

Original research article

**CRP: AN AID TO ASSESS THE SEVERITY,
COMPLICATIONS AND PROGNOSIS OF ACUTE
PANCREATITIS**

¹Dr. Manoranjan UD, ²Dr. Divyarani MN, ³Dr. Abhijit Patil

¹Associate Professor, Department of Surgery, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

²Assistant Professor, Department of Pathology, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

³Assistant Professor, Department of Orthopedics, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

Corresponding Author:

Dr. Abhijit Patil

Abstract

Background: Acute pancreatitis, a routine surgical emergency encountered, intensity of treatment depends on proper prognostic indicators to assess the severity of the disease. The present study investigated the use of C-reactive protein (CRP) as prognosticator of the severity of the disease.

Methods: Fifty-eight patients with acute pancreatitis were studied. Serum samples for measurement of CRP were collected on the day of admission and additionally on the 5th day, CT Balthazar scoring was done in each of the cases and severity was assessed.

Results: The mean serum CRP in people with mild pancreatitis was 39U/l and that in the those suffering with severe pancreatitis was 127.93, this difference was statistically significant ($p<0.001$).

Conclusions: Measurement of CRP levels seems to be an accurate method in order to assess the extent and persistence of the inflammatory process and progression of acute pancreatitis to severity and complications.

Keywords: CRP, acute pancreatitis, severity and complications

Introduction

Discovered by Tillett and Francis in 1930, it was initially thought that CRP might be a pathogenic secretion since it was elevated in a variety of illnesses. The later discovery of hepatic synthesis demonstrated that it is a native protein. CRP was so named because it was first identified as a substance in the serum of patients with acute inflammation that reacted with the somatic 'C' carbohydrate antigen of Pneumococcus.

It is found in the blood plasma, a pentameric protein whose levels are seen to increase to various inflammatory reactions in the body. An acute phase reactant whose levels increase following the increase in the levels of interleukin-6 secreted by T cells and

macrophages.

Measuring and charting CRP values can prove useful in determining disease progress or the effectiveness of treatments.

The acute pancreatitis (acute hemorrhagic pancreatic necrosis) is characterized by acute inflammation and necrosis of pancreas parenchyma, focal enzymic necrosis of pancreatic fat and vessel necrosis (hemorrhage). These are produced by intrapancreatic activation of pancreatic enzymes ^[1, 2]. C reactive protein to changes in the intensity of the inflammatory stimulus suggest that it might be valuable in the assessment and monitoring of acute pancreatitis. The clinical problem of particular interest was to test whether C reactive protein measurements could reflect the severity of the attack and thereby provide a warning of the likely development of pancreatic collections (pseudocyst, abscess and necrosis), which can arise insidiously and be life threatening ^[3, 4].

Changes in the level of CRP are an indication of an on going variation in the pancreatic inflammatory process, thus making it a valuable tool in the assessment, monitoring and the propensity towards developing complications associated with acute pancreatitis like pseudocyst formation, collections, abscess and pancreatic necrosis.

We have studied the intensity of the C reactive protein response and its rate of change in cases of acute pancreatitis of varying severity. The value of this test was compared with the information provided by the white cell count, standard indices of inflammation, were used as reference data.

Determination of the severity of acute pancreatitis is difficult in the early phase after onset, and difficulties are often encountered decision making, if to initiate intensive care during this early phase. Therefore, there is real need for a simple and inexpensive method that can accurately evaluate the severity of acute pancreatitis.

The results indicate that C reactive protein can identify severe pancreatitis which may not be obvious at its onset, and lay the basis for prospective trials.

Methods

Fifty eight patients were enrolled in the study, conducted in department of surgery, Bangalore Medical college and research institute during the period august 2019 to august 2020. Further information regarding the patients clinical features and sociodemographic data was recorded.

58 patients with acute pancreatitis were studied, which included 56 men and 2 women. Patients with presentation more than 48 hours from the onset of symptoms, pancreatic tumor, prior pancreatic surgery, renal or hepatic failure, trauma and diabetic ketoacidosis were excluded from the study.

The diagnosis was based on a plasma amylase value in excess of 1000 IU/l. The patients were treated conventionally, they were discharged from the hospital when the attack was thought to have subsided according to the routine clinical criteria. Ultrasound imaging was done routinely along with all routine blood investigations including CRP on day 1 and 5, serum amylase and lipase.

Computed tomography with Balthazar scoring was performed in each case.

Each attack was classified as mild or severe according to revised Atlanta criteria (2012). A severe attack was defined as one which resulted in more than 10 days in hospital, one which gave rise to a complication such as a pseudocyst, abscess,

collections or at times even death or one which was fatal with organ failure of more than forty-eight hours.

All the patients were closely followed according to the Atlanta criteria, for the development of local (pancreatic collection, ascites, necrosis, and pseudocyst formation) or systemic (ARDS, MODS, septic shock) complications and managed accordingly (ERCP, CT-guided drainage, surgery).

Results

Table 1: Demographic details

	Frequency	Percent	Valid Percent
Female	2	3.4	3.4
Male	56	96.6	96.6
Total	58	100.0	100.0

In our study, out of 58 patients-56 were males, 2 were females.

Table 2: Clinical Diagnosis-Severity

	Frequency	Percent	Valid Percent
Mild	35	60.3	60.3
Moderate	8	13.8	13.8
Severe	15	25.9	25.9
Total	58	100.0	100.0

Table 3: Serum amylase, CRP and Total Leukocyte count Statistics with scoring system

	AMYLA SE	CRP Day 1	CRP Day 5	TLC day 1	TLC day 5	CT BALTHAZAR Score
N Valid	58	58	58	58	58	58
Missing	0	0	0	0	0	0
Mean	1222.52	51.41	64.67	10283.8	11830.1	4.59
Median	1188.00	54.00	50.00	9867.00	9880.00	4.00
Std. Deviation	209.627	27.602	42.294	2344.63	4351.30	2.464
Minimum	1000	11	9	5690	6643	0
Maximum	1997	119	168	16450	22678	9

58 patients with acute pancreatitis were admitted in the General surgery department of Victoria hospital, of which 96.6% of the patients were males, and 25.9% suffered from severe acute pancreatitis in whom one of the local complications such as fluid collection, haemorrhage, and necrosis were identified and appropriate treatment administered. Serum CRP levels between the 2 groups were compared on day 5, and it was noted that in the severe group the mean CRP levels were 127.93 to the mild group in whom it was 39.00. On analysing the data it was noted that the p value is <0.01 and hence significant, indicating that the CRP value of more than 100 is a good prognostic indicator for the progression towards severity with local complications in patients with acute pancreatitis.

Table 4: Clinical diagnosis

Acute pancreatitis	N	CRP day 5	P
Clinical diagnosis			
Mild	35	39.00	<0.01
Moderate	8	58.38	
Severe	15	127.93	
Total	58	64.67	168

Discussion

Acute pancreatitis, regardless its aetiology, leads to the disruption of the normal stimulation-secretion axis within the pancreatic acinar cell. This ultimately triggers a premature enzyme activation system (concerning mainly the metabolism of trypsinogen to trypsin) and a consequent cascade of coactivation of other pancreatic proenzymes (such as proelastase, chymotrypsinogen, procarboxypeptidase, and phospholipase A2), causing autodigestion of the gland^[1, 2, 3, 4]. Blood monocytes and neutrophils migrate to the site of inflammation and secrete inflammatory mediators^[1].

In cases of acute pancreatitis with limited extent of injury, spontaneous resolution of the inflammation occurs. When inflammation persists, mediators are released to the circulation leading to the malfunction of various organs and a systematic inflammatory response (SIRS)^[1, 2, 4]. This progression from acute pancreatic inflammation to SIRS and MODS may often be fulminant as approximately 50-60% of severe acute pancreatitis deaths occur within the first week^[1]. This systemic reaction combined with local complications such as fluid collection, haemorrhage, and necrosis necessitates an early prediction in order to achieve a more aggressive treatment. Most of the deaths reported after the first weeks are due to secondary pancreatic infection and necrosis^[1, 5].

Already from the decade of 1980s staging of the severity of acute pancreatitis using serum criteria was employed^[1, 2, 3]. Many clinical trials have employed the use of either cytokines^[3, 6, 7, 8] or serum amyloid A and procalcitonin (PCT)^[5, 6, 7, 9] as prognosticators of the severity of acute pancreatitis.

C-reactive protein (CRP) that is synthesized by the hepatocytes is a nonspecific inflammatory marker routinely used in assessment of severity of acute pancreatitis^[10].

^{11, 12]}. Its synthesis is induced by the release of interleukins 1 and 6 thus a serum peak is usually delayed (>3rd day of onset of pain)^[10, 11, 12].

Acute pancreatitis, regardless its aetiology, leads to the disruption of the normal stimulation-secretion axis within the pancreatic acinar cell. This ultimately triggers a premature enzyme activation system (concerning mainly the metabolism of trypsinogen to trypsin) and a consequent cascade of coactivation of other pancreatic proenzymes (such as proelastase, chymotrypsinogen, procarboxypeptidase, and phospholipase A2), causing autodigestion of the gland^[10, 12, 14]. Blood monocytes and neutrophils migrate to the site of inflammation and secrete inflammatory mediators^[10].

In cases of acute pancreatitis with limited extent of injury, spontaneous resolution of the inflammation occurs. When inflammation persists, mediators are released to the circulation leading to the malfunction of various organs and a systematic inflammatory response (SIRS)^[10, 15, 16]. This progression from acute pancreatic inflammation to SIRS and MODS may often be fulminant as approximately 50-60% of severe acute pancreatitis deaths occur within the first week^[10, 16]. This systemic reaction combined with local complications such as fluid collection, haemorrhage and necrosis necessitates an early prediction in order to achieve a more aggressive treatment. Most of the deaths reported after the first weeks are due to secondary pancreatic infection and necrosis^[10, 17]. Some authors support that systematic inflammatory response may occur even in the absence of pancreatic necrosis^[18].

Many authors suggest that CRP may accurately predict infected pancreatic necrosis. Other studies over the last few years have suggested that serum levels of CRP may be used to identify patients who are prone to develop local or systemic complications^[18]. Early identification of such patients could lead to a more intensive management that would result to a decreased morbidity and mortality of that potentially fatal disease^[18]. In the present study we identified significantly higher serum levels of Serum CRP levels in the severe group when compared to those with mild to moderate disease. On admission, mean plasma levels of CRP did not show any significant difference between two groups but on day 5, significantly higher values for CRP were observed on the group of patients with severe pancreatitis. In all patients of the mild group resolution occurred with supportive treatment within less than one week and no local or systemic complications were identified. On the contrary, the majority of patients in the severe group developed several either serious (ARDS, MODS, septic shock, pancreatic necrosis) or less important complications.

We believe that the persistence of high levels of CRP levels during the first week of severe acute pancreatitis may be related to the development of late local and systemic complications, The aim of our study was to investigate the correlation of cytokines with the severity and prognosis of acute pancreatitis. Our findings suggest the pivotal role of interleukins to the progression of pancreatic injury to systemic inflammation.

Conclusion

The aim of our study was to investigate the correlation of CRP with the severity and prognosis of acute pancreatitis. Our findings suggest the pivotal role of interleukins to the progression of pancreatic injury to systemic inflammation. Since the development of multiorgan failure decreases dramatically the prognosis in acute pancreatitis patients, it is of paramount importance to promptly identify high-risk patients. Measurement of

CRP levels seems to be an accurate method in order to assess the extent and persistence of the inflammatory process that can contribute to an early and more accurate management of this fragile patient group.

References

1. Mayer JM, Raraty M, Slavin J, *et al.*, Serum amyloid A is a better early predictor of severity than C-reactive protein in acute pancreatitis, *British Journal of Surgery*, 89(2), 163-171.
2. Kingsnorth A. Role of cytokines and their inhibitors in acute pancreatitis, *Gut*. 1997;40(1):1-4.
3. Al Mofleh IA. Severe acute pancreatitis: pathogenetic aspects and prognostic factors, *World Journal of Gastroenterology*. 2008;14(5):675-684.
4. Sandberg A, Borgström A. Early prediction of severity in acute pancreatitis. Is this possible? *Journal of the Pancreas*. 2002;3(5):116-125.
5. Chen CC, Wang SS, Lee FY, Chang FY, Lee SD. Proinflammatory cytokines in early assessment of the prognosis of acute pancreatitis, *American Journal of Gastroenterology*. 1999;94(1):213-218.
6. Štimac D, Fišic E, Milić S, Bilić-Zulle L, Perić R. Prognostic values of IL-6, IL-8 and IL-10 in acute pancreatitis, *Journal of Clinical Gastroenterology*. 2006;40(3):209-212.
7. Jiang CF, Shiau YC, Ng KW, Tan SW. Serum interleukin-6, tumor necrosis factor α and C-reactive protein in early prediction of severity of acute pancreatitis, *Journal of the Chinese Medical Association*. 2004;67(9):442-446.
8. Mayer JM, Raraty M, Slavin J, *et al.*, Serum amyloid A is a better early predictor of severity than C-reactive protein in acute pancreatitis, *British Journal of Surgery*, 89(2), 163-171.
9. Chen CC. Serum markers in the early assessment of severity of acute pancreatitis: which is the most useful? *Journal of the Chinese Medical Association*. 2004;67(9):439-441.
10. Kingsnorth A. Role of cytokines and their inhibitors in acute pancreatitis, *Gut*. 1997;40(1):1-4.
11. Papachristou GI, Whitcomb DC. Inflammatory markers of disease severity in acute pancreatitis, *Clinics in Laboratory Medicine*. 2005;25(1):17-37.
12. Sandberg AA, Borgström A. Early prediction of severity in acute pancreatitis. Is this possible? *Journal of the Pancreas*. 2002;3(5):116-125.
13. Al Mofleh IA. Severe acute pancreatitis: pathogenetic aspects and prognostic factors, *World Journal of Gastroenterology*. 2008;14(5):675-684.
14. Lempinen M, Puolakkainen P, Kempainen E. Clinical value of severity markers in acute pancreatitis, *Scandinavian Journal of Surgery*. 2005;94(2):118-123.
15. Sandberg AA, Borgström A. Early prediction of severity in acute pancreatitis. Is this possible? *Journal of the Pancreas*. 2002;3(5):116-125.
16. Lempinen M, Puolakkainen P, Kempainen E. Clinical value of severity markers in acute pancreatitis, *Scandinavian Journal of Surgery*. 2005;94(2):118-123.
17. Riché FC, Cholley BP, Laisné MJC, *et al.*, Inflammatory cytokines, C reactive protein and procalcitonin as early predictors of necrosis infection in acute necrotizing pancreatitis, *Surgery*. 2003;133(3):257-262.

18. Berney T, Gasche Y, Robert J, *et al.*, Serum profiles of interleukin-6, interleukin-8 and interleukin-10 in patients with severe and mild acute pancreatitis, *Pancreas*. 1999;18(4):371-377.

Accepted on 19/03/2022