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Original Article

C -reactive protein in assessment of severity acute pancreatitis

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Abstract

Background: Acute pancreatitis (AP) is an acute inflammation of the pancreas and clinical evolution is frequently unpredictable. Numerous predictive markers have been studied to assess severity in AP, including clinical assessment, clinical-physiological scoring systems, imaging techniques, and biochemical markers in different body fluids.

Objective: This study was done to see the association between level of CRP and severity of acute pancreatitis.

Methods: 50 patients diagnosed as acute pancreatitis based on operational definition admitted in Dhaka Medical College Hospital was included in the study. Patients' admission date back from 1ST August, 2016 to 31december, 2015. Conservative management started from the date of admission as per standard conservative management protocol. Patients were monitored by RANSON scoring system and categorized as mild if RANSON score is <3 and categorized as severe if the score is ≥3. At the same time serum CRP level was measured on day 2, 3 and 7. Then the correlation between the severity of the disease and measures of CRP was established by unpaired t test and x^2 test.

Results: Over 6 months of study period 50 patients were treated for pancreatitis in different medical and surgical unit of Dhaka Medical College Hospital. Aetiological analysis revealed mostly caused by biliary disease (40%) followed by idiopathic, alcoholic, post ERCP and post traumatic. Based on RANSON score about 34 patient developed mild acute pancreatitis and 16 patient developed severe acute pancreatitis. Then CRP value of this two groups was compared on day 2, 3, 7 by unpaired t test with P value<.001 in all 3 days. ROC curve was plotted to determine specificity and sensitivity with a cut off value of CRP 132mg/l. Sensitivity and specificity was 75% and 55.8% accordingly.

Conclusion: In a patient with acute pancreatitis the use of RANSON scoring system is not always possible as many of the investigation are not easily available in our set up. In our study we have found that serum CRP level is significantly (cut off value 132) higher in patient with sever acute pancreatitis. This will allow high proportion of patients with mild disease to be managed in low-cost hospital beds.

Keywords: Acute Pancreatitis, RANSON scoring system, CRP.

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Introduction

Acute pancreatitis is usually a mild, self-limiting disease that resolves within days. However, about 20–30 per cent of patients develop severe acute pancreatitis[1]. Because most of the morbidity and mortality in severe acute pancreatitis derives from the development of vital organ dysfunction[2], which is not uncommon at an early stage of acute pancreatitis early identification of patients likely to develop organ failure would be of clinical value.

Two general types of scoring system have been applied to pancreatitis. The first type comprises systems that are specific to pancreatitis, such as the Ranson and Imrie (Glasgow) severity scoring systems. The second type correlates non-specific physiological variables with outcome; examples are the APACHE II and III systems[3].

The main problem with Ranson's criteria was that they did not allow prediction until 48 h after admission. Furthermore, these criteria were developed and validated in patients with alcoholic pancreatitis. Imrie and co-workers in Glasgow proposed a similar scoring system, which was validated on patients with gallstone and alcoholic pancreatitis[4].

An increased serum C reactive protein concentration is well recognized as a non-specific response to a wide variety of tissue injuries[5]. Sequential measurements of C reactive protein concentration can be helpful in providing a warning of inflammatory complications in disease-for example, postoperative sepsis and thrombosis-and its response to treatment[6].

The rapid response of C reactive protein to changes in the intensity of the inflammatory stimulus suggests 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[7].

The acute pancreatitis is a very common surgical emergency in our country but the monitoring system for the risk of development of severe disease is yet to be defined. Only when the patient gets worse or develops complications and then that becomes evident in imaging. If it is found that CRP alone is a good indicator, reflecting the severity of the disease, then it will be a cost effective monitoring tool in the management of pancreatitis no such study is carried in our country.

Materials and Methods

50 patient diagnosed as acute pancreatitis based on operational definition admitted in Dhaka Medical College Hospital was included in the study by simple random purposive sampling. Patients' admission date back from 1ST August, 2016 to 31december, 2015. Necessary information was obtained from history, physical examination, investigation, follow up chart, operation note and discharge certificates.

Patient with acute pancreatitis admitted within 24 hours of onset of symptoms were included in the study. Patient admitted after 24 hours of onset of symptoms or later on revealed pancreatic tumour or having renal or hepatic failure were excluded from the study.

Demographic variables (age, sex), were analysed along with local (acute peripancreatic fluid collection, sterile pancreatic necrosis, infected pancreatic necrosis, pleural effusion) complication and systemic (cardiovascular, respiratory, renal failure, hematological) complication.

Serum CRP value were measured on day two, three and seven of admission and scatter matrix plot were drawn with that of RANSON score. Statistical analysis was also done by line plots to see the association between severity of acute pancreatitis with CRP value in three days. ROC curve was plotted for CRP value of day 3.

Results

Among the sample population 62% were male and 38% were female, age varying 21 to 65 years mostly between 41-50 years (38%).

Table 1: Age distribution of the study population (n=50)

Age in years	Number	Percentage
21-30 yrs	02	04
31-40 yrs	10	20
41-50 yrs	19	38
51-60 yrs	15	30
> 60 yrs	04	08
Total	50	100

Table 2: Etiology pancreatitis (n=50)

Etiology	Number	Percentage
Biliary disease	20	40
Idiopathic	13	26
Alcoholic	08	16
Post ERCP	06	12
Post traumatic	03	06
Total	50	100

Table -3: Comparison of monitoring investigations between acute mild and severe Pancreatitis (n=50)

	Acute Pancreatitis		p value
	Mild	Severe	
	n=36	n=16	
	Mean ±SD	Mean ±SD	
Total count	13288.23 (±1233.31)	18887.50 ±2255.91	< 0.001
Haematocrit	42.41 (±2.10)	36.18 (±3.88)	< 0.001
RBS	7.52 (±1.89)	13.56 (±3.86)	< 0.001
Calcium	8.32 (±0.19)	7.24 (±0.61)	< 0.001
Serum creatinine	0.68(±0.10)	1.89(±0.76)	0.01

Table -4: Complications developed in the patients of Acute Pancreatitis (n=50)

Complication	Number	Percentage
Acute fluid collection	19	38
Sterile pancreatic necrosis	13	26
Infected pancreatic necrosis	06	12
SIRS	06	12
ARDS	10	14
Acute kidney injury	05	10
Pleural effusion	30	60
Ascites	10	20
MODS	03	06
DIC	06	12
Death	01	02

Acute peripancreatic fluid collection was found in 19 patient (38%) evident in USG of whole abdomen on the 1st day of admission and on subsequent USG in next 7 days evidence of regression of collection was found in 13 patient. Pleural effusion was found in 30 patients(60%) as evident by USG of W/A but5 not causing any major respiratory complication and all responded with the ongoing conservative management on 7 days follow up. Six patient (12%) developed SIRS but all resolved in first 72 hours.

Sterile pancreatic necrosis was found in 13 patients evident by CT scan with oral and I/V contrast, among them 7 patient responded conservative management the rest went on a state of infected pancreatic necrosis. Three patient developed MODS on 4th to 5th day of monitoring and one of them died on 6th of follow up. Ten patient developed ARDS, five patients (10%) developed AKI, and 06 patients (12%) developed DIC all managed conservatively

Serum CRP value were measured on day two, three and seven of admission and scatter matrix plot were drawn with that of RANSON score. In all three graphs it was found that patient with RANSON score ≤ 3 were clustered around CRP value 80mg/l and with the increasing value RANSON score CRP value also raises accordingly, which firmly establishes CRP value CRP value is higher in patient with acute severe pancreatitis than that of mild variety.

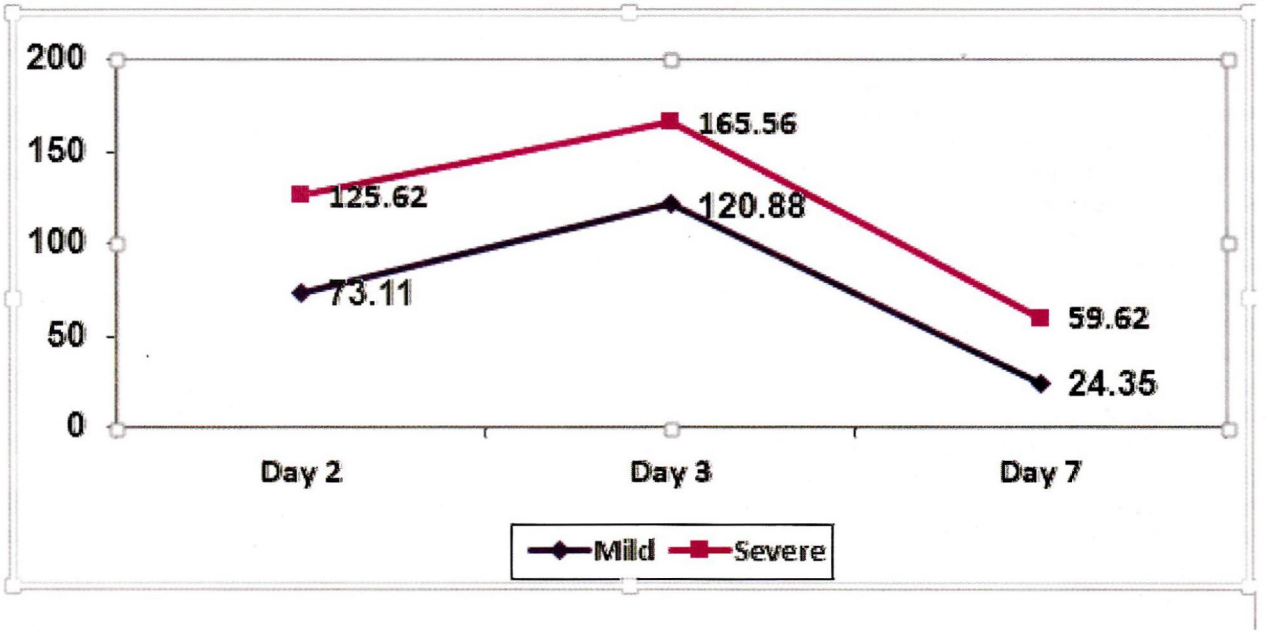

Figure 1: Relation between severity of acute Pancreatitis with CRP level at day 2, day 3 and day 7

Table 5: Relation between CRP level with RANSON score (n=50)

CRP	RANSON score		Total	p value
	< 3	≥ 3		
≤132 mg/l	19	4	23	0.04
> 132 mg/l	15	12	27	
Total	34	16	50	

x^2 test was done

Discussion

In clinical practice, probably the most used prognostic factor in AP is CRP, but it is useful only if it is measured after at least 48 h following the onset of AP. Values greater than 120 mg/L can detect between 67 and 100% of pancreatic necroses8. Others authors proposed a cut-off value of 150 mg/L 9. In the study of Gurleyik et al 10 for a cut-off value of 150 mg/L, CRP had 84.6% Se, 73.8% Sp, 50% PPV, 93.9% NPV and 76.4% accuracy to predict a severe outcome of AP. In the study of de la Pena et all1[1], for a cut-off value of 100 mg/L, CRP had 100% Se and 86% Sp to predict a severe outcome of AP.

In our study out of 50 patient who was taken in sample were admitted within 24 hours of onset of attack were monitored with RANSON scoring system. Aetiological analysis from table 2 it was found that biliary aetiology stands as a large share of the cause and next rank is for idiopathic which does not corresponds with other western study like the study performed by Simon Bota et all. It can be easily explained by the less alcohol consumption in our country. Age distribution of study population showed 88% of study population are between 31 to 60 years. The mean CRP value of severe group on day 3 is 165.56 (±37.32) and that of mild group is 120.88(±44.01) that gave a P value <.001 by unpaired t test. After drawing the ROC curve we had area under the curve was .782 that corresponds with the cut of value of CRP 132mg/l which is very close to the value of CRP found by Gurleyik et al10 study which was 150mg/l. another performed by the Pena et all11 for detecting severity of acute pancreatitis by means of CRP value and they had a CRP value of 100mg/l, which is very close to our cut off value.

Performance diagnostic test with cut off value of CRP 132mg/l gave a sensitivity of CRP (> 132 mg/l) level was 75%, specificity 55.88%, accuracy 62%, positive and negative predictive values were 44.44% and 82.61% respectively. With cut value of CRP 120mg/l shows that sensitivity of CRP (> 120mg/l) level was 87.5%, specificity 55.88%, accuracy 66%, positive and negative predictive values were 48.28% and 90.48% respectively. In the study of Gurleyik et al [27], for a

cut-off value of 150 mg/L, CRP had 84.6% Se, 73.8% Sp, 50% PPV 93.9% NPV and 76.4% accuracy to predict a severe outcome of AP. So statistically both these study support each other.

Selective conservatism with criteria for selecting patients who will benefit from immediate operation will result in a drastic morbidity reduction and costs saving with short hospital stay based on a 48 h observation period. Our experience with abdominal penetrating wounds supports the concept of selective conservatism based on repeated physical examination. In a well established trauma centre this has proven to be highly effective with remarkably low rates of non-therapeutic laparotomies and absence of missed diagnosis of visceral injuries. Peritoneal perforation and haemoperitoneum should not be an indication for routine laparotomy.

By the second day, the median serum concentration CRP was significantly increased in patients who subsequently developed organ failure compared with that in those with mild disease or a local pancreatic complication alone. This is consistent with the concept of a systemic inflammatory response contributing to the development of organ failure in critical illnesses.

Statistical analysis showed that both RANSON score and CRP concentration correlated significantly with pancreatic sepsis. Once again, these findings confirm earlier work and can be explained by the previously described association of CRP with pancreatic necrosis and of Ranson score with severity'

Mayer et al[12] have recently studied the role of CRP in the assessment and monitoring of acute pancreatitis. They found that the main value of CRP is to provide a guide to the severity of inflammation and to indicate the patients' risk of developing pancreatic collections when the CRP values remain high (>100 mg/l) at the end of the first week of the illness.. Mayer also concluded that CRP could differentiate mild and severe attacks of pancreatitis better than the white blood cell count, erythrocyte sedimentation rate, body temperature or concentration of antiproteases.

We believe that measurement of C reactive protein concentration during the first week of the illness may enable radiological imaging techniques to be used to search fruitfully for pancreatic collections in a high risk group. Its measurement along with conservative management and RANSON scoring is good indicator of severity.

Conclusion

In conclusion, in this prospective series of consecutive potentially severe attacks of acute pancreatitis, CRP values in different groups correlated well with the severity of the pancreatitis and with the prognostic signs, which suggests that CRP determinations are of value in the early assessment of the severity of acute pancreatitis. In the individual patient, however, the CRP values seem to provide abetter measure of the severity of the disease than do the prognostic signs. The results are much the same to study that has been done in different times., but the CRP assay is much easier to incorporate into the hospital routine practice.

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