

ORIGINAL RESEARCH

Role of measurement of C-reactive Protein in Acute Pancreatitis

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ABSTRACT:

Acute pancreatitis is an inflammatory process of the pancreas with varying involvement of regional tissues or remote organ systems and with potentially devastating consequences. CRP is an acute phase protein and plasma levels increase in nearly all acute and chronic inflammatory diseases. Thus, the aim of the study was to identifying the role of c-reactive protein in severity stratification of acute pancreatitis. The study was conducted on 50 patients. The results showed that mean age of the patients was 42.82±12.29 years. Majority of patients belonged to 41-50 age group followed by 31-40 age group. Majority of patients were male (52%) and the remaining were females (48%). Most common presenting symptoms were pain, vomiting, abdominal distension and vomiting with pain being reported in majority of patients (96%). It was observed that alcohol was the most common cause of acute pancreatitis as it was seen in 72% of patients. Mortality was seen in 1 patient (2%). It was observed that there was significant correlation coefficient ratio between CRP and hematocrit, calcium, BUN and creatinine. It was observed that majority of patients with CRP level > 150 mg/l had severe acute pancreatitis (p value=0.0004). Overall, these findings highlight the potential utility of CRP in the management of acute pancreatitis and suggests that it may be a useful tool in helping to guide treatment decisions.

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Introduction:

Acute pancreatitis is an inflammatory process of the pancreas with varying involvement of regional tissues or remote organ systems and with potentially devastating consequences.¹ Acute pancreatitis (AP) is common, with an alarming rise in the global incidence.² The clinical course of AP is highly variable, ranging from mild, self-limiting symptoms to multiple organ dysfunction and/or death. Multiple predictive models and scoring systems have been proposed over the years to predict severity of AP including: Ranson score, Glasgow score, and the acute physiology and chronic health evaluation (APACHE).³ These have been shown to have a limited discriminatory ability in predicting mild and severe disease. Since the revision of the Atlanta classification to include a 'moderately severe' pancreatitis group, the utilization of these scoring systems to identify specific disease subgroups may have new connotations and benefits in clinical practice.⁴ Worldwide the incidence of acute pancreatitis varies, from 5 to 80 per 100,000 population. Commonest etiologies being gallstones (40–70%) and alcohol (25–35%). In approximately 10–20% of patients, no etiology is identified. CRP is

probably the most studied serum biomarker and widely recognized marker of inflammation. CRP is an acute phase protein and plasma levels increase in nearly all acute and chronic inflammatory diseases. According to many studies CRP is one of the earliest acute-phase reactants that increase in level and CRP level higher than 170 mg/dl at 48 hours has been reported to be very valuable for predicting severe acute pancreatitis and pancreatic necrosis at any time before 48 hours. Further, the importance of CRP lies in its value for predicting the healing of acute pancreatic inflammation as follow-up CRP levels will correctly reveal which patients will develop complications or which will heal uneventfully.⁵ Thus, the aim of the present study was to assess the value of serum C reactive protein levels as a biochemical severity marker in acute pancreatitis and to find the relationship between C reactive protein levels and severity of acute pancreatitis according to revised Atlanta classification.

MATERIALS AND METHODS

The prospective study included 50 Patients with the diagnosis of acute pancreatitis who met the inclusion criteria and were selected after obtaining written

informed consent. The patients were recruited from emergency ward of Guru Nanak Dev Hospital, Amritsar. This study was undertaken after approval of the Institutional Ethics Committee, Govt. Medical College, Amritsar.

INCLUSION CRITERIA: Patients aged between 18-65 years who presented with first episode of acute pancreatitis. Diagnosis of AP was defined by meeting two of the following three criteria (1) Abdominal pain consistent with pancreatitis, (2) Serum amylase or lipase more than three times the upper limit of normal (3) radiological evidence of AP on CECT, ultrasound or MRI abdomen.

EXCLUSION CRITERIA: Age <18 and >65, Prior episodes of AP or chronic pancreatitis, Post endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis, Patients with incomplete clinical data such as the lack of routine blood test.

DATE COLLECTION: After obtaining informed consent from the patients diagnosed to have acute pancreatitis a detailed history about the symptoms like abdominal pain, nausea, vomiting were asked. A detailed clinical examination to look for abdominal tenderness and rigidity was done. All patients were subjected for following investigations: CBC, RFT, LFT, CRP, Serum Amylase, Serum lipase, ECG, X ray chest and x ray abdomen, Ultrasound abdomen, ABG, Lipid profile

Serum C reactive protein levels were measured within 48 hours of admission.

STATISTICAL ANALYSIS

Data entry was done in MS Excel and computations including proportion and values were calculated using appropriate software. Mean +/- SD was calculated for quantitative data. Chi-square test was applied to measure association between categorical data. P value less than 0.05 were considered statistically significant.

RESULTS

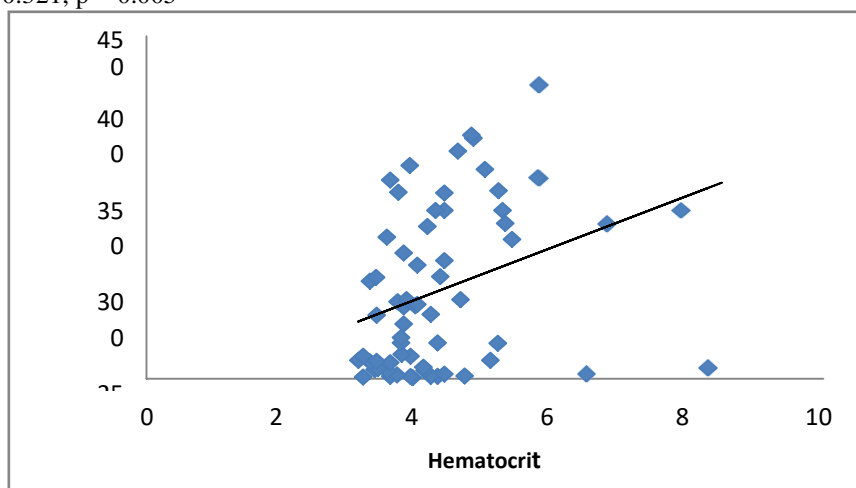
The present study was conducted on 50 patients to know the role of c-reactive protein in severity stratification of acute pancreatitis. It was observed that mean age of the patients was 42.82±12.29 (18-65) years. Majority of the patients (52%) were male while females were only 48%. The study observed that pain (96%), vomiting (60%), abdominal distention (18%), and jaundice (18%) was the most common presenting symptoms. It was observed that 72% patients were consuming alcohol, and there were 42% smokers while 40% patients had both habits. Alcohol was the most common cause of acute pancreatitis as it was seen in 72% of the study population. Mortality was reported in 2% patients. It was found that creatinine, albumin, blood urea, and haematocrit was reportedly normal in 90%, 84%, 80%, and 70% patients respectively. It was observed that majority of the patients (80%) had their calcium in the normal range.

TABLE 1: DISTRIBUTION OF CRP IN THE STUDY POPULATION

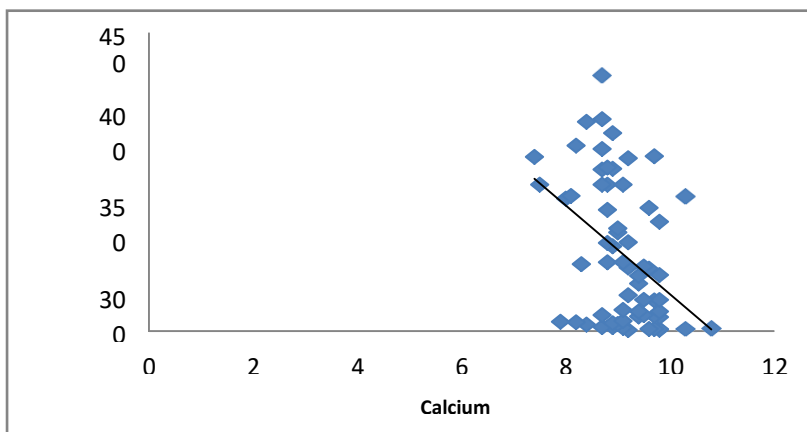
C –Reactive Protein	Number	Percentage
<150	31	62.0
>150	19	38.0

Table 1: showed that 62% had a CRP level less than 150 mg/L and 38% had a CRP level greater than 150 mg/L. It was also observed that maximum patients (24%) had lipase in the range of 101-200. Only 16% patients had lipase above 500. In this study, maximum patients (32%) had amylase between 101-200. About 12% patients had lipase above 500.

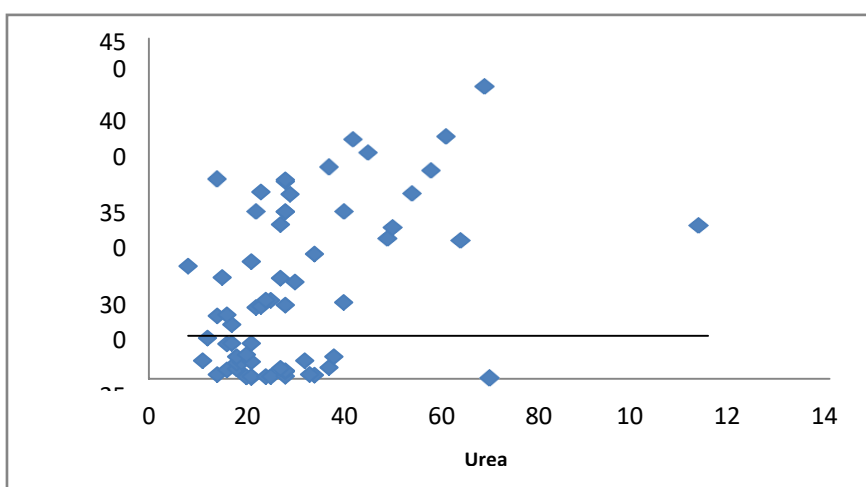
This study has calculated correlation using Pearson correlation between CRP and haematocrit Correlation coefficient: $r = 0.321, p = 0.005$



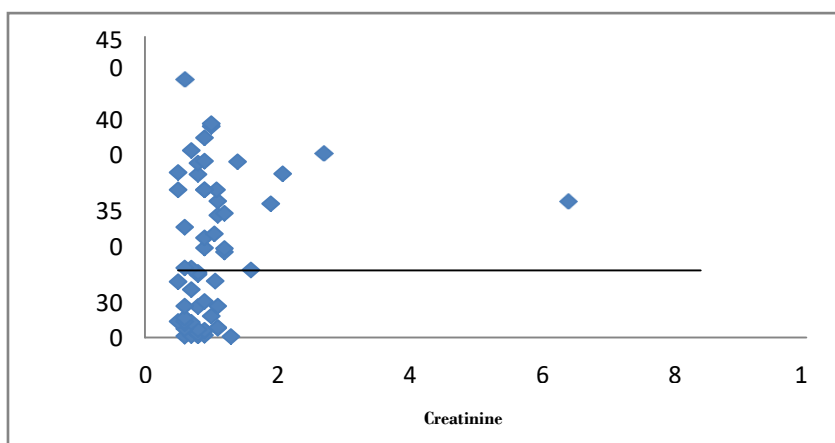
GRAPH 1: Correlation CRP and hematocrit



GRAPH 2: Correlation CRP and Calcium
 Correlation coefficient: $r = -0.403$, $p = 0.001$



GRAPH 3: Correlation CRP and BUN
 Correlation coefficient: $r = 0.416$, $p = 0.0012$



GRAPH 4: Correlation CRP and creatinine
 Correlation coefficient: $r = 0.239$, $p = 0.04$

From the above graphs it was found that there was a significant correlation coefficient ratio between CRP and haematocrit, calcium & renal function tests (creatinine and BUN). The study found out no correlation was found between CRP and AST ($r = -0.162$, $p = 0.312$), ALT ($r = -0.143$, $p = 0.212$), ALP ($r = -0.168$, $p = 0.065$), Bilirubin ($r = -0.164$, $p = 0.162$), and Albumin ($r = -0.148$, $p = 0.222$) using Pearson correlation. It was noticed that acute pancreatitis was mild, moderately severe and severe in 64%, 10% and 26% patients respectively.

TABLE 2: CORRELATION OF CRP WITH ATLANTA CLASSIFICATION OF ACUTE PANCREATITIS

CRP	Severity of Acute pancreatitis			Chi Square	P value
	Mild	Moderate	Severe		
< 150	26	3	3	15.55	0.0004
≥150	6	2	10		

Table 2 showed that majority of the patients with CRP <150 mg/L had mild acute pancreatitis (52%). The study observed that majority of patients (20%) with CRP level ≥150 mg/L had severe acute pancreatitis.

DISCUSSION

The present study was aimed to assess the role of C-reactive protein in severity stratification of acute pancreatitis. This prospective study was performed on 50 patients diagnosed of acute pancreatitis during the study period. There is substantial evidence across the literature outlining the benefits of CRP as an acceptable indicator of AP severity. As a result, it has become one of the most widely utilized biomarkers in clinical practice.

C-reactive protein (CRP) is a protein produced by the liver in response to inflammation. Elevated levels of CRP in the blood can be a marker of inflammation, and can be used to help assess the severity of acute pancreatitis, which is a condition characterized by inflammation of the pancreas. In acute pancreatitis, CRP levels are typically elevated within the first few days after the onset of symptoms. The levels of CRP can be used to help stratify the severity of the condition. Higher CRP levels are generally associated with a more severe case of acute pancreatitis, and may be used to help guide treatment decisions. It's worth noting that CRP levels are not the only factor used to assess the severity of acute pancreatitis.⁶ Other factors that may be considered include the presence of organ failure, the presence of necrosis (tissue death) in the pancreas, and the patient's overall clinical condition.⁷

Demographic status: In the present study there were 26 males contributing to the 52% of study population. This finding was consistent with previous studies by Stimac et al (2013)⁸ and the study of Roberts et al (2013)⁷ which showed only a slight male predominance of 53% and 50.7% respectively. The mean age of the patients was 42.82±12.29 years with majority of subjects (36%) belonging to 41-50 years age group. In contrast to our findings, the studies by Davoret al (2013)⁸ and Roberts et al (2013)⁷ reported a mean age of 61 and 57.7 years respectively. However the findings of our study are in alignment with the study by Thamilselvam et al(2008)⁹ who reported a high prevalence in the age group of 40-60 years. The probable reason for this could be that gall stone disease is not as common here as it is in the west and the predominant cause of AP in this study was alcohol which is more abused by men than women and in younger population comparatively in our country.

General findings and history of patients

In the present study pain (96%), vomiting (60%), abdominal distention (18%), and jaundice (18%) were the most common presenting symptoms. These findings suggest that abdominal pain and vomiting were the predominant complaints reported in our study population. In a reference study by Vinish et al (2014)⁶ it was reported that abdominal pain (96.9%) and vomiting (59.4%) were the predominant complaints seen in the study population. Another study by Milheiro and Medeiros(1995)¹⁰ reported that the predominant symptom in AP was abdominal pain in 100% of patients followed by vomiting in 69.2%. Our study showed that presence of extra pancreatic manifestations in acute pancreatitis had a high probability to be associated with SAP. Significant association with jaundice, fever, dyspnea and oliguria was reported by Akhtar &Shaheen (2004)¹¹ and Jacobs et al (1977)¹².

The study found out that there were 72% patients who were consuming alcohol while 42% were smokers. The study also found out that 40% patients were consuming both alcohol and smoking. These findings suggest that alcohol was the most common cause of acute pancreatitis (72%). In contrast to the findings of our study Roberts et al (2013)⁷ reported that 36.9% patients had gallstone as the predominant etiology of AP followed by alcohol (22.0%). In line with the findings of our study Sekimoto et al (2006)¹³ reported that in the Japanese population alcohol contributed to 37% of AP and the biliary system contributed to 20%, while Akhtar &Shaheen (2004)¹¹ showed that alcohol was the predominant cause in 53 % of patients. These studies have shown parallel results to the present study.

CRP (C - reactive protein)

In the present study it was found that 62% patients had a CRP level less than 150 mg/L. A CRP of > 150 mg /L was taken to predict acute severe pancreatitis. The study found out that 38% patients had an elevated C - reactive protein. The accepted figure by international consensus for prediction of severe acute pancreatitis is an absolute CRP >150 mg/dL within 48 h of admission.¹⁴ Like our study, Vinish et al (2014)⁶ in their study reported that 23 (35.9%) acute pancreatitis patients of the 64-study population had an elevated CRP at 48 hours of admission. The study found out that there was a significant correlation coefficient ratio between CRP and haematocrit,

calcium, creatinine and BUN. Haematocrit, calcium, creatinine and BUN are single prognostic markers in predicting the severity of pancreatitis.¹⁵

Severity of Acute Pancreatitis: In the present study Revised Atlanta Classification was used to determine the severity of acute pancreatitis. The study found out that acute pancreatitis was mild, moderately severe and severe in 64%, 10% and 26% patients respectively. The study reported that majority of the patients with CRP <150 mg/L had mild acute pancreatitis (52%). However, majority of patients (20%) with CRP level \geq 150 mg/L had severe acute pancreatitis. The results signified that there was a significant association between CRP level and severity of acute pancreatitis (p value=0.0004). In a reference study by Vinish et al (2014)⁶ it was reported that CRP predicted severe acute pancreatitis with a good sensitivity and specificity (65.2% and 80.5%). The positive predictive value of CRP in predicting severe acute pancreatitis was 65.2% while it had a negative predictive value of 80.5%. These findings suggest that CRP may play a significant role in severity stratification of acute pancreatitis. These findings are in accordance to studies by Alfonso et al (2003)¹⁶ and Cardoso et al (2013)¹⁷ who took a CRP value of 200 mg /L and 170 mg/L respectively in predicting SAP and necrotising pancreatitis. This study achieves the same association with a CRP cut off of 150mg/L as suggested by previous studies by Wilson et al (1989)¹⁸ and the UK guidelines of management of AP (1998)¹⁹. Thus, this study confirms that a CRP of >150mg/L is as diagnostic as higher levels in predicting severe acute pancreatitis.

Mortality: In the present study mortality was reported in 2% patients. This finding was consistent with the findings of previous studies. Vinish et al (2014)⁶ reported that there were 2 (3.1%) deaths in AP patients; both patients had elevated CRP and the pancreatic predicting scores were positive for SAP. Stirling et al (2017)²⁰ also reported similar findings. Stirling also reported an overall mortality of 2% in acute pancreatitis patients. This is however in contrast to study done by K D John et al (1997)²¹ where mortality reported was 8.1%. This difference in mortality is probably because the study was done on African Black population and black population are significantly more likely to have advanced changes on pancreatic morphology, pancreatic ductal strictures, and decreased pancreatic function.

Conclusion: The present study suggests that C-reactive protein (CRP) can be useful in the severity stratification of acute pancreatitis. The study found that a CRP level of more than 150 mg/L was associated with a higher likelihood of severe acute pancreatitis. Additionally, the study found that elevated CRP levels correlated with certain other markers, such as haematocrit, calcium, creatinine,

and BUN, which may also be useful in predicting the severity of the condition. Overall, these findings highlight the potential utility of CRP in the management of acute pancreatitis and suggests that it may be a useful tool in helping to guide treatment decisions.

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