



CODEN [USA]: IAJPBB

ISSN : 2349-7750

INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

<https://zenodo.org/records/10478950>Available online at: <http://www.iajps.com>

Review Article

PREVALENCE OF GLOBUS SYNDROME AND ASSOCIATED FACTORS: A PROTOCOL FOR SYSTEMATIC REVIEW

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Abstract:

Background: The feeling of globus refers to a consistent or sporadic non-painful perception of a mass or foreign object in the pharynx. The aforementioned clinical disease is often observed in medical practice, characterized by its chronic nature, resistance to treatment, and propensity for recurrence.

Methods: A comprehensive search was conducted using electronic databases, including PubMed, Embase, and Cochrane Library, to identify relevant studies published from 2000 to 2022. The search was limited to English-language studies that examined the prevalence of globus syndrome and other associated factors.

Results: The initial search identified a total of 3052 studies and 59 studies were eligible for inclusion in this systematic review. The elusive origin of globus makes the establishment of standardized inquiry and treatment approaches challenging for individuals experiencing this condition. In order to effectively manage globus, it is essential to engage in meticulous history collection and do nasolaryngoscopy as a first measure. Considering the non-malignant characteristics of the ailment and the contemporary understanding that gastroesophageal reflux disease (GERD) plays a significant role in the development of globus sensation, it is justifiable to pursue empirical treatment including the administration of proton pump inhibitors at a substantial dosage for individuals exhibiting typical globus symptoms. In cases when patients exhibit a lack of response to the treatment, it is advisable to consider doing definitive tests, including endoscopy, multichannel intraluminal impedance/pH monitoring, and manometry. In cases when patients continue to have symptoms after negative examinations, the implementation of speech and language therapy, administration of anti-depressants, and use of cognitive-behavioral therapy have shown potential efficacy.

Conclusion: Globus syndrome is widespread. Research has identified this condition's causes and triggers. Reflux acid may produce globus. Upper esophageal sphincter and motor dysfunction. A full diagnosis is needed since globus syndrome is connected to pharyngeal inflammatory illnesses, upper aerodigestive tract malignancy, tongue base hypertrophy, retroverted epiglottis, thyroid disorders, cervical heterotopic gastric mucosa, and uncommon malignancies. An unknown link exists between mental health and globus, however stress may increase symptoms. Globus evaluation and treatment must involve physical and psychological factors. Many psychological and physical causes induce globus syndrome. Understanding these factors may help clinicians treat this discomfort. This sickness requires further investigation and therapy.

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Please cite this article in press Hanan I Almuzaini et al, . **Prevalence of globus syndrome and associated factors: a protocol for systematic review.**, *Indo Am. J. P. Sci*, 2023; 10 (11).

BACKGROUND:

A well-defined clinical symptom, globus is the non-painful feeling of a lump or foreign body in the throat that may stay for days or weeks at a time and can come back again and again. This symptom often gets better after eating, and it seldom occurs with dysphagia or odynophagia [1]. Up to 46% of otherwise healthy people report having this issue, and its prevalence increases with age (peaking in middle age) [2,3]. This ailment contributes for around 4% of new referrals to ear, nose, and throat (ENT) clinics. Men and women have similar rates of this disease, however women are more likely to seek medical attention when experiencing this symptom [4].

About 2500 years ago, Hippocrates was the first to identify globus pharyngeus [5]. Purcell [6] was the first to provide a detailed description of globus in 1707. He hypothesized that the ailment was caused when the strap muscles in the neck contracted, placing pressure on the thyroid cartilage. Historically, globus has been called "globus hystericus" due to its connection to the menopause and other psychogenic causes. The more correct word "globus pharyngeus" was first used by Malcomson [7] in 1968 when he realized that most individuals suffering globus did not have a hysterical personality. Although its cause is uncertain, globus likely has several contributors. Although evidence is scant, current research has pinpointed psychological and behavioral illnesses, stress, and gastroesophageal reflux disease (GERD) as key contributors to the globus impression. It has been challenging to create standard examination and treatment techniques for afflicted people due to the wide range of possible causes.

Globus syndrome, characterized by the sensation of a persistent lump or foreign body in the throat without an identifiable physical cause, is a common complaint in clinical practice. While it is often considered benign, the exact prevalence and associated factors remain poorly understood. This systematic review aims to synthesize existing literature to determine the

prevalence of Globus syndrome and identify potential associated factors.

METHODS:**Objective**

The primary objectives of this systematic review are as follows:

- To determine the prevalence of Globus syndrome in various populations.
- To identify and describe factors associated with the development of Globus syndrome.

Study Design

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Eligibility Criteria**Types of Studies****Inclusion Criteria:**

- Observational studies (cross-sectional, case-control, cohort studies)
- Interventional studies (clinical trials)
- Case series and case reports

Exclusion Criteria:

- Review articles
- Conference abstracts
- Studies not published in English

Types of Participants**Inclusion Criteria:**

Individuals of any age and gender who have been diagnosed with or reported symptoms of Globus syndrome.

Types of Interventions/Exposure**Inclusion Criteria:**

- Studies reporting the prevalence of Globus syndrome.

- Studies reporting factors potentially associated with the development of Globus syndrome.

Types of Outcome Measures

Primary Outcome:

Prevalence of Globus syndrome in the selected populations.

Secondary Outcomes:

Factors associated with the development of Globus syndrome, including demographic, clinical, psychological, and environmental factors.

Search Strategy

Information Sources

Electronic databases were systematically searched, including but not limited to:

- PubMed/MEDLINE
- EMBASE
- Web of Science
- Scopus

Additional sources:

- Google Scholar
- Hand searching of reference lists of relevant studies

Search Terms

The search strategy included both medical subject headings (MeSH) terms and keywords related to Globus syndrome and associated factors. Search terms may include "Globus hystericus," "Globus sensation,"

and "Globus pharyngeus." The Boolean operators (AND, OR) were used to combine search terms appropriately.

Study Selection

Two independent reviewers screened titles and abstracts of retrieved articles, followed by full-text assessment for eligibility. Discrepancies were resolved through consensus or consultation with a third reviewer.

Data Extraction

Data was extracted from eligible studies using a standardized data extraction form. The data to be collected included study characteristics, participant demographics, prevalence data, and associated factors. Any missing or unclear data was sought from the study authors.

Data Synthesis and Analysis

The extracted data was summarized and synthesized using appropriate statistical and narrative techniques. Meta-analysis would be conducted if feasible and appropriate, with subgroup analyses performed if relevant.

RESULTS:

The initial search identified a total of 3052 studies from PubMed, Embase, Cochrane Library, and CINAHL. After removing duplicates, 1,923 studies were screened based on their titles and abstracts. Of these, 127 full-text articles were reviewed, and 59 studies were eligible for inclusion in this systematic review (Figure 1).

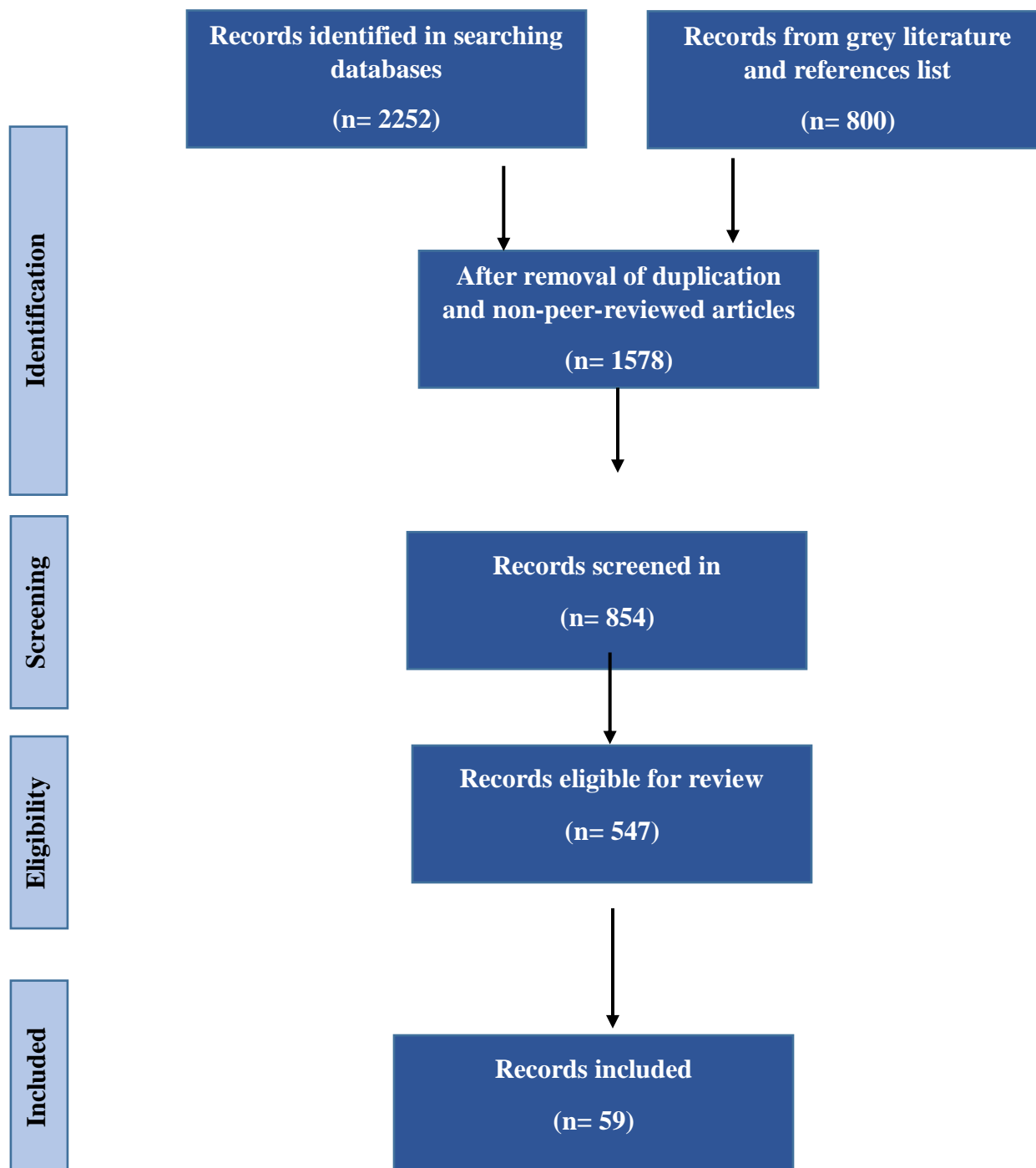


Figure 1: Flow chart of selection process

Prevalence of globus syndrome

Globus is a pretty frequent symptom. A population survey in the United States found that 12.5% of healthy individuals have globus [8]. According to a previous research conducted in the United Kingdom [9], up to 46% of the general public has experienced globus feeling at least once throughout their lives. According to these two surveys, the ratio of females to men is around 2:1. It is estimated that 4% of all new patients examined in ear, nose, and throat clinics have globus [10-11]. Male gender, smoking, and self-perceived breathing problems were predictive of persistent symptoms [11], whereas female gender and intensity of symptoms were the only characteristics shown to be connected with individuals who saw their physicians with globus [12]. According to a case series from a psychosomatic clinic [13], most patients come in the middle stages of life, with a median age of 43 years (range 22-71 years).

Associated factors

Gastroesophageal reflux disease

Though the exact cause of GERD in globus patients is still up for dispute, gastroesophageal reflux (GER) has been proposed as a primary etiology of this symptom, perhaps accounting for 23%-68% of globus patients [10-18].

With the use of a barium swallow, Malcomson [7] was the first to establish a connection between GERD and the globus feeling. Further, Cherry et al. [19] showed

that 10 out of 12 people complained of globus when acid was pumped into the distal esophagus, while Koufman [16] discovered that 58% of patients with globus had incorrect pH findings. Twenty-four hour double-probe pH monitoring revealed pathologic reflux in 72% of patients with globus and hoarseness [20], and GERD patients had a greater globus symptom score compared to healthy controls [21]. After 8 weeks of treatment with a proton pump inhibitor (PPI), globus sensation also enhanced [22]. Several population-based studies have shown a higher incidence of globus among individuals with GERD symptoms [23-25], lending credence to the hypothesis that the two are linked. Non-erosive reflux disease patients were more likely to have the globus symptom than erosive reflux disease patients were in a research [26]. Also, contradictory reports exist [4,27-31]. Many people with globus, however, also suffer from GERD, demonstrating a real link between the two conditions. Direct irritation and inflammation of the laryngopharynx by retrograde flow of gastric contents, also known as laryngopharyngeal reflux (LPR) [15,16,34], and (2) Vagovagal reflex hypertonicity of

the UES triggered by acidification or distention of the distal esophagus [18] have been proposed to explain the association between GERD and the globus sensation [14,32,33].

Abnormal upper esophageal sphincter function

Abnormal UES function has also been hypothesized to be a cause of globus sensation [20,35-38]. Patients reporting a globus feeling are more likely to have hypertension UES than controls (28 percent vs 3 percent) [30], indicating that hypertensive UES is a risk factor for globus. Botulinum toxin injected into the cricopharyngeal muscle of a patient with globus and very high UES pressure reduced the patient's UES pressure and eliminated the globus symptom [35]. Hyperdynamic respiratory UES pressure fluctuations were more common in patients reporting globus in a study of high-resolution manometry in patients with globus feeling, normal controls, and GERD patients without globus [38]. Other research, however, have shown the opposite [39-41].

Esophageal motor disorders

Patients with globus are twice as likely to have esophageal motor abnormalities as the general population, and the incidence of esophageal motor disorders in this population ranges from 6 percent to 100 percent [27,28,31,42]. As much as 67% of globus patients have abnormalities on esophageal manometry, with nonspecific esophageal motility problem being the most common result [31]. According to research [43], the globus feeling may be experienced by patients with esophageal motor abnormalities before the onset of dysphagia. However, proving that the feeling improves after the motor disease is treated is necessary before any etiological importance can be inferred from the abnormality in globus.

Pharyngeal inflammatory causes

Pharyngitis, tonsillitis, and chronic sinusitis with postnasal drip are only few of the disorders that may irritate and inflame the pharynx, leading to heightened local sensitivity and the resulting globus feeling [28,44].

Upper erodigestive tract malignancy

Patients with globus feeling who also present with "high risk" symptoms such weight loss, dysphagia, throat discomfort, and lateralization of pathology should be evaluated for pharyngolaryngeal or upper esophageal cancer [5,45].

Hypertrophy of the tongue base

Extreme enlargement of the base of the tongue, likely caused by the follicles' contact with the posterior wall of the throat, may cause globus. In a study [46], researchers found that individuals who had symptoms of GER were more likely to have hypertrophied follicles near the base of their tongue.

Retroverted epiglottis

Retroverted epiglottis may generate globus feeling by making contact with the base of the tongue or the posterior pharyngeal wall. Partial epiglottectomy has been shown to be effective in relieving symptoms [47,48].

Thyroid diseases

Patients with globus feeling are more likely to have ultrasound-detectable abnormalities in the thyroid than controls [32]. According to research [49], up to a third of people who have a thyroid mass also have globus-like symptoms. Some people have globus pattern symptoms after a thyroidectomy, however this is usually temporary. While the specific mechanism linking globus to thyroid disorders is unclear, some research suggests that a thyroidectomy may alleviate globus symptoms [49–51].

Cervical heterotopic gastric mucosa

Acid production from CHGM seems to generate symptoms comparable to those of GERD, including globus feeling, which has been associated to the existence of cervical heterotopic gastric mucosa (CHGM) [52-54]. After undergoing argon plasma ablation for CHGM, patients who had previously complained of a globus feeling and/or sore throat no longer had these symptoms [55,56]. Infection with *Helicobacter pylori* of the CHGM has recently been linked to the globus symptom [57].

Rare tumors

Patients with globus have been documented to have Merkel cell carcinoma with oropharyngeal metastases, post cricoid lymphangioma, and pharyngeal smooth muscle tumors [58, 60]. These reports show the need of doing further tests on individuals with persistent globus in order to rule out uncommon lesions [32].

Psychological factors and stress

Psychogenic disorders have frequently been suggested to induce or initiate the globus impression. Patients presenting with globus have been reported to have lower levels of extraversion and greater levels of alexithymia, neuroticism, and psychological discomfort (including worry, poor mood, and somatic problems) [61,62]. Also, life stress may have a role in both the origin and the aggravation of symptoms, since

multiple studies have shown an increase in the frequency of stressful life events before symptom start. As many as 96% of people with globus say their symptoms worsen at times of intense emotion [63,64]. However, several studies have revealed no significant abnormalities in globus patients' mental health when compared to healthy controls [4,10,65]. The etiological importance of these psychological traits is unclear [1,65], despite the fact that psychiatric diagnoses are common among those seeking medical attention for globus. However, an explanation other from ascertainment bias has not been proven. Recent research has shown that people with globus who are LPR positive and those who are LPR negative may have distinct mental health outcomes [15,66]. The psychiatric symptoms of globus patients with LPR were less severe than those of non-LPR globus patients [15], while the anxiety ratings of globus patients who did not react to PPI were considerably greater [66].

DISCUSSION:

In this study, we systematically reviewed literature related to globus syndrome which is characterized as a subjective perception of a lump, a retained food bolus, or a sensation of tightness in the throat that occurs in the inter-meal period. This sensation is seen in the absence of dysphagia or odynophagia, pathological reflux, achalasia, or any other motility disorder with a documented pathological etiology. The etymology of the term "globus" remains uncertain now. Idiopathic globus is a medical disorder characterized by the presence of globus without a discernible underlying physiological cause, such as cricopharyngeal spasm, pharyngeal dysmotility, or gastroesophageal reflux (GER) [2].

This implies that idiopathic globus may manifest in individuals who have a previous record of globus sensation, however lack a discernible etiological basis. The aforementioned grievance is prevalent among individuals seeking medical care for ear, nose, and throat conditions, with an estimated occurrence rate that might potentially exceed 5% [3, 4, 5]. However, clinical gastroenterology encounters a very small proportion, namely less than 10%, of patients presenting with solitary globus feelings.

The feeling known as globus pharynges, also referred to as the globus sensation, is frequently linked to mental health difficulties [6, 7, 8]. Although globus is not often seen among psychiatric outpatients, it is regarded as a kind of conversion disorder or a depressive, somatoform personality disorder [9]. This phenomenon persists despite the absence of globus in

individuals without any underlying medical conditions. Nevertheless, there exists a contentious discourse around the psychological findings. There is a suggestion in the literature that persons who have been diagnosed with Globus may be more susceptible to developing somatization disorder, severe depression, generalized anxiety disorder, post-traumatic stress disorder, and drug use or dependency [12]. However, it is important to note that other studies have shown no significant elevation in these conditions [10], [11].

CONCLUSION:

The prevalence of globus syndrome is relatively common, affecting a significant portion of the population. Various studies have provided insights into the factors associated with this condition, shedding light on its potential causes and triggers. Gastroesophageal reflux disease (GERD) appears to be a major contributor to globus sensation, with evidence linking acid reflux to the development and exacerbation of this symptom. Abnormal upper esophageal sphincter function and esophageal motor disorders also play a role in some cases. Other factors such as pharyngeal inflammatory conditions, upper aerodigestive tract malignancy, hypertrophy of the tongue base, retroverted epiglottis, thyroid diseases, cervical heterotopic gastric mucosa, and even rare tumors have been associated with globus syndrome, highlighting the importance of a comprehensive evaluation when persistent symptoms are present. Psychological factors and stress may exacerbate globus symptoms in some individuals, but the exact relationship between mental health and this condition remains complex and not fully understood. It is important to consider the interplay between physical and psychological factors in the assessment and management of globus patients. The etiology of globus syndrome is multifactorial, involving a combination of physical and psychological elements. Understanding these factors can guide clinicians in providing appropriate care and treatment for individuals experiencing this distressing sensation. Further research is needed to gain a deeper understanding of the condition and to refine its diagnosis and management.

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