-78. doi: 10.1093/ije/dyh258.
45. Festi D, Scaioli E, Baldi F, Vestito A, Pasqui F, Di Biase AR, et al. Body weight, lifestyle, dietary habits and gastroesophageal reflux disease. *World J Gastroentero*.

2009;**15**:1690-701. doi: 10.3748/wjg.15.1690.

46. Zheng Z, Nordenstedt H, Pedersen NL, Lagergren J, Ye W. Lifestyle factors and risk for symptomatic gastroesophageal reflux in monozygotic twins. *Gastroenterology* 2007;**132**:87-95. doi: 10.1053/j.gastro.2006.11.019.
47. Malekzadeh R, Nasseri-Moghaddam S, Sotoudeh M. Gastroesophageal reflux disease: the new epidemic. *Arch Iranian Med* 2003;**6**:127-40.
48. Sharma PK, Ahuja V, Madan K, Gupta S, Raizada A, Sharma MP. Prevalence, severity, and risk factors of symptomatic gastroesophageal reflux disease among employees of a large hospital in northern India. *Indian Journal of Gastroenterology* 2011;**30**:128-34. doi: 10.1007/s12664-010-0065-5.
49. Wang X, Pitchumoni CS, Chandrarana K, Shah N. Increased prevalence of symptoms of gastroesophageal reflux diseases in type 2 diabetics with neuropathy. *World J Gastroenterol* 2008;**14**:709-12. doi: 10.3748/wjg.14.709.
50. Ha JO, Lee TH, Lee CW, Park JY, Choi SH, Park HS, et al. Prevalence and Risk Factors of Gastroesophageal Reflux Disease in Patients with Type 2 Diabetes Mellitus. *Diabetes Metab J* 2016;**40**:297-307. doi: 10.4093/dmj.2016.40.4.297.
51. Nishida T, Tsuji S, Tsujii M, Arimitsu S, Sato T, Haruna Y, et al. Gastroesophageal reflux disease related to diabetes: Analysis of 241 cases with type 2 diabetes mellitus. *J Gastroenterol Hepatol* 2004;**19**:258-65. doi: 10.1111/j.1440-1746.2003.03288.x.
52. Lluch I, Ascaso JF, Mora F, Minguez M, Pena A, Hernandez A, et al. Gastroesophageal reflux in diabetes mellitus. *Am J Gastroenterol* 1999;**94**:919-24. doi: 10.1111/j.1572-0241.1999.987_j.x.
53. Sun H, Yi L, Wu P, Li Y, Luo B, Xu S. Prevalence of Gastroesophageal Reflux Disease in Type II Diabetes Mellitus. *Gastroenterol Res Pract* 2014;**2014**:601571. doi: 10.1155/2014/601571.
54. Fujiwara M, Miwa T, Kawai T, Odawara M. Gastroesophageal reflux disease in patients with diabetes: Preliminary study. *J Gastroenterol Hepatol* 2015;**30 Suppl 1**:31-5. doi: 10.1111/jgh.12777.
55. Ke M. How is the autonomic nerve function different between gastroesophageal reflux disease alone and gastroesophageal reflux disease with diabetes mellitus neuropathy? *J Neurogastroenterol Motil* 2011;**17**:430-1;author reply 432-3. doi: 10.5056/jnm.2011.17.4.430.
56. Lee SD, Keum B, Chun HJ, Bak Y-T. Gastroesophageal reflux disease in type II diabetes mellitus with or without peripheral neuropathy. *Journal of neurogastroenterology and motility* 2011;**17**:274. doi: 10.5056%2Fjnm.2011.17.3.274.
57. Kimura Y, Kamiya T, Senoo K, Tsuchida K, Hirano A, Kojima H, et al. Persistent reflux symptoms cause anxiety, depression, and mental health and sleep disorders in gastroesophageal reflux disease patients. *J Clin Biochem Nutr* 2016;**59**:71-7. doi: 10.3164/jcbn.16-9.
58. Yang X-J, Jiang H-M, Hou X-H, Song J. Anxiety and depression in patients with gastroesophageal reflux disease and their effect on quality of life. *World J Gastroenterol* 2015;**21**:4302-09. doi: 10.3748%2Fwjg.v21.i14.4302.
59. Kessing BF, Bredenoord AJ, Saleh CM, Smout AJ. Effects of anxiety and depression in patients with gastroesophageal reflux disease. Clinical gastroenterology and hepatology. *the official clinical practice journal of the American Gastroenterological Association* 2015;**13**:1089-95 e1. doi: 10.1016/j.cgh.2014.11.034.