

Original Research Article**A Study of High Risk Operational Link for Gastritis Assessment (OLGA) Stages in South Indian Subjects****Thara Keloth¹, Marie Moses Ambroise², Thomas Alexander³, Susy S. Kurian⁴**

¹ Senior Resident, Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry-605006, India. ² Associate Professor, Department of Pathology, Pondicherry Institute of Medical Sciences, Puducherry-605014, India. ³ Professor, Department of Gastroenterology, Pondicherry Institute of Medical Sciences, Puducherry-605014, India. ⁴ Professor, Department of Pathology, Pondicherry Institute of Medical Sciences, Puducherry-605014, India.

Abstract**Corresponding Author:**

Marie Moses Ambroise,
Associate Professor,
Department of Pathology,
Pondicherry Institute of Medical
Sciences, Puducherry 605014,
India

E-mail:

drmosesambroise1978@gmail.com

(Received on 15.05.2018,

Accepted on 09.06.2018)

Background: The OLGA staging system which was developed in 2005 assesses the stage of gastric atrophy and also predicts the risk of gastric carcinoma development. High risk OLGA stages carry a significant risk for developing gastric carcinoma. A worldwide study of OLGA gastritis staging showed no cases of high risk OLGA stages in a centre from North India. The present study was undertaken to estimate the prevalence of high risk OLGA stages among dyspeptic patients in a South Indian population and also study the correlation with relevant clinico-pathological parameters.

Materials and Methods: Ninety-six patients attending the Gastroenterology OPD with dyspepsia were studied. Gastric biopsies were collected according to the Sydney-Houston biopsy protocol and were assessed using the OLGA system.

Results: The prevalence rate of high risk OLGA stages (III & IV) in this study was 6.25% and that of low risk OLGA stages (0, I & II) was 93.75%. The prevalence rate of H.pylori in this study was 62%.

Conclusion: The prevalence rate of high risk OLGA stages was 6.25% in subjects with dyspepsia among this South Indian population.

Keywords: Atrophic Gastritis; Gastric Carcinoma; Helicobacter Pylori.

Introduction

Gastric carcinoma is the second most common cancer in Chennai as recorded in the Chennai registry. It accounts for 9.3% of all cancers among men, being second only to lung carcinoma which has a prevalence of 9.8%. On an all Indian basis, the states with the highest prevalence are Arunachal Pradesh (20.7% among men) and Mizoram (15.5% among men) [1,2].

It is generally known that gastric carcinoma is preceded by H.pylori associated chronic atrophic gastritis with or without intestinal metaplasia [3,4].

The OLGA system was developed in 2005 and was derived from the modified Sydney system. The histological OLGA staging is based on the location and extent of atrophy as present in the antrum, the incisura and the corpus. High risk OLGA stages (Stages III and IV) are generally associated with greater risk of developing gastric carcinoma [5-9]. This study was undertaken in order to estimate the prevalence of high risk OLGA stages among dyspeptic patients, since there is a high prevalence of gastric carcinoma in this region of the country. The study also aimed to assess the correlation of OLGA stages with relevant clinico-pathological parameters.

Materials and Methods

Patient selection

This cross-sectional study was carried out over a period of 22 months, from October 2014 to July 2016. Patients who attended the outpatient department of the Gastroenterology services of PIMS with dyspeptic symptoms (abdominal pain, discomfort, vomiting, nausea, burping, belching and bloating) were evaluated with a questionnaire. The questionnaire included details about duration and nature of symptoms, family history of gastric cancer, history of smoking, and alcohol consumption (frequency, amount in volume and duration). The amount of alcohol consumed in grams/week was calculated, using the above details and patients were categorized into four groups in accordance with a previous study: no alcohol, <60g/week (Mild), 60-140g/week (Moderate), >140g/week (Heavy) [10].

Only those who had dyspeptic symptoms for a minimum period of three months were included in the study. Exclusion criteria were as follows: i) bleeding disorders ii) end stage liver disease iii) history of prior gastric surgeries iv) newly diagnosed or past history of gastric cancer v) inadequate biopsy

Endoscopy

Patients were subjected to upper gastrointestinal (GI) endoscopy after obtaining written consent. Biopsies from atleast five sites were obtained according to the Sydney-Houston protocol [11].

Histology

All specimens were routinely processed and sections were stained with Haematoxylin and Eosin (H&E), Alcian blue (for acidic mucin) and modified Giemsa (for H.pylori) stains. The biopsy specimens were assessed by an experienced expert GI Pathologist who was blinded to both the clinical details and endoscopic findings.

The histological slides were assessed for five parameters (H.pylori, activity, chronicity, atrophy and intestinal metaplasia) in the antrum, corpus and incisura angularis separately. Load of H. pylori, grade of atrophy and intestinal metaplasia (IM) were assessed using a four-tier

scale according to the Visual Analog Scale of the modified Sydney system [11]. OLGA stage was determined in each case according to the recommendations of the OLGA staging tutorial (Table 1) [5,6].

Statistical Analysis

The Pearson's Chi-square test and Fisher's Exact test were used for categorical variables. The One-Way ANOVA was used to compare the mean age. A two sided p value less than 0.05 was considered statistically significant for all tests. The data was entered in Microsoft Excel (Microsoft Corp., USA) and analyzed using IBM SPSS Statistics for Windows (version 20.0. Armonk, New York: IBM Corporation).

The study was approved by the Institutional Ethics Committee (IEC) and written informed consent was obtained from all the participants.

Results

A total of 96 cases of dyspepsia were included in the study after applying exclusion criteria. The baseline characteristics and OLGA staging are shown in Table 2. In this study, 93.75% of the 96 cases showed low risk OLGA stages (stages 0, I & II) and 6.25% of cases showed high risk OLGA stages (stages III & IV). There was no significant association of OLGA staging with age, sex and smoking history. The majority of OLGA stage III/IV cases (84%) were above 30 years of age. OLGA staging was significantly associated with alcohol intake. Only two cases had a family history of gastric carcinoma.

About a third of the cases (35.4%) had normal endoscopic study. Another third of cases (29.2%) were diagnosed endoscopically as having gastritis while the remaining third (35.4%) were diagnosed with different lesions including oesophageal and duodenal lesions. Sixty two percent of the total cases were positive for H.pylori. There was significant association of H.pylori load on the surface epithelium with OLGA stages with a 'p' value of 0.022. The H.pylori load showed an increasing trend from stage 0 to stage III and then a decreasing trend towards stage IV (Figure 1).

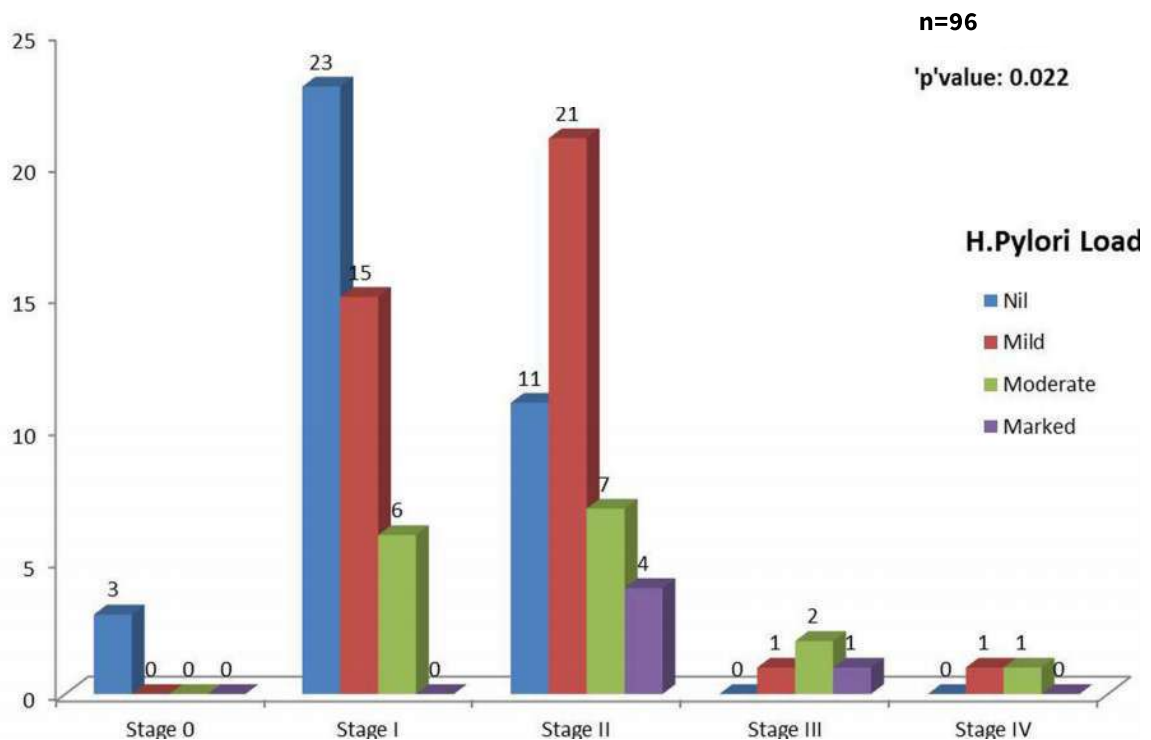
Table 1: OLGA staging system

	Atrophy score	Corpus			
		No atrophy	Mild atrophy	Moderate atrophy	Severe atrophy
Antrum (including incisura)	No atrophy	Stage 0	Stage I	Stage II	Stage II
	Mild atrophy	Stage I	Stage I	Stage II	Stage III
	Moderate atrophy	Stage II	Stage II	Stage III	Stage IV
	Severe atrophy	Stage III	Stage III	Stage IV	Stage IV

Table 2: OLGA staging and baseline characteristics

	Total	Stage 0	Stage I	OLGA staging Stage II	Stage III	Stage IV	P value
Number	96	3 (3.1%)	44(45.8%)	43(44.8%)	4 (4.2%)	2 (2.1%)	
Age mean (SD)	43.5(12.0)	42.7(17.2)	42.3(12.4)	45.4(11.6)	33.8 (6.2)	50 (0)	0.316
Sex							
Female	32(33.3%)	0	19(43.2%)	11 (25.6%)	2 (50%)	0	0.205
Male	64(66.7%)	3 (100%)	25(56.8%)	32 (74.4%)	2 (50%)	2 (100%)	
Smoking							
Smoker	11*(11.5%)	0	5 (11.4 %)	5 (11.6%)	1 (25 %)	0	
Non-smoker	85(88.5%)	3(100 %)	39(88.6%)	38(88.4%)	3 (75 %)	2 (100 %)	0.946
Alcohol							
No alcohol	61(63.5%)	1 (33.3%)	33(75%)	25 (58.1%)	2 (50 %)	0	
Mild alcohol	11(11.5%)	0	6 (13.6%)	5 (11.6%)	0	0	0.003
Moderate alcohol	10(10.4%)	2 (66.7%)	4 (9.1%)	3 (7.0 %)	1 (25 %)	0	
Heavy alcohol	14(14.6%)	0	1 (2.3%)	10 (23.3%)	1 (25 %)	2(100 %)	

* includes 10 current smokers and 1 ex-smoker

**Fig. 1:** Association of H. pylori load with OLGA stages

Shows significant association between the severity of H. pylori load and OLGA stages (2911x1600 pixels)

Intestinal metaplasia was present in 45% of the total cases and majority was of mild or moderate severity. There was a significant association between severity of IM and high risk OLGA stages ($p=0.001$) (Figure 2).

Atrophy and Intestinal Metaplasia according to Location:

Severe atrophy was found most frequently in the incisura (5.2 % of all cases) compared to the antrum (1 %) and corpus (1%). Moderate atrophy was also found most frequently in the incisura (42.7% of all cases) compared to the antrum (41.7% of all cases) and the corpus (4.2%).

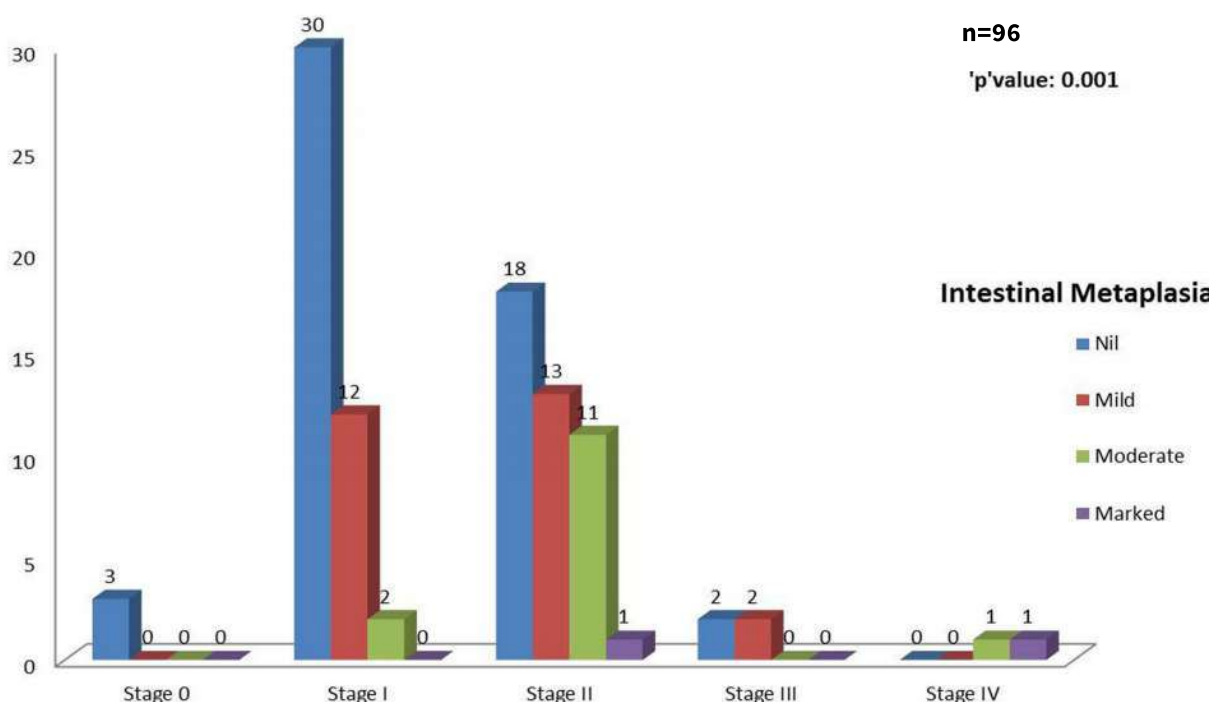


Fig. 2: Association of Intestinal Metaplasia with OLGA stages Shows significant association between the severity of IM and OLGA stages(2911x1600 pixels)

Moderate to severe intestinal metaplasia was found more frequently in the antrum (10.4 % of all cases) as compared to the incisura (6.3 %) and corpus (3.1%).

Discussion

The percentage of high-risk OLGA cases varies across regions. In a long term follow-up study from Italy, Rugge et al found that high-risk OLGA stages constituted 11% of their 93 cases at enrolment and 14 % after a follow-up period of atleast 12 years [7]. After the follow-up period ,only cases with high-risk OLGA at enrolment developed invasive carcinoma and high-grade intra-epithelial neoplasia. In a Chinese study, Zhou et al assessed OLGA in cases of functional dyspepsia and suspected early gastric cancer(EGC) and found the proportion of high-risk OLGA to be 52.1% and 22.4% in the EGC and non-EGC groups [12]. A study from South Korea found 16.6% of cases to be high-risk OLGA [13] whereas a study from Tunisia revealed the proportion to be only 6 % [14]. Our study found 6.25 % cases to be having high-risk OLGA. The age standardised rates for gastric cancer in South Korea, China, Italy, Tunisia and India are 41.8, 22.7, 8.2, 4.2 and 6.1 [15].

A worldwide study of OLGA gastritis staging in young adults (18-40 years) which included a centre from North India (Delhi) [8] and East Asian countries showed prevalence of high risk OLGA stages of 6 % in South Korea in keeping with the high prevalence of gastric carcinoma

in that region. The centre included in the study from North India showed no cases of high risk OLGA stages [8]. Notably the H. pylori prevalence was highest in India (75%) in this multicentre study. Our study did reveal high-risk OLGA in young adults also. Perhaps this reflects the lower incidence of gastric carcinoma in North India compared to the South [16].

High-risk OLGA stages increased significantly with age in both H. pylori positive and negative cases [13]. It is interesting to note that the mean age of high-risk OLGA cases was lower in our study compared to other countries. The mean age of cases in OLGA stage II/III/IV in two Western studies were 64.4/67.1/67.5 and 63.7/60.6/66.4 [17,18]. The Tunisian study revealed them to be 54.6/44.2/58. In our study the mean age was 45.4/ 33.8/50 and majority of stage III cases were found in the 20-40 age group. This could be due to poor sanitary conditions, higher prevalence of H. pylori infection and genetic predisposition. All our high-risk OLGA cases were positive for H.pylori. The Korean study found smoking to be a risk factor for high-risk OLGA. We however did not find a significant association between smoking and high-risk OLGA probably due to the lower number of smokers in our study. In the Korean study, 41.8% of the participants were smokers whereas only 11.5 % were smokers in our study [13]. Globally smoking is acknowledged to be a risk factor for gastric cancer. However tobacco chewing and cigarette smoking did not emerge as high risk factors for gastric cancer in a study

from Chennai region [19]. An earlier study from Mumbai also showed that bidi or cigarette smoking were not high risk factors for gastric cancer [20].

H. pylori is high in prevalence in South India (57.7%), as has been reported in various studies [21-25]. *H. pylori* prevalence in this study (62%) correlates with the reported prevalence in this region. The *H. pylori* load on the gastric surface showed an increasing trend from OLGA stages 0 to III, and a decreasing trend towards stage IV (Figure 2). This is probably explained by less availability of mucus-bicarbonate for this acid sensitive organism in severe gastric atrophy.

The degree of IM generally reflects the severity of atrophic gastritis. The significant association of severe IM with high risk OLGA in this study probably correlates with severe IM being a premalignant lesion.

A previous study showed that the sensitivity and specificity of endoscopy for the histological diagnosis of atrophy was found to be 61.5 and 57.7%, respectively, in the antrum, and 46.8 and 76.4%, respectively, in the body of the stomach [26]. Mucosal inflammation reduces the sensitivity of endoscopy, especially in individuals below 50 years of age [26]. The absence of rugae and the presence of visible vessels in the gastric mucosa can predict severe atrophy but with a relatively low sensitivity [27,28]. A high index of suspicion of gastric atrophy is important in the young age group, and histological confirmation of the diagnosis is necessary [26]. Narrow-band imaging and magnifying endoscopy corresponds better with histology scores [29]. Endoscopic atrophy was not evident in all cases of high-grade OLGA in our study. However we did not attempt a detailed analysis since endoscopic-histology correlation was not our objective.

Biopsy protocols are also important to categorise OLGA because of topographical differences in the atrophy and intestinal metaplasia. The management of precancerous conditions and lesions in the stomach (MAPS) guideline recommends at least four nontargeted biopsies of two topographic sites (at the lesser and greater curvature, from both the antrum and the corpus), in contrast to the modified Sydney Protocol which mandates a biopsy from the incisura angularis also [28]. It is important to include the incisura angularis in the biopsy sampling protocol because atrophy is more prevalent in this location as compared to the corpus and antrum. A recent study by Isajevs et al showed that the proportions of patients in the OLGA high-risk groups was underestimated by 35% when the biopsy protocol did not incorporate an incisura angularis site [30]. Our study also reveals that 50% of the high-risk OLGA cases would be underestimated if the incisura angularis is not included.

Conclusion

In conclusion, the prevalence rate of high risk OLGA stages was 6.25% in subjects with dyspepsia among this South Indian population. The biopsy sampling protocol must routinely include incisura angularis for accurate OLGA staging.

Strengths and Limitations of the Study

The strengths of this study include its prospective nature, adequate sample size and a rigorous biopsy sampling protocol. Non-consecutive selection of cases is a limitation.

References

1. Leading sites of cancer. In: Three Year Report of the PBCRs (2012-2014). Three year Report of Population Based Cancer Registries 2012-2014. [Last accessed on 2018 March 30]. Available from: <http://www.pbcrindia.org>.
2. Comparison of Cancer Incidence and Patterns of all Population Based Cancer Registry. In: Three Year Report of the PBCRs (2012-2014). [Last accessed on 2018 March 30]. Available from: <http://www.pbcrindia.org>.
3. Correa P. The biological model of gastric carcinogenesis. IARC SciPubl 2004;(157):301-10.
4. Ghoshal UC, Chaturvedi R, Correa P. The enigma of *Helicobacter pylori* infection and gastric cancer. Indian J Gastroenterol 2011;29(3):95-100.
5. Rugge M, Genta RM; OLGA Group. Staging gastritis: an international proposal. Gastroenterology 2005;129(5):1806-7.
6. Rugge M, Correa P, Di Mario F, El-Omar E, Fiocca R, Genta RM, et al. OLGA staging for gastritis: A tutorial. Dig Liver Dis 2008;40(8):650-8.
7. Rugge M, Boni MDE, Lli GP, Bona MDE, Giacomelli L, Fassan M. Gastritis OLGA-staging and gastric cancer risk/ : a twelve-year clinico-pathological follow-up study. Aliment Pharmacol Ther 2010;31:1104-11.
8. Rugge M, Kim JG, Mahachai V, Miehke S, Pennelli G, Russo VM, et al. OLGA gastritis staging in young adults and country-specific gastric cancer risk. Int J Surg Pathol 2008;16(2):150-4.
9. Rugge M, Meggio A, Pennelli G, Pisciole F, Giacomelli L, De Pretis G, et al. Gastritis staging in clinical practice: the OLGA staging system. Gut 2007;56(5):631-6.
10. Gao L, Weck MN, Stegmaier C, Rothenbacher D, Brenner H. Alcohol consumption and chronic atrophic gastritis: Population-based study among 9,444 older adults from Germany. Int J Cancer 2009;125(12):2918-22.
11. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and Grading of Gastritis. The Updated Sydney System. International workshop on the histopathology of gastritis, Houston 1994. Am J Surg Pathol 1996;20(10):1161-81.

12. Zhou Y, Li HY, Zhang JJ, Chen XY, Ge ZZ, Li XB. Operative link on gastritis assessment stage is an appropriate predictor of early gastric cancer. *World J Gastroenterol.* 2016;22(13):3670-8.
 13. Nam JH, Choi IJ, Kook MC, Lee JY, Cho SJ, Nam SY, et al. OLGA and OLGIM stage distribution according to age and Helicobacter pylori status in the Korean population. *Helicobacter* 2014;19(2):81-9.
 14. Ben Slama S, Ben Ghachem D, Dhaoui A, Jomni MT, Dougui MH, Bellil K. Helicobacter pylori gastritis: assessment of OLGA and OLGIM staging systems. *Pan Afr Med J* 2016(4);23:28.
 15. Globocan 2012: Estimated cancer incidence, mortality and Prevalence worldwide in 2012. International agency for research on cancer. Downloaded from http://globocan.iarc.fr/Pages/summary_table_site_sel.aspx.
 16. Asthana S, Labani P, Labani S. A review on cancer incidence in India from 25 population-based cancer registries. *J Dr NTR Univ Heal Sci* 2015;4(3):150.
 17. Rugge M, Fassan M, Pizzi M, Farinati F, Sturmiolo GC, Plebani M, et al. Operative link for gastritis assessment vs operative link on intestinal metaplasia assessment. *World J Gastroenterol.* 2011;17(41):4596-601.
 18. Capelle LG, de Vries AC, Haringsma J, Ter Borg F, de Vries RA, Bruno MJ, et al. The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis. *Gastrointest Endosc* 2010;71(7):1150-8.
 19. Sumathi B, Ramalingam S, Navaneethan U, Jayanthi V. Risk factors for gastric cancer in South India. *Singapore Med J* 2009;50(2):147-51.
 20. Rao DN, Ganesh B, Dinshaw KA, Mohandas KM. A case-control study of stomach cancer in Mumbai, India. *Int J Cancer* 2002 10;99(5):727-31.
 21. Misra V, Pandey R, Misra SP, Dwivedi M. Helicobacter pylori and gastric cancer/ : Indian enigma. *World J Gastroenterol* 2014;20(6):1503-9.
 22. Thirumurthi S, Graham DY. Helicobacter pylori infection in India from a western perspective. *Indian J Med Res* 2012;136(4):549-62.
 23. Shah H, Shah P, Jarag M, Shah R, Shah P, Naik K. Prevalence of Helicobacter pylori infection in gastric and duodenal lesions as diagnosed by endoscopic biopsy. *Int J Med Sci Public Health* 2016;5(1):93-6.
 24. Hemalata M, Sahadev R, Nanda N, Preethan KN, Suguna B V. Prevalence of Helicobacter pylori infection and histomorphologic spectrum in endoscopic biopsies. *Int J Biomed Res* 2013;4(11):608-14.
 25. Adlekha S, Chadha T, Krishnan P, Sumangala B. Prevalence of Helicobacter Pylori Infection Among Patients Undergoing Upper Gastrointestinal Endoscopy in a Medical College Hospital in Kerala, India. *Ann Med Health Sci Res* 2014;3(4): 559-63.
 26. Eshmuratov A, Nah JC, Kim N, Lee HS, Lee HE, Lee BH, et al. The correlation of endoscopic and histological diagnosis of gastric atrophy. *Dig Dis Sci* 2010;55(5):1364-75.
 27. Redeen S, Petersson F, Jonsson KA, Borch K. Relationship of gastroscopic features to histological findings in gastritis and Helicobacter pylori infection in a general population sample. *Endoscopy* 2003;35(11):946-50.
 28. Dinis-Ribeiro M, Areia M, de Vries AC, Marcos-Pinto R, Monteiro-Soares M, O'Connor A, et al. Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHS), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED). *Endoscopy* 2012;44(1):74-94.
 29. Saka A, Yagi K, Nimura S. OLGA- and OLGIM-based staging of gastritis using narrow-band imaging magnifying endoscopy. *Dig Endosc* 2015;27(7):734-41.
 30. Isajevs S, Liepniece-Karele I, Janciauskas D, Moisejevs G, Funka K, Kikuste I, et al. The effect of incisura angularis biopsy sampling on the assessment of gastritis stage. *Eur J Gastroenterol Hepatol* 2014;26(5):510-3.
-