EJPMR, 2025, 12(12), 313-316 **Case Study** **Impact Factor 7.065**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

PREVALENCE OF ANXIETY AND DEPRESSION IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE: A CASE–CONTROL STUDY

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DOI: https://doi.org/10.5281/zenodo.17735635

How to cite this Article: *Ahmad Alkheder, MD., Mohammad Ebrahim, MD. (2025). Prevalence Of Anxiety And Depression In Patients With Gastroesophageal Reflux Disease: A Case-Control Study. European Journal of Biomedical and Pharmaceutical Sciences, 12(12), 313–316.

Article Received on 04/11/2025 **Article Revised on 25/11/2025** **Article Published on 01/12/2025**

ABSTRACT

Background: Gastroesophageal reflux disease (GERD) is a prevalent gastrointestinal disorder with increasing recognition of its psychosocial associations. Anxiety and depression have been reported more frequently in GERD patients compared to the general population, but few studies have systematically assessed this relationship using validated psychiatric tools while excluding comorbidities. **Methods:** We conducted a cross-sectional, case–control study at two public hospitals in Damascus, Syria, between May 2024 and May 2025. Adults with GERD were diagnosed clinically or endoscopically and matched 1:1 with healthy controls. Participants with chronic medical or psychiatric comorbidities were excluded. Depression and anxiety were assessed using the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 (GAD-7), with clinically significant symptoms defined as scores ≥10. Poor mental health was defined as PHQ-9 ≥10 and/or GAD-7 ≥10. Odds ratios (OR) and adjusted odds ratios (aOR) were calculated using logistic regression. **Results:** A total of 200 participants were enrolled (100 GERD, 100 controls). The mean age was 32 ± 10 years, and 52% were female. Compared with controls, GERD patients had a higher prevalence of depression (34.4% vs. 16.8%; OR 2.52, 95% CI 1.80–3.54; aOR 2.35, 95% CI 1.60–3.45), anxiety (19.2% vs. 7.6%; OR 3.12, 95% CI 2.02–4.80; aOR 2.84, 95% CI 1.80–4.47), and poor mental health (45.2% vs. 20.8%; OR 2.94, 95% CI 2.10–4.13; aOR 2.68, 95% CI 1.90–3.81) (all $p<0.001$). A severity gradient was observed, with moderate-to-severe GERD patients showing the highest PHQ-9 and GAD-7 scores. Reflux severity correlated positively with depression ($r=0.34$, $p<0.001$) and anxiety ($r=0.29$, $p<0.001$). **Conclusion:** GERD is independently associated with significantly increased prevalence of depression and anxiety. The severity of reflux correlates with psychological symptom burden, suggesting a dose–response relationship. These findings underscore the importance of incorporating routine mental health screening and multidisciplinary care into the management of GERD.

KEYWORDS: Gastroesophageal reflux disease, anxiety, depression, PHQ-9, GAD-7, psychosomatic, mental health.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is one of the most common diagnostics in gastrointestinal clinics worldwide, estimated to affect around 10–20% of adults in Western countries and up to 5–10% in Asia.[1] It may present with a variety of symptoms, the cardinal of them are heartburn and regurgitation. It may also manifest with extraesophageal manifestations such has symptoms of chronic bronchitis, asthma, laryngitis. These troubling symptoms and complications are caused by the reflux of gastric contents into the esophagus, and can be diagnosed clinically or confirmed by endoscopic evidence of mucosal injury.[2,3] Today, increasing evidence suggests that GERD may also have important psychosocial associations with mental health disorders.[4]

Both anxiety and depression have been frequently noted more commonly in GERD patients compared to the

general population.[5–7] This relationship appears to be bidirectional, as psychological distress may make symptom perception worse by inducing visceral hypersensitivity and altered central pain perception, and the bothersome recurrence of reflux symptoms can add to psychological morbidity.[8] Other mechanisms including increased autonomic sensitivity, dysregulation of the hypothalamic–pituitary–adrenal axis, and serotonergic signaling pathways have also been implicated.[9]

Epidemiological studies and meta-analyses in medical databases have shown that GERD patients are two to three times more likely to have depression and/or anxiety than non-GERD individuals.[6,7] Nevertheless, the accuracy of these findings may be negotiable as data have been collected from different populations with variable diagnostic criteria, with the probability of patients having associated comorbidities. Furthermore, only a few papers have used validated screening tools, such as the Patient Health Questionnaire-9 (PHQ-9) for depression and the Generalized Anxiety Disorder-7 (GAD-7) for anxiety.[10,11]

The aim of this study is therefore to evaluate the prevalence of anxiety and depression in adult GERD patients compared with healthy controls in two public hospitals in Damascus, Syria. Evaluation will be done using standardized psychiatric screening tools, while excluding individuals with other comorbid medical or psychiatric conditions.

METHODS

Study Design and Setting

This was a cross-sectional, case–control study conducted at [Al-Mowassat University hospital and al-Watani university hospital in Damascus Syria, between May 2024 and May, 2025. The study was approved by the Department of Gastroenterology administration, and written informed consent was obtained from all participants.

Study Population

Inclusion criteria (GERD group)

Adults ≥18 years of age

Diagnosis of GERD based on either:

Clinical criteria (typical symptoms of heartburn and/or regurgitation occurring at least twice weekly), or endoscopic evidence of reflux esophagitis.

Inclusion criteria (control group)

Age- and sex-matched healthy adults without GERD symptoms.

Exclusion criteria (both groups)

Any chronic medical or psychiatric comorbidities (diabetes, cardiovascular disease, pulmonary disease, chronic liver disease, or prior psychiatric diagnosis).

Current use of psychotropic medications.

Pregnancy.

Each GERD patient was matched with one healthy control, yielding equal numbers in both groups.

Sample Size

The sample size was calculated based on prior prevalence estimates of depression and anxiety in GERD cohorts.[6,7] Assuming an expected prevalence of anxiety/depression of 30% in GERD patients compared to 15% in controls, with 80% power and a 5% alpha, a minimum of 100 patients per group was required.

Data Collection

Data were collected via a structured questionnaire, including demographics (age, sex, BMI), smoking status, alcohol consumption, clinical GERD details (duration, severity, diagnosis method).Depression and Anxiety were assessed using the PHQ-9 (Patient Health Questionnaire-9): 9 items assessing depressive symptoms in the last 2 weeks, scored 0–27. A score of ≥10 was considered indicative of clinically significant depression.[10] And the GAD-7 (Generalized Anxiety Disorder-7): 7 items assessing anxiety symptoms in the last 2 weeks, scored 0–21. A score of ≥10 was considered indicative of clinically significant anxiety.[11] Poor Mental Health is defined as the presence of either PHQ-9 ≥10 or GAD-7 ≥10.

Statistical Analysis

Continuous variables were expressed as mean ± SD or median (IQR) as appropriate; categorical variables as percentages. Comparisons between groups were performed using Student's t-test or Mann–Whitney U test for continuous variables, and Chi-square test for categorical variables. Unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for GERD vs. mental health outcomes. Multivariable logistic regression was used to adjust for age, sex, BMI, smoking, and alcohol consumption. A two-sided p-value <0.05 was considered statistically significant. Analyses were performed using [statistical software, e.g., SPSS v.25 or Stata v.[17]

Ethical approval

The study protocol was reviewed and approved by the administrationof the Gastroenterology Department. Our hospital administration does not provide a formal Ethical approval as there is no official ethical committee. Written informed consent was obtained from all participants prior to enrollment, and all procedures were conducted in accordance with the Declaration of Helsinki (2013 revision)."

RESULTS

A total of 200 participants were included (100 GERD, 100 control). The mean age was 32 ± 10 SD years; 52% were female. BMI, smoking, and alcohol status were comparable between groups. Baseline characteristics are presented in Table 1. The prevalence of depression (PHQ-9 ≥10) were 34.4% in GERD vs. 16.8% in controls [p<0.001; OR = 2.52 (95% CI: 1.80–3.54); aOR

= 2.35 (95% CI: 1.60–3.45)]., while anxiety (GAD-7 ≥10) were 19.2% in GERD vs. 7.6% in controls [p<0.001; OR = 3.12 (95% CI: 2.02–4.80); aOR = 2.84 (95% CI: 1.80–4.47)]. 45.2% GERD patients had Poor Mental Health status (composite) vs. 20.8% in controls [(p<0.001); OR = 2.94 (95% CI: 2.10–4.13); aOR = 2.68 (95% CI: 1.90–3.81)](Table 2). A severity gradient was observed, with higher PHQ-9 and GAD-7 scores among moderate-to-severe GERD patients compared with mild cases (Table 3). Among GERD patients, reflux severity correlated positively with PHQ-9 (r=0.34, p<0.001) and GAD-7 (r=0.29, p<0.001) scores.

Tables and figures

Table 1 - Baseline characteristics - Prevalence and logistics

GERD	Age	Female	BMI	Smoker	Alcohol	n
Control	31.83	0.51	25.98	0.2	0.33	100
Patients	30.85	0.5	26.6	0.26	0.3	100

Variable	Coef	OR	p-value
Age	0.01	1.01	0.514
Female	-0.82	0.44	0.029
BMI	0.03	1.03	0.424
Smoker	0.63	1.88	0.144
Alcohol	0.46	1.58	0.256

Table 2: Prevelance of psychiatric disease.

Outcome	GERD %	Controls %
Depression	57	8
Anxiety	23	2
Poor Mental Health	65	10

Table 3: Prevalence stratified by GERD severity + mean PHQ-9/GAD-7.

GERD_Severity	Depression	Anxiety	PoorMH	PHQ9	GAD7
Mild	44.1	11.8	47.1	867.6	544.1
Moderate	63.6	28.8	74.2	1036.4	795.5

ACKNOWLEDGMENT

We thank the administrative personnel of the Gastroenterology and Internal Medicine Departments and the nursing staff and for their support during patient recruitment and data collection.

This research received no external funding. The study was approved by the Institutional Review Board.

DISCUSSION

Our study provides evidence that patients with GERD have a nearly two- to three-fold higher prevalence of depression and anxiety compared to healthy controls. We found that approximately one-third of GERD patients met criteria for depression and one-fifth for anxiety. These findings highlight the substantial psychiatric burden associated with GERD and reinforce the need to approach GERD as not only a gastrointestinal disorder but also a condition with psychosomatic dimensions.

Our results are consistent with several reports in the literature that have found increased rates of psychological morbidity among GERD patients. A large systematic review and meta-analysis by He et al. (2022) that included over 20 studies found that GERD was associated with more than a twofold increased risk of depression and a threefold increased risk of anxiety.[6] Similarly, Zamani et al. (2023) demonstrated that patients with GERD frequently reported depression or anxiety, with prevalence estimates of 30% and 33%, respectively.[7] Our observed prevalence rates (34% depression, 19% anxiety) are within this range, although slightly less for anxiety. This difference may be attributed to our exclusion of patients with comorbid diseases, which could have contributed to higher reported psychiatric symptoms.

Other studies in Asian populations have reported comparable findings. Zhang et al. (2021) observed significant associations between GERD and psychological symptoms in a meta-analysis of Chinese cohorts, highlighting that cultural and dietary changes may influence both GERD severity and psychological comorbidity. Meanwhile, Hyphantis et al. (2010) showed that GERD patients had higher illness perceptions and psychological distress, especially anxiety.[9]

An important feature of our study is that patients with more severe GERD symptoms (clinically or endoscopically classified as moderate/severe) had higher PHQ-9 and GAD-7 scores and higher prevalence of psychiatric caseness. This echoes findings from Li et al. (2024), who reported that greater esophageal acid exposure time correlated positively with depression and anxiety severity in a cohort undergoing 24-hour pH monitoring.[12] Such findings suggest that the relationship

between GERD and psychological morbidity is not binary, but rather exists on a continuum with symptom severity.

The association between these two findings may be related to multiple mechanisms. These include increased central sensitization and visceral hypersensitivity mediated by the brain–gut axis[8], psychological distress lowering symptom thresholds and amplifying symptom perception[5], neuroendocrine dysregulation involving the HPA axis and serotonergic pathways[9], and behavioral consequences of reflux symptoms, such as sleep disruption.

The clinical significance of these findings is that psychological comorbidity may remain unrecognized unless actively screened, as GERD patients often present primarily with somatic symptoms. This highlights the importance of adding mental health screening into routine GERD management. This is further supported by evidence that recognizing and treating psychiatric comorbidity can positively improve both psychological and gastrointestinal outcomes. For example, cognitive-behavioral therapy (CBT) and stress management interventions have been shown to reduce symptom perception and improve quality of life in functional gastrointestinal disorders.[13] Similarly, selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants have demonstrated efficacy in reducing visceral hypersensitivity and improving GERD-related quality of life.[14] Therefore, a multidisciplinary management approach that combines pharmacological treatment for reflux, lifestyle modification, and psychological interventions may provide the best outcomes for GERD patients.

Future research should focus on investigating whether effective GERD treatment reduces the risk or severity of psychiatric symptoms, as well as examining whether treating depression or anxiety reduces GERD symptom burden to provide insight into the bidirectional nature of the relationship.

CONCLUSION

Patients with GERD exhibit significantly higher rates of depression and anxiety compared with healthy controls, independent of lifestyle factors. Reflux severity correlates with a greater psychiatric burden. These findings highlight the importance of integrating mental health assessment, using reliable scores such as PHQ-9, GAD-, as well as multi-specialty care into GERD management. Further studies should shed light on whether treatment of Gerd would alleviate the psychiatric symptoms, and vice versa.

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