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Barrett's Esophagus in Patients with Gastroesophageal Reflux Disease

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ABSTRACT

Background: Barrett's esophagus a is metaplasia of normal squamous cells that line the lower part of the esophagus and carries a major risk for adenocarcinoma of esophagus. In Asian population, the prevalence of Barrett's esophagus and adenocarcinoma are less common than in Western countries but has been increasing.

Methods: This is a hospital based descriptive study comprising of 120 consecutive patients with symptoms of gastroesophagial reflux disease belonging to both sexes of any age group. The diagnosis of gastroesophagial reflux disease was based on the symptoms like heart burn and regurgitation. Upper gastrointestinal endoscopy was done in all the patients. Four quadrant biopsies were taken from the esophagogastric junction in suspected case of Barrett's esophagus. The diagnosis of Barrett's esophagus was confirmed histopathologically.

Results: There were 44.2% males and 55.8% females, age ranging from 22 to 85 years mean being 44.33±13.37. Of them, gastroesophagial reflux disease was mild in 54.16%, moderate in 21.16% and severe in 16.66%. Upper Gastrointestinal endoscopy revealed non erosive gastroesophagial reflux disease in 50%, erosive in 45%, hiatal hernias in 5% and Barrett's esophagus in 1.6%. Both patients with Barrett's esophagus were elderly and had short segment (<3cm) involvement with no evidence of dysplasia or adenocarcinoma histopathologically.

Conclusions: Endoscopic surveillance with detailed inspection and systematic biopsies is recommended for most patients with Barrett's esophagus. Esophageal carcinoma if detected should be treated at the earliest.

Keywords: Barrett's esophagus; erosive esophagitis; endoscopy; GERD; quadrant biopsies.

INTRODUCTION

Barrett's esophagus is the designation for replacement of the normal squamous epithelium of the distal esophagus by metaplastic intestinal columnar glandular epithelium. Norman R Barrett first described this entity in 1950.[1] The metaplastic epithelium progress through a multi step process to low grade dysplasia, high grade dysplasia and ultimately to adenocarcinoma though the risk is only 0.5% per patient year.[2] The combination of esophageal endoscopy indentifying this mucosal change with a proper knowledge of the gastroesophageal junction and confirming the intestinal metaplasia by biopsy is currently the primary modality for routine disease surveillance.

Barrett's esophagusis a serious complication of Gastroesophageal Reflux Disease (GERD), which is found all over the world though more common in the west[3] and is a major risk for adenocarcinoma of the distal esophagus. Little is known about the aetiology of Barrett's oesophagus. The established predicting factors for Barrettt's esophagus are age >40 years and heartburn,[4] long duration GERD symptoms,[5] male gender[6] and obesity[7] although Barrett's esophagus has also been reported in the general population in asymptomatic persons.[8] The prevalence and incidence of dysplasia or adenocarcinoma in patients witth traditional Barrett's esophagus are significantly higher than in patients with short segment Barrett's esophagus.[9]

There are limited data from Nepal regarding study of GERD and correlation with Barrett's esophagus. This study aims at symptomatology together with invasive upper gastrointestinal endoscopy and biopsy in patients with GERD for the identification of Barrett's esophagus.

METHODS

This is a hospital based descriptive study comprising of 120 consecutive patients with symptoms of GERD attending the OPD and admitted in Gastroenterology ward of Teaching Hospital, College of Medical Sciences,

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Bharatpur, Chitwan, during the period between January 2012 to June 2014. The ethical clearance was taken from the Ethical Review Board and written consent was taken from each respondent or their relatives.

Patients presenting with symptoms of GERD, belonging to both sexes of any age group were included. The diagnosis of GERD was based on the symptoms like heart burn (burning feeling, rising from the stomach or lower chest and radiating towards the neck, throat, and occasionally back), regurgitation (bitter or sour tasting fluid spontaneously coming into the mouth) especially after meals and worsened by stooping or supine position, dysphagia, chest pain and endoscopic findings. Exclusion criteria being patients with known peptic ulcers, esophageal or gastric malignancies, cirrhosis of liver with portal hypertension, frank upper GI bleeding, major psychiatric illness, patients already on H pylori eradication therapy and proton pump inhibitors during the last 4 weeks, non steroid anti inflammatory drugs (NSAIDs), calcium channel blockers, alpha and beta agonist, nitrates, caffeine and pregnancy.

Each patient was subjected to a detailed clinical history regarding symptoms of GERD and comorbidities if any along with a thorough clinical examination including the body mass index (BMI).

Upper Gastrointestinal (UGI) endoscopy was done in all the patients after explaining the procedure. Patient was kept nil per oral for at least 4 to 6 hours before the procedure. Premedication with topical anesthesia with 2% lignocaine was applied before the procedure.The endoscopic findings were classified as nonerosive reflux disease (NERD) if the mucous membrane seemed intact and Erosive esophagitis if there was any evidence of mucosal injury. Erosive esophagitis was further classified by using the Los Angeles classification.[10]

Barrett's esophagus was searched for when a suspected columnar lined esophagus was identified during endoscopy, based on salmon pink mucosa[11] in either a circumferential upward shift of the squamocolumnar junction or in adjacent mucosal tongues. Four quadrant biopsies (four biopsies from each quadrant) was taken from the esophagogastric junction and the specimen was transferred to histopathologist within 24 hours in 10% buffered formalin. The samples were stained with Hematoxylin& Eosin (H&E). The diagnosis of Barrett's esophagus was confirmed histopathologically by evidence of intestinal metaplasia based on the presence of goblet cells which were characterized by distended lateral boarder, compressed basal nucleus and basophilic apical cytoplasm in columnar epithelium. Barrett's esophagus was classified based on the length on endoscopic impression of intestinal metaplasia from the top of the suspected columnar lined epithelium to the gastroesophageal junction into long segment (LSBE) which is defined as equals to or more than 3 cm and short segment Barrett's esophagus (SSBE) which is less than 3 cm.[12]

Results were expressed as mean ± standard deviation. Data was analyzed using Software Package for Social Sciences (SPSS) version 20.

RESULTS

Of these 120 patients, there were 53(44.2%) males and 67 (55.8%) females with mean age being 44.33±13.37 (range 22-85) years. GERD was mild in 54.16%, moderate in 21.16% and severe in 16.66%. BMI was normal in the majority with only 5(4.2%) having grade I obesity. Upper GI endoscopy revealed non erosive mucosa in 60 (50%), hiatal hernia in 6 (5%) and erosive mucosa in 54 (45%). Erosive mucosal lesions were further classified as per Los Angeles classification.[10] Thirty three (27.5%), 11 (9.2%), 7 (5.8%) and 3 (2.5%) patients had Los Angeles A, B, C, and D respectively. (Table 1)

In the erosive mucosal lesion group, Barrett's esophagus was detected in 2 (1.6%) patients. Both were elderly, with long GERD symptoms (>5 years) with short segment involvement and comorbidities. There was no evidence of dysplasia or malignancy in histopathological examination. The details of both patients with Barrett's esophagus are shown below (Table 2).

Table 1. Endoscopic findings in patients with GERD (n=120).

Endoscopic finding	No	%
Non Erosive Reflux Disease (NERD)	60	50.0
Erosive Reflux Disease	54	45.0
LA-A	33	
LA- B	11	
LA- C	7	
LA-D	3	
Hiatal Hernia	6	5.0
Total	120	100.0

Table 2. Profile of patients with Barrett's esophagus (n=2).

Case No	Sex	Age	GERD symptoms		Smoking	Alcohol	BMI	Segment involved	Hiatus hernia	Erosive esophagitis (LA class)	Comorbidity
			duration	severity							
1	Male	78	>10years	severe	Past smoker	No	18.7	short	No	Present (LA-C)	Hypertension
2	Female	85	>5 years	severe	Non smoker	No	22	short	No	Present (LA-C)	Cholelithiasis

LA class-Los Angeles classification[10]

DISCUSSION

Two cases of Barrett's esophagus in a series of 120 patients with chronic GERD are reported, the incidence being 1.6% only. Variable incidence of Barrett's esophagus have been reported in series from different geographic areas for patients with chronic GERD symptoms viz 2.4 to 13.2% in North American and European countries,[13] 2.4% in Iran,[14] 1% from China,[8] 7.3% from Egypt,[15] 1.5% from Turkey,[16] 6.6% from Malaysian population of mixed ethnicity,[17] 2.6% to 23% in Indian patients[18] while a much higher incidence of 25.3% from Germany[19] and 28.18% from an US study[20] have been reported.

The prevalence of Barrett's esophagus in individuals without GERD is uncertain. It was 0.5% reported from China,[8] 0.06% from Hong Kong,[21] 1.6% in Swedish population,[22] 5.6% to 15.25% in elderly people from US[23] undergoing screening colonoscopy for colorectal cancer and with no data from India as yet available.

The risk factors for Barrett's esophagus in our patients were looked for. Both these patients were elderly (mean age being 81.5 years), with long GERD symptoms (>5 years) both had erosive esophagitis (LA-C), with short segment involvement and comorbidities. Sex, dietary factors, alcohol or tobacco use, hiatus hernia and body mass index were not associated with BE. Age > 45 years in patients with BE are reported in most of the series.[4,7,22] However bimodal age distributions is also reported from India.[24]

The length of Barrett's mucosa correlates with the duration of esophageal acid exposure,[25] patients with LSBE experiences significantly more esophageal acid exposure than those with SSBE. The frequency of finding short segment vs long segment BE is variable e.g. 17.72% vs 18.98%,[26] 17% vs 7%,[6] 4.6% vs 1.6%,[17] 66.6% vs 33.3%,[14] 85% vs 15%,[16] 0% vs 8.9%[27] showing short segment BE to be more common. However incidence and prevalence of dysplasia and adenocarcinooma are found to be significantly higher in long segment BE,[9,24,28] as also the prevalence of adenocarcinomas. The cumulative percentage of intestinal metaplasia in endoscopic lengths 1-2 cm and 3-4 cm increased from 30.5% and 44.8% to 63.6% and 88.9% respectively after six endoscopies. Intestinal metaplasia was detected in all patients with greater than 4 cm of the endoscopic BE segment after 2-4 endoscopies. This infers that the endoscopic presence of columnar appearing mucosa cannot be ignored even in absence of intestinal metaplasia on biopsies, may it be a SSBE where also dysplasia and adenocarcinoma can be associated.[12]

Though both our patients with BE did not show evidence of dysplasia or malignancy, they need proper observation and follow up for a longer period for the detection of malignant transformation. There are strong epidemiological evidences from Sweden[3] and Japan[29] that esophageal adenocarcinoma incidence is rising as a complication of chronic GERD and BE. In another study[30] it was reported that BE increases the risk of esophageal cancer, approximately 10 times and esophageal adenocarcinoma approximately 30 times compared with the general population. In a review of 22 resected specimen of adenocarcinoma occurring within 2 cm of the gastroesophageal junction and 22 matched control specimens of resected esophageal squamous carcinoma, Cameron[31] reported that there was high or low grade dysplasia associated with 64% of adenocarcinoma compared to only 5% of controls ($p<0.001$).

The possible role of GERD induced erosive esophagitis leading to BE has not been clearly established, but possible cellular injury and subsequent healing with columnar epithelium has been hypothesized. The pathogenic mechanisms for the two entities may be different, but are often seen together due to shared patient characteristics and risk factors. BE has also been identified in up to 25% of asymptomatic or minimally symptomatic individuals.[32] In a study from Taiwan, 14.5% patients were found to have erosive esophagitis, 2%, Barrett's esophagus, and 7% hiatal hernias which were higher than the previous studies.[33] In another endoscopic follow up study at 5 years in Swedish population, it was found that the erosive esophagitis progressed to a more

severe grade in 13% and to BE in 8.8%. The authors concluded that erosive esophagitis at baseline was independently associated with BE at follow-up.[34] In an Iranian population with chronic GERD symptoms, 66.5% had erosive esophagitis and only 2.4% had BE which showed less existence of BE despite presence of high number of erosive esophagitis.[14] In Turkish population, 12.8% had erosive esophagitis with 0.4% BE and this association was significantly higher in patients with BE (27%, p=0.0001).[16] In our study, 45% had erosive esophagitis and 1.6% had BE, both the patients with BE had chronic severe GERD symptoms with erosive esophagitis (LA-C). Concern exists that BE could be missed during the screening of patients with erosive esophagitis given that BE diagnosis depends on histologic confirmation of specialized columnar metaplasia. It is clearly not understood whether erosive esophagitis is a precursor of BE or can exist concomitantly with BE.

The total number of patients was small. 24 hours PH metry and manometry couldn't be done because of non availability. A special technique like chromoendoscopy and narrow band endoscopy are better options but increases the cost of the procedure. The patients usually do not come for follow up when they become asymptomatic.

CONCLUSIONS

Endoscopic surveillance with detailed inspection and systematic biopsies is recommended for most patients with Barrett's esophagus. Esophageal carcinoma if detected should be treated at the earliest.

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