

# Utility of Endoscopy for Diagnosis of Barrett in a Non-Western Society: Endoscopic and Histopathologic Correlation

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Barrett esophagus is metaplastic transformation of esophageal squamous epithelium to columnar cells. A total of 1370 patients who had undergone upper endoscopy because of dyspeptic complaints were enrolled in the study. Age, sex, alcohol and smoking habits, body mass index, type and duration of symptoms (heartburn, epigastric pain, nausea, vomiting), and use of proton pump inhibitors were evaluated in all patients and recorded on standardized forms. Patients were grouped as normal esophagogastric junction, long-segment Barrett esophagus, and short-segment Barrett. Biopsies were taken from at least 6 points and examined histopathologically. Of the 1370 patients involved in the study, 748 (54.6%) were female and 622 (45.4%) were male. Mean age was  $47.2 \pm 15.30$  years. Short-segment Barrett esophagus was detected in 16 patients, and long-segment Barrett was detected in 11 patients. Although Barrett esophagus was detected in 11 cases that were suspected to have Barrett during endoscopy, histopathology was negative in all cases that were not suspected to have Barrett. Barrett esophagus prevalence was significantly higher in people who used alcohol and tobacco and who had hiatal hernia. Although Barrett esophagus was detected in 40% of cases that were suspected to have Barrett during endoscopy, histopathology was negative in all cases that were not suspected to have Barrett. Barrett was detected in 40.7% of cases that were suspected to have Barrett during endoscopy; histopathology was negative in all cases that were not suspected to have Barrett. Sensitivity of endoscopy is questionable in detection of short-segment Barrett.

*Key words:* Endoscopy – Barrett esophagus – Gastroesophageal reflux – Dyspepsia – Histopathology

Barrett esophagus (BE) is the metaplastic transformation of esophageal squamous epithelium into columnar cells.<sup>1</sup> This histologic alteration is an important complication of gastroesophageal reflux disease (GERD), and it sets the groundwork for adenocarcinoma.<sup>2,3</sup> Diagnosis is made by showing goblet cells and intestinal metaplasia in biopsy specimens taken from the lesions directly seen under endoscopy (Fig. 1).<sup>4</sup> It has an increasing incidence not only in the United States, New Zealand, and Australia, but also in the rest of the developed world.<sup>5,6</sup> Although there are conflicts about the prevalence of BE, reports have demonstrated 1.2% to 25% positivity of BE in endoscopy of asymptomatic patients,<sup>7,8</sup> and 8% to 20% positivity in patients who have GER symptoms.<sup>9</sup> Factors such as hiatal hernia, obesity, and *Helicobacter pylori* (HP) are responsible for BE because they provoke acid reflux.<sup>10</sup> Recently, BE incidence rates raised after the definition of short-segment BE was introduced.

The aim of this study was to compare endoscopic and histopathologic findings in patients who presented with dyspeptic complaints and had upper endoscopy.

## Materials and Methods

A total of 1370 patients who had endoscopy for dyspeptic symptoms between February 2011 and March 2013 were enrolled in the study. Those who had gastric carcinoma, gastrointestinal bleeding during endoscopy, and coagulopathy disorder were excluded from the study. Age, sex, alcohol and smoking habits, heartburn, nausea, vomiting, use of proton pump inhibitors, and duration of symptoms were questioned and recorded on standard forms. Smoking more than 10 cigarettes a day was accepted as habitual smoking.<sup>11</sup> Alcohol abuse was identified according to the *Diagnostic and Statistical Manual of Mental Disorders 5*. Endoscopic examinations were carried out by gastroenterologists or certificated gastrointestinal surgeons using a standard endoscope (Fujinon EPX-4400, System WR, Fujifilm Turkey, Saitama, Japan) under sedation. During the course of endoscopy, esophagogastric junction (EGJ) was examined carefully. Squamocolumnar junction was defined as the line where squamous epithelium turns into salmon-

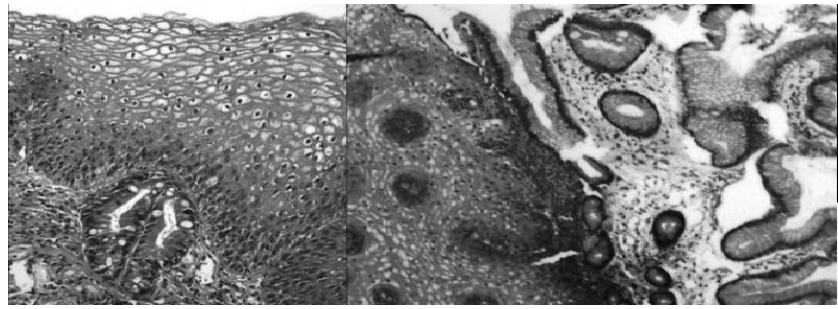
colored columnar mucosa (Fig. 1). Patients were classified as normal EGJ, long-segment BE (intestinal metaplasia  $\geq 3$  cm beginning from EGJ), or short-segment BE (SSBE; intestinal metaplasia  $< 3$  cm beginning from EGJ; Fig. 2).<sup>12–14</sup> The presence of more than 2 cm of distance between EGJ and diaphragmatic notch was accepted as hiatal hernia. When normal EGJ was detected, at least 6 biopsies from different sites were taken and examined histopathologically. Of these 6 biopsies, 4 were taken from the squamocolumnar junction and 2 were taken from the gastric antrum. In BE suspected cases, extra biopsies were taken from all possible quadrants and columnar epithelium sites 1 cm distant from each other. All biopsy materials were stored in 10% formalin solution and stained with hematoxylin-eosin and Alcian Blue (Fig. 2). Pathology specimens were reviewed by senior pathologists.

All patients were notified about the procedures by physicians, and informed consent was taken. Patient data were analyzed using SPSS 15.0 (SPSS Inc, Chicago, Illinois). Student *t*-test and  $\chi^2$  tests were used where appropriate.  $P < 0.05$  was accepted as statistically significant.

## Results

Of the 1370 patients involved in the study 748 (54.6%) were female and 622 (45.4%) were male. Mean age was  $47.2 \pm 15.30$  years. The demographic and clinical characteristics of patients are shown on Table 1. Alcohol use and smoking were significantly higher in male patients. A total of 19.2% of female and 22.6% of male patients were using proton pump inhibitors, and it was not statistically significant (Table 1). Female patients had more complaints of nausea, vomiting, and heartburn. Durations of symptoms were similar in both sexes. HP was positive in 64.8% of patients who had undergone endoscopy, and no significant difference was found between sexes. Endoscopic findings of patients using the classification described elsewhere<sup>15</sup> are listed in Table 2. A total of 27 patients had endoscopically diagnosed BE. Of these, 16 were reported as SSBE and 11 were reported as long-segment BE. Esophagitis was detected in 131 patients, of which 44 (33.5%) were female and 87 (66.5%) were male. The high rate of

**Fig. 1** Histopathology showing specialized intestinal metaplasia with glandular epithelium and characteristic goblet cells. Hematoxylin-eosin [ $\times 50$  (left panel),  $\times 100$  (right panel)].



esophagitis in male patients was statistically significant ( $P < 0.05$ ). Of the 11 patients (40.7%) with histopathologically diagnosed Barrett, 3 were female and 8 were male. There was not a statistically significant difference between sexes. Hiatal hernia was detected in 7 of 11 patients who were histopathologically identified as Barrett, and this was statistically significant ( $P < 0.05$ ). Gastrointestinal symptoms, such as nausea, vomiting, and heartburn, were significantly higher in female sex. Alcohol use and smoking were more frequent among males and it was statistically significant ( $P < 0.05$ ). Durations of symptoms were  $46.1 \pm 27.0$  months in patients with histopathologically proven BE and  $41.2 \pm 27.8$  months in patients who do not have BE, but the difference was not statistically significant. There was no statistically significant difference between sex groups on duration of symptoms ( $44.7 \pm 27.7$  months in female patients and  $43.2 \pm 27.2$  months in male patients). When patients were grouped according to body mass index, 15 were underweight (1.1%), 434 (31.6%) were normal weight, 587 (42.9%) were overweight, and 334 (24.4%) were obese. Obesity frequency in our study population was similar to that of the Turkish population.<sup>16</sup> There was not a statistically significant association between body mass index and BE ( $P > 0.05$ ).

## Discussion

Barrett metaplasia is accepted as a precancerous lesion in the development of esophageal adenocarcinoma. In our study BE prevalence in dyspeptic

patients who had endoscopy was found as 1.97% endoscopically and 0.8% histologically. Studies carried out in different countries have reached different results. A German study has found BE prevalence as 4.2%, and another study made in Japan reported this prevalence as 0.3% to 0.6%.<sup>17</sup> In studies conducted with Turkish patients, histopathologic BE prevalence has been found to be 1.7% and 7.4%.<sup>15,18</sup> In our study, most of the 11 patients with pathologically diagnosed BE were male, and the mean age was 46 years. These results are similar to the findings of other series in medical literature.<sup>19,20</sup>

SSBE could easily be missed when not carefully looked for during endoscopy, and biopsy could easily be taken from the wrong location. In a study by Padda and Ramirez,<sup>21</sup> histopathologic confirmation rates of SSBE and long-segment BE were 38% and 75%, respectively. As with Padda and Ramirez, in our study, only 36% of patients with a diagnosis of having SSBE during endoscopy had histopathologically confirmed BE, whereas most of the patients who were categorized as long-segment BE during endoscopy had histologic BE.

Hiatal hernia is an important factor in the development of GER, which is frequent in patients with BE. In a study by Cameron,<sup>22</sup> hiatal hernia was seen in 96% of patients with BE. In addition, hernia sac was longer and wider in patients with BE.<sup>22</sup> In our study, hiatal hernia was found in 7 of 11 patients (63.3%) who had histopathologically proven BE.

There are controversies regarding the correlation of esophagitis and BE.<sup>23,24</sup> There was no statistical-

**Fig. 2** Salmon-colored columnar mucosa.

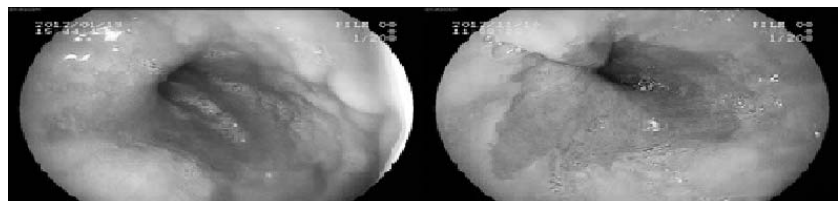


Table 1 Demographic and clinical features

Characteristic	Male (n = 622)	Female (n = 748)	Total (n = 1370)
Age, y, mean $\pm$ SD (%)	46.4 $\pm$ 15.1 (24–90)	47.8 $\pm$ 15.4 (23–87)	47.2
Smoking, no. (%) <sup>*</sup>	237 (38.1)	162 (21.6)	399 (29.1)
Alcohol abuse, no. (%) <sup>*</sup>	122 (19.6)	13 (1.7)	135 (9.8)
Epigastric pain, no. (%)	219 (35.2)	288 (38.5)	507 (36.7)
Nausea, no. (%) <sup>*</sup>	154 (24.7)	360 (48.1)	514 (37.5)
Vomiting, no. (%) <sup>*</sup>	31 (4.9)	103 (13.7)	134 (9.7)
Heartburn, no. (%) <sup>*</sup>	67 (10.7)	113 (15.1)	180 (13.1)
HP positivity, no. (%)	392 (63)	486 (64.9)	878 (64)
Medical treatment, no. (%)	141 (22.6)	144 (19.2)	285 (20.8)
Duration of symptoms, mo, mean $\pm$ SD	44.7 $\pm$ 27.7	43.2 $\pm$ 27.2	43.9

<sup>\*</sup>P < 0.05.

ly significant difference in esophagitis rates of patients who had BE and who did not have BE in our study. In addition, no relationship was found among dyspeptic symptoms (*e.g.*, nausea, vomiting, heartburn) or duration of symptoms and BE in our study. In studies carried out by Spechler *et al*<sup>24</sup> and Nandurkar *et al*,<sup>25</sup> a relation between SSBE and GER was not found. On the contrary, studies by Johnston *et al*<sup>23</sup> Pereira *et al*<sup>26</sup> showed a significant relation between SSBE and GER. Although we did not find a relation between the presence of esophagitis and BE, nonerosive GER disease that cannot be detected during endoscopic examination may be an important factor in the development of BE.

The relationship between HP infection and BE has not been fully identified yet. Moreover, some authors argue that HP infection is an inhibitor of BE development by reducing acid secretion.<sup>27</sup> On the contrary, no relation between HP infection and BE was found in several studies.<sup>28,29</sup> In a such a high-prevalence area as Turkey, it may be difficult to document a relationship between HP infection and

BE. In fact, no significant association was found between HP infection and BE in our study.

There are studies reporting that alcohol use provokes GER and thus indirectly reduces BE, but on the other hand there are studies showing no relation between the two.<sup>30,31</sup> Although some previous studies have shown inverse correlation with wine use<sup>32,33</sup> but positive correlation with liquor use<sup>34</sup> and BE development, some authors have argued that alcohol itself, not the type of the different drinks, was directly related to GERD.<sup>35</sup> Our study found a significant relationship between BE and alcohol abuse and tobacco use, and demonstrates that BE development increases with alcohol abuse and smoking. Further studies are needed to show the mechanisms and results of risks between foods and drinks and BE.

There are certain reports indicating that there exists a discordance between clinical and pathologic diagnosis of BE among endoscopists in different countries.<sup>36</sup> Some authors suggest that the definition of BE should actually be columnar lined esophagus. These further justify the aim of our study.

## Conclusion

Patients with dyspeptic or GERD complaints are candidates for BE screening. It is important to raise awareness about SSBE, although it may yield overdiagnosis of SSBE, which may be another problem for beginners in endoscopy. Although BE was detected 40.7% of cases that were suspected to have BE during endoscopy, histopathology was negative in all cases that were not suspected to have BE, thus proving the importance of a careful endoscopic evaluation. Our study points out the fact that sensitivity of endoscopy is questionable in detection of SSBE.

Table 2 Classification of cases that were diagnosed as Barrett with endoscopy

Endoscopic appearance	Male (n)	Female (n)	Total (n)
Short segment Barrett's			
A	1	1	2
B	5	4	9
C	1	2	3
D	1	0	1
E	1	0	1
Long segment Barrett's	6	5	11
Total (n)	15	12	27

A, Barrett appearance on squamocolumnar junction; B, tongue-like Barrett appearance; C, islet-like Barrett appearance; D, tongue-like Barrett appearance and irregularity on squamocolumnar junction; and E, islet-like Barrett appearance and irregularity on squamocolumnar junction.

Table 3 Comparison of clinical and endoscopic features of patients with and without histopathologic Barrett diagnosis

Characteristic	Pathologic Barrett	No pathologic Barrett
Age, y, mean $\pm$ SD (%)	48.6 $\pm$ 14.8 (20–71)	47.1 $\pm$ 15.3 (23–90)
Female/male, no.	3/8	745/614
Smoking, no. (%) <sup>*</sup>	9 (81)	390 (29)
Alcohol abuse, no. (%) <sup>*</sup>	8 (72)	127 (9)
Heartburn, no. (%)	1 (9)	179 (13)
Nausea, no. (%)	4 (36)	510 (36)
Vomiting, no. (%)	0	134 (10)
Epigastric pain, no. (%)	5 (45)	502 (37)
Duration of symptoms, mo, mean $\pm$ SD	46.1 $\pm$ 27.0	41.2 $\pm$ 27.8
Hiatal hernia, no. (%) <sup>*</sup>	7 (64)	161 (12)
HP positivity, no. (%)	7 (64)	871 (64)
Endoscopic esophagitis, no. (%)	1 (9)	130 (10)
Endoscopic Barrett, no. (%) <sup>*</sup>	11 (40.7)	16 (59.2)
Endoscopic LES floppiness, no. (%)	0	30 (2)

LES, lower esophageal sphincter.

<sup>\*</sup>P < 0.05.

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