Original Research Article

Predictive value of serum C- reactive protein in diagnosis of acute pancreatitis at a tertiary hospital

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Abstract

Background: Acute pancreatitis (AP) is defined as an inflammatory process of the pancreas with possible peripancreatic tissue and multiorgan involvement inducing multiorgan dysfunction syndrome (MODS) with an increased mortality rate. Various biochemical markers like C-reactive protein (CRP), pro-calcitonin and the like are under evaluation as prognostic indicators. Present study was aimed to study predictive value of serum C- Reactive Protein (CRP) in diagnosis of acute pancreatitis at a tertiary hospital. **Material and Methods:** Present study was hospital based, prospective, observational study, conducted patients above 18 years of age and diagnosed with acute pancreatitis as evidenced by the elevated levels of pancreatic enzymes or confirmed by imaging studies. **Results:** During study period 72 patients of acute pancreatitis were studied. In present study majority of cases were from 31-40 years (33.33%) followed by 41-50 years (22.22%). We noted male preponderance (81.94 %) and male to female ratio was 4.54:1. In present study alcoholism was the main etiological factor (73.61%) followed by Biliary/ Gall stones (6.94 %), Choledochal cyst (4.17%), Viral infections (4.17%) and Idiopathic (11.11%). In present study normal CRP levels (<6) were noted in 7 (9.72%) patients, 39 (54.17%) had CRP level 6 -150 and 26 (36.11%) had CRP level >150. CRP level >150 was statistically significantly ($p<0.001$) associated with Ranson's score ≥ 3, thus CRP level >150 was predictor of severe disease. CRP level >150 was statistically significantly ($p<0.001$) associated with CT severity index (CTSI) ≥ 5, thus CRP level >150 was predictor of severe disease. **Conclusion:** A CRP level of 150 mg/L at 48 hours after onset of symptoms can be used as a cut off value to predict a severe disease in patients of acute pancreatitis.

Keywords: CRP, acute pancreatitis, CTSI, Ranson's score.

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INTRODUCTION

Acute pancreatitis (AP) is defined as an inflammatory process of the pancreas with possible peripancreatic tissue and multiorgan involvement inducing multiorgan dysfunction syndrome (MODS) with an increased mortality rate.[1] The severity of acute pancreatitis can range between mild self-limiting pancreatic inflammatory response to pancreatic necrosis leading to life-threatening condition.[2] The severe form of the disease associated with macroscopic hemorrhage and fat necrosis in and around the pancreas. It is important to identify those patients with acute pancreatitis who have an increased risk of mortality. Alcohol consumption and cholelithiasis have been reported as the most common ethological factors in the development of acute pancreatitis. Other less common causes include pancreatic divisum, intraduct papillary mutinous tumour, endoscopic retrograde cholangiopancreatography, hyperlipidemia, drug induced pancreatitis, hypercalcemia, and idiopathic causes.[3,4] C-Reactive Protein (CRP) is one of the acute phase reactants synthesized by the liver in response to interleukin-1 and

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interleukin-6. Various clinical, biochemical and imaging criteria have been proposed as predictors of severity of acute pancreatitis. The role of diagnostic markers (pancreatic enzymes such as amylase and lipase) as prognostic indicators has been a failure. Other biochemical markers like C-reactive protein (CRP), pro-calcitonin and the like are under evaluation as prognostic indicators.[5] Present study was aimed to study predictive value of serum C- Reactive Protein (CRP) in diagnosis of acute pancreatitis at a tertiary hospital.

MATERIAL AND METHODS

Present study was hospital based, prospective, observational study, conducted in Department of General Surgery, Shri Venkateswara Medical College, Hospital & Research Centre, Pondicherry, during January 2017 to December 2018 (2 year). Study approval was taken from institutional ethical committee, India. Study was approved by institutional ethical committee.

Inclusion criteria: Patients above 18 years of age and diagnosed with acute pancreatitis as evidenced by the elevated levels of pancreatic enzymes or confirmed by imaging studies were included.

Exclusion criteria: Patients with chronic pancreatitis and acute on chronic pancreatitis; Patients with questionable diagnosis of other possible abdominal conditions.

Study was explained to patients/relatives and a written informed consent was taken for participation. Cases with confirmed acute pancreatitis were considered for study and diagnosis of acute pancreatitis was confirmed either by a three-fold rise in the level of pancreatic enzymes or by radiological evidence of pancreatic inflammation. Detailed history, examination findings were noted in case record proforma. Routine investigations such as complete blood counts, renal function tests, liver function tests and chest X-ray. Ranson's score and CT severity index (CTSI) were done in all patients. CRP levels were measured 48 hours after the onset of symptoms. All patients were managed conservatively and as per standard operating procedures of surgery department. Local complications such as intra/peri pancreatic collection, necrosis and abscess, and systemic complications such as acute respiratory distress syndrome (ARDS), acute kidney injury (AKI) and multiple organ dysfunction syndrome (MODS) were noted in case record proforma. The local complications were managed conservatively. Among the systemic complications, patients who developed ARDS and MODS were managed in ICU; patients who developed AKI were either managed conservatively with fluid resuscitation or with dialysis. Ranson's score, CTSI and CRP values measured 48 hours after onset of symptoms were noted down for each patient and tabulated. A Ranson's score of more than 3 was considered as severe disease. CRP levels more than 6 was considered to be raised. Patients were followed up until death or discharge. The data tabulated was analysed with SPSS software v23. Descriptive statistics such as mean and percentage was used to describe the data. Pearson coefficient was used to study the correlation between the variables. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

During study period 72 patients of acute pancreatitis were studied. In present study majority of cases were from 31-40 years (33.33 %) followed by 41-50 years (22.22 %). We noted male preponderance (81.94 %) and male to female ratio was 4.54:1.

Table 1: Age and Gender distribution

Age (Years)	No. of patients	Percentage
19 – 30	14	19.44
31 – 40	24	33.33
41 – 50	16	22.22
51 – 60	11	15.28
61 – 70	6	8.33
≥71	1	1.39
Gender		
Male	59	81.94
Female	13	18.06

In present study alcoholism was the main etiological factor (73.61 %) followed by Biliary/ Gall stones (6.94 %), Choledochal cyst (4.17 %), Viral infections (4.17 %) and Idiopathic (11.11 %).

Table 2: Etiological factors

Etiology	No. of patients	Percentage (%)
Alcoholism	53	73.61
Biliary/ Gall stones	5	6.94
Choledochal cyst	3	4.17
Viral infections	3	4.17
Idiopathic	8	11.11

In present study 24 (33.33 %) patients developed complications. Complications noted were pleural effusion (18.06 %), ascites (13.89 %), organ failure (8.33 %), acute fluid collection (6.94 %), pseudocyst (5.56 %), pancreatic necrosis (4.17 %), venous thrombosis (2.78 %) and GI bleeding (1.39 %). All the complications were conservatively managed except for one patient with bilateral pleural effusion for whom bilateral intercostal drainage was done.

Table 3: Complications in acute pancreatitis

Complications	No. of patients	Percentage (%)
Pleural effusion	13	18.06
Ascites	10	13.89
Organ failure	6	8.33
Acute fluid collection	5	6.94
Pseudocyst	4	5.56
Pancreatic necrosis	3	4.17
Venous thrombosis	2	2.78
GI bleeding	1	1.39

In present study normal CRP levels (<6) were noted in 7 (9.72 %) patients, 39 (54.17 %) had CRP level 6 -150 and 26 (36.11 %) had CRP level >150. CRP level >150 was statistically significantly ($p<0.001$) associated with Ranson's score ≥ 3, thus CRP level >150 was predictor of severe disease.

Table 4: Correlation of CRP and Ranson's score

CRP	Ranson's score		Total
	< 3	≥ 3	
< 6	7 (9.72 %)	0	7 (9.72 %)
6-150	37 (51.39 %)	2 (2.78 %)	39 (54.17 %)
≥ 151	4 (5.56 %)	22 (30.56 %)	26 (36.11 %)

CRP level >150 was statistically significantly ($p<0.001$) associated with CT severity index (CTSI) ≥ 5, thus CRP level >150 was predictor of severe disease.

Table 5: Correlation of CRP and CT severity index (CTSI)

CRP	CT severity index (CTSI)		Total
	< 5	≥ 5	
< 6	6 (8.33 %)	1 (1.39 %)	7 (9.72 %)
6-150	35 (48.61 %)	4 (5.56 %)	39 (54.17 %)
≥ 151	7 (9.72 %)	19 (26.39 %)	26 (36.11 %)

DISCUSSION

Acute pancreatitis (AP) is an inflammatory disorder of the pancreas with a multifactorial pathogenesis, in which enzyme activation plays a central role in local pancreatic damage, causing systemic and peripancreatic tissue involvement.[6] There are many scores to help us to differentiate between MAP and SAP, which be generalized severity scores such as the APACHE II , The sequential Organ Failure Assessment (SOFA), Logistic Organ Dysfunction (LOD) or the Multiple Organ Dysfunction (MODS) scores or pancreatitis specific severity scores such as the Ranson Criteria, The Pancreatic Outcome Prediction Score, all which are generally cumbersome but do have their advantages.[7] Limitations of these scoring systems have been either the inability to obtain a complete score until at least 48 hours into the illness (Ranson and Glasgow scores) or the complexity of the scoring system itself (APACHE II). In study by Ganesh BN[8] common local complications were peripancreatic collection (28%) and pancreatic necrosis (12%), while 48 % had systemic complications. 50 % had mild disease and 50 % had severe disease as evidenced by the Ranson's score. In patients with severe disease raised CRP was noted. There was no statistically significant correlation between the CTSI and CRP values. 4 patients with CRP values more than 400 succumbed to the illness. CRP can serve as an inexpensive alternative to the conventional severity assessment methods for the prediction of severity and outcome of patients with acute pancreatitis. Deherkar JA *et al.*,[9] noted that mean serum CRP level of patients with Ranson"s score <3 was significantly higher as compared to mean serum CRP level of patients with Ranson"s score ≥3 (10.54±5.00 mg/l vs 7.29±3.94 mg/l). There was significant association of serum CRP and Ranson's score of patients. Similar findings were noted in present study. Trivikraman *et al.*,[10] found that the sensitivity and specificity of CRP were in predicting severity of acute pancreatitis were 66.7% and 86.3% respectively. The rapid response of CRP to changes in the intensity of the inflammatory stimulus suggests that it might be valuable in the assessment and monitoring of acute pancreatitis. Mathew B *et al.*,[11] studied 90 patients with acute pancreatitis according to CT severity grading, patients were divided into three groups as Group I (mild pancreatitis, n=32 patients), group II (moderate

pancreatitis, n=42) and group III (severe pancreatitis, n=16). The highest C-reactive protein values were detected on day 3 in all groups. There was significant correlation between severe pancreatitis and day 3 CRP with a p value <0.05. The highest sensitivity and negative predictive value (85.71% and 89.04%) was obtained for C-reactive protein cut-off at 150 mg/L. Staubli SM *et al.*,[12] noted that using a cut-off value from 110 to 150 mg/l, the sensitivity and specificity ranged from 38 to 61%, and 89 to 90%, respectively, at the time of hospital admission. Mohan Joshi *et al.*,[13] studied 50 patients of acute pancreatitis, CRP levels of 63mg/dl and above are significantly associated with increased time to recovery (p-0.004). A significant association was seen between the presence of complications and CT Severity Index (CTSI) >7, (p-0.0002). There was no significant correlation or association between the CRP levels and CTSI. High serum CRP levels have predicted prognosis as well as mortality in this study. In study by Khanna AK *et al.*,[14] an elevated CRP level and an increased BISAP score was found to have a statistically significant relation (p = 0.009 and p = 0.0002 respectively) to length of patient's stay in hospital and hence the severity. BISAP and CRP levels had a positive correlation with a p-value of 0.064. Among single biochemical markers, C-reactive protein (CRP) remains the most useful. Despite its delayed increase, peaking not earlier than 72 h after the onset of symptoms, it is accurate and widely available. As a single prognostic marker, an elevated C-reactive protein (CRP) concentration of greater than 150 mg/L indicates that acute pancreatitis has a complicated course with a sensitivity of 85% in the first 72 h after the onset of symptoms.[14] Similar findings were noted in present study. CRP is an acute phase reactant that can serve as an inexpensive alternative to the conventional severity assessment methods for the prediction of severity and outcome of patients with acute pancreatitis.

CONCLUSION

A CRP level of 150 mg/L at 48 hours after onset of symptoms can be used as a cut off value to predict a severe disease in patients of acute pancreatitis. However, further studies on a larger scale are needed for better validation of results and for determining the effects of early intervention in the prevention of a predicted severe disease.

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