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# COMPARISON OF SERUM PEPSINOGEN I AND II AND GASTRIN 17 LEVEL IN PATIENTS MORE THAN 50 YEARS WITH DYSPEPSIA WHO HAVE PRECANCEROUS GASTRIC LESIONS

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## ABSTRACT

**Introduction:** Serum screening systems are useful in monitoring gastric cancer. The present research studied and compared serum levels of pepsinogens, gastrin-17, and *Helicobacter pylori* antibodies in patients with dyspepsia and precancerous lesions by focusing on gastric pathology.

**Materials and methods:** In this cross-sectional study, patients with dyspepsia symptoms from whom gastric biopsy samples were taken during endoscopy entered the present study. The biopsy samples were examined using a rapid urease test (RUT) and histopathology study. Patients with precancerous lesions were considered the case group (40 individuals) and patients with chronic gastritis the control group (88 individuals). Serum pepsinogen I, pepsinogen II, gastrin-17, anti-Helicobacter pylori antibodies, and the gene related to vacuolatingcytotoxinA(vacA) were measured at a private laboratory in Rasht. The information was analyzed by using SPSS 16 and through employing the t-test and the chi-square test.

**Results:** This study included 120 patients with chronic non-atrophic gastritis, 39 with metaplasia, 5 with dysplasia, and 6 with neoplasia. No cases of atrophic gastritis were observed. The percentages of patients with pepsinogen I levels lower than normal and without metaplasia (75.9%)or neoplasia (96.6%) were significantly higher than those with metaplasia (24.1%) or neoplasia (3.4%).

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When the three groups of patients with metaplasia, dysplasia, and atrophic gastritis were combined to form a new group (the precancerous group), there were significant differences between the case and control groups with respect to levels of pepsinogen I and pepsinogen I/ pepsinogen II ratios ($p<0.05$). The frequencies of patients with lower than normal pepsinogen I levels and pepsinogen I/ pepsinogen II ratios in the precancerous group (15 and 20 percent, respectively) were higher than those in the chronic gastritis group (1.1 and 5.7 percent, respectively) ($p<0.05$). The mean pepsinogen I levels and pepsinogen I/ pepsinogen II ratio in the precancerous group (99.57 and 5.89µg/l, respectively) were smaller compared to those in the chronic gastritis group (100.24 and 8.77 µg/l) ($p<0.05$). No significant differences were observed between the groups with respect to pepsinogen II, gastrin-17, or levels of anti-Helicobacter pylori antibodies.

**Conclusions:** Results showed that low pepsinogen I levels and small pepsinogen I to pepsinogen II ratios were useful markers for identifying precancerous lesions. It is recommended that more research with larger sample volumes be carried out to determine the sensitivity and specificity of this test and the possible cutoff values of the mentioned markers.

**Keywords:** Pepsinogen, precancerous lesions, gastrin-17

## INTRODUCTION

Gastric cancer is one of the most prevalent types of cancer in the world, about 870,000 new cases are diagnosed and 650,000 patients die of it per year, 9.9 percent of all new cases of cancer are gastric cancer (1-3), and its incidence rates have rapidly declined in recent years (4-7). Part of this decline has resulted from discovering the main risk factors for it (such as *Helicobacter pylori* and other environmental and nutritional hazards), although this decline started before Helicobacter pylori was discovered. The decline started in countries with low incidence rates including the United States, whereas in countries with high incidence rates the decline has shown a slower trend (8). Statistics show that incidence rates of gastric cancer vary in different countries ranging from 0.6 casesper 100,000 population in Cameroon to 69.6 cases per 100,000 population in Korea for men, and from 0.6 cases per 100,000 population in Gabon to 30.6 cases per 100,000 population in Peru for women. In general, the highest incidence rates were observed in Asia and Latin America (Costa Rica, El-Salvador, and Columbia) both for men and for women and in some African countries (Mali, Congo, and Ruanda) for women. On the contrary, the lowest incidence rates were found in North America and in most African countries both for men and or women (9). Gastric cancer is the fourth most frequent type of cancer in the world. Based on a global evaluation, more than 930,000

new cases of gastric cancer are diagnosed every year and at least 700,000 people die of it annually (10). Although the death rates caused by gastric cancer have noticeably declined in many regions during the past 50 years, yet it is still the second cause of death caused by cancer in the world (11). Moreover, it is the most prevalent malignancy in Iran with the northern and northwestern parts of the country being high risk regions. The incidence rates among men and women in Mazandaran and Golestan Provinces are high, and Ardabil Province has the highest incidence rate in Iran. Incidence rates of gastric cancer are also high in Semnan, Golestan, East Azerbaijan, and Tehran Provinces, whereas Kerman Province in southern Iran has lower incidence rates compared to the northern part of the country (10). Gastric cancer has several developmental stages: it begins with chronic gastritis and progresses to chronic atrophic gastritis, intestinal metaplasia, and to dysplasia. This trend usually starts with infection caused by *Helicobacter pylori* and involves genetic elements and environmental factors (12). Endoscopy and biopsy are the gold standard for determining the reason for the development of the disease in patients with dyspepsia and provide us with information regarding *Helicobacter pylori* infection, presence of atrophy, intestinal metaplasia or dysplasia (and also concerning lesion site) (13). This method is invasive, painful, stressful, and expensive and, therefore, rapid, reliable, inexpensive, and non-invasive tests for screening and monitoring patients with mild to intermediate symptoms of dyspepsia are attracting great interest at present (14). C13 urea breath test and fecal *Helicobacter pylori* antigen are also often used, but they do not provide information about the morphological conditions of gastric mucosa (15-16). Recently, use of the ELISA test for measuring serum pepsinogen I and II, gastrin-17, and the anti-Helicobacter pylori antibodyIgG as non-invasive markers for evaluating functional and morphological conditions of gastric mucosa in patients with dyspeptic symptoms has attracted interest (17-18). Pepsinogen I and II are precursors of pepsin. Pepsinogen I is mainly secreted by the oxyntic glands and is a proprietary marker of the secretory capacity of the stomach body. On the contrary, pepsinogen II is produced by all gastric glands (the fundic, cardiac, and pyloric glands) and also by duodenal glands (Brunner's glands) and is strongly influenced by inflammation of the stomach (19-20). These precursors are secreted in small quantities inside the gastric lumen and one percent of them that are leaked into blood (and can be measured). Gastrin-17 is mainly produced in the gastric antrum, is directly secreted into the blood, and is a proprietary marker of G-cell activity (21). Since few studies have been carried out in Iran on non-invasive methods of screening for precancerous gastric lesions, the present research used non-invasive serological tests (measured serum levels of PGI, PGII, the anti-Helicobacter pylori antibody IgG, and gastrin-

17 and assessed their changes in precancerous lesions and in gastric cancer) instead of gastroscopy and biopsy that are performed for patients over 50 years with dyspepsia.

## METHODOLOGY

This descriptive cross-sectional research was conducted in six months and studied patients over 50 years who visited a professor of digestive diseases and the gastroenterology clinic at Razi Hospital with symptoms of dyspepsia (any feeling of chronic or recurrent pain or discomfort in the epigastric region). If the physician thought that these patients exhibited the indications, the patients underwent endoscopy and biopsy. During endoscopy, three samples were taken from the body, the antrum, and the fundus of the stomach. Moreover, one sample was taken for RUT (Rapid Urease Test) to be examined for *H. pylori*. The samples were placed in 10% formalin and sent to the laboratory for pathological tests. The patients were divided into a case and a comparison group based on the pathology reports, and those with precancerous lesions (such as atrophic gastritis, intestinal metaplasia, and dysplasia) were put in the case group and those with mild non-atrophic gastritis in the comparison group. Those with gastric cancer were informed of it and referred for treatment continuation and follow-up. Personal and general information regarding the patients and the types of their pathology were entered into the questionnaire forms, 5 ml blood samples were taken from each patient and sent to the laboratory, and the concentrations of pepsinogenI, pepsinogen II, gatrin-17, the anti-Helicobacter pylori antibody IgG, and of the Anti-CagA antibodies were measured using the ELISA test and the ratios of pepsinogen I to pepsinogen II were calculated. The person performing the tests did not know the results of endoscopy or the types of precancerous lesions in the patients.

**Ethical considerations:** All information in this project was published in general terms without naming the patients. Moreover, informed consent was obtained from all patients, and those having gastric cancer (shown in the pathology reports) were informed of it and referred for treatment continuation and follow-up.

**Inclusion criteria:** Patients older than 50 years and without kidney or liver failure who did not take PPI, H2 blockers, or antibiotics at least four weeks prior to endoscopy, and had no history of gastroduodenal surgery entered the study, and those who could not tolerate endoscopy or refused it were excluded from the research.

The steps taken and the facilities used in the research were as follows

1. Extraction of the patients' addresses and telephone numbers from the records kept at the pathology laboratories

2. Various questionnaires (forms 1 and 2) to record the patients' particulars and the studied variables
3. Upper endoscopy equipment and materials including 10% Lidocaine spray, upper endoscopy equipment together with the necessary accessories, biopsy forceps
4. Filter paper, formalin solution and the related containers
5. Laboratory facilities and Dr. Afrah pathological Laboratory
6. RUT solution

The information was analyzed using SPSS 16 and employing the t-test and the chi-square test

**RESULTS**

Among the endoscopic biopsy specimens, there were 120 cases of chronic non-atrophic gastritis, 39 of metaplasia, 5 of dysplasia, and 6 of neoplasia, but no cases of atrophic gastritis were observed. The most common complaints were stomach ache (50%) and dyspepsia (35.9%), and the most frequent endoscopic findings erosive gastropathy (46.1%) and hiatal hernia (32%). Twenty eight, 7, 0, and 1 of the patients with chronic gastritis, metaplasia, dyspepsia, or neoplasia had lower than normal PGI values, respectively. The numbers of patients with lower than normal values of PGI and without metaplasia (22 patients) or without neoplasia (28 patients) were significantly higher than among those with metaplasia (7 patients) or with neoplasia (1 patient) ($p<0.05$). The numbers of specimens with higher than normal PGI values in patients with chronic gastritis, metaplasia, dysplasia, or with neoplasia were 58, 18, 1, and 2, respectively.Among patients with chronic gastritis, metaplasia, dysplasia, or with neoplasia, the numbers of specimens with PG I/PG II ratios lower than normal were 2, 0, 2, and 0, respectively. The number of patients with GI/PGII ratios lower than normal among those without neoplasia (Table 2) was significantly larger than those with neoplasia (0) ( $p<0.05$) (Tables 1 and 2). There was a significant relationship between PGI and the types of lesions (precancerous lesions).The percentage of specimens with normal PGI values was larger in the chronic gastritis group (73.9%) than the precancerous group (67.5%). The percentage of PGI values lower than normal was higher (15%) in the precancerous lesion group than in the chronic gastritis group (1.1%) ($p<0.05$) (Table2). The mean PGI value in patients with precancerous lesions (99.57) was significantly lower than that among the patients with chronic gastritis (100.24) ($p<0.05$) (Table3). There was a significant relationship between PGI/PGII ratios and the types of lesions, and the reduction in this ratio among the precancerous group (20%) was greater than the chronic gastritis group (5.7%). The normal

PGI/PGII ratio in the chronic gastritis group (92%) was larger than the precancerous group (80%) ($p<0.05$) (Table2). Furthermore, the PGI/PGII ratio in patients with precancerous lesions (5.89±3.99) was smaller than in those with non-atrophic gastritis (8.77±4.45) ($p<0.05$) (Table3).There were no significant relationships between the types of lesion and PGII, gastrin-17, and the *Helicobacter pylori* antibody ($p<0.05$). The mean age in the group with precancerous lesions (98±9.5) was significantly higher than group with non-atrophic gastritis (65.01±9.2). In patients with smoking history, the percentage with precancerous lesions (10%) was smaller than those with non-atrophic gastritis (11.4%), and relationship assessment was not performed because the number of smokers in this research was low. In patients with drinking history, the percentage of patients with precancerous lesions (0%) was lower than those with non-atrophic gastritis (1.1%). In patients with positive RUT history, the percentage with precancerous lesions (42.5%) was significantly higher than those with non-atrophic gastritis (37.5%).

**Table 1.** Frequency distribution of chronic gastritis, metaplasia, dysplasia, and neoplasia among biopsy samples taken from different parts of the stomach

| Lesion type/lesion location | Antrum (% frequency) | Stomach body (% frequency) | Fundus (% frequency) |
|---|---|---|---|
| Chronic gastritis | 74(57.8) | 78(60.9) | 109(85.2) |
| Metaplasia | 27(21.1) | 14(10.9) | 14(10.9) |
| Dysplasia | 1(0.8) | 3(2.3) | 2(1.6) |
| Neoplasia | 5(3.9) | 0(0.0) | 2(1.6) |

**Table 2.** Comparison of pepsinogen I levels between patients with various lesions shown in endoscopy

| PGI | More than normal | | Normal | | Less than normal | | P value |
|---|---|---|---|---|---|---|---|
| Lesion type | Positive | negative | Positive | Negative | Positive | Negative | |
| Chronic gastritis | 6 (85.76) | 1(14.3) | 86(93.5) | 6(6.5) | 28(96.6) | 1(3.4) | 0.55 |
| Metaplasia | 5 (71.45) | 2(28.6) | 27(29.3) | 65(70.7) | 7(24.1) | 22(75.9) | 0.04 |
| Dysplasia | 0 (0.0) | 7(100.0) | 5(5.4) | 87(94.6) | 0(0.0) | 29(100.0) | 0.36 |
| Neoplasia | 2(28.6) | 5(71.4) | 2(3.3) | 89(96.7) | 1(3.4) | 28(96.6) | 0.009 |

**Table 3.** Comparison of pepsinogen II levels in patients with various lesion types shown in endoscopy

| PGII | More than normal | | Normal | | P value |
|---|---|---|---|---|---|
| Lesion type | Positive | Negative | Positive | Negative | |
| Chronic gastritis | 62(93.9) | 4(6.1) | 58(93.5) | 4(6.5) | 0.60 |
| Metaplasia | 21(31.8) | 45(68.2) | 18(29.0) | 44(71.0) | 0.73 |
| Dysplasia | 4(6,1) | 62(93.9) | 1(1.6) | 61(98.4) | 0.20 |
| Neoplasia | 4(6.1) | 62(93.9) | 2(3.1) | 60(96.8) | 0.44 |

**Table 4.** Comparison of pepsinogen I/pepsinogen II ratios between patients with various lesion types shown in endoscopy

| PGI/PGII ratio | More than normal | | Normal | | Less than normal | | P. value |
|---|---|---|---|---|---|---|---|
| Lesion type | Positive | Negative | positive | Negative | Positive | Negative | |
| Chronic gastritis | 11(84.6) | 21(15.4) | 107(94.7) | 6(5.3) | 2(100.0) | 0(0.0) | 0.34 |
| Metaplasia | 7(53.8) | 6946.2) | 32(28.3) | 81971.7) | 0(0.0) | 2(100.0) | 0.107 |
| Dysplasia | 13(100.0) | 0(0.0) | 108(95.6) | 5(5.4) | 2(100.0) | 0(0.0) | 0.70 |
| Neoplasia | 3(23.1) | 10(76.9) | 3(2.7) | 110(97.3) | 0(0.0) | 2(100.0) | 0.004 |

Since the sample number was small in many cells, the metaplasia and dysplasia lesions were combined to make results of the analysis meaningful, and this new group was compared with the group of chronic gastritis lesions.

**Table 5.** Comparison of frequency distributions of PGI, PGII, PGI/PGII, gastrin-17, and anti-Helicobacter pylori antibody between patients with precancerous lesions and those in the non-atrophic gastritis group

| Group | | Chronic gastritis n=88 Number (percent) | Precancerous n=40 Number(percent) | P. value |
|---|---|---|---|---|
| PG I | Less than normal | 1(1.1%) | 6(15%) | 0.005 |
| | Normal | 65(73.9%) | 27(67.5%) | |
| | More than normal | 22(25%) | 7(17.5%) | |
| PG II | Normal | 44(50%) | 22(55%) | 0.06 |
| | More than normal | 44(50%) | 18(45%) | |
| PG I/PG II | Less than normal | 5(5.7%) | 8(20%) | 0.03 |
| | Normal | 81(92%) | 32(80%) | |
| | More than normal | 92(2.3%) | (0.0) | |
| Gastrin-17 | Less than normal | 1(1.1%) | 0(0.0%) | 0.777 |
| | Normal | 39(44.3%) | 17(42.5%) | |
| | More than normal | 48(54.5%) | 23(57.5%) | |
| Anti-Helicobacter pylori IgG | Positive | 00(0.0%) | 2(5%) | 0.03 |
| | Negative | 88(100%) | 38(95%) | |
| Anti-CagA antibodies | Less than normal | 46(52.9%) | 17(42.5%) | 0.27 |
| | More than normal | 41(47.1%) | 23(57.5%) | |

**Table 6.** Comparison of the means of pepsinogen I, pepsinogen II, pepsinogen I/pepsinogen II, gastrin-17, anti HP, anti-CagA antibodies in patients with precancerous lesions and those with non-atrophic gastritis

| Group | | Mean (standard deviation) | P. value |
|---|---|---|---|
| PG I | Precancerous lesions | 99.57(76.80) | 0.05 |
| | Non-atrophic gastritis | 100.24(62.81) | |
| PG II | Precancerous lesions | 20.05(17.34) | 0.36 |
| | Non-atrophic gastritis | 17.34(11.58) | |
| PG I/ PG II | Precancerous lesions | 5.89(3.99) | 0.001 |
| | Non-atrophic gastritis | 8.77(4.45) | |
| Gastrin-17 | Precancerous lesions | 49.42(84.83) | 0.82 |
| | Non-atrophic gastritis | 30.51(37.68) | |
| Anti-Helicobacter pylori IgG | Precancerous lesions | 40.51(24.70) | 0.68 |
| | Non-atrophic gastritis | 42.38(23.50) | |
| Anti-CagA antibodies | Precancerous lesions | 27.36(35.24) | 0.17 |
| | Non-atrophic gastritis | 19.33(28.29) | |

## DISCUSSION

In the present research, the PG I levels in patients with chronic gastritis and without it and in patients with dysplasia and without it were not significantly different, but its levels in patients

with and without metaplasia and also in patients with and without neoplasia were significantly different. PG I levels were only different in precancerous metaplastic lesions and this factor did not exhibit significant differences in other precancerous lesions (atrophic gastritis or dysplasia). PGI levels and PG I/PG II ratios in the group of patients with precancerous lesions were significantly lower than the group with non-atrophic gastritis. Various similar studies with different designs have been conducted throughout the world. Cao Qet al. (2007) showed that PGI and PG I/Pg II ratiosin patients with atrophic gastritis and gastric cancer declined compared to the healthy group. They concluded that increased serum levels of G-17 and reduced PG I levels and PG I/PG II ratioscould be employed for screening (22).Germanaet al. (2005) noticed that serum levels of PG I, and PG I/PGII ratios, in patients with atrophic gastritis were significantly lower compared to patients with chronic non-atrophic gastritis (23). In another study conducted in Japan in 2009, it was suggested that PG I, PG II, G 17, and HP IgG could be used to distinguish healthy people from those with atrophic gastritis (24). Kwak et al. (2010) in South Korea found an inverse correlation between mean PG I levels and PG I/PG II ratios and the stages of gastritis: the mean PG I levels and PG I/PG II ratios significantly declined with advancing gastritis stages (from stage 0 to high-stage gastritis) (25).In Japan, Ubukata H et al. (2010) carried out a study on patients that were supposed to undergo gastrostomy. They suggested that gastric cancer in pepsinogen negative people may have higher malignant potential compared to pepsinogen positive patients (26). In the United States, Abnet CC et al. (2011) showed in their case-control research that plasma PG I concentrations lower than 50ng/ml and plasma PG II concentration higher than 6.6 ng/mlhad significant relationships with higher risk of gastric cancer. They also noticed that PG I/PG II ratios had a linear relationship with gastric cancer (27). In Chile, a study on atrophic gastritis patients revealed that PG I serum levels of lower than 61.5 μg/ml, PG I/PG II ratios smaller than 2.2, and gastrin concentrations higher than 13.3pmol/l had high accuracies (91-100%) and low sensitivity (56-78%) in detecting atrophy of the upper part of the stomach (28). In research carried out in Finland in 2002 to see if it was possible to diagnose atrophic gastritis and determine its site without performing endoscopy, it was concluded that low serum gastrin 17 and PG I levels were biomarkers for the antrum and body of the stomach (29). In Peru, Colarossi et al. (2011) conducted a case-control study on patients with atrophic gastritis and used people without this disease as the control group. They studied and compared serological profiles of PG I and PG I/PG II ratios and found that there were no differences between the case and control groups with respect to the above mentioned markers, and pepsinogen and gastrin tests were not appropriate for atrophy (30).In the present

research, mean gastrin 17 and PG II concentrations in patients with precancerous lesions were higher than those in patients with atrophic gastritis. In a study carried out in China in 2007, gastrin 17 levels in the atrophic gastritis group 9 that also had dysplasia) was higher than the group without dysplasia. They suggested that lesion site was an important factor that influenced gastrin 17 levels (31). Zhanget al. (2006) showed that PG II levels in chronic atrophic gastritis and in gastric cancer were significantly higher than in healthy groups. Moreover, PG I/PG II ratios in patients with chronic atrophic gastritis and gastric cancer were significantly lower than the other groups (32). Haj Sheykholeslami et al. (2008) carried out a study in Tehran and showed that PG II was a suitable marker in screening for any gastritis from normal mucosa, but PG I, PG I/PGII, gastrin 17, or their combination were not able to select those with precancerous conditions among first-degree relatives of patients with cancer (33).

## CONCLUSIONS

The present research clearly showed that there were significant differences between patients with precancerous lesions and those with chronic gastritis with respect to PG I levels and the PG I/PG II ratios. No significant differences were observed between patients with precancerous lesions and those with chronic gastritis with respect to other markers such as PG II, gastrin 17, and *Helicobacter pylori* antibodies.

## SUGGESTIONS

Considering the high prevalence of gastric cancer, the fact that it can be treated in its early stages and the importance of its early diagnosis in high risk patients, use of noninvasive methods acceptable to patients such as serum markers is very important. We recommend that sensitivity and specificity of pepsinogens for diagnosis shouldbe determined in future studies with more in depth analysis of the data.

## REFERENCES

1. Ferlay, J Bray, F, Parkin, DM, Pisani, P, eds (2001) Gobocan 2000: Cancer Incidence and Mortality Worldwide (IARC Cancer Bases No. 5), Lyon, IARCPress .

2. Lau M, Le A, El-Serag HB. Noncardia gastric adenocarcinoma remains an important and deadly cancer in the United States: secular trends in incidence and survival. Am J Gastroenterol 2006; 101:2485.

3. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin.2005; 55: 74 -108.

4. HAENSZEL W. Variation in incidence of and mortality from stomach cancer, with particular reference to the United States. J Natl Cancer Inst 195 8; 21:213.

5. Mufioz N, Asvall J. Time trends of intestinal and diffuse types of gastric cancer in Norway. Int J Cancer 1971; 8:144.

6. I-Iirayama T. Epidemiology of cancer of the stomach with special reference to its recent decrease in Japan. Cancer Res 1975; 35:3460.

7. Waterhouse, J, Muir C, Correa, P, et al, eds. Cancer incidence in five continents. Vol III. IARC Scientific Publication n0.15.International Agency for Research on Cancer, Lyon, 1976.

8. Fitzsimmons D, Osmond C, George S, Johnson CD. Trends in stomach and pancreatic cancer incidence and mortality in England and Wales, 1951-2000.Br J Surg 2007; 9411162.

9. Correa P, Haenszel W, Cuello C, Tannenbaum S, Archer M. A model for gastric cancer epidemiology. Lancet 1975, 2:58-60.

10- Malekzadeh R, Deral<hshan MH, Malekzadeh Z. Gastric cancer in Iranzi Epidemiology and risk factors. Arch Iran Med, 2009; l2(6):576-5 83.

11- Alberts SR, Cervantes A, van de Velde CJ. Gastric cancer: epidemiology, pathology and treatment. Ann Oncol, 2003; 14 (Suppl. 2): ii31—6.

12- Nardone G, Rocco A, Malfertheiner P. Review article: Helicobacter pylori and molecular events in precancerous lesions. Aliment pharmacolTher, 2004;20:261-270.

13- Schnell GA, Schubert TT. Usefulness of culture, histology, and urease testing in the detection of Campylobacterpylori. Am J Gastroenterol, 1989;84: 133-7.

14- McColl KEL, Murray LS, Gillen D, Walker A, Wirz A, Fletcher J, et al. Randomised trial of endoscopy with testing for Helicobacterpyloricompared with non-invasive H.pyloritesting alone in the management of dyspepsia. Br Med J, 2002;324:999-l002.

15-Graham DY, Klein PD, Evans Jr DJ, Evans DG, Alpert LC, Operkun AR, et al. Campylobacterpyloridetected noninvasively by the 13Curea breath test. Lancet, 1987;23:l174-7.

16-Vaira D, Malfertheiner P, 'Megraud F, Axon AT. Diagnosis of Helicobacter pylori in faction with a new non invasive antigen-based assay.HpSA European Study Group. Lancet, l999; 354:30-3.

17- Korstanje A, den Hartog G, Biemond I, Lamers CB. Theserological gastric biopsy: a non-endoscopical diagnostic approach in management of the dyspeptic patient: significance for primary care based on a survey of the literature. Scand J Gastroenterol, 2002;236:22-6.

18- Oksanen A, Sipponen P, Miettinen A, Sarna S, Rautelin H. Evaluation of bood tests to normal gastric mucosa. Scand J Gastroenterol, 2000;35:791-5.

19- Foltmann B. Gastric proteinases: structure, function, evolution and mechanism of action. Essays Biochem, 1981;17:52-84.

20- Di Mario F, Vianello F, Plebani M. Peptic secretion, clinical and pathophysiological features.Padova: Piccin; 1985.

21- Sipponen P, Ranta P, Helske T, Kaarinainen I, Maki T, Linnala A, et al. Serum levels of amidaded gastrin-l7 and pepsinogen I in atrophic gastritis: an observational case-control study. Scand J Gastroenterol, 2002;37:785-9l.

22- Cao Q, Ran ZH, Xiao SD, Screening of atrophic gastritis and gastric cancer by serum pepsinogen, gastrin-17 and Helicobacter pylori immunoglobulin G antibodies. Journal of Digestive Diseases, 2007;8: 1 5-22.

23- Germana B, Mario F. Di, Cavallaro LG, Moussa AM, Lecis P, Liatoupolou S etal. Clinical usefulness of serum pepsinogens I and II, gastrin-17 and anti-Helicobacter pylori antibodies in the management of dyspeptic patients in primary care. Digestive and Liver Disease, 2005;37:501-508.

24- lijima K, Abe A, Ryosuke K, Koike T, Ohara S, Sipponen P etal. Serum biomarker tests are useful in delineating between patients with gastric atrophy and normal, healty stomach. World Gastroentrol,2009;15(7):853-859.

25-Daugule I, Sudraba A, Chiu HM, Funka K, Ivanauskas A, Janciauskas D, Jonaitis LKiudelis G, Tolmanis I, Vanags A, Lin JT, Kupcinskas L, Leja M. Gastric plasma biomarkers and Operative Link for Gastritis Assessment gastritis stage.Eur J GastroenterolHepatol. 2011 Apr;23(4):302-7.

26-Ubukata H, Konishi S, Nakachi T, Motohashi G, Goto Y, Watanabe Y, Nakada I, Tabuchi T. Characteristics of the serum pepsinogen (Pg) test, and the relationship between Pg test results and gastric cancer outcomes. Scand J Surg. 2010;99(4):20l-7.

27-Abnet CC, Zheng W, Ye W, Kamangar F, Ji BT, Persson C, Yang G, Li HL, Rothman N, Shu XO, Gao YT, Chow WH. Plasma pepsinogens, antibodies against I-lelicobacter pylori, and risk of gastric cancer in the Shanghai Women's Health Study Cohort.Br J Cancer. 2011 Apr 26;lO4(9):l5l 1-6. Epub 2011 Mar l5.

28- Rollan A, Ferreccio C, Gederdini A, Serrano C, Tones J, Harris P. Non- invasive diagnosis of gastric mucosal atrophy in an asymptomatic poulation with high prevalence of gastric cancer. World J Gastroenterol, 2006;12(44):7l72-8.

29-Sipponen P, Ranta P, Helske T, Kéiéiriéiinen I, Méiki T, Lirmala A, Suovaniemi O, Alanko A, Héirkonen M. Serum levels of amidated gastrin-17 and pepsinogen I in atrophic gastritis: an observational case-control study. Scand J Gastroenterol. 2002 Jul;37(7):785-91.

30-Colarossi A, Inga R, Prochazka R, Reyes U, Bussalleu A, Barua RL. [Pepsinogen and gastrin in the noninvasive diagnosis of gastric atrophy.A case-control study in Peruvian population].Rev Gastroenterol Peru. 2011 Apr-Jun;3 l(2):110 5.

31- Zhong Z, Liping S, YueHva G, XuGuang W, Meng Z, Yuan Y. Factors affecting the serum gastrin 17 level: an evidence-based analysis of 3906 serum samples among Chinese. Chinese Journal of Digestive Disease, 2007;8(2):72-76.

32-Zhang XH, Huang B, Wang JL, Li YH, Mi JM, Shen HT, Zhang ZG, Yan X, Xing LX, Wang SJ .Correlation of serum pepsinogen level and gastric mucosal changes of residents in the high incidence area of gastric cancer]. ZhonghuaZhong Liu ZaZhi. 2006 Ju1;28(7):507-11.

33-Haj-Sheykholeslami A, Rakhshani N, Amirzargar A, Rafiee R, Shahidi SM, Nikbin B, Khosravi F, Massarrat S. Serum pepsinogen I, pepsinogen II, and gastrin 17 in relatives of gastric cancer patients: comparative study with type and severity of gastritis. Clin Gastroenterol Hepatol. 2008 Feb;6(2):I74-9.

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