Original Article

FREQUENCY, TYPES AND COMPLICATIONS OF BARRETT'S ESOPHAGUS IN PATIENTS WITH SYMPTOMS OF GASTRO-ESOPHAGEAL REFLUX

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ABSTRACT

Objective: This study was carried out to evaluate the frequency, types and complications of Barrett's esophagus in symptomatic gastro-esophageal reflux patients.

Setting: Department of Pathology, Basic Medical Sciences Institute, JPMC and the Pakistan Medical Research Council, JPMC, Karachi.

Subjects: A total of 100 patients of gastro-esophageal reflux were studied to evaluate the frequency, types and complications of Barrett's esophagus. Endoscopic biopsies were taken and examined with H&E & various special stains like PAS, Alcian blue/PAS, high iron diamine/Alcian blue & Giemsa stains.

Results: Of 100 cases studied, 32 were found to have Barrett's esophagus on microscopy. The remaining 68 cases showed low and high grade changes of gastro-esophageal reflux.

Conclusion: In comparison with studies from western countries, Barrett's esophagus was found to be relatively more common in our population. However, the frequency of complications like ulcer, stricture, dysplasia and adenocarcinoma was lesser.

KEY WORDS: Barrett's esophagus, gastro-esophageal reflux.

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INTRODUCTION

Barrett's esophagus is a pathologic condition in which metaplastic columnar epithelium rather than the normal stratified squamous epithelium lines the distal 3 cms of esophagus. It was first described by Norman Rupert Barrett in 1950 and is now widely accepted to be the consequence of long standing gastro-esophageal reflux[1-7]. The importance of the condition lies in the fact that it produces complications such as ulcer and stricture and has malignant potential[8,9]. It represents an adaptive change in response to the continued foreign (acid-pepsin) environment due to chronic gastro-esophageal reflux. Following repeated cycles of destruction and regeneration a simple columnar type of epithelium more resistant to digestive action finally replaces the destroyed squamous epithelium[10,11].

The frequency of Barrett's esophagus in patients with gastro-esophageal reflux reported in various studies varies from 0.45% to 12.4%[3,5,12].

The diagnosis of Barrett's esophagus requires endoscopic examination and biopsy[13]. On endoscopy Barrett's esophagus has a characteristic velvety-red appearance and contrasts sharply with the grey appearance of the

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squamous epithelium[14]. In the normal esophagus, the squamo-columnar junction is located within 2cm of the gastro-esophageal junction. The diagnosis of Barrett's esophagus should be considered at endoscopy when the squamo-columnar junction is located at a site greater than 2cm above the gastro-esophageal junction[15,16]. An esophageal biopsy is mandatory to establish the diagnosis of Barrett's esophagus.

MATERIAL AND METHODOLOGY

Hundred patients with symptoms of gastro-esophageal reflux attending the out patient clinic of Pakistan Medical Research Council (PMRC), JPMC, Karachi from, 1st January 1992 to 15th May 1993, were studied. The criteria for selection of the patients was the presence of characteristic symptoms of gastro-esophageal reflux e.g.: heart burn, regurgitation and retrosternal pain. The endoscopies were performed with the help of fibre-optic endoscope number 2T10. The location of gastro-esophageal junction was noted (in cm) by taking the upper incisor teeth as a reference point. Barrett's esophagus was endoscopically defined as the presence of characteristic velvety red mucosa extending in the distal esophagus in such a way that the squamo-columnar mucosal junction was displaced at least 3cm proximal to gastro-esophageal junction. The level and length of Barrett's mucosa was noted. Presence of other endoscopic features such as redness, swelling, presence of ulcers and strictures were also noted. Hiatal hernias were distinguished by their non-tubular, pouch-like appearance and the presence of gastric rugae. In cases where Barrett's esophagus was endoscopically noted the biopsy was taken near the proximal extent of Barrett's mucosa also including the mucosa above the squamo-columnar junction. If the endoscopic findings were negative for Barrett's esophagus and apparent macroscopic esophagitis was present or if the endoscopic appearance was interpreted as being normal, the biopsy was taken 2 cm from gastro-esophageal junction. Eight control patients who had no clinical evidence of esophageal disease were chosen from patients undergoing endoscopy for other reasons.

The biopsy specimens were processed routinely for paraffin sections. The sections were stained with haemotoxylin and eosin stain and various special stains like periodic acid-Schiff (PAS), Alcian blue / periodic acidSchiff (AB / PAS), high iron diamine / alcian blue (HID / AB) and Giemsa stain. Sections taken from normal stomach, small intestine and colon were used as controls. The stained sections were studied by light microscope using 4X, lOX and 40X dry objectives. The microscopic features were noted by making two groups of patients. One group included those patients with gastro-esophageal reflux in whom, on microscopy Barrett's esophagus was seen while the other group included patients with gastro-esophageal reflux in whom Barrett's esophagus was not seen.

RESULTS

Of 100 cases studied, 32 were found to have Barrett's esophagus on microscopy. The remaining 68 cases showed low and high grade changes of gastro-esophageal reflux. The age of patients with Barrett's esophagus ranged from 18 to 65 years, mean age was 41.3 years. Male to female ratio was 5.4:1 (Table-I). The average duration of symptoms was 7.9 years with a range of 5 months to 25 years. Maximum number of patients i.e. 12 of 32 (37.5%) had symptoms in the range of 5-10 years. Ten

TABLE–I
Age & sex distribution of 32 patients of gastro-esophageal reflux with Barrett's esophagus

Age groups (Years)	*Male*	*Female*	*Total number*	*Percentage (%)*
11-20	5	0	5	15.63
21-30	5	1	6	18.75
31-40	5	2	7	21.86
41-50	6	2	8	25.00
51-60	3	0	3	9.38
61-65	3	0	3	9.38
Total	27	5	32	100.00

Mean Age : 41.3 years.
Male to female ration 5.4:1.

patients (31.25%) had symptoms for more than 10 years (Table-II). 56% of the patients were addicted to cigarette smoking.

On endoscopy Barrett's mucosa was seen in 27 patients (84%). The length of Barrett's mucosa in maximum number of cases i.e. 11 (40%) was more than 4 cm. Other important endoscopic findings included esophagitis in 81.25% cases, ulcer in 9.37%, erosion in 6.25% and hiatal hernia in 31.25% of cases (Table-III).

TABLE-II
Duration of symptoms of gastro-esophageal reflux in 32 patients with Barrett's esophagus

Duration of symptoms	*No. of patients*	*Percentage (%)*
> 10 years	10	31.25
5 – 10 years	12	37.50
1 – 5 years	6	18.75
< 1 year	4	12.50
Total	32	100.00

TABLE - III
Endoscopic findings in 32 patients of gastro-esophageal reflux with Barrett's esophagus

Endoscopic findings	*No. of patients*	*Percentage (%)*
Barrett's mucosa seen on endoscopy	27	84.37
Barrett's mucosa not seen on endoscopy	05	15.63
Length of Barrett's mucosa		
3 cm	06	22.22
4 cm	10	37.04
> 4 cm	11	40.74
Esophagitis	26	81.25
Erosion	02	6.25
Ulcer	03	9.37
Stricture	00	0.00
Others		
Hiatal hernia	10	31.25
Lax lower esophageal sphincter	02	6.25
Gastritis	03	9.37
Gastric ulcer	01	3.12
Duodenal ulcer	03	9.37

On histopathology one type of metaplastic epithelium i.e., either the gastric cardiac type of epithelium or gastric fundic type of epithelium and specialized columnar epithelium was seen in 29 cases (90.62%). In the remaining three cases (9.38%), a combination of two types was seen. Gastric cardiac type of epithelium (Fig. I) either alone (46.87%) or in combination with other types (9.38%) was found in maximum number of cases i.e. 18 (56.25%). The gastric fundic type (Fig. II) was the least common type found, seen alone in 5 cases only (15.62%) and in combination with other type in 01 case (3.13%). Specialized columnar epithelium (Fig. III) was seen alone in 9 cases (28.12%) and in combination with other type in 02 cases (6.25%). In every case this specialized columnar epithelium took the form of an incompletely differentiated variant of intestinal metaplasia with presence of goblet cells and columnar mucous cells. No Paneth cells were seen (Table-IV).

TABLE-IV
Histopathological findings in 32 cases of gastro-esophageal reflux with Barrett's esophagus

Type of metaplastic columnar epithelium	*No. of patients*	*Percentage (%)*
Gastric cardiac type of epithelium	15	46.87
Gastric fundic type of epithelium	05	15.62
Specialized columnar epithelium	09	28.12
One type of epithelium only	**29**	**90.62**
Gastric cardiac + specialized columnar epithelium	02	6.25
Gastric cardiac + gastric fundic type of epithelium	01	3.13
More than one type of epithelium	**03**	**9.38**

The inflammation in the Barrett's mucosa on histopathology was seen in all the cases. The degree of inflammation which ranged from 1+ to 3+, did not correlate with the type of epithelium present and the length of segment involved. Ulcer was seen in 03 patients (9.37%) and was characterized by necrotic surface with infiltration by polymorphs. In 15 patients Helicobacter like organisms were seen (Table-V).

TABLE - V
Histopathological findings in 32 cases of gastro-esophageal reflux with Barrett's esophagus

Frequency of various associated histopathological features other than metaplastic columnar epithelium

Histopathological findings	*No. of patients*	*Percentage (%)*
Changes in Barrett's mucosa		
Inflammation		
1+	12	37.00
2+	14	43.75
3+	06	18.75
Ulcer		
Positive	03	9.37
Negative	29	90.62
Helicobacter-like organisms:	15	46.87
Dysplasia		
Negative	30	93.75
Indefinite	00	0.00
Low grade	02	6.25
High grade	00	0.00
Adenocarcinoma	00	0.00
Changes in adjacent stratified squamous epithelium		
Low grade changes of gastro-esophageal reflux	24	75.00
High grade changes of gastro-esophageal reflux	08	25.00
Legends		

Figure 1: Photomicrograph showing gastric cardiac type epithelium in a case with Barrett's esophagus. The surface shows columnar mucous secreting cells. The glands are lined by columnar mucous cells. H&E X 100.

Figure 2: Photomicrograph showing high power view of gastric fundic type epithelium in Barrett's esophagus. The parietal and chief cells are evident. H&E X 200.

Figure 3: Photomicrograph showing specialized columnar epithelium in a case with Barrett's esophagus. The surface shows villiform folds with many goblet cells. H&E X100.

DISCUSSION

Barrett's esophagus is a pathologic condition in which the normal squamous epithelium of the distal esophagus is replaced by columnar epithelium. It is believed by most investigators to be an acquired condition secondary to chronic gastro-esophageal reflux[5,11,17,18]. The current study to our knowledge is first of its kind in our population. The observed frequency rate of Barrett's esoppagus in this study was 32% which is higher than reported in other studies (0.45% to 12.4%)[3,5,12]. This could be related to the dietary habits of our population which is known to take high amount of fat and spices, resulting in gastro-esophageal reflux. A probable explanation of the lower frequency of Barrett's esophagus in developed countries may be the frequent use of diagnostic endoscopy and so the patients with reflux symptoms showing esophagitis on endoscopy get screened out and treated. In our country diagnostic endoscopy is not in routine use. It is only performed when the symptoms are of severe intensity and are refractory to treatment. Thus by the time the patients are examined endoscopically, Barrett's esophagus has already developed.

The mean age of patients with Barrett's esophagus in this study was 41.3 years which is slightly lower than reported in other studies[18-20]. Male to female ratio was 5.4:1 in patients with Barrett's esophagus which is in accordance with other studies[18,19,21]. The concept that Barrett's epithelium develops as a consequence of acid-peptic reflux is supported by the data in this study. Similar findings were also observed in other studies[12,15]. The predominant endoscopic finding in patients with Barrett's esophagus was esophagitis. It was seen in 81.25% of the patients. This is in accordance with other studies[15,19,22]. In the present study all the three metaplastic epithelial types as described in the literature were seen on histopathology either alone or in combination. In maximum number-of cases i.e. 56.25%, gastric cardiac type of epithelium was found. This finding is in consistence with other studies[19,20,23]. However, in various other studies, the more frequent type of epithelium seen was specialized columnar type[12,15,24]. The least frequent type of metaplastic epithelium observed in this study was gastric fundic type of epithelium. This finding is also in accordance with other studies[6,25]. In this study, the mucin histochemical findings in various epithelial, types were not much different from other studies[12,26].

In this current study, dysplasia of low grade type was seen in patients with Barrett's epithelium in two cases (6.25%). Similar findings were observed in other studies[6,18]. However, the dysplasia in our study was seen in cardiac type of metaplastic epithelium which is in contrast to the other studies, in which the dysplasia was more frequently seen in specialized columnar epithelium[25-27]. In the present study, adenocarcinoma was not seen in any case with Barrett's esophagus. The frequency of adenocarcinoma in Barrett's esophagus reported in literature ranges from 0-37.5%[20,24,28]. In various studies in which adenocarcinoma in Barrett's esophagus was seen, the most frequent type of metaplastic epithelium was specialized columnar epithelium[29-31]. Since in the present study, the specialized columnar epithelium was not frequently seen, this may be considered as one of the reasons for not finding adenocarcinoma in this study.

The histopathological changes in patients without Barrett's esophagus observed in this study were low and high grade changes of gastro-esophageal reflux as defined according to criteria reported in literature[24].

CONCLUSION

From the present study we conclude that Barrett's esophagus is relatively more common in our population as compared to western countries. However, the frequency of complications like ulcer, stricture, dysplasia and adenocarcinoma were less.

In view of high frequency of Barrett's esophagus in our patients it is recommended that (1) routine endoscopy and biopsy be done in

patients with chronic gastro-esophageal reflux symptoms and (2) periodic endoscopic examination and biopsy be done in patients with Barrett's esophagus for early detection of any complication.

This study, offers the much needed information on the frequency, types and complications of Barrett's esophagus in our patients. However, other important parameters like etiological factors and the malignant potential of the various types ,of the Barrett's esophagus have not been studied. Further study is recommended to look into these aspects of Barrett's esophagus.

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