Barrett's Esophagus in Patients with Symptomatic Gastro-Oesophageal Reflux Disease-Attending in a Tertiary Care Hospital of Bangladesh

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Barrett's esophagus (BE) is a risk factor for oesophageal adenocarcinoma, usually diagnosed during UGI endoscopy for GERD symptoms. GERD is common in Bangladesh. Aim of this study was to detect Barrett's oesophagus with degree of dysplastic change and possible associated risk factors in development of Barrett's esophagus in symptomatic GERD patients in Bangladesh. This observational, cross sectional study was carried out in the department of Gastroenterology of Bangabandhu Sheikh Mujib Medical University (BSMMU) from November 2010 to April 2012. Total 126 patients with GERD symptoms underwent UGI endoscopy where columnar-lined epithelium (CLE) in oesophagus were recognized as mucosal tongues or an upward shift of the squamocolumnar junction and four quadrant biopsy were taken. BE was diagnosed when specialized intestinal metaplasia was detected histologically in suspected CLE. Among 126 study population, 60 had endoscopic sign of CLE, 21 was diagnosed as Barrett's oesophagus. Mean age of patients having Barrett's was 34.67 ± 12.60 (±SD) years, 3 had long segment, 15 had short segment,3 had ectopic mucosal island. Low grade dysplasia were found in 5(23.8%), High grade dysplasia in 1(4.8%) and remaining 15(71.4%) were non dysplastic. In this study age, sex, residence, socioeconomic status, duration of GERD symptoms had no significant influence on development of BE. Smoking, betel nut chewing, NSAIDs, OCP, BMI also showed no effect in developing Barrett's in GERD patients. BE is not uncommon in Bangladesh. No significant risk factors were identified. Further large scale study is recommended.

[Dinajpur Med Col J 2017 Jan; 10 (1):80-88]

Key words: Gastro-oesophageal Reflux Disease (GERD), Barrett's oesophagus

Introduction

Barrett's esophagus (BE) is a consequence of chronic gastro oesophageal reflux disease typically discovered during endoscopic examination for evaluation of GERD symptoms[1] "Barrett's esophagus is a change in the oesophageal epithelium of any length that can be recognized at endoscopy and is confirmed to have intestinal metaplasia by biopsy of the tubular oesophagus and exclude intestinal metaplasia of cardia."[2] It is an acquired disorder associated with oesophageal acid injury.[3] On endoscopic examination, columnar lined-epithelium (CLE) in the oesophagus can be recognized by its characteristic red color, velvet like texture that contrast sharply with pale glossy appearance of adjacent squamous epithelium.[4]

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In BE, squamocolumnar junction is displaced proximal to oesophago gastric junction, which is confirmed by presence of specialized intestinal metaplasia (SIM) on biopsy specimen. The extent of disease relates to the severity of oesophageal acid exposure.[3] It can be long segment (LSBE) and short segment (SSBE) when SIM present in a segment of columnar epithelium extending ≥ 3 cm, < 3 cm respectively. [5]

Longer duration and increased frequency of GERD symptom, male gender, white race[6] alcohol or tobacco use, obesity and hiatal hernia found to be risk factors in some studies.[7] Average age at the time of diagnosis is approximately 55 years. The condition is rare in children <10 years and virtually nonexistent in < 5 years.[8] Among adult symptomatic GERD patient, LSBE is found in 3% to 5% whereas 10% - 20% have SSBE.[9] In western countries the prevalence of BE in general adult population is between 1.6% and 6.8%.[10]

BE is relatively uncommon in Asia. It's prevalence was 2% in Taiwanese population,[11] which was higher than expected, in Malaysia 1.6% (LSBE) and 4.6% (SSBE) .[12] It was as high as 19.9% in Japan, 23.6% in India.[13] although in study by Dhawan et al in 2001 prevalence of BE was 6% in India.[14]. Outside Japan and India it ranged from 0.06% to 6%.[15]

It is a recognized premalignant condition of oesophageal adenocarcinoma (5 years survival of 11%).[15] The risk of cancer in general population with BE is approximately 0.5% / year.[16] The prevalence of GERD in Bangladesh is 19.4% (rural) and 18.1% (urban) respectively.[17,18] To the best of our knowledge, in Bangladesh no study was carried out to see the BE. This study is aimed in detecting BE with degree of dysplasia in symptomatic GERD patient and to assess associated risk factors in development of BE.

Methods

This observational, cross sectional study was carried out in the department of Gastroenterology of Bangabandhu Sheikh Mujib Medical University (BSMMU) from November 2010 to April 2012 Patients of either sex, age 18 years and above ,having GERD symptoms detected by using a questionnaire developed by Carlos Manterola et al. were enrolled in the study. Patients with history of oesophageal carcinoma, cardiac, pulmonary and musculoskeletal disorder of chest were excluded. Total 126 patients completed the study. History of cigarette smoking, alcohol, drugs particularly NSAIDs, H2 antagonist and PPIs were taken. After proper evaluation, explanation and informed written consent, all patients underwent endoscopy by single experienced endoscopist with a forward viewing video endoscope using tropical xylocaine pump spray 10% (Lidocaine 10 mcg/dose). After each endoscopy the endoscope were carefully cleaned and disinfected by first keeping the scope immersed in cidex (2.2-2.4% activated glutaraldehyde solution) for 10 minutes and then rinsing with sterile distilled water. Biopsy forceps were also disinfected and cleaned in similar manner. Endoscopically identification of squamocolumner junction (Z line) and gastroesophageal junction (proximal gastric fold) were done. Barrett's esophagus was suspected when squamocolumner junction was displaced proximal to the gastroesophageal junction and were categorized into long segment (≥3 cm) , short segment (<3 cm) or islands of ectopic mucosa. When such changes observed, four quadrant biopsy were taken. Total four biopsies were taken. The biopsy specimen were put on a container containing buffer formalin and sent to pathology department for histopathological confirmation of Barrett's

oesophagus by the presence of specialized intestinal metaplasia with hematoxylin and eosin (H&E) stain**.** Statistical analysis was done using SPSS (statistical package for social science) program for windows software (version 15). Data were expressed as mean ± SD. Unpaired t test and Chi square test were done for different means and different categorical variables.

Results

Total 126 individuals with GERD symptoms were included in the study. Mean age of patients was 33.52 ± 10.55 (±SD) years with lowest age of 18 years and highest of 60 years. Majority (34.9%) was between 25 to 35 years age group. Among them 71 (56.3%) were female and 55 (43.7%) were male with male and female ratio of 0.77: 1. Among them 67(53.2%) came from rural area and 59(46.8%) came from urban area. 63 (50%) patients were housewife, 20 (15.9%) were students. 95 patients (75.4%) came from lower middle class family with monthly income of <20000 taka. The mean and median duration of GERD symptoms was 4.02 ± 4.91 (±SD) years and 2 years, respectively.

Majority (89 patients, 70.6%) with GERD symptoms had no risk behavior. 19 patients (15.1%) were smoker,18 patients (14.3%) were betel leaf with tobacco chewer .57 patients (45.2%)took NSAIDs, 50 female(70%) took OCP. Most of the patients took antiulcerants (91.3% PPI, 17.5% H2 antagonist) for symptoms. Mean BMI of the study population was 24.49 ± 3.07 with range of 15.6-30.0 kg/m^2 BMI of most of the study population (68.3%) were within normal limit (18-25 kg/m^2). Whereas 23% were overweight (26-30 kg/m^2**),** 0.8% were obese (>30 kg/m^2**)** and 7.9% were under weight (< 18 kg/m^2**).**

Table I: Distribution of endoscopically suspected BE in symptomatic GERD patients

Endoscopy findings	Frequency	Percent
Barrett's (ESBE)	60	47.6
Long Segment	10	16.67
Short Segment	45	75.00
Ectopic mucosal Islands	5	8.33
Non Barrett's	66	52.4
Total	126	100.0

ESBE- Endoscopically suspected Barrett's esophagus

Among 126 study population, endoscopically suspected Barrett's esophagus (ESBE) were 60 (47.6%) and remaining 66 (52%) were labeled as Non Barrett's. Among 60 ESBE patient 75% had short segment, 16.67% long segment Barrett's and 8.33% had Ectopic mucosal islands (Table I)

Table II: Distribution of histopathologically proved BE in symptomatic GERD patients

Histopathology findings	Frequency	Percentage
Barrett's esophagus	21	16.7
Long Segment	03	14.3
Sort Segment	15	71.4
Ectopic mucosal Islands	03	14.3
Non- Barrett's esophagus	105	83.3
Total	126	100

But histologically proved Barrett's esophagus (SIM) were 21 (16.7%), remaining 105 (83.3%) were labeled as Non Barrett's. Among 21 BE pt 71.4% were short segment, 14.3% Long segment and 14.3% were found to have Ectopic mucosal islands (Table II).

Table III: Distribution of dysplasia in Barrett's patients

Dysplasia	Long Segment	Sort Segment	Ectopic mucosal Islands	Total
Low grade dysplasia	1 (33.3%)	4 (26.7%)	0 (.0%)	5 (23.8%)
High grade dysplasia	0 (.0)	1 (6.7%)	0 (.0)	1 (4.8%)
No dysplasia	2 (66.7%)	10 (66.7%)	3 (100.0%)	15 (71.4%)
Total	3 (100.0%)	15 (100.0%)	3 (100.0%)	21 (100.0%)

Among 21 histologically proved Barrett's esophagus, Low grade dysplasia were found in 5(23.8%), High grade dysplasia in 1(4.8%) and remaining 15(71.4%) were non dysplastic. (Table III)

Risk factors for developing Barrett's Esophagus in GERD

Several risk factors like age, sex, residence, socioeconomic status, duration of GERD symptoms, cigarette smoking, betel leaf, tobacco, alcohol, NSAID, H2 antagonist, PPI, OCP, BMI were assessed to see whether they play any significant role in developing Barrett's Esophagus in symptomatic GERD patients .

Table IV(a): Distribution of Histological findings among different age groups

Age (in year)	Histopathology findings		p value*
	Barrett's	Non Barrett's	
≤25	5 (15.2%)	28 (84.8%)	
25-35	8 (18.2%)	36 (81.8%)	
35-45	2 (6.7%)	28 (93.3%)	
>45	6 (31.6%)	13 (68.4%)	
Total	21 (16.7%)	105 (83.3%)	
Mean ± SD	34.67 ± 12.60	33.29 ± 10.15	0.586^{ns}

*t test was done to measure the level of significant. ns-not significant

Among the total study population, the mean age of patients having Barrett's was 34.67 ± 12.60 (±SD) years, whereas in non Barrett's patients was 33.29 ± 10.15 (±SD) years. This difference was not statistically significant (p>0.05) (Table IVa). However, development of Barrett's was observed more above the age of 45yrs (31.6%) than at or below 45yrs (14%) (Table IVb).

Table IV(b): Peak age of Barrett's among study population

Age (in year)	Histopathology findings		p value*
	Barrett's	Non Barrett's	
≤45	15 (14.0%)	92 (86.0%)	0.058^{ns}
>45	6 (31.6%)	13 (68.4%)	
Total	21 (16.7%)	105 (83.3%)	

*Chi-square test was done to measure the level of significant. ns-not significant

Table V: Distribution of Histological findings among sex groups

Sex	Histopathology findings		p value*
	Barrett's	Non Barrett's	
Male	9 (16.4%)	46 (83.6%)	0.936^{ns}
Female	12 (16.9%)	59 (83.1%)	
Total	21 (16.7%)	105 (83.3%)	

*Chi-square test was done to measure the level of significant. ns-not significant

Among 21 Barrett's patients, 9(16.4%) were male and 12(16.9%) were female. Sex difference was not statistically significant (p>0.05). Sex difference was also not statistically significant (p>0.05) among non Barrett's patient. (Table V)

Table VI: Distribution of residence by histological findings

Residence	Histological findings		p value*
	Barrett's	Non Barrett's	
Rural	9 (13.4%)	58 (86.6%)	0.229^{ns}
Urban	12 (20.3%)	47 (79.7%)	
Total	21 (16.7%)	105 (83.3%)	

*Chi-square test was done to measure the level of significant. ns- not significant

Among 21 Barrett's patients, 9(13.4%) patients reside in rural areas and 12(20.3%) were in urban. Residence difference was not statistically significant (p>0.05)

Table VII: Distribution of Monthly family income by histological findings

Monthly family income (in Tk.)	Histopathology findings		p value*
	Barrett's	Non Barrett's	
≤5000	2 (15.4%)	11 (84.6%)	
5000-20000	16 (16.8%)	79 (83.2%)	
>20000	3 (16.7%)	15 (83.3%)	
Total	21 (16.7%)	105 (83.3%)	
Mean ± SD	14119.05 ± 6985.84	14124.76 ± 8007.31	0.998^{ns}

*t test was done to measure the level of significant. ns-not significant

There are no significant difference among Barrett's and non Barrett's patients in different income groups which is shown in TableVII.

Table VIII: Mean (± SD) duration of symptoms among two groups

	Histopathology findings		p*
	Barrett's	Non Barrett's	
Duration of symptoms	5.08 ± 5.26	3.81 ± 4.83	0.281^{ns}

*t test was done to measure the level of significant. ns-not significant

The mean Duration of symptoms of the study population in Barrett's and non Barrett's patients were 5.08 ± 5.26 (±SD) years and 3.81 ± 4.83 (±SD) years respectively. This difference was not statistically significant (p>0.05) (Table VIII).

Table IX: Distribution of personal history on histological findings

personal history	Histopathology findings		p*
	Barrett's	Non Barrett's	
H/O Cigarette smoking	5 (26.3)	14 (73.7)	0.221^{ns}
Betel leaf with chewing tobacco	5 (27.8)	13 (72.2)	0.172^{ns}
Alcohol	0	0	

*Chi-square test was done to measure the level of significant. ns-not significant

Among 19 smokers, 5 (26.3%) subjects were in Barrett's group and 14(73.7%) in non-Barret's group. This difference was not statistically significant (p>0.05). Regarding betel leaf with tobacco chewer 5 (27.8%) patients were in Barrett's group and 13(72.2%) were in non Barrett's group. This difference was also not statistically significant (p>0.05).

Table X: Distribution of drugs history on histological findings

Drugs history	Histopathology findings		p*
	Barrett's	Non Barrett's	
NSAIDS	13 (22.8%)	44 (77.2%)	0.093^{ns}
H2 antagonist	6 (27.3%)	16 (72.7%)	0.142^{ns}
P.P.I	18 (15.7%)	97 (84.3%)	0.323^{ns}
OCP	7 (14.0%)	73 (86.0%)	0.314^{ns}

*Chi-square test was done to measure the level of significant. ns-not significant

Among respondents who took NSAIDs 13(22.8%) were in Barrett's group and 44(77.2%) were in nonBarrett's which was not statistically significant. Regarding H2 antagonist 6(27.3%) in Barrett's and 16(72.7%) in non-Barrett's group, PPI 18(15.7%)in Barrett's and 97(84.3%) in non-Barrett's and OCP 7(14%) in Barrett's and 73(86%) in non-Barrett's group .These difference were also not statistically significant (p>0.05) which is shown in Table 10.

Table XI: Distribution of BMI among Barrett's and non-Barrett's groups

	Histopathology findings		
BMI	Barrett's	Non Barrett's	p*
Under weight	4 (40.0%)	6 (60.0%)	
Normal	14 (16.3%)	72 (83.7%)	
Over weight	3 (10.3%)	26 (89.7%)	
Obese	0 (.0)	1 (100.0%)	
Total	21 (16.7%)	105 (83.3%)	
Mean ± SD	21.09 ± 3.08	22.77 ± 3.00	0.021[s]

*t test was done to measure the level of significant. s-Significant.

Mean±SD of BMI among Barrett's was lower (21.09±3.08) than that of nonBarrrett's group (22.77±3.00) which was statistically significant (p<0.05%) (Table 11)

Discussion

In Western countries, the epidemiology of esophageal cancer has changed considerably over the past decades with a rise in the ratio of adenocarcinoma to squamous cell carcinoma. This is thought due to increased prevalence of Barrett's esophagus among them. Although the prevalence of gastroesophageal reflux is increasing in Asia, the prevalences of Barrett's esophagus (BE) and esophageal adenocarcinoma (EAC) have remained low in most Asian countries.

The present study was the first of its kind in Bangladesh where we had seen frequency of Barrett's esophagus among symptomatic GERD patients. Among 126 study population, Endoscopically suspected Barrett's esophagus (ESBE) were 60 (47.6%) and remaining 66 (52%) were labeled as Non Barrett's. This finding was near about finding of a study done by Akiyama et al[111] in Japan where endoscopically suspected Barrett's esophagus was (43.1%) but higher than other studies in Japan, Korea and Taiwan.[19-23]

Among endoscopically suspected Barrett's patients (60) who underwent biopsy for histopathology - histologically proven Barrett's esophagus were 21 (16.7%). Remaining 105(83.3%) of the study subjects were labeled as Non Barrett's. This observation is comparable with study of Western countries, Japan, India and china[9,21,24] but higher than Korea, Taiwan, Iran and Turkey.[22,23,25,26] Among 21 BE pt 15 (71.4%) were short segment, 3(14.3%) Long segment and 3(14.3%) were found to have Ectopic mucosal islands.

Among 21 histologically proven Barrett's esophagus, Low grade dysplasia were found in 5(23.8%),High grade dysplasia in 1(4.8%) and remaining 15(71.4%) were non dysplastic. Mean age of patients having Barrett's was 34.67 ± 12.60 (±SD) years, which is lower than other countries of Asia where the mean age of patients with BE ranges from 51.1 to 66.7 years.[20,23,27] However development of Barrett's was observed more above the age of 45yrs(31.6%) than at or below 45yrs (14%) among symptomatic GERD patients.

The mean Duration of symptoms of the study population in Barrett's and non Barrett's patients were 5.08 ± 5.26 (±SD) years and 3.81 ± 4.83 (±SD) years respectively. This difference was not statistically significant

(p>0.05). Regarding sex distribution, there was slightly female predominance. Among Barrett's patients, 9(16.4%) were male and 12(16.9%) were female. Sex difference was not statistically significant (p>0.05). This observation inconsistent with studies from Asian countries which showed that men are more likely to have BE with a male/female ratio of approximately 1.93–2.09.[23, 27]

Among 21 Barrett's patients, 9(13.4%) patients reside in rural areas and 12(20.3%) were in urban . Residence difference was not statistically significant (p>0.05). Most of the patients came of lower middle socioeconomic family. The mean(± SD) of monthly family income in Barrett's and non Barrett's patients were 14119.05 ± 6985.84 (±SD) taka and 14124.76 ± 8007.31 (±SD) taka respectively. This difference was not statistically significant (p>0.05).

Among 19 smokers, 5 (26.3%) subjects were in Barrett's group and 14(73.7%) in non-Barret's group . This difference was not statistically significant (p>0.05). Similar results also found by Cygil CP et al[28] and Conio M et al[29] among western population but Akiyama T et al[30] and Kim JH et al[31] found that there were increased risk of BE among smokers. Regarding betel leaf with tobacco chewer 5 (27.8%) patients were in Barrett's group and 13(72.2%) were in non-Barrett's group. This difference was also not statistically significant (p>0.05).

Among respondents who took NSAIDs 13(22.8%) were in Barrett's group and 44(77.2%) were in non-Barrett's which was not statistically significant. Regarding H2 antagonist 6(27.3%) in Barrett's and 16(72.7%) in non-Barrett's group, PPI 18(15.7%) in Barrett's and 97(84.3%) in non-Barrett's and OCP 7(14%) in Barrett's and 73(86%) in non-Barrett's group. These difference were also not statistically significant (p>0.05).

Mean±SD of BMI among Barrett's was lower (21.09±3.08) than that of nonBarrrett's group (22.77±3.00) which was statistically significant (p<0.05%) (Table XI). This observation showed no association between BMI and BE which was similar to a meta-analysis by Cook et al.[32] who concluded that there was no association between BMI and Barrett's esophagus when the control group comprised GERD patients, but there was a positive association when cases were compared to population controls. However a retrospective study in Japanese patients with fatty liver disease suggested that abdominal obesity was a risk factor for BE.[33]

Conclusion

Previously it was thought that Barrett's esophagus is a disease of western populations. It's prevalence is low in Asian countries due to low dietary fat intake, genetic factors and low body mass index.[14] Among Asian countries, highest prevalence were observed in Japan and India which was reflected in this study. So we conclude that Barrett's esophagus is not uncommon in our country. In this study no significant influence were observed among smokers, betel nut chewers or patients taking NSAIDs, PPI, H_2antagonist and OCP. BMI also showed no effect developing Barrett's in GERD patients.

Limitations

There are several limitations of this study: sample size was too small and study period was short. This study was conducted in a tertiary care hospital. So, the observation of this study may not the reflection of the country. Dietary habit may influence in progression of Barrett's esophagus among GERD pts. But full dietary habits among the study subjects were not evaluated in this study. In this study four quadrant biopsies,

one from each quadrant were taken but eight biopsies, taking two from each quadrant is the standard protocol.

Recommendation

Considering the results and limitations of the study we propose the following recommendation:

- Large scale population based prospective studies are needed to find out the prevalence of Barrett's esophagus in our country.
- Dietary influence on development of Barrett's esophagus (if any) should be studied.
- These patients should be followed up for long time – so that exact nature of short segment, long segment and development of adenocarcinoma could be find out.

Refference

1. Layergren J, Bergstrom R, Lindgren A, Nyren O. Symptomatic Gastroesophageal reflux as a risk factor for oesophageal adenocarcinoma.N Engl J Med 1999;340:825-31.
2. Wang KK, Sampliner RE. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. Am. J.Gastroenterol. 2008; 103: 788–97.
3. MA J, Thomas loughney . Esophageal manometry and Ambulatory 24 hours PH Monitoring in patients with short and long Segment Berretts Esophagus. The American journal of Gastroenterology,1998; 93:134-9.
4. Spechler SJ. Gastroesophageal reflux disease and its complications.In: FriedmanSI,MC Quaid KR and Grendell JH (editors):Current diagnosis and treatment Gastroenterology-second edition,MC Graw –Hill,New York,2003:266-282.
5. Phillips RW, Wong RK. Barretts esophagus:Natural history , incidence, etiology and complications. Gastroclinics North AM 1991;20:791-815.
6. Cameron AJ, Ott BJ, Payne WS. The incidence of adenocarcinoma in columnar lined (Barretts) oesophagus. N Engl J Med.1985;313:857-859.
7. Avidan B, Sonner A, Schnell TG, Sontag SJ. Hiatal Hernia and acid reflux frequency predict presence and length of Barretts esophagus.Dig Dis Sci 2002;47:256-264.
8. Hassall E: Esophageal metaplasia: Definition and prevalence in childhood. Gastrointestinal Endosc 2006;64:676-7.
9. Spechler SJ. Barretts oesophagus .N Engl J Med 2002;346:836-42.
10. Rex DK,Cummings OW, Shaw M. Screening for Barrett's esophagus in colonoscopy patients with or without heartburn . Gastroenterology 2003;125:1670-7.
11. Yeh. C, Has CT, HO As, Sampliner RE, Fass R. Erosive esophagitis and Berretts esophagus in Taiwan.A higher frequency than expected.Dig Dis sci 1997;42:702-706.
12. Rajendra S, Kutty K, Karim N. Ethnic differences in the prevalence of endoscopic esophagitis and Barretts esophagus.Dig Dis sci.2004 Feb,49(2):237-42.
13. Punia RS, Arya S, Mohan H, Dusija A, Bal A. Spectrum of clinicopathological Changes in Barrett's Oesophagus. J. Assoc. Physicians of India 2006;54:187-9.
14. Dhawan PS, Alvares JF, Vova IM . Prevalence of short segments of specialized columnar epithelium in distal oesophagus;Association with gastroesophageal reflux. Indian J.Gastroenterol.2001;20:144-7.
15. Chang CY, Cook MB, Lee YC, Lin JT, Ando T . Current status of Barrett's

esophagus research in Asia. J. Gastroenterol.Hepatol. 2011; 26: 240–46.
16. Shaheen NJ, Crosby MA, Bozymski EM. Is there publication bias in the reporting of cancer risk in Barrett's esophagus?Gastroenterology 2000; 119: 333–8.
17. Rokonuzzaman SM. Epidemiological study of GERD in a Rural Population using a Validated Questionnaire. Thesis work, Dept of Gastroenterology, BSMMU, January 2006.
18. Shahed MM. Epidemiological study of GERD in an Urban Population using a Validated Questionnaire . Thesis work, Dept of Gastroenterology, BSMMU, January 2006.
19. Fujiwara Y, Higuchi K, Shiba M . Association between gastroesophageal flap valve, reflux esophagitis, Barrett's epithelium, and atrophic gastritis assessed by endoscopy in Japanese patients. J. Gastroenterol. 2003; 38: 533–9.
20. Okita K, Amano Y, Takahashi Y. Barrett's esophagus in Japanese patients: its prevalence, form, and elongation. J. Gastroenterol. 2008; 43: 928–34.
21. Azuma N, Endo T, Arimura Y. Prevalence of Barrett's esophagus and expression of mucin antigens detected by a panel of monoclonal antibodies in Barrett's esophagus and esophageal adenocarcinoma in Japan. J. Gastroenterol. 2000; 35:583–92.
22. Park JJ, Kim JW, Kim HJ. The prevalence of and risk factors for Barrett's esophagus in a Korean population: a nationwide multicenter prospective study. J. Clin. Gastroenterol. 2009; 43:907–14.
23. Chang CY, Lee YC, Lee CT. The application of Prague C and M criteria in the diagnosis of Barrett's esophagus in an ethnic Chinese population. Am.J. Gastroenterol. 2009; 104: 13–20.
24. Mathew P,Joshi AS,Shukla A and Bhatia SJ. Risk factors for Barrett's esophagus in Indian patients with gastroesophageal reflux disease. J. Gastroenterol.Hepatol. 2011; 26: 1151–56.
25. Nasseri-Moghaddam S, Malekzadeh R, Sotoudeh M. Lower esophagus in dyspeptic Iranian patients: a prospective study. J. Gastroenterol. Hepatol. 2003; 18: 315–21.
26. Bayrakci B, Kasap E, Kitapcioglu G, Bor S. Low prevalence of erosive esophagitis and Barrett esophagus in a tertiary referral center in Turkey. Turk. J. Gastroenterol.2008; 19: 145–51.
27. Akiyama T, Inamori M, Iida H. Alcohol consumption is associated with an increased risk of erosive esophagitis and Barrett's epithelium in Japanese men. BMC Gastroenterol. 2008; 8: 58.
28. Caygill CP, Johnston DA, Lopez M. Lifestyle factors and Barrett's esophagus. Am.J. Gastroenterol. 2002; 97: 1328–31.
29. Conio M, Filiberti R, Blanchi S. Risk factors for Barrett's esophagus: a case-control study. Int. J. Cancer. 2002; 97:225–9.
30. Akiyama T, Inamori M, Akimoto K. Risk factors for the progression of endoscopic Barrett's epithelium in Japan: a multivariate analysis based on the Prague C & M Criteria. Dig. Dis. Sci. 2009; 54: 1702–7.
31. Kim JH, Rhee PL, Lee JH. Prevalence and risk factors of Barrett's esophagus in Korea. J. Gastroenterol. Hepatol. 2007; 22: 908–12.
32. Cook MB, Greenwood DC, Hardie LJ, Wild CP, Forman D. A systematic review and meta-analysis of the risk of increasing adiposity on Barrett's esophagus. Am. J. Gastroenterol. 2008; 103:292–300.
33. Akiyama T, Yoneda M, Inamori M. Visceral obesity and the risk of Barrett's esophagus in Japanese patients with non-alcoholic fatty liver disease. BMC Gastroenterol. 2009; 21: 56.