PREVALENCE OF GASTRO-ESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH VOICE DISORDERS

A dissertation submitted in part fulfillment of MS Branch IV, ENT examination of the Tamil Nadu Dr. MGR Medical University, to be held in April 2011

Department of Otorhinolaryngology

Christian Medical College, Vellore

CERTIFICATE

This is to certify that the dissertation entitled '**Prevalence of gastroesophageal reflux disease in patient with voice disorders**' is the bonafide original work of Dr Maldhure Swati Vijay submitted in fulfillment of the rules and regulations for the MS Branch IV, ENT examination of the Tamil Nadu Dr. MGR Medical University, to be held in April 2011.

Guide:

Dr Mary Kurien
Professor and Head Unit II
Dept. of Otorhinolaryngology
Christian Medical College & Hospital,
Vellore – 632 004

Co – investigators:

Dr Ashok Chacko

Professor and Head,

Dept. of Gastroenterology,

Christian Medical College & Hospital,

Vellore – 632 004

Dr Amit Kumar Dutta

Assistant Professor,

Department of gastroenterology,

Christian Medical College & Hospital,

Vellore – 632 004

Department of Otorhinolaryngology

Christian Medical College, Vellore

CERTIFICATE

This is to certify that the dissertation entitled '**Prevalence of gastroesophageal reflux disease in patient with voice disorders**' is the bonafide original work of Dr Maldhure Swati Vijay submitted in fulfillment of the rules and regulations for the MS Branch IV, ENT examination of the Tamil Nadu Dr. MGR Medical University, to be held in April 2011.

Dr Achamma Balraj
Professor and Head,
Dept of Otorhinolaryngology,
Christian Medical College & Hospital
Vellore – 632 004

Acknowledgements

I would like express a deep sense of gratitude towards my professor and guide Dr Mary Kurien for all her encouragement, wisdom and expert guidance throughout the work on my thesis.

I am extremely grateful to Dr Ashok Chako, Head of department, and Dept of Gastroenterology for allowing me to conduct this study in collaboration with Gastroenterology department. I am also extremely thankful to Dr Amit Kumar Dutta, Assistant Professor, Department of Gastroenterology for his excellent guidance and encouragement and for sparing his valuable time to help me in the execution of this study.

I wish to thank Dr. Achamma Balraj, Professor and Head of Otorhinolaryngology, CMC, and Vellore for facilitating this study.

I would like to thank Mr. Solomon Christopher and Mr. Vasanth for patiently understanding and helping me with the analysis of the data. I would also like to thank Mr Sathiya murthi for editing and compiling the study material.

I am grateful to every ENT surgeon and Speech therapists for meticulous screening of patients, and to the patients who consented to be a part of this study. I owe my gratitude to all my professors, seniors and colleagues for their encouragement. A special thanks to friends who gave me their time, concern, support, and any help I needed; and my family, especially my husband, for supporting me throughout the work on this study.

And to God for his blessings, which helped me complete this study.

Table of Contents

AIM

To determine the prevalence of gastro-esophageal reflux disease in patients with voice disorders.

OBJECTIVES:

1. To determine the prevalence of gastro esophageal reflux disease (GERD) in patients with voice disorders.

2. To determine prevalence of laryngopharyngeal reflux (LPR) in patients with gastro-esophageal reflux disease by validating the following, in patients with gastro-esophageal disease:

    A. Kaufmann Reflux Symptom Index

    B. Reflux Finding Score

PRESENT KNOWLEDGE AND REVIEW OF LITERATURE

INTRODUCTION

Acid reflux is a common problem in 4-10% of patients coming to ENT out patient departments. A recent study of voice and reflux disorders revealed that 55% - 60% patients had laryngopharyngeal reflux.[1] Anti-reflux therapy is usually used as an empirical treatment for patients with hoarseness, where no other cause has been identified by examination.[2]

Gastro-esophageal reflux disease (often abbreviated to GERD or GORD) is defined as the retrograde flow of gastric contents into the oesophagus or above. Gastro-esophageal reflux disease is characterized by symptoms and/or signs of mucosal injury of the oesophagus or upper aerodigestive tract secondary to this reflux. [3]

Laryngopharyngeal reflux refers to backflow of acid from stomach to throat. Otolaryngological manifestation of acid reflux includes a wide range of laryngeal and pharyngeal symptoms and constellation of symptoms is called laryngopharyngeal reflux.[4] Patients with laryngopharyngeal reflux suffer from change in voice, burning sensation in substernal / epigastric, regurgitation, dysphagia ,throat pain, ,cough, foreign body sensation in throat, or frequent throat clearing. Laryngopharyngeal reflux is a major cause of laryngeal inflammation and present with constellation of symptoms different from classic gastro-esophageal disease. The goal of this study is to estimate prevalence of gastro-esophageal disease for the management of laryngeal and voice disorder**.**

NORMAL LARYNGEAL ANATOMY [5]

The larynx is an extraordinary versatile organ capable of many rapid and subtle adjustments and capable of sound production over a wide range of pitch and loudness. The structural framework of the larynx is consisting of nine cartilages, their connecting membranes and ligaments.

Cartilages of larynx: (Figure 1)

Thyroid cartilage: The thyroid cartilage develops from the 4th arch cartilage.[7, 6] Thyroid cartilage is covered by outer thick perichondrium and inner thin perichondirum. Attachment of the anterior commisure of vocal cord lacks perichondrium.

Cricoid cartilage: It is a signet ring shaped cartilage, with a thin anterior arch and a broader posterior lamina, which has facets for articulation with the arytenoids cartilage. This forms a crucial joint in the production of voice.

Epiglottic cartilage: It is a leaf like hyaline cartilage. Thyroepiglottic ligament connects it to thyroid cartilage and hyoepiglotttic ligament connects it to the hyoid superiorly.

Arytenoid cartilages: These are paired pyramidal cartilage rests upon the cricoid lamina with two processes (vocal and muscular), an apex and a base. The concave base articulates with the cricoid cartilage in a synovial joint.

Minor cartilages: The corniculate cartilage (cartilage of santorini) is located just above the apices of arytenoids. The cuneiform cartilage (cartilage of wriesberg) is found in the superior aspect of the aryepiglottic folds. These cartilages provide rigidity to the membranes, which function as ramparts that guides the food bolus away from the larynx.

Ligaments of larynx

Quadrangular membrane: On both side of larynx, the membrane extends from the lateral edge of the epiglottis to the arytenoid cartilage posteriorly. The superior border of the membrane is a free edge corresponding to AE folds. Each membrane's lower edge is also free and it extends from the epiglottis to the vocal process of the arytenoids corresponding to the false vocal cords which is also known as the ventricular bands. The superior and inferior edges of this membrane are thickened giving rise to the aryepiglottic ligament and the vestibular ligament.

Triangular membrane (conus elasticus): The triangular membrane is paired and together forms the connus elasticus. Its base is located anteriorly attached to both thyroid and cricoid cartilage. Each membranes apex is attached to the vocal process of arytenoids. The free superior edge of this membrane is forming the vocal ligament.

Mucous membrane: It is continuous with the lining of pharynx above and the trachea below. This membrane is particularly rich in mucous glands in the region of the laryngeal ventricle (ventricle of Morgagni). It is closely adherent to the epiglottis, the aryepiglottic ligament and the vocal cords. The epithelium of larynx is either squamous, ciliated columnar or transitional. The superior half of the posterior surface of the epiglottis, the upper part of the aryepiglottic folds, posterior commisure and vocal cords are covered by squamous epithelium.

Laryngeal muscles: (Figure 2)

The laryngeal muscles can be divided into three groups: intrinsic, extrinsic, and accessory.

Intrinsic muscles:

The intrinsic muscle of the larynx may be classified according to their effect on the shape of glottis and the vibratory behavior of the vocal fold. They are adductors, abductors, relaxers and tensor muscles.

The articulation between the cricoid and arytenoid cartilages is a complex one, involving sliding arytenoid and rotation about its vertical axis. Arytenoid movement is the composite of all the actions of the intrinsic muscles acting together.

The Posterior Cricoarytenoid Muscle (PCA): The posterior cricoarytenoid is the sole abductor of the vocal folds. This muscle originates from the posterior surface of the cricoid cartilage and inserts into the muscular process of the arytenoid cartilage. The role of the whole PCA during phonation is controversial. It is widely accepted that the PCA pulls the vocal folds apart after phonation.

The Interarytenoid Muscle (IA): The interarytenoid muscle is an unpaired muscle that originates from the posterior surface of each arytenoid cartilage. It approximates the posterior ends of the arytenoid cartilages, thus playing an important role in both the phonatory and the sphincteric mechanisms of the larynx.

The lateral Cricoarytenoid Muscle (LCA): The lateral cricoarytenoid muscle originates from the cricoid arch and inserts onto the muscular process of the arytenoid cartilage. Contraction of the muscle adducts the vocal folds.

The Thyroarytenoid Muscle (TA): The thyroarytenoid muscle is the most important muscle for phonation. This muscle is composed of two basic compartments: a medial part, the vocalis, which is more involved in phonation; and a lateral part, the muscularis, which is more involved with adduction. Depending on the myofibrillar ATPase reaction, muscle fibers are divided into a fast and slow type. These slow fibers are arranged in a gradient with the medial edge of the muscle approaching 100% slow twitch and gradually changing into almost 100% fast twitch at the lateral edge.

Table showing Intrinsic muscle and their actions

Function of Laryngeal Muscles in Vocal cord Adjustments·					
	CT (cricothyroid)	TA (thyroarytenoid)	LCA (Lateral cricoarytenoid)	IA (Interarytenoid)	PCA (posterior cricoarytenoid)
Position	Paramedian	Adduct (Membranous portion)	Adduct (Entire fold)	Adduct (Cartilaginous portion)	abduct ––
Level	Lower	Lower	Lower	--	Elevate
Length	Elongate	Shorten	Elongate	(Shorten)	Elongate
Thickness	Thin	Thicken	Thin	(Thicken)	Thin
Edge	Sharpen	Round	Sharpen	--	Round
Cover	Stiffen	Slacken	Stiffen	(Slacken)	Stiffen
Transition	Stiffen	Slacken	Stiffen	(Slacken)	Stiffen
Body	Stiffen	Stiffen	Stiffen	(Slacken)	Stiffen

Extrinsic muscles:

The cricothyroid muscles are located on the exterior surface of the larynx, each consist of two parts. It stretches the vocal fold and sharpens its edge, indicating that they are an important determinant of the pitch of the acoustic signal of the vibrating vocal folds.

Laryngeal neuromuscular anatomy:

The larynx is innervated by two main branches of the vagus nerve: the superior and recurrent laryngeal nerves. The superior laryngeal nerve (SLN) bifurcates into two nerves: the internal and the external. The internal supply the sensory innervation to the entire mucosa of the larynx above the vocal folds. The external SLN supply motor innervation to the cricothyroid muscle. The recurrent laryngeal nerves are the main of motor innervation to the larynx. They supply motor innervation to the laryngeal muscles in the following sequence: posterior cricoarytenoid, interarytenoid, lateral cricoarytenoid, thyroarytenoid. Only the interarytenoid muscle receives bilateral innervation.

Anatomy of glottic region (Figure 3)

The glottis consists of two portions; the intermembranous portion or the anterior glottis and the intercartilagenous portion, or the posterior glottis. The anterior glottis can be regarded as the phonatory glottis whereas the posterior glottis is considered the respiratory glottis. The vocal fold is defined as the fold like structure that lies between the anterior commisure and vocal process of arytenoids.

Histological structure of vocal cord (Figure 4)

Vocal cord is made of mucosa and muscle. The mucosa in turn, consists of epithelium and lamina propria. Around the vocal fold edge, the epithelium is stratified squamous epithelium. The lamina propria can be divided into three layers. The superficial layer of lamina propria mainly consists of amorphous substance and it is loose and pliable. Elastic and collagenous fibers as well as fibroblast are sparse. This layer is called the Reinke's space. It is this layer which vibrates during phonation. If it becomes stiffened with pathologies such as inflammation, scar or tumor, its vibration will be disturbed. This results in voice problems. The intermediate layer consists primarily of elastic fibers, whereas the deep layer consists chiefly of collagenous fibers. The structure that consists of intermediate and deep layer of the lamina propria is called the vocal ligament. The vocalis muscle forms the main body of vocal cord. The five histological layers are reclassified into three parts -

The cover: consisting of epithelium and the superficial lamina propria.

The transition: consist of intermediate and the deep layer of lamina propria

The body: consists of the vocalis muscle.

PHYSIOLOGY OF PHONATION (Figure 5,6)

The larynx is the major source of sound used during speaking. Phonation is the generation of sound by vibration of vocal cords.

THEORIES OF PHONATION [5]

It is based on three theories.

a) Aerodynamic or myoelastic theory: (Van de Berg - 1958) this theory postulates that vocal cords are subject to well established aerodynamic and physical forces. There is a building up of infraglottic air column, and its pressure act on the vocal folds which are kept tensed by the tonic contraction of the laryngeal muscles. This increased infraglottic pressure forces the vocal cords apart and it is set in vibration, once again the pressure falls, vocal cords recoil following which the subglottic pressure raises. The mode and frequency of vibration is dependent on properties of the cord and interplay of the intrinsic muscles of the larynx.

b) Neuromuscular or clonic theory (Husson): This is not accepted now. This states that each new vibratory cycle is initiated by nerve impulses transmitted from brain to the vocalis muscle by way of the vagus nerve. This means that the frequency of vocal cord vibration is dependent on rate of impulses delivered. There was very little conclusive evidence to support this theory.

c) Cavity tone or transient theory (Wills) this states that larynx functions simply to supply puffs of air that might excite the supraglottal resonating cavity. This explains sound production based on the resonation chambers alone.

Normal voice : A normal voice falls within the accepted ranges of pitch, loudness , and quality found in a majority of individuals of the same age and sex. Abnormal vocal fold vibrations take many forms, each of which creates acoustic patterns that cause the voice to be perceived as disordered.

Common voice Complaints

Hoarseness means change in voice. This term is used by patients to describe changes in their voice quality.

Dysphonia means abnormal voice, but the degree of dysphonia does not correlate with any particular specific cause. It may present with mild, moderate, or severe dysphonia.

The symptoms of dysphonia may be further subclassified, as Diplophonia (double-tone) and Dysresonance (change in the resonance of the voice). Voice breaks exemplify pitch-specific dysphonias. Odynophonia implies uncomfortable or painful speaking. Vocal fatigue is a common symptom among voice disorder patients and implies the development of symptoms (dysphonia or odynophonia) sometime after the initiation of vocalization.[7, 6]

Aphonia is used to describe the loss of voice; such patients may still be able to communicate in a quiet environment using the airstream for articulation, but the glottis does not participate in phonation. The sound of an aphonic, then is characteristically no voice or extreme breathiness.

NORMAL ESOPHAGEAL ANATOMY [7]

The esophagus is a muscular tube connecting the pharynx to the stomach, acting as a channel for the transport of food. However, its structure and function is much more complex. The proximal margin of the tubular esophagus is the upper esophageal sphincter (UES), the functional unit correlating anatomically with the junction of the inferior

pharyngeal constrictor and cricopharyngeus. The esophagus extends distally 18 to 26 cm within the posterior mediastinum as a hollow muscular tube to the lower esophageal sphincter (LES). The LES is a 2- to 4-cm-long focus of tonically contracted thickened circular smooth muscle that lies within the diaphragmatic hiatus. The esophageal wall is comprised of four layers: mucosa, submucosa, muscularis propria, and adventitia. (Figure 7). The esophagus has no serosa, which makes it unique to the rest of the gastrointestinal (GI) tract. The mucosa is normally composed of stratified squamous epithelium, lamina propria, and the muscularis mucosa. Lymphatic drainage begins in the lamina propria. The muscularis propria consists of both skeletal and smooth muscle. The proximal 5% to 33% is skeletal muscle, the middle 35% to 40% is mixed, and the distal 50% to 60% is smooth muscle. The muscles are arranged into inner circular and outer longitudinal layers.

The smooth muscle portions of the esophageal body are innervated by the vagus nerve, which controls peristalsis under physiologic conditions. Neural innervation of the esophagus is from the myenteric or Auerbach's plexus, located between the two muscle layers and from Meissner's plexus, which is located in the submucosa. The myenteric plexus is responsible for esophageal peristalsis, whereas Meissner's complex is the site of afferent sensory input.

Although the precise interaction between morphology and function of the nerve plexuses is not entirely clear, there are two main neurotransmitters within the myenteric plexus. Excitatory stimulation from acetylcholine mediates contraction of both the longitudinal and circular muscle layers. Inhibitory neurons predominantly affect the circular muscle layer via nitric oxide. Excitatory stimulation from acetylcholine has its largest effect proximally, whereas inhibitory effect of nitric oxide is seen distally.[7]

ESOPHAGEAL PHYSIOLOGY [7](Figure 8)

Functionally, the UES, the esophageal body, and the LES act in a coordinated manner to allow normal swallowing. Swallowing begins when a food bolus is propelled into the pharynx from the mouth. This oropharyngeal phase of swallowing is voluntary, whereas the esophageal phase that follows is involuntary. In rapid sequence and with precise coordination, the larynx is elevated and the epiglottis seals the airway. A rapidly progressing pharyngeal contraction then transfers the bolus through the relaxed UES into the esophagus. As the UES closes, a progressive circular contraction begins in the upper esophagus and proceeds distally along the esophageal body to propel the bolus through the relaxed LES. Peristaltic pressures normally ranging from 30 to 180 mmHg are generated. The measured pressure tends to be lower in the more proximal portions of the esophagus and greater in the distal smooth muscle portions.

The pressures may also vary with the consistency of the bolus itself. The LES subsequently closes with a prolonged contraction, preventing movement back into the esophagus. The mechanical effect of peristalsis is a stripping wave that strips the esophagus clean from its proximal to its distal end. Secondary peristalsis is a progressive contraction in the esophageal body that is induced by stimulation of sensory receptors, rather than a swallow. Distention by residual food bolus or the refluxed gastric contents are usually the stimulants.[7]

GASTRO-ESOPHAGEAL REFLUX DISEASE

Gastro-esophageal reflux disease (often abbreviated to GERD or GORD) is defined as the retrograde flow of gastric contents into the oesophagus or above. Gastro-

esophageal reflux disease is characterized by symptoms and/or signs of mucosal injury of the oesophagus or upper aerodigestive tract secondary to this reflux.[3]

Typical symptoms of gastro-esophageal reflux disease include heartburn and regurgitation. The reflux episodes often occur at night in the supine (lying face up) position or if the patient bends forward. Most patients with symptoms of gastro-esophageal reflux disease will exhibit little or no objective evidence on examination .The complications of gastro-esophageal reflux disease include peptic stricture, dysphagia, odynophagia, oesophagitis and Barrett's oesophagus . The etiology of gastro-esophageal reflux disease is not certain, but there are several factors which may contribute. These factors are delayed gastric emptying, impaired function of the lower esophageal sphincter and incomplete esophageal clearance. Other factors such as infection (e.g. Helicobacter pylori), obesity, allergy, smoking, food intolerance and swallowing dysfunction have also been suggested. [3]

LARYNGOPHARYNGEAL REFLUX:

First coined by Kaufman in 1981, laryngopharyngeal reflux (LPR) has also been recognized under other aliases including extraesophageal reflux, reflux laryngitis, and posterior laryngitis. Laryngopharyngeal reflux (LPR) is a syndrome associated with a constellation of symptoms including laryngitis, hoarse voice, chronic cough, and other complaints and believed to be caused by the retrograde flow of stomach contents into the laryngopharynx , this being a supra-esophageal manifestation of gastroesophageal reflux disease (GERD).[8]

Laryngopharyngeal reflux (LPR) went unrecognized as a clinical entity until 1968 when the first reports linking LPR with the development of vocal process granulomas

(contact ulcer) appeared in the otolaryngology literature. Since that time, LPR has been reported to be associated with a host of laryngeal conditions, including muscle tension (functional) dysphonia, subglottic stenosis, laryngospasm, pachydermia, leukoplakia, and vocal cord carcinoma. The most common symptoms associated with LPR are hoarseness, dysphagia, globus pharyngeus, chronic throat clearing and cough, and excessive throat mucus. [9] Common laryngeal findings of LPR are localized or diffuse laryngeal edema, opalescence and/or hypertrophy of the posterior commisure, erythema, granulation, and, sometimes, granuloma formation. Classic posterior laryngitis (red arytenoids and piled-up interarytenoid mucosa) is not seen in most patients with LPR. Instead, laryngeal edema, not erythema, is by far the most common laryngeal finding.[9]

Although LPR is now a widely recognized clinical entity, the incidence of this disease process remains unknown.

Hoarseness /change in voice

Otolaryngologists navigate through the multiple causes of hoarseness when treating patients. In case of nonspecific physical / laryngeal findings, symptom overlap with common voice disorders, and lack of consensus about diagnostic tests, empiric Proton Pump Inhibitors (PPI) therapy has been recommended for suspected LPR. As a result, patients may receive ineffective or unnecessary medical treatment.[10]

Differentiating LPR from other common voice disorders is also required. Similar to LPR, Muscle tension dysphonia (MTD) patients may present with hoarseness, reduced vocal stamina, increased effort to talk, pain with phonation, excessive throat phlegm, and throat complaints.[11] MTD is common, occurring in 20% to 40% of patients with voice complaints and reportedly coexists with LPR in 35% to 78% of voice patients.[9,11]

Whether MTD and LPR are related or whether the association represents the co-existence of two common voice disorders is not known.[12] Although MTD may be a sign of glottal insufficiency, patients may not have any organic laryngeal pathology.[13] Furthermore, nonspecific signs of erythema and edema were the two most common physical examination findings reported in a survey of community and academic otolaryngologists for diagnosing LPR.[10] However, laryngeal findings depend on the use of flexible laryngoscopy, and the presence of erythema demonstrated low interrater reliability. Because LPR is currently and frequently diagnosed based on minimal, nonspecific laryngeal findings, patients with MTD may be misdiagnosed as having LPR and receive inappropriate treatment.[10,11]

GERD (hoarseness, globus pharyngeus, throat itching, throat clearing) dominate in the group of LPR patients. Combination of three atypical symptoms (hoarseness, throat itching, globus pharyngeus) separates significantly LPR patients and healthy persons. In the case when characteristic laryngoscopic findings are found and LPR is suspected, the symptom of idiopathic hoarseness in 90.2% of cases allows to determine the patient to the LPR patients' group. However, in this study LPR was evaluated by symptoms score and laryngoscopic findings with histology of esophagitis. .[14]

Jae ho chung et al, also observed that vocal polyps, reinke's edema, and laryngopharyngeal reflux disease (LPR) all include edematous changes of the vocal cords. Vocal fold edema and diffuse laryngeal edema are also important findings of LPR that are included in the RFS suggested by Belafsky.[15] Pathologic LPR could be associated with Reinke's edema and vocal polyps as a causative factor of vocal cord swelling.[16]

Reflux Symptom Index [17]

Reflux symptom index is a self administered nine-item symptom index for assessment of symptoms in patients with suspected LPR. The assessment can be complete in less than 1 minute. The scale for individual item ranges from 0 (no problem) to 5(severe problem), with maximum total score of 45. Koufman et al, observed 95% upper confidence limit of RSI in controls was 13.6, hence RSI of more than 13 was considered abnormal. [17]

Koufman RSI included the following items:

1. Hoarseness of voice / voice problems : scores 0 - 5.
2. Clearing your throat: scores 0 - 5
3. Excess throat mucous / post nasal drip: scores 0 – 5
4. Difficulty in swallowing food / liquids / pills: scores 0-5
5. Cough after eating / lying down: scores 0-5
6. Breathing difficulty / choking: scores 0-5
7. Annoying cough: scores 0-5
8. Sticky sensation in throat / lump in throat: scores 0-5
9. Heart burn / chest pain: scores 0-5

Cowell et al, also defined and validated a GERD questionnaire in order to asses the severity and response to treatment, but it was found to be lengthy and relied purely on GERD symptoms.[17,18] Shaw et al later on developed a 12 –item questionnaire for GERD , on symptoms such as burning and pain behind breastbone, acid taste in mouth, movement of materials upward from the stomach, and burning and pain in the upper stomach, which are very difficult to be assessed by patient. [17, 19] Koufman's RSI was found to be short

and easy questionnaire for patients. . Koufman [17] had evaluated 25 patients with clinical laryngopharyngeal reflux, (confirmed with 24 hours dual probe esophageal pH metry) with the 9-item questionnaire and validated the Reflux Symptom Index.

Reflux Finding Score (RFS)

The RFS is an 8-item scale that attempts to document the clinical severity of LPR. It is easily administered, takes less than 1 minute to complete, and manifests excellent inter- and intraobserver reproducibility. Although each item on the RFS is entirely subjective, the overall finding score reliably documents LPR.[15]

This scoring is prepared by the surgeon after performing a laryngeal examination.[15, 20]

1. Subglottic oedema: 0 - absent, 2 - present.
2. Ventricular obliteration: 2 - partial, 4 - complete
3. Erythema / Hyperemia: 2 - arytenoids involved, 4 - diffuse
4. Vocal fold oedema: 1 - mild, 2 - moderate, 3 - severe, 4 - polypoidal
5. Diffuse laryngeal oedema: 1 - mild, 2 - moderate, 3 - severe, 4 - obstruction
6. Posterior commissure hypertrophy: 1 - mild, 2 - moderate, 3 - severe and 4-obstruction.
7. Granuloma / Granulation: 0 - absent, 2 - present
8. Thick mucous: 0 - absent, 2 - present.

Total score: from 0 – 26

A score of 7 indicates possible presence of laryngopharyngeal reflux.[14, 16]

The most frequent finding of persons with LPR is posterior laryngeal hypertrophy, seen in 85% of all patients. Koufman first described subglottic edema, also called pseudosulcus vocalis, in 1995. It refers to subglottic edema that extends from the anterior commisure to the posterior larynx. Ventricular obliteration is a relatively frequent finding in patients with LPR (80%). Swelling of the true and false vocal folds causes this space to be poorly visualized (obliterated). With partial ventricular obliteration the ventricular space is reduced and the false fold edge is indistinct. With complete ventricular obliteration, the true and false folds appear to touch and there is no true ventricular space. Laryngeal erythema/hyperemia is a relatively nonspecific finding that is significantly dependent on the videoendoscopic equipment. True vocal fold edema is graded as mild (1 point) if only slight swelling exists and moderate (2 points) when it becomes more perceptible. Edema is graded as severe (3 points) when swelling of the cord becomes sessile. Finally, polypoid degeneration of the true vocal fold contributes 4 points to the RFS.[14, 24] Diffuse laryngeal edema is judged by the size of the airway relative to the size of the larynx. It is graded as mild (1 point) to obstructing (4 points). Hypertrophy of the posterior commisure is a frequent finding in LPR. It is graded as mild (1 point) when there is a mustache-like appearance of the posterior commisure mucosa and moderate (2 points) when the posterior commisure mucosa is swollen enough to create a straight line across the back of the larynx. Posterior commisure hypertrophy is graded as severe (3 points) when there is bulging of the posterior larynx into the airway and obstructing (4 points) when a significant portion of the airway is obliterated (Fig. 4). The final two items on the RFS are granuloma/granulation tissue and thick endolaryngeal mucus.[15]

Auditory perceptual evaluation

Auditory-perceptual evaluation is the most commonly used clinical voice assessment method, and is often considered a gold standard for documentation of voice disorders. This view has arisen for many reasons, including the fact that voice quality is perceptual in nature and that the perceptual characteristics of voice have greater intuitive meaning and shared reality among listeners than do many instrumental measures. Other factors include limitations in the validity and reliability of instrumental methods and lack of agreement as to the most sensitive and specific instrumental measures of voice quality. Perceptual evaluation has, however, been heavily criticized because it is subjective. [21]

The most commonly used perceptual evaluation systems have many similarities in terms of the voice features evaluated and definitions of those features. The GRBAS (Grade, Roughness, Breathiness, Asthenia and Strain) , CAPE-V (Consensus Auditory-Perceptual Evaluation of Voice) , Stockholm Voice Evaluation Approach and the Perceptual Voice Profile , for example, all incorporate the perceptual features of breathy, rough and strain.[21]

In auditory perceptual assessment, every patient was asked to say some specific sentences and sustained vowel like /a/,/l/ and /o/. Voice assessment was carried out by a phoniatrician for overall grade of dysphonia, character of voice and pitch of voice.[1, 21]

1) Overall grade – Normal/ Slight / Moderate
2) Characters - Normal / Breathy / Strained / Strained and leaky
3) Pitch – Decrease/ Diplophonia / Increase

24 hours dual probe esophageal pHmetry

24 hours dual probe pH metry was done using Comfortec plus single use dual probe pH meter (Sandhill scientific).The pH probes were calibrated in pH 7 and pH 4 buffer solutions according to the manufacturer's instructions. The probe is a 1.5 mm diameter nasopharyngeal catheter with a wireless digital Sandhill scientific transmitter worn externally. The semi-disposable silicon rubber catheters (ComforTec Plus disposable pH probes; Sandhill Scientific) were used for this study. These catheters contain dual-channel glass electrodes within each single silicon rubber catheter "a double probe". Probes were available with various intersensor distances. This allows a probe to be selected that would place the distal esophageal sensor 5 cm above the LES and the proximal sensor at the superior border of or just above (within 1 cm) the UES. Patients were asked to wear the device for a 24-hour period and were encouraged to participate in normal daily activities. Each subject carried two transmitter receivers, one for each of the catheters (esophageal and oropharyngeal). Each catheter contains a transmitter, which wirelessly sends the data to a separate monitor worn by the patient. Monitors contain a digital memory card to record events marked for meals, position, and chief complaint. Once the pH study was completed, the volunteer returned to have the catheters removed, the data from the digital recorder was downloaded to a password-protected computer, and the data was analyzed with DataView software. The software generated a graphical tracing of the study events and also created a report of any reflux events. [22]

Traditionally, a pH cutoff of less than 4 is used in clinical studies of patients with reflux; however, recently some have suggested that pH levels >4 may be important in LPR. George sun et al [22] showed that for the distal pH probe, the 95th percentile for total percent time pH < 4 is 4.52%. The external validity of these findings comes from its

consistency with prior reports using the traditional pH catheter. In 1974, Johnson and Demeester[23] reported 95% cutoff (normal value) of 4.2% for total % time pH < 413; and in 1992 Richter et al. reported a similar value of 5.78% in a larger group of patients. In study by George sun et al [22], the distal esophageal pH data is also consistent with normal values reported recently for the wireless pH probes of 5.3%.

Appropriately collected normative data for this location is important to compare findings to those of patients with extra-esophageal symptoms. Their results suggest that the 95th percentile for the total % time pH < 4 in the oropharyngeal location was 0.02% confirming infrequent reflux of acid in this location.[22] The results for the oropharyngeal probe were lower than previous reports using standard pH probes 1 cm to 2 cm above the UES of 0.1% to 0.2%.[22] Other studies have assessed normal pH values in the proximal esophageal location just below the UES. These studies found normal values ranging from 0.9% to 1.1%, which are slightly higher than the values for the pH probe reported here and for those with probes above the UES.[22]

Parameters measured are:

1) Acid exposure percentage time (overall) – Proximal > 0.02 %significant [22]

Distal > % 4 significant [22]

2) Total number of reflux episodes – Proximal

Distal

3) Demester and Johnson's score for gastro-esophageal reflux disease >/= 14.7 was significant.[23]

Material & Methods

a) Study Design:

This was a prospective, descriptive cross sectional study.

b) Subjects:

The study patients were those who attended the ENT Out Patient Clinics of Christian Medical College & Hospital with history of change in voice for more than three weeks.

Inclusion criteria:

- More than 18 years of age
- Any gender

Exclusion criteria:

- Laryngeal papillomatosis
- Carcinoma larynx
- Vocal cord palsy
- Hypothyroidism
- Neurological deficits causing change in voice

- Have received proton pump inhibitors
- Received H2 receptor antagonists
- Receiving calcium channel blockers
- Receiving anti dopminergic drugs like domperidone
- Receiving α and β blockers
- Allergic to any anesthetic agent
- Chronic pulmonary disease, asthma
- Heart disease
- Scleroderma
- Pregnancy

d) Informed Consent:

Informed consent was taken from all patients being enrolled in the study. The consent form is attached as Appendix A.

e) Methods:

A detailed evaluation of patient in out patient department was done which included age, sex, profession, level of voice user, history of voice abuse, addiction, diet, and use of any drug. Patient then underwent nasopharyngolaryngoscopy, voice analysis

(mainly included auditory perceptual evaluation) and 24 hours dual probe esophageal pH metry.

Severity of symptoms for laryngopharyngeal reflux was assessed using Kaufmann reflux symptom index. Laryngopharyngeal reflux on nasopharyngolaryngoscopy was assessed using reflux finding score. Patients' voice was evaluated by speech therapist /audiologists in ENT department. They were then admitted under the department of gastroenterology for 24 hours dual probe esophageal pH metry. The overall acid exposure time and number of episodes of reflux for proximal and distal esophagus were analyzed. Demester and Johnson score for gastroesophageal reflux disease was noted.

Detailed history was taken and all patients were divided into one of the following level of voice users:

Level of voice users [27]

Level I - elite vocal performers (singers & actors)

Level II - professional voice users (teachers, lecturers, barristers)

Level III - non-vocal professionals (businessmen, doctors & lawyers)

Level IV - non-vocal non-professionals (housewives & farmers)

They were then evaluated for various symptomatology using accepted symptom indices.

1) Koufman Reflux Symptom index [17]

All patients were given a questionnaire to answer. It contains about 9 questions. Patient were requested to award scores according to their symptoms.

Questionnaire

Within last month how did the following problems affect you?

0 = No problem, 5 = severe problem.

1. Hoarseness of voice / voice problems: scores 0 – 5
2. Clearing your throat: scores 0 – 5
3. Excess throat mucous / post nasal drip: scores 0 – 5
4. Difficulty in swallowing food / liquids / pills: scores 0-5
5. Cough after eating / lying down: scores 0-5
6. Breathing difficulty / choking: scores 0-5
7. Annoying cough: scores 0-5
8. Sticky sensation in throat / lump in throat: scores 0-5
9. Heart burn / chest pain: scores 0-5

Koufman Reflux Symptom Index score of more than 13 indicates laryngopharyngeal reflux. [17]

2) Auditory perceptual assessment [21]

- Overall grade

  Normal

  Slight

  Moderate

- Characters

  Normal

  Breathy

  Strained

  Strained and leaky

- Pitch

  Decrease

  Diplophonia

  Increase

These patients then underwent flexible fibreoptic laryngoscopy and the following indices were noted by the primary investigator.

4) Reflux Finding Score [15]

1. Subglottic oedema: 0 - absent, 2 - present.

2. Ventricular obliteration: 2 - partial, 4 – complete

3. Erythema / Hyperemia: 2 - arytenoids involved, 4 – diffuse (figure 9)

4. Vocal fold oedema: 1 - mild, 2 - moderate, 3 - severe, 4 – polypoidal (figure 10)

5. Diffuse laryngeal oedema: 1 - mild, 2 - moderate, 3 - severe, 4 – obstruction (figure 11)

6. Posterior commissure hypertrophy: 1 - mild, 2 - moderate, 3 - severe and 4- obstruction posterior airway.

7. Granuloma / Granulation: 0 - absent, 2 – present (Figure 12)

8. Thick mucous: 0 - absent, 2 - present.

Total score: from 0 - 26

A score of 7 indicates possible presence of laryngopharyngeal reflux [15].

5) 24 hours dual probe esophageal pH metry: [22, 23]

These patients then underwent 24 hours pH metry monitoring using dual esophageal probe (Figures 13, 14,15).

They were admitted for 24 hours after pH probe insertion. The position of the pH probe is confirmed using videofluoroscopy. (Figure 16)

Parameters measured are:

1) Acid exposure percentage time (overall) – Proximal > 0.02 %significant [22]

Distal > 4 %significant [22])

2) Demester and Johnson score for gastro-esophageal reflux disease >/= 14.7 significant .[23]

Data was collected using a detailed performa, which has been attached as Appendix B. The Data spreadsheet has been attached as Appendix C.

f) Instruments:

An Olympus and flexible fibreoptic scope was used for nasopharyngolaryngoscopy. (Figure 17, 18) Voice analysis was done by speech therapist in the ENT department. Twenty-four hours dual probe pH metry was done using Comfortec plus single use dual probe pH meter (Sandhill scientific).

g) Calculation of Sample Size:

Calculated by the formula:

$$n = \frac{4 \times p \times q}{d^2}$$

Where, n – sample size
p – Prevalence of gastro-esophageal disease in voice disorder (80%)
q – 100 – p (20)
d – Precision value (10)

Hence, $n = 4 \times 80 \times 20 / 10^2$

$= 6400 / 100 = 64$

Sample size = 64

h) Statistical Analysis:

The categorical data is presented as frequency with percentages .the continuous data with normal distribution are presented as mean with standard deviation, while, non normally distributed data is presented as median with range. The prevalence will be calculated along with 95% CI.

Comparison between categorical variables are done using Fishers exact test. Continuous variables were compared using Mann Whitney's U test.

A p value of </= 0.05 is considered statistically significant.

Results and Analysis

Table 1:

Prevalence of gastroesophageal reflux disease in patients with voice disorders.

GERD	No. of patients	Percent	Cumulative Percent
Absent	19	63.3	63.3
Present	11	36.7	100.0
Total	30	100.0	

Total 30 patients were enrolled in this study. On basis of 24 hours esophageal pH metry (Demester Johnson score >/=14.7) was found that 11 patients had gastroesophageal reflux disease, ie.prevalence of gastroesophageal reflux disease in patients with voice disorders with 36.7%.

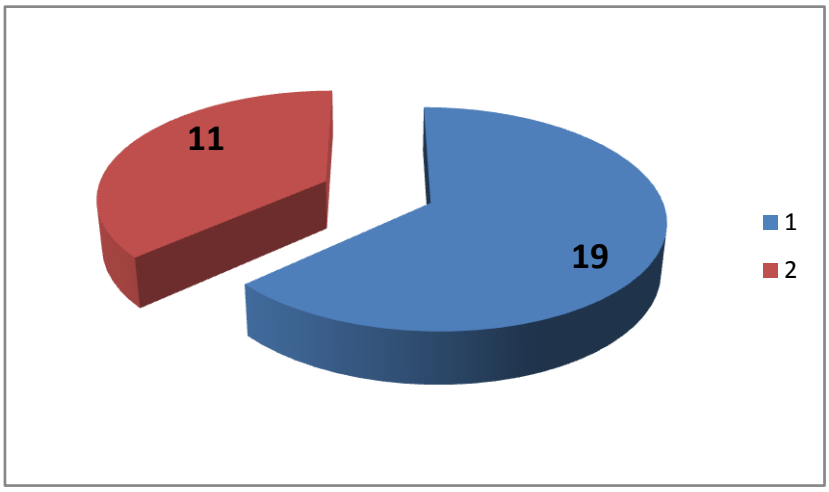

Figure I 1: GERD 2: No GERD

Table 2:

Age distribution

Gerd	No of patients	Mean +/- SD	Range
Absent	19	38.32 +/- 9.7	19-61
Present	11	38.73+/- 10.8	19- 61

The mean age of patients who had GERD was 38.7+/-10.8, ranging from 19 to 61 years. The majority of patients studied fell within the 30-50 year group. However, mean age of patients who did not have GERD was also close 38.3+/-9.7

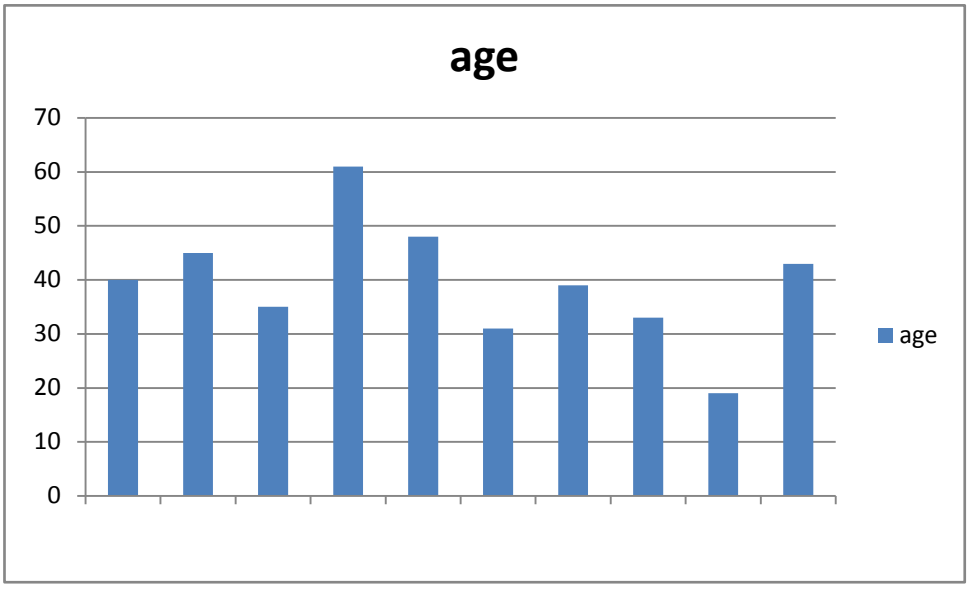

Figure II

Table 3:

Sex distribution

Sex	GERD		Total
	Absent	Present	
Male	11 (61.1%)	7 (38.9%)	18
Female	8 (66.7%)	4 (33.3%)	12
Total	19 (63.3%)	11 (36.7%)	30

30 patients were enrolled in this study. Out of these 30 patients who underwent Questionaire, endoscopy and pHmetry 18 (38.9%) were men and 12 (36.7%) were women.

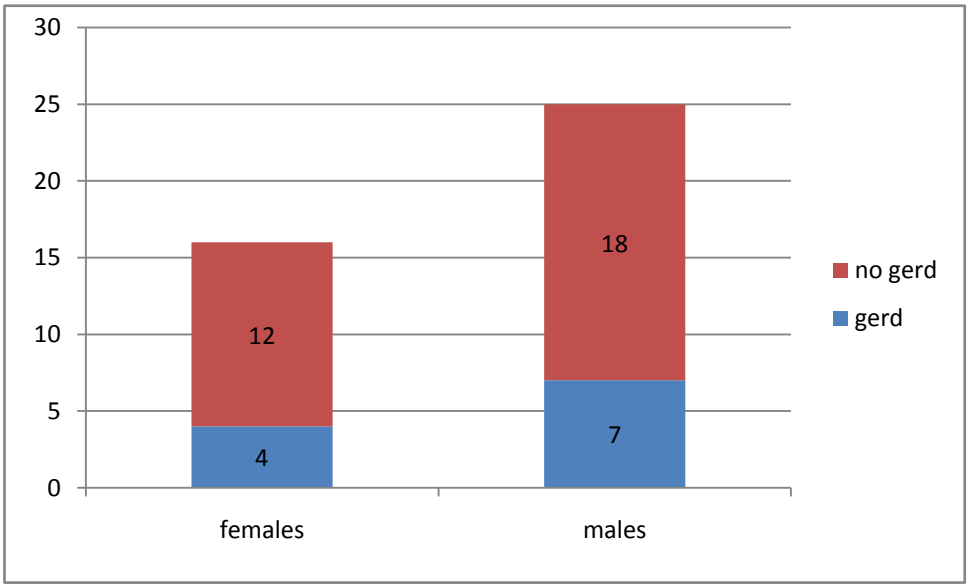

Figure III

Table 4:

Predominance of Level of voice user in GERD

Level of voice users	No GERD	GERD	Total
Level II	5 (26.3%)	1 (9%)	6
Level III	6 (31.6%)	5 (45%)	11
Level IV	8(42.1%)	5 (45%)	13

In patients with GERD, 91% were level III & IV voice users (45.5% each), and only 9% were level II voice users. There were no patients who belonged to level I voice users. However, when level II voice users were compared with level III & IV using Fisher's exact test, no statictical significance was observed (p value = 0.37) .

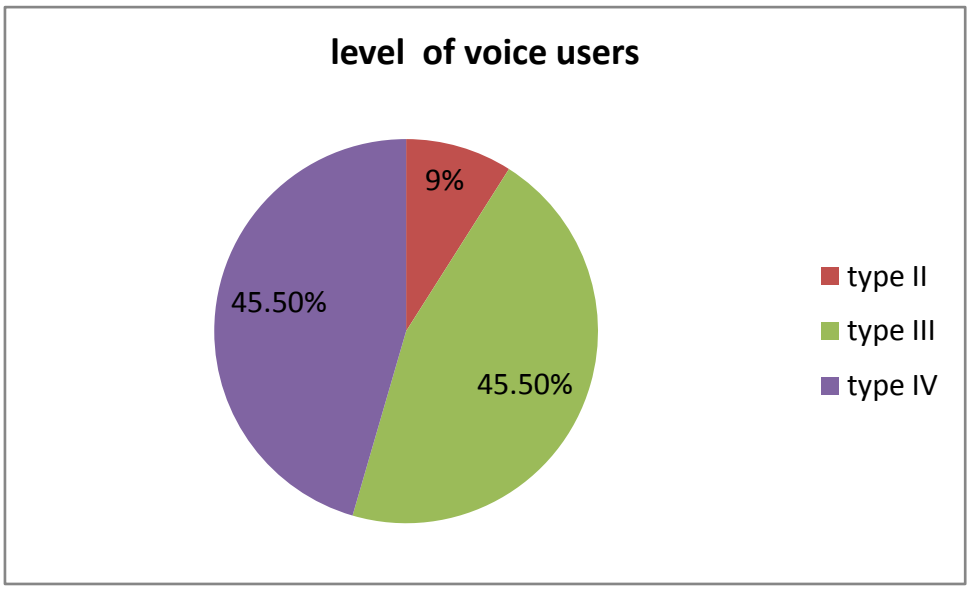

Figure IV

Table 6:

Smoking and gastroesophageal reflux disease

Smoking	GERD		Total
	Absent	Present	
Absent	14 (60.9%)	9 (39.1%)	23
Present	5 (71.4%)	2 (28.6%)	7
Total	19	11	30

In questionnaire, it was also found that only 2 (18.2%)patients who had gerd were smoking, whereas 5(26.3%) patients who did not have gerd were addicted to smoking.

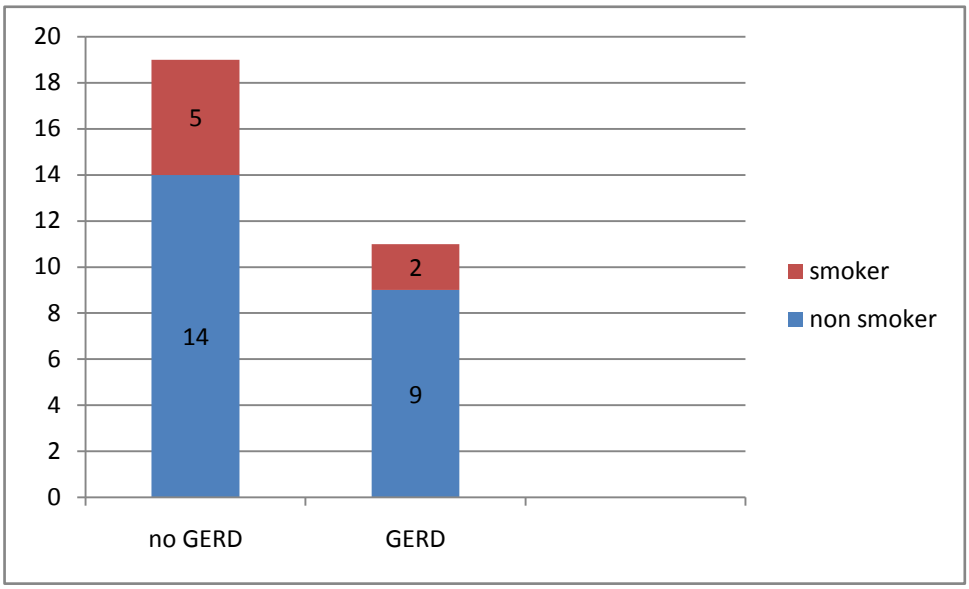

Figure V

Table 7:

Alcohol and gastroesophageal reflux disease

Alcohol consumption	GERD		Total
	Absent	Present	
Absent	17 (60.7%)	11 (39.3%)	28
Present	2 (100.0%)	0 (0%)	2
Total	19 (63.3%)	11 (36.7%)	30

Statistically, no correlation was found between alcohol, voice changes and gastroesophageal reflux disease.

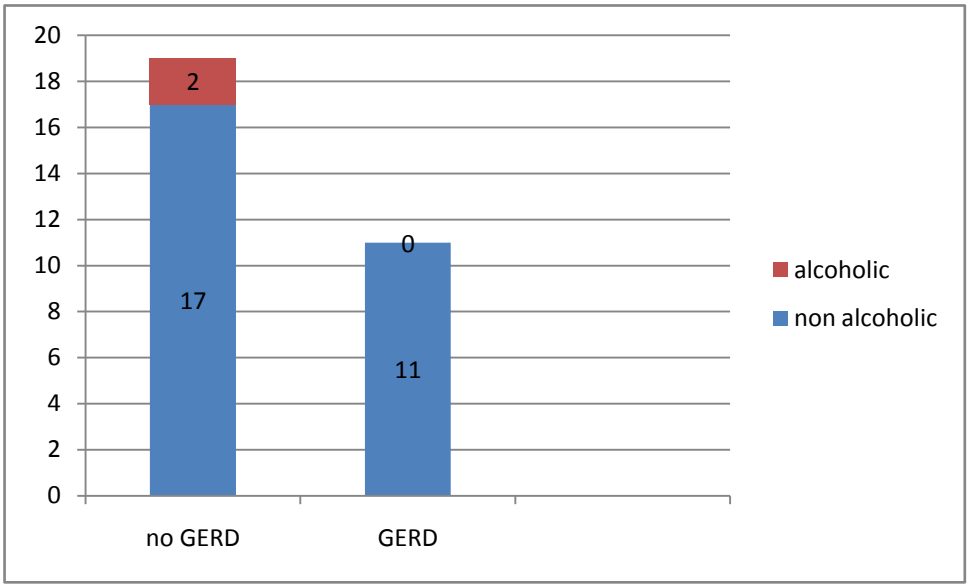

Figure VI

Table 8:

Duration of change in voice and gastroesophageal reflux disease

	GERD	
	Absent	**Present**
Duration of change in voice (median) in months	**9.0**	**12.0**

The median duration of history of change in voice in patients with GERD was about 12 months, however in patients who did not have gerd, the median was 9 months. Hence, there was longer duration of change in voice in patients with GERD. The comparison between the two were done using Mann Witney's U test, but results were not statistically significant.

Table 9:

Koufman Reflux Symptom Index

Reflux Symptom Index (RSI)	No. of patients	Percentage
Negative	23	76.7
Positive	7	23.3
Total	30	100

On basis of Koufman Reflux Symptom Index, only 7 (30%) out of 30 patients, had RSI of more than or equal to 13 which is significant for laryngopharyngeal reflux.

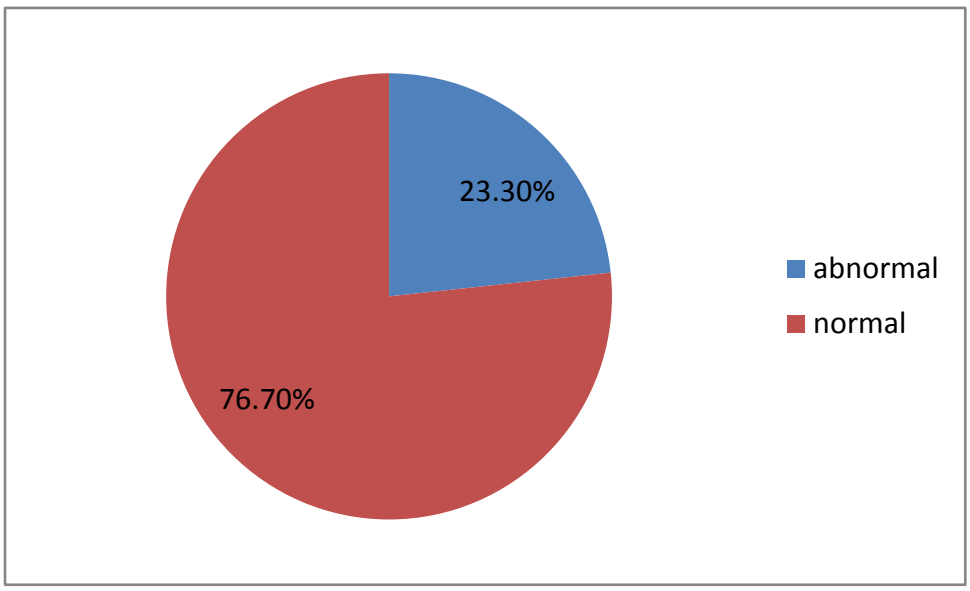

Figure VII

Table 10:

Koufman Reflux Symptom Index & GERD

Reflux Symptom Index	GERD		Total
	absent	Present	
Negative	14 (73.7%)	9 (81.8%)	23 (76.7%)
Positive	5 (26.3%)	21 (18.2%)	7 (23.3%)
Total	19	11	30

When Koufman Reflux Symptom Index was compared with Demester Johnson score, it was observed that out of the 7 patients whose RFI was >/= 13, only 2 (18.2%) patients had Demester Johnson score of >/= 14.7.Hence, only 2 patients had laryngopharyngeal reflux on 24hours dual esophageal pH metry, as compared to 7 patients on RSI and 11 patients with GERD as per Demester Johnson score.

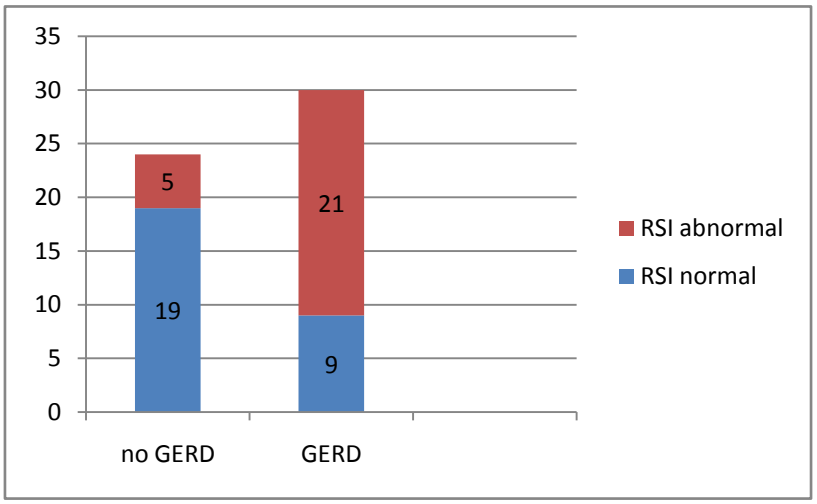

Figure VIII

Table 11:

Reflux Finding Score

Reflux Finding Score (RFS)	No. of patients	Percentage
Negative	18	60
Positive	12	40
Total	30	100

Out of the 30 patients who under flexible nasopharyngolaryngoscopy,as per the Reflux Finding Score (RFS >/=7), 12 (40%) patients were found to have laryngopharyngeal reflux.

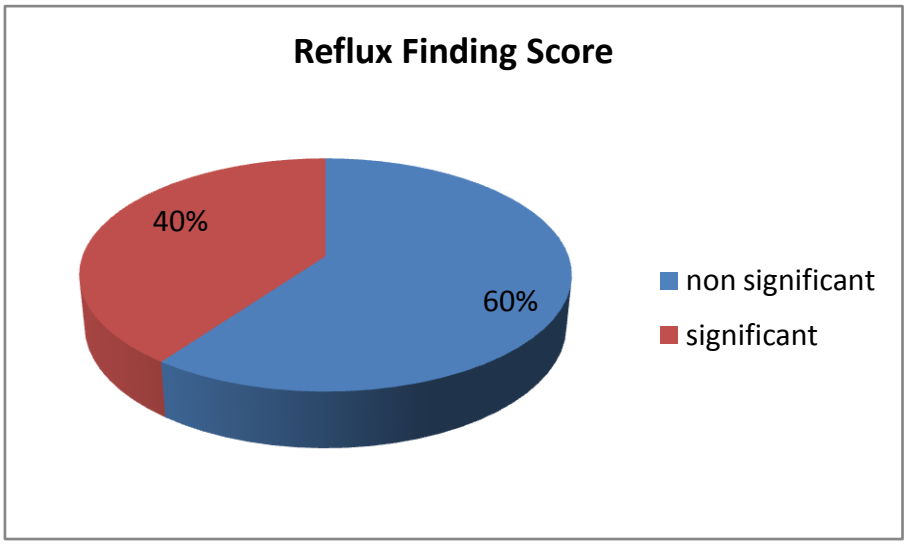

Figure IX

Table 12:

Reflux Finding Score & gastroesophageal reflux disease

Reflux Finding Score	GERD		Total
	Absent	Present	
Absent	14 (77.8%)	4 (22.2%)	18
Present	5 (41.7%)	7 (58.3%)	12
Total	19	11	30

When Reflux Finding Score (RFS) was compared with Demester Johnson score, it was observed that out of the 12 patients whose RFS was >/= 7, only 7 (58.3%) patients had Demester Johnson score of >/= 14.7.Hence, only 7 patients had laryngopharyngeal reflux on 24hours dual esophageal pH metry , as compared to 12 patients on RFI and 11 patients with gerd as per Demester Johnson score. (p value – 0.063)

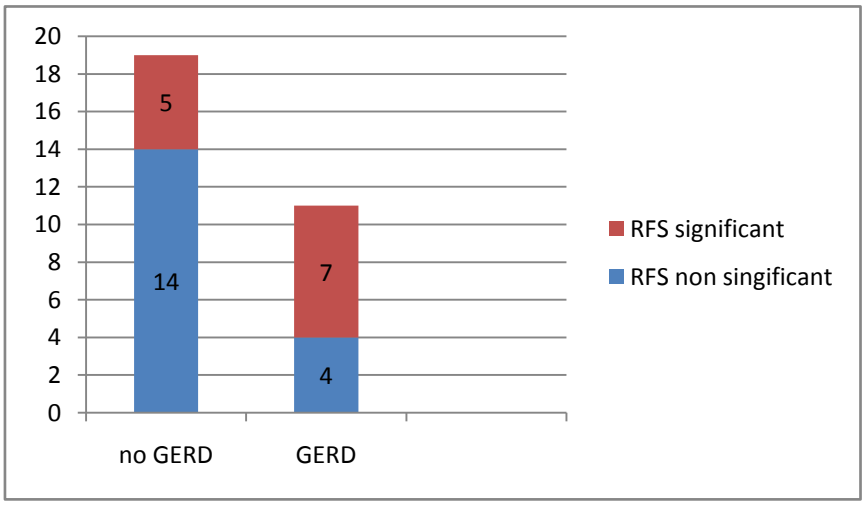

Figure : X

Table 13:

Koufman Reflux Symptom Index versus Reflux Finding Score

Koufman Reflux Symptom Index			
Reflux Finding Score	**Negative**	**Positive**	**Total**
Negative	16 (88.9%)	2 (11.1%)	18
Positive	7 (58.3%)	5 (41.7%)	12
Total	23	7	30

On comparing RFS and RSI, it was observed that, 5 (41.7%) patients who had laryngopharyngeal reflux on RSI, also had laryngopharyngeal reflux on RFS, in comparison to 7 patient who had laryngopharyngeal reflux as per RSI and 12 patient as per RFS.

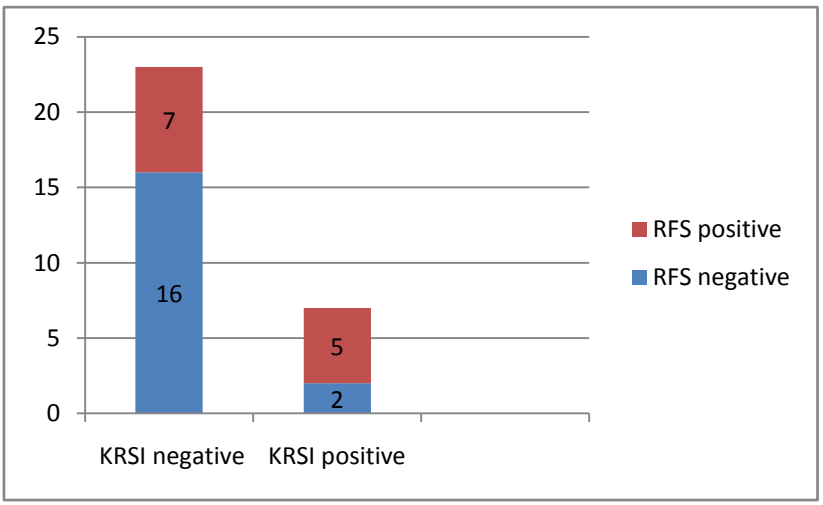

Figure: XI

Table 14:

Acid reflux in proximal esophagus

Proximal Acid reflux	No of patients	Percent
Absent	27	90.0
Present	3	10.0
Total	30	100.0

On 24 hours dual probe esophageal pH metry, it was observed that only 3 (10%) of patients had proximal overall acid exposure percentage time more than or equal to 0.02%, out of the thirty patients who under went pH metry.

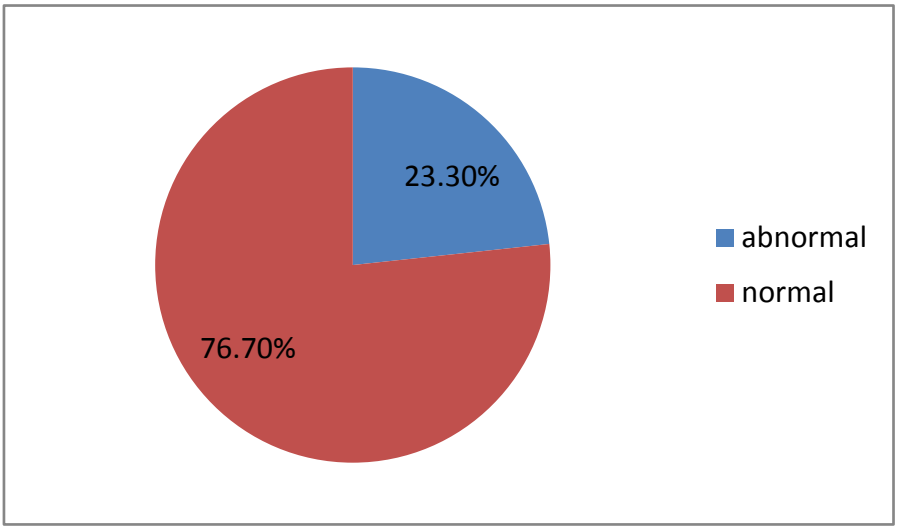

Figure : 12

Table : 15

Proximal acid exposure & Koufman Reflux Symptom Index

Proximal Acid exposure	Koufman Reflux Symptom Index		Total
	Absent	Present	
Absent	20 (87%)	7 (100%)	27 (90%)
Present	3 (13%)	0	3 (10%)
Total	23	7	30

When patients, whose proximal overall acid exposure percentage time was significant (>0.02%) were compared with patients with abnormal Koufman RSI , it was observed that there was no statically significant co-relation between the two (p value = 1.00).

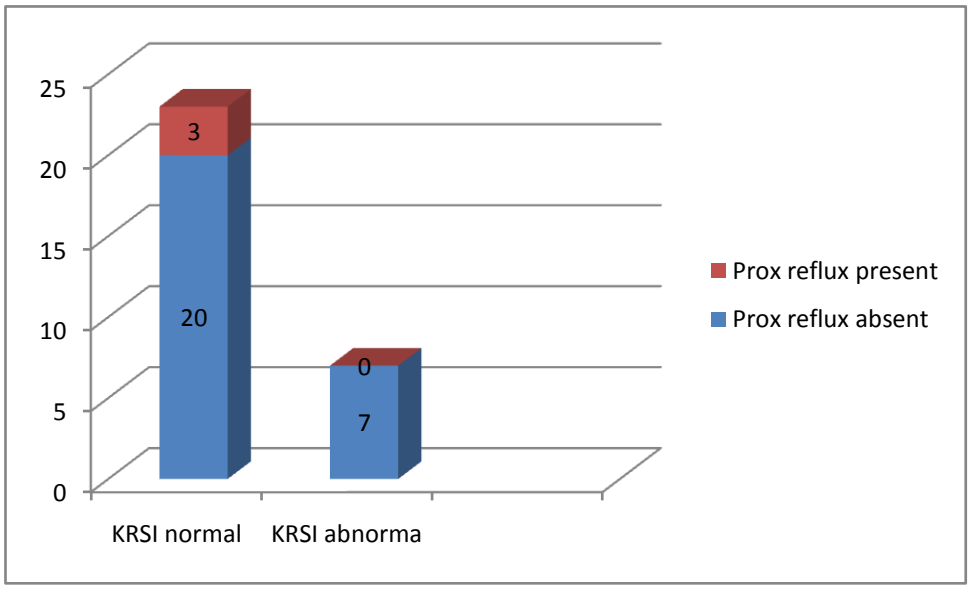

Figure XIII

Table 16:

Proximal acid exposure & Reflux Finding Score

Proximal acid exposure	Reflux Finding Score		Total
	Absent	Present	
Absent	16 (88.9%)	11 (91.7%)	27 (90%)
Present	2 (11.1%)	1 (8.3%)	3 (10%)
Total	18	12	30

When patients, whose proximal overall acid exposure percentage time was significant (>0.02%) were compared with patients with abnormal RFS, it was observed that here also, there was no statically significant co-relation between the two (p value = 1.00).

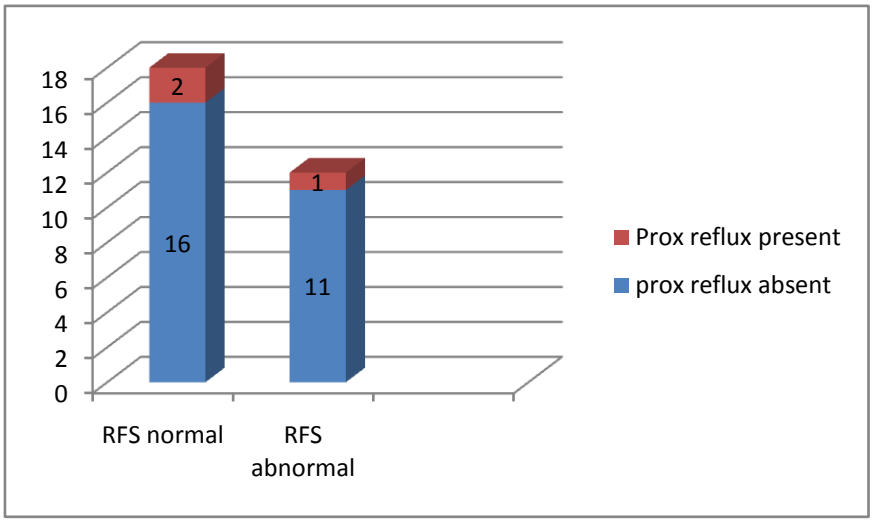

Figure XIV

DISCUSSION

Gastro-esophageal reflux disease is a common problem in patients coming to the ENT out patient department [1, 9]. They present with various complaints including cough, foreign body sensation in the throat, frequent clearing of throat, throat pain, change in voice and burning sensation in chest. When a patient undergoes evaluation for voice disorder, various causes such as vocal polyps, vocal cord nodules, Reinke's edema, muscle tension dystonia, etc are to be ruled out. Where no other cause for change in voice is identified, patient is most often given anti-reflux therapy as an empirical treatment. [1] Hence, it is important to determine the prevalence of gastro-esophageal reflux disease in voice disorder, so that the empirical treatment of voice disorder with antireflux therapy can be justified.

Gastro-esophageal reflux disease (often abbreviated to GERD or GORD) is defined as the retrograde flow of gastric contents into the oesophagus or above. It is characterized by symptoms and/or signs of mucosal injury of the oesophagus or upper aerodigestive tract secondary to this reflux.[3] Laryngopharyngeal reflux (LPR) is a syndrome associated with a constellation of symptoms including throat pain, hoarse voice, chronic cough, and other complaints and believed to be caused by the retrograde flow of stomach contents into the laryngopharynx, this being a supra-esophageal manifestation of gastroesophageal reflux disease (GERD) .[8]

According to Nora Siupsinskiene et al [25] Laryngopharyngeal reflux (LPR) is a gastrointestinal (GI) and otolaryngologic condition related to but distinct from gastroesophageal reflux disease (GERD). They also suggest that that LPR and GERD represent different entities of reflux disease. It is important to note that although most patients with LPR do not have GERD, some patients do indeed have both LPR and GERD. [25]

Peter Belafsky et al [15] and James Koufman et al [9] assessed patients with voice disorder and reported prevalence of laryngopharyngeal reflux disease to be 50%. Naeem Makhadoom et al[1] studied thirty patients with voice disorder and observed that 80% patients had gastroesophageal reflux disease. This was contrary to our study of thirty patients with voice change which revealed that eleven of them had gastroesophageal reflux disease on 24 hours dual esophageal pH metry on basis of Demester Johnson Score (more than or equal to 14.7). [23] The prevalence of (GERD) in our patients with voice disorder thus being 36.7%.

James Koufman et al [9] and Naeem Makhadoom et al[1] reported mean age of their patients with gastroesophageal reflux disease approximately 54 years and 42.5 years, respectively. The mean age of patients who had gastroesophageal reflux disease in our study was 38.7+/- 10.8 years, ranging from 19 to 61 years of age. This probably could be one of the reasons that our study revealed lower prevalence of GERD.

Among the 11 patients who had gastroesophageal reflux disease based on Demester Johnson score seven (63.6%) were male and four (36.3%) were females. However, other studies have found to prevalence of gastro-esophageal disease to be more in females.[1, 9, 15] The predominance of gastroesophageal reflux disease in males could be due to the fact that none of the female patients in our study gave history of smoking or consuming alcohol. Besides various addictions like smoking, tobacco chewing and alcoholism are relatively uncommon among females in India.

Patients were divided into 4 levels of voice users as graded by Koufman and Blalock [27,] depending on their profession, where level I were elite vocal performers (singers & actors), level II were professional voice users (teachers, lecturers, barristers),

level III were non-vocal professionals (businessmen, doctors & lawyers) and level IV were non-vocal non-professionals (housewives & farmers). It was observed that in patients who had gastroesophageal reflux disease, only one (9%) patient belonged to level II voice user and rest 10 (91%) patients belonged to level III & IV voice users (45% each). Hence, it can be interpreted from our study, that voice disorders in level II voice users are probably due to voice overuse and not due to gastroesophageal reflux disease, where as change in voice in level III and IV voice users could be attributed to gastroesophageal reflux disease.

We also evaluated all our 30 patients on the basis of smoking and alcohol consumption. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) focuses on the epidemiology of alcohol abuse, and defines risk categories based on the quantity of alcohol (number of standard drinks) consumed. Definitions of a "standard drink" vary among sources and countries, ranging from 8 to 12 g of alcohol .[24] The NIAAA defines a standard "drink" as one that contains 12 g of alcohol, and is equivalent to 360 mL (12 oz) of beer, 150 mL (5 oz) of wine, or 45 mL (1.5 oz) of 80 proof distilled spirits.[24] Questionnaire smoking data included the intensity of its use and the ages smoking started and stopped. A current smoker was someone who smoked cigarettes during the month prior to the interview date. A nonsmoker was someone who smoked less than 20 packs over their lifetime.[30] Limited data were also available on pipe, chewing tobacco, and cigar use. It was observed that among thirty patients in our study, seven were smokers, and only 2 (18.2%) of them had gastroesophageal disease .Surprisingly, of the thirty patients, only 2 patients consumed alcohol, none of whom had gastroesophageal reflux disease. Statistically, no correlation was found between smoking, alcohol consumption, voice disorder and gastroesophageal reflux disease in our study. Considering the sphincter relaxing action of smoking and alcohol consumption, this could probably be due to the

small sample size of patients in our study.[28, 29, 30] No definite data was available in the reported article correlating smoking and alcohol consumption with GERD / LPR.

The duration of change of voice in patients under study ranged from 1 month to 10 years, the median being 12 months for those with GERD and nine for those without GERD. All the 30 patients presenting with change in voice were subjected to a questionnaire which included Koufman Reflux Symptom Index consisting of 9 items and scoring from 0-5 according to severity of symptoms. A score of more than or equal to 13 was significant for laryngopharyngeal reflux.[17] A proximal overall acid exposure percentage time of >/= 0.02% on pH metry is suggestive of reflux in the proximal esophagus resulting in laryngopharyngeal reflux. In our study, according to Koufman Reflux Symptom Index, seven (30%) patients were found to have laryngopharyngeal reflux. Of these seven patients, only 2 (18.2%) were found to have gastroesophageal reflux disease according to Demester Johnson score and none of them had significant proximal overall acid exposure percentage time. This could be because Koufman Reflux Symptom Index is very subjective and can vary from patient to patient according to their threshold for various symptoms. Besides, it could also be due to small sample size.

Patients in this study underwent fibreoptic nasopharyngolaryngoscopy and were analyzed on basis of Reflux Finding Score. A score of more than or equal to seven was significant.[17] It was observed that 12 patients had laryngopharyngeal reflux according to Reflux Finding Score, of which seven (58.3%) patients had GERD as per Demester Johnson score and only one (8.3%) patient had proximal overall acid exposure percentage time significant on pH metry.

One hypothesis to explain the low incidence of confirmed gastroesophageal reflux disease and low proximal acid reflux on dual probe esophageal pH metry (accepted confirmatory test for laryngopharyngeal reflux) [22] is that the laryngopharyngeal epithelium is more sensitive to reflux-related injury than esophageal epithelium. Therefore, smaller amounts and less episodes of reflux are capable of causing damage and presenting with various laryngeal symptoms. [25] In addition, Fass et al [26] explained that vasovagal reflex is another potential mechanism responsible for supra-oesophageal manifestations of gastro-esophageal reflux disease. The reflex is triggered by acidification of the distal portion of the oesophagus and by micro-aspirations. Stimulation of vagal afferents in response to gastric content triggers a vagovagal reflex that induces bronchospasm, cough, foreign body sensation throat, frequent throat clearing etc.[26] This could probably explain the high Reflux Score and negative proximal acid reflux on pH metry in our study group.

Laryngopharyngeal reflux (LPR) and gastroesophageal reflux (GERD) are not totally different entities of reflux disease but rather represent different aspects of the spectrum of reflux disease.

Limitations

1. In dual probe esophageal pH metry, the probe was not inserted with help of esophageal manometry. Hence the placement of proximal and distal probe could vary from patient to patient and interfere with pH metry reports.

2. The length of esophagus also varies from patient to patient and gender. The length of pH metry probe being constant, the placement of probe and interpretation of results may vary.

3. Cost of the dual pH metry probe and overnight hospital stay for completion of investigations may have contributed to the small sample size.

CONCLUSION

1) The prevalence of gastro-esophageal reflux disease (GERD) in our patients with voice disorder was 36.7%.

2) There was no significant statistical co-relation between Koufman Reflux Symptom Index, Laryngopharyngeal reflux and GERD.

3) There appears to be some co-relation between Reflux Finding Score, Laryngopharyngeal reflux and GERD (*p* value- 0.063). Further evaluation including increase in the sample size may provide significant results.

4) Unlike other studies, GERD in voice disorder patients was predominant in males in our study.

5) Voice disorder in level II voice user was due to voice overuse and in level III & IV voice user were probably due to GERD.

6) There was no statistical co-relation between GERD, voice disorder, smoking and alcohol in our study.

Bibliography

1. Naeem Mahhadoom, Ali Abouloyoun, Hassan A, Khatid O. Dbafar, Zohair J. Gazzaz, Badr A,Azab. Prevalence of gastro-esophageal reflux disease in patients with laryngeal and voice disorders. Saudi Med J 2007;28 (7):1068-71

2. Cohen JT, Gill Z.The Reflux Symptom Index – a clinical tool for diagnosis of laryngopharyngeal reflux. Harefuab, 2005;144: 826-9, 912.

3. Hopkins C, Yousaf U,Pederson M. Acid reflux treatment for hoarseness. The Cochrane library Oxford. Wiley publishing,January 2006;25(1):50-54

4. Messallam TA, Stemple JC, Sobeih TM, Fluru RG. Reflux Symptom Index versus Reflux Finding Score .Ann Otol Rhinol Laryngol, 2007 Jun;116(6):436-40.

5. Neil Weir. Anatomy of larynx and tracheo bronchial tree. In: Scott brown. Gleeson M Editor,6th ed Butterworth Heinemann Publisher,1997,Vol1,ch12,p1-18

6. Rubin Js, Stataloff RT, Korovin GS. Voice disorders : presentation and classification. In: Diagnosis and treatment of voice disorders, 2nd ed, Delmar learning Publisher,2003,p17-26

7. Jason F. Vollweiler, Michael F. Vaezi. Anatomy & physiology of esophagus. In :Cummings CW .Editors. Otolaryngology head and neck surgery, 4th ed, Elsiver Mosby, 2005,ch 80, p1836 – 37

8. Maximillian Groome, James P. Cotto, Marina Borland, Shirley McLeod, David A. Johnston, John F. Dillon. Prevalence of Laryngopharyngeal Reflux in a population with Gastroesophageal Reflux. Laryngoscope. August 2007;117(8):1424–28.

9. James A. Koufman, Milan R. Amin, Margeurite Netti. Prevalence of reflux in 113 consecutive patients with laryngeal and voice disorders. Otolaryngology– Head and Neck Surgery, October 2000;123(4):385-8

10. Seth M. Cohen, C.Gaelyn Garrett. Hoarseness: Is It Really Laryngopharyngeal Reflux? Laryngoscope, 2008;118:363–6

11. Altman KW, Atkinson C, Lazarus C. Current and emerging concepts in muscle tension dysphonia: a 30 month review. J Voice, 2005;9:261–7.

12. Angsuwarangsee T, Morrison M. Extrinsic laryngeal muscular tension in patients with voice disorders. J Voice, 2002;16:333–43.

13. Belafsky PC, Postma GN, Reulbach TR, Holland BW, KoufmanJA. Muscle tension dysphonia as a sign of underlying glottal insufficiency. Otolaryngol Head Neck Surg, 2002;127:448–51.

14. Ruta Pribuisiene, Virgilijus Uloza, Laimas Jonaitis. Typical and atypical symptoms of laryngopharyngeal reflux disease, Medicina,2002;38:7

15. Peter C. Belafsky, Gregory N. Postm, James A. Koufman. The Validity and Reliability of the Reflux Finding Score (RFS).Laryngoscope, August 2001;111:1313–17

16. Jae Ho Chung, Kyung Tae,Yong Seop Lee, Jin Hyeok Jeong, Seok Hyun Cho, Kyung Rae Kim, Chul Won Park, and Dong Soo Han. The significance of laryngopharyngeal reflux in benign vocal mucosal lesions. Otolaryngology–Head and Neck Surgery,2009;141:369-73.

17. Peter CA, Gregory NA, James AA Koufmann. Validity and reliability of Reflux Symptom Index, Voice journal, June 2002;16(2):274–77

18. Colwell HH, Mathias SD, Pasta DJ, Henning JM, Hunt RH. Development of a health-related quality-of-life questionnaire for individuals with gastroesophageal reflux disease: a validation study. Digestive Diseases and Sciences,1999 Jul;44(7):1376-83.

19. Michael J Shaw, Nicholas J Talley, Timothy J Beebe, Todd Rockwood, Rolf Carlsson , Susan Adlis, A Mark Fendrick, Roger Jones, John Dent, Peter Bytzer. Initial validation of a diagnostic questionnaire for gastroesophageal reflux disease. The American Journal of gastroenterology,2001;96:52–57

20. Mesut S T, M. Cemkockar, Olgakoc¸ Kar ,Alpeir Celik. Laryngopharyngeal reflux finding scores correlate with gastroesophageal reflux disease and Helicobacter pylori expression. Acta Oto-Laryngologica, 2006;126: 958-61

21. Jennifer Oates. Auditory-Perceptual Evaluation of Disordered Voice Quality, Pros, Cons and Future. Directions Folia Phoniatr Logop, 2009;61:49–56

22. George Sun, Srikant Muddan, James C. Slaughter, Sean Casey, Eric Hill, Farnoosh Farrokhi, C. Gaelyn Garrett, Michael F. Vaezi. A New pH Catheter for Laryngopharyngeal Reflux: Normal Values. Laryngoscope,August 2009;119:1639-43

23. Johnson LF, Demeester TR. Twenty-four-hour pH monitoring of the distal esophagus. A quantitative measure of gastroesophageal reflux. The American journal of gastroenterology, October 1974;62(4):325-32

24. Dufour, MC. What is moderate drinking? Defining "drinks" and drinking levels. Alcohol Res Health, 1999;23:5.

25. Nora Siupsinskiene , Kestutis Adamonis , Robert J. Toohill. Quality of Life in Laryngopharyngeal Reflux Patients. Laryngoscope, March 2007;117(3);480–84.

26. R. Fass, S. R. Achem , S. Harding, R. K. Mittal, E. Quigley. Review article: Supra- esophageal manifestations of gastro-oesophageal reflux disease and the role of night-time gastro- oesophageal reflux. Alimentary Pharmacology & Therapeutics, December 2004;20(9):26–38

27. Koufman, Blalock.Voice disorders: presentation and classification. In : Greene, Mathieson.Editors. The Voice and Its Disorders, 6th ed, Whurr Pubhlishers, p 121-144.

28. Hashimoto Hiroko, Nakazakikaoru. Negishi Michiko, Torai Akira Wada, Takashi, Matsushima Masato.A study of effect of smoking and alcohol on gastroesophageal reflux disease. Tokyo Jikeikai Medical Journal, 2004;119(1):77-85

29. Ai Kubo, T.R. Levin, Gladys Block, Gregory Rumore, Charles P, Quesenberry Jr., Patricia Buffler, Douglas A. Corley. Cigarette Smoking and the Risk of Barrett's Esophagus. NIH Public Access, April 2009;20(3):303–11

30. Ahmad Mostaghni, Davood Mehrabani, Farnaz Khademolhosseini, Seyed Jalil Masoumi, Fariba Moradi, Najaf Zare, Mehdi Saberi-Firoozi. Prevalence and risk factors of gastroesophageal reflux disease in Qashqai migrating nomads, southern Iran. World J Gastroenterol, February 28,2009;15(8):961-65

Appendix – A

Informed Consent

Prevalence of gastro- esophageal reflux disease in patients with laryngeal & voice disorders

Study Number:

Subject's Initials:

Subject's Name:

Date of Birth / Age:

Please initial box

(i) I confirm that I have read and understood the information sheet dated for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am

free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

Information sheet

"Gastro-esophageal reflux disease" is a illness in which the acid from stomach regurgitates back into the esophagus (food pipe) due to various reasons like weakness of esophageal sphincters, increased secretion of acid, neural problems, etc. This acid can also regurgitate from esophagus (food pipe) to larynx (wind pipe) and pharynx in certain individuals, when it is called "**laryngopharyngeal reflux**". This can lead to various symptoms like cough, difficulty in swallowing food, sore throat, change in voice, weak voice, chest pain, neck pain etc. However, presently there are controversies on association of voice disorder and gastro-esophageal reflux disease and their management.

A study is thus being conducted in our hospital, in order to asses the prevalence of gastro-esophageal reflux disease in patients with voice disorder. At the end of study, we hope to improve the management of these patients.

The study includes all the patients coming to voice clinic with primarily voice and laryngeal disorder. The subjects will have to answer a questionnaire and undergo a detail ear, nose and throat examination. Later he/she will then undergo two procedures – Flexible nasopharyngolaryngoscopy and 24 hours esophageal pH metry.

a) Flexible nasopharyngolaryngoscopy :

It is a simple office procedure to visualize vocal fold movements using flexible nasopharyngolaryngoscope under local anesthesia.

b) 24 hours esophageal pH metry;

Dual pH catheter (2mm) is passed through the nasal cavity into pharynx and then into esophagus. The pharyngeal probe is positioned 2 cm above the Upper esophageal sphincter, while the lower probe is placed 5 cm above the lower esophageal sphincter.

Esophageal pH is onitored for 24 hrs in various postures and duration of reflux is assessed.

These procedures are not associated with any added risk or complications, apart from those normally associated with endoscopy.

The subject will be assessed on the basis of above procedures and confirmed to have gastro-esophageal reflux disease and prescribed treatment as well.

Since all of the above procedures are part of routine investigations for evaluation of voice disorder and gastro-esophageal reflux disease, the subject will have to bear the cost of the procedures.

If you are willing to participate in this study, you will be required to sign in the following consent form.

Appendix – B

Proforma for data collection

Name

Hospital No

Age

Sex

Profession

Level of voice user

HISTORY:

Change in voice –

Burning sensation in substernal / epigastric

Regurgitation

Dysphagia

Throat pain

Cough

Foreign body sensation in throat

Throat clearing

ETIOLOGICAL FACTORS:

Voice overuse

Smoking (in terms of pack years)

Alcohol intake (amount)

Fatty food

Drugs

Kaufmann reflux symptom index

Suspected and control patients are given a questionnaire to answer. It contains about 9 questions. Patient is supposed to award scores according to their symptoms.

Within last month how did the following problems affect you?

0 = No problem, 5 = severe problem.

1. Hoarseness of voice / voice problems :	0	1	2	3	4	5
2. Clearing your throat:	0	1	2	3	4	5
3. Excess throat mucous / post nasal drip:	0	1	2	3	4	5
4. Difficulty in swallowing food / liquids / pills:	0	1	2	3	4	5
5. Cough after eating / lying down:	0	1	2	3	4	5
6. Breathing difficulty / choking:	0	1	2	3	4	5
7. Annoying cough:	0	1	2	3	4	5
8. Sticky sensation in throat / lump in throat:	0	1	2	3	4	5
9. Heart burn / chest pain	0	1	2	3	4	5

Reflux symptom index score of more than 10 indicates laryngopharyngeal reflux.

Auditory perceptual assessment

Overall grade

Normal

Slight

Moderate

- Characters

Normal

Breathy

Strained

Strained and leaky

- Pitch

Decrease

Diplophonia

Increase

Reflux finding score

This scoring is prepared by the surgeon after performing a laryngeal examination.

1. Subglottic oedema: 0 - absent, 2 - present.

2. Ventricular obliteration: 2 - partial, 4 - complete

3. Erythema / Hyperemia: 2 - arytenoids involved, 4 - diffuse

4. Vocal fold oedema: 1 - mild, 2 - moderate, 3 - severe, 4 - polypoidal

5. Diffuse laryngeal oedema: 1 - mild, 2 - moderate, 3 - severe, 4 - obstruction

6. Posterior commissure hypertrophy:

1 – mild , 2 - moderate, 3 - severe and 4 - obstruction.

7. Granuloma / Granulation: 0 - absent, 2 - present

8. Thick mucous: 0 - absent, 2 - present.

Total score: from 0 - 26

A score of 7 indicates possible presence of laryngopharyngeal reflux.

24 ours esophageal pH metry :

1) Acid exposure percentage time (overall) – proximal

- Distal

2) Demester and Johnson score

Appendix C - Data sheet

S.No.	Vot	Evo	Esm	Eal	Eff	Edg	Khov	Kcyt	Ketm	Kdis	kcae	kbd	kac	klit	khb	KRSI	Aog	ach	apt	Rso	rvo	reh	rvfo
1	4	1	0	0	0	0	4	0	0	0	0	0	0	3	0	7	2	3	1	0	0	4	0
2	4	1	0	0	1	0	4	2	0	3	0	0	0	2	0	11	1	3	1	0	0	4	1
3	4	1	1	0	1	0	3	2	1	0	0	3	0	4	4	16	1	3	1	0	0	4	0
4	3	1	1	0	1	0	3	2	0	0	3	0	1	2	0	11	2	3	1	0	0	2	1
5	4	1	0	0	1	0	5	2	0	0	0	0	0	2	0	9	1	1	0	0	0	4	2
6	2	1	0	0	0	1	3	3	0	1	0	0	0	3	0	10	1	3	1	0	0	4	1
7	3	1	0	0	1	0	5	3	0	0	0	0	1	3	0	12	1	3	0	0	0	4	0
8	3	1	0	0	1	0	4	2	0	0	0	0	0	2	0	8	2	3	0	0	0	4	0
9	4	1	0	0	0	0	5	0	0	0	0	0	0	2	0	7	1	3	1	0	0	2	0
10	2	1	0	0	1	0	5	0	0	0	0	0	0	0	0	5	1	3	1	0	0	2	0
11	4	1	0	1	1	0	4	2	2	0	0	0	0	2	2	10	1	3	1	0	0	4	1
12	3	1	1	0	1	0	4	3	0	0	0	0	2	0	0	9	2	3	1	0	0	2	1
13	3	1	1	0	1	0	2	2	0	0	0	0	0	0	2	6	1	3	1	0	0	4	0
14	3	1	0	0	1	0	4	2	0	0	0	0	1	2	0	9	3	3	1	0	0	4	0
15	4	1	0	0	1	0	3	1	0	0	0	0	0	2	0	6	1	1	1	0	0	2	0
16	2	1	1	0	1	0	5	3	0	0	0	0	0	2	0	10	1	3	1	0	0	2	1
17	3	1	0	0	0	0	5	2	0	0	0	0	0	2	0	9	1	3	1	0	0	2	0
18	4	1	0	0	1	1	2	2	0	0	0	0	0	2	4	10	1	2	0	0	0	2	0
19	2	1	0	0	0	0	5	2	0	0	2	0	0	1	0	10	3	3	1	0	0	2	1
20	4	1	0	0	1	1	4	3	0	3	2	0	2	2	0	16	2	3	1	0	0	4	0
21	4	1	0	0	0	0	4	3	0	0	0	0	3	2	0	12	2	3	1	0	0	4	2
22	3	1	0	0	0	0	4	3	2	0	1	0	1	3	3	17	1	3	1	0	0	4	0
23	3	1	1	0	1	0	4	0	0	0	0	0	2	0	0	6	1	1	0	0	0	2	0
24	3	0	0	0	0	1	3	0	0	0	0	3	0	3	4	13	1	3	1	0	0	4	2
25	2	1	0	0	0	0	4	3	2	0	0	0	0	3	1	13	2	3	1	0	0	4	0
26	4	0	0	0	0	0	4	2	0	0	2	0	0	4	0	12	1	3	1	0	0	4	0
27	3	1	1	1	1	0	3	1	1	0	0	0	0	2	2	9	1	1	1	0	0	0	0
28	2	1	0	0	0	0	4	3	2	0	0	0	1	3	0	13	1	3	1	0	0	0	0
29	4	1	0	0	1	0	4	2	2	0	0	0	0	3	0	11	1	3	1	0	0	2	0
30	4	1	0	0	1	1	2	2	2	4	1	0	3	1	0	15	1	1	1	0	0	4	2

rvfo	rdlo	rpch	rg	rtm	RFI	Aet_p	Aet_d	Ne_p	Ne_d	Djs	duration
0	0	0	0	2	6	0	0	0	15	1	1
1	0	0	0	2	7	0	0	0	15	0	1.5
0	0	0	2	2	8	0	0	0	29	1	12
1	0	0	2	2	7	0	0	0	30	1	36
2	0	0	0	0	6	0	1	0	27	1	1
1	0	2	0	0	7	0	0	0	14	1	120
0	0	1	0	2	7	0	0	0	36	1	2
0	0	0	2	0	6	0	0	0	3	0	3
0	0	0	0	0	2	0	0	0	0	0	120
0	0	0	2	0	4	0	0	0	0	0	4
1	0	0	2	2	9	1	0	1	15	0	3
1	0	0	2	0	5	0	0	1	11	0	48
0	0	0	2	0	6	0	0	0	6	0	7
0	0	0	2	2	8	0	0	0	42	1	2
0	0	0	0	2	4	0	0	0	5	0	12
1	1	0	0	0	4	0	0	1	4	0	6
0	0	0	2	2	6	1	1	15	88	1	24
0	0	0	0	2	4	0	0	0	19	1	24
1	0	0	2	0	5	0	0	0	0	0	12
0	0	2	0	2	8	0	0	0	0	0	24
2	0	0	0	2	8	0	0	0	9	1	18
0	0	0	0	0	4	0	0	0	18	0	5
0	0	0	0	0	2	0	0	0	12	0	60
2	1	0	0	2	9	0	1	0	21	1	9
0	0	0	2	2	8	0	0	0	0	0	36
0	0	0	0	0	4	0	0	0	5	0	4
0	0	0	0	0	0	1	0	0	5	0	24
0	0	0	2	2	14	0	0	0	2	0	2
0	0	0	0	2	4	0	0	0	6	0	9
2	0	2	0	0	6	0	0	0	9	0	12