



## A Study on C-Reactive Protein as an Inflammatory Marker in Comparison with CT Severity Index of Balthazar in Predicting Severity of Acute Pancreatitis

Basil Mathew<sup>1</sup>, Rajagopalan G<sup>2\*</sup>, Sabu S Jeyasekharan<sup>3</sup> and Bala Vidyasagar<sup>3</sup>

<sup>1</sup>Department of Urology, Stanley Medical College, Chennai, India

<sup>2</sup>Department of Surgery, Jawaharlal Institute of Post Graduate Medical Education and Research, India

<sup>3</sup>Department of Surgery, Dr. Jeyasekharan Hospital and Nursing Home, India

### Abstract

**Introduction:** To determine relation between the C-reactive protein and acute pancreatitis, and to estimate the prognostic value of C-reactive protein in early Prediction of severity of acute pancreatitis.

**Material and Methods:** During 2013-14, 90 patients with acute pancreatitis were included in the study. The clinical data, diagnostic procedures, and laboratory values were analyzed. C-reactive protein concentration in serum was measured on day 1, 2, and 3 after admission and a CT scan was done 72 h after admission. According to CT severity grading, patients were divided into three groups. Group I which is mild pancreatitis consisted of 32 patients, group II which is moderate pancreatitis consisted of 42 patients and group III which is severe pancreatitis consisted of 16 patients. The presence of correlation if any, between elevated levels of C-reactive protein and severity of acute pancreatitis in each group was analyzed by Spearman's test and was found to be significantly correlating with a p value <0.05 on day 3 CRP in patients with severe disease. The sensitivity, specificity, positive and negative predictive values for different C-reactive protein concentration cut-off (100 mg/l to 170 mg/l) were calculated.

**Result:** 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.

**Conclusion:** The results of our study show that C-reactive protein values increase significantly in early stages of acute pancreatitis and it is an important prognostic marker of severe pancreatitis with pancreatic necrosis. The highest sensitivity and negative predictive value for CRP is 150 mg/L in severe pancreatitis. The patients with C-reactive protein below 150 mg/l are at low risk to develop severe pancreatitis with pancreatic necrosis.

**Keywords:** Acute pancreatitis; C-reactive protein; Pancreatic necrosis

### Introduction

Acute pancreatitis is a disease with wide clinical variation, which makes its diagnosis complex. Serum amylase measurement is a standard diagnostic method, although it was shown to be unable to recognize in 19% to 32% of acute Pancreatitis patients. The severity of acute pancreatitis forms a continuum, and the average mortality rate approaches 2% to 10%. Most of the cases are mild and conservative treatment results in a rapid recovery in most of them. However, severe acute pancreatitis constitutes 15% to 20% of all cases. In recent decades, mortality rate of severe acute pancreatitis has decreased from 30% to 80% to 15% to 20% [1,2].

There are important reasons to define and stratify the severity of acute pancreatitis. First, on admission, it is important to identify patients with potentially severe acute pancreatitis who require aggressive early treatment. Second, in a secondary care setting, clinicians need to identify such patients for possible transfer to specialist care. Third, for specialists who receive such referrals, there are advantages to stratifying these patients into subgroups based on the presence of persistent organ failure and local or systemic complications. The Atlanta classification defines three degrees of

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#### \*Correspondence:

Rajagopalan G, Department of Surgery,  
Jawaharlal Institute of Post Graduate  
Medical Education and Research,  
Puducherry - 6, India, Tel: +91-  
8220408324;

E-mail: prash1108@gmail.com

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severity: Mild acute pancreatitis, moderately severe acute pancreatitis, and severe acute pancreatitis [3,4].

Terminology that is important in this classification includes transient organ failure, persistent organ failure, and local or systemic complications. Transient organ failure is organ failure that is present for <48 h. Persistent organ failure is defined as organ failure that persists for >48 h. Local complications include peripancreatic fluid collections and acute necrotic collections, while systemic complications can be related to exacerbations of underlying comorbidities related to the acute pancreatitis.

C-Reactive Protein (CRP) is one of the acute phase reactants synthesized by the liver in response to interleukin-1 and interleukin-6. Many studies conclude that levels of CRP above 150 mg/L at 48 h discriminate severe from mild disease. At 48 h, CRP above 150 mg/L has a sensitivity, specificity, positive predictive value, and negative predictive value of 80, 76, 67, and 86 percent, respectively, for severe acute pancreatitis [5]. CRP rises steadily in relation to the severity of pancreatitis, is inexpensive to measure, and testing is readily available [6,7]. As a result, it can be used to help predict the severity of pancreatitis, especially at 48 h. The rise in CRP level was correlated with CT severity index of Balthazar in determining the severity of illness in acute pancreatitis.

## Materials and Methods

This was a longitudinal analytical study of inpatients clinically diagnosed as acute pancreatitis who presented to the department of surgery, Dr. Jeyasekaran Hospital, Nagercoil, Tamilnadu from January 2014 to December 2015 for a period of 2 yrs. A total of 90 patients with acute pancreatitis were analyzed during this study period. For all patients who presented with signs and symptoms of acute pancreatitis, a detailed history including patient details, symptomatology and positive examination findings were recorded as per the proforma.

Serial C-reactive protein levels were assessed at 24, 48 and 72 h after the admission and the time gap between the onset of symptoms and maximal elevation of C-reactive protein were assessed and there by correlating with the severity of disease which was further assessed with CECT abdomen. Patients were categorized in to three groups (mild, moderate and severe) based on the CT severity index of pancreatitis. Spearman's correlation test was done to find out significance of correlation between CT severity index and CRPs of all three days.

The sensitivity, specificity, positive predictive value and negative predictive value were calculated for the day showing significant correlation. Receiver Operator Characteristics curve (ROC) was plotted to find out whether a particular day CRPs would be a good predictive marker of the severity of the disease. The Area under the curve was also generated to depict the same. The cut off value of CRP with the maximum sensitivity and specificity was inferred from the ROC curve. SPSS version 16.0 software was used to perform statistical analysis.

## Results and Observations

A total of 90 patients diagnosed with acute pancreatitis were enrolled in the study during a period from January 2014 to December 2015. The aim of the study was to establish the presence of correlation if any, between elevated levels of C-reactive protein and severity of acute pancreatitis, which was analyzed by Spearman's test and was

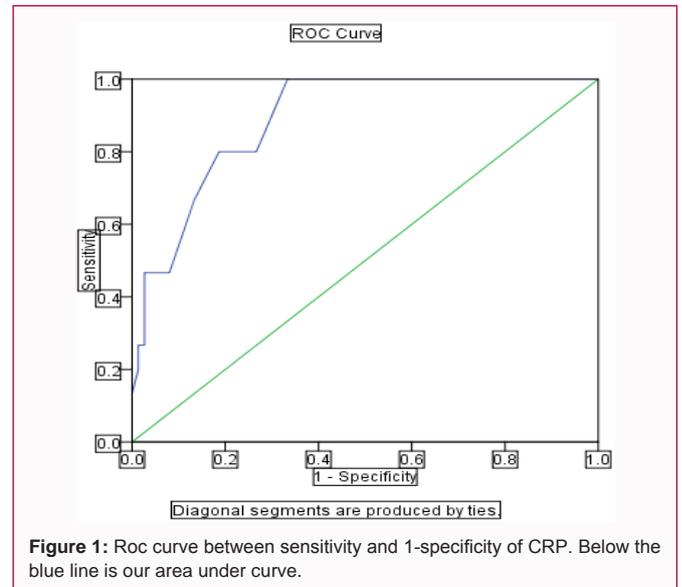


Table 1: Stratification of severity using ct severity index.

CT Severity Index	Description of Pancreatitis	No. of Patients	Percentage
1-3	Mild	32	35.56%
4-6	Moderate	43	47.78%
7-10	Severe	15	16.67%

Table 2: Mean CRP's of moderate and severe pancreatitis groups.

CRP	CT Severity Index	Mean	Standard Deviation	P Value
Day 1	Moderate	40.2791	27.91	0.517
	Severe	45.4667	21.73	
Day 2	Moderate	105.93	25.26	0.06
	Severe	122.67	29.73	
Day 3	Moderate	148.2	22.02	0.001
	Severe	176.2	25.45	

Table 3: Sensitivity and specificity of CRP values on day 3.

CRP Value (Mg/L)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
100	72	28	25	75
110	72	39.33	25	83.33
120	73.08	45.36	26.39	86.27
130	79.41	50.54	36.99	87.04
140	79.59	61.54	52.7	84.85
150	<b>85.71</b>	<b>73.03</b>	<b>66.67</b>	<b>89.04</b>
160	82.43	65.71	83.56	63.89
170	80.68	63.64	94.67	29.17

found to be significantly correlating with a p value <0.05 on day 3 CRP.

CT severity index was the gold standard test adopted to find out the severity of pancreatitis. Patients were divided in to three groups based on CT severity index. As per Table 1, most of the patients fall under mild and moderate variety of pancreatitis. This finding was similar to that of the world literature.

Mean CRP's of moderate and severe group were calculated. Regression analysis was done to find out which group of severity in

**Table 4:** Area under roc curve.

Area	Standard Error <sup>a</sup>	Aymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.891	0.37	0	0.819	0.963

day 3 would be predictive of the CT severity Index. Regression analysis revealed significant prediction between severe category of CRPs of day 3 and CT severity index. ROC curve was also generated to find out the cut-off with maximum sensitivity and specificity. Receiver operator characteristics curve which is a plot between the sensitivity and specificity of CRP was done to calculate the accuracy as the area under the curve would denote the significance of association.

As per CT severity index only patients with moderate and severe pancreatitis would develop complications of the same, which would add on to the morbidity of disease status. Hence patients in these groups were selected for further study.

Table 2 tabulates the mean CRP's in moderate and severe group of pancreatitis in all 3 days. When a P value was calculated between the mean CRP's of each day, significance could only be elicited for day 3 values.

As mentioned above, Spearman's correlation coefficient was <0.05 on day 3 CRP. The moderate and severe groups were chosen for further analysis as the patients in these groups had higher chance of development of complications as documented by previous studies [8,9,10,11].

- Mean CRP's of moderate and severe group were calculated.
- Regression analysis was done to find out which group of severity in day 3 would be predictive of the CT severity Index. Regression analysis revealed significant prediction between CRPs of severe category on day 3 and CT severity index.
- The sensitivity and specificity of different values of CRP on day 3 was calculated taking CT severity index as the gold standard test.

Table 3 tabulates the sensitivity, specificity, positive predictive value and negative predictive values of CRP on day 3, taking CT severity index as the gold standard. A cut off of 150 mg/L gave highest sensitivity and specificity followed by 160 mg/L.

Receiver operator characteristics curve was generated to find out the cut-off with maximum sensitivity and specificity. ROC curve was done to calculate the accuracy and area under the curve. ROC curve is a plot between the sensitivity and 1-specificity of CRP. Table 4 tabulates the total area under ROC curve for CRP values of day 3 which was found to be 89.1%. Figure 1 shows the ROC curve characteristics and area under curve.

## Discussion

Acute pancreatitis continues to challenge clinicians due to the varied clinical course and outcome which cannot be predicted. Most of the mild and even moderately severe forms of pancreatitis resolve with minimal morbidity. It is almost always the severe form of acute pancreatitis which results in increase in morbidity, the mortality rate of which is 15% to 20% as per a study conducted by Mofodi et al. [11]. This is where the importance of a widely available and inexpensive serum marker which can predict the severity of pancreatitis so that the treatment strategy could be determined.

In our study conducted in The Department of General surgery at Dr. Jeyasekaran Hospital and Nursing Home from January 2014 to December 2015 for a period of two years, 90 patients with acute pancreatitis were studied. Clinical history, physical examination findings and laboratory investigations were recorded for each patients including serial CRP monitoring for the first 3 days after admission. A CT scan was done 72 h after admission and CT severity index was estimated and the patients were categorized in to 3 groups mild, moderate and severe based on the severity of disease (Table 1).

Patients were divided in to 3 groups based on CT severity index in to mild, moderate and severe form of pancreatitis and the incidence of each of these groups were 35.5%, 47.7% and 16.6% respectively. This observation was comparable to a study conducted by Isenmann et al. which found out the incidence of severe form of pancreatitis to be 15% to 20% [12].

C-Reactive Protein (CRP) is one of the acute phase reactants made by the liver in response to interleukin-1 and interleukin-6. It is a nonspecific marker of inflammation and its use has been widely studied in pancreatitis. But no studies could specify a cut off value for CRP when it could predict severe form of acute pancreatitis [13]. In a study conducted by Treister et al. there was a significant elevation of CRP after 72 h of onset of symptoms in case of severe pancreatitis with necrosis [14].

In our study, serial CRP values were obtained in all patients for the first 3 days. Mean CRP for moderate and severe group of pancreatitis based on CT severity index were calculated (Table 2). The CRP values on 3<sup>rd</sup> day after admission in moderate and severe form of pancreatitis (as predicted by CT) differed significantly with a P value <0.05 (Table 2). This observation concludes that even though the CRP values are elevated in every case of acute pancreatitis, high value of CRP on the 3<sup>rd</sup> day after the onset of symptoms suggest that the patient has severe pancreatitis and has a high probability of pancreatic necrosis. This observation is similar to that of study conducted by Treister et al. [14].

The sensitivity, specificity, positive predictive value and negative predictive values of C-reactive protein in predicting the severity of acute pancreatitis were calculated, taking CT severity index as the gold standard test. The above mentioned parameters were calculated for a series of CRP values from 110 mg/L to 170 mg/L as illustrated in Table 3. CRP value of 150 mg/L had the highest sensitivity and specificity of 85.71 and 73.03 respectively. This observation was similar to study conducted by Larvin et al. [15] and Dervenis et al. [16].

## Conclusion

C-reactive protein is an early predictor for severity of acute pancreatitis which has high sensitivity, high positive predictive value, and rapid in its assay, readily available in all clinical laboratories and relatively cheap. A CRP level of 150 mg/L on 3<sup>rd</sup> day after onset of symptoms can be used as a cut off value to predict a severe disease and CT scan which is an expensive investigation can be reserved for patients with a CRP value of greater than 150 mg/L on 3<sup>rd</sup> day after onset of symptoms.

## References

1. Satoh K, Shimosegawa T, Masamune A, Hirota M, Kikuta K, Kihara Y, et al. Nationwide epidemiological survey of acute pancreatitis in Japan. *Pancreas*. 2011;40(4):503-7.
2. Hirota M, Shimosegawa T, Masamune A, Kikuta K, Kume K, Hamada, et

- al. The sixth nationwide epidemiological survey of chronic pancreatitis in Japan. *Pancreatology*. 2012;12(2):79-84.
3. Vege SS, Gardner TB, Chari ST, Munukuti P, Pearson RK, Clain JE, et al. Low mortality and high morbidity in severe acute pancreatitis without organ failure: A case for revising the Atlanta classification to include "moderately severe acute pancreatitis". *Am J Gastroenterol*. 2009;104(3):710-15.
  4. Petrov MS, Windsor JA. Classification of the severity of acute pancreatitis: How many categories make sense? *Am J Gastroenterol*. 2010;105(1):74-6.
  5. Larvin M. Assessment of clinical severity and prognosis. In: *The Pancreas*. Beger HG, Warshaw AL, Buchler MW, editors. Blackwell Science, Oxford. 1998. p. 489.
  6. Büchler M, Malfertheiner P, Schoetensack C, Uhl W, Beger HG. Sensitivity of antiproteases, complement factors and C-reactive protein in detecting pancreatic necrosis. Results of a prospective clinical study. *Int J Pancreatol*. 1986;1(3-4):227-35.
  7. Leese T, Shaw D, Holliday M. Prognostic markers in acute pancreatitis: Can pancreatic necrosis be predicted? *Ann R CollSurg Engl*. 1988;70(4):227-32.
  8. Singh VK, Bollen TL, Wu BU, Repas K, Maurer R, Yu S, et al. An assessment of the severity of interstitial pancreatitis. *Clin Gastroenterol Hepatol*. 2011;9(12):1098-103.
  9. Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. *Gut*. 2004;53(9):1340-4.
  10. Muckart DJ, Bhagwanjee S. American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference definitions of the systemic inflammatory response syndrome and allied disorders in relation to critically injured patients. *Crit Care Med*. 1997;25(11):1789-95.
  11. Mofidi R, Duff MD, Wigmore SJ, Madhavan Kk, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. *Br J Surg*. 2006;93(6):738-44.
  12. Isenmann R, Buechler M, Uhl W, alfertheiner P, Martini M, Beger HG. Pancreatic necrosis: An early finding in severe acute pancreatitis. *Pancreas*. 1993;8(3):358-61.
  13. Wilson C, Heats A, Shenkin A, Imvie CW. C-reactive protein, anti proteases and compliment factors as an objective marker of severity in acute pancreatitis. *Br J Surg*. 1989;76(2):177-81.
  14. Triester SL, Kwodley KV. Prognostic factors in acute pancreatitis. *J Clin Gastroenterol*. 2002;34(2):167-76.
  15. Larvin M. Assessment of clinical severity and prognosis. In: *The Pancreas*. Beger HG, Warshaw AL, Buchler MW, editors. Blackwell Science, Oxford. 1998;14:489-90.
  16. Dervenis C, Johnson CD, Bassi C, Bradley E, Imrie CW, McMahon MJ, et al. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini Consensus Conference. *Int J Pancreatol*. 1999;25(3):195-210.