ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2017 August 28; 23(32): 5829-6008

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

Contents

Weekly Volume 23 Number 32 August 28, 2017

CASE REPORT

LETTERS TO THE EDITOR

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORIAL OFFICE
Jin-Lei Wang, Director
Yuan Qi, Vice Director
Ze-Mao Gong, Vice Director
World Journal of Gastroenterology
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLICATION DATE
August 28, 2017

INSTRUCTIONS TO AUTHORS
Full instructions are available online at http://www.wjgnet.com/bpg/gerinfo/204

ONLINE SUBMISSION
http://www.f6publishing.com

World Journal of Gastroenterology

Submit a Manuscript: http://www.f6publishing.com

World J Gastroenterol 2017 August 28; 23(32): 5945-5953

DOI: 10.3748/wjg.v23.i32.5945

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Observational Study

Changes with aging in gastric biomarkers levels and in biochemical factors associated with *Helicobacter pylori* infection in asymptomatic Chinese population

Jin-Hua Shan, Xiao-Juan Bai, Lu-Lu Han, Yuan Yuan, Xue-Feng Sun

Jin-Hua Shan, Department of Gerontology and Geriatrics, the First Affiliated Hospital of China Medical University, Shenyang 110001, Liaoning Province, China

Xiao-Juan Bai, Lu-Lu Han, Department of Gerontology and Geriatrics, Shengjing Hospital of China Medical University, Shenyang 110004, Liaoning Province, China

Yuan Yuan, Department of Tumor Research, the First Affiliated Hospital of China Medical University, Shenyang 110001, Liaoning Province, China

Xue-Feng Sun, Department of Kidney, General Hospital of Chinese People's Liberation Army, Beijing 100853, China

ORCID number: Jin-Hua Shan (0000-0002-1130-0784); Xiao-Juan Bai (0000-0003-3890-8391); Lu-Lu Han (0000-0002-8306-4506); Yuan Yuan (0000-0002-9314-3371); Xue-Feng Sun (0000-0002-6569-6737).

Author contributions: Shan JH and Bai XJ conceptualized and designed the study; Shan JH and Han LL collected the data; Shan JH and Bai XJ performed analysis and interpretation of the data; Shan JH drafted the manuscript; Bai XJ and Sun XF obtained funding support; Yuan Y provided administrative, technical and material support.

Supported by the National Basic Research Program of China (973 Program), No. 2007CB507405, No. 2013CB530803 and No. 2013CB530804.

Institutional review board statement: This study was reviewed and approved by the Medical Ethics Committees of the General Hospital of Chinese People's Liberation Army and China Medical University.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: There are no conflicts of interest to report.

Data sharing statement: No additional data are available.

Manuscript source: Unsolicited manuscript

Correspondence to: Dr. Xiao-Juan Bai, Department of Gerontology and Geriatrics, Shengjing Hospital of China Medical University, Shenyang 110004, Liaoning Province, China. baixj@sj-hospital.org
Telephone: +86-24-23516346

Received: April 14, 2017
Peer-review started: April 17, 2017
First decision: May 16, 2017
Revised: May 29, 2017
Accepted: July 12, 2017
Article in press: July 12, 2017
Published online: August 28, 2017

Abstract

AIM

To observe changes in gastric biomarker levels with age and effects of *Helicobacter pylori* (*H. pylori*) infection in a healthy population, and explore factors associated with gastric biomarkers.

METHODS

Three hundred and ninety-five subjects were selected and underwent physical examinations, biochemical tests, and measurement of serum pepsinogen (PG)

Ⅰ and Ⅱ, gastrin-17 (G-17) and *H. pylori* antibody levels. Analyses were made by Student's *t*-test, ANOVA, Pearson's correlation and multiple linear regressions.

RESULTS

PGII levels were higher in the ⩾ 65-years-old age group ($P < 0.05$) and PGI/PGII were lower in the ⩾ 75-years-old age group ($P = 0.035$) compared to the 35-44-years-old age group. Levels of low-density lipoprotein cholesterol (LDL-C) were higher ($P = 0.009$) in *H. pylori*-infected subjects that were male. LDL-C levels were higher in 55-74-years-old age group ($P < 0.05$) for *H. pylori*-infected subjects and 45-64-years-old age group ($P < 0.05$) for non-infected subjects compared to 35-44-years-old age group. Hp-IgG level positively correlated with PGⅠ, PGⅡ and G-17 ($P < 0.001$, $P < 0.001$, $P = 0.006$), and negatively correlated with PGI/PGII ($P < 0.001$). Creatinine positively correlated with PGⅠ, PGⅡ and G-17 ($P < 0.001$, $P < 0.001$, $P < 0.001$). Fasting blood glucose (FBG) positively correlated with PGⅠ/PGⅡ and G-17 ($P < 0.001$, $P = 0.037$). Age positively correlated with PGII and G-17 ($P = 0.005$, $P = 0.026$).

CONCLUSION

PGII levels increased while PGI/PGII declined with age in a healthy population. *H. pylori* infection had an effect on raising LDL-C levels to increase the risk of atherosclerosis in males, especially those of elderly age. Age, *H. pylori* infection, levels of renal function and FBG were associated with levels of pepsinogens and gastrin.

Key words: *Helicobacter pylori* antibody; Pepsinogen; Gastrin; Gastric ageing

Core tip: Our study showed that in an entire healthy population, levels of serum pepsinogen (PG) Ⅱ increased while PGⅠ/PGⅡ declined with age. We discovered that *Helicobacter pylori* (*H. pylori*) infection had an effect on raising levels of low-density lipoprotein cholesterol to increase the risk of atherosclerosis in males, especially those who are elderly. We also found that age, *H. pylori* infection, serum levels of renal function indicators and fasting blood glucose (FBG) were associated with levels of serum PGs and gastrin; it was assumed that they may influence the secretory function of gastric mucosa and that abnormal serum levels of FBG and renal function might participate in the occurrence and development of gastric diseases.

Shan JH, Bai XJ, Han LL, Yuan Y, Sun XF. Changes with aging in gastric biomarkers levels and in biochemical factors associated with *Helicobacter pylori* infection in asymptomatic Chinese population. *World J Gastroenterol* 2017; 23(32): 5945-5953 Available from: URL: http://www.wjgnet.com/1007-9327/full/v23/i32/5945.htm DOI: http://dx.doi.org/10.3748/wjg.v23.i32.5945

INTRODUCTION

Ageing of the gastric tract is an early manifestation of overall ageing, and mainly presents as a decline in the secretory function of the gastric mucosa. Histomorphological studies have demonstrated that atrophy of gastric mucosa increases with age[1-3]. In addition, studies have also shown that *Helicobacter pylori* (*H. pylori*) infection plays an important role in the progression of gastric mucosa lesions[4]. It has been demonstrated that the prevalence of *H. pylori* infection increases with age, and *H. pylori* is closely related with the occurrence and development of peptic ulcers, chronic atrophic gastritis and gastric cancer[5,6].

Serum pepsinogen (PG) levels reflect the number of glands and cells in gastric corpus mucosa. Therefore, they can reflect the secretory function of the gastric mucosa[7-10]. It has been reported that the levels of serum PGs are influenced by age, sex, pathophysiologic status of gastric mucosa and *H. pylori* infection[11]. Thus, serum PGs are indicators of the functional and morphological status of gastric corpus mucosa, and lower serum levels of PGⅠ or PGⅠ/PGⅡ represent existence and degree of atrophy in gastric corpus mucosa[12].

Serum level of gastrin-17 (G-17) can act as a biomarker that reflects the function and structure of gastric antral mucosa. Combining serum PG and G-17 levels has been shown to provide diagnostic information on gastric mucosa[13-16], and may also reflect the degree of gastric aging. Non-invasive biomarker tests may, therefore, evaluate the secretory function of gastric mucosa and differentiate pathological conditions, such as *H. pylori*-associated gastritis and atrophic gastritis, from the healthy condition by combining tests for PGs, G-17 and *H. pylori*-immunoglobulin G (Hp-IgG)[17].

Previous studies have investigated patients with peptic ulcer, chronic atrophic gastritis and gastric cancer. To date, few studies have observed levels of the aforementioned biomarkers and effects of *H. pylori* infection in a healthy ageing population nor explored the associated factors. In our study, we selected PGs and G-17 as gastric biomarkers and measured their serum levels along with Hp-IgG. The aim of the current study was to observe changes in gastric biomarker levels with age in a healthy Chinese population and effects of *H. pylori* infection on biochemical tests, as well as to explore associated factors which influence the levels of gastric biomarkers.

MATERIALS AND METHODS

Study subjects

This was a cross-sectional study of a healthy population, defined as having no respiratory, cardiovascular,

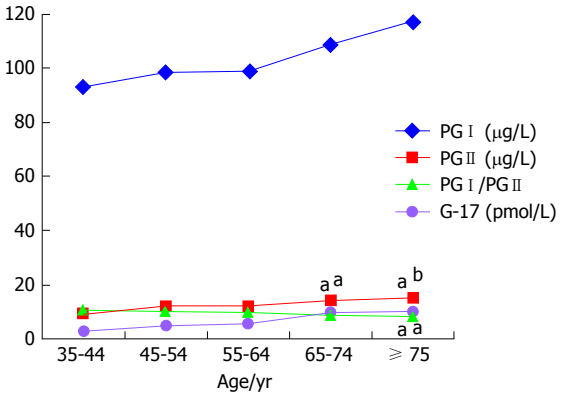

Figure 1 Comparison of serum gastric biomarker levels in various age groups. There was no significant difference in serum levels of PGI and G-17 between each age group with increasing age. In contrast, serum levels of PGII increased with age, and were significantly higher in subjects ≥ 65-years-old compared to 35-44-years-old group. The ratio of PGI/PGII decreased with age, and was significantly lower in subjects ≥ 75-years-old compared to 35-44-years-old group. The "a" denotes comparison with 35-44-years-old age group, $^{a}P < 0.05$, $^{b}P < 0.01$. G-17: Gastrin-17; PG Ⅰ: Pepsinogen Ⅰ; PG Ⅱ: Pepsinogen Ⅱ.

digestive, neurological, endocrine or urinary system diseases, as well as having absence of neoplastic and chronic infectious diseases and no history of psychiatric disorders. We screened 505 healthy persons out of 1500 volunteers in Shenyang, China between September 2007 and June 2008. The screening included inquiries on medical history, symptoms, smoking, alcohol intake, diet and family history obtained by a questionnaire that was completed by each participant. Physical examinations (*i.e.*, electrocardiogram, chest radiograph, *etc.*) were carried out along with biochemical tests, including assessments of fasting blood glucose (FBG), blood lipids, liver function, renal function and uric acid levels.

A total of 395 subjects (168 males and 227 females) out of the 505 persons, having a mean age of 59.4 years (range: 37-87 years), were enrolled from November 2010 to May 2011 by the same screening method. Patients with circulatory, respiratory, endocrine, neurological, digestive, urinary diseases and chronic infections or neoplastic diseases, or abnormal physical examinations and test results, as well as those with psychiatric disorders or who were unable to complete instructions and self-evaluations were excluded. Blood samples were obtained and sera were stored (within 2 h of collection) at -75 ℃ until use for measurement of gastric biomarker levels (within 6 mo).

Informed consent was obtained from each participant. This study was reviewed and approved by the Medical Ethics Committees of General Hospital of Chinese People's Liberation Army and China Medical University.

Serological assays

Serum PGI and PGII, G-17 and *H. pylori* antibody levels were measured with enzyme-linked immunosorbent assay (ELISA)[18] (Biohit Oyj, Laippatie 1, FIN-00880 Helsinki, Finland). All procedures were carried out according to the manufacturer's instructions.

Study groups

Subjects were divided into five age groups (35-44, 45-54, 55-64, 65-74 and ≥ 75 years). Hp-IgG-positive or -negative groups (Hp-IgG-positive defined as serum Hp-IgG ≥ 35 EIU)[19] were also established.

Statistical analysis

Serum biomarker levels and serum biochemical tests were analyzed in *H. pylori*-positive and *H. pylori*-negative patients, separately in male and female subjects, by Student's *t*-test. Levels of serum gastric biomarkers among age groups and levels of serum gastric biomarkers and biochemical tests among age groups divided by *H. pylori* infection status were compared by ANOVA, and multiple comparisons were carried out by the Bonferroni method (homogeneity of variance) or Tamhane method (heterogeneity of variance). Relationships among serum gastric biomarker levels, age and biochemical tests were analyzed by Pearson's correlation coefficient matrix. Serum gastric biomarkers as dependent variables and other related factors as independent variables were analyzed by multiple linear regression analysis with stepwise method and multiple-colinearity. For all statistical analyses, we used SPSS V.17.0, and a two-sided *P* value of < 0.05 was considered statistically significant.

RESULTS

Comparison of serum gastric biomarker levels in various age groups

There was no significant difference in serum levels of PG Ⅰ and G-17 between each age group with increasing age. In contrast, serum levels of PGII increased with age, and were significantly higher in subjects ≥ 65-years-old compared to the 35-44-years-old group ($P = 0.024$, $P = 0.004$). The ratio of PG Ⅰ/PG Ⅱ decreased with age and was significantly lower in subjects ≥ 75-years-old compared to those in the 35-44-years-old group ($P = 0.035$) (Table 1 and Figure 1).

Comparison of serum gastric biomarker levels by H. pylori infection status

Compared to non-infected subjects, serum levels of PG Ⅰ, PG Ⅱ and G-17 were significantly higher ($P < 0.001$, $P < 0.001$, $P = 0.025$), while the ratio of PG Ⅰ/PG Ⅱ was significantly lower ($P < 0.001$), in the *H. pylori*-infected subjects (Figure 2).

Comparison of serum biochemical tests between H. pylori infection statuses by sex

There was no significant difference in serum levels of biochemical tests between *H. pylori*-infected and non-infected female subjects. In males, levels of low-density lipoprotein cholesterol (LDL-C) were higher (*P*

Table 1 Comparison of serum gastric biomarker levels in various age groups

	35-44 yr, *n* = 58	45-54 yr, *n* = 84	55-64 yr, *n* = 117	65-74 yr, *n* = 76	⩾ 75 yr, *n* = 60	F	*P* value
PG Ⅰ, μg/L	92.98 ± 5.16	98.47 ± 4.15	98.65 ± 3.66	108.56 ± 8.01	117.04 ± 8.30	2.326	0.056
PGⅡ, μg/L	9.65 ± 0.73	12.26 ± 0.91	12.43 ± 0.76	14.23 ± 1.17[1a]	15.33 ± 1.25[1b]	3.915	0.004
PG Ⅰ/PGⅡ	10.94 ± 0.44	9.89 ± 0.40	9.67 ± 0.36	9.29 ± 0.61	8.71 ± 0.52[1a]	2.407	0.049
G-17, pmol/L	2.93 ± 0.55	5.10 ± 1.29	5.75 ± 1.49	9.93 ± 3.00	10.03 ± 3.18	1.950	0.101

Data are presented as mean ± SD. [1]Comparison with the 35-44-years-old group, [a]*P* < 0.05, [b]*P* < 0.01. G-17: Gastrin-17; PG Ⅰ: Pepsinogen Ⅰ; PGⅡ: Pepsinogen Ⅱ.

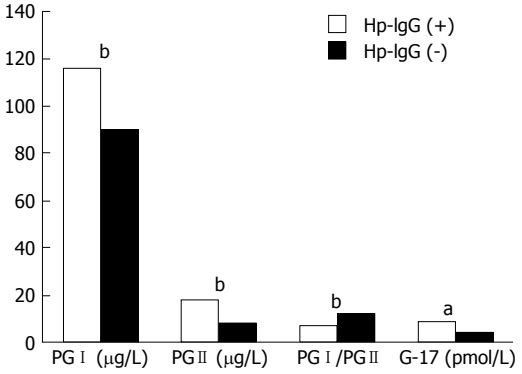

Figure 2 Comparison of serum gastric biomarker levels by *Helicobacter pylori* infection status. Compared to non-infected subjects, serum levels of PG Ⅰ, PGⅡ and G-17 were significantly higher, while the ratio of PG Ⅰ/PGⅡ was significantly lower in *Helicobacter pylori*-infected subjects. [a]*P* < 0.05, [b]*P* < 0.01. G-17: Gastrin-17; PG Ⅰ: Pepsinogen Ⅰ; PGⅡ: Pepsinogen Ⅱ.

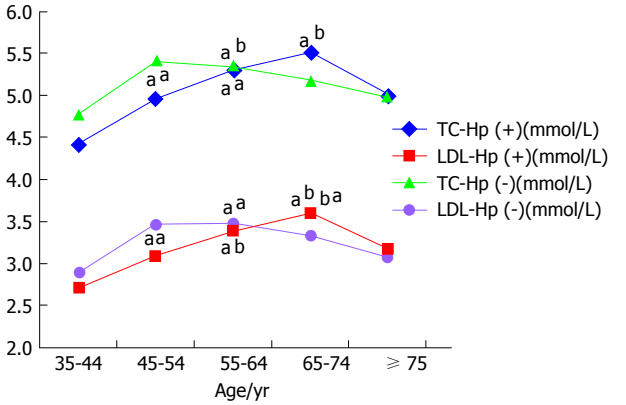

Figure 3 Comparison of serum cholesterol levels in various age groups by *Helicobacter pylori* infection status. In *H. pylori*-infected subjects, serum levels of TC and LDL were significantly higher in subjects between 55- and 74-years-old compared to those in the 35-44-years-old age group. In non-infected subjects, serum levels of TC and LDL were significantly higher in subjects between 45- and 64-years-old compared to those in the 35-44-years-old age group. The "a" denotes comparison with the 35-44-years-old age group and the "b" denotes comparison with the 45-54-years-old age group, [a]*P* < 0.05, [b]*P* < 0.01. *H. pylori*: *Helicobacter pylori*; LDL-C: Low-density lipoprotein cholesterol; TC: Total cholesterol.

= 0.009) in *H. pylori*-infected subjects compared to non-infected subjects (Table 2).

Comparison of serum gastric biomarker levels and biochemical tests in various age groups by H. pylori infection status

There was no significant difference in serum levels of gastric biomarkers between each age group with increasing age in *H. pylori*-infected subjects. In non-infected subjects, levels of serum PGⅡ increased with age and were significantly higher in subjects ⩾ 75-years-old compared to subjects between 35- and 54-years-old (*P* = 0.007, *P* = 0.004).

In *H. pylori*-infected subjects, serum levels of total cholesterol (*P* = 0.002, *P* = 0.001) and LDL-C (*P* = 0.016, *P* = 0.002) were significantly higher in subjects between 55- and 74-years-old compared to those in the 35-44-years-old age group. In non-infected subjects, serum levels of total cholesterol (*P* = 0.023, *P* = 0.035) and LDL-C (*P* = 0.015, *P* = 0.006) were significantly higher in subjects between 45- and 64-years-old compared to those in the 35-44-years-old group (Table 3 and Figure 3).

Correlation analysis among serum gastric biomarker levels, age and biochemical tests

Age positively correlated with serum levels of Hp-IgG, PG Ⅰ, PGⅡ and G-17 (*P* = 0.038, *P* = 0.001, *P* < 0.001, *P* = 0.005) and negatively correlated with ratio of PG Ⅰ /PGⅡ (*P* = 0.002). Levels of serum Hp-IgG positively correlated with serum levels of PG Ⅰ, PGⅡ and G-17 (*P* < 0.001, *P* < 0.001, *P* = 0.038) and negatively correlated with ratio of PG Ⅰ/PGⅡ (*P* < 0.001).

Levels of serum PG Ⅰ positively correlated with serum levels of uric acid, creatinine and cystatin-C (*P* < 0.001, *P* < 0.001, *P* < 0.001). Levels of serum PG Ⅱ positively correlated with serum levels of creatinine and cystatin-C (*P* < 0.001, *P* < 0.001). Levels of serum G-17 positively correlated with serum levels of FBG, creatinine and cystatin-C (*P* = 0.018, *P* = 0.011, *P* = 0.037).

Levels of serum Hp-IgG were strongly associated with serum levels of PGⅡ and PG Ⅰ/PGⅡ (*r* = 0.592, *P* < 0.001; *r* = -0.587, *P* < 0.001), and levels of serum PGⅡ were strongly associated with serum levels of PGI and PG Ⅰ/PGⅡ (*r* = 0.682, *P* < 0.001; *r* = -0.588, *P* < 0.001)(Table 4).

Analysis of factors associated with serum levels of gastric biomarkers

With serum PGI as a dependent variable, serum levels of creatinine, Hp-IgG and FBG positively correlated with levels of serum PG Ⅰ (*P* < 0.001, *P* < 0.001,

Table 2 Comparison of serum biochemical tests between *Helicobacter pylori* infection statuses by sex

	Male			Female		
	Hp-IgG (+), *n* = 81	Hp -IgG (-), *n* = 87	*P* value	Hp-IgG (+), *n* = 104	Hp-IgG (-), *n* = 123	*P* value
TG, mmol/L	1.33 ± 0.11	1.30 ± 0.17	0.875	1.24 ± 0.06	1.26 ± 0.06	0.767
TC, mmol/L	5.07 ± 0.11	4.80 ± 0.09	0.052	5.16 ± 0.09	5.42 ± 0.09	0.050
HDL-C, mmol/L	1.31 ± 0.04	1.35 ± 0.03	0.381	1.52 ± 0.03	1.54 ± 0.03	0.575
LDL-C, mmol/L	3.30 ± 0.10	2.99 ± 0.07	0.009	3.26 ± 0.09	3.48 ± 0.08	0.071
FBG, mmol/L	5.45 ± 0.09	5.26 ± 0.06	0.073	5.29 ± 0.06	5.27 ± 0.09	0.857
Cr, μmol/L	72.58 ± 1.76	73.26 ± 1.40	0.760	60.66 ± 2.59	55.34 ± 0.89	0.054
Cys-C, mg/L	0.93 ± 0.02	0.91 ± 0.02	0.520	0.88 ± 0.03	0.81 ± 0.02	0.059
UA, μmol/L	339.05 ± 8.19	337.48 ± 9.04	0.898	265.13 ± 6.19	273.22 ± 5.30	0.319

Data are presented as mean ± SD. *H. pylori*-IgG (+) is defined as *H. pylori*-IgG ⩾ 35 EIU. Cr: Creatinine; Cys-C: Cystatin-C; FBG: Fasting blood glucose; HDL-C: High-density lipoprotein cholesterol; Hp-IgG: Helicobacter pylori-immunoglobulin G; LDL-C: Low-density lipoprotein cholesterol; TC: Total cholesterol; TG: Triglycerides; UA: Uric acid; *H. pylori*: *Helicobacter pylori*.

Table 3 Comparison of serum gastric biomarker levels and biochemical tests in various age groups by *Helicobacter pylori* infection status

	35-44 yr *n*1 = 21 *n*2 = 37	45-54 yr *n*1 = 39 *n*2 = 45	55-64 yr *n*1 = 57 *n*2 = 60	65-74 yr *n*1 = 36 *n*2 = 40	⩾ 75 yr *n*1 = 33 *n*2 = 27	F	*P* value
PGI, μg/L							
Hp-IgG (+)	89.43 ± 7.46	100.03 ± 6.45	90.25 ± 5.10	92.61 ± 12.23	94.95 ± 13.47	0.824	0.920
Hp-IgG (-)	83.6 ± 6.47	81.28 ± 3.89	83.96 ± 5.04	96.67 ± 10.31	105.49 ± 8.08	1.730	0.143
PGII, μg/L							
Hp-IgG (+)	14.68 ± 1.08	18.45 ± 1.34	17.47 ± 1.16	19.52 ± 1.46	19.51 ± 1.91	1.393	0.260
Hp-IgG (-)	6.80 ± 0.58	6.89 ± 0.41	7.64 ± 0.46	9.46 ± 1.42	10.23 ± 0.76[1b2b]	1.115	0.011
PGI/PGII							
Hp-IgG (+)	7.92 ± 0.53	7.17 ± 0.39	7.03 ± 0.38	6.65 ± 0.58	6.97 ± 0.52	0.662	0.616
Hp-IgG (-)	12.66 ± 0.41	12.25 ± 0.42	12.18 ± 0.39	11.68 ± 0.89	10.85 ± 0.80	1.163	0.353
G-17, pmol/L							
Hp-IgG (+)	4.11 ± 0.74	9.81 ± 2.58	8.18 ± 2.17	7.16 ± 0.95	13.7 ± 4.79	1.258	0.285
Hp-IgG (-)	2.26 ± 0.73	1.02 ± 0.26	3.44 ± 2.03	12.43 ± 5.65	5.54 ± 3.90	2.254	0.066
TC, mmol/L							
Hp-IgG (+)	4.42 ± 0.14	4.96 ± 0.14	5.30 ± 0.11[1b]	5.51 ± 0.19[1b]	5.00 ± 0.15	6.604	< 0.001
Hp-IgG (-)	4.77 ± 0.10	5.41 ± 0.17[1a]	5.35 ± 0.13[1a]	5.18 ± 0.16	4.98 ± 0.14	2.709	0.031
LDL-C, mmol/L							
Hp-IgG (+)	2.71 ± 0.14	3.10 ± 0.12	3.40 ± 0.11[1a]	3.60 ± 0.17[1b2a]	3.17 ± 0.14	7.291	< 0.001
Hp-IgG (-)	2.89 ± 0.09	3.47 ± 0.15[1a]	3.48 ± 0.11[1b]	3.33 ± 0.13	3.08 ± 0.13	3.544	0.008
FBG, mmol/L							
Hp-IgG (+)	5.25 ± 0.08	5.22 ± 0.13	5.38 ± 0.12	5.46 ± 0.12	5.44 ± 0.08	0.791	0.532
Hp-IgG (-)	5.01 ± 0.06	5.21 ± 0.08	5.29 ± 0.08	5.34 ± 0.08	5.39 ± 0.34	1.186	0.318
Cr, μmol/L							
Hp-IgG (+)	56.95 ± 2.57	60.38 ± 2.35	63.79 ± 1.71	63.61 ± 3.04	81.4 ± 7.24[1a]	4.974	0.001
Hp-IgG (-)	59.19 ± 2.05	62.78 ± 1.95	61.20 ± 1.67	63.53 ± 2.29	73.19 ± 3.40[1b2a3b]	4.174	0.003
Cys-C, mg/dL							
Hp-IgG (+)	0.69 ± 0.02	0.78 ± 0.02[1a]	0.84 ± 0.02[1b]	0.97 ± 0.03[1b2b3a]	1.19 ± 0.07[1b2b3b]	19.952	< 0.001
Hp-IgG (-)	0.71 ± 0.02	0.78 ± 0.02	0.83 ± 0.02[1b]	0.93 ± 0.03[1b2b]	1.14 ± 0.04[1b2b3b4b]	28.435	< 0.001

Data are presented as mean ± SD. Hp-IgG (+) is defined as Hp-IgG ⩾ 35 EIU. *n*1: number in the Hp-IgG (+) group; *n*2: number in the Hp-IgG(-) group. [1]35-44-years-old group, [2]45-54-years-old group, [3]55-64-years-old group, [4]65-74-years-old group, [a]*P* < 0.05, [b]*P* < 0.01. Cr: Creatinine; Cys-C: Cystatin-C; FBG: Fasting blood glucose; G-17: Gastrin-17; Hp-IgG: *Helicobacter pylori*-immunoglobulin G; LDL-C: Low-density lipoprotein cholesterol; PG Ⅰ: Pepsinogen Ⅰ; PG Ⅱ: Pepsinogen Ⅱ; TC: Total cholesterol.

P = 0.037), while serum levels of G-17 negatively correlated with levels of serum PG Ⅰ (*P* < 0.001). With serum PGII as a dependent variable, serum levels of creatinine, Hp-IgG and age positively correlated with levels of serum PG Ⅱ (*P* = 0.006, *P* < 0.001, *P* = 0.007). With PG Ⅰ/PG Ⅱ as a dependent variable, serum levels of FBG positively correlated with PGI/PGII (*P* < 0.001), while serum levels of Hp-IgG, G-17 and age negatively correlated with PG Ⅰ/PG Ⅱ (*P* < 0.001, *P* < 0.001, *P* = 0.024). With serum G-17 as a dependent variable, age and serum levels of creatinine, Hp-IgG and FBG positively correlated with levels of serum G-17 (*P* = 0.032, *P* < 0.001, *P* = 0.037, *P* = 0.045), while serum levels of PGI and uric acid negatively correlated with levels of serum G-17 (*P* < 0.001, *P* = 0.009)(Table 5).

DISCUSSION

A European gastric biomarkers test[17] has been developed to measure serum PG and G-17 levels, and

Table 4 Correlation matrix among serum gastric biomarker levels, age and biochemical tests

	Age	PG Ⅰ	PG Ⅱ	PG Ⅰ/Ⅱ	G-17	Hp-IgG	TG	TC	HDL-C	LDL-C	FBG	UA	Cr	Cys-C	BMI
Age	1	0.161[b]	0.215[b]	-0.155[b]	0.140[b]	0.104[a]	-0.009	0.108[a]	0.010	0.136[b]	0.145[b]	0.148[b]	0.265[b]	0.548[b]	-0.016
		0.001	0.000	0.002	0.005	0.038	0.854	0.033	0.844	0.007	0.004	0.003	0.000	0.000	0.781
PG Ⅰ		1.000	0.682[b]	0.047	-0.140[b]	0.260[b]	-0.014	-0.066	-0.051	-0.023	0.056	0.188[b]	0.301[b]	0.355[b]	0.011
			0.000	0.357	0.005	0.000	0.788	0.188	0.308	0.654	0.266	0.000	0.000	0.000	0.843
PGⅡ			1.000	-0.588[b]	0.149[b]	0.592[b]	-0.029	-0.062	-0.075	-0.019	-0.005	0.077	0.209[b]	0.278[b]	0.006
				0.000	0.003	0.000	0.571	0.216	0.135	0.705	0.915	0.124	0.000	0.000	0.913
PG Ⅰ/Ⅱ				1.000	-0.384[b]	-0.587[b]	0.035	0.032	0.040	0.027	0.074	0.080	-0.019	-0.060	0.003
					0.000	0.000	0.488	0.532	0.427	0.590	0.140	0.112	0.712	0.234	0.961
G-17					1.000	0.105[a]	0.055	-0.020	-0.068	-0.016	0.119[a]	-0.062	0.129[a]	0.105[a]	-0.023
						0.038	0.279	0.695	0.177	0.749	0.018	0.219	0.011	0.037	0.690
Hp- IgG						1.000	0.000	-0.025	-0.062	-0.004	0.057	0.009	0.058	0.095	0.006
							0.985	0.618	0.220	0.938	0.257	0.865	0.250	0.059	0.919
TG							1.000	0.278[b]	-0.327[b]	0.145[b]	0.166[b]	0.156[b]	0.059	0.068	0.048
								0.000	0.000	0.004	0.001	0.002	0.243	0.176	0.402
TC								1.000	0.295[b]	0.896[b]	0.123[a]	0.023	-0.032	-0.039	0.111
									0.000	0.000	0.015	0.647	0.530	0.442	0.053
HDL-C									1.000	0.032	-0.093	-0.282[b]	-0.176[b]	-0.164[b]	0.017
										0.528	0.064	0.000	0.000	0.001	0.762
LDL-C										1.000	0.149[b]	0.074	0.000	0.022	0.085
											0.003	0.142	10.000	0.664	0.138
FBG											1.000	0.119[a]	0.111[a]	0.086	0.034
												0.018	0.027	0.086	0.558
UA												1.000	0.465[b]	0.403[b]	-0.003
													0.000	0.000	0.961
Cr													1.000	0.706[b]	-0.010
														0.000	0.858
Cys-C														1.000	-0.026
															0.648
BMI															1.000

[a]$P < 0.05$, [b]$P < 0.01$. BMI: Body mass index; Cr: Creatinine; Cys-C: Cystatin-C; FBG: Fasting blood glucose; G-17: Gastrin-17; Hp-IgG: *Helicobacter pylori*-immunoglobulin G; LDL-C: Low-density lipoprotein cholesterol; PG Ⅰ: Pepsinogen Ⅰ; PG Ⅱ: Pepsinogen Ⅱ; TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: Triglyceride; UA: Uric acid.

Hp-IgG antibodies by ELISA technique. Compared to endoscopic biopsy findings, the test classified the subjects into groups with "healthy" or "diseased" gastric mucosa with 94% accuracy, 95% sensitivity and 93% specificity. Compared to endoscopic histological findings, the accuracy of the biomarkers test in diagnosing atrophic gastritis was 87%, with a sensitivity of 40% and a specificity of 94%. Combined testing of Hp-IgG, PG and G-17 levels is of great clinical significance for general assessment of gastric mucosa secretion.

It has been previously shown that levels of serum PG Ⅰ decreased with age. Levels of serum PGII increased with age, but declined in participants aged over 60. Ratio of PG Ⅰ/PG Ⅱ decreased with age, but it increased after age 60[20]. It has also been observed that levels of PGI and PG Ⅱ increased with age. In a healthy population, levels of PG Ⅰ and PG Ⅱ varied amongst age groups, and the average PG level was highest in the senile group[21].

Our study showed that in the entire healthy study population, levels of serum PG Ⅱ increased with age, while the ratio of PG Ⅰ/PG Ⅱ decreased with age. The correlation between age and PG Ⅱ is stronger and more significant than that of PG Ⅰ; possibly, the distribution of PG Ⅱ-secreting cells is more extensive, and this could

Table 5 Factors associated with serum levels of gastric biomarkers

Dependent variable	Associated factors	Non-standard coefficient		Standard coefficient	*P* value
		B	SE	β	
PGI	Constant	50.347	200.845		0.798
	Cr	0.712	0.138	0.273	0.000
	Hp-IgG	0.334	0.066	0.263	0.000
	G-17	-0.647	0.138	-0.247	0.000
	FBG	70.859	30.744	0.110	0.037
PGII	Constant	-10.657	20.078		0.426
	Hp-IgG	0.120	0.010	0.556	0.000
	Cr	0.058	0.021	0.131	0.006
	Age	0.089	0.033	0.129	0.007
PGI /PGII	Constant	90.251	10.461		0.000
	Hp-IgG	-0.054	0.004	-0.520	0.000
	G-17	-0.075	0.009	-0.349	0.000
	FBG	10.037	0.255	0.177	0.000
	Age	-0.033	0.015	-0.101	0.024
G-17	Constant	-140.817	80.992		0.100
	Age	0.192	0.089	0.1240	0.032
	PGI	-0.103	0.022	-0.269	0.000
	Cr	0.228	0.063	0.228	0.000
	Hp-IgG	0.058	0.027	0.119	0.037
	UA	-0.042	0.016	-0.160	0.009
	FBG	30.054	10.520	0.112	0.045

Cr: Creatinine; FBG: Fasting blood glucose; G-17: Gastrin-17; Hp-IgG: *Helicobacter pylori*-immunoglobulin G; PGⅠ: Pepsinogen Ⅰ; PGⅡ: Pepsinogen Ⅱ; UA: Uric acid.

be one of the reasons to explain this finding. Since the ratio of PGⅠ/PGⅡ reflects the degree of atrophy in gastric mucosa, the current study indicated that atrophy of gastric mucosa occurred and developed with increasing age in a non-invasive serological method.

It has been suggested that serum levels of PGI and PGII significantly correlated with age in *H. pylori*-positive subjects. Increased PGⅠ and PGⅡ levels associated with age in a healthy population were caused by increased rates of *H. pylori* infection. Levels of PGⅠ and PGⅡ were dependent on the presence of *H. pylori* infection[22]. It was suggested that serum levels of G-17, PGI and PGⅡ increased in subjects with *H. pylori* infection, especially PGⅡ, while the ratio of PGⅠ/PGⅡ decreased.

Hypergastrinemia and hyperpepsinogenemia may be secondary to *H. pylori* infection[23,24]. The results of the current study on the effects of *H. pylori* infection on serum gastric biomarker levels were consistent with those of previous studies, and it was suggested that *H. pylori* infection had a closer correlation with PGⅡ than with PGⅠ and may influence the levels of PGⅡ more.

It has been shown that *H. pylori* infection was independently associated with elevated LDL-C levels and contributed to the atherosclerotic process[25]. The current study showed the difference on levels of serum LDL-C between *H. pylori*-infected and non-infected male subjects, which suggested an effect of *H. pylori* infection on raising levels of LDL-C in males. Meanwhile, the highest level of LDL-C was found in the middle-aged group (45-64 years) in non-infected subjects, while in *H. pylori*-infected subjects it was found in the elderly group (55-74 years). Increased LDL-C level is a risk factor for the development of atherosclerosis, and the current study indicated that Hp infection may increase the risks of atherosclerosis in males, especially those of elderly age.

It has been reported that renal function status may influence levels of serum PG and gastrin. Levels of serum PG and gastrin were found to be increased in patients with renal function insufficiency. This may have been due to reduced renal clearance of PG and gastrin[26,27]. There have been few studies investigating the relationship between renal function and serum PG and gastrin in a healthy population. The current study showed that age and serum levels of Hp-IgG, creatinine and FBG were the main factors associated with levels of serum PG and G-17. Since different levels of PG and G-17 represent different pathophysiological status of gastric mucosa, it was assumed that age, *H. pylori* infection, and serum levels of FBG and markers of renal function may influence the secretory function of gastric mucosa, and that abnormal serum levels of FBG and renal function might participate in the occurrence and development of gastric diseases.

In summary, the current study observed changes in gastric biomarker levels with age and effects of *H. pylori* infection in a healthy Chinese population, and explored factors associated with gastric biomarkers. Our data provide a theoretical basis for the recognition of gastric aging and its related diseases, which is of important clinical significance. However, there are some limitations in the study. Firstly, the sample size was relatively small and may, therefore, not represent the whole healthy population. Secondly, we found the effects of *H. pylori* infection and the correlation between gastric biomarkers and other associated factors, but the

mechanisms are not clear. More studies are needed to illustrate the mechanisms in the future.

COMMENTS

Background

Combined testing of *Helicobacter pylori* (*H. pylori*)-immunoglobulin G (Hp-IgG), pepsinogen (PG) and G-17 levels is of great clinical significance for general assessment of gastric mucosa secretion, and may also reflect the degree of gastric aging. Previous studies have investigated patients with peptic ulcer, chronic atrophic gastritis and gastric cancer. To date, few studies have observed levels of the gastric biomarkers and effects of *H. pylori* infection in a healthy ageing population nor explored the associated factors.

Research frontiers

Non-invasive biomarker tests may evaluate the secretory function of gastric mucosa, and distinguish pathological conditions, such as atrophic gastritis, from the healthy condition by combining tests for PGs, G-17 and Hp-IgG. Lower serum levels of PGI or PGⅠ/PGⅡ represent existence and degree of atrophy in gastric corpus mucosa. Studies have indicated that serum levels of PGs and G-17 are related to *H. pylori* infection and age, and could be significantly influenced by *H. pylori* infection. Furthermore, it has been shown that *H. pylori* infection was independently associated with elevated low-density lipoprotein cholesterol (LDL-C) levels and contributed to the atherosclerotic process.

Innovations and breakthroughs

The current study observed changes in gastric biomarker levels with age and effects of *H. pylori* infection in a healthy Chinese population, and explored factors associated with gastric biomarkers. This study showed that in the entire healthy study population, levels of serum PGII increased while PGI/PGII declined with age, which indicated that atrophy of gastric mucosa occurred and developed with increasing age, observed *via* a non-invasive serological method. Meanwhile, we discovered that *H. pylori* infection had an effect on raising levels of LDL-C to increase the risk of atherosclerosis in males, especially those of elderly age. Moreover, it is suggested that age, *H. pylori* infection, serum levels of renal function and fasting blood glucose (FBG) were associated with levels of serum PGs and gastrin.

Applications

In this study, the authors' discovered that *H. pylori* infection had an effect on raising levels of LDL-C to increase the risk of atherosclerosis in males, especially those who were elderly, which indicated that *H. pylori* infection should be afforded a more important status and given active treatment in elderly males to prevent atherosclerotic diseases. This study suggested that age, *H. pylori* infection, serum levels of renal function and FBG were associated with levels of serum PGs and gastrin. It was assumed that serum levels of renal function and FBG may influence the secretory function of gastric mucosa, and abnormal serum levels of FBG and renal function might participate in the occurrence and development of gastric diseases.

Terminology

H. pylori: A curved Gram-negative bacillus which is found in gastric mucosa; *H. pylori* is closely related with multiple gastric diseases, such as peptic ulcers, chronic atrophic gastritis and gastric cancer. PG: A precursor of pepsin which is mainly secreted by cells in the gastric corpus and can be divided into two groups, PGⅠ and PGⅡ; serum PG levels reflect the number of glands and cells, as well as the secretory function in gastric corpus mucosa. G-17: A hormone which is mainly secreted by G cells in gastric antrum and plays multiple physiological roles; serum level of G-17 reflects the number of cells and the secretory function in gastric antral mucosa.

Peer-review

The authors have carried out a detailed study of biomarkers and *H. pylori* infection in a large cohort of patients. The manuscript is detailed, the study well carried out and the data is comprehensive and complex.

REFERENCES

1 **Kang JM**, Kim N, Kim JH, Oh E, Lee BY, Lee BH, Shin CM, Park JH, Lee MK, Nam RH, Lee HE, Lee HS, Kim JS, Jung HC, Song IS. Effect of aging on gastric mucosal defense mechanisms: ROS, apoptosis, angiogenesis, and sensory neurons.*Am J Physiol Gastrointest Liver Physiol* 2010; **299**: G1147-G1153 [PMID: 20724528 DOI: 10.1152/ajpgi.00218.2010]

2 **Park KS**. [Aging and digestive diseases: at the view of the functional change of gastrointestinal tract]. *Korean J Gastroenterol* 2011; **58**: 3-8 [PMID: 21778797]

3 **Salles N**. Basic mechanisms of the aging gastrointestinal tract. *Dig Dis* 2007; **25**: 112-117 [PMID: 17468545 DOI: 10.1159/000099474]

4 **Malfertheiner P**, Megraud F, O'Morain C, Bazzoli F, El-Omar E, Graham D, Hunt R, Rokkas T, Vakil N, Kuipers EJ. Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. *Gut* 2007; **56**: 772-781 [PMID: 17170018 DOI: 10.1136/gut.2006.101634]

5 **Massarrat S**, Haj-Sheykholeslami A, Mohamadkhani A, Zendehdel N, Rakhshani N, Stolte M, Mirzaei M, Saliminejhad M, Saeidi S, Shahidi M. Precancerous conditions after H. pylori eradication: a randomized double blind study in first degree relatives of gastric cancer patients. *Arch Iran Med* 2012; **15**: 664-669 [PMID: 23102241]

6 **Chen TS**, Lee YC, Li FY, Chang FY. Smoking and hyper-pepsinogenemia are associated with increased risk for duodenal ulcer in Helicobacter pylori-infected patients. *J Clin Gastroenterol* 2005; **39**: 699-703 [PMID: 16082280]

7 **Kiyohira K**, Yoshihara M, Ito M, Haruma K, Tanaka S, Chayama K. Serum pepsinogen concentration as a marker of Helicobacter pyloriinfection and the histologic grade of gastritis; evaluation of gastric mucosa by serum pepsinogen levels. *J Gastroenterol* 2003; **38**: 332-338 [PMID: 12743772 DOI: 10.1007/s005350300060]

8 **Derakhshan MH**, El-Omar E, Oien K, Gillen D, Fyfe V, Crabtree JE, McColl KE. Gastric histology, serological markers and age as predictors of gastric acid secretion in patients infected with Helicobacter pylori. *J Clin Pathol* 2006; **59**: 1293-1299 [PMID: 16644877 DOI: 10.1136/jcp.2005.036111]

9 **di Mario F**, Cavallaro LG. Non-invasive tests in gastric diseases. *Dig Liver Dis* 2008; **40**: 523-530 [PMID: 18439884 DOI: 10.1016/j.dld.2008.02.028]

10 **Sun LP**, Gong YH, Wang L, Gong W, Yuan Y. Follow-up study on a high risk population of gastric cancer in north China by serum pepsinogen assay. *J Dig Dis* 2008; **9**: 20-26 [PMID: 18251790 DOI: 10.1111/j.1443-9573.2007.00321.x]

11 **Sun LP**, Gong YH, Wang L, Yuan Y. Serum pepsinogen levels and their influencing factors: a population-based study in 6990 Chinese from North China. *World J Gastroenterol* 2007; **13**: 6562-6567 [PMID: 18161928 DOI: 10.3748/wjg.13.6562]

12 **Iijima K**, Abe Y, Kikuchi R, Koike T, Ohara S, Sipponen P, Shimosegawa T. Serum biomarker tests are useful in delineating between patients with gastric atrophy and normal, healthy stomach. *World J Gastroenterol* 2009; **15**: 853-859 [PMID: 19230047 DOI: 10.3748/wjg.15.853]

13 **Broutet N**, Plebani M, Sakarovitch C, Sipponen P, Mégraud F; Eurohepygast Study Group. Pepsinogen A, pepsinogen C, and gastrin as markers of atrophic chronic gastritis in European dyspeptics. *Br J Cancer* 2003; **88**: 1239-1247 [PMID: 12698190 DOI: 10.1038/sj.bjc.6600877]

14 **Kikuchi R**, Abe Y, Iijima K, Koike T, Ara N, Uno K, Asanuma K, Asano N, Imatani A, Shimosegawa T. Low serum levels of pepsinogen and gastrin 17 are predictive of extensive gastric atrophy with high-risk of early gastric cancer. *Tohoku J Exp Med* 2011; **223**: 35-44 [PMID: 21222340]

15 **Cao Q**, Ran ZH, Xiao SD. Screening of atrophic gastritis and gastric cancer by serum pepsinogen, gastrin-17 and Helicobacter pylori immunoglobulin G antibodies. *J Dig Dis* 2007; **8**: 15-22 [PMID: 17261130 DOI: 10.1111/j.1443-9573.2007.00271.x]

16 **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; **6**: 174-179 [PMID: 18237867 DOI: 10.1016/j.cgh.2007.11.016]
17 **Storskrubb T**, Aro P, Ronkainen J, Sipponen P, Nyhlin H, Talley NJ, Engstrand L, Stolte M, Vieth M, Walker M, Agréus L. Serum biomarkers provide an accurate method for diagnosis of atrophic gastritis in a general population: The Kalixanda study. *Scand J Gastroenterol* 2008; **43**: 1448-1455 [PMID: 18663663 DOI: 10.1080/00365520802273025]
18 **González CA**, Megraud F, Buissonniere A, Lujan Barroso L, Agudo A, Duell EJ, Boutron-Ruault MC, Clavel-Chapelon F, Palli D, Krogh V, Mattiello A, Tumino R, Sacerdote C, Quirós JR, Sanchez-Cantalejo E, Navarro C, Barricarte A, Dorronsoro M, Khaw KT, Wareham N, Allen NE, Tsilidis KK, Bas Bueno-de-Mesquita H, Jeurnink SM, Numans ME, Peeters PH, Lagiou P, Valanou E, Trichopoulou A, Kaaks R, Lukanova-McGregor A, Bergman MM, Boeing H, Manjer J, Lindkvist B, Stenling R, Hallmans G, Mortensen LM, Overvad K, Olsen A, Tjonneland A, Bakken K, Dumeaux V, Lund E, Jenab M, Romieu I, Michaud D, Mouw T, Carneiro F, Fenge C, Riboli E. Helicobacter pylori infection assessed by ELISA and by immunoblot and noncardia gastric cancer risk in a prospective study: the Eurgast-EPIC project. *Ann Oncol* 2012; **23**: 1320-1324 [PMID: 21917738 DOI: 10.1093/annonc/mdr384]
19 **He CY**, Sun LP, Gong YH, Xu Q, Dong NN, Yuan Y. Serum pepsinogen II: a neglected but useful biomarker to differentiate between diseased and normal stomachs. *J Gastroenterol Hepatol* 2011; **26**: 1039-1046 [PMID: 21303408 DOI: 10.1111/j.1440-1746.2011.06692.x]
20 **Rollan A**, Ferreccio C, Gederlini A, Serrano C, Torres J, Harris P. Non-invasive diagnosis of gastric mucosal atrophy in an asymptomatic population with high prevalence of gastric cancer. *World J Gastroenterol* 2006; **12**: 7172-7178 [PMID: 17131482 DOI: 10.3748/wjg.v12.i44.7172]
21 **Miki K**, Fujishiro M, Kodashima S, Yahagi N. Long-term results of gastric cancer screening using the serum pepsinogen test method among an asymptomatic middle-aged Japanese population. *Dig Endosc* 2009; **21**: 78-81 [PMID: 19691778 DOI: 10.1111/j.1443-1661.2009.00839.x]
22 **Kim HY**, Kim N, Kang JM, Park YS, Lee DH, Kim YR, Kim JS, Jung HC, Song IS. Clinical meaning of pepsinogen test and Helicobacter pylori serology in the health check-up population in Korea. *Eur J Gastroenterol Hepatol* 2009; **21**: 606-612 [PMID: 19293719 DOI: 10.1097/MEG.0b013e3283086757]
23 **Leung WK**, Wu MS, Kakugawa Y, Kim JJ, Yeoh KG, Goh KL, Wu KC, Wu DC, Sollano J, Kachintorn U, Gotoda T, Lin JT, You WC, Ng EK, Sung JJ; Asia Pacific Working Group on Gastric Cancer. Screening for gastric cancer in Asia: current evidence and practice. *Lancet Oncol* 2008; **9**: 279-287 [PMID: 18308253 DOI: 10.1016/S1470-2045(08)70072-X]
24 **Massarrat S**, Haj-Sheykholeslami A, Mohamadkhani A, Zendehdel N, Aliasgari A, Rakhshani N, Stolte M, Shahidi SM. Pepsinogen II can be a potential surrogate marker of morphological changes in corpus before and after H. pylori eradication. *Biomed Res Int* 2014; **2014**: 481607 [PMID: 25028655 DOI: 10.1155/2014/481607]
25 **Gong Y**, Wei W, Jingwei L, Nannan D, Yuan Y. Helicobacter pylori Infection Status Correlates with Serum Parameter Levels Responding to Multi-organ Functions. *Dig Dis Sci* 2015; **60**: 1748-1754 [PMID: 25599961 DOI: 10.1007/s10620-015-3522-2]
26 **Furgała A**, Błaut-Kadzielska U, Stojakowska M, Dobrek Ł, Mazur M, Machowska A, Thor PJ. Gastric dysfunction in dialysed patients with chronic renal failure. *Folia Med Cracov* 2012; **52**: 39-55 [PMID: 23697214]
27 **Gong Y**, Wang W, Li Y, Yuan Y. Serum Indicators Reflecting Gastric Function May Also Correlate with Other Extragastric Diseases. *Gastroenterol Res Pract* 2015; **2015**: 867495 [PMID: 26339238 DOI: 10.1155/2015/867495]

P- Reviewer: Bramhall S, Lombardo L, Yamaoka Y **S- Editor**: Qi Y
L- Editor: Filipodia **E- Editor**: Zhang FF

Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

ISSN 1007-9327