



Full Length Research Paper

Depression and Anxiety in Patients with Persisting Gastroesophageal Reflux Disease

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Abstract

Background: Gastroesophageal reflux disease (GERD) is a common condition faced in the internal medicine outpatient clinic. The response rate to proton pump inhibitors and other anti-GERD measurements elicited questions about associated symptoms. Psychiatric comorbidity could be responsible for poor response to medical treatment. These associations are poorly investigated. **Aim of the work:** The current study aimed to estimate the prevalence of depression and/or anxiety and associated factors among patients with GERD. **Patients and Methods:** The study included 220 subjects (110 with GERD and 110 age and sex matched controls). Each participant completed a structured, self-administered hospital anxiety and depression scale questionnaire (HADS), and Reflux Disease Questionnaire. In addition, patient demographics, medical history, gastrointestinal manifestations, height, weight and body mass index (BMI) was documented. **Results:** There was slight female sex predominance (58.2% were females), from rural areas (62.7%) and were married (77.3%), with no significant difference between groups. Obesity was significantly increased in GERD than control group (19.1% vs 9.1% respectively). Anxiety, depression and concomitant anxiety and depression were reported in 23.6%, 13.6% and 13.6%, compared to 7.3%, 8.6% and 8.6% in the control group with the same order. In addition, all GERD symptoms score was significantly increased in GERD than control group. **Conclusion:** Results confirmed the reciprocal relationship between GERD and psychiatric disorders (anxiety and depression). Psychiatric comorbidity should be evaluated in patients with GERD and properly treated.

Keywords: Anxiety; Depression; Psychiatric disorder; GERD.

Introduction

Gastroesophageal reflux disease (GERD) is chronic disease caused by retrograde flow of gastroduodenal contents to the esophagus, leading to development of frequent symptoms of heart burn and regurgitation with mucosal damage⁽¹⁾. GERD is relatively common condition, affecting about 10-20% of individuals in the Western Nations and 18-28% in North America⁽²⁾, 5% among Asians⁽³⁾, and 7.3% among Egyptians⁽⁴⁾. However, a higher prevalence rate was reported from Saudi Arabia (23.5-45.4%)⁽⁵⁻⁷⁾, which greatly reduced in endoscopy-based studies^(8,9).

Diagnosis of GERD could be based on symptoms only, but had low sensitivity⁽¹⁰⁾. In early GERD, upper gastrointestinal endoscopy had a low sensitivity when used to confirm diagnosis, as some patients with clinical GERD had normal endoscopic findings⁽¹¹⁾. However, pH manometry had a sensitivity and specificity around 90% and 95% respectively^(12,13).

Medical management strategy for GERD usually achieved by proton pump inhibitors (PPIs). However, 20 to 30% of patients still complain from GERD symptoms irrespective of medical therapy⁽¹⁴⁾. Persisting symptoms of GERD could cause discomfort, impair quality of life and psychological stress⁽¹⁵⁾. The link between GERD and psychiatric health had been reported in previous studies.

A reciprocal link between the brain and gastrointestinal (GI) tract is known, where emotional distress can affect GI function, and GI stress can lead to mental and emotional stress. In addition, psychological stress could increase the severity of GIT symptoms and decrease response to medications^(16,17). In addition, no sufficient global studies established the link between GERD and psychological factors, including depression and anxiety, with inconsistent results^(18,19). Data on the prevalence of anxiety and depression in patients with GERD are lacking. Thus, we conducted the current study to estimate the prevalence of anxiety and depression and associated factors among patients with GERD presented to Al-Azhar University hospital (Damietta).

Subjects and methods

This study was designed as a case control study included 220 subjects (110 with GERD and 110 age and sex matched controls). The sample size for study group was calculated based on prevalence rate of 7.3% for GERD in Egyptian populations⁽⁴⁾. The equation used was n (sample size) = $[(Z_{1-\alpha/2})^2 * p(1-p)]/d^2$, where $Z_{1-\alpha/2}$ is the standard normal variate (at 5% type 1 error) and equal 1.96, (p) is the expected proportion in populations according to previous or pilot studies and (d) is the absolute error or precision (5%). The estimated sample size was 100 and with consideration of 10% drop down rate, we used 110 as a proper sample size for the study group, and with 1: 1 ratio, another 110 were included as a control group. The study was carried out from January 2017 through January 2019.

Ethical considerations: the study protocol was approved by the local institutional review board (IRB) of Damietta Faculty of Medicine, and we obey the ethical principles of Declaration of Helsinki. All participants signed an informed consent, and their confidentiality, and right of withdrawal without harm were guaranteed.

Inclusion criteria were: 1) acceptance to participate (consent), persistent symptoms of GERD after 8-weeks of once-daily proton pump inhibitors (PPI) therapy; while exclusion criteria were: 1) Gastroesophageal carcinoma, 2) Active peptic ulcer based on upper GIT endoscopy findings, 3) A history of gastrectomy, 4) subjects with symptoms of other functional gastrointestinal disorder except reflux from the control group, 5) patients with mental illness, and 6) patients with abnormal laboratory tests (e.g, hemoglobin and fasting blood sugar).

After full explanation of the study and its aims to participants, each of them was asked to complete a structured, self-administered questionnaire [including patient demographic, medical history, and GIT manifestations] and hospital anxiety and depression scale (HADS) questionnaire. Height and body weight were measured and the body mass index (BMI) was calculated.

"Anxiety includes feelings of fear, worry and apprehension, but depression is linked to feelings of sadness, sorrow, hopelessness and gloom"⁽²⁰⁾.

The HADS is a well-validated screening tool, which consists of 7 questions to assess anxiety symptoms (HADS-A) during the last week and 7 to assess depression (HADS-D), and also as a measure of co-morbid anxiety and depression. Each item score 0–3, with 0 = no symptom present. A score of eight or more indicated presence of anxiety and/or depression⁽²¹⁾. We used this questionnaire due to its wide use in primary and clinical care settings.

All upper GIT endoscopies were done by the same gastroenterologists. The traditional white light endoscopes (Olympus GIF-H260 and GIF-H290 series; Olympus Optical Co, Tokyo, Japan) was used. Before endoscopy, all subjects were submitted to physical examination of gastrointestinal complaints. GERD was defined clinically as the existence of heartburn (feeling of retrosternal burning sensation) and/or acid regurgitation (sensation of reflux of stomach contents into the mouth or the hypopharynx) occurring at least once a week⁽²²⁾. Patients with endoscopically proven erosive/ulcerative GERD were excluded.

To confirm association between psychiatric symptoms and GERD, patients were asked to complete Reflux Disease Questionnaire to assess reflux symptoms (retrosternal burning, retrosternal pain, regurgitation, and acid taste in the mouth). In short, this questionnaire assigns a score for each typical reflux symptom using a 6-point Likert scale (0–5)⁽²³⁾.

Statistical analysis: All data were expressed according to its type [i.e., numerical data were expressed as means \pm SD] or as numbers (percentages) for qualitative data. Comparison between groups was achieved by student [t] test or Chi square for quantitative and qualitative data respectively. P value < 0.05 was considered significant.

Results

In the current work, patient age ranged between 22 and 66 years and the majority of them were in their fifties; with slight female sex predominance (58.2% were females), and there was no significant difference between study and control groups regarding patient's age, weight, height, body mass index (BMI) or sex distribution. The majority of our patients live in rural areas (62.7%) and married (77.3%), with no significant difference between groups. However, obesity was significantly increased in GERD than control group (19.1% vs 9.1% respectively). GERD was significantly increased in patients with higher education. But no significant difference was found between groups regarding smoking, hypertension or diabetes (Table 1).

In the current work, patients with GERD had significantly higher score of hospital anxiety and depression scale in anxiety, depression and total domains than control group. In GERD, anxiety, depression and concomitant anxiety and depression were reported in 23.6%, 13.6% and 13.6%, compared to 7.3%, 8.6% and 8.6% in the control group with the same order. In addition, all GERD symptoms score was significantly increased in GERD than control group (Table 2). In the current study, all GERD symptoms score was significantly increase in patients with GERD and Anxiety than those with GERD without anxiety (Table 3). Similarly, results were documented for those with GERD and depression in comparison to those with GERD without depression except retrosternal pain which showed non significant differences (Table 4).

Table (1): Variable associated with GERD on univariate analysis

| | | GERD | Control | Total | Test | P |
|--------------------------|--------------|-------------|-------------|-------------|-------|--------|
| Age (years) | | 46.2±9.2 | 44.7±9.7 | 45.4±9.5 | 1.20 | 0.22 |
| Weigh(kg) | | 73.3±11.3 | 70.8±8.3 | 72.1±9.9 | 1.86 | 0.06 |
| Height (m) | | 1.696±0.054 | 1.689±0.049 | 1.693±0.052 | 1.06 | 0.28 |
| BMI (kg/m ²) | | 25.4±3.5 | 24.8±2.4 | 25.1±3.0 | 1.60 | 0.11 |
| Sex | Male | 48(43.6%) | 44(40.0%) | 92(41.8%) | 0.29 | 0.58 |
| | Female | 62(56.4%) | 66(60.0%) | 128 (58.2%) | | |
| Residence | Urban | 43 (39.1%) | 39 (35.5%) | 82 (37.3%) | 0.31 | 0.57 |
| | Rural | 67 (60.9%) | 71 (64.5%) | 138 (62.7%) | | |
| Obesity | Obese | 21(19.1%) | 10(9.1%) | 31(14.1%) | 4.54 | 0.033* |
| | Non-obese | 89(80.9%) | 100(90.9%) | 189(85.9%) | | |
| Marital status | Single | 6(5.5%) | 6(5.5%) | 12(5.5%) | 0.12 | 0.93 |
| | Married | 84(76.4%) | 86(78.2%) | 170(77.3%) | | |
| | Divorced | 20(18.2%) | 18(16.4%) | 38(17.3%) | | |
| Education | Primary | 7(6.4%) | 16(14.5%) | 23(10.5%) | 14.75 | 0.002* |
| | Middle | 35(31.8%) | 50(45.5%) | 85(38.6%) | | |
| | Higher | 34(30.9%) | 30(27.3%) | 64(29.1%) | | |
| | Postgraduate | 34(30.9%) | 14(12.7%) | 48(21.8%) | | |
| Smoking | Never | 86(78.2%) | 88(80.0%) | 174(79.1%) | 0.11 | 0.94 |
| | Current | 10(9.1%) | 9(8.2%) | 19(8.6%) | | |
| | Ex-smoker | 14(12.7%) | 13(11.8%) | 27(12.3%) | | |
| Hypertension | | 10.0(9.1%) | 5(4.5%) | 15 (6.8%) | 1.78 | 0.18 |
| Diabetes | | 13(11.8%) | 7(6.4%) | 20 (9.1%) | 1.98 | 0.16 |

Table (2): Comparison between cases and controls regarding anxiety and depression

| | | GERD | Control | Total | Test | P |
|---------------------|-------------------------|------------|------------|------------|-------|---------|
| HADS-A | Mean±SD | 7.76±3.86 | 6.23±2.13 | 7.0±3.20 | 3.63 | <0.001* |
| | Min. – Max. | 4-18 | 4-15 | 4-18 | | |
| HADS-D | Mean±SD | 5.83±3.40 | 4.30±2.14 | 5.06±2.94 | 3.95 | <0.001* |
| | Min. – Max. | 2-16 | 3-16 | 2-16 | | |
| HADS-T | Mean±SD | 13.50±6.44 | 10.54±3.88 | 12.02±5.51 | 4.12 | <0.001* |
| | Min. – Max. | 7-32 | 8-31 | 7-32 | | |
| Anxiety | | 26(23.6%) | 8(7.3%) | 34(15.5%) | 11.27 | 0.001* |
| Depression | | 15(13.6%) | 4(3.6%) | 19(8.6%) | 6.97 | 0.008* |
| Anxiety-Depression | | 15(13.6%) | 4(3.6%) | 19(8.6%) | 6.97 | 0.008* |
| GERD symptoms score | Regurgitation | 2.28±0.73 | 0.90±0.42 | 1.59±0.91 | 17.11 | <0.001* |
| | Acid taste in the mouth | 2.19±0.72 | 0.13±0.47 | 1.16±1.20 | 25.07 | <0.001* |
| | Retrosternal burning | 2.15±0.69 | 0.14±0.49 | 1.14±1.17 | 24.81 | <0.001* |
| | Retrosternal pain | 0.12±0.43 | 0.027±0.16 | 0.08±0.32 | 2.27 | 0.024* |

Table (3): Association between GERD symptoms score and anxiety in the GERD group

| | Positive | Negative | Test | P |
|-------------------------|-----------|-----------|-------|---------|
| Regurgitation | 3.26±0.78 | 1.97±0.34 | 11.95 | <0.001* |
| Acid taste in the mouth | 3.07±0.79 | 1.91±1.41 | 9.76 | <0.001* |
| Retrosternal burning | 2.96±0.82 | 1.90±0.39 | 8.90 | <0.001* |
| Retrosternal pain | 0.50±0.79 | 0.02±0.11 | 5.74 | <0.001* |

Table (4): Association between GERD symptoms score and depression in the GERD group

| | Positive | Negative | Test | P |
|-------------------------|-----------|-----------|------|---------|
| Regurgitation | 3.40±0.51 | 2.10±0.59 | 8.01 | <0.001* |
| Acid taste in the mouth | 3.07±0.78 | 2.05±0.60 | 5.73 | <0.001* |
| Retrosternal burning | 2.93±0.79 | 2.03±0.59 | 5.21 | <0.001* |
| Retrosternal pain | 0.26±0.45 | 0.11±0.42 | 1.35 | 0.19 |

Discussion

In this study we assessed the association between GERD from one side and each of anxiety and depression from the other side. Patients with GERD had higher scores and percentages of anxiety, depression and both conditions when compared to control group. In addition, the GERD symptoms scores were significantly higher among those with anxiety than those without anxiety in patients of

GERD group. These results confirm the bidirectional relationship (association) between GERD and psychiatric disorders (mainly anxiety and depression). These results could be explained by the close connection between gastrointestinal tract and the brain. The emotional stress could affect the gastrointestinal function leading to different diseases. In addition, gastrointestinal disease and stress could affect the mental and emotional well-being. The severity of functional gastrointestinal diseases can be changed by psychological factors, altering the pain perception through the stimulation on the gut-brain axis, which also applied to GERD⁽¹⁸⁾. Thus, it is crucial to address the psychological disorders accompanying GERD as the treatment of GERD in the existence of psychological disorders can become hindered⁽¹⁶⁾. Kimura *et al.*⁽²⁴⁾ also stated that patients who had poor or no response to proton pump inhibitors (PPI) were more likely to show high values of anxiety and depression. In the current work, GERD showed no association with patient age. This disagrees with previous study conducted by He J, *et al.*,⁽²⁵⁾. This could be attributed to different study designs and sample size. The female sex was higher in the current work, but the difference between study and control groups was statistically non-significant. These results are in line with Alsuwat *et al.*⁽⁷⁾ who reported that, the relationship between GERD and gender was not of statistical significance. In the current work, GERD was associated with higher education, the results which is different than previous studies reported that, higher education was associated with a lower prevalence of GERD⁽²⁶⁾, though other studies found no link between education and GERD⁽⁷⁾.

On the other side, previous studies revealed that, the symptoms of GERD were more prevalent in whom with higher education^(22,27). These results are supported by the current work. Our results are in agreement with previous studies reported that, anxiety and depression are closely related to the GERD and reflux esophagitis⁽²⁸⁻³¹⁾. The pathophysiological mechanisms underlying the relationship between psychological factors and GERD are not fully understood. However, there are potential possibilities. One explanation is that depression and/or anxiety are secondary to GERD, which in turn increases the sensitivity of patients to GERD symptoms. The second possibility is that delayed gastric emptying in patients with depression and/or anxiety will increase transient lower esophageal sphincter (LES) relaxation due to the influence the central nervous system, which in turn can aggravate gastroesophageal reflux^(28, 30).

Results of the current work are in line with Bilgi *et al.*⁽³²⁾ who reported that, patients with GERD were significantly more depressed than the control group. Anxiety level was significantly higher in GERD than those of the control groups. In addition, Oh JH, *et al.*⁽³³⁾ also found an association between depression and anxiety and GERD. Furthermore, Jansson *et al.*⁽²⁰⁾ concluded that, anxiety and depression are strongly associated with reflux symptoms. In short, results of the present study confirmed the interrelationship between GERD and psychiatric disorders (anxiety and depression).

Conflict of interest: none

Financial disclosure: none

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