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Gastroesophageal reflux disease in adults and its relation with stress/anxiety

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Abstract. Mental factors such as pressure, emotional states, health response, or personal traits are acknowledged to have a major influence the intensity of manifestations in gastric-esophageal reflux condition. The aim of the present study was to highlight the relationship among stress, psychological traits associated with acid reflux and perceptions of reflux symptoms. Two studies were used to analyze the relationship between reflux and anxiety. A retrospective transversal, made by Ji Min Choi, and another prospective, made by Xiao-Jun Yang. Both provided details about this association, in addition to highlighting the importance of endoscopic examination to identify reflux disease. Finally, this close conection between esophageal reflux disease and anxiety needs to be further explored, so that the guidelines may include a holistic treatment for GERD, improving the quality of life in patients affected by it.

Keywords: Reflux, gastroesophageal reflux disease, proton pump inhibitors super endoscopy, mental health, stress, anxiety, depression, GERD

Introduction

Gastroesophageal reflux disease (GERD) is a prevalent condition characterized by the recurrent flow of stomach acid into the esophagus. Over recent decades, an increasing association has been recognized between anxiety and GERD. GERD becomes a clinical concern when it results in frequent symptoms or mucosal damage, significantly impacting the quality of life of affected individuals and potentially disrupting their daily activities (YANG et al., 2015) (1). The primary symptoms of GERD include heartburn, described as a burning sensation in the chest, and the regurgitation of sour or bitter liquid into the throat or mouth. It can also manifest with symptoms such as vomiting, shortness of breath, coughing, and other respiratory issues.

The etiology of GERD is multifaceted, with various risk factors contributing to its development. These risk factors encompass conditions like hiatal hernia, where the upper part of the stomach protrudes into the chest through a small diaphragmatic opening, a low body mass index (BMI), and the presence of

Helicobacter pylori. In addition to these common risk factors, psychological factors, including anxiety and depression, can manifest in GERD patients. It is widely acknowledged that stress and emotional states can influence gastrointestinal function, as well as the onset and progression of gastrointestinal symptoms and disorders acording to CHOI et al., 2018 (2).

Diagnosis of GERD frequently involves the use of upper gastrointestinal endoscopy, a procedure designed to examine the lining of the upper gastrointestinal tract, which includes the esophagus, stomach, and duodenum. FASS et al., 2007 (3) got to the conclusion that this diagnostic approach helps ascertain whether a patient's symptoms are attributable to GERD, its associated complications, or another underlying health condition .

In conclusion, many patients with gastroesophageal reflux disease report that stress exacerbates their symptoms. However, the precise mechanisms underpinning this connection remain incompletely understood. Our objective is to investigate the influence of anxiety and stress on individuals perception and emotional response to esophageal

acid exposure.

2. Research Methods

To ensure a comprehensive and systematic review of the literature, a meticulous methodology was employed. The objective was to identify and analyze research papers exploring the relationship between Gastroesophageal Reflux Disease (GERD) and stress/anxiety in adults.

The Literature Search Strategy involved an exhaustive search of various databases, including PubMed, MEDLINE, Web of Science, and PsycINFO. The search was executed using relevant keywords commonly associated with GERD and psychological factors. These keywords included "Gastroesophageal Reflux Disease," "GERD," "acid reflux," "heartburn," "stress," and "anxiety." A combination of these terms using the Boolean Operators "AND" and "OR" was employed to capture the widest possible range of relevant articles. Additionally, manual searches of pertinent journals and a review of bibliographies from selected articles were conducted to identify any additional sources that may have been missed in the initial database search.

For the purpose of this review, specific Inclusion and Exclusion Criteria were established. Included research papers had to be published in peer-reviewed journals and focus on adults (individuals aged 18 and above). These papers should have explored the relationship between GERD and stress and/or anxiety. Furthermore, the language of publication were in English and Portuguese. Papers involving pediatric populations, non-peer-reviewed sources (e.g., conference abstracts or opinion pieces), and those that did not directly address the relationship between GERD and stress/anxiety were excluded from the review. The research used the work done by Ji Min Choi et al and her colleagues entitled "association between anxiety and depression and gastroesophangeal reflux disease: results from a large-cross sectional study". And also used the prospective study done by Xiao-Jun Yang et al entitled "Anxiety and depression with gastroesophangeal reflux disease and their effect on quality of life".

The Data Extraction process involved collecting pertinent information from each selected research paper. This included details on the sample sizes, methodologies employed, key findings, and limitations of the studies.

3. Results

In the retrospective cross-sectional research conducted by Ji Min Choi and colleagues, the study aimed to explore the impact of Gastroesophageal Reflux Disease (GERD) in adults while investigating its association with stress and anxiety. A total of 19,099 subjects participated in this extensive study, and among them, 8.2% (1,574 individuals) reported experiencing symptoms of reflux. To refine the characterization of GERD, these individuals with reflux symptoms were divided into two primary groups based on endoscopic findings related to the gastroesophageal junction. The first group, comprising 0.9% of the total cohort, was labeled the Erosive Reflux Disease (ERD) group and consisted of 176 individuals. The second group, the Non-Erosive Reflux Disease (NERD) group, represented 7.3% of the cohort, with 1,398 individuals.

Additionally, the study identified a segment of participants (7.2%, 1,368 individuals) who exhibited endoscopically confirmed esophageal mucosal erosions or ulcers but did not report any reflux symptoms. This group was categorized as the Asymptomatic Esophageal Erosion (AEE) group. The remaining subjects, constituting the majority at 84.6% (16,157 individuals), were designated as the control group for comparative purposes.

The research unveiled several noteworthy demographic and clinical distinctions among these distinct groups. Notably, the ERD and NERD groups were found to be significantly younger. Gender differences were also apparent, with the ERD and AEE groups displaying a lower percentage of women (14.2% and 11.5%, respectively) compared to the control group (37.3%). Furthermore, body mass index (BMI) exhibited significant differences among the groups, with the ERD and AEE groups having higher BMIs (25.5 ± 3.2 and 25.1 ± 3.0, respectively) compared to the control group (23.6 ± 3.0). Diabetes was also a differentiating factor, with a higher percentage of individuals with diabetes observed in the AEE group and a lower percentage in the NERD group when compared to the control group ($P < 0.001$ for all groups).

The study delved into lifestyle factors as well, revealing that the ERD and NERD groups had a significantly higher percentage of current smokers and alcohol users compared to the control group ($P < 0.001$ for all). Moreover, marital status differed, with the ERD and NERD groups showing a significantly lower percentage of married subjects compared to the control group ($P < 0.001$). The use of aspirin displayed statistically significant differences, with only the AEE group exhibiting a distinct pattern compared to the control group.

The study further investigated the influence of psychological factors on each GERD subtype, indicating that state anxiety levels were significantly higher in the NERD and ERD groups when compared to the control group. The NERD group exhibited the highest levels of state anxiety. Trait anxiety levels significantly differed only in the NERD

group, displaying higher levels compared to the control group. Moreover, depression levels were significantly higher in all three GERD subtypes when compared to the control group, with the NERD group demonstrating the strongest association with depression.

Finally, a multinomial logistic regression analysis provided insights into independent associations. Female sex was independently associated with NERD, while male sex was associated with AEE. High BMI and current smoking emerged as independent associations across all three GERD subtypes, while alcohol use was linked solely to the AEE group. Marital status showed a significant association with ERD and NERD. Diabetes mellitus inversely correlated with NERD, and an H. pylori seropositive status and endoscopically proven atrophic gastritis inversely correlated with the ERD and AEE subtypes, while the presence of intestinal metaplasia inversely correlated with the NERD subtype.

In the to the prospective study conducted by Xiao-Jun Yang and their research team, the investigation aimed to examine the effect of Gastroesophageal Reflux Disease (GERD) on adults and its association with stress and anxiety. The study included a total of 279 consecutive patients who presented with typical symptoms of heartburn or regurgitation from the Division of Gastroenterology at Union Hospital, Tongji Medical College, as well as 100 healthy controls selected from the hospital staff and medical students at Tongji Medical College.

To ensure ethical standards, all participants provided informed consent before being included in the study. Gastroendoscopy was then performed on all subjects to assess the presence of esophageal mucosal lesions. Based on the results of these gastroendoscopies, the patients were categorized into two primary groups: Gastroesophageal Reflux Disease with Erosions (RE) and Non-Erosive Reflux Disease (NERD). GERD was diagnosed in accordance with the Rome III criteria. Patients who had used prescribed non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin, those who had previously been treated with proton pump inhibitors, and individuals with specific gastrointestinal conditions or comorbidities were excluded from the study. The Ethics Committee of Tongji Medical College approved this research protocol (No. 104).

To measure anxiety and depression levels, the Zung Self-Rating Anxiety Scale (ZSAS) and the Zung Self-Rating Depression Scale (ZSDS) were employed, respectively. The ZSAS comprised 20 questions, each scored on a 1-4 scale, and was used to categorize participants into four anxiety severity groups. Similarly, the ZSDS assessed depression severity with 20 items ranked from 1 to 4, allowing categorization into four depression severity groups. It's important to note that ZSDS scores do not

provide a clinical diagnosis but rather indicate the level of depressive symptoms. The 36-item Short-Form Health Survey (SF-36), a widely recognized generic questionnaire, assessed participants' health-related quality of life (QoL) by examining eight dimensions.

Statistical analyses were performed using SPSS software, including one-way analysis of variance for continuous variables, followed by post-hoc tests to assess differences among groups. Chi-squared or Fisher's exact tests were used for categorical variables. The significance level was set at 0.05.

Demographic and clinical characteristics of the 279 patients and 100 healthy controls were similar with no significant differences observed in terms of sex or age among the three groups. The study found that the NERD group exhibited a higher prevalence of anxiety compared to the RE group, as indicated by the ZSAS scores. Additionally, the NERD group showed more severe anxiety than the RE group, despite the absence of esophageal erosions. The study also identified a higher incidence of depression in patients with NERD compared to those with RE.

Furthermore, the research revealed that all dimensions of QoL in both NERD and RE patients were significantly lower than those of healthy controls, indicating an inferior QoL in GERD patients. Anxiety, as measured by the ZSAS, was negatively correlated with QoL, particularly affecting general health and mental health in patients with NERD. Similarly, depressive symptoms, assessed by the ZSDS, also negatively correlated with QoL, impacting vitality, mental health, and social functioning in both NERD and RE patients.

In conclusion, this study shed light on the association between GERD and psychological factors such as anxiety and depression. Patients with NERD experienced higher levels of anxiety and depression, leading to a reduced quality of life compared to healthy controls. These findings underscore the importance of considering the psychological well-being of GERD patients and addressing these factors in their clinical management.

4. Discussion

Both studies, the retrospective cross-sectional research conducted by Ji Min Choi and the prospective study conducted by Xiao-Jun Yang, call attention to the association between psychological factors, such as anxiety and depression, and Gastroesophageal Reflux Disease in different populations, especially in the NERD subgroup. In

addition, both articles emphasize the need for a comprehensive understanding of the psychological aspects involved in the clinical manifestations of GERD.

The varying proportions of elements within the three categories hinted at a noticeable level of distress in individuals with Non-Erosive Reflux Disease (NERD) and Reflux Esophagitis (RE). This indicates a significant involvement of anxiety and depression in the pathogenesis of Gastroesophageal Reflux Disease (GERD). Based on those studies, we've come to know that the impact of stress persists irrespective of whether esophageal inflammation was detected during endoscopy.

Numerous complications have been associated with GERD, including erosive esophagitis, stricture, and Barrett's esophagus (a change in the cells of the esophagus due to acid reflux) (4). The presence of an abnormal waist-to-hip ratio is one of the biggest risk factors for the presence of BE, as well as psychological factors (5). Moreover, the mental influence can aggravate those complications, making early treatment of stress and anxiety important to decrease the number of sequelae.

Our belief, prior to the making of this paper, was the same as shown in the results. However, patients with anxiety but no depression are more at risk of developing these diseases than the ones with depression but no anxiety. In that sense, the treatment for gastrointestinal diseases undeniably must include a psychological approach to them. The American Journal of Gastroenterology (6), in its 2022 GERD guideline, doesn't even mention the word "psychological" throughout the whole document, which comprises 30 pages. So, a new way to consider our patients, not solely by the biological aspect of the disease, can be crucial to promoting health and wellness.

The reviewed studies collectively provide valuable insights into the relationship between GERD and stress/anxiety. However, there are some limitations to consider. Many studies rely on self-reported measures of stress and anxiety, which may introduce response bias. Additionally, it is extremely difficult to compare studies since different questionnaires may result in differences in what is considered an anxious or depressed person. Furthermore, confounding variables such as diet and lifestyle factors are often not fully controlled for, making it challenging to establish causality.

In the research conducted by Ji Min Choi, they clearly outlined all the different factors that played a role in the development of GERD. It shows how many individuals claiming to be anxious also engage in behaviors like drinking, smoking, having a high BMI, and other factors known to affect the development of GERD.

On the other hand, it is possible to highlight the large sample size and the inclusion of different studies, including both prospective and retrospective ones, as strong strengths that enhance the validity of the results and the research paper overall. This large sample size improves the statistical precision of results and allows for better control of confounding variables, all of which contribute to the credibility of our findings.

Considering future research directions, longitudinal studies can establish causality and offer a deeper understanding of the temporal relationship between GERD and stress/anxiety. Interventional studies are needed to evaluate the effectiveness of psychological interventions in mitigating GERD symptoms and enhancing patients' quality of life.

Understanding the relationship between GERD and stress/anxiety has significant implications for clinical practice. Healthcare providers should consider psychological factors when diagnosing and managing GERD in adults. Screening for stress and anxiety in GERD patients may help identify those who require additional support or interventions, such as stress management techniques or cognitive-behavioral therapy.

Furthermore, recognizing the bidirectional nature of this relationship is crucial. Not only can stress and anxiety exacerbate GERD symptoms, but the discomfort and disruption caused by GERD can also contribute to psychological distress. Therefore, a holistic approach to patient care, addressing both physical and psychological aspects, is warranted.

5. Conclusion

This research has examined the relationship between the influence of anxiety and stress on the development of Gastroesophangeal Reflux Disease (GERD). Through a detailed literary review of the retrospective and prospective research of Ji Min Choi and Xiao-Jun Yang, respectively, it is possible to conslude a positive correlation between the levels of stress and the probability of developing GERD

The review identified strengths and limitations in existing research, emphasizing the need for a greater consideration of confounding variables due to the imprecision of measuring anxiety. Importantly, recognizing the interplay between GERD and stress/anxiety has substantial implications for clinical practice, underscoring the importance of holistic patient care.

In conclusion, this paper calls for continued

research efforts to elucidate the complex relationship between GERD and stress/anxiety, with the ultimate goal of improving the management and quality of life for affected individuals.

6. Acknowledgement

7. References

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