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Original Research Article

C reactive protein as a prognostic indicator of severity in patients with acute pancreatitis

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ABSTRACT

Background: Acute pancreatitis ranges from a mild illness to a severe disease with high morbidity and mortality. Severity affects the treatment and outcome. The existing scoring systems for assessment of its severity require are time consuming and expensive. This study was an attempt to evaluate the effectiveness of C-reactive protein (CRP) as a prognostic indicator and a marker of severity of acute pancreatitis.
Methods: This was a prospective observational study conducted between among 50 patients diagnosed with acute pancreatitis. The Ranson's score and CTSI was calculated for these patients. CRP levels were measured 48 hours after the onset of symptoms. They were observed for the development of local and systemic complications, and outcome. These were compared with the CRP values. 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: 30 of the 50 patients had no local complications. 14 patients (28%) had peripancreatic collection and 6 (12%) had pancreatic necrosis. 24 of the 50 patients had systemic complications (48%). 25 patients had mild disease and 25 had severe disease as evidenced by the Ranson's score. These 25 patients with severe disease also had raised CRP ($p<0.05$). There was no statistically significant correlation between the CTSI and CRP values. 4 patients with CRP values more than 400 succumbed to the illness.
Conclusions: 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.

Keywords: Acute pancreatitis, CRP, Prognostic indicator, Severity of disease

INTRODUCTION

The incidence of acute pancreatitis has increased over the past 20 years. It has been documented as one of the most common causes of hospital admission for gastrointestinal illness.[1] The disease ranges from a mild self-limiting illness which improves with supportive care, to a severe illness with multiple organ failure and high mortality. Around 10-20% patients have a rapidly progressive inflammatory response associated with prolonged length of hospital stay and significant morbidity and mortality. The mortality rate in patients with mild pancreatitis is less than 1 while that in patients with severe pancreatitis ranges from 10-30%.[2] Alcohol consumption and cholelithiasis have been reported as the most common ethological factors in the development of acute pancreatitis. Other documented causes include pancreatic divisum, intraduct papillary mutinous tumour, endoscopic retrograde cholangiopancreaticography, hyperlipidemia, drug induced pancreatitis, hypercalcemia, and idiopathic causes.[3] The diagnosis of acute pancreatitis is made by clinical, biochemical and radiological methods. The classical history and examination findings should raise a clinical suspicion of acute pancreatitis. The diagnosis had traditionally been made by the threefold rise in the levels of pancreatic enzymes. In acute pancreatitis, the

pancreatic enzymes amylase, lipase, elastase, and trypsin are simultaneously released into the bloodstream.[4] Lipase has a higher diagnostic accuracy compared to amylase as the serum lipase levels are elevated for a longer period.[5]

Despite the etiology, the treatment of acute pancreatitis remains more or less the same, and is largely dependent upon the severity of the illness. Hence, the assessment of severity of acute pancreatitis has been of interest for decades now. Various methods has been developed for the assessment of severity and thus the prediction of outcome of acute pancreatitis. These include acute physiology and chronic health evaluation (APACHE) II, Ranson's score, CT severity index, bedside index for severity in acute pancreatitis, and measurement of acute phase reactants and procalcitonin.[6,7] Of these, the APACHE II scoring system has shown to have the highest accuracy in predicting severe acute pancreatitis when compared with other scoring systems.[8] However, most of these scores involve the measurement of multiple parameters, which can be time consuming and expensive. Hence, there is a need for development of a simpler and inexpensive test to assess the severity of acute pancreatitis and predict the outcomes.

C reactive protein (CRP) is a pentameric protein synthesized by the liver, whose levels rise in response to any inflammatory process. CRP is an acute-pchase reactant protein that is primarily induced by the IL-6 action on the gene responsible for transcription of CRP during the acute phase of an inflammatory/infectious process. It's levels rise in plasma after about 48 hours after the initiation of the inflammatory process. High levels of CRP, greater than 10 mg/dL, are associated with infection about 80% of the time. If the level exceeds 50%, then that number rises to around 94%.[9] Being nonspecific, it cannot be used in the diagnosis of acute pancreatitis. However, being an acute phase reactant, it has the potential to serve as an indicator of severity and as a prognositic indicator. It has the added advantage of being inexpensive. This study was an attempt to evaluate the effectiveness of CRP as a prognostic indicator and a marker of severity of acute pancreatitis.

METHODS

This was prospective observational study done from July to August 2019 at Victoria hospital. 50 patients were included in the study.

Selection 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.

Patients below age 18 and patients not consenting for participation in the study were excluded.

Statistical analysis

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.

50 patients presenting to Victoria Hospital, who were diagnosed with acute pancreatitis were selected for the study after obtaining verbal consent. The 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. These patients were subjected to 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) was calculated for all the patients. CRP levels were measured 48 hours after the onset of symptoms.

The patients were managed conservatively and were followed up until death or discharge. They were observed for the development of 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). 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. Patient data such as age, sex, etiology of pancreatitis, values of pancreatic enzymes, local and systemic complications (if any), 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.

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

The age of the patients ranged from 19-60 years with a mean of 37.56±11.10 years. Most of the patients belonged to the 31-40 age group. 38 (76%) of the patients were males and 12 (24%) were females. There was no significant difference in the CRP levels between males and females.

The etiology of acute pancreatitis in our study is depicted in Table 1.

Table 1: Etiology of acute pancreatitis.

Etiology	Number	Percentage
Alcohol induced	30	60
Biliary pancreatitis	15	30
Hypertriglyceridemia	4	8
Drug induced pancreatitis	1	2

60% of the patients had alcohol induced acute pancreatitis, 30% had biliary pancreatitis, 8% had hypertriglyceridemia as the etiological factor while 2% had drug induced pancreatitis.

Analysis is the enzyme levels revealed the following. The mean amylase was 700 with a standard deviation of 465, and the mean lipase was 644 with a standard deviation of 344. These values did not show a statistically significant correlation with CRP values (p >0.05) (Table 2).

Table 2: Analysis of enzyme levels.

Enzyme	Mean	Standard deviation	P value	Correlation with CRP
Amylase	700	465	>0.05	None
Lipase	644	344	>0.05	None

Of the 50 patients, 30 had no local complications while 20 developed local complications. 14 patients (28%) had peripancreatic collection and 6 (12%) had pancreatic necrosis (Figure 1).

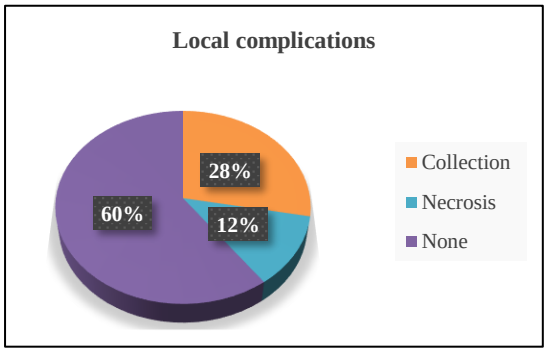

Figure 1: Local complications of acute pancreatitis.

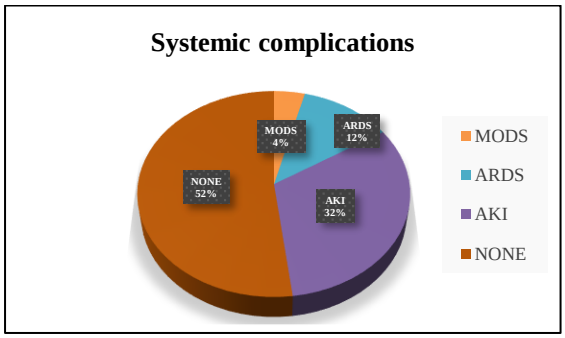

Figure 2: Systemic complications of acute pancreatitis.

24 of the 50 patients had systemic complications (48%). Of these, 16 patients had AKI, 2 patients had ARDS and 2 patients had MODS (Figure 2). Of the 16 patients with AKI, 8 underwent dialysis, while 8 were managed with fluid resuscitation alone.

On assessment of the Ranson's score calculated for the patients, it was observed that 25 patients had Ranson's score <3 (mild disease) while 25 had >3 (severe disease) (Table 3).

Table 3: Ranson's score of patients.

Ranson's score	Number of patients	Percentage
<3	25	50
>3	25	50

32 patients had CTSI between 0-3, 13 patients had CTSI between 4 - 6 while 5 patients had CTSI between 7 - 10 (Table 4).

Table 4: CTSI of patients.

CTSI	Number of patients	Percentage
0-3	32	64
4-6	13	26
7-10	5	10

On analysis of the CRP values, it was found that the 25 patients who had severe disease as categorised by Ranson's score also had raised CRP values, while the rest had normal values of CRP. There was a positive correlation between the Ranson's score and CRP values (p<0.05), while there was no such correlation noted between CTSI and CRP. Of the 50 patients, 46 survived while 4 succumbed to the illness. The CRP levels of the patients who died was more than 400.

DISCUSSION

This prospective observational study was conducted among 50 patients diagnosed to have acute pancreatitis, to evaluate the role of CRP as a prognostic marker in predicting the severity and outcome of acute pancreatitis. It was observed in this study that the CRP values have a positive correlation with the Ranson's score, while they had no correlation with the CTSI or the levels of the enzymes. CRP levels of more than 400 was an indicator for mortality.

CRP is an acute phase reactant produced by the hepatocytes. Its level rises in inflammatory conditions10. The synthesis of CRP in the liver is induced by cytokines such as interleukins. The time duration between onset of symptoms and rise of CRP is usually around 72 hours. This delayed rise of CRP levels and its non-specific nature as an inflammatory marker are the disadvantages of its practical use.[11] Despite this, its wide availability, ease of measurement and the fact that it is inexpensive, make it the most frequently used single biomarker for

assessment of severity of acute pancreatitis.[10] However, before measurement of CRP, other inflammatory conditions such as cholangitis and pneumonia should be ruled out.[11] Few of the reports on the role of CRP in predicting acute pancreatitis were not promising. Tenner et al. reported that CRP has no significant predictive role in assessing the severity of AP in the first 72 hours after admission.[12] However, the findings of this study is consistent with the findings of Deherkar et al, who concluded that measured CRP was a simple and effective method to assess the severity of acute pancreatitis.[12-13] Pezzelli et al found that CRP values greater than 100 mg/l indicate severe acute pancreatitis in 60-80% of the patients with pancreatitis.[14]

This is also consistent with the findings of Joshi et al who found that high serum CRP levels accurately predicted the prognosis and mortality of the patients with acute pancreatitis.[15] Trivikraman et al found that the sensitivity and specificity of CRP were in predicting severity of acute pancreatitis were 66.7% and 86.3% respectively.[16] Fossard et al stated that standard scores and CRP remain the most effective methods in routine use for the prediction of severity of acute pancreatitis between Day 2 and 317. Aaron et al noted in their study that the interval change in the CRP is a comparable measure to absolute CRP in the prognostification of severity of acute pancreatitis.[18] They suggested that a rise of >90 mg/dl from admission or an absolute value of >190 mg/dl at 48 hours predicts severe disease with the greatest accuracy.

The role of CRP could also be extended to determine the outcomes of Acute Pancreatitis following treatment, as evidenced by Wang et al in their study.[19] They concluded that lower serum CRP levels prior to and after treatment led to better therapeutic effects of ulinastatin combined with somatostatin in patients with severe acute pancreatitis. However, more studies are needed in this regard for better validation.

CONCLUSION

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. 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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