



## A prospective study of Barrett's oesophagus in patients with Gastro Oesophageal Reflux Disease.

### KEYWORDS

Gastro Oesophageal Reflux Disease(GORD), Barrett's oesophagus, oesophageal adenocarcinoma, endoscopy, hiatal hernia.

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### ABSTRACT

The most common of oesophageal diseases is Gastro Oesophageal Reflux Disease (GORD). The GORD, if left unchecked, progresses to reflux oesophagitis which in turn develops into Barrett's oesophagus. The most important complication of Barrett's oesophagus is carcinoma oesophagus, which has very poor prognosis as compared to the other carcinoma. In our prospective study, patients with symptoms of GORD who did not have any serious co morbid condition were studied with the upper gastro intestinal endoscope as the primary tool of investigation. The most common finding clinching a diagnosis of GORD is the oesophagitis. Hiatal hernia is a common association to both the conditions. Males, increasing age, chronic GORD, increased BMI, smoking were proved risk factors for the development of Barrett's oesophagus. The proper treatment with endoscopic surveillance can prevent the further development of the pathology into adenocarcinoma.

### INTRODUCTION:

The gastro oesophageal reflux is considered a disease, if the reflux material causes troublesome symptoms and/or complications. This definition is given by the Montreal International consensus.<sup>1</sup> The Barrett's oesophagus develops in 10 to 15 percent of patients with Gastro Oesophageal Reflux Disease(GORD). This is an important complication because, this is the first step in the metaplasia – dysplasia – carcinoma sequence, which ultimately ends in the formation of adenocarcinoma of the oesophagus. Barrett's oesophagus is defined as macroscopically, the presence of salmon pink columnar mucosa of any length proximal to the gastrooesophageal junction. The microscopic criteria of presence of intestinal metaplasia is also included in the definition.<sup>2,3</sup> The types are, long segment(>=3cm), short segment(<3cm), ultra short segment (cardiac mucosa with intestinal metaplasia), and sub squamous(intestinal metaplasia in squamous epithelium) Barrett's oesophagus.<sup>4</sup> The condition is easily diagnosed by the upper gastro intestinal endoscopy. The risk factors include chronic GORD, male gender, increasing age, obesity, smoking and hiatal hernia. There is decrease in risk with Helicobacter pylori Cag A+ strain infection.

The permanent attenuation of the collar sling fibres in the Lower Oesophageal Sphincter(LOS), is the primary pathology in GORD.<sup>5</sup> In such patients, the intake of a heavy fatty meal, which delays gastric emptying, increases distension of stomach and hence a transient sphincter uptake, which further attenuates the defence mechanism against the reflux in the gastro oesophageal junction.<sup>6</sup> This leads to the symptoms and complications of GORD.

The various theories for formation of Barrett's oesophagus include, trans differentiation of stem cells or migration of submucous or gastric cells. The first step involved are the replacement of squamous mucosa with cardiac mucosa, which is channelized by the gene Bone Morphogenetic Protein 4(BMP 4).<sup>7</sup> The next step is the intestinalization of cardiac mucosa. There may be differentiation into oxynto cardiac cells, mediated by the Sonic Hedgehog(Shh) gene<sup>8</sup>, or into intestinal goblet cells, programmed by the Caudal - type homeobox 2(Cdx - 2)<sup>9</sup>. Shh is activated if the pH is <3 and Cdx - 2 is activated if the pH is >6. The treatment for the condition is PPI's and prokinetics.

### AIM AND OBJECTIVES:

The aim of the study is to, prospectively study the patients with the symptoms of GORD, with the aid of an endoscope, in an attempt to,

1. study natural history i.e. regression/progression of the condition and its complications, including Barrett's oesophagus, with treatment.

2. histopathological study of the endoscopic biopsies, in the view of studying the progression of the disease.

### MATERIALS AND METHODS:

The patients referred from all other departments for endoscopy in M.K.C.G. medical college hospital, Brahmapur, Odisha from September 2014 to August 2016 are selected for the study, according to the following inclusion and exclusion criteria. The inclusion criteria includes, patients with symptoms like heart burn, regurgitation, water brash, dysphagia, atypical symptoms of respiratory system like cough, asthma and repeated respiratory infections. The patients who were haemodynamically unstable, with uncorrected coagulopathies, epigastric pain radiating to left shoulder, terminally ill patients, patients in whom informed consent couldn't be obtained were excluded.

The patients in the study underwent a meticulous scrutiny by history and examination. Then after obtaining an informed consent, they were subjected to video endoscopy by the standard method.

The criteria used in the study are given below:

1. Gastro oesophageal junction – the upper end of proximal gastric folds and the lower end of oesophageal palisade vessels.

2. Any oesophagitis, mucosal breaks is taken as evidence of GORD.

3. Any cephalad displacement of "Z line" more than 1cm, any tongues of salmon pink patch of mucosa extending from the "Z line", any Salmon pink patch of mucosa in the middle of normal oesophageal mucosa is taken as potential site of Barrett's oesophagus, and biopsy is taken.

4. Flap valve is graded by visualising it by retroflexion of endoscope at the stomach (Incompetent LOS).

5. Gastric rugal folds residing 2cm proximal to the hiatus is taken as hiatal hernia.

Multiple endoscopic biopsies to be taken, wherever indicated. The follow up period was in an interval of 3months.

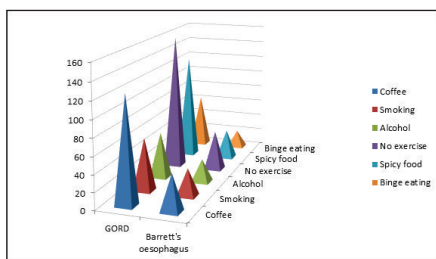
### OBSERVATION:

Total number of patients included in the study were 623. The

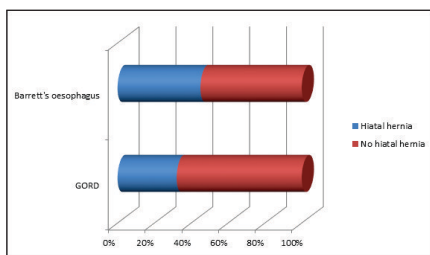
afore mentioned inclusion and exclusion criteria was followed in selecting these patients. The number of patients with GORD, Barrett's and carcinoma oesophagus at initial presentation were 196, 60 and 12 respectively.

**Table 1. Age and sex distribution of the oesophageal pathologies.**

AGE GROUP	GORD MALES	GORD FEMAL ES	BARRET T'S OE SOPHAG US - MALES	BARRET T'S OES OPHAG US - FE MALES	CARCIN OMA OESOPH AGUS - MALES	CARCIN OMA OE SOPHAG US - FE MALES
15 – 20 YRS	2(1%)	1 (0.5%)	-	-	-	-
21- 30 YRS	4(2%)	2(1%)	-	-	-	-
31 -40 YRS	3(1.5%)	4(2%)	2(3.3%)	1(1.6%)	-	-
41 – 50 YRS	32(16.3 2%)	18 (9.1%)	4(6.6%)	2(3.3%)	-	-
51 – 60 YRS	34(17.3 4%)	19(9.87 %)	9(15%)	3(5%)	1(8.3%)	1(8.3%)
61 – 70 YRS	30 (15.3%)	18 (9.1%)	16 (26.6%)	6 (10%)	6 (50.2%)	2 (16.6%)
71 – 80 YRS	19(9.87 %)	10(5.1 %)	12 (20%)	5(8.6%)	1(8.3%)	1(8.3%)



**Chart 1. Risk factor association in GORD and Barrett's oesophagus.**



**Chart 2. Hiatal hernia association with GORD and Barrett's oesophagus.**

**Table 2. Various symptom presentation in the oesophageal disorders**

Symptoms	No endoscopic finding N=355 (100%)	GORD N=196 (100%)	Barrett's oesophagus N=60(100%)
Actual triad(heart burn, regurgitation, dysphagia)	7(1.9%)	53(27.3%)	10(16.6%)
Heart burn	114(32.1%)	7(3.5%)	1(1.6%)
Regurgitation	28(7.8%)	9(4.5%)	1(1.6%)
Heart burn + regurgitation <1 episode/week >=1 episode /week 1 episode at night/month	17(4.7%)	29(14.8%)	16(26.6%)

Atypical symptoms	186(52.5%)	4(2%)	1(1.6%)
Heart burn + regurgitation + atypical symptoms	3(1%)	94(47.9%)	31(52%)

**Table 3. various endoscopic findings in the patients undergoing endoscopy for symptomatic GORD..**

ENDOSCOPIC FINDING	NO. OF PATIENTS(% OF PATIENTS)
NO FINDING	355(56.98%)
OESOPHAGITIS	143(22.9%)
EROSIONS	44(7.16%)
ULCERS	9(1.4%)
BARRETT'S OESOPHAGUS	60(9.6%)
CARCINOMA OESOPHAGUS	12(1.96%)

**Table 4. Follow up of patients**

Follow up after	Decrease in severity of oesophagitis	No oesophagitis	Barrett's oesophagus recovery
1 month	22	36	-
2 months	18	30	-
3 months	12	46	12
6 months	8(13.8%)	50(86.2%)	17

Many of the patients are lost to follow up and only 58 patients could be followed up. The patients who had been followed up too found it difficult to modify their life style and only PPI treatment has been instituted. The effect of the drugs were excellent and the patients in the unsatisfactory group were always defaulters of the drug.

**DISCUSSION:**

Our study has its findings in par with the international studies of , Anderson et al(2007)<sup>10</sup>, Edelstein et al(2007)<sup>11</sup>, Kendall et al(2012)<sup>12</sup> and even older studies like, Leiberman et al(1997)<sup>13</sup>.

The association of alcohol and smoking with GORD is obvious in western studies. But in a conservative culture of India, the intake of alcohol is less. Important factor is that, the females are not habituated to alcohol or smoking. The decreased smoking habits and intake of alcohol in Indian society, is compensated by the high intake of the spicy foods and life style habits like lying down immediately after meals. This has made the overall incidence of GORD similar to that of western population.

There is an increased risk of both GORD and Barrett's oesophagus with increase in BMI. The people who are of the habit of taking more fatty food have more of BMI. The intake of fatty food is a risk factor for both the conditions.

The association of hiatal hernia in oesophagitis and Barrett's oesophagus is higher in the western study. Our study shows an association lesser than the western studies but a definite association is obvious.

**SUMMARY:**

A total of 623 patients were studied. 56.98% of these patients, i.e., 355 patients had only symptoms of GORD but endoscopy had no findings.

GORD was found in 196 patients, i.e., 31.46% of patients. Male : Female ratio was, 1.77 :1. The disease was prevalent in the age group, 51 – 60 years. In present study, the risk association was found with, life style like lack of exercise, dietary habits like tea and coffee, spicy food and addiction to alcohol and smoking and other forms of tobacco. The most common symptom is heart burn. It was seen in 93.5% of patients. The most common endoscopic finding was, oesophagitis and is found in 143 patients, i.e. 22.9% of patients studied. Hiatal hernia was found to be associated with GORD in nearly 32.1% of patients studied.

Barrett's oesophagus was found in 9.6% of patients with GORD, i.e., 60 patients. Male : Female ratio was, 3:1. The most common age group to be affected was, 61 - 70 years. The risk association was found as the same with GORD. Heart burn was present in 96.8% of patients, which makes it the most common presenting symptom. The most common endoscopic finding was, short segment oesophagus and there was only "Z line" changes and there were no islands or tongues of salmon pink mucosa. Only "Z line" changes was found in 71.7% of patients. The longer the symptoms, the longer is the segment of Barrett's oesophagus. Also, the findings of islands and tongues of Barrett's oesophagus increase with the increasing duration of symptoms. The intestinal metaplasia was seen in 22.2% of patients.

#### CONCLUSION:

The most common oesophageal disorder is GORD. This makes the UGIE an inevitable tool in symptomatic GORD patients. The different stages of the disease progression can be easily diagnosed by the UGIE biopsy. And when the dysplasia is confined to the mucosa of the oesophagus, it can be easily ablated by endoscopic mucosal resection. The patient, though have to be kept in constant endoscopic surveillance, the morbidity and mortality of invasive procedures on oesophagus is overcome. The oesophageal disorders are identified and proper minimally invasive therapy is instituted at the early stage of the disorder. The endoscope can thus keep in check the oesophageal disorders, which have been on the rise for the last four decades. Soon endoscopy will become, what the pap smear is of cervical cancer, for the cancers plaguing the upper gastro intestinal system.

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