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

**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 Helicobacter 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 PG1/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 PG I, PG II 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 PG I, PG II and G-17 (P < 0.001, P < 0.001, P < 0.001). Fasting blood glucose (FBG) positively correlated with PG I/PG II 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

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Core tip: Our study showed that in an entire healthy population, levels of serum pepsinogen (PG) II increased while PG I/PG II 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.

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[5-13]. 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[2,6].

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 PG I or PG I/PG II 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,
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 September 2007 to May 2008. 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) were also established.

**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 35-44-years-old group. The ratio of PG I/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, and "b" with ≥ 75-years-old compared to 35-44-years-old group. The "a" denotes comparison with 35-44-years-old age group, and "b" with ≥ 75-years-old.

**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 (heterogeneity 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 /PGII 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/PGII 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

| Age/yr       | n   | PG I (μg/L) | PG II (μg/L) | PG I/PG II | G-17 (pmol/L) |
|--------------|-----|-------------|--------------|------------|---------------|
| 35-44 yr, n = 58 |     | 9.28 ± 5.16 | 9.84 ± 4.15  | 9.65 ± 3.66 | 2.93 ± 0.55   |
| 45-54 yr, n = 84 |     | 10.03 ± 3.18| 10.76 ± 3.26 | 10.86 ± 3.01| 5.10 ± 1.29   |
| 55-64 yr, n = 117|    | 108.56 ± 8.01| 117.04 ± 8.30| 115.04 ± 8.10| 9.75 ± 1.49   |
| 65-74 yr, n = 76  |    | 2.32 ± 0.55  | 3.05 ± 0.76  | 2.12 ± 0.65  | 9.03 ± 0.70   |
| ≥ 75 yr, n = 60  |    | 1.95 ± 0.45  | 2.32 ± 0.55  | 2.03 ± 0.45  | 9.35 ± 0.56   |

Data are presented as mean ± SD. *Comparison with the 35-44-years-old group, *P < 0.05, *P < 0.01. G-17: Gastrin-17; PG I : Pepsinogen I ; PG II : 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, PG II and G-17 were significantly higher, while the ratio of PG I/PG II was significantly lower in Helicobacter pylori-infected subjects. *P < 0.05, *P < 0.01. G-17: Gastrin-17; PG I : Pepsinogen I ; PG II : Pepsinogen II.

Comparison of serum gastric biomarker levels and biochemical tests in various age groups by Helicobacter 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 PG II 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, PG II and G-17 (P = 0.038, P = 0.001, P < 0.001, P = 0.005) and negatively correlated with ratio of PG I/PG II (P = 0.002). Levels of serum Hp-IgG positively correlated with serum levels of PG I, PG II and G-17 (P < 0.001, P < 0.001, P = 0.038) and negatively correlated with ratio of PG I/PG II (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 PG II and PG I/PG II (r = 0.592, P < 0.001; r = -0.587, P < 0.001), and levels of serum PG II were strongly associated with serum levels of PG I and PG I/PG II (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 = 104                                                     |
|                | Hp-IgG (-), n = 87                                                    | Hp-IgG (-), n = 123                                                    |
|                | P value                                                               | P value                                                               |
| TG, mmol/L     | 1.33 ± 0.11                                                           | 1.30 ± 0.17                                                           | 0.875 | 1.24 ± 0.06 | 0.767 |
| TC, mmol/L     | 5.07 ± 0.11                                                           | 4.80 ± 0.09                                                           | 0.052 | 5.16 ± 0.09 | 0.542 |
| 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 |
| FBC, 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; FBC: Fasting blood glucose; 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 | 45-54 yr | 55-64 yr | 65-74 yr | ≥ 75 yr | F      | P value |
|----------------|----------|----------|----------|----------|---------|--------|---------|
|                | n1 = 21  | n1 = 39  | n1 = 57  | n1 = 36  | n1 = 33 | n2 = 37 | n2 = 45 | n2 = 60 | n2 = 27 | n2 = 27 |
| PG1, μg/L      | 89.43 ± 7.46 | 100.03 ± 6.45 | 90.25 ± 5.10 | 92.61 ± 12.23 | 94.95 ± 13.47 | 0.824 | 0.920 |
| PG1, μg/L      | 83.6 ± 6.47 | 81.28 ± 3.89 | 83.96 ± 5.04 | 96.67 ± 10.31 | 105.49 ± 8.08 | 1.730 | 0.143 |
| PG1, μg/L      | 14.68 ± 1.08 | 18.45 ± 1.34 | 17.47 ± 1.16 | 19.52 ± 1.46 | 19.51 ± 1.91 | 1.393 | 0.260 |
| PG1, μg/L      | 6.80 ± 0.58 | 8.69 ± 0.41 | 7.64 ± 0.46 | 9.46 ± 1.42 | 10.23 ± 0.76ab | 1.115 | 0.011 |
| PG1, μg/L      | 7.92 ± 0.53 | 7.17 ± 0.39 | 7.03 ± 0.38 | 6.65 ± 0.58 | 6.97 ± 0.52 | 0.662 | 0.616 |
| PG1, μg/L      | 12.66 ± 0.41 | 12.25 ± 0.42 | 12.18 ± 0.39 | 11.68 ± 0.89 | 10.85 ± 0.80 | 1.163 | 0.353 |

Data are presented as mean ± SD. H. pylori-IgG (+) is defined as H. pylori-IgG ≥ 35 EIU. n1: number in the Hp-IgG (+) group; n2: number in the Hp-IgG(-) group. 35-44-years-old group, 45-54-years-old group, 55-64-years-old group, ≥ 65-years-old group. P < 0.05. P < 0.01. Cr: Creatinine; Cys-C: Cystatin-C; FBC: Fasting blood glucose; TG: Triglycerides; UA: Uric acid; H. pylori: Helicobacter pylori.

P = 0.037), while serum levels of G-17 negatively correlated with levels of serum PG I (P < 0.001). With serum PG1 as a dependent variable, serum levels of creatinine, Hp-IgG and age positively correlated with levels of serum PG1 (P = 0.006, P < 0.001, P = 0.007). With PG I/PGII as a dependent variable, serum levels of FBG positively correlated with PG1/PGII (P < 0.001), while serum levels of Hp-IgG, G-17 and age negatively correlated with PG I/PGII (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 PG I 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      | 1.000 | 0.219 | 0.215 | 0.166  | 0.304 | 0.104  | 0.010| 0.136| 0.145  | 0.146  | 0.145 | 0.148 | 0.265| 0.548 | -0.016|
| PG I     | 1.000 | 0.001 | 0.002 | 0.005  | 0.038 | 0.384  | 0.343| 0.074| 0.004  | 0.033  | 0.007 | 0.004 | 0.003 | 0.000 | 0.781 |
| PG II    | 1.000 | 0.000 | 0.003 | 0.000  | 0.035 | 0.052  | 0.161| 0.135| 0.138  | 0.074  | 0.019 | 0.005 | 0.077 | 0.209 | 0.278 |
| PG I/II  | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.105| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.913 |
| G-17     | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| HP-IgG   | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| TG       | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| HDL-C    | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| LDL-C    | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| FBG      | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| UA       | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Cr       | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Cys-C    | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| BMI      | 1.000 | 0.000 | 0.000 | 0.000  | 0.000 | 0.000  | 0.000| 0.000| 0.000  | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |

*P < 0.05; **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 I 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 PG II 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 PG I 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[23].

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
be one of the reasons to explain this finding. Since the ratio of PG I /PG II 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 PG II, 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 PG II than with PGI and may influence the levels of PG II 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

### Table 5 Factors associated with serum levels of gastric biomarkers

| Dependent variable | Associated factors | Non-standard coefficient | Standard coefficient | β | P value |
|--------------------|--------------------|--------------------------|----------------------|---|---------|
| PGI                | Constant           | 50.347                   | 200.845              | 0.119 | 0.138 |
|                   | 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 |
| PGI /PGII         | Constant            | 90.251                   | 10.461               | 0.129 | 0.000 |
|                   | Cr                  | -0.054                   | 0.004                | -0.520 | 0.000 |
|                   | Hp-IgG              | -0.075                   | 0.009                | -0.349 | 0.000 |
|                   | G-17                | 10.037                   | 0.255                | 0.177 | 0.000 |
|                   | Age                 | -0.035                   | 0.015                | -0.101 | 0.024 |
| G-17              | Constant            | -140.817                 | 80.992               | 0.124 | 0.032 |
|                   | Age                 | 0.192                    | 0.089                | 0.022 | 0.000 |
|                   | 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 | 0.007 |
|                   | 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; PG I : Pepsinogen 1 ; PG II : Pepsinogen 2; UA: Uric acid.
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 PG I/PG II 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 PGIII 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, especially those who were elderly, which indicated that 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.

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, PG I 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.

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