The Incidence Of Barrett's Esophagus In Iraqi Patients With Erosive Gastroesophageal Reflux Disease

*Qasim L. Abbas C.A.B.M.
**Bassim A. Asker C.A.B.M., F.I.C.M.S (GE&H)

Abstract

Background: Barrett's esophagus is the condition in which columnar epithelium replaces the squamous epithelium that normally lines the distal esophagus. The diagnosis of Barrett's esophagus is based on the endoscopic findings and confirmed by the presence of specialized intestinal metaplasia in esophageal biopsy specimens. Barrett's esophagus is common in the western world ,present in about 10% of patients with GERD who undergo endoscopy and perhaps 1% of the general population. Barrett's esophagus is predominantly a disease of middle-aged white males and two to three times more common in men than women.

Aim of the Study:
To verify the incidence of Barrett's esophagus in Iraqi patients with erosive GERD.

Patients And Methods: Patients who were discovered to have erosive GERD when underwent OGD were included . During endoscopic examination a careful assessment of GEJ, squamocolumnar junction,and hiatus hernia was made. Erosive GERD was graded according to Savary-Miller Classification. Biopsies 2 cm above the Z-line were obtained and examined for evidence of esophagitis, cardiac type metaplasia, and intestinal metaplasia

Results: 115 patients (78 males and 37 females) were included, the median age was 46 years. The shortest duration of illness was 1 month and the longest was 20 years. Cardiac metaplasia (CM) was histologically confirmed in 8 (7.0%) patients; Barrett's metaplasia (BM) was confirmed in 12 (10.4%) patients. Two patients with Barrett's metaplasia (2 out of 12"16.7%") also were diagnosed as having low and high-grade dysplasia. The mean age of patients with CM was 47.9 years and that for BM was 49.6 years. Patients with CM and BM were predominantly males. Symptom duration was longer in BM group. BM and CM were seen more frequently in erosive GERD of grades I & II than in grade III & IV. Hiatus hernia was also seen more frequently in BM group.

Conclusion: approyimately of patent with erasion gird were diagnosed with rant. epavhey male gender longer duvet of GERD symptom and hiatus hernia were confirmed as risk factarfor BM

*The gastroenterology and hepatology teaching hospital

**The gastroenterology and hepatology teaching hospital

INTRODUCTION

Barrett's esophagus is the condition in which columnar epithelium replaces the squamous epithelium that normally lines the distal esophagus. The condition develops when gastroesophageal reflux disease (GERD) damages the squamous esophageal mucosa and the injury heals through a metaplastic process in which columnar cells replace squamous ones.

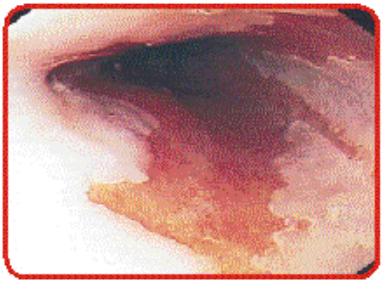

Figure (1) classic Barrett's esophagus, with tongues of salmon-colored mucosa extending proximally from the gastroesophageal junction into normal pale esophageal mucosa

The diagnosis of Barrett's esophagus is based on the endoscopic findings of columnar epithelium lining the distal esophagus and confirmed by the presence of specialized intestinal metaplasia in esophageal biopsy specimens (figure1).To document the finding of columnar epithelium in the distal esophagus,the endoscopist must identify both the squamo-columnar junction (SCJ) and gastroesophageal junction (GEJ).The juxtaposition of pale squamous epithelium and reddish columnar epithelium forms a visible line called the z- line or the squamocolumnar junction.The gastroesophageal junction,the point at which the esophagus ends and the stomach begins,is the most proximal part of the gastric folds. Often the Z line and the gastroesophageal junction coincide.when the Z line is located above the GEJ,there is a columnar lined segment of esophagus' Barrett's esophagus is common in the western world ,present in about 10% of patients with GERD who undergo endoscopy and perhaps 1% of the general population. Barrett's esophagus is predominantly a disease of middle-aged white males and two to three times more common in men than women.It is rare in non white population,especially African-American and Asians,and is uncommon outside of North America ,Europe,and Australia, possibly related to higher rates of H.pylori infection and less severe GERD[2]The average age at the time of diagnosis is approximately 55 years,but it has been reported in children older than 5 years[3] The prevalence of Barrett's esophagus increases with age,paralleling that of reflux esophagitis,but the length of the columnar-lined segment remains remarkably stable even over years of endoscopic followup[4]Families are reported with multiple members having Barrett's esophagus,some with cancer affecting more than one generation[5]. Most patients have classic reflux symptoms,but approximately 25% discovered at endoscopy have no esophageal complaints[6]. The classic histologic finding in Barrett's esophagus is a distinctive,specialized,intestinal metaplasia with acid mucin-containing goblet cells easily seen on hematoxylin and eosin-stained sections with an alcian blue PH 2.5 stain (figure2). It occupies most or all of the columnar lined area and is the type of epithelium in which adenocarcinoma arises[7,8]. The epithelium is composed mainly of goblet cells

interspersed between intermediate mucous cells, both in the surface and glandular epithelium. mature absorptive intestinal cells with a well defined brush border are rare.[9,10] t was classically considered that the three types of mucosa had a zonal distribution from intestinal to cardiac to fundic mucosa joining the upper part of the stomach. However, some mapping studies have demonstrated in most Barrett's oesophagus a patchwork of the three mucosal types, with a predominance of the intestinal mucosa.[11,12]

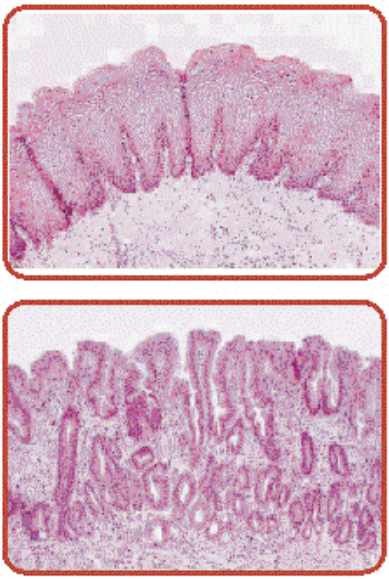

Figure (2)
Sections from the resected specimen (hem atoxylin and eosin, ¬100) demonstrated norm al esophageal squam ous epithelium (left). intestinal m etaplasia or Barrett's epithelium , defined as villiform , specialized columnar epithelium with goblet cells(right).

Some controversy exist over the classification of the Barrett's esophagus[2].classic or "long segment" Barrett's esophagus requires at least 3 cm of columnar-lined esophagus and is the best studied Barrett's subset with traditional demographic features and increased risk for developing adenocarcinoma." short segment"Barrett's esophagus refers to shorter lengths < 3 cm or tongues of columnar epithelium in the distal esophagus with intestinal metaplasia on biopsy. This entity is three to five times more common than long segment variant and its risk of cancer appears to be lower.Intestinal metaplasia at the esophagogastric junction refers to microscopic findings on biopsy but no visible esophageal columnar epithelium at endoscopy, and reported in 10% to 32% of biopsies from unselected patients, many without reflux symptoms[13]. Women and African-Americans have a higher frequency of this lesion than patients with long or short segment Barrett's esophagus. The etiology is controversial, some people suggest this is the earliest form of GERD[14], whereas others believe these changes are secondary to H.pylori infection[15] Importantly the cancer risk is minimal, if atall Patients with long segment Barrett's esophagus have an estimated 30 to 125 times increased risk of developing esophageal cancer compared with the general population[16]. Over the past 20 years, the incidence of squamous cell carcinoma has stayed constant, while the incidence of adenocarcinoma of the esophagus and esophagogastric junction has risen five fold. Despite this cancer risk, most patients with Barrett's esophagus die of unrelated causes. Nearly 95% of patients who developed cancer did not know they had antecedent Barrett's esophagus[17]. Epidemiologic data suggest

that the mean interval from developing Barrett's esophagus to cancer maybe 20 to 30 years[3].

Aim of the Study:

To verify the incidence of Barrett's esophagus in Iraqi patients with erosive GERD.

PATIENTS AND METHODS

The study group included 115 patients who were referred to the endoscopy unit in the Gastroenterology & Hepatology Teaching Hospital between Jan. 2006 and Jan. 2008, and were discovered to have erosive gastroesophageal reflux disease (erosive GERD) during endoscopic examination. All patients entering the study were requested to complete a symptom questionnaire concerning the presence of symptoms of GERD (heartburn, regurgitation, waterbrash, odynophagia, nausea and vomiting) [18,19,20] and epigastric pain, and a history of smoking, alcohol intake and nonsteroidal anti-inflammatory drugs (NSAID) intake. All endoscopic examinations were performed by one of the senior endoscopists using a standard video upper endoscope (Olympus GIF-Q240Z, Tokyo, Japan). During endoscopic examination a careful assessment of the following points was made:

- The appearance of the gastroesophageal junction was carefully inspected (GEJ; defined as the junction of the proximal gastric folds and the tubular esophagus)[18]
  - The squamocolumnar junction was also identified as the point where the squamous mucosa joined the red-color columnar mucosa[18]
  - Hiatus hernia (defined as the gastric folds seen > 2 cm above the diaphragmatic hiatus)[19]

.Erosive GERD was graded according to Savary-Miller Classification[21] as in table (1). Four quadrant biopsies (2 from each quadrant) 2 cm above the Z-line, regardless of its location, were obtained. The specimens were then examined for evidence of:

- esophagitis (defined as the presence of polymorphonuclear leukocytes, eosinophils or an increased number of lymphocytes in the esophageal epithelium, degeneration of the basal cell layers of the squamous epithelium with exocytosis of inflammatory cells, or inflammation in the lamina propria),
- cardiac and fundic type metaplasia was defined as columnar metaplasia with glands containing mucous cells,
- intestinal metaplasia (defined as the presence of specialized absorptive columnar epithelium with Goblet cells).[22,23,24]

And Dysplasia defined as neoplastic change of the epithelium that remains confined within the basement membrane of the gland from which it arises (i.e. intraepithelial neoplasia).[24]

The biopsy specimens were examined by a single expert pathologist with special interest in gastrointestinal pathology.

Statistical analysis was performed using the SPSS software package, version 7.5. The chi squared test was used to compare categorical data.

Table (1) Savary-Miller Classification

Grade I	Single, erosive, or exudative lesion on 1 longitudinal fold
Grade II	Multiple erosions on more than 1 longitudinal fold
Grade III	Circumferential erosions
Grade IV	Ulcer, stricture, or short esophagus, isolated or associated with grades I-III
Grade V	Barrett's esophagus ± grades I-III

RESULTS

During the 2 year period of the study,115 patients (78 males and 37 females) were included, the median age was 46 years (range: 16-84 years). The shortest duration of illness was 1 month and the longest was 20 years(the mean 38 m and the range 3 240 m in males;and the mean 10 m and the range 1-171 m in females). Demographic and clinical characteristics of patients are shown in Table 2.

Characteristic	Male (n = 78)	Female (n = 37)	Entire group (n = 115)
Age (years; range)	47 (16 84)	45 (21 65)	46 (16 84)
Symptom duration months:mean (range)	38 (3 240)	10 (1 171)	96 (2 240)
Heartburn *	43(55%)	18(48.6%)	61(53%)
Regurgitation	12(15.4%)	8(21.6%)	20(17.4%)
Nausea *	20(25.6%)	9(24.3%)	29(25.2%)
Vomiting	4(5%)	5(13.5%)	9(7.8%)
Epigastric pain	11(14%)	7(18.9%)	18(15.6%)
Dysphagia *	9(11.5%)	3(8%)	12(10.4%)
Smoking *	17(21.7%)	-	17(21.7%)
Alcohol consumption *	5(6.4%)	-	5(6.4%)
NSAIDs intake	10(12.8%)	5(13.5%)	15(13%)

*P(0.05)

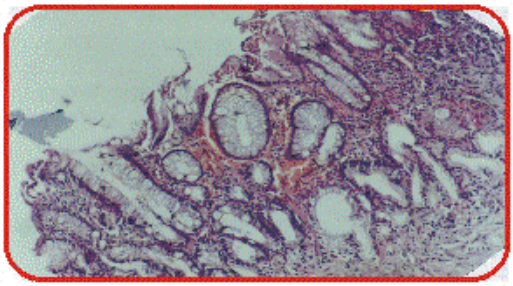

Figure (4)
GERD with intestinal metaplasia (H&E;X100)

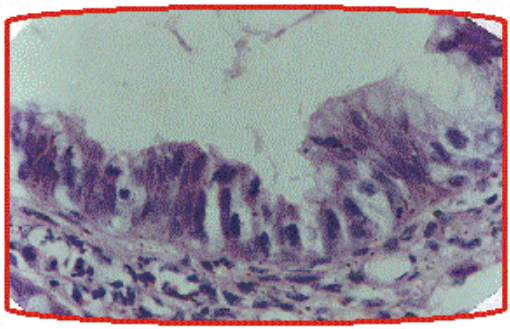

Figure (5)
GERD with intestinal metaplasia and low-grade dysplasia (H&E;X100)

The mean age of patients with CM was 47.9 years and that for BM was 49.6 years. patients with reflux esophagitis alone were predominantly males (67.4% vs 32.6% females), also patients with reflux esophagitis and CM were mainly males (62.5% vs 37.5% females, CM = 8), similarly patients with reflux esophagitis and BM were predominantly males (75% vs 25% females, BM =12). Although gastrointestinal symptoms such as heartburn, epigastric pain, and nausea were seen more frequently in male patients and male patients had more social habits such as smoking and alcohol consumption, there was no significant difference between these three groups.

Symptom duration was longer in the RE+BM group than in the other two groups (RE alone and RE+CM); 96 [2240] vs 12 [1162] and 48 [2211] months, respectively, ($p < 0.05$).

Table 5 shows the endoscopic characteristics of patients according to the histopathological features.

Table (5): histopathological groups in relation to the endoscopic characteristics of the study group

Feature	RE(n=95)	CM(n=8)	BM(n=12)
Grade I	34(35.8%)	3(37.5%)	6(50.0%)
Grade II	36(37.9%)	4(50.0%)	3(25.0%)
Grade III	16(16.8%)	1(12.5%)	2(16.7%)
Grade IV	9(9.5%)	-	1(8.3%)
Hiatus hernia	40(34.8%)	4(50.0%)	8(66.7%)*

*P<0.01

BM and CM were seen more frequently in erosive GERD of grades I & II than in grade III & IV.

In CM [3/8 patients (37.5%), 4/8 (50.0%), 1/8 (12.5%)] were in grades I, II& III

In BM [6/12 patients (50%), 3/12 (25%), 2/12 (16.7%), and 1/12 (8.3%)]were in grades I, II, III & IV respectively.
Hiatus hernia was seen more frequently in RE+BM group (66.7%) than RE+CM (50%) and RE alone group (34.8%) with (P < 0.01).

DISCUSSION

Barrett's metaplasia has been accepted as a premalignant lesion of the esophagus which can lead to the development of adenocarcinoma of the esophagus. Therefore the lower esophagus and the cardia have been the focus of extensive research over the past decade. This is mostly because of a dramatic increase in the incidence of adenocarcinoma of the GEJ over the past decade in Western countries.[25,26,27,28,29]
In the present study, we found that 10.4% of patients who had endoscopic GERD had Barrett's metaplasia and 7% had cardiac metaplasia. We could only find a single similar study in the literature estimating the incidence of Barrett's metaplasia in patients with endoscopic GERD, all other studies in this field had focused on the incidence or prevalence of Barrett's esophagus in the general population or in patients with GERD symptoms both erosive and non erosive.

Differences between the reported prevalence of BE have been observed among studies from different countries. In Germany, prevalence of BE was reported to be 4.2%, however, BE prevalence was reported to be 8.4% in Jordan.[16] In another study from Turkey, Dincer et al. reported a very low prevalence (1.7%) of BE in their study population, although the number of patients studied was quite small (n = 60), they concluded that this finding may be

related to the relatively younger mean age of patients."The incidence of BE in our study group is higher than other studies because our hospital is a tertiary referral center and we specifically selected those patients with endoscopic GERD, while others studied the general population or those with symptoms of GERD only. But it is similar to or even lower "considering our specific study group" than western reports which indicate prevalence rates of 5\19%.[3,9,11,14,15] In a previous Iraqi study done in the Gastroenterology and Hepatology Teaching Hospital in 2002, the incidence of BE was 22% in patients with GERD symptoms.

"We also found that BE is seen predominantly in older age groups and males. These results are similar to the previous studies that reported a higher prevalence in older groups of patients and males."

However Vontilainenet al. found that the male to female ratio of BE patients was 1."[3] Hirota et al. have also reported an equal distribution of BE between males and females."[1]

We also found a significant correlation between the symptom duration and the presence of BE, which demonstrates that longer duration of acid/bile reflux to esophagus is a risk factor for developing BE.

Our study revealed that esophagitis is one of the risk factors in the development of BE, also Barrett's metaplasia was seen more frequently in erosive GERD of grades I & II (75%) than in grades III & IV (25%) because early grades of GERD were more common in our patients. Results of previous studies investigating the association between erosive esophagitis and BE were controversial. While some of those studies found no correlation between esophagitis and BE,"[4] Voutilainen et al. demonstrated that junctional specialized columnar epithelium was associated with erosive esophagitis, suggesting that specialized columnar epithelium may be a result of GERD."Hiatus hernia is known to be more common a."In our study, hiatus hernia was found in 66.7% (n= 8/12) of patients with BE ; in 50% (n=4/8) of patients with CM and in only 34.8% (n= 40/95) of patients without BE or CM (P < 0.01). It has been known that hiatus hernia presence may lead to GERD which can cause BE."Dysplasia associated with Barrett's esophagus is also considered a premalignant lesion.In our study dysplasia was confirmed in 16.6% of patients with BM (n= 2/12) , the 2 patients were both males over60 years,having the symptoms for long time, one with grade II GERD and having hiatus hernia while the otherwith grade III GERD. This result is lower than that reported by Hirota et al. which reported dysplasia in45% of his BM patients."

in patients with Barrett's metaplasia than in healthy controls. A recent study by Cameron demonstrated that 96% of his patients with BE harbored a hiatus hernia."[1] In our study, hiatus hernia was found in 66.7% (n = 8/12) of patients with BE ; in 50% (n=4/8) of patients with CM and in only 34.8% (n = 40/95) of patients without BE or CM (P < 0.01). It has been known that hiatus hernia presence may lead to GERD which can cause BE."Dysplasia associated with Barrett's esophagus is also considered a premalignant lesion.In our study dysplasia was confirmed in 16.6% of patients with BM (n= 2/12) , the 2 patients were both males over 60 years,having the symptoms for long time, one with grade II GERD and having hiatus hernia while the other with grade III GERD. This result is lower than that reported by Hirota et al. which reported dysplasia in 45% of his BM patients."[1]

In conclusion approximately,10% of patients with erosive GERD were diagnosed with Barrett's esophagus. Male gender , longer duration of GERD symptoms and hiatus hernia were confirmed as risk factors for BM.

REFERENCES

1. Stuart Jon Spechler,M.D.N Engl J Med, 2002 346:11 ,March 14.

2. Falk GW: Barrett's esophagus,Gastroenterology,2002122:1569.

3. Hassel E: Barrett's esophagus:New definitions and approaches in children. J pediatric gastroenterol Nutr. ,1993,16:345. 4. Cameron A,Lomboy C: Barrett's esophagus: age,prevalence and extent of columnar epithelium . Gastroenterology ,1992,103:1241

5.Drovdlic CM.Goddard KAB,Chak A,et al:Demographic andphenotypic features of 70 families segregating Barrett's esophagus and esophageal adenocarcinoma. J.Med Genet ,2003 40:651

6. Johnson DA,Winters C, J.Clinical Gastroenterology,1987 9:23.

7. Paull A,Trier JS,Dalton MD,et al:The histolo

histolo
gic spectrum of Barrett's esophagus.N Engl J Med,1976, 295:476.
8. Zwas F , Shields HM, Doos WG, et al. Scanning electron microscopy of Barrett's epithelium and its correlation with light microscopy and mucin stains. Gastroenterology1986;90:193241.
9. Hassall E . Columnar-lined esophagus in children. Gastroenterol Clin North Am 1997;26:53348
10.Oberg S , DeMeester TR, Peters JH, et al. The extent of Barrett's esophagus depends on the status of the lower esophageal sphincter and the degree of esophageal acid exposure. J Thorac Cardiovasc Surg 1999;117:57280.
11.Cameron AJ, Carpenter HA. Barrett's esophagus, high-grade dysplasia, and early adenocarcinoma: a pathological study. Gastroenterol 1997;92:58691
12.Chatelain D , Flejou JF. High-grade dysplasia and superficial adenocarcinoma in Barrett's esophagus: histological mapping and expression of p53, p21 and Bcl-2 oncoproteins. Virchows Arch 2003;442:1824.
13.Sharma P: Recent advances in Barretts esophagus.Semin Gastrointest.Dis. ,1999,10:93
14.Oberg S,Peter JH,DeMeester TR,et al: Inflammation and specialized intestinal metaplasia of cardia mucosa is amanifestation of gastroesophageal reflux disease.Surg,1997 .226:522.g
15.Astroesophageal reflux and H.pylori infection.Gastroenterology,1998 114:633.
16.Sharma P,McQuaid K,Dent J,et al:ACritical review of the diagnosis and management of Barretts esophagus Gastroenterology,2004 127:310.
17.Dulai G,Guha S,Kahn KL,et al: preoperative prevalence of Barretts esophagus inesophageal adenocarcinomaGastroenterology ,200212:26
18.Carlsson R,çDent J,çBolling-Sternevold E,çet al:çThe usefulness of structured questionnaire in the assessment of symptomatic Gastroesophageal reflux disease. Scand J Gastroenterol. symptomatic Gastroesophageal reflux disease. Scand J Gastroenterol.
19. Klauser AG,çSchindlebeck NE,çMuller-Lissner SA:Symptoms Of gastro-oesophageal reflux disease. Lancet .Brzana RJ,□ KochKL:
20. Gastroesophageal reflux diseasepresenting with intractable nausea. Ann Intern Med
21. Ollyo JB,□ Lang F,□Fontolliet C,□ Monnier P:□ Savary-Miller's new endoscopic grading of reflux-oesophagitis: A reproducible, logical, complete and useful classification.simple,□ Gastroenterology□□ □A100.
22.Gerson LB, Shetler K, Triadafilopoulos G. Prevalence of Barrett's esophagus in asymptomatic individuals. Gastroenterology2002;123:4617.
23. Hirato WK, Loughney TM, Lazas DJ, Maydonovitch CL, Rholl V, Wong RKH. Specialized intestinal metaplasia, dysplasia and cancer of the esophagus and esophagogastric junction: prevalence and clinical data.Gastroenterology 1999; 116: 27785.
24.Chandrasoma PTR, Ma Y, Peters J, Demeester T. Histologic Classification of patients based on mapping biopsies of the gastroesophageal junction Am. J. Surg. Pathol. 2003; 27:92936.
25. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF Jr. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. JAMA 1991; 265:12879.
26. Blot WJ, Devessa SS, Fraumeni JF Jr. Continuing climb in rates of esophageal adenocarcinoma: an update. JAMA 1993;270:1320.
27. Powell J, McConkey CC. Increasing incidence of adenocarcinoma of the gastric cardia and adjacent sites. Br. J. Cancer 1990; 62:4403.
28.Spechler SJ. Barrett's oesophagus: Diagnosis and Management. Baillieres Best Pract. Res. Clin. Gastroenterol.

2000; 14: 85779.
29. Jankowski JA, Perry I, Harrison RF. Gastro-esophageal cancer: death at the junction. Br. Med. J.
2000; 321: 19 26.
30. Sharma P, McCallum RW, Lundell L. The geoprevalence of Barrett's esophagus. (Paper presented at the Sixth OESO World Congress; September
2000, Paris, France).
31. Dincer D, Besisik F, Sahin E, Demir K. Intestinal metaplasia of the gastric cardia: a study form Turkey. Hepatogastroenterol.
Dincer D, Besisik F, Sahin E, Demir K. Intestinal metaplasia of the gastric cardia: a study form Turkey. Hepatogastroenterol.
2002; 49: 11536.
32. Spechler SJ. The columnar lined esophagus. History, Clin.terminology, and clinical issues. Gatroenterol. North Am.
1997; 26: 45566.
33. Spechler SJ. Short and ultrashort Barrett's esophagus what does it mean? Semin. Gastrointest. Dis.
1997; 8: 5967.
34. Spechler SJ, Goyal RK. The columnar lined esophagus, intestinal metaplasia, and Norman Barrett. Gastroenterology1996;
110: 61421.
35. Chalasani N, Wo JM, Waring JP. Racial differences in the histology, location, and risk factrs of esophageal cancer. J. Clin. Gastroenterol.
1998; 26: 113.
36. Bassim A.Asker, Amira Shubbar, Luay Al-Khurry:Clinical, endoscopi
c and histological evaluation of eleven Iraqi patients with BE. IJGE 2005; 5:10-17.
37. Gerson LB, Edson R, Lavori PW, Triadafilopoulos G. Use of a Simple symptom questionnaire to predict Barrett's esophagus in patients with symptoms of gastroesophageal reflux. Am. J. Gastroenterol.
2001; 96: 200512.
38. Voutilainen M, Farkkila M, Juhola M et al. Specialized Columnar epithelium of the esophagogastric junction: prevalence and associations. Am. J. Gastroenterol.
39. Johnston MH, Hammond AS, Laskin WL et al. The prevalence And clinical characteristics of short segments of specialized Intestinal metaplasia in the distal esophagus on routine endoscopy. Am. J. Gastroenterol.
1996; 91: 150711.
40. Spechler SJ, Zeroogian JM, Antonioli DA, Wang HH, Goyal RK. Prevalence of metaplasia at the gastroesophageal junction. Lancet
1994; 344: 5336.
41. Cameron AJ. Barrett's esophagus: prevalence and size of hiatal hernia. Am. J. Gastroenterol.
1999; 94: 20549.
42. Avidan B, Sonnenberg A, Schnell TG, Sontag SJ. Hiatal hernia and acid reflux frequency predict presence and length of Barrett's esophagus. Dig. Dis. Sci. 2002; 47: 25664. 1.figure (1): N Engl J Med. ,1999, 343:19.
2.figure (2): N Engl J Med. ,1999, 343:19