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Clinical Importance of C - Reactive Protein in Predicting in Patients with Acute Severe Pancreatitis

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Abstract

Introduction: Acute Pancreatitis is a disease of unpredictable outcomes early intervention can prevent the development of acute severe pancreatitis which develops in 20 to 30% of patients with Acute Pancreatitis. The progression of the disease and the development of complications are mainly due to the release of proinflammatory cytokines leading to third space volume loss. C–reactive protein (CRP) being an acute phase reactant is elevated in the ensuing inflammation of the pancreas, this elevation when above 150 mg/L has been noted to be a predictive marker of the development of acute severe pancreatitis.

Aim & Objective: determine the role of C –reactive protein in predicting acute severe pancreatitis, the secondary aims were to determine the role of Bedside Index for Severity in Acute Pancreatitis (BISAP), Harmless Acute Pancreatitis Score (HAPS), and Systemic Inflammatory Response Syndrome (SIRS) scores in predicting Acute severe pancreatitis.

Methods*:* This is an observational study; we enrolled 64 consecutive patients with acute pancreatitis from the period of august 2021 to September 2021. At government nagapattinam medical college& hospital, nagapattinam in the department of general Surgery. On admission, pancreatic severity scores were determined using the BISAP, HAPS, and SIRS scores. After 48 hours of admission blood levels of CRP were measured, a CRP level of >150mg/L was taken as a cutoff to predict acute severe pancreatitis. The CRP levels and pancreatitis predicting scores were then evaluated against Computerized Tomography of the abdomen taken 72 hours after admission to predict acute severe pancreatitis.

Results: Acute severe pancreatitis according to CT was found in 23 patients in the study population of 64.CRP predicted the presence of acute severe pancreatitis in 15 out of the 23 patients with a specificity of 85.2%. CRP had a significant correlation in predicting acute severe pancreatitis (p value=0.0002). BISAP, HAPS, and SIRS scores had a Specificity of 69.6%, 97.6%, and 97.6% respectively in predicting acute severe pancreatitis. All the scores predicted significantly (p-value 0.0001) the occurrence of a severe episode. Analyzing in between the scores none of the scores fared better than the other.

Conclusion*:* C - reactive protein (CRP) of 150 mg/L at 48 hours of admission is an excellent predictor that predicts acute severe pancreatitis. The BISAP, HAPS, and SIRS scores on admission are also good markers to predict acute severe pancreatitis. All scores predict acute severe pancreatitis with equal efficacy

Keywords: CRP, Pancreatitis, BISAP, HAPS, SIRS, Severe, Computerized Tomography

Introduction

Acute pancreatitis (AP) is a major debilitating disease of the gastrointestinal tract, having high morbidity and thus creating a huge physical, financial and emotional stress to the affected individual. None of the other acute abdominal differentials have an outcome that is so unpredictable at presentation as compared to that of acute pancreatitis. [1]Two-thirds of patients would improve with supportive therapy, while the other third develops serious local and systemic complications due to an intense inflammatory response, which may progress to multiorgan failure and/or pancreatic necrosis with a 20%to 30% risk of mortality. A triage of AP patients on admission would be ideal at least for two reasons. [2]First, more vigorous and intensive resuscitation would be required for those with severe acute pancreatitis (SAP). Second, a belligerent treatment attitude might be required in patients with a poor prognosis with endoscopic papillotomy, peritoneal lavage, or urgent pancreatectomy, but seldom required in those with mild attacks. An aggressive first 24-48 hours management may alter the course of SAP, the mortality increases more than four times in SAP if there is a > 24-hour delay in transferring a patient to the intensive care unit. Ironically, the first 48hours is when it is most difficult to distinguish between mild and severe acute pancreatitis, but identifying vulnerable patients is essential for a guided treatment plan. [3]The best predictor of outcome in AP is the absence or presence of pancreatic necrosis. The degree of necrosis predicts morbidity and mortality. 30% of pancreatic necrosis patients develop infection of the necrotic tissue, in this group, there is morbidity is around 80% and mortality ranging from 6 to 40%. Single laboratory parameters have also been evaluated for the differentiation between acute mild and severe pancreatitis, from commonly available investigations which are generalized markers of injury such as hematocrit, Blood urea nitrogen, serum creatinine, to markers of inflammation such as C-Reactive Protein, Serum Amyloid A Protein, Interleukins and Procalcitonin along with which are the pancreas-specific injury markers [4,5]

Methods:

This is an observational study; we enrolled 64 consecutive patients with acute pancreatitis from the period of August 2021 to September 2021.At Government Nagapattinam Medical college & Hospital, Nagapattinam in the Department of General Surgery On admission, pancreatic severity scores were determined using the BISAP, HAPS, and SIRS scores. After 48 hours of admission blood levels of CRP were measured, a CRP level of >150mg/L was taken as a cutoff to predict acute severe pancreatitis. The CRP levels and pancreatitis predicting scores were then evaluated against Computerized Tomography of the abdomen taken 72 hours after admission to predict acute severe pancreatitis.Inclusion criteria: Age > 18 years .The Atlanta classification was used for the diagnosis of AP. Exclusion criteria: Patients who had any of the following were excluded from the study.Age <18 years,Chronic pancreatitis,Severe acute pancreatitis on admission,Pregnant women,Hematologic diseases,Connective tissue disorders,Collagen vascular diseases.A total of sixty-four (n=64) patients with acute pancreatitis were enrolled in the study based on the inclusion criteria and the set of exclusion criteria out of the 114 persons seen. Clinical history was elicited in detail with special emphasis on abdominal pain, abdominal distention, decreased urine output, vomiting, blood vomitus, blackish stool, breathlessness, chest discomfort, swelling of legs, fever, yellowish discoloration of eyes or urine, and substance abuse (alcohol and smoking) Blood pressure, Pulse rate, Temperature, Respiratory rate, Oxygen saturation in peripheral blood (SpO2) was measured using standard procedures. Clinical examination was done with special attention for abdominal guarding, rebound tenderness, impaired mental status, a respiratory system for breath sounds. Serum Amylase: Estimation was done by kinetic colorimetric method (Spin React, Spain)Serum Lipase: Estimation was done by kinetic colorimetric method, CRP: Estimation was done by PCR turbid latex method, Liver Function Tests, Blood urea, Serum creatinine, Blood Glucose, Serum Triglycerides, Serum Calcium: Estimation was done using COBAS autoanalyzer. Computerized Tomography: was done using Toshiba Aquilion 64 (Japan)

Results

A total of 64 patients with acute pancreatitis were studied. The patients were divided into two groups, those with mild pancreatitis and those with severe acute pancreatitis. Both moderately severe acute

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pancreatitis and severe acute pancreatitis were considered severe acute pancreatitis.

Table 1: Distribution of Cases About Age & Gender

Age group	Male (%)	Female (%)	Total (%)
18-29	13 (20.3)	3 (4.7)	16 (25.0)
30-39	23 (35.9)	2 (3.1)	25 (39.0)
40-49	9 (14.1)	3 (4.7)	12 (18.8)
50-59	7 (10.9)	1 (1.6)	8 (12.5)
>60	3 (4.7)	0	3 (4.7)

TABLE: 1 80% of the study population. Men were predominating in the study group where they contributed to 85.9% of the study population. The mean age of presentation of acute pancreatitis was 37.7 years.

Table 2: Symptom on Presentation

Symptom	Present	Absent
Pain	62(96.9%)	2 (3.1%)
Vomiting	38 (59.4%)	26(40.6%)
Abdominal distention	11(17.2%)	53(82.8%)
Jaundice	11(17.2%)	53 (82.8%)
Fever	7 (10.9%)	57 (89.1%)
Oliguria	5 (7.8%)	59(92.2%)
Dyspnoea	5 (7.8%)	59 (92.2%)
UGI bleed	1 (1.6%)	63(98.4%)

TABLE:2 In this study, Pain was the predominant presenting complaint seen in 96.9% of the study population, while the least common presenting complaint or associated symptom was upper gastrointestinal bleed which was seen only in one individual. Extrapancreatic manifestations were seen in a frequency of 1.6% to 17.2%.

Table 3: Baseline Investigations

Parameter(Normal values)	Normal	Not withinNormal limits
Bilirubin (<1.2 mg/dl)	31(50.0%)	31(50.0%)
AST (<40 IU/mL)	29(45.3%)	35(54.7%)
ALT(<40 IU/mL)	42 (65.6%)	22(34.4%)
Albumin (>3 gm/dl)	55(85.9%)	9(14.1%)
Blood Urea(< 40 mg/dl)	53 (82.8%)	11(17.2%)
Creatinine (<1.2 mg/dl)	57(89.1%)	7(10.9%)
Hematocrit (44%)	45(70.3%)	19(29.7%)

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TABLE :3 Amylase and lipase were taken for the diagnosis of acute pancreatitis; amylase and lipase were elevated significantly in 52 and 54 patients respectively. Patients who did not have significantly elevated amylase and lipase levels were diagnosed using abdominal pain and CT findings. The mean amylase and lipase levels were 623.23 U/L and 890.21 U/L respectively.

Table 4: Distribution of Crp in The Study Population

C –reactive protein	Number	Percentage
<150	41	64.1
>150	23	35.9

TABLE:4 A CRP cut of 150 mg/L was taken as a cut-off to differentiate between mild and severe pancreatitis. The majority 64.1% had a CRP level less than 150 mg/L. Normal CRP levels <6 mg/L were seen in 11 individuals. Lactate dehydrogenase was performed in 31 patients out of 64 patients.LDH levels were < 350 IU/L in 6 patients and increased (> 350IU/L) in 25 patients.

Table 5: Distribution of Pancreatitis According to Scoring Systems

Scoring System	Positive for MAP	Positive for SAP
SIRS	45(70.3%)	19 (29.7%)
BISAP	47(73.4%)	17(26.6%)
HAPS	48(75.0%)	16(25.0%)

TABLE:5 Three scoring systems (SIRS, HAPS, and BISAP) were used to predict the severity of acute pancreatitis. If the patient had two or more of the SIRS criteria, the patient was considered positive for SAP. In the HAPS system, if the patient had all three criteria as negative, then he was considered HAPS positive for MAP. While considering the BISAP system, the patient was considered positive for MAP, if he/she had three or less than three criteria. Patients were classified as mild and severe acute pancreatitis based on the scoring systems their distribution

Table 6: Analysis Crp with Ct in Predicting Severe Acute Pancreatitis

CRP	Severity based on CT		Chi-square	P-value
	1	2 & 3		
< 150	33	8	13.37	0.0002
≥ 150	8	15		

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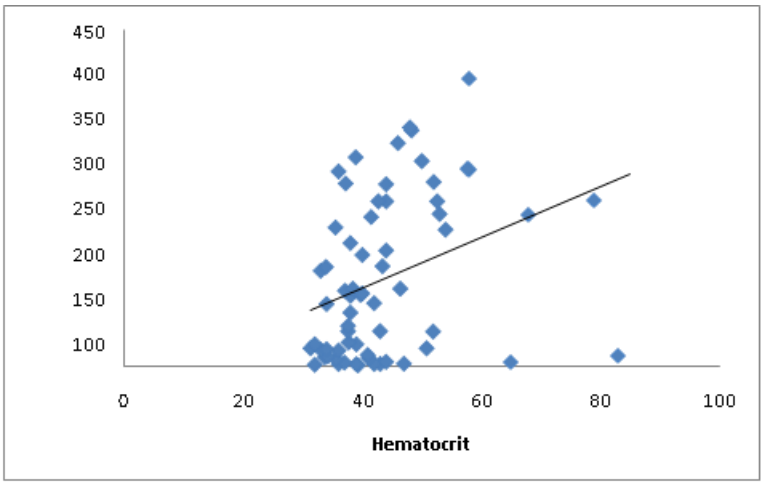
TABLE:6 Analyzing the primary aim of the study to correlate between CRP levels and severity of pancreatitis taking into consideration, CRP had a significant correlation in predicting SAP (p value=0.0002) and in predicting acute necrotizing pancreatitis (p value=0.0004)

GRAPH 1: Correlation CRP and hematocrit



GRAPH :1 CRP predicted severe acute pancreatitis with a sensitivity of 65.2% and a specificity of 80.5%. The Positive predictive value of CRP in predicting SAP was 65.2% while it had a negative predictive value of 80.5%. A correlation was calculated using Pearson correlation. Correlation coefficient r = 0.335, p = 0.007.

Table:7 Analysis Of Pancreatic Predictive Scores

Score	MAP	SAP	Severity based on CT			Chi-square	P-value
			1	2	3		
SIRS	45	19	1	4	14	42.73	0.0001
BISAP	47	17	1	4	3	37.71	0.0001
HAPS	48	16	1	2	13	38.18	0.0001

TABLE:7 All the three pancreatitis predicting scores had a significant say in predicting SAP, with more or less similarity (P-value =0.0001), when compared to the severity of pancreatitis on CT.16 patients were HAPS negative out of the 23 patients with an elevated CRP. There was a significant association of CRP and HAPS with a p-value of 0.0001.19 patients were SIRS positive out of the 23 patients with an elevated CRP. There was a significant association of CRP andSIRS with a p-value of 0.0001. All scores had a significant association with CRP, but none were superior tothe other in predicting SAP.

Discussion

Acute pancreatitis is undoubtedly a disease in which the progression can be greatly altered by early intervention. Numerous scores and single prognostic markers have been suggested to predict the severity of pancreatitis on admission or after a couple of days, this by itself suggests none of the available scores or markers are the gold standard to predict the severity of the disease. [6] In this study CRP and pancreatitis predicting scores SIRS, BISAP and HAPS were analyzed to predict the severity of pancreatitis. Scores that had many markers may have had an increased sensitivity but simpler and easily available

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scores and markers were taken. In our country where resources are limited, the simplest and the most economical of the scores or markers are the ones that would have a great impact on society in the prediction of severity in AP. Abdominal pain (96.9%) and vomiting (59.4%) were the predominant complaints seen in the study population.[7] This is similar to the study by Chávez Rossell et.al who stated the predominant symptom in AP as abdominal pain in 100% followed by vomiting in 69.2%. A symptom association of extrapancreatic manifestations to the occurrence of SAP was done, which showed that the presence of Extra pancreatic manifestations in acute pancreatitis had a high probability to be associated with SAP [8]. In this study, there was a significant association with jaundice, fever, dyspnea, and oliguria which is similar to the study by Chiari H. U¨et.al.Thus this study further emphasizes the well-known fact of the need for aggressive fluid management in AP thus preventing volume depletion, which may lead to the development and progression of SAP. In this study alcohol was the predominant cause of AP seen in 68.8% while a biliary cause of pancreatitis was seen only in 10.9% of the study population, contrary to Roberts who reported from the UK that 36.9% of patients had gallstone as the predominant etiology of AP followed by alcohol (22.0%).[9] Other Causes of AP were seen in 13 patients in the study group, one patient had carcinoma pancreas, one was tropical pancreatitis and 2 patients had pancreatic divisum. In 9 patients etiology was not known and an evaluation was not attempted due to the first episode of acute pancreatitis. A CRP of > 150 mg /L was taken to predict acute severe pancreatitis, 23 (35.9%) patients of the 64 study population had an elevated CRP at 48 hours of admission.15of the 23 patients who had a significant elevation of CRP had CT features of SAP (P = 0.0002), while 12 of the 23 patients with significant elevation of CRP had Necrotising pancreatitis on CT (P = 0.0004).[10] The Positive predictive value of CRP in predicting SAP was 65.2% while it had a negative predictive value of 80.5%. This is similar to previous studies which have stated an at 48 hours CRP had a sensitivity ranging from 65% to100% and a positive predictive value of 37% to 77%.41(64.1%) patients of the study population had mild pancreatitis, while 23(35.9%) patients had SAP as determined by CT, which is taken as a standard to predict the severity of pancreatitis. [11]The reason could be that in our population there is a delay in presentation to the hospital as the patients seek over-the-counter medications or complementary and alternative forms of medicine for the most common symptom of abdominal pain or it could be that of a referral bias.[12]Three pancreatic scores were taken in the study HAPS, BISAP, and SIRS, all of which have easily obtainable variables and can be calculated at the time of admission. This study evaluated the efficacy of these scores in comparison with CRP and CT severity in predicting SAP. This study suggests all the pancreatic predictive scores have an excellent predictive value in predicting severe acute pancreatitis. [13]None of the scores were superior to the other in predicting SAP. BISAP score in this study had a Sensitivity and Specificity of 69.6% and97.6% in predicting SAP with a PPV of 94.1% and an NPV of 85.1%. HAPS score in this study had a Sensitivity and Specificity65.2% and 97.6%in predicting SAP with a PPV 93.8% of and an NPV of 83.3% [14,15]

Conclusions

C - reactive protein (CRP) of 150 mg/L at 48 hours of admission was able to predict Severe Acute Pancreatitis in 65.1% and Acute Necrotising Pancreatitis in 52.1%. The Pancreatic Predicting Scores BISAP, HAPS, and SIRS scores predicted significantly the occurrence of severe acute pancreatitis. CRP was significantly associated with BISAP, HAPS, and SIRS scores in predicting severe acute pancreatitis. None of the studied scores BISAP, HAPS, and SIRS scores were superior to the other. The presence of Extrapancreatic symptoms was associated with acute severe pancreatitis especially dyspnea and oliguria. Alcohol was the predominant etiology in this study. Patients who were young mostly in the third decade were more commonly affected with acute pancreatitis.

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