Evaluation of C-reactive Protein, Blood Urea Nitrogen and Hematocrit as Independent Predictors of Severity of Acute Pancreatitis

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Abstract

Background: Different modalities are available for predicting severity of acute pancreatitis. A single marker with high sensitivity and specificity is yet to be identified. This study intends to find out the utility of C- reactive protein (CRP), Hematocrit (HCT) and Blood Urea Nitrogen (BUN) in predicting the severity of acute pancreatitis.

Methods: A total of 117 patients admitted with acute pancreatitis were included. A predesigned structured questionnaire was used for recording data. Clinical parameters and biochemical tests were recorded on admission and on day 3 and day 5 of admission. CT scan was performed in all patients. CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) were done on admission. Every patient was followed regularly for identification of organ failure or any other complication. Statistical analysis was done with SPSS.

Result: Among 117 patients, 67(57.3%) were male and 50(42.73%) were female with a mean age of 47.99±15. Among the patients the etiology was found to be biliary, hypertriglyceridemia, alcohol, malignancy and post-ERCP complications in 25(21.4%), 23(19.7%), 8(6.8%), 3(2.6%), 2(1.7%) cases respectively. In 53(45.3%) cases no definite etiology could be found. 83(70.9%) patients had mild, 15(12.8%) had moderately severe and 19(16.2%) had severe acute pancreatitis. The mean CRP (mg/L), Hematocrit (HCT) (%) and Blood Urea Nitrogen (BUN) (mg/dl) were 60.61±81.2,37.23±4.8 and 17.40±9.61respectively. ROC curve evaluating the role of CRP in predicting severity of acute pancreatitis showed an AUC of 0.851. A cut off point of 160 mg/L showed highest sensitivity (73.7%), specificity (98%), positive predictive value (PPV) (87.5%) and negative predictive value (NPV) (95%). ROC curve evaluating the role of HCT in predicting severity of acute pancreatitis showed an AUC of 0.954. A cut off point of 42.50% showed highest sensitivity (89.5%), specificity (96.9%), positive predictive value (PPV) (85%) and negative predictive value (NPV) (97.9%). ROC curve evaluating the role of BUN in predicting severity of acute pancreatitis showed an AUC of 0.971. A cut off point of 25.66mg/dl showed highest sensitivity (94.7%), specificity (94.9%), positive predictive value (PPV) (78.3%) and negative predictive value (NPV) (98.9%).

Conclusion: CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) can be taken into consideration for predicting severity of acute pancreatitis early in the course of disease

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Introduction

Acute pancreatitis accounts for 3% of all cases of abdominal pain admitted to hospital[1]. The incidence of acute pancreatitis appears to be increasing[2]. As the population is becoming increasingly overweight, the incidence of gallstones, the most common cause of acute pancreatitis, is rising. Whereas gallstones and alcohol appear to be the cause of acute pancreatitis in the majority of cases, many other conditions like hypertriglyceridemia predispose to acute pancreatitis to varying degrees.[3]

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About 80% of all cases are mild and have a favorable outcome. Of the rest 20% of patients with severe disease, almost all (98%) die within the first week, usually from multiorgan failure. After this time the majority of deaths result from sepsis, especially that complicating infected necrosis. On admission, it is possible to predict patients at risk of this complication.[1]

Predicting severity of pancreatitis early in the course of disease is critical to maximize therapy and to prevent and minimize organ dysfunction and complications. Unfortunately, the management of patients with acute pancreatitis is complicated by the inability to distinguish mild from severe disease during the early stages.[3] Severe acute pancreatitis has a poor prognosis and early prediction of the severity helps us in taking appropriate steps to halt the disease progression and to reduce development of complications. Several predictors (biochemical parameters, clinico-biochemical scores and radiological scores) have been used to predict the severity of acute pancreatitis. But a simple, inexpensive, routinely available and highly accurate predictor is however not yet available.

C-Reactive Protein (CRP), an acute-phase reactant produced by the liver, is used extensively in Europe as a marker of severe pancreatitis. CRP is inexpensive to measure and readily available.[4] A high hematocrit (HCT) on admission, or 1 that fails to decrease after 24 hours of rehydration, is thought to be a sign of hemoconcentration from retroperitoneal fluid loss and thus is a marker of severe disease.

Several prognostic scoring systems, including the Ranson criteria and BISAP, incorporate BUN levels for the prediction of mortality in patients with acute pancreatitis.[5,6] Hemoconcentration has been shown to be an accurate predictor of necrosis and organ failure. Both the BUN level and the hematocrit are routine laboratory tests that may provide information on changes in intravascular volume status. CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) may be very useful in the early prediction of severity of acute pancreatitis and can guide us to initiate effective management before the development of complications.

Several studies have been conducted to establish their role in the early prediction of severity of acute pancreatitis. But no such study is done in our country till now. This study aims at establishing the role of CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) in the prediction of severity of acute pancreatitis.

Methods

This prospective and observational study was done in the department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), Square Hospitals Ltd, Dhaka, Bangladesh from January, 2018 to June, 2019. Patients aged more than 18 years, admitted with abdominal pain and fulfilling the diagnostic criteria of acute pancreatitis by clinical history, physical examination, biochemical tests and different imaging modalities were included in this study.

Patients attending after 72 hours after the onset of abdominal pain, patients having chronic pancreatitis, chronic kidney disease, serious co-morbid conditions like COPD, heart failure and patients suffering from severe infection or inflammation of any other organ system were excluded from the study. Patients unwilling to give voluntary consent to participate in the study were also excluded. Consecutive type of non-probability sampling technique was applied to enroll the patients.

Prior to the commencement of this study, the research protocol was approved by the Ethical Review Committee (ERC) of the institution. The aims and objective of the study along with its procedure, alternative diagnostic methods, risk and benefits were explained to the patients in easily understandable local language and then informed consent was taken from each patient.

A predesigned structured questionnaire was used for recording all the data. To detect etiology of acute pancreatitis, liver function test, fasting lipid profile, USG of abdomen were done in all cases. Demographic data like age, sex, BMI; clinical data like presence of abdominal pain, severity and radiation of abdominal pain, abdominal lump, anemia, fever, GCS score, vital parameters were recorded. Laboratory data like CBC with HCT, CRP, BUN, serum creatinine, FBS, HbA1c, serum amylase, serum lipase, serum bilirubin, serum albumin, AST, ALT, alkaline phosphatase, serum LDH, fasting lipid profile, ABG, CA 19.9, USG and CT scan of upper abdomen findings were recorded. Laboratory tests were done on admission and CBC with HCT, CRP, BUN, serum creatinine, ABG were repeated on day 3 and on day 5 of admission to follow up the patient.

Computedtomography (CT) scan was performed in all patients after 72 hours of admission for detectionofthe development of fluid collections, the extent of inflammation, and necrotic changes. Attacks of acute pancreatitis were classified as mild, moderately severe and severe according to revised Atlanta criteria and with the help of modified Marshall scoring system for organ failure. Every patient was followed regularly for identification of organ failure or any other complication. Data were analyzed by computer analysis method using SPSS version 22.

Statistics

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean, standard deviation, and categorical variables as frequencies and percentages. ROC curve was plotted for evaluating the test accuracy of CRP, HCT and BUN as a predictor severity of acute pancreatitis, which yielded different cutoff points. The cutoff points with highest sensitivity and specificity were further evaluated by chi-square (X^2) test. A p-value of <0.05 was considered as significant.

Result

A prospective observational study was carried out to evaluate the role of CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) in predicting severity of acute pancreatitis. Total 117 patients with acute pancreatitis, who fulfilled the inclusion criteria, were included in this study. The result of the study is presented in following tables and diagrams.

Table I: Demographic, clinical and biochemical characteristics of the study population (n=117)

Parameters	Result
Age (years)	47.99±15.90
Sex (Male)	67(57.3)
Contributing factor	
Smoking	36(30.8)
Alcohol	10(8.5)
Tea/ coffee	93(79.5)
OCP	3(2.6)
DM	82(70.1)
BMI	25.36±3.4
Clinical features	
Abdominal pain	117(100.0)
Nausea/ vomitting	109(93.2)
Fever	24(20.5)
Duration of hospital stay	8.04±4.26
HCT	37.23±4.80
Blood urea nitrogen	17.40±9.61
CRP	60.61± 81.2

Values are expressed as mean±SD. Values within the bracket are expressed as percentage.

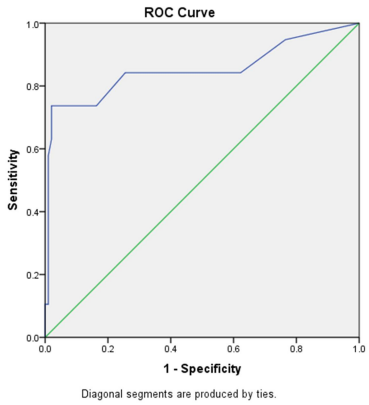

Figure 1. ROC curve showing test accuracy of CRP in the prediction of severity of acute pancreatitis (AUC=0.851, p<0.001).

Table II: Evaluation of different cutoff points of CRP as a predictor of severity of acute pancreatitis (n=117)

Cutoff points for CRP (mg/L)	Sensitivity	Specificity
104	73.7	93.9
136	73.7	96.9
160	73.7	98.0
185	63.2	98.0
202	57.9	99.0

Table III: Performance test of CRP as a predictor of severity of acute pancreatitis (n=117)

CRP (mg/L)	Severity		Total	p-value
	Severe acute pancreatitis	Mild and moderate severe acute pancreatitis		
CRP ≥ 160	14 (73.7)	2 (2)	16 (13.67)	<0.001
CRP < 160	5 (26.3)	96 (98)	101 (86.32)	
Total	19 (100.0)	98 (100.0)	117 (100.0)	

Chi-square(X^2) test was done to measure the level of significance.

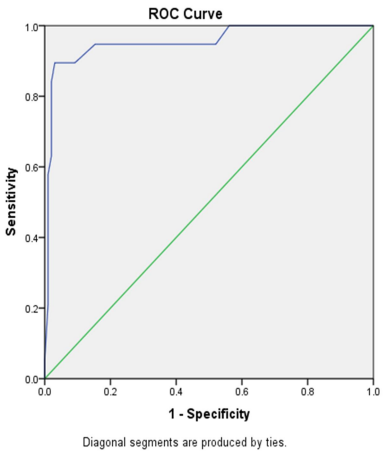

Figure 2. ROC curve showing test accuracy of HCT in the prediction of severity of acute pancreatitis (AUC=0.954, p<0.001).

Table IV: Evaluation of different cutoff points of Hematocrit (HCT) as a predictor of severity of acute pancreatitis (n=117)

Cutoff points for HCT (%)	Sensitivity	Specificity
37.50	94.7	67.3
40.05	89.5	90.8
42.50	89.5	96.9
44.40	68.4	98.0

Table V: Performance test of Hematocrit (HCT) as a predictor of severity of acute pancreatitis (n=117)

HCT (%)	Severity		Total	p-value
	Severe acute pancreatitis	Mild and moderate severe acute pancreatitis		
HCT ≥ 42.5	17 (89.5)	3 (3.1)	20 (13.67)	<0.001
HCT < 42.5	2 (10.5)	95 (96.9)	97 (86.32)	
Total	19 (100.0)	98 (100.0)	117 (100.0)	

Chi-square(X^2) test was done to measure the level of significance.

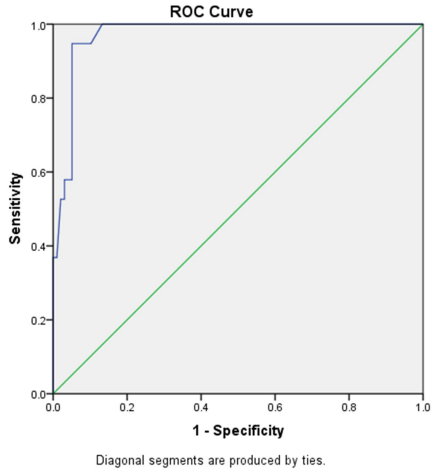

Figure 3: ROC curve showing test accuracy of BUN in the prediction of severity of acute pancreatitis (AUC=0.971, p<0.001).

Table VI: Evaluation of different cutoff points of BUN as a predictor of severity of acute pancreatitis (n=117)

Cutoff points for BUN (mg/dl)	Sensitivity	Specificity
19.57	100	86.7
22.65	94.7	91.8
25.66	94.7	94.9
28.25	57.9	94.9

Table VII: Performance test of BUN as a predictor of severity of acute pancreatitis (n=117)

BUN (mg/dl)	Severity		Total	p-value
	Severe acute pancreatitis	Mild and moderate severe acute pancreatitis		
BUN ≥ 25.66	18 (94.7)	5 (5.1)	23 (19.66)	<0.001
BUN < 25.66	1 (5.3)	93 (94.9)	94 (80.34)	
Total	19 (100.0)	98 (100.0)	117 (100.0)	

Chi-square(X^2) test was done to measure the level of significance

Discussion

A prospective observational study was carried out to evaluate the role of CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) in predicting severity of acute pancreatitis. Total 117 patients with acute pancreatitis, who fulfilled the inclusion criteria, were included in this study.

Among the patients, 67(57.3%) patients were male and 50(42.73%) patients were female. Mean age of the study population was 47.99±15.90 (mean± SD) with minimum age 18 years and maximum age 95 years. In a study by Albulushi et al.[7] found the mean age of acute pancreatitis of 47 years among which 55 % were male and 45% were female. The mean age and sex difference of the above study correlate with this study. Out of 117 patients, 36(30.8%) were smoker and 10 (8.5%) were alcoholic. 55(47%) patients were overweight and 12 (10.3%) patients were obese. Mean BMI was 25.36±3.4. Haque MM found that mean BMI was 25.88±2.95.[8]

The mean CRP (mg/L), Hematocrit (HCT) (%) and Blood Urea Nitrogen (BUN) (mg/dl) were 60.61±81.2, 37.23±4.8 and 17.40±9.61 respectively. Average duration of hospital stay was 8.04±4.26 days. Haque MM[8], in his study also found that mean HCT was 32.9±7.5, mean BUN was 21.7±7.2and average duration of hospital stay was 7.8±2.5 days. All of which is almost similar to these study results.

In this study, 25(21.4%) cases were gall stone pancreatitis, 23(19.7%) cases were due to hyper triglyceridaemia, 8(6.8%) cases were due to alcohol, 3(2.6%) cases were due to malignancy, 2 (1.7%) cases due to post ERCP complications, 2(1.7%) cases were due to gall stones and hypertriglyceridemia and 1 (0.9%) cases were due to hyper triglyceridaemia and alcohol (figure 1). In 53(45.3%) cases no definite etiology could be found. Al-Karawi et al. found that 67.5% cases of acute pancreatitis were due to biliary cause; alcohol was responsible in 1.8% of cases and 17% cases were due to unknown cause.[9] In another study, Chang et al. found gall stone as etiology in 34.1% of cases and alcohol in 33.6% cases and hyper triglyceridaemia in 12.3% of cases.[10]

High prevalence of hypertriglyceridemia in this study could be explained by increased prevalence of DM, obesity and metabolic syndrome among the study population. And the low prevalence of alcohol as etiology of acute pancreatitis could be due to social custom as well as religious belief.

Out of 117 patients 83(70.9%) had mild acute pancreatitis according to revised Atlanta criteria, 15(12.8%) patients had moderately severe acute pancreatitis and 19(16.2%) patients had severe acute pancreatitis (figure 2). Cho et al.[11] found 13% cases as severe acute pancreatitis, 8% cases as moderately severe and 79% cases as mild acute pancreatitis in their study which is similar to our study.

ROC curve evaluating the role of CRP in predicting severity of acute pancreatitis showed an AUC of 0.851. A cut off point of 160 mg/L showed highest sensitivity (73.7%), specificity (98%), positive predictive value (PPV) (87.5%) and negative predictive value (NPV) (95%). Khanna et al.[12] in their study found an AUC of 0.91 for CRP in predicting severity of acute pancreatitis and a CRP level of 150 mg/L showed highest sensitivity (86.2%), specificity (100%), positive predictive value (PPV) (100%) and negative predictive value (NPV) (88.6%), which are quite similar with our study.

One study showed that a hematocrit greater than 44% had a sensitivity of 72% on admission and of 94% after 24 hours in detecting organ failure. The negative predictive value at 24 hours was 96%. Although one study from Germany found no correlation between admission hematocrit and organ failure, most investigators have found hematocrit to be important in the management of patients with acute pancreatitis.[13]In our study, ROC curve evaluating the role of HCT in predicting severity of acute pancreatitis showed an AUC of 0.954. A cut off point of 42.50% showed highest sensitivity (89.5%), specificity (96.9%), positive predictive value (PPV) (85%) and negative predictive value (NPV) (97.9%).

ROC curve evaluating the role of BUN in predicting severity of acute pancreatitis showed an AUC of 0.971. A cut off point of 25.66 mg/dl showed highest sensitivity (94.7%), specificity (94.9%), positive predictive value (PPV) (78.3%) and negative predictive value (NPV) (98.9%). Wu and colleagues recently performed a large observational cohort study on data from 69 U.S. hospitals and found that BUN may be superior to Hgb (but not hematocrit).[6] For every 5 mg/dL increase in BUN during the first 24 hours, the age- and gender-adjusted odds ratio for mortality increased by 2.2. Of multiple routine laboratory tests examined, BUN yielded the highest accuracy in determining mortality at 24 and 48 hours.[6]

Conclusion

This study evaluated the role of CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) in predicting severity of acute pancreatitis. All three of them performed quite well in this regard. So, CRP, Hematocrit (HCT) and Blood Urea Nitrogen (BUN) can be taken into consideration for predicting severity of acute pancreatitis early in the course of disease

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