

Clinical ,Endoscopic and Histopathological Evalution Of eleven Iraqi Patients with Barrett's Esophagus

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Background :Barrett's esophagus (BE) is consequence of chroinc gastroesophageal reflux, in which the normal epithelium of distal esophagus is replaced by specialized epithelium that is hitologically characterized by two different types of cells: goblet cells and columnar epithelium .

The true prevalence of BE is difficult to define because of lack of endoscopic surveys of normal population. However,it is estimated that 1% of the population has BE .

Objective:Clinical ,endoscopic and histological analysis of Iraqi patients with Barretts esophagus .

Design:Prospective case descriptive study .

Setting :Gastroenterology &Hepatology Teaching Hospital .

Method :During the period (July 2001-January 2002) patients with typical symptoms of gastroesophageal reflux disease were endoscoped after clinical evalution .Modified Savary – Miller grading system were followed. Methylene Blue staining was carried to increase the yield of endoscopic dignosis of intestinal metaplasia .Biobsy was taken every 2 cm, starting at 2cm above gastroesophageal junction .

Result :Fifty patients were included ,they were 34 male and 16 female ,mean age 47 years,with mean duration of illness of 6.1 years,88% were erosive reflux disease with 9 patients had grade I ,21 grade II,10 grade III and 4 patients with grade IV .Four cases were diagnosed as Barrett`s esophagus during endoscopic evaluation and after methylene staining the yield was increased to 2.5 fold .Histological analysis of esophageal biobsy revealed 24/50 squamous epithelium changes of GERD ,26/50 metaplastic columnar epithelium, and out of those 26 cases with metaplastic columnar epithelium eleven cases of BE were diagnosed.

In conclusion survey and careful detection of BE on endoscopy for all patients with long duration of sympons of GERD particularly male gender should be carried.

Introduction:

The condition known as Barrett's esophagus (BE) was first described by Norman Barrett in 1950, Barrett considered, incorrectly, that peptic ulceration of esphagus arising in gastric type epithelium associated with an esophageal stricture to be because of congenitally short esophagus. Subsequent studies have shown that lower esophagus itself becomes lined by metaplastic epithelium. ⁽¹⁾

BE is the most sever histological consequence of chronic gastroesophageal reflux. Although its pathogenesis is unclear, Barrett's mucosa is metaplastic columnar epithelium that has replaced the native squamous epithelium. ⁽²⁾ BE is the only known precursor of esophageal and esophagogastric junction adenocarcinoma. ^(3,4)

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Barrett's adenocarcinoma develops via a multiple process recognized phenotypically as histological sequence of metaplasia – lowgrade dysplasia (LDG) Highgrade dysplasia (HGD) – adenocarcinoma. Consequently, during the past 10 years, scientific interest in Barrett's esophagus has grown in parallel with rising incidence of adenocarcinoma of distal end of esophagus,. early recognition of BE is necessary in order to prevent cancer. To achieve early recognition endoscopic screening of patient with presistant reflux disease, careful inspection of distal esophogus, general use of high resolution endoscopes, and the use of staining method and careful biopsy technique may be helpful. ⁽⁵⁾

This study was carried aiming at clinical, endoscopic, and histopathological detection of Iraqi patients with BE.

Patient and methods :

This study was conducted at Iraqi Center of Gastroenterology, during a six months period from (mid of July 2001 to the January, 2002).

I – Criteria of Patient Inclusion :

Patients with typical symptoms of GERD (heart burn and/or regurgitation by recumbency or bending and releived by antacids, symptom must be present twice a week for at least 3 month), ⁽⁶⁾, who were pretreated sufficiently with acid suppression therapy for at least six weeks, were included in this study. History and clinical examination were carried for every patient with full information regarding smoking, alcohol intake, cholecystectomy and NSAID ingestion.

II – Endoscopy :

An upper endoscopy was carried out for every patient by same endoscopist, using Olympus Videoendoscope GEXQ 230. The procedure was carried under local anesthesia (Xylocaine 10% oral spray) taking care to record distances using centimeter markings on the endoscopic shaft. With respect to esophagus a careful assessment was made at endoscopic procedure of the following points :

- 1-Distance of squamucolumnar junction (SCJ) and gastroesophageal junction from incisor teeth.
- 2 - The presence and length of hiatus hernia.
- 3 - The presence and grading of esophagitis.
- 4- Endoscopic complication of GERD (stricture,ulcer)
- 5 – Diagnosis of columnar lined esophagus (Barrett's).

1. The gastroesophageal junction[GEJ] was defined by expansion of tubular esophagus into saccular stomach and by the upper margin of gastric mucosal folds.

This site should be determined with esophageal lumen minimally distended and during the absence of active prestaltic activity. The junction of the squamous epithelium (pearly pink) and columnar epithelium (orange-red) appear after minimum inflation as slightly irregular or undulating line called Z line. ^(7,5)

2. After the SCJ is identified the next step is endoscopic diagnosis of hiatus hernia (an anatomic abnormality characterized by displacement of SCJ 2cm. above the diaphragmatic hiatus). ⁽⁸⁾

Endoscopic diagnosis of size and length of hiatus hernia is carried by following the important points :

- a . Idetification of gastroensophageal junction by transition from tubular esophagus to saccular stomach or by upper margin of gastric folds.
- b. Determination of the level of diaphragmatic hiatus.
- c . The length of hiatus hernia is recorded as the distance from gastroesophageal junction to the diaphragmatic hiatus.

3. The extent and severity of esophagitis are assessed using modified Savary-Miller classification of esophagitis. ⁽⁹⁾

Grade I : Single or multiple erosion, on a signal fold : erosion may be erythematous or erythematous-exudative.

Grade II : Multiple erosion affecting more than one longitudinal fold : erosion may be confluent.

Grade III : Circumferential erosion.

Grade IV : Ulcer(s), stricture(s).

4. Endoscopic complication of GERD including stricture, permanent narrowing of the lumen ,(used for a short less than 1 cm non-distensible segment in tubular organ) and ulcer. ⁽⁷⁾

5. Diagnosis of columnar line esophagus (Barrett's) is achieved by :

- a . Endoscopy.
- b . Staining method.
- c . Endoscopic biopsy procedure.

a . Endoscopy:

detection of endoscopic feature associated with greatest chance of finding of intestinal metaplasia are :

Mucolysis	10 - 20 ml of 1% acetic acid solution for 2 minute
Staining	10 – 20 ml of 0.5 % methylene blue solution for 2 minute
Lavage	Rinsing off superficial methylene blue with 10 – 20 ml 1% acetic acid

Table. (1) – Methylene Blue Staining Method. ⁽⁵⁾

c . Endoscopic Biopsy Procedure :

Endoscopic biopsy was taken with spiked biopsy forceps (KW2415s) starting at 2 cm. above visible mucosal GEJ every 2 cm. for at least 2 – 3 levels, or higher up according to length of metylene blue staining mucosal lesion. Two quadrant biopsies were taken every 2 cm. and every two-quadrant biopsy stored in separated container, (i.e. one container for each two-quadrant biopsy). All the samples were fixed in neutral buffered formalin for 48 hours and paraffin embedded, serial sections, 4 mm thick, were cut from each sample and stained with heamatoxyline and eosin.

Biopsy specimens were examined by general pathologist and then reviewed by second

1 . Long segment of esophageal columnar lining (more than 3 cm).

2 . A jagged, irregular squamuo columnar junction (length > 1 cm, width > 5 mm).

3 . Prominent squamous columnar junction.

4 . Discrete patches of columnar epithelium in distal esophagus. ⁽¹⁰⁾

b . Staining method using methylene blue dye :
Specialized spray catheter (PW-6p-I) was used for application of methylene blue in lower third (distal 8 cm) following the methods listed in table. (1)

pathologist with gastrointestinal interest, with emphasis on description of the following points :

1 . Type of eqithelium lined mucosa :

- a . Squamous epithelium
- b . Metaplastic columnar epithelium
- c . Subset of metaplastic columnar epithelium: Reflux carditis. - Oxynto cardiac mucosa.
- d . Presence of intestinal metaplasia.
- e . Preseence and grading of dysplasia.

2 . Squamous epithelium changes of GERD :

- a . Basal cell hyperplasia.
- b . Thickened esophageal squamous ephthelium.
- c . Eosinophilic infiltration.
- d . Mixed cell infiltration.
- e . Severity of mucosal inflammation.

Results:

Out of total fifty patients who have met criteria of clinically suspected GERD, eleven case of BE were diagnosed.

They were 9 male and 2 female (M/F 4.5:1) of age range 14 – 76 years mean (45 yr.) out of 11 patients with BE 8 of them with duration of illness more than 24 month. The shortest duration of illness was one year and longest 7 yr. Heart burn as main problem was reported in all cases followed by epigastric pain (54.6%) belching (18%) and dysphagia (18.1%). Alcohol drinking was reported by only one male and smoking by 3/11 (27.2%).Table (2) All the 11 cases on endoscopy were erosive reflux esophagitis, and according to modified Savary - Miller classification, it was found that 2 patients had

grade I, 5 grade II, 2 grade III and 2 patients with grade IV.

Hiatus hernia was seen in 6/11 (M/F 5:1). Two patients had stricture at level of GEJ and ulcer in another patient.

Methylene blue staining was carried for every patient, and it was found to increase the yield of endoscopic detection of BE by 2.5 folds. Only 4 patients were suspected to have BE by endoscopy, but after MB staining the number increased to 10. In addition to this, one positive BE by biopsy did not take the MB stain, (i.e. False negative).

Endoscopic feature of BE after MB staining revealed 5 cases of short segment(SSBE), 3 cases of long segment(LSBE), 2 of circumferential type(CBE) and one case did not take the MB stain.Table (3) .

Case.no	Age (Years)	Sex	Duration of illness (months)	illness Age of onset of (years)	Smoking
1	50	M.	>24	47	-ve
2	14	M.	<24	13	-ve
3	50	M.	<24	49.5	+ve
4	65	M	<24	64.2	+ve
5	55	M.	>24	53	-ve
6	34	F.	>24	28	-ve
7	73	M.	>24	70	-ve
8	27	F.	>24	24	-ve
9	29	M.	>24	22	-ve
10	68	M.	>24	66	-ve
11	76	M.	>24	74	+ve

Table(2)Demographic and Clinical feature of BE Patients

Case.no	Age (Years)	Sex	Endoscopic Grading	Length of H.H.	Endoscopic Feature of BE after MB Staining	Staining MB
1	50	M.	Grade II	.3c.m.	SSBE	+ve
2	14	M.	Grade III	4c.m.	SSBE	+ve
3	50	M.	Grade II	-ve	SSBE	+ve
4	65	M.	Grade IV	5 cm.	CBE	+ve
5	55	M.	Grade II	.3cm.	SSBE	+ve
6	34	F.	Grade I	-ve	-ve	-ve
7	73	M.	Grade I	-ve	SSBE	+ve
8	27	F.	Grade IV	.3cm	LSBE	+ve
9	29	M.	Grade II	4c.m.	LSBE	+ve
10	68	M.	Grade III	-ve	CBE	+ve
11	76	M.	Grade II	-ve	LSBE	+ve

Table(3) Endoscopic Feature of BE Patients

Age Years	Sex	Duration of illness	Main Symptomes	EndoScopic Grading	H.H	M. B
50	M.	> 24 m.	H.B + Ep. pain	Grade II R.E	+ ve	+ ve
55	M.	< 24 m.	H.B + Dysph.	Grade IV R.E	+ ve	+ ve

Table (4) Clinical &Endoscopic Feature of BE Patient with LGD

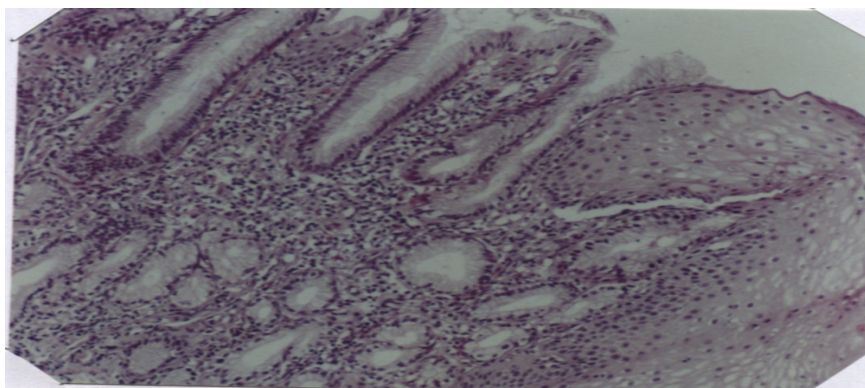


Figure –1 Reflux Carditis of BE Patient

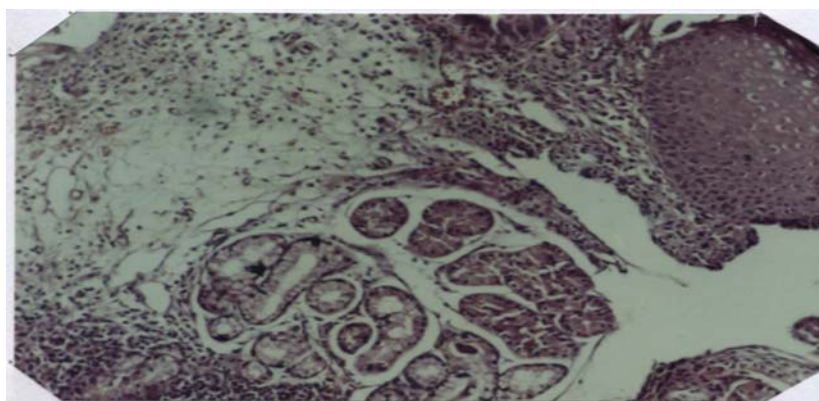


Figure-2 Oxynto-Cardic Mucosa

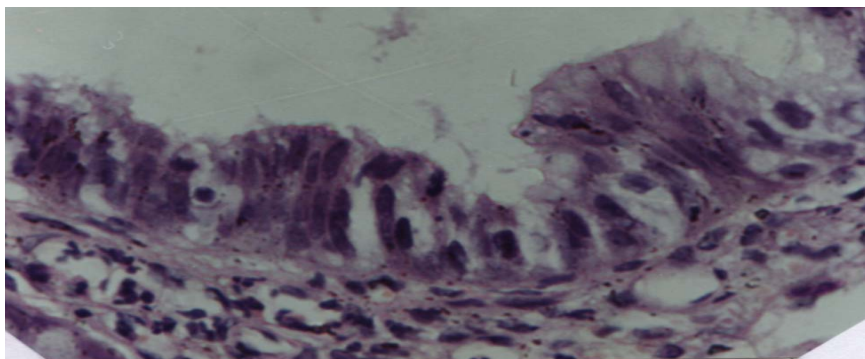


Figure -3 BE with LGD

Discussion:

While there is no doubt that GERD is rather common, however, the percentage of BE is not well looked into and studied in our community, which stimulated the conduct of this study. Out of fifty cases with GERD eleven were diagnosed to have BE, mounting to 22% of the total. As far our center is tertiary center it partly explains this high percentage of BE, in addition, to the known observation that our patient's seek advice very late in most of situation, and if they do, the availability of the drugs were drastically affected over the last twelve years.

Analysis of our eleven cases of BE demonstrates that male to female ratio is 4.5:1, this is mid way between what is reported at different population. Wienkbeck & Barnert reported a male preponderance of 10:1, While Cameron & Gospe multicentric study survey reported a frequency of 2 male : 1 female, also M. Vieth, et al reported a ratio of 2.23:1 and Andrello, et al reported a ratio of 1.5: 1. ^(11,12,13,14,15).

The mean age (45 years) of our BE patients is comparable to mean age of other reports. Eisen, et al reported in his work on the relationship between GERD and its complication with BE, in which the study based on (79) case patient with BE and 180 control patient at university of North Carolina, each case patient was matched to one control patient whose indication for endoscopy was GERD and one control patient who underwent endoscopy for other indication, they concluded, on average, patient with BE developed reflux symptoms at an earlier age than age-gender matched control patients and also had a longer duration of symptoms. Complications of reflux, including esophagitis, stricture and ulceration, were reported significantly more frequent than either group control patient. ⁽¹⁶⁾

These risk factors are similarly observed in our study group of BE, where eight of our patients had duration of illness more than 24 months, with earlier age of onset of GERD symptoms (one of the patients had his symptom started at 13 years of age (case No. 2).

Two of the three cases reported stricture in our study were associated with BE and one out of two cases with ulcer associated with BE as well.

Spechler et al reported that BE observed in (8 – 20%) of patients with reflux esophagitis. and 44% of those with peptic stricture. ⁽¹⁷⁾

Andrell, et al in their study on endoscopy finding of BE concluded that most of them having rather grad I & II esophagitis, which is similar to our finding in which, seven of our BE cases had grade I, II and the rest four were grade III, IV. ⁽¹⁵⁾

In spite of the use of three parameters for differentiation between H.H and BE, our endoscopic recognition of BE fell behind the histological diagnosis 4, 11 respectively. In a study carried by Grunwald, et al, where they endoscoped 1000 consecutive patients with histologically proved BE, they were able to diagnose only 62.2%. Endoscopist failed to recognize nearly four of every ten patients with Barrett's metaplasia, ⁽⁵⁾ similarly M. Vieth and Stolte in retrospective analysis of 1068 consecutive patients with histologically confirmed BE found that endoscopic diagnosis was made in 62% of the cases. ⁽¹⁴⁾

In our study the review of slides by second pathologist with gastrointestinal interest, uncovered a discrepancy with the results, in which four cases were falsely diagnosed as BE, but they were reflux carditis (columnar lined esophagus without intestinal metaplasia) and on the other hand, two cases diagnosed as reflux carditis were found to be BE.

John D, et al suggested that dual reading may be needed in community hospital setting for all suspected BE pathology specimens ⁽¹⁸⁾. Our results of having no BE in normal looking esophagus on endoscopy, confirmed the recommendation by Spechler which stated *it is not recommended that endoscopist routinely obtain biopsy specimens from a healthy appearing distal esophagus to look for specialized intestinal metaplasia.* ⁽¹⁹⁾

The two cases of dysplasia were of low grade. Table No. (4) Fig. No. (3) demonstrated clinical and endoscopic findings of patient with dysplastic BE.

In conclusion survey and careful detection of BE in endoscopy in all patients with long duration of symptoms of GERD particularly male gender should be established.

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