FREQUENCY OF NECROTIZING PANCREATITIS IN PATIENTS OF ACUTE PANCREATITIS WITH RAISED CRP

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ABSTRACT

Objective: To determine the frequency of necrotizing pancreatitis in patients of acute pancreatitis with raised C-reactive protein above 150 mg/l.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted over a period of 9-months (1st November 2010 to 30th July 2011) at surgical department of Combined Military Hospital and Military Hospital, Rawalpindi.

Patients and Methods: Forty three patients from surgical out patient department (OPD) at CMH, MH Rawalpindi fulfilling the inclusion criteria was selected and informed written consent taken. The diagnosis of pancreatitis was made by trainees and consultants clinically and with the aid of raised serum amylase level. After diagnosis serum CRP was measured on admission. CT-scan with IV contrast was carried out on 7th day of diagnosis and presence of pancreatic necrosis was noted.

Results: Necrotizing pancreatitis was found in 3 out of 43 patients (7%). CRP of all patients of necrotizing pancreatitis was greater than 150mg/l.

Conclusion: A CRP level of greater than 150 mg/l is highly suggestive of acute necrotizing pancreatitis.

Keywords: Acute Pancreatitis, C-Reactive protein, CT-Scan with IV contrast, Necrotizing pancreatitis.

INTRODUCTION

Acute pancreatitis is an acute condition presenting with abdominal pain and is usually associated with raised pancreatic enzyme levels in the blood and urine. Pancreatic necrosis occurs in 20% of patients with severe acute pancreatitis[1]. About one third of patients with acute severe pancreatitis die in early phase of attack from multiple organ failure, while deaths occurring after first week of onset are due to infective complications. Accurate early prediction of severity is essential to direct clinical care. Ranson , APACHE-II and Glasgow scores , routinely used for prediction of severity in acute pancreatitis are cumbersome to calculate and require upto 48 hours for complete calculation[2]. Contrast enhanced computed tomography (CT) scanning has become the gold standard for detecting and assessing the anatomical severity of pancreatitis[3]. The pancreatic necrosis is characterized by either pathologically confirmed necrosis of the parenchyma or fat in the interstitial space. There was no up-taking shown by the parenchyma contrast medium sized >3 cm or more than 30% of the gland on dynamic CT (Balthazar's criteria)[4].

While serum enzymes such as amylase and lipase are helpful in the diagnosis of pancreatitis, these have no prognostic value. Several recent research studies have suggested additional markers that may have prognostic value, including acute phase reactants such as C-reactive protein. CRP rises up to 50,000-fold in acute pancreatitis. It rises within 6 hours, and peaks at 48 hours[5].

Measuring and charting C-reactive protein values can prove useful in determining disease progress or the effectiveness of treatments. 150 mg/dl is currently the limit of discrimination of the severe from mild one[5]. The highest sensitivity and negative predictive value (94.1% and 95.7% respectively) was obtained for C-reactive protein cut-off at 150 mg/l[1].

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The rationale of doing the study on this topic is that C-reactive protein assay is simple, quick to perform, provides useful clinical information and is more likely to be of value and to be adopted into routine clinical practice than multiple factor scoring systems, like Ranson and Glasgow scores. Reproducibility of international data in Pakistani population was the main objective of this study.

MATERIAL AND METHODS

This was a descriptive studycarried out in department of Surgery, Combined Military Hospital and Military Hospital, Rawalpindi from1st November 2010 till 30th July 2011.

All males and females, alcoholics or non-alcoholics presenting with a combination of clinical features suggestive of acute pancreatitis including severe upper abdominal pain radiating to back and elevation of serum amylase four times above normal with raised CRP were included in the study.Previously diagnosed cases of acute pancreatitis as well as those with a history of previous pulmonary disease, diabetes and hypertension were excluded from the study.

After approval from hospital ethical committee, over a period of 9-months, 43 patients were prospectively recruited fulfilling the inclusion criteria. After diagnosis, serum CRP was measured by latex agglutination method on the day of admission (approx. 24-48 hours of onset of symptoms). Contrast enhanced CT-scan of the admitted patients was carried out on 7th day of diagnosis and findings of pancreatic necrosis were recorded (fig-1 and 2). The data was analyzed by the statistical package for social sciences (SPSS) version 13.0.

RESULTS

A total of 43 cases were included in the study after observing inclusion and exclusion criteria. Table-1 summarizes sample demographics.

It was observed that CRP rose in all patients with acute pancreatitis.It rose above 150 mg/l in only 3 patients and the same were observed to have necrotizing pancreatitis on CT-scan. Of the rest 40 having CRP less than 150 mg/l none had pancreatic necrosis.

Interestingly none of female patients developed necrotizing pancreatitis (table-2) and incidence of acute pancreatitis was quite low in females in our set despite the fact that cholelithiasis is quite common in females.

Table-1: Demographics of study group.

Mean age	**48.93 + 5 Years**
Male to female ratio	5.1:1
Cause of pancreatitis	Gall stones 43 Alcoholism 0
Mean hospital stay	Necrotizing pancreatitis 28+5 days Non-necrotizing pancreatitis 11+ 3 days

Table-2: Frequency of necrotizing pancreatitis confirmed on contrast enhanced CT scan.

		CECT findings		**Total**
		Necrotizing Pancreatitis	No Necrosis	
CRP-Level	CRP Level more than 150 mg/l	3 (100%)	0	3
	CRP Level less than 150 mg/l	0	40 (100%)	40
Total		3 (7%)	40 (93 %)	43

DISCUSSION

One of the most relevant features of acute pancreatitis is the great unpredictability in clinical severity. Most patients with acute pancreatitis (80–85% in most series) present with a mild and self-limiting disease, while 15–20% of patients with acute pancreatitis develop some major local and/or systemic complications of the disease, often leading to multiple organ failure and death[1]. In the currently used classification system of Atlanta severe acute pancreatitis is defined to be associated with specific clinical manifestations, Ranson's prognostic criteria ≥3 points or APACHE II ≥8, multiple organ dysfunction (MOD) in the course of systemic inflammatory response syndrome (SIRS), and pancreatic necrosis[4,6]. Since 1974, when John Ranson reported the first prognostic scoring system for acute pancreatitis, a large variety of multifactorial systems and single biochemical markers have been extensively evaluated with the aim of predicting the severity of the disease.

In spite of these research efforts, the need for early prognostic evaluation of acute pancreatitis had been strongly questioned as methods for determination of most markers are hardly applicable to the daily routine of an emergency laboratory and application of most prognostic scoring systems is cumbersome needing up to 48 hours for quantification. The risk of severe acute pancreatitis is increased at Glasgow's or Ranson's score ≥3 in 48 hours, APACHEII on admission ≥8, BMI ≥30, abdominal wall bruising,abnormal chest radiograph and serum creatinine >2 mg/dl on admission, Balthazar's score ≥4, CRP >150 mg/dl at 48 hours, and hematocrit >44%[4].

C-reactive protein has been found to be an important prognostic marker of pancreatitis severity with the highest sensitivity and negative prognostic value to predict development of pancreatic necrosis[7]. CRP is an acute phase reactant that starts rising within 6 hours of an insult (including acute pancreatitis) under influence of Interleukin-6 , peaks at around 48 hours and then declines with a half-life of 19 hours[8]. Its concentration in healthy human serum is usually lower than 10 mg/l. A C-reactive protein level greater than 150 mg/L in first 4 days of attack or 120mg/L at the end of first week has a predictive value for severity of acute pancreatitis similar to other criteria[7].

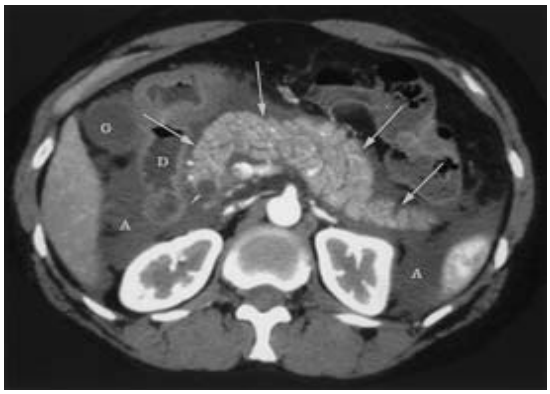

Figure-1: Contrast enhanced computed tomography scan of interstitial pancreatitis (n=43).

Studies have found that C-reactive protein is an important prognostic marker of pancreatic necrosis with the highest sensitivity and negative prognostic value given the cut-off is 110 mg/l. The patients with C-reactive protein

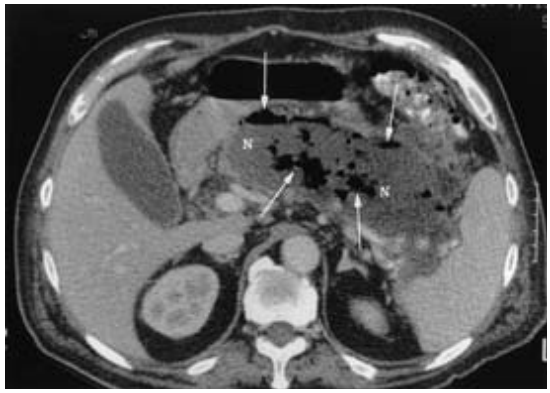

Figure-2: Contrast enhanced computed tomography scan of infected pancreatic necrosis. A few bubbles of air (arrows) are present in the encapsulated necrotic tissue.

below 110 mg/l were low risk to develop pancreatic necrosis[1]. C-reactive protein (CRP) has been widely used in the early risk

assessment of patients with acute pancreatitis. The Bedside Index for severity in AP (BISAP). It was found that CRP measured at approximately 48 hours after hospital admission (CRP48) had a prognostic accuracy for severity, pancreatic necrosis, and in hospital mortality in AP better than CRP measured at any other timing. It has also been observed that the optimal CRP cutoff points at 48 hours for severity, Pancreatic necrosis, and In hospital mortality in acute pancreatitis varied from 170mg/l to 190mg/l[9].

It was concluded in another study that in acute pancreatitis, a CRP value of less than or equal to 200 mg/l obtained at 72 hours of symptom onset was useful for ruling out the presence of necrosis with a high degree of probability[10]. In our study CRP raised in all patients of acute pancreatitis but we selected cut-off value 150 mg/l for necrotizing pancreatitis. (Table-2) We measured the value at admission i.e. 24-48 hours of onset of symptoms and found the value of 150 mg/l to be predictive of necrotizing pancreatitis. The patients with C-reactive protein below 150 mg/l were found to be at low risk to develop pancreatic necrosis.

Studies showed that C-reactive protein concentrations was the best discriminator between mild and complicated attacks, these differences were highly significant from day 2 (the morning after admission) to day 8. The concentrations providing the best results were found to be greater than or equal to 210 mg/l for the peak C-reactive protein (on the second, third or fourth day) and greater than or equal to 120 mg/l for the C-reactive protein at the end of the first week.

In our study out of 43 patients, value of CRP of 40 patients of acute pancreatitis was less than 150mg/l (cut-off value we selected for our study) and none of them had pancreatic necrosis on CE-CT scan. Of the 3 patients who developed necrotizing pancreatitis on contrast enhanced CT scan abdomen all had CRP values >150 mg/l. (Table-2 and fig-1). Although we didn't compare scoring system in our study with CRP but we established that value of 150mg/l is better predictor than 210 mg/l because in our study all the patients with CRP >150 mg/l developed necrotizing[11]. A lower cutoff limit is expected to be more sensitive in predicting pancreatic necrosis although it may also be less specific. .

Other studies have shown that a C-reactive protein (CRP) value over 150 mg/l was the only autonomous predictor of mortality on admission into the emergency unit, whereas the computed tomography severity index and the elevated CRP value over 150 predicted significantly and independently morbidity and mortality on admission into the ICU. This study also clearly showed that raised CRP had clear relation with probability of necrotizing pancreatitis and may be extrapolated to increased morbidity and mortality[12].

CONCLUSION

Of the parameters explored over the years, CRP is still the single best biochemical marker to predict severity of acute pancreatitis The patients with C-reactive protein below 150 mg/l are low risk to develop pancreatic necrosis where as those with CRP greater than 150 mg/l is highly suggestive of acute necrotizing pancreatitis. CRP is available, simple and economical biochemical parameters that can help us predict complications of acute pancreatitis in the early phase of the disease. It is also less cumbersome than other criteria[3] as Ranson's, APACHE-II or Glasgow scores.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

AUTHORS CONTRIBUTION

Adeel Habib, data analysis/manuscript, Junaid Mansoor, references, Shahzar Malik, literature review, Muhammad Pervaiz, supervisor, Ammara Adeel, data analysis.

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