

**ROLE OF FLEXIBLE UGIE & RAPID UREASE TEST IN GLOBUS PHARYNGEUS**Meenakshi Kekre<sup>1</sup>, Jyoti Ranjan Das<sup>2</sup>, Abhiraj Tiwari<sup>2</sup>, Smriti Saxena<sup>3</sup><sup>1</sup>Professor & HOD, <sup>2</sup>Assistant Professor, <sup>3</sup>Senior Resident, Department of Otorhinolaryngology & Head and Neck Surgery.*Corresponding Author: Meenakshi Kekre, Email ID: [dolmeena@yahoo.com](mailto:dolmeena@yahoo.com)***Abstract:**

*Globus refers to the painless perception of a lump or foreign object in the throat. It is persistent or intermittent. The etiology is uncertain. Establishing standard investigation and treatment strategies for affected patients continues to pose a challenge. For managing the globus, careful history taking and complete nasal, larynx, and pharynx examination are essential. The investigation involves cervical spine x-ray, thyroid profile, upper G I endoscope, X-ray nose pns for sinusitis. Among the various causes, gastroesophageal reflux disease is a major cause with a proton pump inhibitor as treatment. If individuals do not respond to this treatment, conclusive evaluations, such as endoscopy to examine gastritis, duodenitis, esophagitis,, and a urease test for H. pylori, should be considered. Pylori should be considered. We conducted UGIE in 30 patients after ruling out other causes and in 23 patients (76.66 %) showed digestive tract inflammation. Rapid Urease test was found to be positive in 16 patients (65.21%).*

**Keywords:** *Globus, Gastroesophageal reflux disease, Upper G I Endoscopy, H pylori, Rapid urease test.*

**INTRODUCTION:**

Globus Pharyngeus, constituting approximately 5% of all new ENT referrals, is a common disorder with an uncertain origin. Patients often report a sensation of a foreign object or tightness in the throat, and there is a slight predominance among females. The term "globus hystericus" was coined by Purcell in 1707, with "globus" derived from the Latin word for "ball" and "hystericus" suggesting a presumed psychological element to the disorder.

The Oxford English Dictionary formally defined it in 1794 as "a choking sensation, resembling a lump in the throat, experienced by hysterical individuals." Traditionally, individuals presenting with symptoms of globus were directed to psychiatric evaluation.

In 1968, the disorder underwent a renaming and became known as globus pharyngeus. Recently, globus pharyngeus has been defined as (i) the persistent or intermittent sensation of a lump or foreign body in the throat lasting at least 12 weeks, (ii) the occurrence of this sensation between meals, (iii) the absence of dysphagia and odynophagia, and (iv) the absence of pathological conditions such as gastroesophageal reflux (GERD), achalasia, or other motility disorders with recognized pathological bases (e.g., scleroderma of the esophagus).

Due to the uncertain etiology of globus, the initial approach involves careful history-taking and naso-laryngo-pharyngoscopy. Empirical therapy, involving a high dose of proton pump inhibitors and antacid syrup, is prescribed. In cases where patients do not respond to this therapy, further assessments such as multichannel intraluminal impedance/pH monitoring, manometry, and endoscopy should be considered.

Upper gastrointestinal endoscopy (UGIE) comes in two types: flexible and rigid. Flexible endoscopy, conducted as a daycare invasive procedure under topical anesthesia, commonly reveals inflammation of the digestive tract, such as gastritis, duodenitis, or esophagitis. *Helicobacter pylori* (*H. pylori*) is identified as a common cause for these findings. *H. pylori* is a prevalent chronic infection worldwide, affecting approximately 50% of the population, with the majority being asymptomatic.

*H. pylori* induces an inflammatory response in the mucosal layer, characterized by neutrophils, lymphocytes, plasma cells, and macrophages, leading to epithelial cell degeneration and injury. Gastritis is typically more severe in the antrum. All patients diagnosed with gastritis, duodenitis, or esophagitis should undergo testing for *H. pylori*, which can be done through invasive and noninvasive methods.

Among noninvasive methods, the urea breath test and stool antigen tests are considered more feasible and accurate than serologic testing. Despite being invasive, endoscopy allows for biopsy and offers various testing methods such as histology, culture, or rapid urease tests. While numerous studies exist on the etiology of globus pharyngeus, there is a limited body of research on the value of endoscopy and rapid urease tests for *H. pylori* in this patient group.

To address this gap, we initiated a prospective study with two objectives: 1. to assess the role of flexible Upper G I endoscopy in patients with globus pharyngeus to identify various causes and 2.

To show the importance of urease test in case of digestive tract inflammation in this group is found.

## **MATERIALS AND METHODS-**

The study was conducted in our institution for a period of 1 year. It was an opd based prospective, observational study. Total 30 patients in age group above 18 yrs. with only complaint of foreign body sensation in throat for 6 months or more were evaluated. Exclusion criteria were (1) age <18 years and (2) patients with typical symptoms like difficulty in swallowing, regurgitation of food, burning sensation over throat, abdominal fullness (3) already investigated with a previous UGIE or RUT.

Detail history was taken. Complete nose, oral cavity, oropharynx examination with all the required investigations were done. Blood test like complete blood count, sugar, thyroid profile, X ray cervical spine, X ray soft tissue neck, X ray nose PNS, diagnostic nasal endoscopy were also done. As for all patient's examination findings and reports were normal, flexible UGIE was planned.

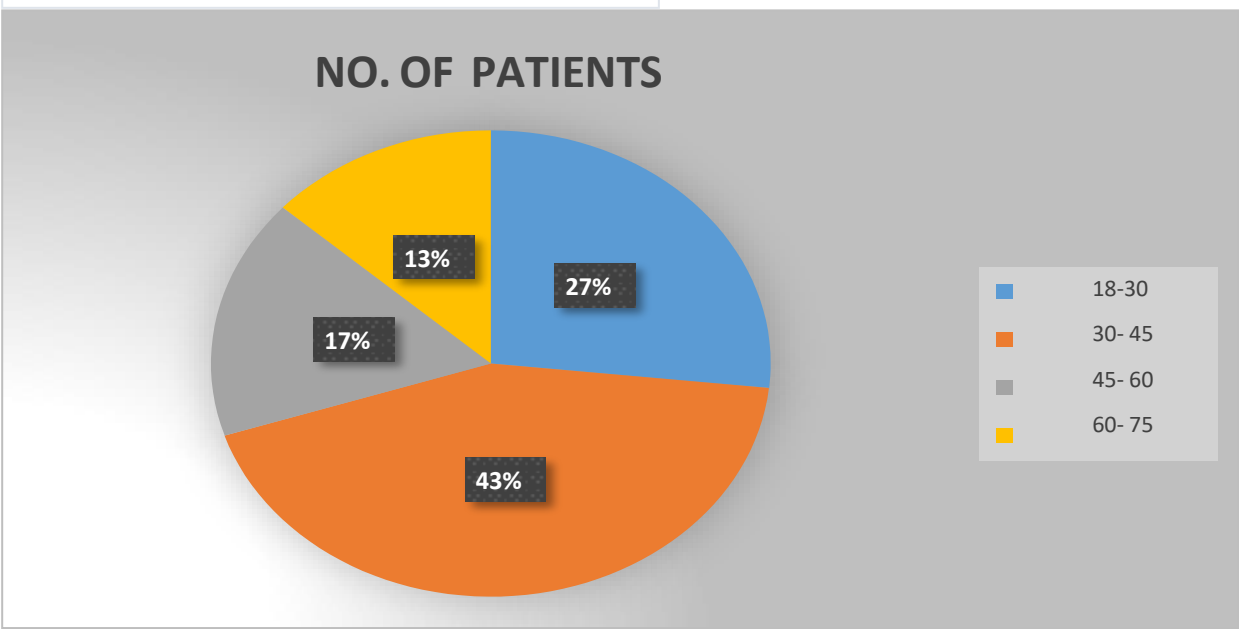
Patients were advised to come to opd with empty stomach on the day of UGIE. Proper consent was taken.

After topical application of lignocaine spray over throat and patient in left lateral position with a mouth gag, flexible endoscopy was done and findings were noted. Patients with findings like gastritis, gastroduodenitis, esophagitis were also undergone Urease test to obtain H. Pylori after taking samples from the inflammatory area.

## **RESULT:**

TABLE 1-Age Distribution

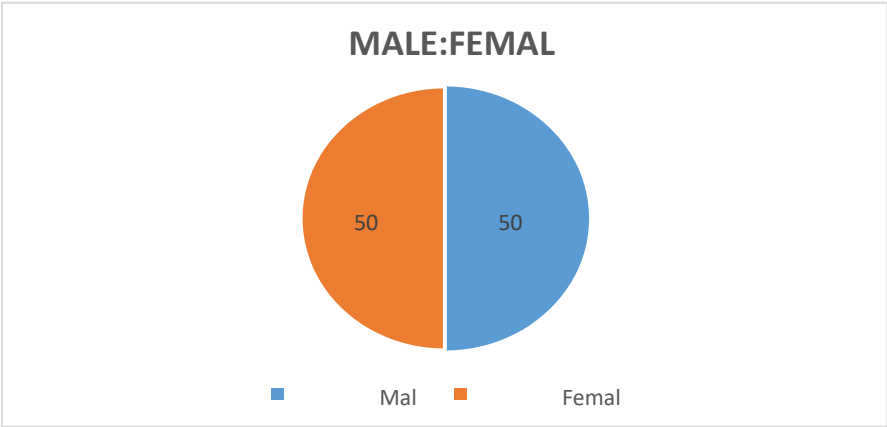
AGE (yrs.)	No. of patients
18-30	08
30- 45	13
45- 60	05
60- 75	04
Total	30



Out of 30 patients 15 were male and 15 were female.

TABLE 2-Sex Distribution

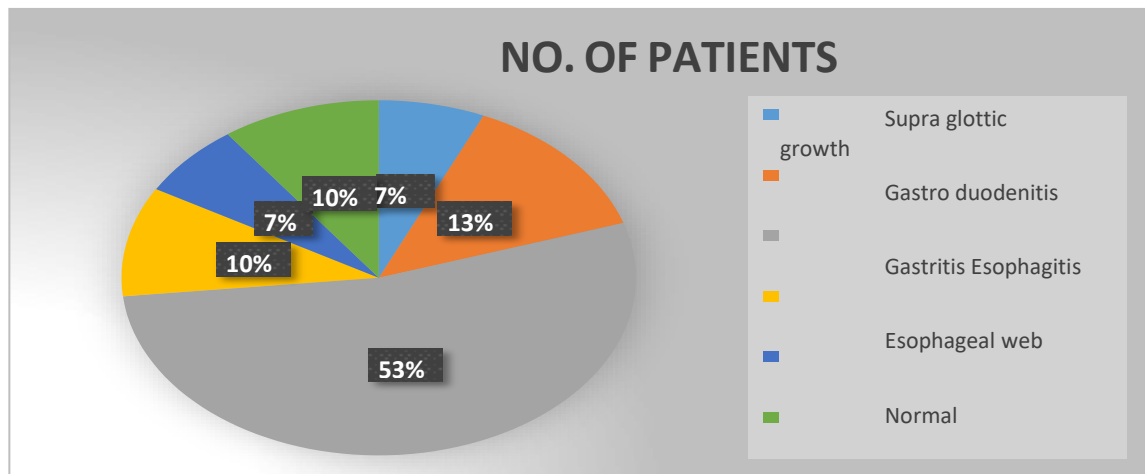
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Supraglottic growth were seen in 2 patients (6.66%). Biopsy was taken which showed squamous cell carcinoma. Endoscopy showed gastro-duodenitis in 4 patients (13.33%). It was normal in 3 patients (10 %). 16 patients (53.33%) were having antritis.3 patients (10%) showed esophagitis. Esophageal varices were found in 2 patients (6.66%).

TABLE 3

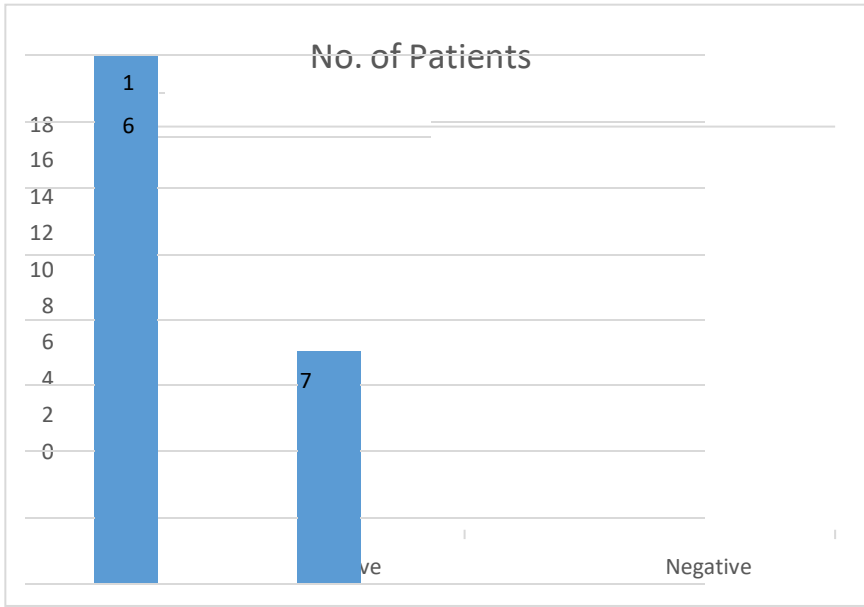
UGIE FINDINGS	NO. OF PATIENTS
Supra glottic growth	02
Gastro duodenitis	04
Gastritis	16
Esophagitis	03
Esophageal web	02
Normal	03
Total	30



So we had total 23 patients (76%) with findings of gastritis, gastro-duodenitis and esophagitis. Samples were taken from the inflammatory areas like gastric antrum, duodenum 1st part, lower end of esophagus and rapid urease card test was done. Out of 23, 16 patients (69.56%) were found to be urease positive.

Table 4

RUT RESULT	No. of Patients
Positive	16
Negative	07
Total	23



**DISCUSSION:**

Globus pharyngeus or globus sensation is the painless sensation of a lump in the throat and maybe described as a foreign body sensation, a tightening or choking feeling. It is often associated with persistent clearing of the throat, chronic cough, hoarseness, and catarrh.<sup>7</sup> Globus pharyngeus makes up 4% of ear, nose, and throat (ENT) referrals and is reported to have been experienced by up to 45% of the population.<sup>7</sup>

The aetiology of globus pharyngeus include cricopharyngeal spasm, lingual tonsil, cervical osteophytosis, hiatus hernia, gastro-oesophageal reflux, sinusitis, post-nasal drip, goitre, foreign body, anxiety, and, very rarely, hypopharyngeal cancer. The regurgitation of stomach acid and digestive enzymes induces chronic inflammation of the laryngopharynx resulting in symptoms. Studies have reported reflux in 23–68% of patients with globus sensation. However, some report a similar rate in asymptomatic control patients.<sup>7</sup>

It is thought that gastro-oesophageal reflux is likely to be the cause in a subgroup of patients but cannot explain all cases.<sup>8</sup>

Oesophageal motility disorder is another aetiological factor. Studies suggest an association between upper oesophageal sphincter function and globus sensation, with one showing elevated sphincter pressure in 28% of patients with globus pharyngeus compared with 3% of controls.<sup>7</sup> Psychological factors may also play a role. There is increased reporting of stressful life events prior to development of symptoms and research suggests that as many as 96% of patients with globus sensation report an exacerbation of symptoms during times of emotional stress. All patients found to have gastritis, duodenitis, esophagitis should be tested for *H. pylori*. There are both invasive and noninvasive methods.

Of all the noninvasive methods, the urea breath test and stool antigen tests are the most feasible and are more accurate than serologic testing. Although invasive, endoscopy allows for biopsy and includes a variety of methods for testing such as histology, culture, or rapid urease test.

The rapid urease test (RUT) is a popular diagnostic test in that it is a rapid, cheap and simple test that detects the presence of urease in or on the gastric mucosa.

While there are a number of studies in the literature examining the exact etiology of this disorder, relatively few studies to date have addressed the value of endoscopy and rapid urease test for Pylori in this group.

It is for this reason that we initiated this prospective study, with the objectives 1. to evaluate the role of flexible Upper GI endoscopy in these globus pharyngeus patients to ascertain the various causes and 2. To show the importance of urease test in case of digestive tract inflammation in this group is found.

## **MATERIALS AND METHODS-**

The study was conducted in our institution for a period of 1 year. It was an opd based prospective, observational study. Total 30 patients in age group above 18 yrs. with only complaint of foreign body sensation in throat for 6 months or more were evaluated. Exclusion criteria were (1) age <18 years and (2) patients with typical symptoms like difficulty in swallowing, regurgitation of food, burning sensation over throat, abdominal fullness (3) already investigated with a previous UGIE or RUT.

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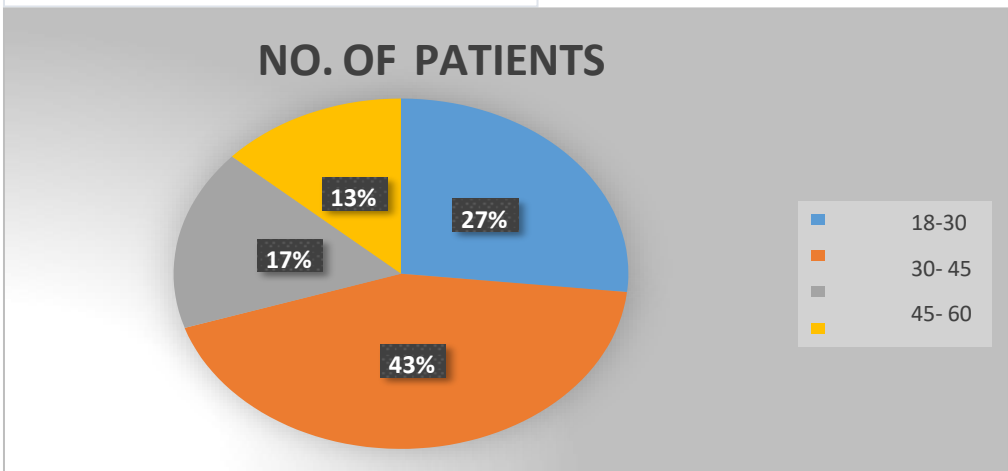
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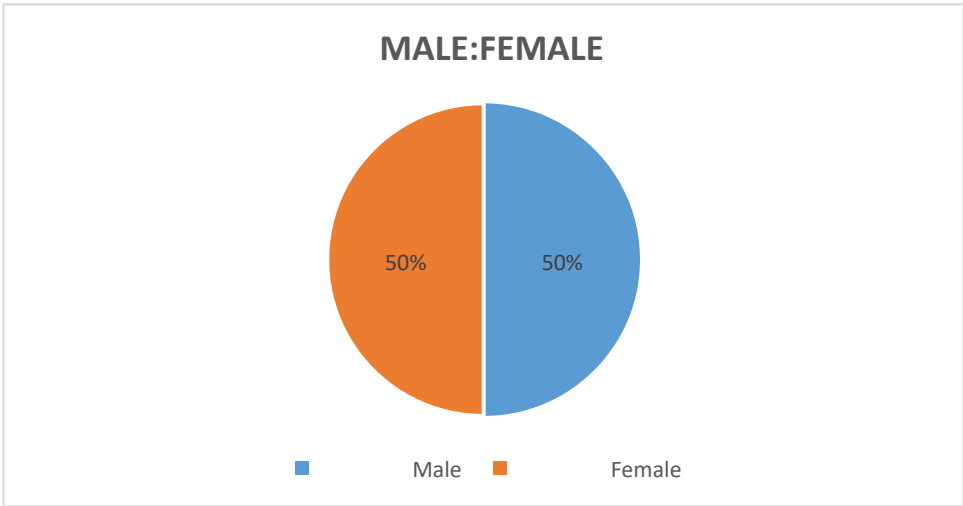




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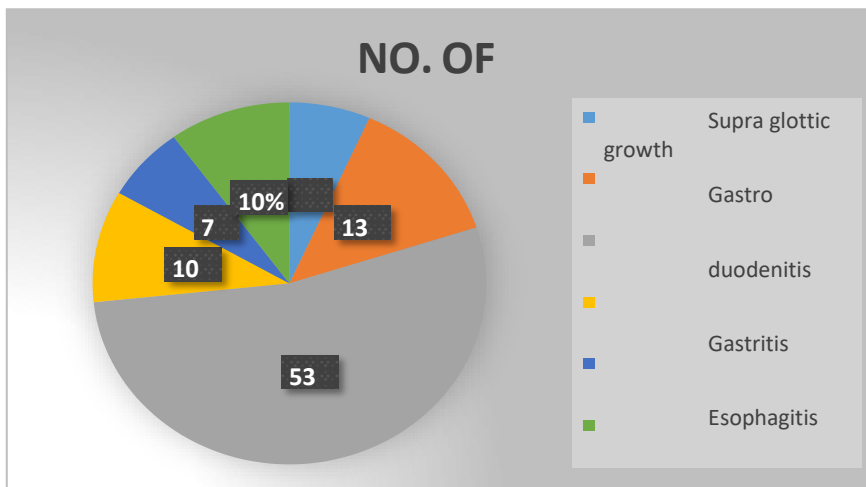
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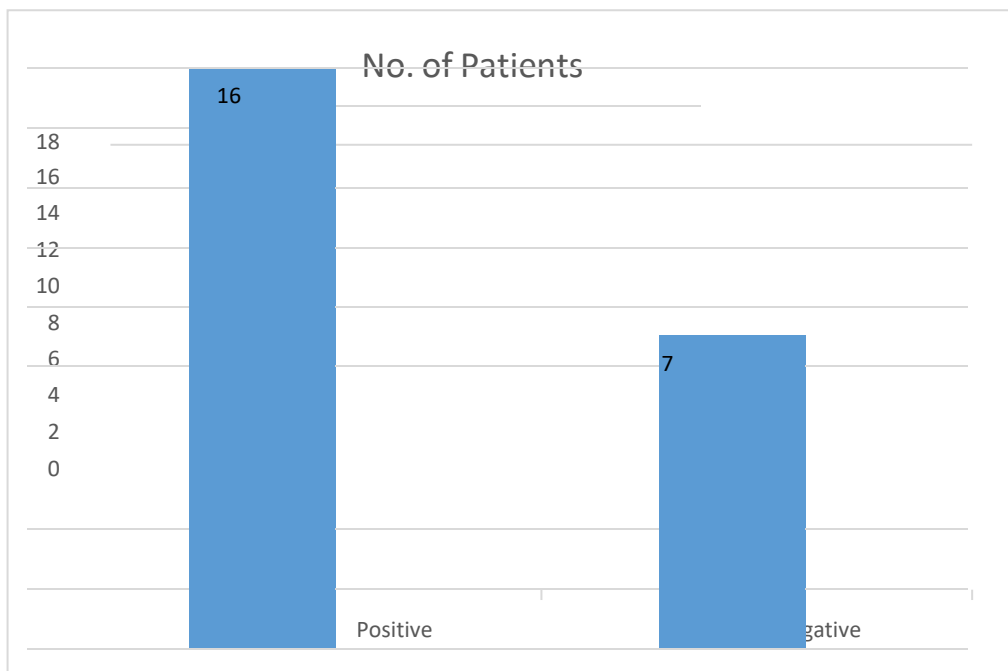
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**DISCUSSION-**

Globus pharyngeus, also known as globus sensation, refers to the painless perception of a lump in the throat and can be characterized as a feeling of a foreign object, tightness, or choking. It is commonly linked with frequent throat clearing, persistent cough, hoarseness, and catarrh. Globus pharyngeus accounts for 4% of referrals to ear, nose, and throat (ENT) specialists and is estimated to be encountered by as much as 45% of the population.<sup>7</sup>

The etiology of globus pharyngeus encompasses various factors, including cricopharyngeal spasm, lingual tonsil, cervical osteophytosis, hiatus hernia, gastro-oesophageal reflux, sinusitis, post-nasal drip, goitre, foreign body, anxiety, and, infrequently, hypopharyngeal cancer (Reference 1).

Chronic inflammation of the laryngopharynx, induced by the regurgitation of stomach acid and digestive enzymes, leads to the manifestation of symptoms. Studies have indicated reflux in 23–68% of individuals with globus sensation, with some reporting a comparable rate in asymptomatic control subjects <sup>[1]</sup>. While gastro-oesophageal reflux is considered a likely cause in a subset of patients, it does not account for all cases <sup>[1]</sup>. Additionally, oesophageal motility disorder has been identified as another contributing factor, with research showing an association between elevated upper oesophageal sphincter pressure and globus sensation in a significant proportion of patients <sup>[1]</sup>.

Psychological factors may also contribute to the development of globus pharyngeus, as evidenced by increased reports of stressful life events preceding symptom onset. Studies suggest that up to 96% of patients with globus sensation experience symptom exacerbation during periods of emotional intensity <sup>[9]</sup>. Diagnostic questionnaires for somatization, panic, and generalized anxiety disorders incorporate inquiries about globus pharyngeus symptoms <sup>[8]</sup>.

The diagnosis of globus pharyngeus relies on a comprehensive evaluation of the patient's history and examination findings. Patients commonly describe the presenting complaint as a lump or ball in the throat, throat swelling, or itching. Symptoms may be intermittent, but persistent or worsening conditions are more concerning <sup>[10]</sup>. The typical site of symptoms is central and suprasternal. Globus sensation is often noticed during swallowing, saliva ingestion, or eating and drinking, emphasizing the importance of assessing the relationship to food and swallowing. Pain on swallowing is not a typical feature of globus sensation. Inquiries about reflux symptoms, throat clearing, cough, hoarseness, anxiety, psychological distress, sleep quality, and lifestyle habits, including alcohol and tobacco use, are essential. Additionally, red flag symptoms associated with cancer, such as persistent hoarseness, progressive dysphagia, dysphagia for solids, pain on swallowing, haemoptysis, and unexplained weight loss, should be specifically addressed <sup>[11]</sup>.

During consultations, healthcare providers should consider the patient's ideas, concerns, and expectations, as many individuals presenting with globus sensation are apprehensive about the possibility of cancer <sup>[12]</sup>. In general practice, a thorough examination of the head and neck, including palpation of the neck to examine the thyroid gland and cervical lymph nodes, is crucial. The examination of the oropharynx and oral cavity should include an assessment for any signs of growth, ulceration, and postnasal drip. Additionally, the nose should be inspected for evidence of inflamed mucosa and polyps, which could be potential causes of globus pharyngeus. An abnormal neck or oral examination should lead to an immediate referral to secondary care <sup>[12]</sup>.

The majority of globus pharyngeus cases can be effectively managed in primary care with proton pump inhibitors (PPI) and antacids. If symptoms persist, further investigations such as pH monitoring, barium swallow, manometry, and upper gastrointestinal endoscopy (UGIE) are recommended. Upper GI endoscopy is considered the standard diagnostic test for esophagitis, gastritis, and duodenitis, providing information on the extent of involvement. Although upper GI endoscopy exhibits good specificity (90-95%), its sensitivity is relatively low <sup>[13]</sup>.

Early signs of acid reflux in endoscopy include erythema and edema, but these findings are nonspecific and depend on the quality of the endoscopic image <sup>[14]</sup>. Reliable endoscopic signs include friability (indicative of easy bleeding due to capillary enlargement in response to acid near the mucosal surface) and red streaks in the ridges of esophageal folds, extending upward from the esophageal junction <sup>[15]</sup>. Additionally, upper GI endoscopy can reveal any supraglottic growth, and if present, a biopsy can be performed simultaneously.

In cases of gastritis, esophagitis, or duodenitis, biopsies should be taken from the affected areas for the rapid urease test for *H. pylori*. Gastric urease, which produces ammonia from urea, plays a role in neutralizing acid and protecting the stomach, serving as a biomarker for *H. pylori* presence. Key clinical tests for *H. pylori*, such as the rapid urease test and urea breath test, are based on gastric urease activity. The choice of rapid urease test depends on factors such as availability, cost, and ease of use <sup>[16]</sup>.

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In regions where cost is a significant consideration, locally made tests may involve a solution containing 2 g of urea in 100 mL of 0.01 M sodium phosphate buffer, pH 6.5, with added phenol red and sodium azide. A positive rapid urease test requires approximately 10<sup>5</sup> H. pylori in the biopsy sample to produce a positive reaction with an agar-based test <sup>[17]</sup>. It is noteworthy that the organisms tend to concentrate on or near the surface of the specimen, and some investigators have used opened forceps to scrape gastric mucus, ensuring a high concentration of bacteria-rich material for the test <sup>[18]</sup>.

In general, the concentration of H. pylori is typically highest in the antrum. However, if a patient has recently taken proton pump inhibitors (PPIs), the concentration may be significantly reduced, leading to a potential false negative test result<sup>[19]</sup>. Another factor contributing to false negative tests, particularly in regions where atrophic gastritis is prevalent, is the presence of intestinal metaplasia, which often lacks H. pylori. It is recommended to obtain at least two large-cup biopsies from visually normal mucosa, one from the antrum and one from the corpus, while avoiding obvious areas of intestinal metaplasia. Subsequently, the two biopsies should be combined within the same test well <sup>[17,20]</sup>.

The sensitivity of various Rapid Urease Test (RUT) assays as primary diagnostic tests is generally high, ranging between approximately 80% and 100%, with a specificity ranging from 97% to 99% <sup>[17,21]</sup>.

Regarding the treatment of H. pylori infection, there are diverse regimens available. Su Young Kim and Jun-Won Chung have provided a comprehensive summary of these regimens in their paper <sup>[22]</sup>

Treatment	Regimen	Duration	Recent First-Line Eradication Rate (ITT)	Recommendations According to Guidelines
				recommended by MAA
Bismuth quadruple therapy (BQT)	PPI standard dose bid Bismuth standard dose qid Metronidazole 500 mg tid Tetracycline 500 mg qid	7–14 d	82.8% [107], 88.2% [44], 91.5% [108]	First-line: recommended by ACG, MAA, TOR, and KCHUGR (optionally) Rescue: recommended by ACG, MAA, TOR, and KCHUGR
Concomitant therapy (non-bismuth quadruple therapy)	PPI standard dose bid Clarithromycin 500 mg bid Amoxicillin 1g bid Metronidazole 500 mg bid	10–14 d	84.6% [106], 90.1% [109], 93.5% [110]	First-line: recommended by ACG, MAA, and TOR Rescue: recommended by ACG and MAA
Sequential therapy	PPI standard dose bid Amoxicillin 1g bid (first half only) Clarithromycin 500 mg bid (for the second half only) Metronidazole 500 mg bid	10–14 d	69.5% [106], 82.0% [111], 87.0% [112]	First-line: optionally recommended (not ideal) by ACG Rescue: not recommended in all guidelines

Treatment	Regimen	Duration	Recent First-Line Eradication Rate (ITT)	Recommendations According to Guidelines
	(for the second half only)			
Hybrid therapy	PPI standard dose bid Amoxicillin 1g bid Clarithromycin 500 mg bid (for the second half only) Metronidazole 500 mg bid (for the second half only)	14 d	85.8 % [75], 92.8% [113]	First-line: optionally recommended (not ideal) by ACG Rescue: not recommended in all guidelines
Levofloxacin-based therapy	Levofloxacin can be given as triple therapy or quadruple therapy.	10–14 d	85.5% [76], 94.0% [77]	First-line: recommended by ACG Rescue: recommended by ACG, MAA, and TOR
Rifabutin-based therapy	PPI standard dose bid Amoxicillin 1g bid Rifabutin 150 mg bid	10 d	83.8% [93]	First-line: not recommended in all guidelines Rescue: optionally recommended (third or fourth-line) by MAA and TOR



Treatment	Regimen	Duration	Recent First-Line Eradication Rate (ITT)	Recommendations According to Guidelines
Potassium-competitive acid blocker based therapy	P-CAB can be given as triple therapy or quadruple therapy by replacing PPI with P-CAB.	7–14 d	89.2% [104], 90.2% [114]	Not stated in algorithm of guidelines
<i>H. pylori</i> treatment based on antibacterial susceptibility test	Tailored therapy according to AST results	7–14 d	92.7% [31], 92.9% [115]	MAA recommends to perform AST after the failure of second-line treatment.

The results of tailored therapy based on AST are excellent, and it is expected to play a role in improving *H. pylori* treatment in the future. Efforts to facilitate the application of AST in clinical practice are required.

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ITT, which stands for intention to treat, is a commonly used term in clinical research. STT, or standard triple therapy, involves a specific treatment regimen. PPI, an acronym for proton pump inhibitor, is another key component in certain therapeutic approaches. The term KCHUGR refers to the Korean College of Helicobacter and Upper Gastrointestinal Research, while JSHR stands for the Japanese Society for Helicobacter Research. The MAA, or Maastricht V/Florence Consensus <sup>[10]</sup>, provides essential guidelines in the field. BQT denotes bismuth quadruple therapy, as recommended by the American College of Gastroenterology clinical guideline (ACG) <sup>[4]</sup>. The TOR, or Toronto Consensus <sup>[9]</sup>, is another significant reference in this context. CTT, or concomitant therapy, is a treatment approach that involves multiple agents simultaneously. P-CAB, or potassium-competitive acid blocker, is another therapeutic agent worth mentioning. The term AST pertains to antimicrobial susceptibility testing, an important aspect in determining appropriate treatment strategies.

In our study, 16 patients showed Urease test positive for H. Pylori. They were prescribed tab amoxycillin 1gm bd and clarithromycin 500 mg bd for 2 weeks along with PPI and antacid syrup. All patients were symptomatically improved after the complete course of medications.

#### **CONCLUSION:**

Globus pharyngeus can be diagnosed with proper history and examination. Routine treatment involves oral PPI and antacid syrup. There are various causes and for each cause particular investigation can be done like hemogram for anemia, thyroid profile test for hypo or hyperthyroidism, X ray nose pns for sinusitis, X ray cervical spine for prominent osteophytes, X ray soft tissue neck for prevertebral widening. If no cause is found, other investigations like pH monitoring, esophageal manometry, barium swallow, UGIE (rigid and flexible) can be advised. Among these, Flexible UGIE is opd based procedure, quick, cheap and biopsy can be taken from any growth or inflammatory areas in upper digestive tract. If gastritis, esophagitis or duodenitis is seen sample should be taken for rapid urease test.

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**AUTHORS CONTRIBUTORS:** All authors contributed to the study concept design and manuscript writing.

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IMAGE 1. ESOPHAGITIS



IMAGE 2. DUODENITIS



IMAGE 3. PROLIFERATIVE GROWTH OVER AE FOLD    IMAGE 4. GASTRITIS