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ORIGINAL ARTICLE

Relation between *Helicobacter pylori* and atrophic gastritis in elderly: Estimation of serum (gastrin 17 and pepsinogen-I) as novel biomarkers

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KEYWORDS

Helicobacter pylori;
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Elderly

Abstract *Background:* Serum levels of gastrin-17 (S-G-17) and pepsinogen I (S-PGI) are biomarkers of gastric antral and corpus mucosa, respectively. We determined whether these tests, together with the assay of *Helicobacter pylori* antibodies, are a nonendoscopic tool for the diagnosis of atrophic gastritis.
Objectives: To study the relation between *H. pylori* infection and atrophic gastritis in the elderly through the estimation of gastrin 17 and pepsinogen I as novel noninvasive diagnostic biomarkers.
Material and methods: The present study included sixty individuals suffering from gastritis there were divided into two groups. Group (I): Thirty patients having *H. pylori* infection aged above 65 years. Group (II): Thirty patients without *H. pylori* infection aged above 65 years. All individualswere subjected to diagnostic upper-gastrointestinal endoscopy and specific gastric biomarkers (serum gastrin-17, serum pepsinogen I/II).

Abbreviation: *H. pylori*, *Helicobacter pylori*; PGI, Pepsinogen I; PGII, Pepsinogen II; G, Gastrin

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Results: Serum pepsinogen I, II, ratio and gastrin 17 decrease with increasing grade of atrophy of the antrum respectively. Serum pepsinogen I, II, gastrin 17 were significantly lower in mild, moderate, and severe gastritis compared to superficial gastritis patients.
Conclusion: The diagnosis of atrophic gastritis obtained with the blood test panel of G.17, SPG I/II and *H. pylori* antibodies is in good agreement with the endoscopic and biopsy finding. The panel is a tool for nonendoscopic diagnosis and screening of atrophic gastritis.

1. Introduction

Aging is a basic natural and biological process that goes on continuously in every individual and is responsible for changes affecting the organs by the passage of time. It starts with the onset of life and is terminated by death.[1]

H. pylori infection increases with age. Its prevalence was found to approach 75% in patients above 65 years of age.[2–4]

A recent retrospective study has found that *H. pylori* infection is associated with the majority of cases of symptomatic gastritis in the elderly patients.[5]

Recent studies have demonstrated a clear association between gastric colonization with *H. pylori*, gastritis and peptic ulcer disease.[6,7] Other epidemiological studies have also shown an association between infections with *H. pylori* and gastric cancer, the evidence is so complete that the world health organization has recently categorized *H. pylori* as a category I carcinogen.[8–12]

Gastric atrophy characterized by the loss of antrum glands is considered a precursor of gastric adenocarcinoma since *H. pylori* increases the risk of gastric adenocarcinoma. It was been classified as a class I oncogenic factor,[13] despite the central role of atrophic gastritis as a major risk factor for gastric carcinoma. Its diagnosis and its grading and proper assessments are done poorly or not at all in clinical practice.[14]

Because *H. pylori* infection is a necessary causative factor in the majority of cases of gastric cancer, eradication of the infection will very likely reduce the incidence of gastric cancer.[14]

The assays of serum/plasma pepsinogen I, pepsinogen II and pepsinogen I/pepsinogen II ratio in addition to gastrin 17 are easy tools for assessment of the presence or absence of atrophic gastritis even in a clinical setting whereas endoscopy is not available.

1.1. The aim of this work

To study the relation between *H. pylori* infection and atrophic gastritis in the elderly through the estimation of serum (gastrin-17 and pepsinogen-I) as novel noninvasive diagnostic biomarkers.

2. Methods

The present study included 60 individuals suffering from gastritis divided into two groups.

Group (I): Thirty patients having *H. pylori* infection aged above 65 years.

Group (II): Thirty patients without *H. pylori* infection aged above 65 years.

All patients included in the study were recruited from Main University Hospital and Fever Hospital.

2.1. Exclusion criteria

Patients with any other disease causing gastric insult were excluded from the study as were patients with diabetes mellitus, autoimmune diseases, chronic systemic infection, liver disease, chronic renal diseases and neoplastic disorders and also patients receiving drugs known to affect the gastric mucosa.

After taking a written consent from all patients, they were subjected to:

2.2. Endoscopy and biopsy sampling

Diagnostic upper gastrointestinal endoscopy was performed in all patients, two biopsies were taken from antrum to detect *H. pylori*, one for rapid urease and the other one for histopathological examination.

The biopsy specimens were immediately placed in a fixative (10% buffered formalin). The formalin fixed specimens routinely processed and embedded in paraffin blocks were serially cut and mounted on glass slides. The slides were stained with the conventional H&E stain. The prepared section was carefully examined by the light microscope and scored semi-quantitatively according to the updated Sydney classification system.[15]

2.3. Blood samples

The basal blood samples for the measurement of PGI, PGII, and gastrin 17 were obtained with the subjects in recumbent position, after an overnight fast, after venipuncture, serum and plasma sample were centrifuged and therefore kept at room temperature for 2 h. Before analysis samples were frozen at −20 °C for the latter assay of gastrin and pepsinogen.

Diagnosis of atrophic gastritis by the blood test panel in delineation of patients with different topographic types of atrophic gastritis took place ;with the blood test panel an algorithm and a computer program (Gastrosuft, Bioint Plc) were used.

Three criteria for the best discrimination of gastritis of different types were obtained from previous studies.[15,16]

2.4. Laboratory tests

2.4.1. Gastropanel test

(a) Estimation of *H.* pylori IgG by ELISA with references negative < 30, positive > 30.[17]
(b) Estimation of pepsinogen I by ELISA with reference range of 30–105 μg/l.[17]
(c) Estimation of gastrin 17 by ELISA with a reference range of 1–10 mmol.[17]

Table 1 Demographic data in the studied groups.

	H. pylori	*n*	Min	Max	Mean	SD	*t*	*P*
Age (years)	Negative	30	62	81	69.4	5.04	0.585	0.561
	Positive	30	65	78	70.1	3.69		
BMI (kg/m^2)	Negative	30	17	24	21.2	2.20	0.483	0.631
	Positive	30	17	24	20.9	2.07		

* *P* is significant if < 0.05.

Table 2 Relation between degree of gastritis and the other parameters.

	Gastritis degree	*n*	Mean	SD	*F*	*P*	LSD
Pepsinogen 1	Superficial	27	122.4	41.75	56.052	0.000*	Superficial vs others Mild vs moderate and severe
	Mild	9	66.0	22.36			
	Moderate	11	19.6	4.34			
	Severe	13	9.6	5.31			
Pepsinogen 2	Superficial	27	52.3	27.31	10.399	0.000*	Superficial and mild vs moderate and severe
	Mild	9	40.8	28.90			
	Moderate	11	18.5	17.03			
	Severe	13	13.3	14.23			
Pepsinogen 1/2 ratio	Superficial	27	3.7	3.85	3.606	0.041*	Superficial and mild vs moderate and severe
	Mild	9	3.2	3.23			
	Moderate	11	1.8	1.01			
	Severe	13	1.2	1.06			
Gastrin	Superficial	27	31.4	25.29	3.169	0.031*	Superficial and mild vs moderate and severe
	Mild	9	31.3	20.07			
	Moderate	11	15.8	11.19			
	Severe	13	15.3	5.22			
H. pylori antibody	Superficial	27	16.6	4.09	37.575	0.000*	Superficial vs others
	Mild	9	34.5	13.85			
	Moderate	11	37.4	4.84			
	Severe	13	41.4	10.60			

* *P* is significant if < 0.05.

Table 3 Relation between *H. pylori* and degree of gastritis.

	H. pylori		X2	*P*
	Negative	Positive		
Superficial	27			
	90.0%			
Mild	3	6		
	10.0%	20.0%		
Moderate		11	57.00	0.000*
		36.7%		
Severe		13		
		43.3%		
	30	30		

* *P* is significant if < 0.05.

(d) Estimation of serum pepsinogen II by ELISA with reference range of 4–9 ng/ml.[17]
(e) Estimation of pepsinogen I/II ratio by ELISA with reference range of 3–20.

2.5. Statistical methods

The Data were collected and entered into the personal computer. Statistical analysis was done using Statistical Package for Social Sciences (SPSS/version 17) software.

Arithmetic mean, standard deviation, for categorized parameters, chi-square test was used while for numerical data *t*-test was used to compare two groups while for more than two groups ANOVA test was used, least significant differences (LSD) was basically a *t*-test used only when the *F*-value is significant to detect the presence of significance between each of the two groups. The level of significance was 0.05.

3. Results

The mean age was 69.4 ± 5.04 years in *H. pylori* +ve group and 70.1 ± 3.69 years in *H. pylori* −ve group. There was no significant difference between both groups (*P* is significant if < 0.05) (Table 1).

The mean body mass index (BMI) was 21.2 ± 2.20 kg/m^2 in *H. pylori* +ve group and 20.9 ± 2.07 kg/m^2 in *H. pylori* −ve group. There was no significant difference between both groups. (*P* is significant if < 0.05) (Table 1).

The mean serum pepsinogen I was significantly lower in *H. pylori* +ve group (23.9 ± 21.84) unit compared to *H. pylori* −ve group (117.4 ± 43.47). (*P* is significant if < 0.05) (Table 2).

The mean serum pepsinogen II was significantly lower in *H. pylori* +ve group (23 ± 23.31) unit compared to *H. pylori* −ve group (48.1 ± 28.94). (*P* is significant if < 0.05) (Table 2).

The mean serum pepsinogen I/II ratio was significantly lower in *H. pylori* +ve group (1.4 ± 0.98) unit compared to

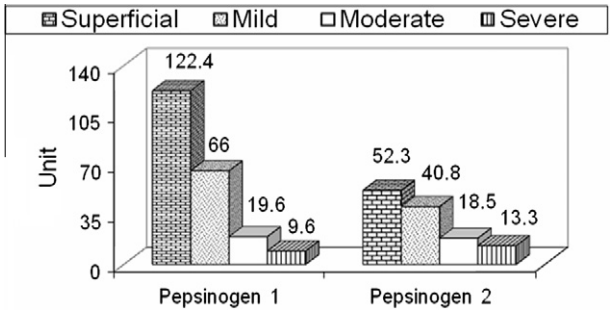

Figure 1 Relation between degree of gastritis and pepsinogen I and II.

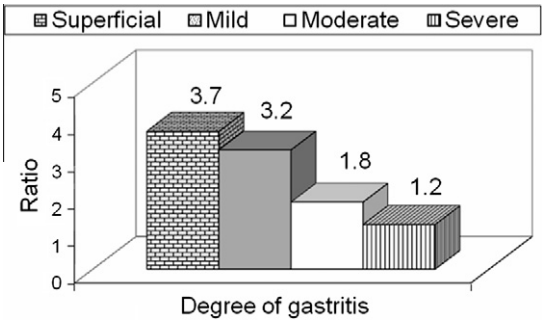

Figure 2 Relation between degree of gastritis and pepsinogen I/II ratio.

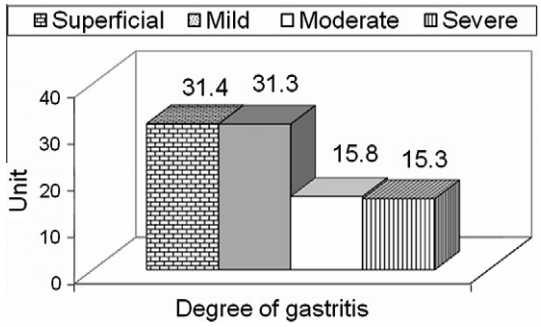

Figure 3 Relation between degree of gastritis and serum gastrin.

H. pylori −ve group (4.1 ± 3.85). (*P* is significant if <0.05) (Table 2).

The mean serum gastrin was significantly lower in *H. pylori* +ve group (32.8 ± 25.92) compared to *H. pylori* −ve group (17.3 ± 8.24). (*P* is significant if <0.05) (Table 2).

The mean serum pepsinogen I was significantly lower in mild, moderate and severe gastritis patients compared to superficial gastritis patients and it was significantly lower in moderate and severe gastritis patients compared to mild gastritis patients. (*P* is significant if <0.05) (Table 3, Fig. 1).

The mean serum pepsinogen II was significantly lower in moderate and severe gastritis compared to superficial and mild gastritis patients. The mean serum pepsinogen I/II ratio was significantly lower in moderate and severe gastritis patients compared to superficial and mild gastritis patients. (*P* is significant if <0.05) (Table 3, Figs. 1 and 2).

The mean serum gastrin was significantly lower in moderate and severe gastritis patients compared to superficial and mild gastritis patients. (*P* is significant if <0.05) (Table 3, Fig. 3).

The mean *H. pylori* antibody was significantly higher in mild, moderate and severe gastritis patients compared to superficial gastritis patients (Fig. 4).

As regards serum pepsinogen I at cut off value <97, sensitivity was 100%, specificity 81.5%, positive predictive value 86.81, negative predictive value 100% and accuracy 91.7% in detecting atrophic gastritis (Table 4).

As regards serum pepsinogen II at cut off value <52 sensitivity was 93.9%, specificity 63% positive predictive value 75.6%, negative predictive value 89.5% and accuracy 80% in detecting atrophic gastritis (Table 4).

As regards serum pepsinogen I/II ratio at cut off value <1.82 sensitivity was 66.7% specificity 66.7%, positive predictive value 71.0% negative predictive value 62.1% and accuracy 66.7% in detecting atrophic gastritis (Table 4).

As regards serum gastrin at cut off value <28 sensitivity was 90.9%m specificity 44.4% positive predictive value 66.7%, negative predictive value 80%, accuracy 70% in detecting atrophic gastritis (Table 4).

4. Discussion

The present study indicates that, in association with *H. pylori* testing, the serum level of G-17 and PGI can be used as biomarkers of gastritis and atrophic gastritis in the antrum. In the present study S.G.17 decreased with increasing grade of antral atrophy among *H. pylori* infected patient. Correspondingly S-PGI decreased with increasing grade of antral atrophy in a way that has been demonstrated in many previous studies.[18–24]

Studies by using all three blood tests (*H. pylori* antibody assay, SG17, and SPGI as panels were done and by using the gastro soft computer program to generate the diagnosis it was possible to delineate the patients with advanced atrophic gastritis with a reasonably high accuracy. The data from the present prospective study among gastritis patients were comparable with those from observational case, control study[25] and prospective Italian study,[26] these three studies suggested that the overall accuracy of the panel in the diagnosis of atrophic gastritis is approximately 80% when compared with the diagnosis from endoscopy and biopsies.

Serum PG known to be a marker for gastritis serum PG has been reported to be a marker for atrophic gastritis[27,28] and is

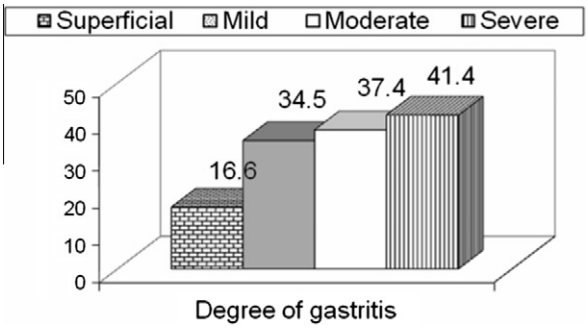

Figure 4 Relation between degree of gastritis and *H. pylori* antibody.

Table 4 Evaluation of different markers in prediction of atrophic gastritis.

	Cut off value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Serum pepsinogen 1	< 97	100.0	81.5	86.8	100.0	91.7
Serum pepsinogen 2	< 52	93.9	63.0	75.6	89.5	80.0
Serum pepsinogen 1/2 ratio	< 1.82	66.7	66.7	71.0	62.1	66.7
Serum gastrin	< 28	90.9	44.4	66.7	80.0	70.0

used for the eradication of *H. pylori*[29–31] Moreover low PG concentration defines groups at high risk of gastric cancer and adenoma[32,33] in describing the relationship between gastritis and pepsinogen concentrations, Samloff et al.[27] used the term ''serologic biopsy'' and Miki et al.[28] reported that I:II ratio was correlated with the extent of atrophic gastritis.

Diagnosis of atrophic gastritis by biopsy specimen is often unreliable and the interobserver variation is large in particular in antral biopsy. This may be due to the fact that atrophic lesions are often patchy due to the fact that atrophic lesions are often patchy and a limited number of biopsy specimens may easily result in under or over diagnosis, the existing inflammation may also bias the microscopic appearance that leads to over estimation of atrophic gastritis due to artificial impression of loss of glands. It is conceivable that the blood test panel avoids these biases.[34]

Therefore the blood test panel is not a direct test for cancer or peptic ulcer but it may reveal patients who are at risk for this disease and when endoscopy is mandatory.[34]

5. Conclusion

From the study we concluded that *H. pylori* is common in the elderly and it is the most important cause of atrophic gastritis in the elderly. Atrophic gastritis in the elderly is considered as a major risk factor for gastric carcinoma. The diagnosis of atrophic gastritis obtained with the blood test panel of SG17 SPGI, ratio and *H. pylori* antibodies is in good agreement with the endoscopic and biopsy findings.

Our study recommends that the blood test panel is a noninvasive alternative in the initial examination of patient dyspepsia. The panel helps to identify easily and nonendoscopically patients with atrophic gastritis in the antrum.

References

1. Williams GC. Pleotropy, natural selection and the evolution of senescence. *Sci Aging Knowl Environ 2001* 2001(1);13.
2. Lijima K, Ohara S, Koike T. Gastric acid secretion of normal Japanese subjects in relation to *Helicobacter pylori* infection, aging and gender. *Scand J Gastroenterol* 2004;**39**:709–16.
3. Brenner H, Arndt U, Stegmaier C. Is *Helicobacter pylori* infection a necessary condition for noncardia gastric cancer. *Am J Epidemiol* 2004;**159**:252–8.
4. Kountenras J, Zavos CH. Pyloric infection and reflex esophagitis. *Gut* 2004;**53**:912.
5. Bhala N, Newton J. Upper gastrointestinal alarms in older people. *Lancet* 2005;**366**:982–3.
6. Kountouras J, Boziki M, Gavalas E. Eradication of *Helicobacter pylori* may be beneficial in the management of Alzheimer disease. *J Neurol* 2009;**256**:758–67.
7. Pilotto A. Aging and upper gastrointestinal disorders. Best pract res chin. *Gastroenterol* 2004;**18**(Suppl.):75–81.
8. Correa P, Fox J, Fathom T, et al. *Helicobacter pylori* and gastric carcinoma. *Cancer* 1990;**60**:2569–74.
9. Forman D, Newall DG, et al. Association between infection and *Helicobacter pylori* and risk of gastric cancer evidence from investigation. *Br Med* 2003;230–4.
10. Who infection with *Helicobacter pylori* in: Schorpsanas, liver flucks and *Helicobacter pylori*. Lyon: International agency for research on cancer 1994; 61:177.241.
11. Nilt consensus conference *Helicobacter pylori* in peptic ulcer disease. J Am Med assoc 1994; 274:65–69.
12. Suzuki M, Mitura S, Semester, et al. *Helicobacter pylori* elicits gastric mucosal cell damage associated with dyplasia. *Gut* 2002;**5**:230–1.
13. Fadden DW, Valle J, Varis K, et al. Gastorduodenal disease in the elderly patient. *Sur Clin North Am* 1994;**74**:113.
14. Varis K, Sipponen P, Laxen F, Samloff IM, Huttunen JK, Talor PR, et al. Ant the Helsinki Gasritis Study Group. Implications of serum pepsinogen in early endoscopic diagnosis of gastric cancer and dysplasia. *Scand J Gastroenterol* 2000;**35**:950–6.
15. Di-Mario F, Moura AM. Serological biopsy in the first degree relative patients with gastric cancer affected by *Helicobacter pylori* infection. *Scand J Gastroenterol* 2003;**38**:1223–7.
16. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of International workshop on the histopathology of gastritis, Houston 1994. *Am J Surg Pathol* 1996;**20**(10):1161–81.
17. Broutert N, Plebani M. Pepsinogen, I pepsinogen II and gastrin as markers of atrophic gastritis in European dyspeptics. *Br J Cancer* 2003;**88**:1247–59.
18. Varis K, Samloff IM, Ihamaki T, Siurala M. An appraisal of tests for severe atrophic gastritis in relatives of pernicious anemia. *Dig Dis Sci* 2009;**24**:187–91.
19. Miki K, Ichinose M, Yahagi N, Suzuki T, Oka M, Shimizu Y, et al. Efficiency of gastric screening system using serum pepsinogen test. *Second international gastric cancer congress, Munich, Germany* 1997;**10**:27–30.
20. Broutet N, Plebani M, Sakarovitch C, Sipponen P. Pepsinogen A, Pepsinogen C and Gastrin as markers of atrophic chronic gastritis in European dyspeptics F Megraud and the Europygast Study Group. *British Journal Cancer* 2003;**88**:1239–47.
21. Korstanje A, van Eeden S, Offerhaus JA, Waltman FL, Hartog G, Roelandse FW, et al. Comparison between serology and histology in the diagnosis of advanced gastric body atrophy: a study in a Dutch primary community. *J Clin Gastroenterol.* 2008;**42**:18–22.
22. Morana E, Guida L, Cavallaro LG, Merli 2 R, Zuppardo R, Cavestro R, et al. Gastrin-17 (G-17): a serological bio-marker for diagnosis of gastroesophageal reflux disease (GERD). *Digest Liv Dis* 2008;**40**:S77.
23. Cavallaro LG, Maini A, Novenne A, Morana E, Merli R, Venerito M, et al. Serum pepsinogen II as a marker of both *Helicobacter pylori* and acetyl salicylic – acid related gastritis. *Helicobacter* 2006;**11**:395.
24. Germanà B, Di Mario F, Cavallaro LG, Moussa AM, Lecis P, Liatopoulou S, et al. Clinical usefulness of serum pepsinogens I and II, gastrin-17 and anti-*Helicobacter pylori* antibodies in the management of dyspeptic patients in primary care. *Dig Liver Dis* 2005;**37**:501–8.

25. Sipponen P, Ranta P, Helske T, Kaarainen Im Maki T, Linnala A, et al. Serum levels of amidated gastrin-17 and pepsinogen I in atrophic gastritis. An observational case-control study. *Scand J gastroenterol* 2002;**37**:785–91.
26. Nicolini G, Zagari R, Pozzato P, Lunedei V, De Lucal L, Antonini F, et al. Diagnosis of atrophic gastritis based upon a combination of three non-invasive tests: preliminary results of the lciano-Monghidoro project. *J Gastroenterol Hepatol* 2002;**17**:A264.
27. Samloff IM, Varis K, Ihamaki T, Siurala M, Rotter JI. Relationships among serum pepsinogen I, serum pepsinogen II, and gastric mucosal histology: a study in relatives of patients with pernicious anemia. *Gastroenterology* 1982;**83**:204–9.
28. Miki K, Ichinose M, Shimizu A, Huang SC, Oka H, Furihata C, et al. Serum pepsinogens as a screening test of extensive chronic gastritis. *Gastroenterol Jpn* 1987;**22**:133–41.
29. Di Mario F, Cavallaro LG, Moussa AM, Caruana P, Merli R, Maini A, et al. Usefulness of serum pepsinogens in *Helicobacter pylori* chronic gastritis: relationship with inflammation, activity, and density of the bacterium. *Dig Dis Sci* 2006;**51**:1791–5.
30. Furuta T, Kaneko E, Baba S, Arai H, Futami H. Percentage changes in serum pepsinogens are useful as indices of eradication of *Helicobacter pylori*. *Am J Gastroenterol* 1997;**92**:80–4.
31. Di Mario F, Moussa AM, Cavallaro LG, Caruana P, Merli R, Bertolini S, et al. Clinical usefulness of serum pepsinogens II in the management of *Helicobacter pylori* infection. *Digestion* 2004;**70**:167–72.
32. Hunter FM, Correa P, Fontham E, Ruiz B, Sobhan M, Samloff IM. Serum pepsinogens as markers of response to therapy for *Helicobacter pylori* gastritis. *Dig Dis Sci* 1993;**38**:2081–6.
33. Miki K, Ichinose M, Ishikawa KB, Yahagi N, Matsushima M, Kakei N, et al. Clinical application of serum pepsinogen I and II levels for mass screening to detect gastric cancer. *Jpn J Cancer Res* 1993;**10**:1086–90.
34. Kodoi A, Yoshihara M, Sumii K, Haruma K, Kajiyama G. Serum pepsinogen in screening for gastric cancer. *J Gastroenterol* 1995;**30**:452–60.