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ROLE OF FLEXIBLE UGIE & RAPID UREASE TEST IN GLOBUS PHARYENGEUS

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Abstract:

Globus is non-painful sensation of a lump or foreign body in the throat. It is persistent or intermittent. The etiology is uncertain. it remains difficult to establish standard investigation and treatment strategies for affected patients. For managing globus, careful history taking and complete nasal, larynx, pharynx examination are essential. 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 patients are nonresponsive to this therapy, definitive assessments such as endoscopy for gastritis, duodenitis, esophagitis and urease test for H. Pylori should be considered. We conducted UGIE in30 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, Rapidurease test.*

INTRODUCTION:

Globus Pharyngeus is a common disorder of indeterminate origin and constitutes about 5% of all new ENT referrals [1]. Patients commonly describe the sensation of a foreign body or tightness in the throat, and the literature reports a slight female preponderance [2]. It was first described by Purcell in 1707 who coined the term globus hystericus, the word globus originating from the Latin meaning “ball” and “hystericus” reflecting the then assumed psychological component of the disorder [3].

It was defined in the Oxford English Dictionary in 1794 as “a choking sensation, as of a lump in the throat, to which hysterical persons are subject,” and traditionally patients presenting with globus symptomatology were referred to psychiatrists.

The disorder was renamed globus pharyngeus in 1968 [4]. Globus Pharyngeus has more recently been defined as (i) a persistent or intermittent sensation of a lump or foreign body in the throat for at least 12 weeks, (ii) occurrenceof the sensation between meals, (iii) absence of dysphagia and odynophagia, (iv) absence of pathological gastroesophageal reflux (GERD), achalasia, or other motility disorder with a recognized pathological basis (e.g., scleroderma of the oesophagus) [5].

Due to the uncertain etiology of globus, as a first step careful history taking and naso-laryngo-pharyngoscopy should be done. Empirical therapy with a high dose of proton pump inhibitors and antacid syrup are prescribed. If patients are nonresponsive to this therapy, definitive assessments such as multichannel intraluminal impedance/pH monitoring, manometry and endoscopy should be considered.

UGIE is of 2 types- flexible and rigid. Flexible endoscopy is a daycare invasive procedure under topical anesthesia. The most common endoscopy finding is inflammation of the digestive tract like gastritis, duodenitis, esophagitis. Helicobacter Pylori (H. Pylori) is one of the causes for the above findings. H. pylori is the most common chronic infection worldwide, with a prevalence of approximately 50%; however, the majority of the infected individuals are asymptomatic [6]

It causes an inflammatory response with neutrophils, lymphocytes, plasma cells, and macrophages within the mucosal layer and causes epithelial cell degeneration and injury. Gastritis is more usually severe in the antrum. 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 andincludes a variety of methods for testing such as histology, culture, or rapid urease test. While there are a number of 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 testfor 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 G I 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 thisgroup 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.

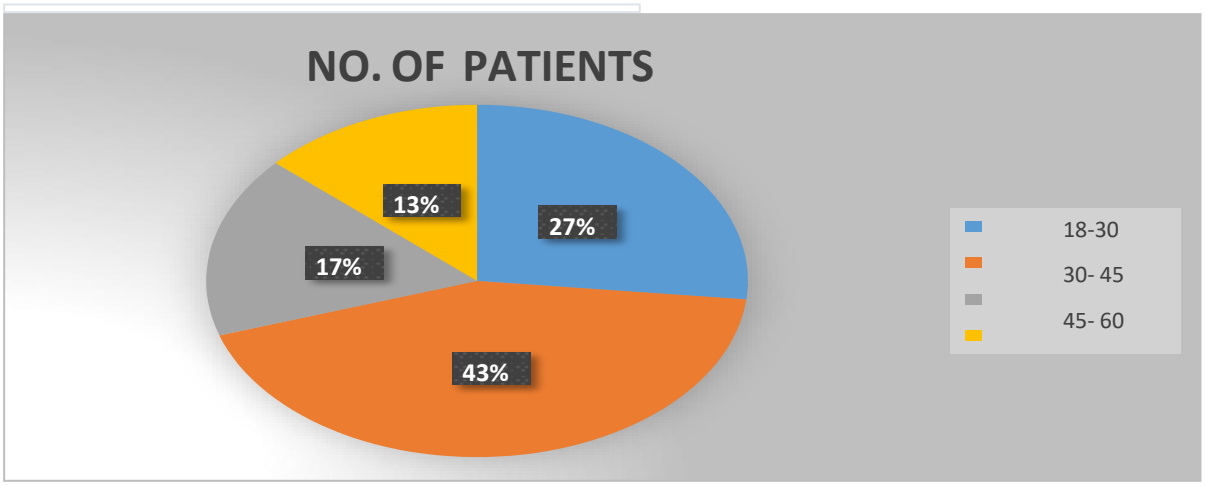
Patients were advised to come to opd with empty stomach on the day of UGIE. Proper consent was taken.

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

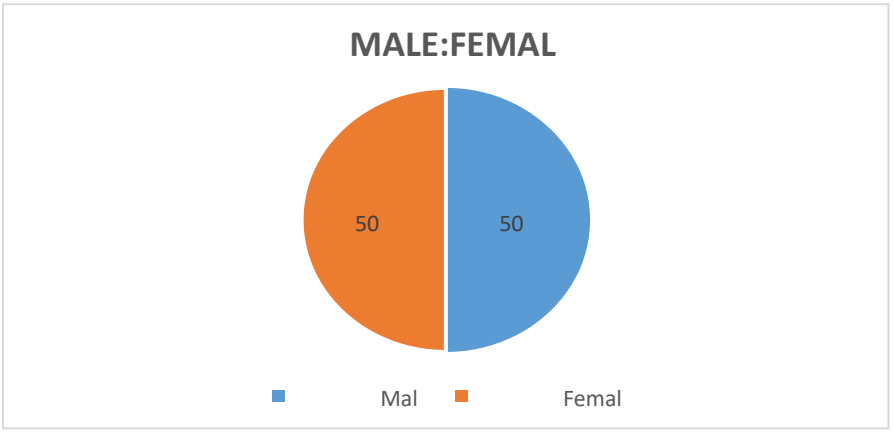
AGE (yrs.)	No. of patients
18-30	08
30- 45	13
45- 60	05
60- 75	04
Total	30



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

TABLE 2-Sex Distribution

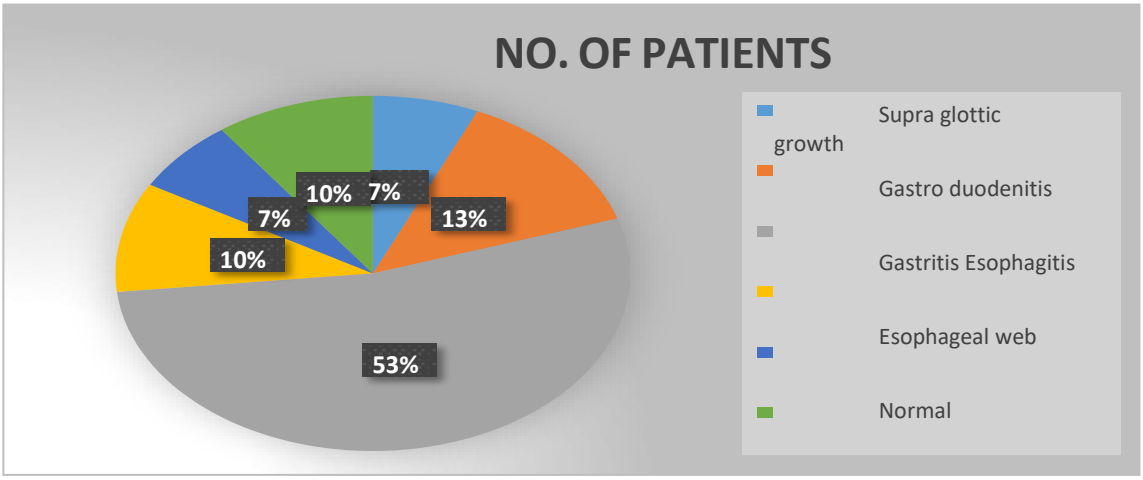
Male	15
Female	15
Total	30



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

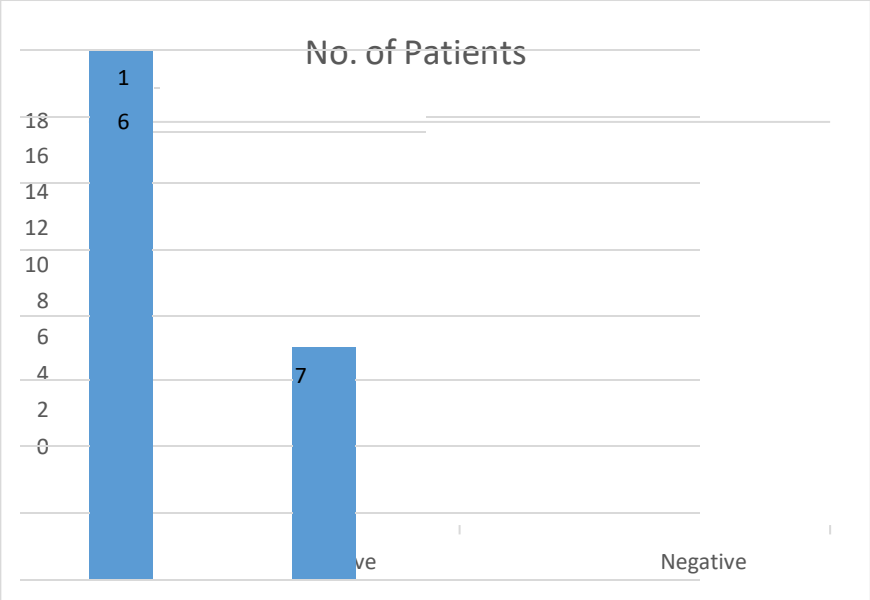
UGIE FINDINGS	NO. OF PATIENTS
Supra glottic growth	02
Gastro duodenitis	04
Gastritis	16
Esophagitis	03
Esophageal web	02
Normal	03
Total	30



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, duodenum1st part, lowerend 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.[7] 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.[7]

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 reporta similar rate in asymptomatic control patients.[7]

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

Oesophageal motility disorder is another aetiological factor. Studies suggest an association between upper oesophageal sphincter function and globus sensation, with one showing elevatedsphincter pressure in 28% of patients with globus pharyngeus compared with 3% of controls.[7] 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 more severe in the antrum. 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 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 testfor 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 G I 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 thisgroup is found.

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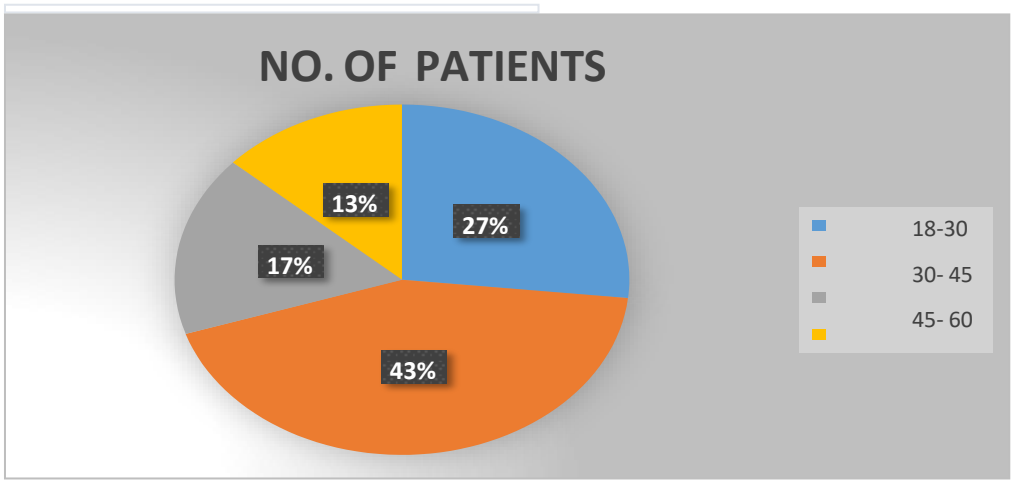

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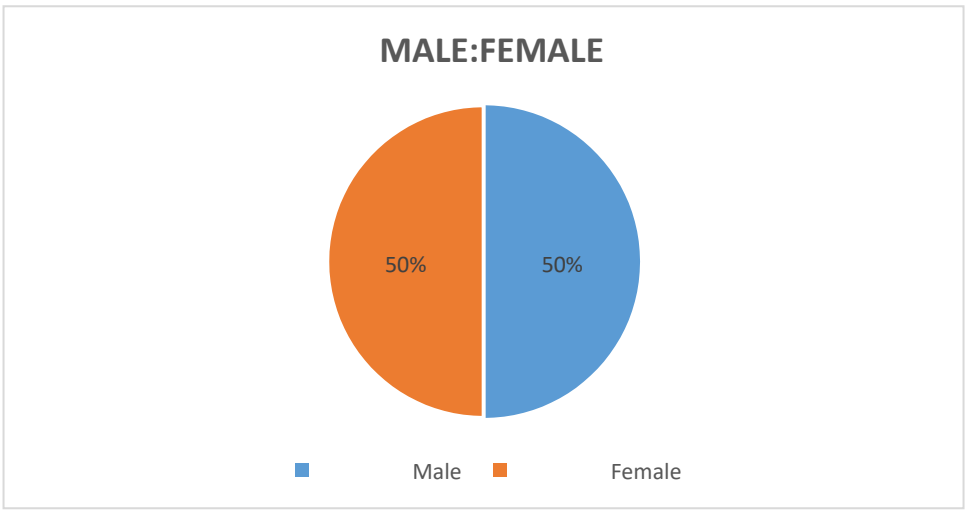

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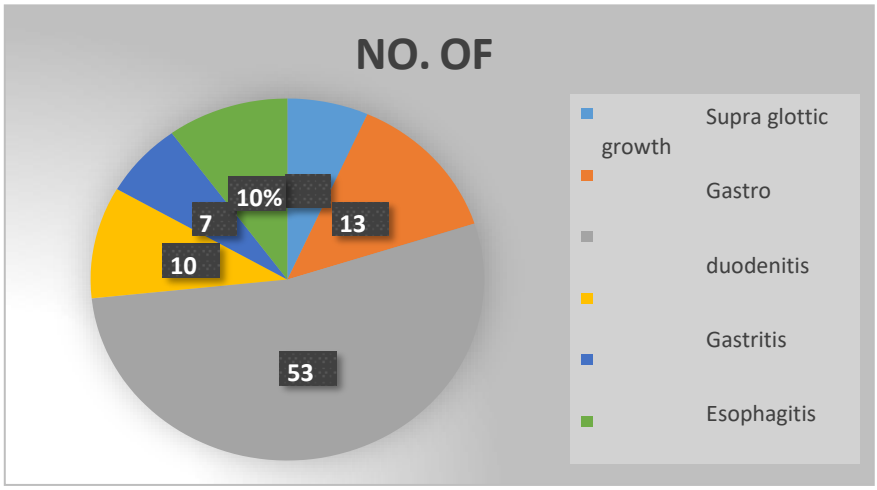

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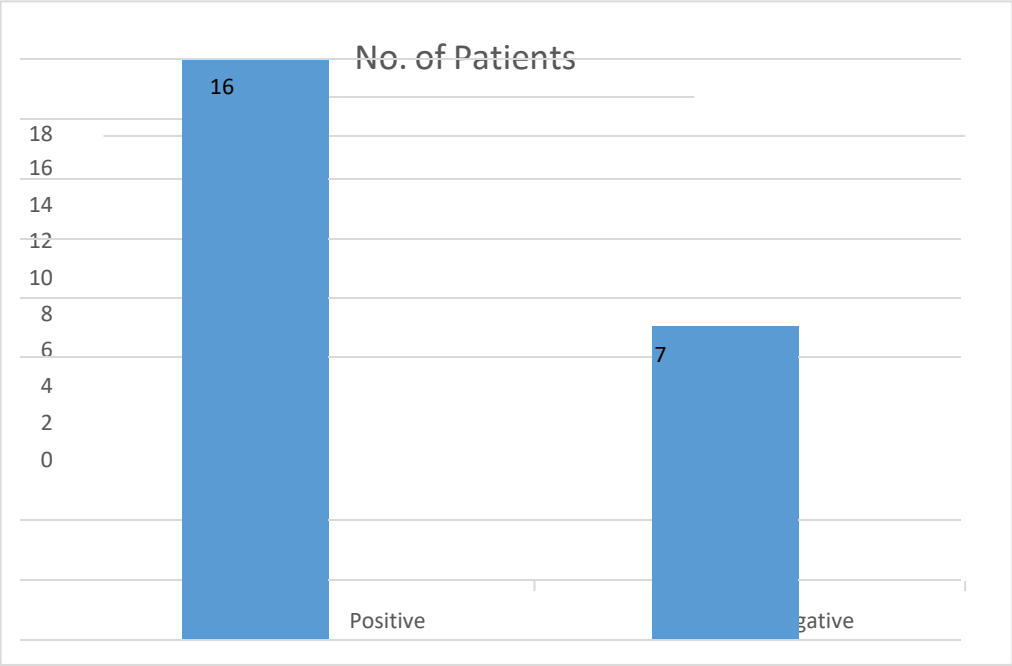

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A diagnosis of globus pharyngeus is based on history and examination. The presenting complaint may be described like a lump or ball in the throat, throat swelling, or itching. The symptoms often come and go but constant or worsening symptoms are more concerning.[10] The site of symptoms is typically, the central and suprasternal. Globus sensation is often noticed while swallowing their own saliva or eat and drink, so it may be helpful to ascertain the relationship to food and swallowing. Pain on swallowing is not typical of globus sensation.Reflux symptoms and other symptoms such as throat clearing, cough, hoarseness, anxiety and psychological distress, poor sleep along, habits like alcohol, tobacco along with the duration should be asked. Although cancer very rarely presents as globus pharyngeus,[11] it is important toask about red flag symptoms such as persistent hoarseness, progressive dysphagia or dysphagiafor solids, or pain on swallowing, haemoptysis, and weight loss. As in every consultation the patient's ideas, concerns, and expectations should be considered; many patients presenting withglobus sensation are worried about cancer.[12]

In general practice, a full examination of the head and neck is important. The neck should be palpated, ensuring the thyroid gland and cervical lymph nodes are examined.

Oropharynx and oral cavity should be assessed for any growth, ulceration, post nasal drip. The nose should be checked for evidence of inflamed mucosa, polyps, considered as a cause for globus pharyngeus.An abnormal neck or oral examination should prompt urgent referral to secondary care.[12]

Most cases of globus pharyngeus can be managed in primary care following by PPI and antacid. If the symptoms are not improved, investigation like pH monitoring, barium swallow, manometer and UGIE should be advised. Upper GI endoscopy is the standard test used for diagnosis of esophagitis, gastritis and duodenitis. it also tells us the extent of involvement. The upper GI endoscopy has good specificity (90-95%) and low sensitivity[13]. The earliest finding of acid reflux in endoscopy is erythema and edema, there are nonspecific and these finding are dependent on the endoscopic quality of image [14]. The reliable endoscopic signs are a) Friability (refers to tendency for easy bleeding) as a result of capillary enlargement in response to acid nearthe mucosal surface. b) Red streaks are found in the ridges of the esophageal folds; they have upward extension from the esophageal junction [15].It can also show any supra glottic growth and if present, biopsy can be taken at the same time. Incase of gastritis, esophagitis, duodenitis, biopsy should be taken from the affected area for rapid urease test for H.Pylori. Gastric urease, neutralizes acid by producing ammonia from urea diffusing from the blood and potentially protects the stomach. It allows the organism to colonizethe acidic stomach and serves as a biomarker for the presence of H. pylori. Important clinical tests for H. pylori, the rapid urease test and urea breath test, are based on gastric urease. Rapid urease tests use gastric biopsies or mucus placed in a device containing urea and an indicator of pH change, typically phenol red[16]. Choice of RUT test depends on availability, cost, and ease of use. In regions where cost is a significant issue, tests are often made locally from a solution containing 2 g of urea in 100 mL of0.01 M sodium phosphate buffer, pH 6.5, into which 10 mL of a 0.5% (w/v) phenol red and 20 mg of sodium azide are added. A positive RUT requires approximately 10^5 *H. pylori* in the biopsy sample to produce a positivereaction with an agar-based test[17]. The organisms tend to localize on or near the surface of the specimen such that most of the tissue is “extra” and does not contribute to the reaction. Some investigators have used opened forceps to scrape gastric mucus to ensure that a high concentration of bacteria-rich material is obtained [18].

Generally, the concentration of *H. pylori* is highest in the antrum, however, if the patient has recently taken proton pump inhibitors (PPIs) the concentration can be markedly reduced resulting in a false negative test[19.]Another common cause of false negative tests, especially in areas where atrophic gastritis is common, is the presence of intestinal metaplasia which is oftendevoid of *H. pylori*. At least two large-cup biopsies be taken from normal appearing mucosa, one from the antrum and one from the corpus, avoiding obvious areas of intestinal metaplasia. The two biopsies are then combined within the same test well [17, 20]

The sensitivity of various RUT tests as primary diagnostic tests is high and has been reported tovary between approximately 80% and 100% with a specificity between 97% and 99% [17,21]

There are various treatment regimens for the H.Pylori infection. Su Young Kim and Jun-Won Chung in their paper summarized the different regimen.[22]

Regimens for the treatment of *Helicobacter pylori* infection.

Treatment	**Regimen**	**Duration**	**Recent First-Line Eradication Rate (ITT)**	**Recommendations According to Guidelines**
Standard triple therapy (STT)	PPI standard dose bid Amoxicillin 1 g bid Clarithromycin 500 mg bid	7–14 d	63.9% [105], 74.1% [106]	First-line: optionally recommended by KCHUGR and JSHR Rescue: limited

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	
H. pylori 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.

ITT, intention to treat; STT, standard triple therapy; PPI, proton pump inhibitor; KCHUGR, Korean College of Helicobacter and Upper Gastrointestinal Research [116]; JSHR, Japanese Society for Helicobacter Research [117]; MAA, Maastricht V/Florence Consensus [10]; BQT, bismuth quadruple therapy; ACG, American College of Gastroenterology clinical guideline [4]; TOR, Toronto Consensus [9]; CTT, concomitant therapy; P-CAB, potassium-competitive acid blocker; AST, antimicrobial susceptibility test.

In our study, 16 patients showed Urease test positive for H. Pylori. They were prescribed tab amoxyciilin 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 pHmonitoring, 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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Su Young Kim[1] and Jun-Won Chung[2,*] Antibiotics (Basel). 2020 Aug; 9(8): 436.

IMAGE 1. ESOHAGITIS IMAGE 2. DUODENITIS

IMAGE 3. PROLIFERATIVE GROWTH OVER AE FOLD

IMAGE 4. GASTRITIS