Original Article

The role of pepsinogen test among the patients with gastric cancer

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Summary:

Background: Identification the relationship of pepsinogen test (pepsinogenI and I /pepsinogen II ratio) and gastric cancer patients make the gastric cancer early diagnosed and prolong the life surviving rate.

Patients and Methods: Serum pepsinogen I and pepsinogen II (PG I and PG I / PG II ratio) measured in 50 patients with gastric cancer ,30 gastritis patients diagnosed , and 16 healthy control by using enzyme immunoassay in those study groups, and the results of PG I and PG I / PG II ratio were comparing to 50 gastric cancer patients whom diagnosed histopathologically according the stomach regions, while the gastritis patients diagnosed endoscopically.

Results: This study showed that the age of patients with gastric carcinoma range between 25 and 80 years with mean age of 47.5 in females and 66.5 years in males(P=0.004). Immunologically, this study revealed that the serum pepsinogen I level was reduced less than 70nmg/dl and it was detected in 37(74%, P=0.008), 17(56.6%) and 5(31.2) in gastric carcinomatose patients, gastritis patients and healthy control respectively. While PG I /PG II ratio was found < 3 in 34(68%, P=0.007) of the stomach cancer patients, 15(50%) in patients control and 4(25%) in healthy control. In this study there is a high prevalence of positive result of PGI (89.1%, P=0.00 highly significant) in corpus-fundus region of stomach as compared to PGI/PGII ratio(44.12%, P=0.493).This study showed that the PGI is more sensitive (74%),and more accuracy (72.72%)than PG I /PG II ratio,while it is more specific (75%) than PGI.

Conclusion: Pepsinogen I and pepsinogen II (PGI and PG I / PG II ratio) are useful as non-invasive method for diagnosis of the precancerous diseases in the stomach, and it is sensitive and specific test, but it did not precisely reflect disease dissemination and pathological type. Gastric cancer was significantly high in age group 45-65 years.

Key Word: Carcioma of stomach, pepsinogen .

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Introduction:

Carcinoma of the stomach is the fourth most common cancer in the world and the second cause of death from neoplasm. Most stomach cancers start in the mucosa, cancers beginning in different site may produce different symptoms and tend to have different outcome. The location can also affect some of the treatment options that is available(1).In general, malignant gastric neoplasm is a disease of elderly, the male to female ratio is about 2:1 but when it effect younger patients the male to female ratio is close to one, and there is a high preponderance of blood type (A)(2,3) Gastric carcinoma is a multifactorial disease, different studies revealed a correlation between the incidence of malignant gastric neoplasm in various population and the prevalence of Helicobacter pylori infection ,environmental factors (such as N-nitroso)(4), genetic factor, partial gastrectomy for benign disease(5),premalignant disease of stomach (as atrophic gastritis, verrucous gastritis) and the family history of stomach cancer specially first degree relation who have had gastric cancer are more likely to develop this disease(6,7). The distribution of gastric cancer within the stomach is39% in the proximal third, 17% in the middle third, 32% in the distal third and 12% involving the entire stomach (8,9). From functional point of view, the stomach can be divided schematically three region cardiac, corpus-funds (oxyntic)and antrum-pylorus (pyloric)(10).

In the beginning of the 1980s, American gastroenterologist M.Samloff proposed a serological determination of pepsinogen (the proenzyme of pepsins) as a simple and non-invasive method for evaluation gastric peptic secretion(11).The correlation between the level of serum pepsinogen and the severity of gastric mucosa lesion, confirmed histologically, induced Samaloff to consider serum pepsinogen as a" serological biopsy" Pepsinogen, produced by stomach, can be divided into two groups according to their immunological properties :pepsinogen I (PGI or PGA)and pepsinogen II (PG II or PGC) (12).Pepsinogen I is secreted exclusively in the fundus and corpus region (normal value more than 70 ng/dl) while pepsinogen II is secreted in all reigns of the stomach , thus the elevation of level of both PG I , PG II , and the PG I /PG II ratio (normal ratio more than 3)can provide important information on

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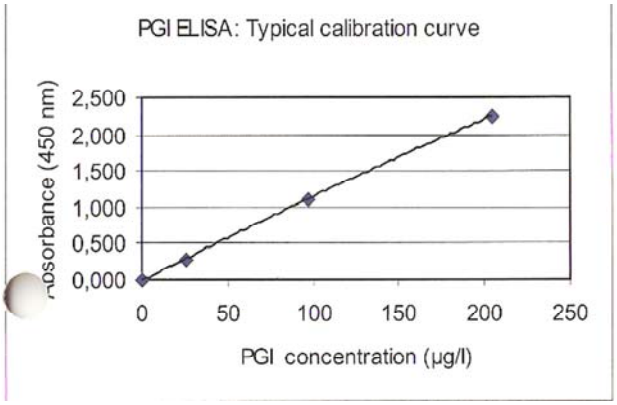
the histological and functional "status "of gastric mucosa.(10), especially its low leveling concentration and ratio which has been reported in patients with atrophic gastritis and intestinal metaplasia (3). Human pepsingen originating from stomach mucousa are immunchemically classified into distinct group pepsinogen1 or (pepsinogen A) and pepsinogen II or (pepsinogenC) according to Dr.Samloffs in 1971, they are secreted into gastric lumen and their small portion into blood circulation which reflect to us condition of the stomach mucousa. However, it has been found that reduced level of PG1<70 mg/L (70 nmg<dl) and PG I /PG II ratio <3 are recommended for endoscopical and histological examination to look for a tumor in the stomach (3, 12).

Material and Methods:

A cross section study was conducted in a period between January ,till the end of June 2005. The patients were individual attending the ward of Baghdad teaching hospital (endoscopic department).A total of 96 individual (50 patients with gastric cancer ,30 patients with gastritis and 16 normal healthy control).The cancer of the stomach patients includes 50 patients (24 males,26 females) with an age range 25-80 years old ,while patients with gastritis include 30 patients (17 males,13 females) with an age ranged from 20 to 75 years old .For purpose of comprise , a control matched group with an age ranged from 19-70 years old , with sex of(9 males,7 females).

Blood of study groups were collected and the serum stored at -20 until used for the quantitative estimation of serum human IgG antibodies to pepsinogen I and pepsinogen II by using Enzyme Linkage Immuno-Sorbant Assay kits (ELISA technique) method (indirect type).The intensity of coloration produced was proportional to the PG I, PG II concentration in the sample or standard. The absorbance of each well was read at 450 against substrate blank and the result were calculated by interpolation from standard curve which was constructed in the same assay as the sample, then location of the average absorbance for each sample on the vertical axis was done and the corresponding PG I or PG II concentration was read on the horizontal axis . Diagram(1).

All of the 50 gastric carcinoma patients, the endoscopic biopsies of them were put in disposable sterile plain tube contain5 ml of formalin then prepare it for staining and examine under microscope, while 30 gastritis patients diagnosed endoscopically.



Diagram(1).Stander curve of immunometric enzyme immunoassay for quantitative determination of PGI and PGII in human serum.

The student t test and chi-sequar test were used to compare soluble factor level among patients and control group and to test for associations between variables. P-value of 0.05 or less was designated as a significant.

Results:

Age of patients with gastric carcinoma in this study ranged between 25-80 years with mean age of 47.5 years and 66.5 years of females and males respectively . The age group 45-54 years occupy the highest percentage 15 (30%) of the cancer patients study age group , ,beside that the incidence of gastric carcinoma in age group above 45 years had (76%) ,where as (24%) occurring in age group below 45 years with a statistically significant P value (0.004). while the age of gastritis patients was ranged between 20-74 years with mean age of 45 years for females and 47 years for males a statistically not significant P value(0.306). There were 24(48%) males and 48(52%) females of cancer patients meaning there is not considerable difference in sex of the patients study sample. Table (1)

Table (1): Age and sex distribution of cases enrolled in the study groups showed the highest percentage of gastric cancer patients in age group 45-54 years.

Age groups (years)	Gastric cancer			Gastritis			H. Control		
	NO. %	F	M	NO. %	F	M	NO. %	F	a
15-24	0 0	0	0	3 10	2	1	4 25	2	2
25-34	5 10	3	2	9 30	5	4	5 1.25	3	2
35-44	7 14	5	2	7 20.3	2	5	4 25	0	4
45-54	15 30	10	5	4 10.3	1	3	0 0	0	0
55-64	11 22	4	7	4 10.3	2	2	2 12.5	1	1
65-74	10 20	4	6	3 10	1	2	1 6.25	1	0
75-84	2 4	0	2	0 0	0	0	0 0	0	0
TOTAL	50 100%			30 00%			16 100%		
χ^2 test P-value	0.025			0.306			0.497		
Sig.	S			NS			NS		

Total= P value (0.004 HS) < 0.05

From the 50 patients of gastric cancer, pepsinogen I level was found < 70 ng/dl in 37 (74%) patients with a statistically significant P value(0.008), while from 30 gastritis patients showed 17 (56.6%) which consider as positive marker for precancerous diseases of the stomach and gastric cancer .In healthy control group the PG I was found < 70 ng/dl in 5(31.2%) out of 16 persons.

The pepsinogen I /pepsinogen II ratio was found less than 3.0 in gastric cancer patients, gastritis patients and healthy control as 34(68%), 15(32%), and4 (25%) respectively with a statistically significant P value(0.007) , so this detection consider a significant result for stomach cancer . Table (2).

Table (2): The comparison of PGI concentration & PGI /PGII ratio in patients with Ca. stomach, gastritis and healthy control.

Study groups		PGI *				PG I/ PGII ratio**			
		Positive (<70 ng/dl)		Negative (>70 ng/dl)		Positive (<3)		Negative (>3)	
		No.	%	No.	%	No.	%	No.	%
Ca stomach No.50		37	74	13	26	34	68	16	32
Gastritis No. 30		17	56.6	13	43.4	15	50	15	50
Healthy control No.16		5	31.2	11	68.8	4	25	12	75
χ^2 test	P-value	0.008				0.007			
	Sig.	HS				HS			

The percentage of positive results of PGI and PGI/PGII ratio comparing to gastric cancer (which diagnosed histopathologically) location in the stomach regions, we found that the corpus-fundus region had high prevalence (89.1%) for PGI with a statistically significant P value(0.00),(2.7%) in cardiac region, and (8.1%) in antrum region comparing to PGI/PGII ratio which had (55.88%) corpus-fundus region, and (44.22%) in antrum region with no significant P value(0.493).Table(3)

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Table (3): The percentage of positive result of PGI & PGI / PGII in gastric cancer according to the stomach region.

Stomach regions		(+ve) PGI < 70 ng/dl NO. %	(+ve) PGI/PGII ratio <3 NO. %
Cardiac		1 2.7	0 0
Corpus-fundus		33 89.1	19 55.88
Anrtum		3 8.1	15 44.12
Total		37 100	34 100
χ^2 test	P-value	0.00	0.493
	Sig.	HS	NS

This study showed that the PGI is more sensitive (74%),and more accuracy (72.72%) than PG I /PG II ratio, while it is more specific (75%) than PGI as show in ROC Curve(Receiver Operator Characteristic) for PGI and PG I /PG II ratio. Diagram (2) & (3).

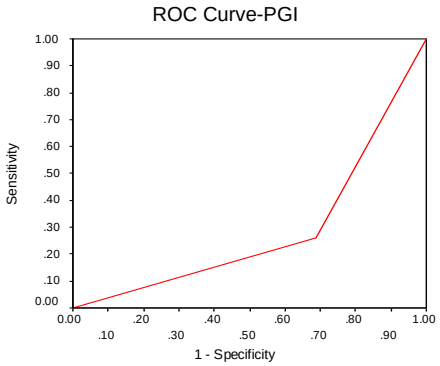

Diagram (2): Show the validity tests of PGI, sensitivity (74%), specificity (68.8%) and accuracy (72.72%)

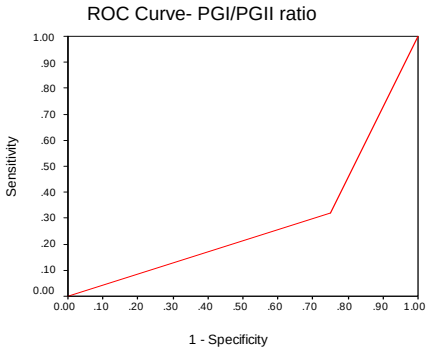

Diagram (2): Show the validity tests PGI /PGII ratio, sensitivity (68%), specificity (75%) and accuracy (69.7%)

Discussion:

Gastric carcinoma is a global healthy problem of major proportions which ranked second in the males (after lung cancer) and fourth in the females (after malignancy of the breast ,cervix uteri, and colon/rectum) (13). In this study we found that the gastric carcinoma occurs in males(48%) and females(52%) which is relatively equal because the little number of study group(only 50) and the number of females more than males so itis not similar to other studies which referred that the gastric cancer is twice as common in men as women.(14,15).in other hand this study showed that the mean age for females was 47.5 years and for males was 66.5 years This study observed that the age group 45-54 years had a peak incidence (30%) among others age groups ,beside that the incidence of gastric carcinoma in age group above 45 years had (76%) ,where as (24%) occurring in age group below 45 years. This finding is in consistence with Isaac H. etal (14) who showed that the prevalence of gastric cancer has a peak incidence at this age with a statistically significant P value (0.004). Obviously, in this study the pepsinogen I level was less than 70 ng/dl in 37 (74%), and in 17 (56.6%) patients as positive marker for gastric carcinoma and gastritis

patient respectively, because the correlation between low concentration level of PGI and gastritis which is in agreement with several other reported studies (16,17) whom found that the serum PGI level reliably correlates with the number of chief cells in the gastric corpus mucosa ,correspondingly, the loss of chief cells results in a linear decrease in serum PGI below 70 ng/dl with statistically highly significant P value(0.008) . While13 (26%) gastric carcinoma patients and 13 (43.4%) gastritis patient showed their serum level more than 70 ng/dl which not precisely reflect disease dissemination or stage for stomach cancer patients and type of gastritis(dueto infection, atrophy or other causes)(10,12).

This study observed that the PGI/PGII ratio when it is low(less than 3.0) detected in 34 (68%) in gastric cancer patients and in 15 (50%) in gastritis patients as positive results due to lesion of stomach mucosa which conformed Yoshihara etal and R.C.G. Russell etal (18,19) whom showed that the PGI/PGII ratio is decreases linearly with increasing in the grade of stomach tumor with statistically highly significant P value(0.007),in other hand the atrophic gastritis rising the risk of gastric cancer to (5 fold) when the PGI/PGII ratio is low. While 16(32%) gastric cancer patients and 15 (50%) gastritis patients their ratio more than3.0 which not reflect disease dissemination or stage for stomach cancer patients and type of gastritis (due to infection, atrophy or other causes) and this finding is in agreement with R.C.G. Russell etal (19).

The pepsinogen method (PG I& PG I /PGII ratio) has been introduced in Japan to screen persons at high risk for stomach cancer give result that survival rate was 49% among all stomach carcinoma patients and 85% among Screening Participants with initial diagnosis of stomach cancer, while the survival rate of stomach cancer in the USA was currently 22%, because they not used the pepsinogen method for screening persons at high risk for stomach cancer (2,6).

In this study ,we take 50 patients with gastric carcinoma who were diagnosed histopathologically ,and compared their effects to the positive results for PGI(< 70ng/dl), and PGI /PGII ratio(<3) according the stomach regions, we found that when the gastric cancer in corpus-fundus region there is a high prevalence of the positive results for PGI (89.1%) with highly significant P value(0.00) which is in agreement with Samloff, etal and Varisk, etal(3,20), while the effect of gastric cancer to positive results for PGI /PGII ratio occurred in corpus-fundus region as(55.88),and in antrum region as (44.22) with no statistical significant P value (0.493). From this study, we detected that the PGI is more sensitive (74%) than PGI/PGII ratio, but it is less specific (68%)than PGI/PGII ratio(75%) .In other hand we observed that the PGI is more accuracy (72.72%) than PGI/PGII ratio (69.7%) .as show in diagram(2,3) ROC Curve (Receiver Operator Characteristic) .The pepsinogen test,enable the establishment with high reliability of whether the mucosa of the stomach is normal and healthy or not .In patients with healthy gastric mucosa the risk of all main gastric diseases is very low.(21). Moreover it can help general practitioners and gastroenterologist to decide about further evaluation (e.g. upper GI endoscopy) and established lines of treatment of patients with dyspepsia symptoms(22,23) .

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Conclusion:

Pepsinogen I and pepsinogen II (PGI and PG I / PG II ratio) are a useful non-invasive method,the testing promotes the identification of the premalignant diseases in the stomach and high risk gastric cancer patients, and it is sensitive and specific test, however it did not precisely reflect disease dissemination, clinical stages, symptoms and pathological type.

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