Study the Effect of COVID19 Vaccines on PIP, GIP and Some of Pancreatic Enzymes in Iraqi Men

Hamed Ali Hamed*, Ashwak I.AL-obaedi *
Tikrit University, College of Science , Dep of Chemistry. *
*AL-Iraqia University,Researches&Islamic studies center.

Abstract:
The gole of the current research was assess influence of COVID19 Vaccines on prolactin inducible protein (PIP), Glucose insulintropic peptide (GIP),Amylase.Lipase Enzyme, in Iraqi men. Altered in some levels of hormones and other biochemical parameters may be accompany the vaccine of covid19.Amylase, Lipase, GIP,PIP,Ferritin, and Age They were estimated in 100 persons which is vaccinated in Pfizer–BioNTech Vaccine (PBV). Results indicated a statistical significantly rise in the mean of Amylase,lipase,GIP,PIP, and Decrease in ferritin level, when compared with the healthy controls (n=50).
Key Words*:* Amylase, Lipase, GIP, PIP,Covid 19 vaccine, Ferritin.

Introduction:
Coronaviruses are a kind of virus that may infected people as well as animals and cause disease(1). SARS-CoV-2 is spread by breathing fumes or coming into contact with an infected surface and then contacting the nose, mouth, and eyes. Instances may be contagious all through the duration of signs and symptoms (2). The new virus spread quickly, generating an outbreak within China and then a global epidemic, with a rise of cases in many nations during the world.(3).Numerous immunizations have been developed to guard against the covid19 as a result of the global coronavirus pandemic 2019, also known as COVID-19. The efficiency of these immunizations as a COVID-19 preventative in all individuals has been demonstrated.[4]. Only a few occurrences of acute pancreatitis have been documented recently, despite the fact that several less common adverse effects have also been mentioned.[5]. One theory postulated the covid 19 virus targeted of pancreas because ACE2 was very emotional in islet capillary. (6).subsequent observational investigations revealed increase Up to 31% of COVID-19 patients had pancreatic enzyme (amylase and lipase) in their blood , and dissection derived from COVID-19 patients indicated necrosis and bleeding in pancreas cell. This condition may lead to severe pancreatitis with a shortage of insulin production. (7). Based on molecular mimicry, the hypothesized that COVID-19 mRNA immunization caused an immunological reaction that concluded in pancreatic damage. (8). Cieslewicz recorded one case of Acute pancaretitis damage in a young woman, 29 years, twenty hours after receiving the BioNTech-Pfizer COVID-19 mRNA vaccine [9]. The worldwide a collection of personal case security reports from instances that involves the pancreas maintained by the World Health Organization (WHO). There are 313 instances of severe pancreatitis, 9 cases of chronic pancreatitis, 17 cases of pancreatitis with necrosis, 8 cases of

pancreatic cysts, 5 cases of pancreatic failure, 4 cases of pancreas hypertrophy, and 3 cases of pancreatic infarction. Pancreatic haemorrhage (2), pancreas steatosis (2), pancreatitis recurrence (2), Pancreatic duct narrowing (1), enzyme pancreatic abnormalities (1), and pancreatic stenosis (2) .(10)

Materials and Methods*:*

Patients.

In a current study fifty samples from pearsons that appeared to be in good health, and 100 blood samples from males between the ages of 20 and 40 who had received vaccinations and were fasting have been obtained.

Serum biocamicals and other parameters.

Blood samples(10ml) was obtained following 12 h of fasting conditions . The levels of serum Amylase , Lipase, PIP,GIP,Ferritin ,was measured. The measurements were done according to the manufacturing kits (ELK,Biotechnelogy,China) for PIP,GIP,ferritin, using Elisa Technique. Amylase, lipase was measured by (Human .liquicolor) using manual method.

Statistical analysis:

Data was analyzed done with the Version of the program GraphPad Prism 7. Simple measurements of average and variation from the mean (SD) values was employed to show data. To ascertain, analysis of variance was employed. whether the difference between distinct means (quantitative data) was significant. (ANOVA), verify whether there is a difference between more than two independent means. When the $P \leq 0.05$, statistical significance was taken into account. Pearson correlation was used to determine the relationship between two quantitative factors determined.. The correlation coefficient value (r) can be positive (direct correlation) or negative (inverse correlation) with value <0.3 represent no correlation, 0.3-<0.5 represent weak correlation, 0.5-<0.7 moderate strength, >0.7 strong correlation. In addition to correlation the r^2 was calculated (The coefficient of determination), i.e. when value of r=0.58, then $r^2=0.34$, this indicates that understanding the values of x, or vice versa, can account for34% of the variation in y value ranges. (ROC) Additionally, analysis employed. The ROC curve's AUC provides insight into how well a measured parameters may distinguish among three groups, one of which is a comparison group.

Results:

The results of current study showed that the 100 vaccinated men by Pfizer–BioNTech Vaccine (PBV) have significant increasae in mean of Amylase,Lipase,GIP,PIP,Concentration,($p \leq 0.05$),(Table1)fig(1),(2),(3),
(4),(5), and significant decreased in mean of ferritin , compared with healthy control.

Table(1)The descriptive analysis including (Mean±SD) and p-values of Amylase,Lipase,GIP ,PIP,ferritin, Age for patients and control groups.

Parameter	Healthy controls		Class A		Class B		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age years	25.9	4.39	27.26	4.809	25.8	5.448	0.4421
Lipase U/L	27.44	2.847	34.14	2.079	32.76	3.886	0.0267
Amylase U\L	47.26	8.549	60.66	3.939	57.73	6.025	0.0353
Ferritin ng\mL	165.1	12.09	122.8	6.227	96.48	11.23	<0.0001
PIP ng\mL	11.78	0.858	15.36	1.149	18.76	2.327	0.0001
GIP pg\mL	224.7	19.78.	486.1	45.7	281.9	42.08	<0.0001

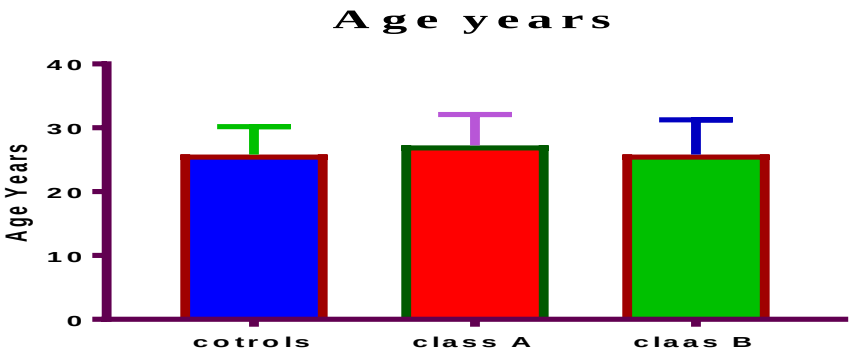


Fig. (1): Mean+ S.D for Age in Control and Patients

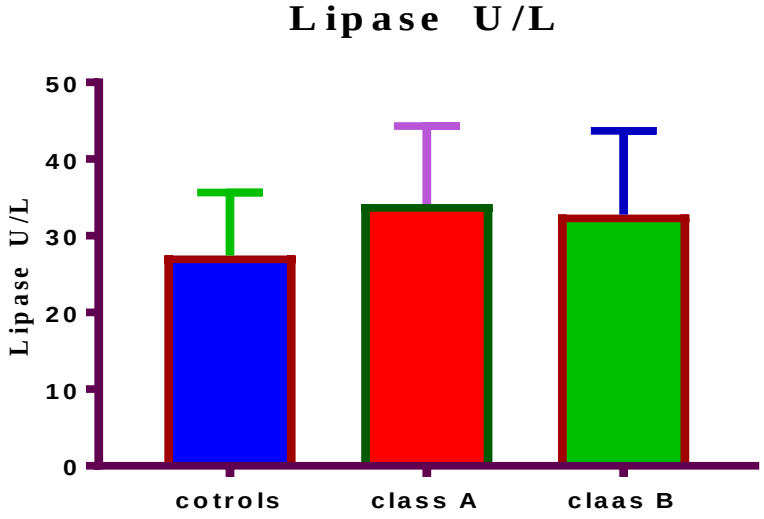


Fig. (9): Mean+ S.D for Lipase in Control and Patients

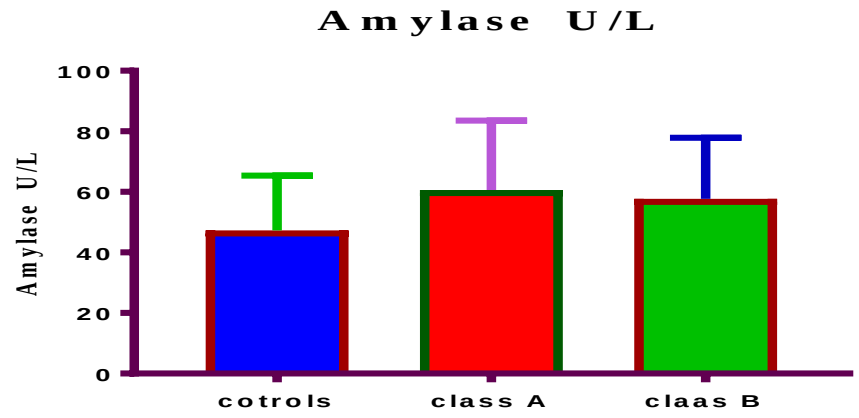


Fig. (10): Mean+ S.D for Amylase in Control and Patients

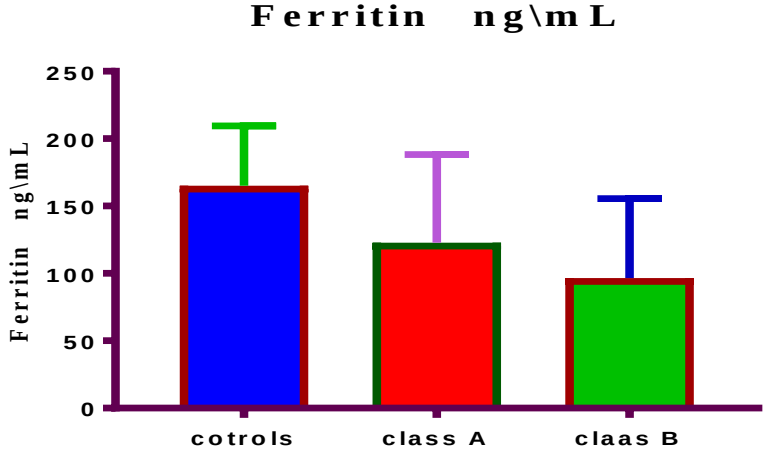


Fig. (13): Mean+ S.D for Ferritin in Control and Patients

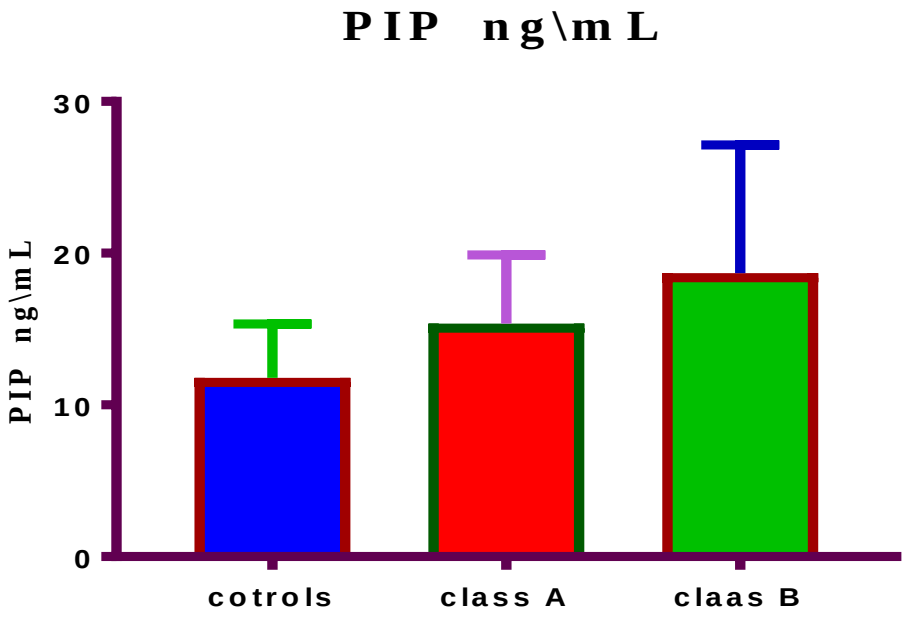


Fig. (15): Mean+ S.D for PIP in Control and Patients

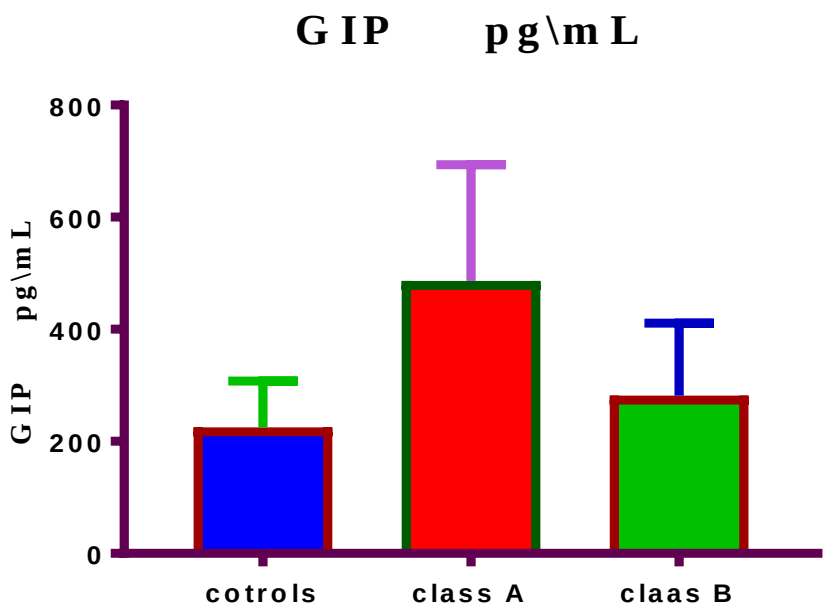


Fig. (18): Mean+ S.D forGIP in Control and Patients

Discussion:

There are fewer instances suggesting a link between immunization and acute pancreatitis.(11). Regarding the COVID-19 vaccine, There are now four incidences of acute pancreatitis. includes the instance described in the immunization trial report for BNT162b2. These incidents happened shortly after the first or second dosage of the BNT162b2 vaccination, anywhere from a few hours to days. (12). Obstructive pancreatitis was described in the acute pancreatitis case in the BNT162b2 vaccination study, which rules out the vaccine as the cause of the **pancreatitis in this case. (12).**

Arecent metaanalysis discovered that individuals with COVID-19 who had rise lipase in blood, defined as any increase of lipase over the URL, had a roughly three-fold greater chance of having bad clinical results, such as the requirement for ICU hospitalization, mechanical air conditioning, or death [13]. Manay Studies in individuals with COVID-19 who did not have acute pancreatitis reported having increased lipase activity. However, the relationship between lipase activity and fatality has not yet been clarified (14). Uncertainty surrounds the mechanism through which the COVID-19 vaccinations cause pancreatitis.

According to Wang et al., all nine COVID-19 patients with pancreatic damage supported the concept that hyperamylasemia was not necessarily linked to pancreatic injury. (increased serum amylase) had considerably higher levels of creatinine than COVID-19 individuals who had not had pancreatic damage.. Moreover, one hyperamylasemia patient also had diarrhea.(15). In individuals with COVID-19, increased pancreas enzymes were seen without any signs of pancreatitis. In addition to the symptoms of COVID-19, patients may also have diabetes, renal damage, and intestinal irritability due to elevated pancreatic enzyme levels.. The cause of increased pancreatic enzymes is

gastroenteritis, and we may identify this rise by observing increased the permeability of the gut in the reaction to inflammation, which encourages the subsequent absorption of Amylase and lipase are examples of large molecules.. (16).

in the present study showed that vaccination recipients had higher levels or activities of the enzymes lipase and amylase than the healthy control group. The outcome is consistent with previous studies. Julia et al. revealed that none of the COVID-19 patients who were 2 of 71 patients (2.8%) who had lipase increase of >3ULN experienced severe pancreatitis. (17). Rasch et al. found that in severe COVID-19 cases, high lipase activity without the normal symptoms of pancreatitis in its acute stage was a common finding related with Syndrome of acute respiratory distress [18]. And with Wang et al.(15), declreard of 52 COVID-19 pneumonia patient were the topic of a study from Wuhan, China, which discovered elevated blood amylase and/or lipase levels in 9 cases (17.3%). High amylase activity was linked to serious illness outcomes in a research that included 1378 COVID-19 participants (19).Walter T et al. [20] About a European male aged 43 man who received the COVID-19 mRNA vaccination from Pfizer and BioNTech and afterwards acquired idiopathic AP.

GIP,PIP too increased in vaccine recipients versus healthy control, May be The glycoprotein CD4 cluster, which is present on the outer surface of immune cells such dendritic cells, T helper cells, and macrophages, has been demonstrated to bind to PIP.. These cells are all essential for maintaining immunological systems that are innate and adaptive, preventing the invasion of foreign pathogens like viruses and bacteria, and regulating the amounts of mRNA and protein and the propagation of diseases increases with the use of androgens, progesterone, glucorticoids together with prolactin or growth hormone, and other cytokines, such as IL-1, IL-4, and IL-13. All of these conditions may contribute to elevated PIP levels.

likewise regarded GIP increased in levels may be the Active macrophages express greater quantities of TNF- and IL-6, and pro-inflammatory markers can increase insulin resistance. Notably that GIP increased in insulin resistence. And other interpretion, has been discovered how the DPP-4/CD26 molecule works, plus to its previously described connection to the ACE2 receptor also activates T lymphocytes and maintains lymphocyte functionality to interface with the S1 domain of the SARS-CoV-2 viral spike glycoprotein. A deficiency of DPP4 and a rise in GIP may be caused by this disease.

Rreceiver operator curve (ROC):

Rreceiver operator Analysis of the curve (ROC) was utilized. to compare the validity of selected parameters when used as a test to predict a covid 19 differentiating it from healthy controls. ROC analysis can be used for set the optimal cut-off point for each parameter, which can also provide the definition for “abnormal” or “positive” test value for the tested parameter when associated with a diagnosis of covid 19.

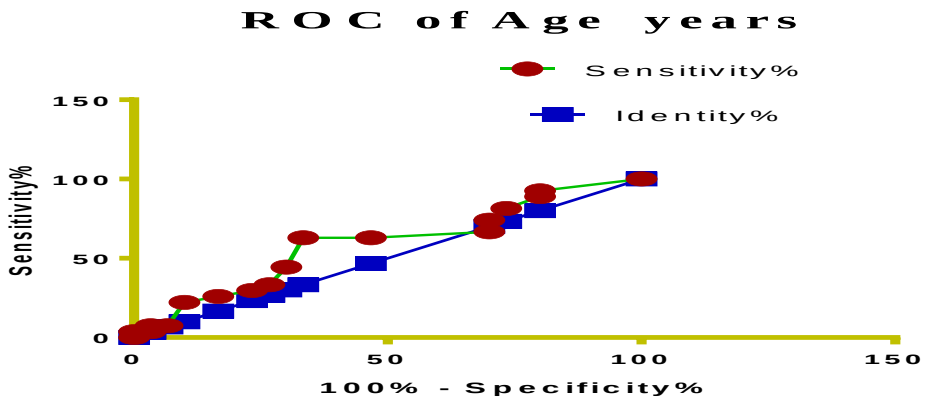
Table(2)The descriptive analysis including (AUC,S.Error) and p-values of Amylase,Lipase,GIP ,PIP,ferritin, Age for patients and control groups

Parameter	AUC	S. Error	95% confidence interval	P-value
Age years	0.5951	0.07638	0.4454 to 0.7448	0.2185
Lipase U/L	0.7167	0.06722	0.5849 to 0.8484	0.0050
Amylase U\L	0.6519	0.07362	0.5076 to 0.7961	0.0493
Ferritin ng\mL	0.7395	0.06761	0.607 to 0.872	0.0019
PIP ng\mL	0.7481	0.06973	0.6115 to 0.8848	0.0013
GIP pg\mL	0.9364	0.03095	0.8758 to 0.9971	<0.0001

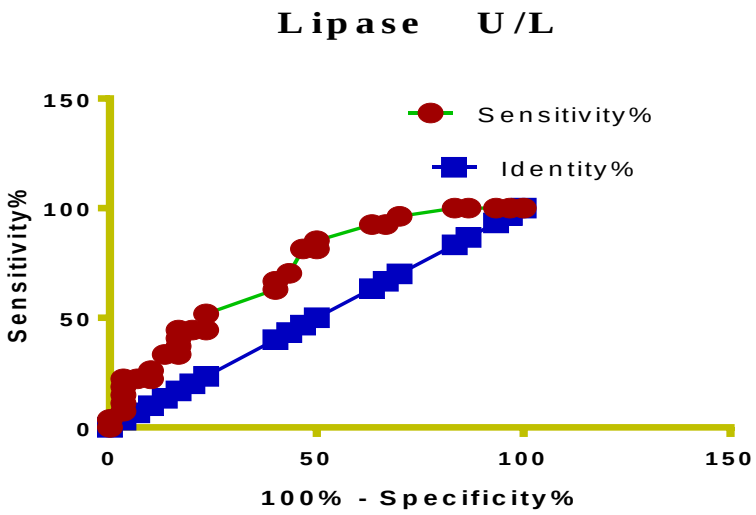
Table(3)The descriptive analysis including (cutt-of value) sensitivity and Specificity % of Amylase,Lipase,GIP ,PIP,ferritin, Age for patients and control group.

parameter	Positive if cut-off value	Sensitivity%	Specificity%
Age years	> 26.5	62.96	66.67
Lipase U/L	> 29.5	62.96	60
Amylase U\L	> 55.5	55.56	56.67
Ferritin ng\mL	< 138.5	66.67	70
PIP ng\mL	> 13.5	74.07	70
GIP pg\mL	> 298.5	81.48	83.33

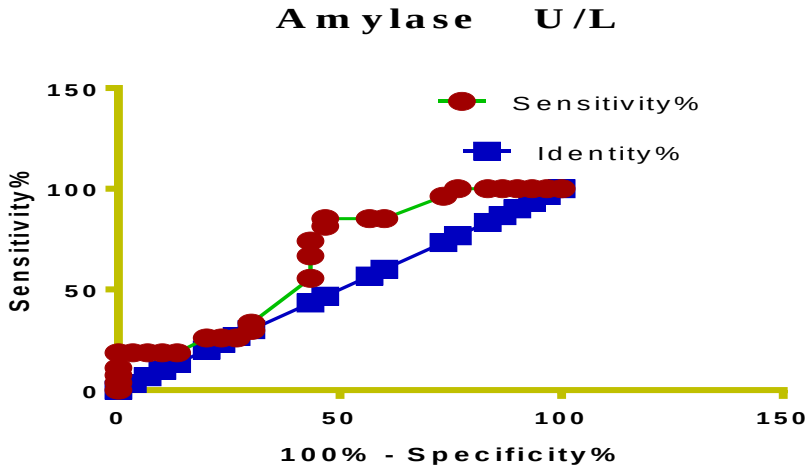
Roc of AGE: **1-**



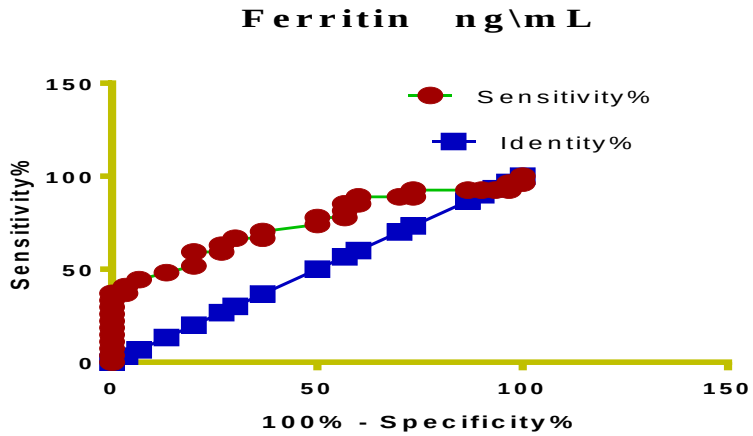
2- **Roc of lipase.**



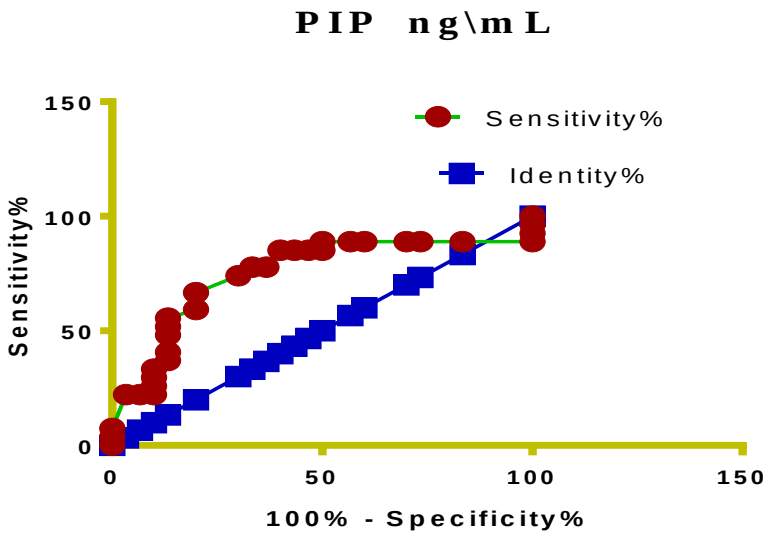
3- **Roc of amylase.**



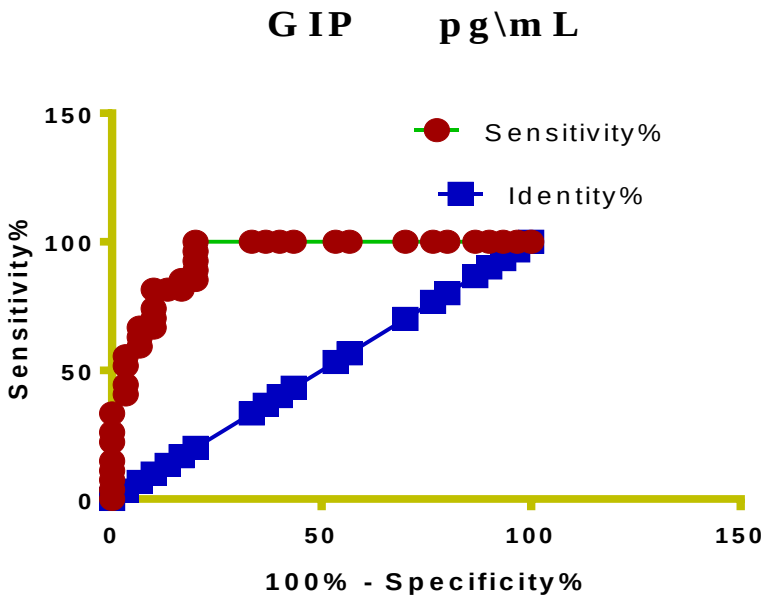
4- **Roc of ferritin.**



5- **Roc of PIP.**



6- **Roc of GIP.**



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