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

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ABSTRACT

BACKGROUND - AIMS

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 assessed.

RESULTS

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

CONCLUSIONS

Measurement of CRP levels seem 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.

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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.

Acute pancreatitis is a major cause of acute abdominal pain. The clinical presentation of the acute pancreatitis is variable. Most of these patients recover without specific complications. Some patients; however, display severe complications such as pancreatic ascites and pancreatic necrosis; these patients show high morbidity and mortality.

Acute pancreatitis is highly variable in clinical presentation and severity. Both anatomic and physiologic criteria are used to stage the severity of acute pancreatitis. Balthazar and Ranson developed a grading system for severity based on CT findings. This computed tomography severity index (CTSI) is derived by assessing the degree of pancreatic and peri-pancreatic inflammation, fluid collection and parenchyma necrosis. The acute phase reactant C-reactive protein (CRP) is the best established and most available predictor of inflammation.

The acute pancreatitis (acute haemorrhagic pancreatic necrosis) is characterised by acute inflammation and necrosis of pancreas parenchyma, focal enzymatic necrosis of pancreatic fat and vessel necrosis (haemorrhage). These are produced by intrapancreatic activation of pancreatic enzymes. C-reactive protein 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,

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abscess, and necrosis), which can arise insidiously and be life threatening.

Changes in the level of CRP are an indication of an ongoing 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 in 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.

MATERIAL AND METHODS: 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 tumour, 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 48 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:

		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	f	2	3.4	3.4	3.4
	m	56	96.6	96.6	100.0
	Total	**58**	**100.0**	**100.0**	
Sex					

		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Mild	35	60.3	60.3	60.3
	Moderate	8	13.8	13.8	74.1
	Severe	15	25.9	25.9	100.0
	Total	**58**	**100.0**	**100.0**	
Clinical Diagnosis					

		Amylase	**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	10283.81	11830.19	4.59
Median		1188.00	54.00	50.00	9867.00	9880.00	4.00
Std. Deviation		209.627	27.602	42.294	2344.633	4351.306	2.464
Minimum		1000	11	9	5690	6643	0
Maximum		1997	119	168	16450	22678	9
Statistics							

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; and in mild group, 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.

Acute pancreatitis Clinical diagnosis	N	CRP day 5	p
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 week 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)[5,6,7,8] as prognosticators of the severity of acute pancreatitis.

C-reactive protein (CRP) that is synthesised by the hepatocytes is a nonspecific inflammatory marker routinely used in assessment of severity of acute pancreatitis.[7,8,10] 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).[8,9,10]

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.[8,9,10,11] Blood monocytes and neutrophils migrate to the site of inflammation and secrete inflammatory mediators.[8]

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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.[12] Early identification of such patients could lead to a more intensive management that would result to a decreased morbidity and mortality of this potentially fatal disease.[12]

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 2002;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, et al. 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, et al. 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, et al. 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. 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.
9. Papachristou GI, Whitcomb DC. Inflammatory markers of disease severity in acute pancreatitis. Clinics in Laboratory Medicine 2005;25(1):17–37.
10. Lempinen M, Puolakkainen P, Kemppainen E. Clinical value of severity markers in acute pancreatitis. Scandinavian Journal of Surgery 2005;94(2):118–123.
11. 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.
12. 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.