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RESEARCH ARTICLE

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Analysis of serum gastrin-17 and *Helicobacter pylori* antibody in healthy Chinese population

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Abstract

Background: Gastrin-17 (G-17) and *Helicobacter pylori* (*H pylori*) antibody are widely used in the screening of gastric diseases, especially in gastric cancer. In this study, we aimed to evaluate the value of G-17 and *H pylori* antibody in gastric disease screening.

Methods: Healthy males and females (1368 and 1212, respectively) aged between 21-80 years were recruited for the study. Serum G-17 value was measured using ELISA, and *H pylori* antibodies were measured using Western blotting. Statistical analyses were performed using the chi-square, Mann-Whitney *U*, and Kruskal-Wallis *H* tests.

Results: Serum G-17 level was higher in the *H pylori*-positive group than in the negative group. Serum G-17 level was higher in the type 1 *H pylori*-positive group than in the type 2 *H pylori*-positive group. Further, serum G-17 level was higher in females than in males and showed significant differences among different age-groups, with changes in trend proportional to the age. The positive rate of *H pylori* infection in all the subjects was 58.29% and did not show a significant difference between males and females. However, it showed significant differences among different age-groups, with the changing trend proportional to the age.

Conclusion: Analysis of serum G-17 level and *H pylori* antibody typing is valuable in gastric disease screening. Every laboratory should establish its own reference interval for G-17 level.

KEYWORDS

age, gastric disease, gastrin, gender, *Helicobacter pylori* antibody

1 | INTRODUCTION

Helicobacter pylori (*H pylori*) is a gram-negative, spiral-shaped bacterium that is known to have infected more than half of the world's population and is the only pathogenic bacteria currently known to survive in the human stomach. *Helicobacter pylori* is listed as grade 1 carcinogen in the list of carcinogens published by the World Health Organization. It changes the structure and function of the gastric mucosa following infection, eventually leading to a variety of gastric diseases.[1-3]

Gastrin-17 (G-17) is an important gastrointestinal hormone which is mainly secreted by the gastrointestinal G cells. It stimulates the secretion of gastric acid and pepsinogen, promotes proliferation of the gastric mucosal cells, enhances the motility of the gastrointestinal tract, and promotes the secretion of pancreatic juice and bile.

It also reflects the functional status of the gastric mucosa and plays an important role in the occurrence and development of gastrointestinal tumors.[4-6]

As an important constituent of "serological biopsy" of gastric mucosa, *H pylori* antibody and G-17 are widely used in clinical diagnosis of gastric diseases. Serum G-17 levels are thought to be closely related to *H pylori* infection, and several studies have attempted to explore and demonstrate their relationship.[7-9] Most of the studies were performed on patients with gastric diseases, and limited number of studies have used healthy human subjects. In this study, we analyzed the level of serum G-17 and *H pylori* antibodies in healthy Chinese population to explore their diagnostic potential in the screening of gastric diseases.

2 | MATERIALS AND METHODS

2.1 | Subjects

In this study, we performed retrospective analysis of 1368 apparently healthy males and 1212 apparently healthy females (aged 21-80 years) who performed physical examinations at the Health Examination Center of The People's Hospital of Guangxi Zhuang Autonomous Region between February 2018 and February 2020. Serum G-17 and *H pylori* antibody were simultaneously tested as examination items in all the subjects. The exclusion criteria of the subjects in our study were as follows: 1. Individuals with a history of administration of special medication (including proton pump inhibitors and H_2 receptor antagonists among others) within 2 weeks prior to the physical examination; 2. individuals with a history of gastric diseases such as gastritis, gastric ulcer, and gastric cancer; 3. individuals with a history of stomach surgery; 4. individuals with severe heart, liver, or kidney insufficiency; 5. individuals with a long-term history of smoking or drinking; and 6. individuals with known infectious diseases. This study was approved by the ethics committee of The People's Hospital of Guangxi Zhuang Autonomous Region.

2.2 | G-17 Enzyme-linked immunosorbent assay (ELISA)

All the individuals were required to maintain fasting for more than 10 hours prior to drawing of blood. Fasting blood samples were collected into BD Vacutainer blood collection tubes (Becton Dickinson, allowed to clot for at least 30 minutes at room temperature, and then centrifuged for 10 minutes at 1200 g to obtain the serum. Serum G-17 value was measured using ELISA (Biohit). All procedures were carried out according to the manufacturer's instructions. Reference interval of G-17 in normal population provided by the instructions was 1 ~ 7 pmol/L, but it was recommended that every laboratory establishes its own reference interval.

2.3 | *H pylori* antibody testing using Western blot analysis

Samples were prepared as described above for G-17. Serum *H pylori* antibodies were measured using Western blot analysis (Blot). The test principles were as follows: *H pylori* antigens were electrophoresed on sodium dodecyl sulfate (SDS)-polyacrylamide gel, separated according to the molecular weights, and then transferred to nitrocellulose membrane. The *H pylori* antibodies present in the serum react with the antigens on the nitrocellulose membrane and were visualized with the addition of enzyme-labeled antigens and color reagents. A positive zone appeared colored on the membrane. All procedures were carried out according to the manufacturer's instructions. Interpretations of the *H pylori* antibody typing were performed as follows: Negative result: only quality control zone appeared on the color rendering zone; type 1 *H pylori* antibody: CagA and VacA zone simultaneously appeared or either of the two appeared; and type 2 *H pylori* antibody: UreA and UreB zone simultaneously appeared or either of the two appeared, CagA and VacA zone did not appear.

2.4 | Statistical analysis

All the experimental data were analyzed with SPSS statistics 22.0 software. Serum G-17 levels were expressed by median (25th percentile, 75th percentile) (M; P25 ~ P75). Positive rates of *H pylori* between males and females, among the different age-groups, were compared using chi-square test; serum G-17 levels between the males and females were compared using Mann-Whitney *U* test; serum G-17 levels among different age-groups were compared using Kruskal-Wallis *H* test; serum G-17 levels among the three groups based on different *H pylori* infection status were compared using Kruskal-Wallis H test at first, and Mann-Whitney *U* test was then used to make pairwise comparison if a significant difference was detected by Kruskal-Wallis *H* test. The level of statistical significance was set at $P < .05$.

3 | RESULTS

3.1 | Comparison of serum G-17 levels among the three groups based on different *H pylori* infection status

The serum G-17 level was 3.30 (1.51 ~ 6.61) in the 1023 subjects with type 1 *H pylori* infection, 1.50 (0.73 ~ 3.40) in the 481 subjects with type 2 *H pylori* infection, and 0.94 (0.57 ~ 1.77) in the 1076 subjects with no *H pylori* infection. The differences in the serum G-17 levels among the three groups were significant ($P = .000$; Table 1).

3.2 | Comparison of serum G-17 level between males and females

The serum G-17 level was 1.59 (0.76 ~ 4.04) in all the subjects, 1.50 (0.67 ~ 4.01) in males, and 1.68 (0.86 ~ 4.09) in females. Thus, the serum G-17 level in females was higher than that in males ($P = .005$; Table 2; Figure 1).

3.3 | Comparison of serum G-17 level among different age-groups

The serum G-17 levels in the different age-groups of 21-30, 31-40, 41-50, 51-60, and >60 years were 1.46 (0.67 ~ 3.77), 1.35 (0.66 ~ 4.01), 1.59 (0.79 ~ 3.80), 1.77 (0.85 ~ 4.26), and 1.89 (0.89 ~ 4.41), respectively. The serum G-17 levels showed significant differences among the age-groups ($P = .000$), with the changing trend proportional to the age (Table 2; Figure 1).

TABLE 1 Serum G-17 levels in the three groups based on different *H pylori* infection status

Hp infection status	Number	G-17 (pmol/L)
Hp-1 positive	1023	3.30 (1.51 ~ 6.61)
Hp-2 positive	481	1.50 (0.73 ~ 3.40)
Hp negative	1076	0.94 (0.57 ~ 1.77)

3.4 | Comparison of *H pylori* positive rates between males and females

Helicobacter pylori -positive rate was 58.29% in all the subjects, 57.46% in males, and 59.24% in females. There was no significant difference in the positive rate between males and females ($P = .379$). The type 1 *H pylori* positive rates were 39.33% and 40.02% in males and females, respectively, and there was no significant difference between them ($P = .747$). The type 2 *H pylori* positive rates were 18.13% and 19.22% in males and females, respectively, and showed no significant difference ($P = .479$; Table 2; Figure 2).

3.5 | Comparison of *H pylori* positive rates among different age-groups

Helicobacter pylori positive rates in the different age-groups of 21-30, 31-40, 41-50, 51-60, and >60 years were 45.32%, 52.22%, 60.47%, 66.98%, and 66.95%, respectively, and showed significant differences ($P = .000$) among the age-groups. The changes in the trend were proportional to the age (Table 2; Figure 2).

4 | DISCUSSION

Gastrin is mainly synthesized and secreted by the G cells in the gastric antrum. G-17 is the most important form of gastrin in blood circulation.[6,10,11] In our study, serum G-17 levels were higher in females

TABLE 2 *H pylori*-positive rates and serum G-17 levels in different genders and age-groups

Age	Gender	Hp-1 (%)	Hp-2 (%)	Hp (%)	G-17 (pmol/L)
21-30	Male	30.20 (74/245)	14.29 (35/245)	44.49 (109/245)	1.06 (0.58 ~ 3.73)
	Female	28.81 (68/236)	17.37 (41/236)	46.19 (109/236)	1.66 (0.88 ~ 3.78)
	Male + female	29.52 (142/481)	15.80 (76/481)	45.32 (218/481)	1.46 (0.67 ~ 3.77)
31-40	Male	33.75 (107/317)	17.03 (54/317)	50.79 (161/317)	1.28 (0.62 ~ 3.52)
	Female	39.41 (106/269)	14.50 (39/269)	53.90 (145/269)	1.39 (0.70 ~ 4.52)
	Male + female	36.35 (213/586)	15.87 (93/586)	52.22 (306/586)	1.35 (0.66 ~ 4.01)
41-50	Male	40.70 (116/285)	19.30 (55/285)	60.00 (171/285)	1.47 (0.71 ~ 3.56)
	Female	41.59 (94/226)	19.47 (44/226)	61.06 (138/226)	1.67 (0.90 ~ 4.04)
	Male + female	41.10 (210/511)	19.37 (99/511)	60.47 (309/511)	1.59 (0.79 ~ 3.80)
51-60	Male	43.89 (115/262)	21.76 (57/262)	65.65 (172/262)	1.82 (0.82 ~ 4.58)
	Female	47.60 (129/271)	20.66 (56/271)	68.27 (185/271)	1.69 (0.93 ~ 3.98)
	Male + female	45.78 (244/533)	21.20 (113/533)	66.98 (357/533)	1.77 (0.85 ~ 4.26)
>60	Male	48.65 (126/259)	18.15 (47/259)	66.80 (173/259)	1.89 (0.78 ~ 4.27)
	Female	41.90 (88/210)	25.24 (53/210)	67.14 (141/210)	1.89 (0.93 ~ 4.65)
	Male + female	45.63 (214/469)	21.32 (100/469)	66.95 (314/469)	1.89 (0.89 ~ 4.41)
Total	Male	39.33 (538/1368)	18.13 (248/1368)	57.46 (786/1368)	1.50 (0.67 ~ 4.01)
	Female	40.02 (485/1212)	19.22 (233/1212)	59.24 (718/1212)	1.68 (0.86 ~ 4.09)
	Male + female	39.65 (1023/2580)	18.64 (481/2580)	58.29 (1504/2580)	1.59 (0.76 ~ 4.04)

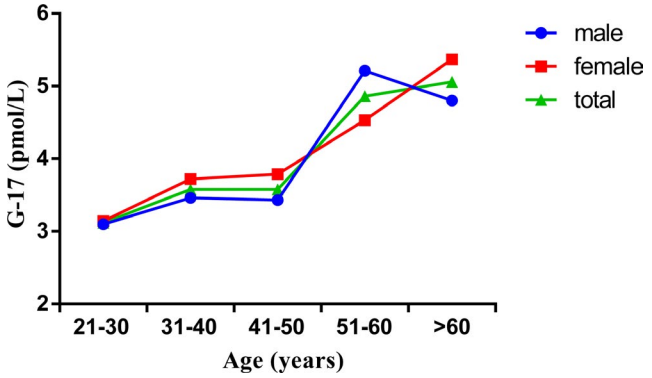

FIGURE 1 Serum G-17 levels in different genders and age groups

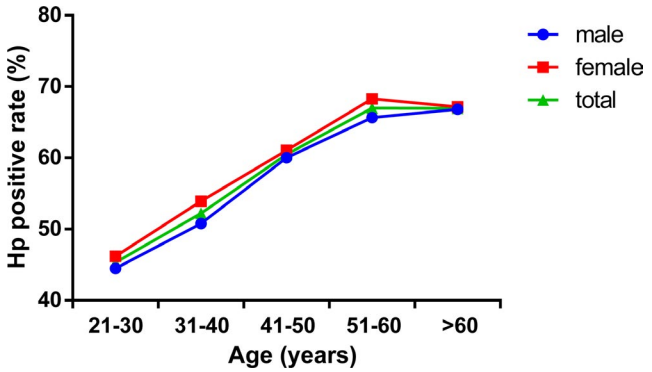

FIGURE 2 *H pylori* positive rates in different genders and age groups

than in males. However, in age-group of 51-60 years, the serum G-17 levels were higher in males than in females. This difference may be related to the changes in hormones that occur in women during menopause. Some previous studies have reported differences in serum G-17 levels between males and females, while some others have reported no difference.[12-14] G-17 is an unstable indicator which is affected by many factors. It shows variations in different regions and populations, such that the difference between males and females also varied. Serum G-17 levels also showed significant differences in different age-groups, the change in the trend was proportional to the age.

Helicobacter pylori is a curved gram-negative bacillus which is found in the gastric mucosa and is typically acquired during childhood. *Helicobacter pylori* infection rates change with public sanitary conditions, socioeconomic factors, and hygiene habits and tend to increase with age. *Helicobacter pylori* infection is globally distributed, and more than half of the world's population are carriers of the microorganism, with a higher prevalence in the developing countries compared to the developed countries.[15-17] Previous studies have reported an *H pylori* infection rate of 50 ~ 80% in China. Consistent with this report, the *H pylori* infection rate in our study was 58.29%.[18,19] Measurement of *H pylori* antibody in our study was conducted using a typing test. The type 1 *H pylori* produces vacuolating cytotoxin (VacA) and cytotoxin-associated protein (CagA) and is more infectious and pathogenic than the type 2 *H pylori* which produces urease subunit A/B (UreA/B) and no cytotoxins.[20-22]

In the *H pylori*-infected group, 68.02% were infected with type 1 *H pylori*, and 31.98% were infected with type 2 *H pylori*. These data showed that most of the *H pylori* infection in our region were caused by type 1 *H pylori* and demonstrated that the type 1 *H pylori* was more infectious than type 2 *H pylori*. The positive rate of *H pylori* infection showed no significant difference between males and females. Some previous studies reported differences in the positive rate of *H pylori infection* between males and females, while some others reported no difference.[23,24] *H pylori* infection status also changed depending on different regions and populations, such that the difference between males and females also varied. The positive rate of *H pylori* infection among different age-groups showed significant differences, and the changes in the trends were proportional to the age.

Studies have suggested that *H pylori* infection stimulates gastrin secretion, leading to an increase in the serum G-17 level.[25,26] In our study, the serum G-17 level in *H pylori*-positive group was higher than in the *H pylori*-negative group. Further, the serum G-17 level in type 1 *H pylori*-positive group was also higher than in the type 2 *H pylori*-positive group. It is reported that *H pylori* infection increases urea and ammonia in the stomach, and decreases gastric acid, resulting in an increase in G-17 secretion.[27,28] Compared to type 2 *H pylori*, the type 1 *H pylori* produces VacA and CagA, which was more pathogenic to the gastric mucosa. The serum G-17 levels in subjects with type 1 *H pylori* infection were higher than in subjects with type 2 *H pylori* infection, which also demonstrates that type 1 *H pylori* has more pathogenic to the gastric mucosa than type 2 *H pylori*.

The reference interval of serum G-17 level in normal population according to the manufacturer's instructions was 1 ~ 7 pmol/L. However, it was recommended that each laboratory needs to establish its own reference interval. Both, increase or decrease of serum G-17 levels indicates a risk of gastric disease. Gastrin is mainly synthesized and secreted by the G cells in the gastric antrum. Gastrin levels often decrease when a lesion develops in the gastric antrum and conversely increase when a lesion develops in the gastric body.[29] Serum G-17 levels in our study were slightly lower than that in previous reports.[30-32] As an unstable indicator, G-17 is influenced by many factors, including people from different regions with different diets and lifestyle habits. Given that several factors may affect serum G-17 levels, every laboratory needs to establish its own reference interval for G-17, and the statistical data pertaining to the serum G-17 levels in our study would serve as a reference for our laboratory.

Although none of the subjects in our study had any history of gastric diseases, screening of serum G-17 and *H pylori* antibody can help in the identification of high-risk population and allow for intervention in the early stage of the disease.

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