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Give space between C and reactive Protein as an early Predictor of acute Pancreatitis: An Observational Study

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Abstract

Background and Aim: In the early risk stratification of acute pancreatitis, C-reactive protein (CRP) is being used extensively worldwide. There are few studies that show that CRP is useful in predicting pancreatic necrosis which is a determinant of severe pancreatitis. Aim of the present study was to assess the role of CRP as a prognostic indicator in acute pancreatitis.

Material and Methods: A total of 128 patients that were diagnosed to have acute pancreatitis were included in the study. Data collected from the patient's record (file/EMR) and organised in an Excel sheet that contained basic demographic data (age and gender), cause, APACHE score, length of hospital/intensive care unit (ICU) stay and the CRP level. Blood samples for CRP and biochemical markers for the APACHE II score were routinely drawn and processed on admission.

Results: The patients were divided into two groups, those with mild pancreatitis and those with severe acute pancreatitis. Men were predominating in the study group where they contributed to 85.9% of the study population. Mean age of presentation of acute pancreatitis was 37.7 years. Amylase and lipase were taken for the diagnosis of acute pancreatitis; amylase and lipase were elevated significantly in 104 and 108 patients respectively. Twenty eight patients had an elevated CRP > 150 in BISAP positive patients. There was significant association of CRP and BISAP.

Conclusion: Acute pancreatitis is a life-threatening disease with a wide spectrum of clinical symptoms. The job of diagnostic markers as prognostic pointers has been a disappointment. However, CRP as a prognostic marker has shown promising results in earlier studies.

Keywords: Amylase, Acute pancreatitis, C reactive protein, Pancreatic Necrosis

Introduction

Acute pancreatitis, the sudden inflammatory process of the pancreas is a common disease that has a variable clinical course, and its severity is often difficult to predict.[1]Although this condition does resolve in some cases without any medical intervention and patients can make full recovery within a relatively short period, there are others who end up developing severe complications that could be fatal. Acute pancreatitis (AP) is an inflammatory condition which may be mild or severe; in severe cases, pancreatic enzymes can cause damage to the gland itself.[1, 2]

AP has many different etiologies, and overall mortality is 5% to 10%. Most cases (80% to 90%) are mild or self-limited and have a good prognosis. The remaining 10% to 20% of cases warrant monitoring in intensive care units due to pancreatic necrosis or distant organ damage. Severe AP cases usually require surgical intervention, and overall mortality can be up to 40%.[3, 4]

Acute Pancreatitis is a disease of unpredictable outcome; early intervention can prevent the development of acute severe pancreatitis which develops in 20 to 30% of patients with Acute

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Pancreatitis.[5] The progression of the disease and the development of complications are mainly due to the release of proinflammatory cytokines leading to third space volume loss. C –reactive protein (CRP) being an acute phase reactant is elevated in the ensuing inflammation of the pancreas , this elevation when above 150 mg/L has been noted to be a predictive marker of the development of acute severe pancreatitis.[6]

In the early risk stratification of acute pancreatitis, C-reactive protein (CRP) is beingused extensively worldwide.[7] There are few studies that show that CRP is useful in predicting pancreatic necrosis which is a determinant of severe pancreatitis. There not many studies reported from our country using CRP to differentiate between MAP and SAP which is the need of the hour for better use of our limited resources as it is a simple and an efficacious way to triage acute pancreatitis patients. Considering its peak at only 48-72 hours, so cannot be used to access severity in the therapeutic window of pancreatitis (first 72 hours).[8] CRP is also elevated in conditions like coronary heart disease, insulin resistance, diabetes, dental disorders, smoking, overweight, obesity, Alzheimer's disease, rheumatoid arthritis and cancer.[9] Hence the aim of the present study was to assess the role of CRP as a prognostic indicator in acute pancreatitis.

Materials & Methods

The present study is the observational study that was done in the medical college and the associated hospital. A total of 128 patients that were diagnosed to have acute pancreatitis were included in the study. Variables (age, sex), were recorded along with local complication and systemic complication. The ethical committee was informed about the study, and the ethical clearance certificate was obtained prior to the start of the study.

The inclusion criteria and exclusion criteria were as follows: the patients with more than age of 18 years and those who satisfy the Atlanta classification for diagnosis of acute pancreatitis were included in the study. Patients who had any of the following were excluded from the study: Age < 18 years, already diagnose with chronic pancreatitis, severe acute pancreatitis on admission, Pregnant women, Hematologic diseases, Connective tissue disorders, Collagen vascular diseases.

Data collected from the patient's record (file/EMR) and organised in an Excel sheet that contained basic demographic data (age and gender), cause, APACHE score, length of hospital/intensive care unit (ICU) stay and the CRP level. Blood samples for CRP and biochemical markers for the APACHE II score were routinely drawn and processed on admission. Collected data analysed to assess the possible statistical significance of the variables and to present the data accordingly. Their CRP levels were sent on second day of admission and CT scan done after 72 hours of admission.

All the data collected in proforma were entered in Microsoft excel sheet and SPSS software version 21 was used for statistical calculations. Chi-square test with Fischers exact was used to calculate p value and find the significant association between CRP and different variables. Serial C reactive proteins levels were analyzed at 72 hours. Computed tomography with oral and IV contrast agents was done at 72 hours after admission and CT severity Index with CT grade and necrosis grade was ascertained.

Results

A total of 128 patients of acute pancreatitis were studied. The patients were divided into two groups, those with mild pancreatitis and those with severe acute pancreatitis. Both moderately severe acute pancreatitis and severe acute pancreatitis were considered as severe acute pancreatitis. Young and middle age persons were the predominant population of the study i.e., < 50 years constituted > 80% of the study population. Men were predominating in the study group where they contributed to 85.9% of the study population. Mean age of presentation of acute pancreatitis was 37.7 years.

In the present study, Pain was the predominant presenting complaint seen in 98% of the study population, while the least common presenting complaint or associated symptom was upper gastrointestinal bleed which was seen only in one individual. Extra pancreatic manifestations were seen in a frequency of 1.8% to 19.4%.

Amylase and lipase were taken for the diagnosis of acute pancreatitis; amylase and lipase were elevated significantly in 104 and 108 patients respectively. Patients who did not have significantly elevated amylase and lipase levels were diagnosed by means of abdominal pain and CT findings.

All individuals underwent CT Abdomen. Eighty two patients had a normal study or had mild

pancreatic or peri pancreatic inflammation. Forty six patients had pancreatic or peripancreatic fluid collection with or without accompanying necrosis of the gland. Severity on CT was classified into 3 groups, Group 1: Normal CT or mild enlargement of the gland ,Group 2 :presence of pancreatic or peri pancreatic fluid collection and Group 3-presence of necrosis.

Twenty eight patients had an elevated CRP > 150 in BISAP positive patients. There was significant association of CRP and BISAP with p value of 0.0001.

Table 1: Distribution of CRP in the patients

C reactive protein	Number of patients
< 150	82
> 150	46

Table 2: Symptoms on presentation

Symptoms	Present	Absent
Pain	124	4
Vomiting	76	52
Abdominal distention	22	106
Fever	22	106
Jaundice	14	114
Oliguria	10	118
Dyspnoea	10	118

Table 3: Analysis CRP with CT in Predicting Severe Acute pancreatitis

CRP	Severity basedon CT		Chi square	P value
	1	2 &3		
< 150	66	16	15.21	.0001
> 150	16	30		

Discussion

Acute pancreatitis is undoubtedly a disease in which the progression can be greatly altered by early intervention. Numerous scores and single prognostic markers have been suggested to predict the severity of pancreatitis on admission or after a couple of days, this by itself suggests none of the available scores or markers are the gold standard to predict the severity of the disease.[10, 11] In this study CRP and pancreatitis predicting scores BISAP were analyzed to predict the severity of pancreatitis. Scores which had many markers may have had an increased sensitivity but simpler and easily available scores and markers were taken.

In our country where resources are limited, the simplest and the most economical of the scores or markers are the ones which would have a great impact on the society in the prediction of severity in AP Epidemiology.[12] In the study population of 110 were male contributing to 86.5% of the study population. This is higher than studies from the Mediterranean by Stimac et al[13] and the study of Roberts[14] from UK who showed only a slight male predominance of 53% and 50.7% respectively. The probable reason could be that gall stone disease is not as common as it is in the west, the predominant cause of AP in this study being alcohol which is more abused by men than women and are young comparatively in our country.

Symptoms Abdominal pain (96.9%) and vomiting (59.4%) were the predominant complaints seen in the study population. This is similar to the study by Milheiro et al[15] who stated the predominant symptom in AP as abdominal pain in 100% followed by vomiting in 69.2%. A symptom association of extra-pancreatic manifestations to the occurrence of SAP was done, which showed that the presence of extra pancreatic manifestations in acute pancreatitis had a high probability to be associated with SAP.

In this study there was a significant association with jaundice, fever, dyspnea and oliguria which is similar to the study by Abbasi and Jacobs et al.[7] Thus this study further emphasizes the well known fact of the need of aggressive fluid management in AP thus preventing volume depletion, which may lead on to the development and progression of SAP.

C - reactive protein A CRP of > 150 mg /L was taken to predict acute severe pancreatitis, 46 (35.9%) patients of the 128 study population had an elevated CRP at 48 hours of admission. 30 of the 46 patients who had a significant elevation of CRP had CT features of SAP (P = 0.0002), while 24 of the 46 patients with significant elevation of CRP had Necrotising pancreatitis on CT (P = 0.0004). Thus drawing on a conclusion that CRP had a significant association in predicting severity of pancreatitis, which is in accordance to studies by Alfonso and Cardoso who took a CRP value of 200 mg /L and 170 mg/L respectively in predicting SAP and necrotising pancreatitis. This study achieves the same association with a CRP cut off of 150mg/L as suggested by recent studies by Wilson. Thus this study confirms that a CRP of >150mg/L is as diagnostic as higher levels in predicting SAP.

The Positive predictive value of CRP in predicting SAP was 65.2% while it had a negative predictive

value of 80.5%.This is similar to previous studies which have stated a at 48 hours CRP had a sensitivity ranging from 65% to 100% and a positive predictive value of 37% to 77%. 82 patients of the study population had mild pancreatitis, while 46 patients had SAP as determined by CT, which is taken as standard to predict the severity of pancreatitis. Incidence of SAP is similar to study by Svetlana. The reason could be that in our population there is a delay in presentation to the hospital as the patients seek over the counter medications or complementary and alternative forms of medicine for the most common symptom of abdominal pain or it could be that of a referral bias.

Conclusion

Acute pancreatitis is a life-threatening disease with a wide spectrum of clinical symptoms. The job of diagnostic markers (pancreatic enzymes like amylase and lipase) as prognostic pointers has been a disappointment. However, CRP as a prognostic marker has shown promising results in earlier studies. CRP levels can give a prior insight about the undergoing inflammatory process.

Ethical Approval is taking from institutional ethical committee

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