



Gastroesophageal reflux disease (GERD): prevalence and association with Psychological Disorders among medical sciences students

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Abstract: Background: With respect to the high prevalence of psychological distress as a risk factor for GERD among medical sciences students, a high frequency of GERD is probable in this group of society. This study examined the frequency of GERD and its relationship with psychological disorders among the students of Hormozgan University of Medical Sciences.

Method: This is a cross-sectional study by Using stratified random sampling, 630 students were included in the study. Montreal criterion was used for weekly assessment of them in terms of having GERD symptoms and Psychological disorders were assessed using the General Health Questionnaire (GHQ-28).

Result: A total of 600 questionnaires, out of 630 distributed, were completed correctly and completely (participation rate 95.23%, female 63.3%). According to the Montreal criteria, 89 subjects (14.8%) had GERD. The relationship between age, Sex, marital status and year of education with the occurrence of GERD was significant. A significant difference exists between the controls and the GERD group in terms of general mental disorder ($p < 0.002$), somatic symptoms ($p < 0.002$), social dysfunction ($p < 0.011$) and anxiety ($p < 0.002$), while despite the difference in depression subscale, it was not statistically significant ($p < 0.341$).

Conclusion: Like other similar research, study results showed that GERD prevalence among the students did not exceed general population despite high frequency of mental disorders among medical sciences students. Although, the robust relationship between mental disorders and GERD represents the need for further attention to mental aspects in treating and following up patients. Anxiety disorders might be more important than depression in causing the GERD.

1. Introduction

Normal regurgitation of stomach contents into esophagus is often short-term and does not result in clinical signs and esophageal damage. However, it is considered morbidity when macroscopically damages the esophagus, creates clinical signs, and reduces the quality of life (2, 1).

Gastroesophageal reflux disease (GERD) is a frequent condition and its prevalence varies according to definitions, population studied, and geographical location (5-3). For example, in a review study by El-serag *et al.* (2013), the disease's prevalence was 8.8%-27.8% in Europe and North America, while it was reported less

than 10% in studies in East Asia (5). The prevalence of GERD is increasing in some parts of the world, including some Asian countries such as Iran (8-6), so that according to a recent study using a standardized questionnaire in Iran, the prevalence of the disease has been reported from 12.8% to 21% (11-9,4). This disease is of particular importance, because it imposes an economic burden upon society, reduces life quality, and creates complications such as esophageal ulcer, esophageal stricture, Barrett's esophagus, and causes upper gastrointestinal bleeding (14-12,6). On the other hand, Barrett's esophagus and GERD are important risk factors for esophageal cancer (13). Psychological stress is stated as a reason for GERD, because it causes signs of GERD through increasing gastric acid secretion, reducing gastric emptying, and increasing perceptual sensitivity to acid in the esophagus (16,15). According to various studies, a significant correlation has been proposed between anxiety disorders, depression, and somatization with the disease (21-17). On the other hand, medical education environments negatively affect academic performance and students' physical and mental health through producing different types of stress. For example, according to a study by Liselotte N *et al.* on 2246 medical students, at least 82% of them suffered from a physical or mental distress (24-22); this can increase the possibility of simultaneous presence of GERD in students. However, there is a very limited number of studies about this disease in students, and in contrary to expectations, the values reported on the prevalence of the disease in students was not more than the general population; further, it was less in some cases. For example, the prevalence of GERD have been reported as 9% and 6.3% in two studies conducted on students in Iran (25,14) and 0.9% in a study on students in China (26). These rates are small regarding the general population in Iran and China.

In addition to the limited number of studies on the disease in students and unexpected results obtained, no study has been performed so far regarding the association of psychological disorders and GERD among students.

Given the very limited number of studies on GERD in students, and considering the relationship between the disease and mental and physical stress, and its impact on quality of life, as well as the importance of students' health, the present study attempted to evaluate the prevalence of GERD and its relation with psychological disorders in students of the Bandar Abbas University of Medical Sciences.

2. Materials and Methods

2.1. Research design and sampling

The study population included all students at the Hormozgan University of Medical Sciences. This cross-sectional study was carried out through the stratified randomized sampling method. According to previous studies, the prevalence of gastroesophageal reflux disease and mental disorders is 20% (9) 28% (27), respectively. These figures were used to estimate the sample size, which was obtained 600 people at the significance interval of 95% and power of 95%, using Cochran formula.

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 [p_1(1-p_1) + p_2(1-p_2)]}{(p_1 - p_2)^2}$$

The University consisted of about 2100 students, and the sample size of 630 people accounted for about 30% of all students, therefore, according to the stratified sampling method, 30% of each category of students was enrolled in the study. Students were classified as follows; first- to seven-year medical students into seven categories, first- to four-year allied health and paramedical students (all disciplines) into four categories, and first- to six-year dental students into six categories. Inclusion criteria were finishing the first semester and the participants' consent, and the exclusion criterion was lack of cooperation of the subjects during the study (failure to complete the questionnaire or to cooperate in the study process). The selected individuals were ultimately examined by a general practitioner (GP) in terms of GERD using the Montreal criteria. A clinical psychologist (unaware of the results of interviews with GP) also examined the students in terms of psychological disorders using the 28-item General Health Questionnaire (GHQ). To study the psychological disorders in subjects with and without GERD, the two groups were matched in terms of some variables. To this end, the students without GERD who were matched with those with GERD in terms of number, gender, year of education, and field were randomly selected as the control group and were compared with the students with GERD in terms of psychological disorders.

2.2. Measurement tools

The data collection instrument was a three-partite questionnaire including demographic details (age, gender, GPA, field of study, degree (year), residence), the Montreal criteria for diagnosis of GERD, and the 28-item GHQ questionnaire to assess mental health.

Montreal criterion: heartburn and/or regurgitation at least once a week (28 ,5) (heartburn: burning sensation in the back of the sternum; regurgitation: returning of acidic or non-acidic contents of stomach into the mouth or throat).

28-item General Health Questionnaire (GHQ-28): It consists of 28 questions which are about somatic symptoms, anxiety, social dysfunction, and depression, each with 7 questions. Goldberg traditional scoring method was used in this study as 0-0-1-1; meaning that choices A and B were scored zero and choices C and D were scored one. Therefore, if each of the 28 symptoms exists more than usual (choice C) it is scored 1, and hence the maximum score will be 28. If the total score of a person in the GHQ-28 is 6 or more, the person have not general mental health. Also, a score of 2 or more in each of the four areas of depression, anxiety, social dysfunction, and somatic symptoms is considered impairment in that field, numerous studies throughout the world showed high levels of reliability and validity of the questionnaire (33-29). The reliability and validity of the Persian version of this questionnaire has been approved among Iranians. The sensitivity, specificity, and the error rate have been reported as 84.7%, 93.8%, and 8.2%, respectively. The questionnaire's reliability is also high (Cronbach's alpha: 0.85) (35-33 ,29).

2.3. Statistical analyses

The data were extracted using SPSS-20 and statistically analyzed with the help of the research statistical adviser. The data were analyzed through *t*-test to compare the mean of quantitative variables between the two groups and Chi-square for qualitative items. Difference levels of equal or more than 0.5 were considered significant.

3. Results

3.1. Demographic findings

A total of 600 questionnaires, out of 630 distributed, were completed correctly and completely with a response rate of 95.23%. From the 600 subjects studied, 220 (36.7%) were male and 380 (63.3%) were female. The participants' age range was 16-40 years with a mean of 21.58 ± 2.12551 years.

3.2. Main findings

According to the Montreal criteria, 89 subjects (14.8%) had GERD with a confidence interval of 95%.

Also 74 students (12.3%) had heartburn and 66 (11%) had regurgitation. There was a statistically significant difference between men and women at risk of heartburn and regurgitation (Table 1).

Table 1: The prevalence of GERD signs based on sex

GERD symptoms	Men number (%)	Women number (%)	Total number (%)	<i>p</i> -value
Heartburn	38 (17.3%)	36 (9.5%)	74 (12.3%)	0.007
Regurgitation	39 (17.7%)	27 (7.13%)	66 (11%)	0.000

3.3. Association of demographic variables with GERD

The mean age of patients with and without GERD was 22.00 ± 2.03 and 21.50 ± 2.13 years, respectively, and the difference was statistically significant at the level of $p < 0.043$. The prevalence of GERD was 22.3% ($n = 49$) in men and 10.5% ($n = 40$) in women, and the difference between women and men was statistically significant at the level of $p < 0.000$.

There was no significant association regarding the variables such as discipline, residence, and GPA with the occurrence of GERD, however, the relationship between marital status and year of education with the occurrence of GERD was significant (Table 2).

Table 2: The prevalence of GERD based on demographic variables

Component		Prevalence	Percent (%)	<i>p</i> -value
Sex	Female	40	10.5	0.000
	Male	49	22.3	
Marital status	Single	84	16	0.036
	Married	5	6.7	
GPA	Achievement	44	13.1	0.203
	No achievement	45	17	
Residence	Dormitory	72	15.5	0.414
	Non dormitory	17	12.5	
Discipline	Medicine	30	21.1	0.070
	Dentistry	4	8.3	
	Allied health	42	14	
	Health	13	11.7	
Year of education	First	28	16.4	0.003
	Second	10	6	
	Third	16	14.5	
	Fourth	19	21.3	
	Fifth	6	26.1	
	Sixth	7	28	
	Seventh	3	21.4	

3.3. Association between psychological disorders and GERD

As in Table 3, a significant difference exists between the controls and the GERD group in terms of general mental disorder. Regarding the subscales of GHQ, significant differences were observed between the GERD and control groups in somatic symptoms, anxiety, and social dysfunction, while despite the difference between the two groups in depression subscale, it was not statistically significant. The mean scores of GERD group were higher than the control group in all of these scales.

Table 3: The relative prevalence of general mental disorder, somatic symptoms, anxiety, depression, and social dysfunction in patients with GERD and controls

	Control number (%)	GERD number (%)	<i>p</i> -value
General mental disorder	6 (6.7%)	22 (24.7%)	0.002
Anxiety	21 (23.6%)	42 (47.2%)	0.002
Social dysfunction	16 (18%)	32 (36%)	0.011
Somatic symptoms	13 (14.6%)	32 (36%)	0.002
Depression	14 (15.7%)	20 (22.5%)	0.341

4. Discussion

To our knowledge, this study is the first one regarding the prevalence of GERD and its association with Psychological disorders in students. In this study, the number of GERD cases was 89 (14.8%) with a confidence interval of 95%. Also, 74 (12.3%) and 66 (11%) students had heartburn and regurgitation, respectively.

In a review article by El-serag *et al.* in 2013, the prevalence of GERD was 18.1%-27.8% in North America, 2.5%-7.8% in East Asia, 8.8%-25.9% in Europe, and 8.7%-33.1% in Middle East. The results were derived from studies in which the diagnosis was made based on heartburn and/or regurgitation and these symptoms occurred at least once a week (5). In a review article based on 15 studies from 1999 to 2010, the prevalence of GERD in Iran has been reported about 6.8% to 33% based on the weekly occurrence of GERD symptoms (4). The differences in the reported prevalence of GERD arise from different definitions and approaches, various studied communities, and invalid questionnaires used in these studies (4,3), although a reason for this difference in results may be the continued prevalence of the disease in some parts of the world such as North America, East Asia, and developing Caucasian countries like Iran in the past two decades (8-5). For example, the prevalence of endoscopic reflux esophagitis in East Asia has increased from 3.4-5% before 2000 to 4.3-15.7% after 2005 (4). By the way, based on a few recent studies which have used standard methodology and questionnaires, the prevalence of GERD have been reported about 12.8 to 21% in Iran (9,4) (11, which is more than the countries in East Asia and Africa, and almost equal to the American and European countries (36,5,4). Thus, according to this study, the prevalence obtained for students in Iran is roughly equal to the average prevalence of GERD in the general population and Western countries.

While, psychological stress, as a risk factor and even one of the causes of GERD (37,25,16,15), is higher in medical students than the general population (24-22). In addition, there are many other risk factors for developing GERD in students such as consuming more tea and coffee than the general population (38,25), which can predict the higher prevalence of the disease in students compared with the general population. However, despite these risk factors in students, the prevalence of GERD is lower in students than the general population based on the present and other studies conducted on students (26,25,14). For example, in a study on students in China in 2011, using the criterion of Montreal, the prevalence of GERD was 0.9% which was much less than the general population of China (40,39,26); this low prevalence of GERD compared with the general population was attributed to lower BMI and younger studied population.

This is despite the fact that in most studies, the prevalence of other gastrointestinal functional disorders, such as IBS and dyspepsia, with the same diagnostic criteria and in the same geographic area, was higher in students than the general population (46-40,26); This difference was attributed to causes such as lower age, higher physical and mental stress, poor eating habits, and consumption of cola and caffeine in students compared to the general population (53-47).

This represents risk factors and different causes regarding each of these gastrointestinal functional disorders and perhaps reflects the fact that, although based on the results of various studies, mental disorders are significantly associated with dyspepsia, IBS, and GERD, and even directly contribute to creation of these disorders, but, the importance of mental disorders in predicting GERD is not as much as other FGIDs such as IBS and dyspepsia, Other factors such as age and BMI are of greater importance in GERD. This might be due to that in patients with GERD, there is just a high relationship between non erosive subgroup and mental disorders and, erosive cases are associated with such causes as hiatal hernia, esophageal dysmotility, and greater esophageal acid exposure (56-54).

Higher educational level is a factor that can justify the lower incidence of this disorder in students compared with other gastrointestinal functional disorders, since a significant correlation exists between low levels of education and the signs of reflux based on various studies (58,57,38,9,6)..

In two separate studies on medical students in 2001 and non-medical students in 2005, 9% and 6.3% of students suffered from heartburn or regurgitation, respectively, once or more per week (25,14); these values are lower than ours. This difference may be due to the non-uniformity of the populations studied, because in the study on medical students, only one input has been investigated, while our study showed a meaningful relationship between year of education and GERD. Thus, the results cannot be well compared. On the other hand, the higher prevalence of GERD in this research compared with previous studies may arise from an increased incidence of the disease in recent years in Iran (8-5).

In a study on students in China in 2011, using the criterion of Montreal, the prevalence of GERD was 0.9% (26), which was much less than our result; this difference may be due to higher prevalence of this disease in Iran than in China and the countries of East Asia (36,5,4).

Prevalence of GERD symptoms

The prevalence of heartburn was higher than acid regurgitation in the present study. Based on a review article conducted in 2005, among the symptoms of GERD, acid regurgitation occurs more than heartburn; this is consistent with the results of our study in terms of the prevalence of GERD symptoms (38).

In a study on 620 students of Tabriz Azad University in 2006, the prevalence of GERD was higher in women than men, although this difference was not significant; and in contrast to our study, the prevalence of pharyngeal acid reflux was more than other symptoms(25). In a study on general population in Iran, the prevalence of acid reflux was also higher than other symptoms (59).

Demographic factors

The mean age of patients with GERD was higher than the mean age of those without GERD ($p<0.043$), although there is no consensus regarding the significant relationship between the disease and age, most studies suggested increased prevalence of the disease with age (59, 38, 25, 8).

In this study, the prevalence of GERD and its signs was significantly higher in men than in women. While based on a review article in 2005, the results about association of the disease with sex are inconsistent and do not imply a definite relation (38), and even the results of many studies on the general population (9, 6) (59, 38, 25) and medical sciences students(25) suggest that the prevalence of these diseases is higher in women.

There was also no significant correlation regarding the variables such as discipline, residence, and GPA with the prevalence of GERD; this finding was consistent with the results of a study performed on medical students (25).

The prevalence of GERD in the present study was significantly higher in single than married people. While according to the general population-based studies, the prevalence of dyspepsia was higher among married people (9). However, no significant correlation was found in another study performed on medical students (25).

In this study, there was also a significant relationship between year of education and the prevalence of GERD. Although in most studies, a significant relationship existed between low educational levels and reflux (58, 57, 38, 9, 6), the prevalence of GERD in the present study was more in higher years of education, which may be due to increased mental and physical stress arisen from less sleep times and more activities because of increased years of education and changes in living conditions of students (52, 26).

The relationship between Psychological disorders with GERD

According to the 28-item GHQ test, the results of our study showed a significant difference between the controls and GERD group in terms of general mental disorder and subscales of somatic symptoms, social dysfunction, and anxiety, while despite the difference between the two groups in depression subscale, it was not statistically significant. The mean scores of GERD group were higher than the control group in all of these scales.

In the study by Baker *et al.*, a positive relationship was found between psychological stress and a subgroup of patients with gastroesophageal reflux disease in the general population (19). According to a study in USA, the prevalence of GERD was higher in people with psychiatric disorders such as major depression and bipolar disorder than the control group (60). Based on two studies on general population in China, patients with GERD had significantly higher scores of depression and anxiety compared with healthy individuals, although the difference in anxiety scores between the two groups was greater than the difference in depression scores (62, 61). Based on a case-control study by Najmeh Al-Taha *et al.*, performed on general population using the GHQ-28 questionnaire to assess Psychological disorders, a significant positive correlation has been reported between the occurrence of GERD and general mental disorder, depression, and anxiety (11).

In a study in Poland, 32% of people with heartburn suffered from anxiety, while the prevalence of depression in these patients was only 10% (63).

According to a study by Núñez-Rodríguez *et al.*, the mean score of people with GERD was significantly higher compared with the control group in terms of disorders such as somatization, obsessiveness, interpersonal sensitivity, phobia, and psychotic symptoms, although the difference in depression scores between the two groups was not significant (64). According to a study by Jansson *et al.*, anxiety without depression increases the risk of reflux 3.2 times in adults, while depression without anxiety results in 1.7 times increase in risk of reflux (65). As the results suggest, in contrast to depression, anxiety has a strong association with GERD. This may be due to the difference of GERD subgroups in association with mental disorders, because one of the main reasons suggested about non-erosive reflux disease (NERD), which constitute approximately 70% of GERD, is the increased esophageal sensitivity (55). While based on Rubenstein *et al.*, anxiety and somatization were significantly associated with individuals' hypersensitivity to acid injection and esophagus balloon dilation, while its relationship with depression was not significant (66). In addition, the study of Nam *et al.* demonstrated that patients with NERD had significantly higher scores of anxiety and somatization than patients with erosive reflux disease (ERD), and healthy individuals, while this difference was not significant in terms of depression (67). Therefore, these results along with those of the present study emphasize somehow the association and higher role of anxiety disorders in GERD compared with depression, especially in NERD patients.

Based on a case-control study by Najmeh Al-Taha *et al.*, performed on general population using the GHQ-28 questionnaire, a significant positive correlation has been reported between the occurrence of GERD and social dysfunction (11).

According to the study by Wong *et al.*, absenteeism and its negative effects on social life is significantly higher in people with GERD than those without it (61). In a study on medical students in Tabriz, quality of life was significantly reduced in patients with GERD compared with those without the disorder (25). These results are consistent with those of our study regarding the relationship of GERD and social dysfunction.

The study also showed that a significant correlation exists between somatic symptoms and GERD. In two studies by Locke *et al.* and Diaz-Rubio *et al.*, a direct significant relationship was found between GERD and psychosomatic symptoms in western populations; this is consistent with our results (18 ,17).

Jonhston *et al.* reported a significantly higher prevalence of somatization in patients with GERD than in healthy individuals (21).

Meanwhile, some studies proposed visceral hypersensitivity as a reason for GERD signs such as heartburn, especially in cases of NERD (70-68), although the cause of increased hypersensitivity remains unclear, some studies proposed mucosal barrier dysfunction, esophageal inflammation, upregulation of nociceptors, and centrally mediated esophageal sensitivity (mental stress or central sensitization of spinal neurons) as reasons (72 ,71 ,15).

Regarding mental stress, studies have shown that psychological stress may produce symptoms of GERD through increasing gastric acid secretion, reducing gastric emptying, and increasing perceptual sensitivity to acid in the esophagus (16 ,15). However according to the studies by Bradley *et al.* and MH Núñez-Rodríguez *et al.*, although stress and mental disorders cause and exacerbate the symptoms of GERD and are highly associated with GERD, no relationship was found between stress and mental disorders with studied parameters such as esophageal pH and endoscopic findings, and the relationship between stress and GERD symptoms has been attributed to the possible role of stress in increasing the sensitivity of individuals to stimulation of the esophagus (73 ,64). In addition, the lack of a direct relationship between the severity of GERD and exposure of the esophagus to acid and endoscopic finding such as severe pathologic damage of mucous, especially in cases of NERD (75 ,74 ,69 ,68) , along with the results of the present and other studies that reported the strong association between somatoform disorders, such as somatization, with GERD ,17 ,11) (64 ,21 ,18, as well as higher prevalence of mental disorders and anxiety in NERD cases compared with ERD (76 ,75), all imply the impact of psychological factors on perception of somatic symptoms by patients with GERD and in particular, those with NERD.

The mentioned items somehow emphasize some of the reasons stated for visceral hypersensitivity in patients with GERD which are not related to the gastrointestinal tract, such as stress and associated psychological disorders as well as changes in central sensory processing. This shows the role of mental stress and mental disorders in creation of GERD symptoms, especially heartburn and pathogenesis of NERD cases.

5. Conclusion

Like other similar research, study results showed that GERD prevalence among the students did not exceed general population despite high frequency of mental disorders among medical sciences students. This indicates that mental disorders are less important than other functional gastrointestinal disorders (FGID) in predicting GERD and other factors such as age and BMI are of greater importance in GERD. The robust relationship between mental disorders and GERD represents the need for further attention to mental aspects in treating and following up such patients, especially NERD cases and those with heartburn-predominant symptoms. On the other hand, anxiety disorders might be more important than depression in causing the disease. A strong association between somatoform disorders and GERD, along with other symptoms, indicates the role of central sensory processing changes in improving visceral sensitivity in GERD patients.

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