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ORIGINAL RESEARCH

Explores the Relationship Between Serum Pepsinogen Levels and Gastric Mucosal Changes in Relation to *Helicobacter pylori* Status in the Eastern Province of Sierra Leone

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Background: Pepsinogen I and pepsinogen II are widely used as diagnostic markers in gastric mucosal diseases such as gastric atrophy and pangastritis, and in assessing the risk of progression to gastric cancer. This study assesses the relationship between serum pepsinogen levels and changes in the gastric mucosa and stomach lining, stratified by *Helicobacter pylori* status. We also evaluate the significance of the serum pepsinogen ratio (PGI/PGII ratio) as a biomarker of atrophic gastritis and intestinal metaplasia that may progress to gastric cancer.

Methods: A total of 84 patients presenting with dyspeptic symptoms or indigestion were recruited for the study. The hallmark diagnostic criteria for atrophic gastritis are serum PGI < 70 ng/mL, and for pangastritis, serum PGII > 20 ng/mL. The serum *Helicobacter pylori* antibody is negative when the concentration is <30 AU/mL (no infection in the gastric mucosa) and positive when the concentration is ≥30 AU/mL (presence of infection in the gastric mucosa) using POCT immunoassay.

Results: Our findings defined the diagnosis of serum *Helicobacter pylori* infection optimal cut-off points concentration of >25 AU/mL with a sensitivity of 100% and specificity of 95%, atrophic gastritis a PGI < 73 ng/mL, with a sensitivity of 100% and specificity of 97%, and pangastritis a PGII > 18.25 ng/mL with a sensitivity of 100% and specificity of 97.8%, respectively. We defined a PGR ratio ≤ 3 As a risk of precancerous conditions, with a sensitivity of 100% and a specificity of 97.8%. We categorize patients with PGR ≤ 3 as low risk, and those patients with a PGI/PGII ratio < 2.5 (high risk) and < 1.5 (very high risk), who may be at risk of developing gastric precancerous lesions that may progress to gastric cancer.

Conclusion: A low PGI, high PGII, and a PGI/PGII ratio ≤ 3 Sensitive biomarkers to identify patients at risk of developing pangastritis and gastric precancerous lesions in the absence of endoscopic gastric mucosal biopsy.

Keywords: pepsinogen, *Helicobacter pylori*, atrophic gastritis, pangastritis, PGI/PGII ratio

Introduction

The gold standard for diagnosing gastric mucosal disease is endoscopic gastric mucosal biopsy, followed by histopathological examination of the specimens for various conditions, including gastritis, *Helicobacter pylori* infection, and gastric precancerous lesions (gastric atrophy and intestinal metaplasia)[1,2] However, the availability of trained personnel for diagnosis and endoscopic surveillance is challenging in Sub-Saharan Africa, especially in Sierra Leone. Without a golden standard for diagnosis and surveillance, serum biomarkers for pepsinogen and *Helicobacter pylori* should be explored for

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to identify who is at risk of developing gastric atrophy and intestinal metaplasia.[3,4] Most of the patients' present symptoms make it difficult for clinicians to differentiate between pangastritis, gastric atrophy, and gastric cancer. Roughly 7–45% of the general population experienced symptoms of indigestion, also called dyspepsia (belly pain and a feeling of fullness soon after you start eating, rather than a specific disease). However, it is not clear which population is at risk of developing pangastritis, GA, and gastric cancer that may warrant invasive procedures. Clinical guidelines recently reported in Asia and Europe suggest pepsinogen for the testing of non-invasive identification of individuals at higher risk of gastric cancer.[5–7] Miki et al evaluated more than 40 meta-analyses, including approximately 300,000 individuals. They suggested that a test on serum pepsinogens is not appropriate for gastric cancer screening but may be a valuable biomarker for the identification of high-risk individuals who may need further medical checks, such as endoscopic or surveillance endoscopic studies.[8]

Pepsinogen as a Marker of Gastric Mucosal Disease

Pepsinogen I (PGI) and Pepsinogen II (PGII) are inactive precursors of pepsin, a specific functional enzyme crucial for protein digestion in the stomach. PGI is principally produced by the chief cells and the gastric fundus gland (upper part of the stomach). PG II is produced by the pyloric gland in the gastric antrum (lower part of the stomach) and the duodenal gland (proximal duodenal mucosa). Acid secretion factors such as gastrin, cholecystokinin, acetylcholine, and histamine, as well as *Helicobacter pylori* infection, stimulate pepsinogen secretion. Pepsinogen I and pepsinogen II are diagnostic markers for gastric mucosal diseases, including gastric atrophy, gastritis, and gastric cancer.[4,9,10]

Helicobacter pylori Infection and Serum Pepsinogen

Helicobacter pylori infection is linked to increased serum pepsinogen levels and contributes to the development of gastric diseases such as gastritis and gastric cancer. Several studies have also reported that serum pepsinogen I and II are significantly higher in patients with *Helicobacter pylori* infection than in those without[11–13] Therefore, measuring pepsinogen levels, particularly the PGI/PGII ratio, can be a valuable tool for assessing the presence and severity of *Helicobacter pylori* infection and monitoring eradication therapy. This study aims to evaluate the three serological biomarkers (serum *Helicobacter pylori*, pepsinogen I, and pepsinogen II) for diagnosing pangastritis and gastric atrophy, and to assess their association with gastric cancer screening.

Results

General Characteristics of the Patient Groups and Descriptive Statistics of Serum Biomarkers

In our study, 84 patients were included: 49 males (58.3%) and 35 females (41.7%), with a mean age of 30.33±16.02 years (Table 1). The serum concentration ranges of all the biomarkers were determined as follows: serum *Helicobacter pylori* (5–199.9 AU/mL), serum pepsinogen I (PGI) (2.5–160 ng/mL), and pepsinogen II (PGII) (2.0–80 ng*/mL*), respectively, as shown in Table 1. The serum *Helicobacter* antibody negative and positive are defined as serum concentration of *Helicobacter* antibody less than *30 AU/mL* (negative) and greater than *30 AU/mL* (positive). Of the total 84 patients included in the study, 43 patients (25 males, 18 females) were negative with a mean range of 8.0±0.94, and 41 patients (24 males, 17 females) were positive with a mean range of 89.69±7.22, as shown in Table 1. The Mann–Whitney test showed statistical significance between the negative (<30 AU/mL) and positive (>30 AU/mL) groups, with a p-value < 0.001 (Table 1). The serum pepsinogen levels (PGI, PGII) negative and positive were defined negatively when PGI ≥ 70 ng/mL with mean range 129.8±6.03 (20 males, 15 females) and PGII < 20 ng/mL with mean range 6.4±0.79 (25 males, 21 females), positive when PGI < 70 ng/mL with mean range 24.64±3.5 (29 males, 20 females) and PGII > 20 ng/mL with mean range 50.62±3.6 (24 males, 14 females) respectively as shown in Table 1. The Mann–Whitney test revealed statistical significance between the negative (PGI ≥ 70 ng/mL, PGII < 20 ng/mL) and positive (PGI < 70 ng/mL, PGII > 20 ng/mL) groups, with a p-value of <0.001, as shown in Table 1.

Table 1: Baseline characteristics of patient groups and descriptive statistics of serum biomarkers.

Variables	Serum helicobacter pylori in AU/mL		Serum Pepsinogen I (PG I) in ng/mL)		Serum Pepsinogen II (PG II) in ng/mL	
Global						
Age (N, Mean ±SD)	84 (30.33±16.02) years		84 (30.33±16.02) years		84 (30.33±16.02) years	
Range	5-199.9AU/mL		2.5-160ng/mL		2.0-80ng/mL	
All sample summary	**Negative**	**Positive**	**Negative**	**Positive**	**Negative**	**Positive**
	<30AU/mL	≥30AU/mL	≥70ng/mL	<70ng/mL	<20ng/mL	≥20ng/mL
Range (min-max)	5.0-25.73	30.02-199.9	72.7-160	2.5-69.	2-18.8	20.3-80
Median	5.0	82.67	159.7	14.40	2.25	49.15
N, Mean ± S.E	(43),8.03±0.94	(41),89.69±7.22	(35)129.8±6.03	(49)24.64±3.5	(46) 6.4±0.79	(38)50.62±3.6
Gender						
Male (N, %)	25(29.8%)	24(28.6%)	20(23.8%)	29(34.5%)	25(29.8%)	24(28.6%)
Female ((N, %)	18 (21.42%)	17(20.23%)	15(17.9%)	20(23.8%)	21 (25%)	14(16.7%)
Mann-Whitney test						
p-value	**p<0.0001**		**p<0.0001**		**p<0.0001**	
ROC curve area						
p-value	**p<0.0001**		**p<0.0001**		**p<0.0001**	
Wilcoxon signed rank test						
p-Value	**p<0.0001**		**p<0.0001**		**p<0.0001**	

Notes: N: indicates numbers, % percentages, and p< 0.05 is considered statistically significant. Bold p-value = statistically significant.
Abbreviations: SD, standard deviation; S.E., standard error; ROC, Receiver Operating Characteristics.

Serum Diagnosis of Helicobacter pylori Infection, Atrophic Gastritis, Pangastritis, and Determination of the Best Threshold Value of Serum Biomarker Using the ROC Curve

To further validate our findings for detecting serum *Helicobacter pylori* infection and the presence of atrophic gastritis and pangastritis using all three biomarkers. The *Helicobacter pylori* antibody infection occurs when the serum concentration is less than 30 AU/mL in the gastric mucosa (<30 AU/mL, no infection), and a positive *Helicobacter pylori* infection occurs when the serum concentration is above 30 AU/mL in the gastric mucosa (>30 AU/mL, presence of infection). Of the total 84 patients in the study, 41 had *Helicobacter pylori* infection (48.88%), and 43 had no infection (51.2%), as shown in Table 1. The unpaired *t*-test reveals statistical significance between negative *Helicobacter pylori* infection and positive *Helicobacter* infection with $p < 0.0001$, as shown in Figure 1a. We also conduct an ROC analysis to determine the optimal cutoff point of the test and assess its diagnostic accuracy. We detected the serum *Helicobacter pylori* test is capable of detecting *helicobacter pylori* in the serum sample with a concentration >25 AU/mL (Area under = 1, p-value < 0.0001), the sensitivity is also 100% (91–100 confidence interval) and specificity 95% (84–99% confidence interval) with a Likelihood ratio 21.50 as shown in Figure 1a. This indicates that the test is accurate for detecting serum *Helicobacter pylori* antibody infection in the gastric mucosa, without requiring a urea breath test. For the diagnosis of atrophic gastritis (loss of gastric body/fundus function) and pangastritis (inflammation of the entire stomach lining), serum pepsinogen levels (PGI, PGII) were used. The hallmark diagnostic criterion for identifying individuals at risk of developing atrophic gastritis is

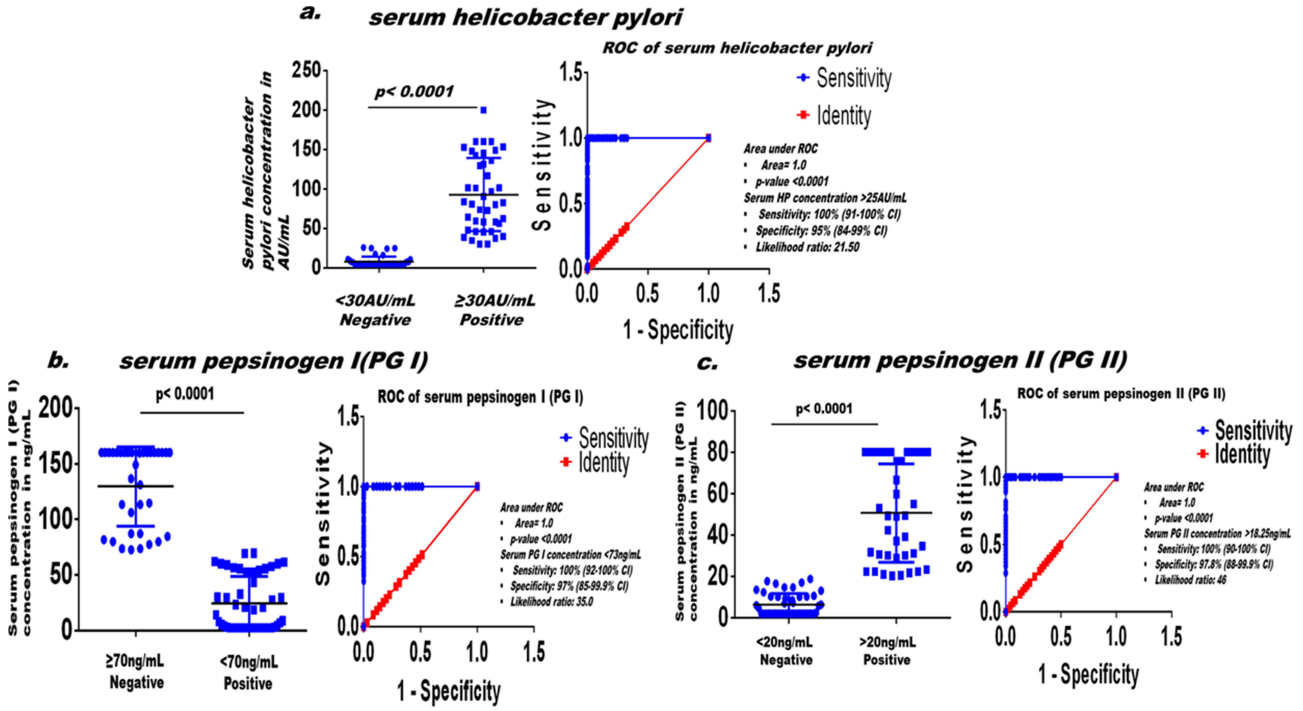

Figure 1 (**a**) The negative and positive serum *Helicobacter pylori* infection. The serum *Helicobacter pylori* test can detect *Helicobacter pylori* in serum samples at concentrations >5 AU/mL, with 100% sensitivity (91–100% confidence interval) and 67.44% specificity (51–80% confidence interval), and a likelihood ratio of 3.071. At a concentration >25 AU/mL, the sensitivity is 100% (91–100% confidence interval) and the specificity is 95% (84–99% confidence interval), with a Likelihood ratio of 21.50. (**b**) The normal (negative) and abnormal (positive) serum pepsinogen I levels. The serum pepsinogen I (PG (I) test is capable of detecting pepsinogen in the serum sample with a concentration >69.9 ng/mL with 97.96% sensitivity (89–99.9% confidence interval) and 100% specificity (90–100% confidence interval) At concentration <73 ng/mL, the sensitivity is 100% (92–100 confidence interval) and specificity 97% (85–99% confidence interval) with Likelihood ratio 35.0 (**c**) The normal (negative) abnormal (positive) serum pepsinogen II levels. The serum pepsinogen II (PG II) test can detect pepsinogen in the serum sample at concentrations >18.25 ng/mL, with 100% sensitivity (90–100% confidence interval) and 97.8% specificity (88–99.9% confidence interval), and a likelihood ratio of 46.0. At concentrations >2.25 ng/mL, sensitivity is 100% (90–100% confidence interval), and specificity is 50% (34–65% confidence interval), with a Likelihood ratio of 2.0, and $p < 0.05$ is considered statistically significant.

serum PGI < 70 ng/mL, and the diagnostic criterion for pangastritis is serum PGII > 20 ng/mL, as shown in Table 1 respectively. Of the total of 84 patients included in the study, 49 patients were at risk of atrophic gastritis (58.33%), 38 were at risk of pangastritis (45.24%% %), 35 patients had healthy fundus function (41.67%), and 46 patients lacked gastritis (54.7%), as shown in Table 1. The unpaired *t*-test shows statistical significance between atrophic gastritis, pangastritis, and healthy individuals with intact fundus and entire stomach lining, as shown in Figure 1b and c ($p < 0.0001$). Using the ROC analysis as shown in Figure 1b, serum PGI is capable of aiding in the diagnosis of atrophic gastritis <73.0 ng/mL (Area under = 1, p-value < 0.0001), the sensitivity is 100% (92–100 confidence interval) and specificity 97% (85–99% confidence interval) with a likelihood ratio 35.0. The serum PGII is capable of aiding in the diagnosis of pangastritis when the level exceeds 18.25 ng/mL (Area under the curve = 1, p-value < 0.0001), with 100% sensitivity (90–100% confidence interval) and 97.8% specificity (88–99.9% confidence interval), yielding a likelihood ratio of 46.0 as shown in Figure 1c. We also compare related disease and non-disease samples using the Wilcoxon signed-rank test for all three biomarkers, demonstrating statistical significance for all biomarkers ($p < 0.0001$), as shown in Table 1. This suggests that the three biomarkers can be used as alternative measures to aid in diagnosing gastric mucosal diseases non-invasively, where access is limited, or personnel are scarce for evaluating gastric mucosa using standard endoscopic biopsy or gastric histology.

Variables and Mean Serum Helicobacter pylori and Pepsinogen Concentrations Among Age Groups

All 84 patients enrolled were divided into three age groups: 13–33 years, 34–55 years, and >55 years, as shown in Table 2, to determine the mean concentrations by age group. The age range 13–33 years, in which 15 females (17.85%),

Table 2: Variables and mean concentration of serum helicobacter pylori and pepsinogen among age groups (mean ±SE).

Variables	**Age:13-33years**		**Age: 34-55years**		**Age :>55years**	
Gender (N = 84)						
Female (N)	15		14		6	
Male (N)	17		25		7	
Serum Helicobacter pylori status	Female	Male	Female	Male	Female	Male
Negative (<30AU/mL)						
N, Mean ±S. E	8 (10.90±3.1)	11(6.1±0.49)	6(11.21±4.21)	12(6.7±1.7)	5(11.5±4.2)	2(5.0±0.00)
min-max	5.0-25.0	5.0-9.35	5.0-30.0	5.0-25.73	5-25.0	5.0-5.0
median	5.97	5.0	5.43	5.0	5.0	5.0
Positive (≥30AU/mL)						
N, Mean ±S. E	7(107.2±21.9)	6(94.98±13.67)	8(94.21±16.	13(93.77±13.5)	1(116.8±0.00)	5(72.77±20.7)
min-max	45.7-199.9	58.43-136.4	30.04-160	37.50-160	116.8	34.65-148.9
median	80.02	93.53	83.20	101.5	116.8	59.67
Serum pepsinogen I (PG I)	Female	Male	Female	Male	Female	Male
Negative (≥70ng/mL)						
N, Mean ±S.E	4 (99.98±20.12)	5(148.7±11.3)	7(122±13.7)	9(137.5±10.38)	4(128.9±19.2)	5(142.7±17.26)
min-max	72.9-159.7	103.6-160	81.9-160	73.3-160	77.6-160	73.7-160
median	83.65	160.0	131.0	160	137.4	160
Positive (<70ng/mL)						
N, Mean ±S.E	11 (21.89±7.02)	12(15.29±6.5)	7(16.9±7.5)	16(41.8±6.2)	2(5.70±3.20)	2(32.25±29.75)
min-max	2.5-69.60	2.50-60.20	2.5-52.9	2.50-80.0	2.50-9.0	2.5-62.0
median	18.80	3.70	3.20	53.45	5.750	32.25

(*Continued*)

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Table 2: (Continued).

Variables	Age:13-33years		Age: 34-55years		Age :>55years	
Serum pepsinogen II (PG II)	Female	Male	Female	Male	Female	Male
Negative (<20ng/mL)						
N, Mean ±S.E	11 (5.48±1.7)	9(3.3±0.89)	8(5.4±1.6)	13(10.25±1.58)	2(4.5±2.5)	2(2.0±0.00)
min-max	2.0-18.80	2.8-8.8	2.0-13.5	2.0-17.70	2.0-7.0	2.0-2.0
median	2.0	2.0	3.3	10.10	4.5	2.0
Positive (>20ng/mL)						
N, Mean ±S.E	4 (41.78±12.99)	8(41.06±5.90)	6 (52.4±11.8)	12(55.66±6.8)	4(70.6±9.40)	5(36.04±11.02)
min-max	22.40-80.0	20.3-66.60	21.8-80	22.40-80.0	42.40-80	10.60-75.80
median	32.35	34.4	52.95	51.15	80.0	23.40

Abbreviations: N: number, SE.: Standard error.

17 males (20.23%), aged 34–15 years in which 14 females (16.6%), 25 males (29.7%) and aged ≥55 years in which six females (7.1%) and seven males (8.3%) respectively, as shown in Table 2. The mean concentration for negative *Helicobacter pylori* antibody (no infection) and positive *Helicobacter pylori* antibody (presence of infection) for all the age groups includes negative (<30 AU/mL, no infection): age 13–33 years: females (10.90±3.1), males (6.1±0.49), age 34–54 years; females (11.21±4.21), males (6.7±1.7) and age ≥55 years; female (11.5±4.2) and males (5.0±0.00) respectively. Positive *Helicobacter pylori* (>30 AU/mL, presence of infection): age 13–33 years: females (107.2±21.9), males (94.98±13.67), age 34–54 years; females (94.21±16.1), males (93.77±13.50), and age ≥55 years; females (116.8 ±0.00) and males (72.77±20.7) as shown in Table 2, respectively. These results suggest that *Helicobacter pylori* colonizes the human stomach lining in similar concentrations, irrespective of age. A higher risk of *Helicobacter pylori* infection damaging the stomach is associated with a family history and a diet rich in carbohydrates, following a similar pattern across all ages. This data further indicates that, if no proper dietary measures are taken, hand-washing is neglected, or access to clean water is limited, every individual is at risk of *Helicobacter pylori* infection throughout their lifespan. Serum pepsinogen levels (PGI, PGII) reflect the status of the gastric mucosa and indicate whether patients are at risk of atrophic gastritis or intestinal metaplasia, which may increase the risk of gastric cancer. Measuring serum PGI and PGII is a well-established, non-invasive approach that can be used as an alternative method for identifying the risk of gastric cancer, especially in healthcare facilities where endoscopic biopsy personnel are not available. Hence, the mean concentration of PGI and PGII in various age groups are as follows: The mean concentration for negative PGI (≥70 ng/mL, healthy gastric mucosa) positive PGI (<70 ng/mL, atrophic gastritis) for all the age groups includes: negative (≥70 ng/mL, healthy gastric mucosa): age 13–33 years: females (99.98±20.12), males (148.7±11.3), age 34–54 years; females (122±13.7), males (137.5±10.38) and age ≥55 years; female (128.9±19.2) and males (142.7±17.26) respectively. Positive (<70 ng/mL, atrophic gastritis): age 13–33 years: females (21.89±7.02), males (15.29±6.5), age 34–54 years; females (16.9±7.5), males (41.8±6.2), and age ≥55 years; females (5.70±3.20), males (32.25±29.75), as shown in Table 2, respectively. The mean concentration for negative PGII (<20 ng/mL, healthy stomach lining) and positive PGII (>20 ng/mL, pangastritis) for all the age groups includes: negative (<20 ng/mL, healthy stomach lining): age 13–33 years: females (5.48±1.7), males (3.3±0.89), age 34–54 years; females (5.4±1.6), males (10.25±1.58) and age ≥55 years; female (4.5 ±2.5) and males (2.0±0.0) respectively. Positive (>20 ng/mL, pangastritis): age 13–33 years: females (41.78±12.99), males (41.06±5.9), age 34–54 years; females (52.4±11.8), males (55.66±6.83), and age ≥ 55 years; females (70.6±9.4) and males (36.04±11.02) as shown in Table 2, respectively. These data suggest that PGI tends to vary with age due to the loss of parietal cells in the gastric mucosa, while PGII increases with age throughout the body. These data further indicate that as we age, people's risk of developing gastric atrophy varies due to environmental lifestyle and socioeconomic status, and a reciprocal increased risk of pangastritis.

Correlation Between Serum Pepsinogen Levels, PGI/PGII Ratio, and Serum Helicobacter pylori with Age

We examined PGI, PGII, PGI/PGII ratio (PGR), and serum *Helicobacter pylori*. Although PGI tends to decline with age due to loss of parietal cells in the gastric mucosa, PGI concentration varies across age groups, and there is a weak positive correlation between PGI level and age ($r = 0.03236$, $p = 0.0869$), as shown in Figure 2a. This data indicates that the loss of parietal cells in the gastric mucosa varies with age, influenced by individuals' environmental lifestyle and socioeconomic status. The concentration of PGII tends to increase with age, with $r = 0.2208$ and $p = 0.0435$, as shown in Figure 2b, although the correlation is weakly positive. This data suggests that acid production in the stomach lining tends to increase as we age. Our findings also show no correlation between the PGI/PGII ratio and serum *Helicobacter pylori* levels with age, $r = 0.051$, $p = 0.647$, and $r = 0.051$, $p = 0.644$, respectively, as shown in Figures 2c and d).

Diagnostic Value of Serum Pepsinogen Level to Discriminate Gastric Mucosa and Helicobacter pylori Status

The serum pepsinogen levels in the gastric mucosa could reflect the status of the patients, whether they have normal gastric mucosa (N), diffuse gastritis with normal mucosa (DN), diffuse gastritis with abnormal mucosa (DA), and

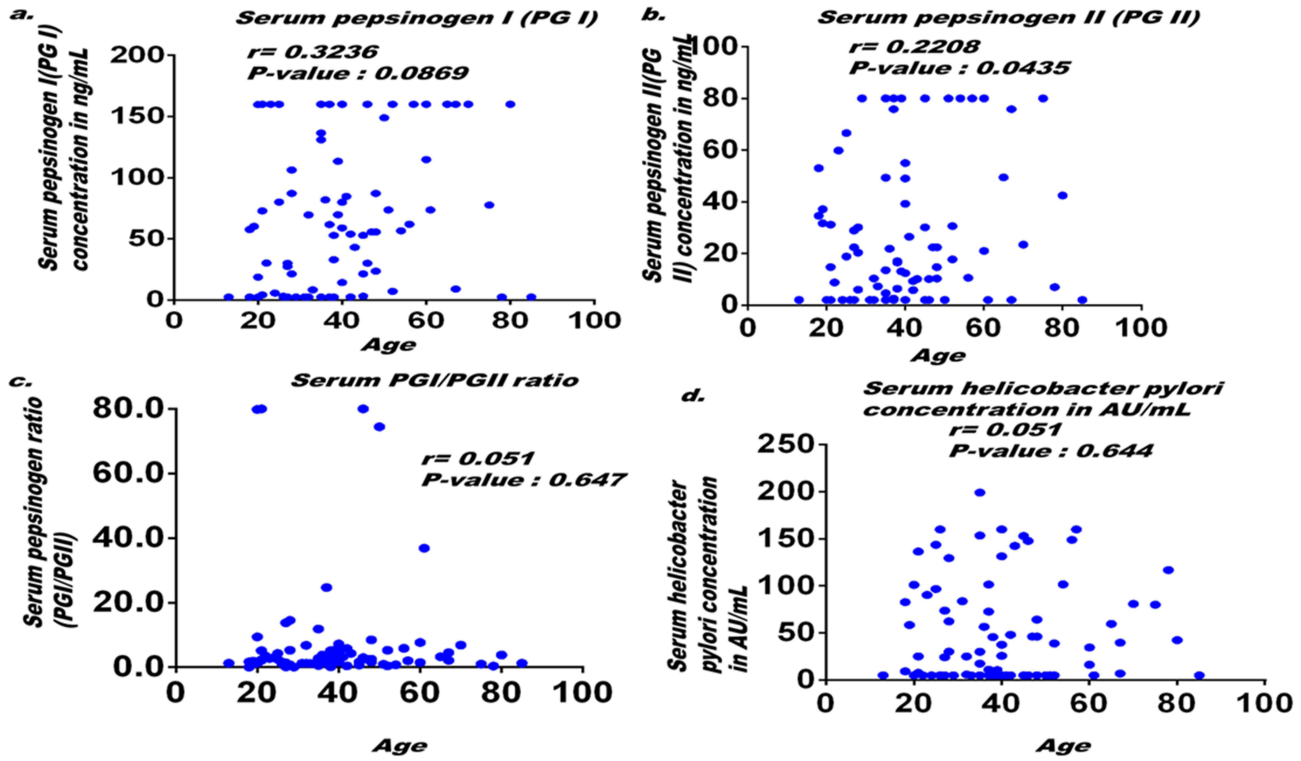

Figure 2 Correlation between serum pepsinogen level, PGI/PGII ratio, and serum *Helicobacter pylori* with age. (**a**) serum pepsinogen I (PGI) correlation with age, r = 0.3236, p = 0.0869, (**b**) serum pepsinogen II (PGII) correlation with age, r = 0.2208, p = 0.0435, (**c**). Serum PGI/PGII ratio correlation with age, r = 0.051, p = 0.647; (**d**) serum *Helicobacter pylori* concentration correlation with age, r = 0.051, p = 0.644. r: Spearman coefficient; positive weak correlation <0.4, positive moderate correlation >0.4 and <0.6 and positive strong correlation >0.6 values with age, p < 0.05 considered statistically significant, and p > 0.05 not statistically significant.

atrophic gastritis (GA), respectively. This non-invasive procedure will guide clinicians to tailor their management of patients who may present with symptoms of indigestion or epigastric pain. In this research, we developed a diagnostic criterion using the serum pepsinogen levels: normal gastric mucosa defined as follows: PGI ≥ 70 ng/mL, PGII < 20 ng/mL, diffuse gastritis with normal mucosa defined as follows: PGI ≥ 70 ng/mL, ↑ PGII > 20 ng/mL, diffuse gastritis with abnormal mucosa defined as follows: ↓PGI < 70 ng/mL, ↑ PGII > 20 ng/mL, and atrophic gastritis defined as follows: ↓PGI < 70 ng/mL, PGII < 20 ng/mL, respectively. Of the 84 patients, 10 have normal gastric mucosa; of these, five have *Helicobacter pylori* infection and five do not, as shown in Table 3. This data suggests that individuals with a negative *Helicobacter pylori* infection may experience symptoms related to reflux esophagitis, bile reflux, or drug-induced or

Table 3 Diagnostic Value of Serum Pepsinogen Level to Discriminate Gastric Mucosa and *Helicobacter pylori* Status

Variables	Number	sPGI (ng/mL)	sPGII (ng/mL)	PGI/PGII Ratio
Gender (N, *Total*)	*84*			
Male (N, *Mean ± SE*)	*49*	*73.75±8.80*	*27.43±3.75*	*7.06±2.33*
Female (N, *Mean ± SE*)	*35*	*61.04±9.70*	*25.12±4.99*	*7.82±2.99*
***Clinical outcome* (N, *Mean ± SE*)**				
Normal gastric mucosa (PGI ≥70 ng/mL, PGII < 20 ng/mL)	*10*	*119.±13.04*	*7.33±2.046*	*39.53±11.02*
Diffuse gastritis with normal mucosa (PGI ≥ 70 ng/mL ↑ PGII > 20 ng/mL)	*25*	*134.1±6.626*	*55.08±4.65*	*3.06±0.36*
Diffuse gastritis with abnormal mucosa (↓PGI < 70 ng/mL↑ PGII > 20 ng/mL)	*13*	*36.87±6.67*	*42.52 ±6.32*	*1.112±0.241*

(*Continued*)

Table 3 (Continued).

Variables	Number	sPGI (ng/mL)	sPGII (ng/mL)	PGI/PGII Ratio
Atrophic gastritis (↓PGI < 70 ng/mL, PGII < 20 ng/mL)	*36*	*20.22±3.90*	*6.11±0.86*	*3.711±0.77*
p-value		***<0.0001***	***<0.0001***	***<0.0001***
Helicobacter pylori status				
Negative (<30 AU/mL) (N, Mean ± SE)				
Normal gastric mucosa (PGI ≥ 70 ng/mL, PGII < 20 ng/mL)	*5*	*110.0±18.37*	*7.02±3.355*	*40.81±15.93*
Diffuse gastritis normal mucosa (PGI ≥ 70 ng/mL ↑ PGII > 20 ng/mL)	*9*	*122.7±11.13*	*65.86±7.139*	*2.31±0.525*
Diffuse gastritis with abnormal mucosa (↓PGI < 70 ng/mL↑ PGII > 20 ng/mL)	*5*	*19.04±11.04*	*43.78±10.38*	*0.634±0.359*
Atrophic gastritis (↓PGI < 70 ng/mL, PGII < 20 ng/mL)	*25*	*12.80±3.90*	*5.21±1.055*	*3.18±1.001*
p-value		***<0.0001***	***<0.0001***	***0.0022***
Positive (≥30 AU/mL) (N, Mean ± SE)				
Normal gastric mucosa (PGI ≥ 70 ng/mL, PGII < 20 ng/mL)	*5*	*128.0±19.69*	*7.64±2.74*	*38.24±17.09*
Diffuse gastritis normal mucosa (PGI ≥ 70 ng/mL ↑ PGII > 20 ng/mL)	*16*	*140.6±8.05*	*49.02±5.65*	*3.48±0.45*
Diffuse gastritis with abnormal mucosa (↓PGI < 70 ng/mL↑ PGII > 20 ng/mL)	*8*	*48.01±5.87*	*41.73±8.52*	*1.411±0.287*
Atrophic gastritis (↓PGI < 70 ng/mL, PGII < 20 ng/mL)	*11*	*37.07±6.85*	*8.173±1.33*	*4.90±1.05*
p-value		***<0.0001***	***<0.0001***	***0.0002***

Notes: p < 0.05 consider statistically significant. Bold p-values = statistically significant.
Abbreviations: N, number; SE, Standard error; sPGI, serum pepsinogen I; sPGII, serum pepsinogen II; ↑, increase; ↓, decrease; PGI/PGII ratio, serum pepsinogen I/serum pepsinogen II ratio.

viral/bacterial infections. In contrast, individuals with a positive *Helicobacter pylori* infection may experience indigestion. Those diagnosed with diffuse gastritis with normal mucosa of 9 are negative for *Helicobacter pylori* infection, and 16 are positive for *Helicobacter pylori* infection, as shown in Table 3. For patients diagnosed with diffuse gastritis and abnormal mucosa, five are negative for *Helicobacter pylori* infection and eight are positive, as shown in Table 3. The patient was diagnosed with atrophic gastritis; 25 cases were negative for *Helicobacter pylori* infection, while 11 cases were positive, as shown in Table 3. These data suggested that people can develop pangastritis with normal or abnormal mucosa and atrophic gastritis with or without *Helicobacter pylori* infection. We also further affirmed our findings by comparing the diagnostic criteria serum pepsinogen levels, which revealed that there was a statistically significant difference between the four parameters (N vs DN, DA & GA, $p < 0.0001$, $p < 0.0001$ and $p < 0.0001$), respectively, as shown in Figure 3a–c).

Validation of the Serum PGI/PGII Ratio for the Diagnosis of Gastric Mucosal Lesions

The validity measurement estimates calculated the serum PGI/PGII ratio (sPGR) and defined the cut-off point of sPGR ≤ 3 for diagnosing gastric mucosal lesions. As shown in Table 4, 33 patients have a sPGR > 3 which are considered as healthy gastric mucosal with a median ratio of 5.8 and 12.75 of 75% percentile and 51 patients have a sPGR ≤ 3, which are deemed to have gastric mucosal lesions with a median ratio of 1.40 and 2.1 of 75% percentile, respectively. We also further affirmed our findings by comparing serum pepsinogen ratios which revealed that there was a statistically significant as shown in Figure 4a ($p < 0.0001$). Furthermore, we validate the sPGR using the ROC curve analysis to determine the sensitivity and specificity as shown in Table 5, in which sPGR of various cut-off point were determined: sPGR < 3.05 has sensitivity of 100% (93–100% confidence interval) and specificity 96.97% (89–99% confidence interval), sPGR < 3.150 has sensitivity of 100% (93–100% confidence interval) and specificity 96.97 (84–99%

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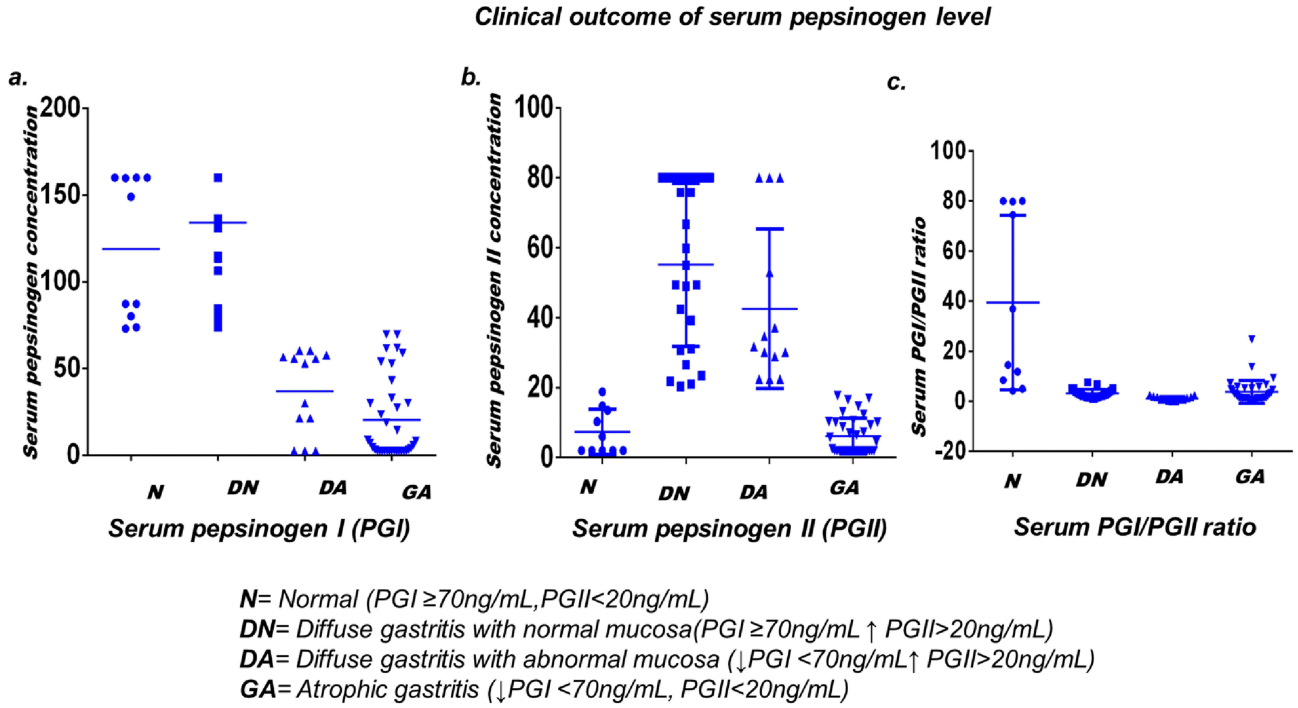

Figure 3 (**a** and **b**) The clinical outcome serum pepsinogen I and Pepsinogen II and PGI/PGII ratio with diagnostic criteria: normal gastric mucosa defined as: PGI ≥ 70 ng/mL, PGII < 20 ng/mL, diffuse gastritis with normal mucosa defined as: PGI ≥ 70 ng/mL, ↑ PGII > 20 ng/mL, diffuse gastritis with abnormal mucosa defined as: ↓PGI < 70 ng/mL, ↑ PGII > 20 ng/mL, and atrophic gastritis defined as: ↓PGI < 70 ng/mL, PGII < 20 ng/mL (**c**) The serum PGI/PGII ratio of Normal gastric mucosa (N), diffuse gastritis with normal mucosa (DN), diffuse gastritis with abnormal mucosa (DA) and atrophic gastritis (GA).

confidence interval) and likelihood of 33, sPGR < 3.3 has sensitivity of 100% (93–100% Confidence interval) and specificity 93% (79–99% confidence interval) and likelihood of 16.50, sPGR < 3.55 has sensitivity of 100% (93–100% confidence interval) and specificity 90 (75–99% confidence interval) and likelihood of 11 and sPGR < 3.850 has sensitivity of 100% (93–100% confidence interval) and specificity 87 (71–96% confidence interval) and likelihood of 8.25 respectively as shown in Table 5. Using the ROC analysis as shown in figure 4b serum PGR is capable of aiding individual's with healthy and abnormal gastric mucosa with sPGR < 3.050 (Area under = 1, p-value < 0.0001), the sensitivity is 100% (93–100 confidence interval) and specificity 97% (89–99% confidence interval). These data suggest that PGR < 3 is more sensitive and specific for differentiating healthy gastric mucosa from gastric mucosal lesions.

Serum PGI/PGII Ratio and Risk of Developing Intestinal Metaplasia That Progresses to Gastric Cancer

In this research, we further categorize our patients using the serum pepsinogen ratio (PGR) and diagnostic criteria described above to assess the risk of developing intestinal metaplasia that can progress to gastric cancer. We defined the

Table 4 Summary of Serum PGI/PGII Ratio (sPGR)

Variables	PGI/PGII Ratio > 3	PGI/PGII Ratio ≤ 3
Number (N)	*33*	*51*
Median	*5.8*	*1.40*
Mean ± S.E	*16.43±4.244*	*1.472±0.1184*
75% percentile	*12.75*	*2.1*

Abbreviations: N, number; S.E, Standard error; PGI/PGII ratio, serum pepsinogen I/serum pepsinogen II.

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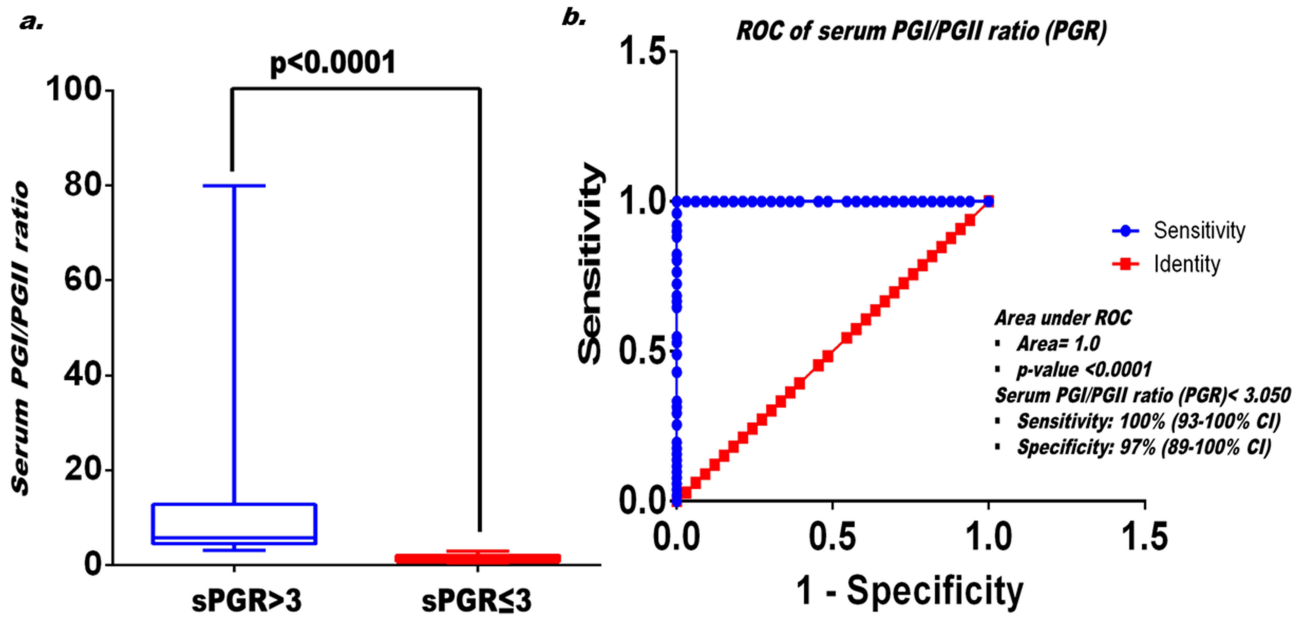

Figure 4 (**a**) The serum pepsinogen I and serum pepsinogen II ratio (sPGR) for healthy gastric mucosa (>3) and gastric mucosal lesions (≤3). (**b**) The ROC curve analysis of the PGI/PG II ratio ≤ 3: It is capable of detecting gastric mucosal lesions with 100% sensitivity (93–100% confidence interval) and 97% specificity (89–100% confidence interval), and $p < 0.05$ is considered statistically significant.

serum PGI/PGII ratio ≤ 3 As a risk of developing atrophic gastritis or intestinal metaplasia, which may warrant clinicians to perform endoscopy surveillance or endoscopy biopsy on suspected patients. We classified our patients into four categories: no risk (sPGR > 3), Low risk (sPGR < 3 and > 2.5), high risk (sPGR < 2.5 and > 1.5), and very high risk (sPGR < 1.5). Ten patients diagnosed with normal gastric mucosa without stomach inflammation do not have any risk of atrophic gastritis or intestinal metaplasia, as shown in Table 6. Twenty-five patients are diagnosed with diffuse gastritis with normal mucosa, 10 of which have no-risk (sPGR > 3) of atrophic gastritis/intestinal metaplasia, three are low-risk (sPGR ≤ 3) that may be recommended for endoscopy, seven are high-risk (sPGR < 2.5) that need endoscopy surveillance and biopsy, and 5 are very-high-risk (sPGR < 1.5) that need urgent endoscopy and biopsy, as shown in Table 6. Thirteen patients were diagnosed with diffuse gastritis with abnormal mucosa, 5 of whom have a high risk (sPGR < 2.5) of atrophic gastritis/intestinal metaplasia that need endoscopy surveillance and biopsy, and 8 are very high risk (sPGR < 1.5) that need urgent endoscopy and biopsy, as shown in Table 6. Thirty-six patients were diagnosed of atrophic gastritis; 14 of which have no risk (sPGR > 3) of intestinal metaplasia, 2 are low risk (sPGR ≤ 3) that may be recommended endoscopy, 6 are high risk (sPGR < 2.5) that needs endoscopy surveillance and biopsy and 14 are very high risk (sPGR < 1.5) that need urgent endoscopy and biopsy as shown in table 6. We further validate our findings using one-way ANOVA and Dunnett's multiple comparison test, with patients having normal gastric mucosa and intact stomach lining serving as

Table 5 Validity Estimates of Serum PGI/PGII Ratio (PGR)

PGI/PGII Ratio	Sensitivity	95% CI	Specificity	95% CI	Likelihood Ratio
<3.050	100.0	93.02% to 100.0%	100.0	89.42% to 100.0%	
<3.150	100.0	93.02% to 100.0%	96.97	84.24% to 99.92%	33.00
<3.300	100.0	93.02% to 100.0%	93.94	79.77% to 99.26%	16.50
<3.550	100.0	93.02% to 100.0%	90.91	75.67% to 98.08%	11.00
<3.850	100.0	93.02% to 100.0%	87.88	71.80% to 96.60%	8.250

Abbreviations: PGI/PGII ratio, serum pepsinogen I/serum pepsinogen II; 95% CI, 95% Confidence interval.

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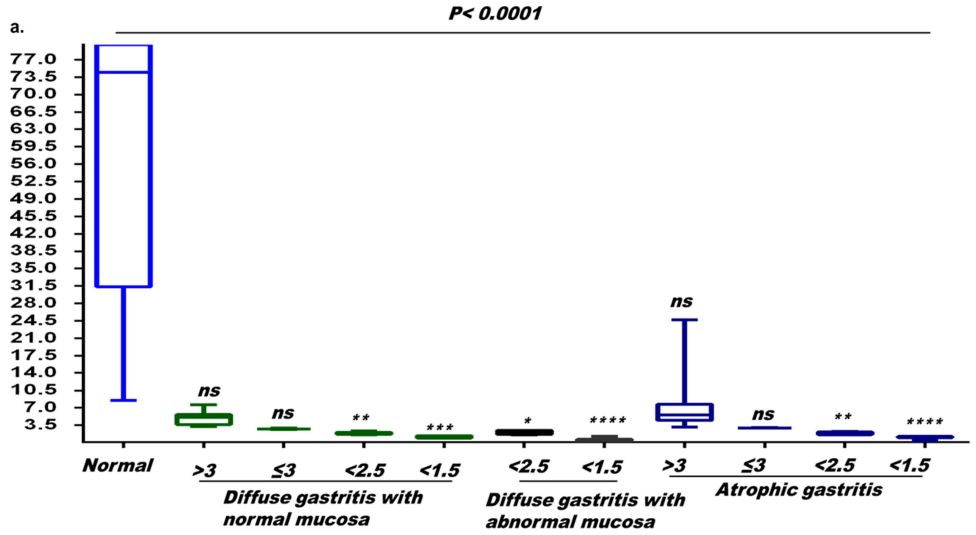

Figure 5 (**a**) Serum PGI/PGII ratio (PGR) of gastric mucosal lesions and risk of diffuse gastritis with normal or abnormal mucosa and atrophic gastritis: The patient is classified into four categories: no risk (PGR > 3), Low risk (PGR ≤ 3 and > 2.5), high risk (PGR < 2.5 and > 1.5), and very high risk (PGR < 1.5). $p < 0.05$ is considered statistically significant, and ns: no statistically significant. The healthy gastric mucosa PGR is used as the control. *$p < 0.05$, **$p < 0.01$, ***$P < 0.001$, and ****$P < 0.0001$.

the control against other clinical outcomes as shown in Figure 5a. For patients with diffuse gastritis and normal mucosa, those with high-risk and very high-risk sPGR showed statistically significant differences ($p < 0.01$ and $p < 0.001$, respectively). In contrast, patients with no risk and low risk showed no statistically significant difference, as shown in Figure 5a. The patient with diffuse gastritis and abnormal mucosa, characterized by only high-risk and very high-risk PGR, showed statistically significant differences ($p < 0.05$, $p < 0.0001$), as illustrated in Figure 5a. For patients with atrophic gastritis, high- and very-high-risk PGR were statistically significant ($p < 0.01$ and $p < 0.001$, respectively). In contrast, no-risk and low-risk patients showed no statistically significant difference, as shown in Figure 5a. These data indicated that only high-risk and very high-risk patients need endoscopy and biopsy.

Combination of Serum PGI/PGII Ratio and Serum Helicobacter pylori Status Risk for Developing Intestinal Metaplasia That Progresses to Gastric Cancer

We evaluate the use of PGI/PGII ratio (PGR) and serum *Helicobacter pylori* status to assess the patients who are at risk of developing atrophic gastritis and intestinal metaplasia, which may progress to gastric cancer. The patients who are negative for *Helicobacter pylori* infection (N = 44) are categorized as follows: 4.55% are low-risk (sPGR < 3), 11.36%

Table 6 Serum PGI/PGII Ratio Cutoff Value and Grading Risk That Progresses to Gastric Cancer

PGI/PGII Ratio Cutoff Value and Grading	**Number**	**>3 No Risk**	**≤3 Low Risk**	**<2.5 High Risk**	**<1.5 Very High Risk**
***Clinical outcome* (N, *Mean* ± *S.E*)**					
Normal gastric mucosa (PGI ≥ 70 ng/mL, PGII < 20 ng/mL)	*10*	*10 (56.56±9.2)*	*0*	*0*	*0*
Diffuse gastritis with normal mucosa (PGI ≥ 70 ng/mL ↑ PGII > 20 ng/mL)	*25*	*10(4.95±0.46)*	*3(2.78±0.06)*	*7(1.98±0.1)*	*5(1.22±0.12)*
Diffuse gastritis with abnormal mucosa (↓PGI < 70 ng/mL↑ PGII > 20 ng/mL)	*13*	*0*	*0*	*5(2.03±0.19)*	*8(0.53±0.160)*
Atrophic gastritis (↓PGI < 70 ng/mL, PGII < 20 ng/mL)	*36*	*14(7.14±1.5)*	*2(2.95±0.5)*	*6(1.88±0.13)*	*14(1.072±0.09)*

Abbreviations: PGI/PGII ratio, serum pepsinogen I/serum pepsinogen II; N, number; S.E, Standard error; PGI, serum pepsinogen I; PGII, serum pepsinogen II; ↑, increase; ↓, decrease.

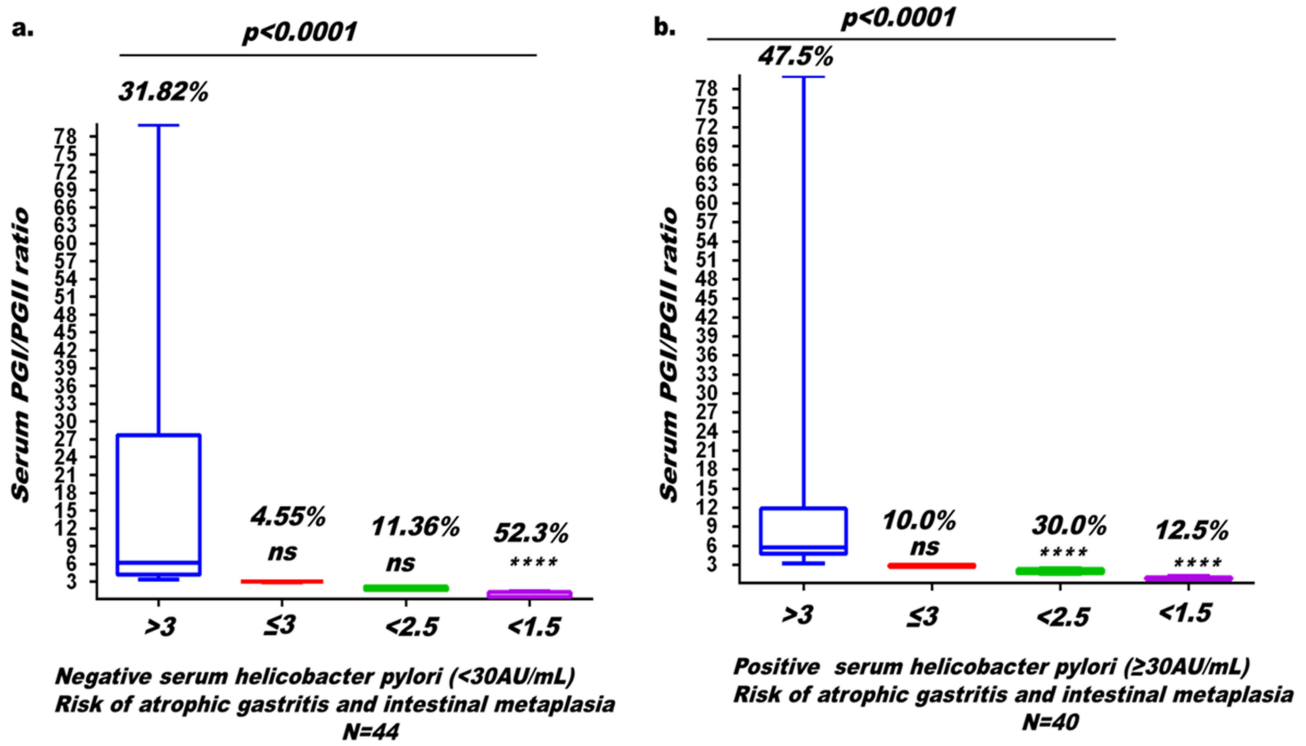

Figure 6 Combination of serum PGI/PGII ratio and serum *Helicobacter pylori* status risk for developing atrophic gastritis and intestinal metaplasia that progresses to gastric cancer: (**a**) Negative serum *Helicobacter pylori* (<30 AU/mL), N = 44; (**b**) Positive serum *Helicobacter pylori* (≥30 AU/mL), N = 40. The patient is classified into four categories: no risk (PGR > 3), Low risk (PGR ≤ 3 and > 2.5), high risk (PGR < 2.5 and > 1.5), and very high risk (PGR < 1.5). $p < 0.05$ considered statistically significant, and ns: not statistically significant. (N) number of patients ****$p < 0.0001$.

are high-risk (sPGR < 2.5), and 52.3% are very high-risk (sPGR < 1.5), as shown in Figure 6a. These data suggested that patients without *Helicobacter pylori* infections are also at risk of developing atrophic gastritis and intestinal metaplasia that may progress to gastric cancer. When we combined the above criteria with negative *Helicobacter pylori* infection, using one-way ANOVA and Dunnett's multiple comparison test, we found that patients with sPGR < 1.5 ($p < 0.001$) who are negative for *Helicobacter pylori* infection require endoscopy and biopsy. Of those patients with *Helicobacter pylori* infection (N = 40), 10.0% of those are low-risk with (PGR < 3), 30.0% are high-risk (PGR < 2.5), and 12.5% were very high-risk (PGR < 1.5) as shown in Figure 6b. These data suggested that patients with the presence of *Helicobacter pylori* infections may have a double risk of developing atrophic gastritis and intestinal metaplasia that may progress to gastric cancer. When we combined the above criteria and positive *Helicobacter pylori* infection using one-way ANOVA and Dunnett's multiple comparisons using sPGR ratio >3 as usual compared to other sPGR, we found out that patients positive for *Helicobacter pylori* infection with PGR < 2.5 and < 1.5 ($p < 0.001$ and $p < 0.001$) need endoscopy and biopsy, respectively, as shown in Figure 6b.

Discussion

Gastric cancer and atrophic gastritis are screened and diagnosed principally by endoscopy and biopsy. However, due to cost-effectiveness and discomfort, several non-invasive tests have recently been reported as reliable tools for the diagnosis of the presence of atrophic gastritis and gastritis at the site of the gastric mucosa and risk of intestinal metaplasia that may progress to gastric cancer.[9,11,14] As the severity of atrophic gastritis and pangastritis increases due to excessive acid secretion or *Helicobacter pylori* infection, the function of the gastric mucosa is compromised, and pepsin production is affected. Therefore, measuring serum pepsinogen levels (PGI, PGII) and *Helicobacter pylori* status are useful markers for assessing gastric mucosal status.

Low levels of serum pepsinogen I (sPGI) and a low PGI/PGII ratio (sPGR) are associated with severe atrophic gastritis and intestinal metaplasia that may increase the risk of gastric cancer.[4,13] In addition, severe atrophic gastritis may

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affect the gastric mucosa acidity, intrinsic factor, and ascorbic acid level, which are essential for dietary vitamin B12 and iron absorption, respectively. Severe atrophic gastritis and pangastritis are associated with decreased intrinsic factor secretion, which, in turn, impairs vitamin B12 absorption, leading to pernicious anemia 15,16. Although various cut-off values have been reported for atrophic gastritis, pangastritis and *Helicobacter pylori* infection, a serum pepsinogen I (PGI) level ≤70 ng/mL, serum pepsinogen II level for pangastritis >10.0 ng/mL and serum *Helicobacter pylori* antibody infection level ≥34 AU/mL with sensitivity ranging from 73.2 −84.6 and a specificity of 70% to 97.9%, respectively,[8,15,16] in this study, we discovered that the definition of serum *Helicobacter pylori* antibody infection with a concentration >25 AU/mL with a sensitivity of 100% (91–100 confidence interval) and specificity of 95% (84–99% confidence interval) with Likelihood ratio 21.50, the serum pepsinogen I (PG I) for atrophic gastritis) at concentration <73 ng/mL, the sensitivity is 100% (92–100 confidence interval) and specificity 97% (85–99% confidence interval) with Likelihood ratio 35.0 and the serum pepsinogen II (PG II) for pangastritis at a concentration >18.25 ng/mL with 100% sensitivity (90–100% confidence interval) and 97.8% specificity (88–99.9% confidence interval) with a likelihood ratio of 46.0, respectively. These findings correspond with several clinical studies reported.[17–19]

The serum pepsinogen levels (PGI, PGII) correlate positively with age, despite a low coefficient, as noted in previous studies. Additionally, we investigated the relationship between serum pepsinogen levels and *Helicobacter pylori* antibodies with age. Our data show a positive correlation between serum pepsinogen levels and age, with a low coefficient, and no correlation between *Helicobacter pylori* antibodies and age. These findings are consistent with previous studies reported.[20–22]

Our analysis of serum pepsinogen levels was used to assess the status of the gastric mucosa and the risk of inflammation in the stomach lining. We developed the following criteria to differentiate healthy gastric mucosa, pangastritis, and atrophic gastritis, respectively: normal gastric mucosa defined as PGI ≥ 70 ng/mL, PGII < 20 ng/mL, diffuse gastritis with normal mucosa defined as PGI ≥ 70 ng/mL, ↑ PGII > 20 ng/mL, diffuse gastritis with abnormal mucosa defined as ↓PGI < 70 ng/mL, ↑ PGII > 20 ng/mL, and atrophic gastritis defined as ↓PGI < 70 ng/mL, PGII < 20 ng/mL. Our findings show that pangastritis, with intact, inflamed, and atrophic gastric mucosa, can develop without *Helicobacter pylori* infection. Furthermore, we use the above criteria to assess serum *Helicobacter pylori* antibody status.

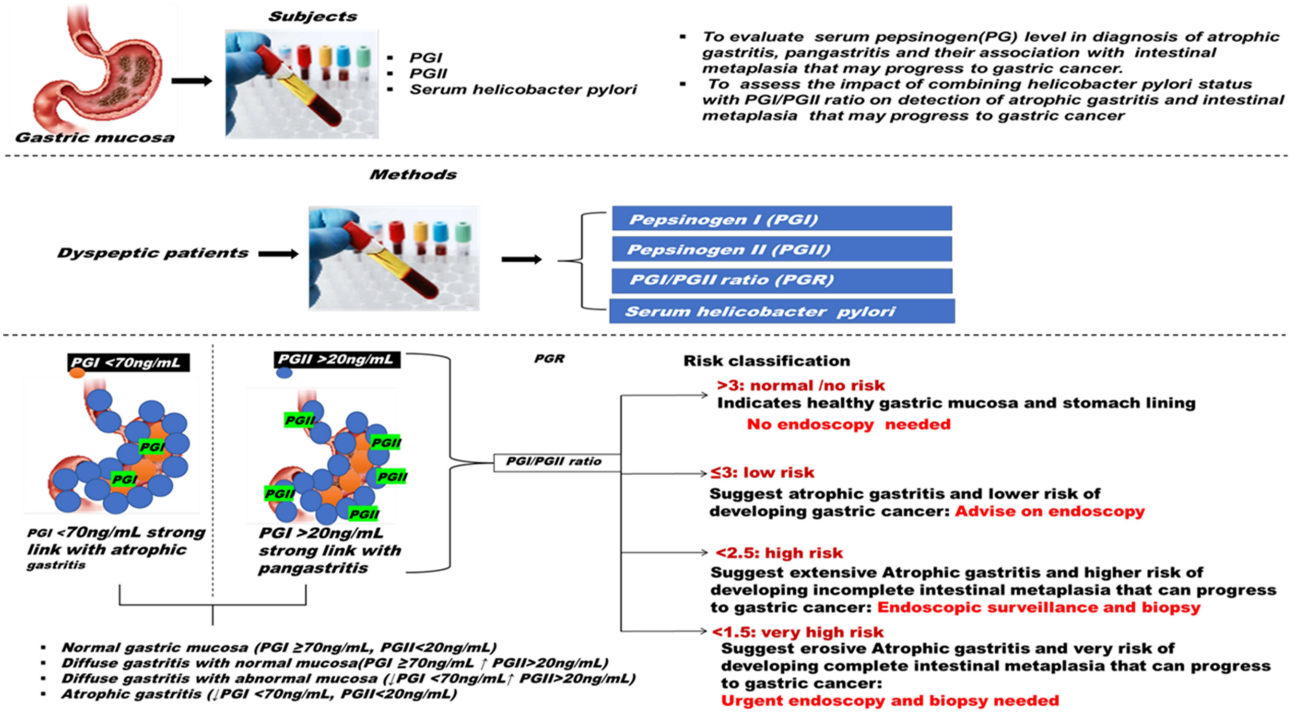

Figure 7 Summarized the evaluation of serum pepsinogen levels (PGI, PGII) and serum *Helicobacter pylori* status blood markers, serum PGI/PGII ratio risk classifications for endoscopic gastric mucosa status for screening atrophic gastritis and intestinal metaplasia that may progress to gastric cancer.

Our findings confirmed that higher serum pepsinogen levels may result from *Helicobacter pylori* infection-induced inflammation in the gastric mucosa, consistent with findings reported in similar studies.[11,12,23]

In meta-analyses by Miki et al, more than 40 studies were included, with approximately 300,000 individuals. They suggested that a test of the serum pepsinogen ratio (PGR) is not appropriate for gastric cancer screening, but may be a valuable biomarker for identifying high-risk individuals who may need further medical checks, such as endoscopic or surveillance endoscopic studies.[8,10] The recommended cut-off points of the PGI/PGII ratio (PGR) ≤ 3 And it has the highest diagnostic performance for atrophic gastritis (reversible state) and intestinal metaplasia, with minimal chance of returning to normal 4,8,13. In this research, we defined the PGI/PGII ratio ≤ 3, the risk of developing atrophic gastritis or intestinal metaplasia may warrant clinicians performing endoscopy surveillance or biopsy of suspected patients. We classified our patients into four categories: no risk (PGR > 3), Low risk (PGR ≤ 3 and > 2.5), high risk (PGR < 2.5 and > 1.5), and very high risk (PGR < 1.5), respectively. Those with low-risk PGR are considered to have reversible atrophic gastritis with minimal risk of intestinal metaplasia that does not warrant endoscopic surveillance. Those with PGR < 2.5 and 1.5 are labelled as high risk and very high risk of irreversible atrophic gastritis and intestinal metaplasia that may progress to gastric cancer and require endoscopy and biopsy for prevention of gastric cancer, respectively as illustrated in Figure 7, and correspond to other similar studies as reported. Also, we examined the PGR with the serum *Helicobacter pylori* status, and results prove that patients with negative *Helicobacter pylori* antibodies, only those with PGR < 1.5, should be considered for early gastric cancer screening using endoscopic surveillance, compared to positive *Helicobacter pylori* antibody with PGR < 2.5 and < 1.5, respectively.

Conclusion

This study concluded that the diagnosis of serum *Helicobacter pylori* antibody infection, atrophic gastritis, PGI < 73 ng/mL, and pangastritis, PGII > 18.25 ng/mL, respectively. The PGI/PGII ratio (PGR) should be used as a guide to identify patients at risk of developing atrophic gastritis and intestinal metaplasia that may progress to gastric cancer, especially in developing nations where there is a lack of experienced personnel for endoscopic biopsy of the gastric mucosa. Those with high-risk PGR < 2.5 and very high risk with PGR 1.5 should be referred to an endoscopic gastroenterologist for early gastric cancer screening with endoscopy and biopsy.

Population and Methods

Study Population

This was a cross-sectional of study of symptomatic population of indigestion or bloating living in the Eastern region of Sierra Leone between January 2024 and March 2025. Inclusion criteria are symptomatic patient with indigestion with no treatment of histamine receptor blockers/proton pump inhibitors (PPIs)/antacids and antibiotics/bismuth-containing medication. Those with dyspeptic symptoms/indigestion on treatment with proton pump inhibitors (PPIs)/histamine receptor blockers/antacids, and antibiotics or bismuth-containing medication were excluded from the study. This research was conducted at Expresscare Medical Clinic, Kenema, Eastern Province, Sierra Leone. Finally 84 patients that met the inclusion criteria were included in study. Although no age restrictions were imposed in the study and sample were predominantly composed of middle-age and elderly patient. Patient-informed consent and demographic characteristics include age, sex, socioeconomic status, and educational level.

Sample Collection

Overnight fasting venous blood samples were collected from the subject to measure serum pepsinogen I, serum pepsinogen II, and serum *Helicobacter pylori* antibody. Two millilitres (2 mL) of venous whole blood were collected in three different non-anticoagulant tubes (no additives) from other sites for each patient, purchased from Jiangsu Yuli Medical Instrument, China, and incubated at room temperature for 30 minutes. After 30 minutes of incubation, the venous blood was centrifuged at 10,000 g for 10 minutes at room temperature. The centrifuge was purchased from Shenzhen Vegas Biotech Co., Ltd, China. The supernatant was transferred to three clean tubes and re-centrifuged for 2 minutes in a microcentrifuge purchased from Akmlab Scientific Zhejiang Co., Ltd, China, to remove any residual

material. The three samples collected from each patient were assessed for hemolysis and lipidemia to ensure accurate testing. The hemolyzed and lipidemic samples were discarded, and then the non-hemolyzed and non-lipidemic samples were tested immediately without storage. The serum *Helicobacter pylori* and pepsinogen levels were used according to the manufacturer's cut-off point. The pepsinogen I/Pepsinogen II ratio cut-off point was adopted from Miki et al.[8] The serum *Helicobacter pylori* and pepsinogen I and II were purchased from Hipro-Biotechnology Co., Ltd, China, using their POCT Immunoassay Hurricane machine (HP-083/4 Hurricane: Model: HPO83-II).

Assessment of Serum Pepsinogen and Helicobacter pylori Antibody

The serum concentration of *Helicobacter pylor*i in the sample was determined using a POCT Immunoassay Hurricane machine (HP-083/4 Hurricane: Model: HPO83-II) following the manufacturer's instructions. The serum *H. pylori* antibody concentration: negative <30 AU/mL (no infection) and positive >30 AU/mL. A positive result highly indicates the gastritis associated with *Helicobacter pylori* infection. Low serum pepsinogen I indicates atrophic gastritis, and high pepsinogen II indicates pangastritis. The ratio of Pepsinogen I/ Pepsinogen II ratio (PGR) <3 It is associated with an increased risk of atrophic gastritis and gastric cancer.

Limitation of the Study

The serum pepsinogen levels and *Helicobacter pylori* level are useful biomarker for screening gastric atrophy and evaluating gastric cancer risk in areas where upper gastrointestinal endoscopy is absent or where lack of personnel for upper GI endoscopy. The serum pepsinogen levels are suitable for risk stratification and not golden standard for gastric mucosal diseases. The cohort is study was avoided due to hard control of unknown external factors such as lost of follow-up or changing habit of patient or pass away over the long period as result of poor socio-economic status. Also this study often span over years making it vulnerable to bias results.

Statistical Analysis

Statistical analysis was done using GraphPad Prism version 6. The data is expressed in mean ±standard error, except otherwise stated. A two-sided significance level of $p < 0.05$ was considered statistically significant for all tests. Group compares concerning serum values of *H. pylori*, PGI and PG II, as well as the PG-ratio have been performed by Mann–Whitney *U*-test, Receiver Operating Characteristic (ROC) curve to plot actual positive rate (sensitivity) against a false positive rate (1 – specificity) at different threshold value to assess the diagnostic performance of the test cut-off value including the area under the curve following the standard guidelines[24] and Wilcoxon rank test was used to determine the difference in the distribution of concentration. A student unpaired *t*-test was used to compare the difference between negative and positive serum concentrations of PGI, PGII, and *Helicobacter pylori*. We calculated Spearman's rank correlations between serum concentrations of PGI, PGII, and *Helicobacter pylori*, and applied the Kruskal–Wallis test to the nonparametric data. Univariate ANOVA was used to analyze interference, followed by Dunnett's *t*-test to compare the means of multiple positive groups against the negative group.

Abbreviations

GA, atrophic gastritis or gastric atrophy; PGR, serum pepsinogen I/serum pepsinogen II ratio; AU/Ml, arbitrary concentration units; ng/mL, nanograms per millilitre.

Data Sharing Statement

The generated data are included in the manuscripts, and the raw data are available on request from the corresponding author.

Ethical Declaration

This research was approved by the Institutional Review Board of the Eastern Technical University (ETUSL-IRB), and written ethical approval was obtained from the Committee of the Expresscare Medical Clinic (CEMC) in accordance with the relevant guidelines of the Helsinki Declaration (Research number not available). Written informed consents

were obtained from all participants, and those under 18 years of age had their written permission obtained from their parents or guardians. If participants were illiterate, the study and consent forms were explained verbally in local languages, and an informed consent form was obtained from the legal guardian, who provided their fingerprint, as approved by the Institutional Review Board of Eastern Technical University, Sierra Leone. Participants who refused to participate were excluded from the study, but this exclusion does not affect their management. The rights, safety, and dignity of all participants were respected.

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Author Contributions

All authors took part in the drafting, critical review of the article, data collection, editing, formal analysis and final approval of the revised version of the paper before submission for publication. All authors made a significant contribution to the work reported. Whether in the study in the design, execution of the work, conception, acquisition of data, analysis and interpretation of results. Every author took part is drafting, revising the article and agreed which journal the manuscript is submitted.

Smith AO writing the original draft, data analysis, software and interpretation of the data.

Smalle IO Writing-review, software, editing and validation.

Rhoda AM conceptualization, validation and projection administration.

Jones AF data curation, formal analysis, writing-review and editing.

Mbaimba Koroma date curation, correlation of results, software and formal analysis.

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Disclosure

The authors declared no conflict of interest.

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