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What are Predictive Factors for Developing of Barrett's Esophagus in Patients with Gerd—our Experience

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SUMMARY

Introduction: Barrett's esophagus (BE) is a condition in which the normal squamous epithelium of the esophagus is replaced with metaplastic intestinal-type epithelium. This epithelium can progress sequentially from metaplasia to low-grade dysplasia, then to high-grade dysplasia and finally to invasive adenocarcinoma. Many factors that appear to be risk factors for the presence of BE include obesity, the presence of hiatal hernia, and interestingly, the absence of *Helicobacter pylori* infection. **The aim:** of this study was to determine the predictive factors for progression of gastroesophageal reflux disease (GERD) to BE. **Methods:** 42 patients with endoscopically diagnosed and histopathologically verified BE were

included in this prospective study. We analysed predictive factors such as: age, sex, obesity, alcohol consumption and smoking, reflux symptom duration in this patients, prevalence of short and long segment of BE, and the presence of hiatal hernia. After endoscopic examination of these patients, the presence of BE was verified with histopathological examination and finally, infection with *H. pylori* was determined. **Results:** Among 42 subjects, 25 (59%) were males and 17 (41%) were females, with mean age of 52.8 ± 3.28 years. Obesity was present in 24 of 42 patients (57%). 27 of 42 patients (64%) were smokers. Symptom duration in this patients was approximately 9.4 years. From total number of patients, 52% were with SSBE and 48% patients were with LSBE. Hiatal hernia was present in

64% of patients, of which 66% were with LSBE and 34% with SSBE. In these patients, prevalence of infection with *H. pylori* was present in 12% of cases, 9.5% in patients with SSBE and 2.5% in patients with LSBE. **Conclusions:** The important risk factors for appearance of BE in GERD patients were male sex, middle age, smoking and alcohol consumption. Obesity is an important factor for development of BE. Most of patients with BE also had hiatal hernia, in majority of cases these were patients with LSBE. The prevalence of infection with *H. Pylori* in patients with BE was lower and this may predict a protective role of this microorganism.

Key words: Barrett's esophagus, GERD, obesity, hiatal hernia, predictive factors.

1. INTRODUCTION

Barrett's esophagus (BE) is defined as a change in the esophageal mucosa, from normal squamous epithelium to columnar epithelium with intestinal metaplasia (1, 2, 3). Gastroesophageal reflux disease (GERD) is accepted as the primary etiologic factor for BE. There is compelling evidence that BE is a precursor lesion for adenocarcinoma of the esophagus (2, 4, 5). BE is found in about 2% of the adult population, and in 3-5% of persons with GERD. Many factors that appear to be risk factors for the presence of BE include obesity, the presence of hiatal hernia, and interestingly, the absence of *Helicobacter pylori* infection. Speculation is that all of these factors contribute to BE by increas-

ing the risk and severity of acid reflux (6, 7).

2. AIM OF THE STUDY

The aim of this study was to determine predictive factors of developing Barrett's oesophagus in our patients with GERD.

3. MATERIAL AND METHODS

In this study we analysed data from the prospective database of 42 patients at the Endoscopic Service of Internal Clinic in Prishtina. All patients diagnosed with Barrett's esophagus in the period: January 2008 – December 2010, were included in the study.

The demographic and clinical data of all patients with BE: age, gender, obesity, smoking, alcohol consump-

tion, duration of reflux symptoms (pyrosis, regurgitation and vomiting). All patients underwent upper GI endoscopy. During the endoscopic examination was determined if the patient had Barrett's esophagus, which pathology was diagnosed based on a histopathologic finding of specialized intestinal metaplasia in endoscopic biopsies. The positions of endoscopic landmarks were determined in centimeters from the teeth, with documentation of the level of oesophagitis and the squamocolumnar junction, the length of columnar-lined lower oesophageal mucosa and the upper limit of gastric folds. The extent of Barrett's esophagus was defined as the distance from the gastro-esophageal junction to the location of the

highest point of the squamocolumnar junction. The presence of hiatal hernia was marked—if present and measured at the same time. Biopsy specimen were taken by method of “four quadrant biopsy” every 2 cm starting at the top of the rugal folds. Biopsy specimen were fixed with 10% buffered formalin and embedded in paraffin wax. Serial sections were then cut and stained with haematoxylin-eosin by the pathologist in Institute of Pathology – University clinical center (UCC) of Prishtina, whereas alcian blue, Giemsa and imunohistochemistry stain were made in the UCC of Skopje. During endoscopical examination, the gastroesophageal junction was defined as the point at which the tubular oesophagus ended and the gastric rugal folds began. A columnar-lined oesophagus was identified when the squamocolumnar junction (SCJ) or any part of its circumference extended above the gastroesophageal junction. Patients with an irregular SCJ had biopsy samples obtained from glandular mucosal tongues extending into the oesophagus.

A biopsy specimen from antrum was also taken, in order to determine the eventual presence of *H. pylori* infection.

In this study were included patients with endoscopically and histopathologically verified diagnose of BE, age from 18-80, both male and female gender. Exclusion criteria were: columnar mucosa in the distal esophagus but no intestinal metaplasia on biopsy and patients with BE who have undergone endoscopic ablation therapy or enrolled in chemoprevention trials.

We collected the data and analysed them statistically, using the T-test. The results were presented through respective figures.

4. RESULTS

The 42 subjects included 25 (59%) were male and 17 (41%) were female, with mean age 52.8 ± 3.28 years. 15 patients (36%) were in the age-group 50-59 years.

Among total number of patients (42), 24 were obese (57%). 27 were smokers (64%), meanwhile alcohol

drinkers were 19 patients (45%).

Mean duration of symptoms was 9.4 ± 1.72 years.

Among 42 patients with Barrett's esophagus, 22 were with short segment (52%), the rest (20 patients) were with long segment of Barrett's esophagus (48%).

Concerning the hiatal hernia, 27 of 42 patients diagnosed with Barrett's esophagus (64%) also had hiatal hernia, of which 18 (66%) were LSBE, and 9 patients (34%) were SSBE ($p < 0.05$).

The presence of *Helicobacter pylori* infection was settled through quick test of urease (HUT test, Astra GmbH). The test was positive in 5 patients or 12%, of which 4 patients 9.5% were among SSBE group of patients, whereas one patient (2.5 %) was among LSBE group of patients ($p < 0.01$).

5. DISCUSSION

GERD is accepted as the primary etiologic factor for BE, which is in turn the major predisposing condition for esophageal adenocarcinoma. BE is thought to be the result of esophageal epithelial response to injury (8).

From results of our study we noticed that male patients were represented significantly higher in the total number of patients with BE, comparing to female patients ($p < 0.05$). The most represented age-group (with BE) was 50-59 years. Smoking (64%) and alcohol consumption (45%) were very common among these patients. These results, also the duration of symptoms of BE, were very similar with the results from the latest literature.

Hiatal hernia distorts the anatomy the normally protects against reflux by reducing pressure at the lower esophageal sphincter,

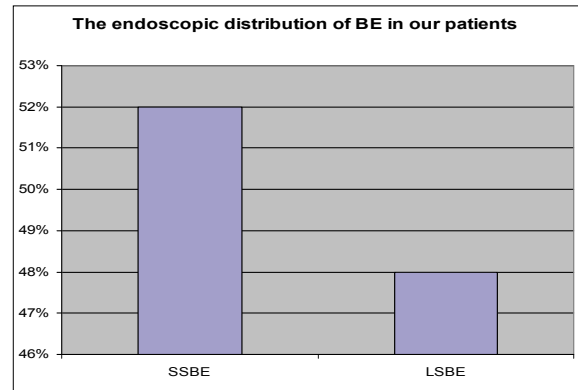


Figure 1. The endoscopic distribution of BR in our patients

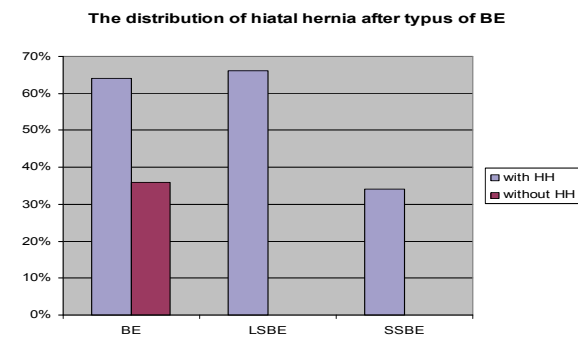


Figure 2. The distribution of hiatal hernia after typus of BE

creating an acidic hernia sac between the diaphragm and the esophagus, and decreasing the efficacy of peristalsis (9). Considering the hiatal hernia, it was significantly more present in patients with long segment of BE, than in those with short segment of BE (66% vs. 34%). One recent study, same as our study, shows that of 50 patients with GERD who developed BE, 63% had the finding of a hiatal hernia (10). Another study demonstrated that longer length of hiatal hernia correlated with longer segment of BE (11).

GERD, BE and esophageal adenocarcinoma have all been associated with the presence of obesity. The relationship between GERD and obesity is thought to be in part due to increased gastroesophageal sphincter gradient (12), intraabdominal pressure (13), and increased incidence of hiatal hernia in obesity (14). This is also confirmed by our results: obesity was present in 57% of our patients. A recent retrospective case-control study showed a strong direct relationship between mean visceral adipose tissue and BE when comparing patients with and with-

out BE who had undergone both endoscopy and an abdominal CT scan at a large Veterans Hospital (15). A similar correlation between body mass index and BE was found in another study, with an adjusted odds ratio of 1.35 for each five-point increase in BMI (16).

Helicobacter pylori, in contrast to obesity and hiatal hernia, may affect the risk of BE by physiologic rather than anatomic means. *Helicobacter pylori* may affect the risk of BE because can decrease gastric acidity through activity of urease (17).

The fact that *H. pylori* may be protective against BE is a contrast to its well established status as a risk factor for peptic ulcer disease and gastritis, and indeed eradication of *H. pylori* for PUD (18, 19, 20, 21, 22). Results of our study showed a low prevalence of *H. pylori* infection among patients with BE (12%). The data from the literature have also shown a low prevalence of *H. pylori* infection among these patients. In a similar study of 251 patients undergoing endoscopy, *cagA+* *H. pylori* was present in 44% of 25 controls, 36% of 36 patients with GERD, 20% of 10 patients with SSBE, and 0% of 18 patients with LSBE. The delimitation of our study was the absence of method for determining *cagA+* strains of *H. pylori*.

6. CONCLUSIONS

Referring to the results of our study, we came to these conclusions:

Age-group 50-59 years, male gender, smoking and alcohol consumption are important predictive factors in developing BE among patients with GERD.

Obesity is also an important factor in developing BE, as long as it was significantly represented

Most of patients with BE also had hiatal hernia, especially patients with long segment of BE.

The prevalence of *H. pylori* in-

fection in patients with BE, especially in those with LSBE was very low, which suggests the possibility of protective role of this microorganism.

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