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Estimation of Blood Urea Nitrogen as an Indicator of Severity in Acute Pancreatitis.

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ABSTRACT

Background: Acute pancreatitis (AP) is an acute inflammatory process of the pancreas with variable involvement of the pancreas, regional tissues around the pancreas, or remote organ systems. The aim of study was to evaluate Blood urea nitrogen (BUN) as an indicator of severity and single prognostic indicator in acute pancreatitis and to Compare BUN with Ranson's and BISAP criteria in prediction of SAP and mortality. **Methods:** A prospective observational study, total 72 patients participated in this study. All Patients presenting to the Emergency and Outpatient Departments of Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar from October 2015 to September 2016 with suspicion of acute pancreatitis. **Results:** In the study, of these 66 (91.7%) were male and 6 (8.3%) were female. Mean age of the study subjects was 38.47 + 11.01. Mean age of patients with SAP was slightly higher than with non severe pancreatitis (41.89 vs. 37.33) but not statistically significant (p=0.55). 75% of the Pancreatitis was due to alcohol (54 out of 72), followed by gallstones in 13.88% (10/72). **Conclusion:** BISAP score within the first 24 hours of admission stratifies patients according to their risk of mortality and onset of organ failure.

Keywords: Acute Pancreatitis, blood urea nitrogen, Ranson's and BISAP criteria.

INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas with variable involvement of the pancreas, regional tissues around the pancreas, or remote organ systems. In 80% of the cases the disease is mild, with interstitial oedema, and leads to recovery within days or weeks.[1,2]

Severe acute pancreatitis is a significant medical and surgical problem. Identification of patients at risk for complications and mortality early, within 24 hours, so called golden hours or therapeutic window in the course of acute pancreatitis (AP) is an important step in improving outcome.[1] Predicting severity and course of pancreatitis early in the course of disease helps to manage patient better and minimize organ dysfunction.

Although severe pancreatitis occurs in less than 30% of cases, it accounts for more than 90% of the mortality attributed to AP.[6] To improve the survival rate in patients with acute pancreatitis, severity assessment during the initial examination is extremely important to ensure the quick and accurate diagnosis of severe cases ,to commence appropriate initial treatment, and, if necessary, to transfer the patient to an advanced specialist medical institution.[7]

Several clinical, biochemical and imaging parameters help in grading severity of disease during first week. Current methods of risk stratification in AP have important limitations. The Ranson and modified Glasgow score contain data not routinely collected at the time of hospitalization like LDH.[3-5] In addition, both require 48 hours to complete, missing a potentially valuable early therapeutic window. [6]

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Aims and Objectives

The purpose of the study was to evaluate blood urea nitrogen (BUN) as an indicator of severity and single prognostic indicator in acute pancreatitis and to Compare BUN with Ranson's and BISAP criteria in prediction of SAP and mortality.

MATERIALS AND METHODS

Study Design:
The prospective observational study

Samplings:
Total 72 patients participated in this study.

Setting and Study population: All Patients presenting to the Emergency and Outpatient

Departments of Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar from October 2015 to September 2016 with suspicion of acute pancreatitis.

Inclusion criteria

1. Only patients with symptoms of <24 hours were included in the study.
2. Only Patients admitted in medical, surgical and gastroenterology ward with diagnosis of AP.

Exclusion Criteria

1. Patients with changes of chronic pancreatitis or diagnosis in doubt.
2. Patients presenting ≥24 hours after symptom onset.
3. Patients with known chronic renal failure

The diagnosis of AP was based on the presence of two of the following three features: (i) abdominal pain characteristic of AP, (ii) serum amylase and / or lipase ≥ 3 times the upper limit of normal, and (iii) characteristic findings of AP on abdominal imaging (USG/CECT scan).

Data was collected on standard preformed, detailing the medical history, physical examination and investigations. The worst (most extreme) value for vital signs within the first 24 h and 48 hours were recorded. Patients under treatment were followed up for development of severe disease or death of the patient.

BUN values were obtained at admission, at 24 hours and 48 hours. Data from all these investigation were utilized for assessing scores for the various scoring systems as: Ranson, Balthazar and BISAP. BISAP scores were calculated using data from the first 24 h from admission and the Ranson's score using data from the first 48 hours. All patients were followed up throughout the hospital stay and the outcome of disease noted.

Statistical Analysis

Data entry was done using Microsoft Excel 2010 version and analysis using SPSS version 17 trial version. Univariate analysis for continuous variables was conducted with the unpaired Student's t test. Categorical variables were analyzed by the chi square test or Fisher's exact test. 'p' value of <0.05 is taken as a measure of significance. 'p' value of <0.01 is taken as highly significant.

RESULTS

72 patients with Acute Pancreatitis were included in the study, of these 66 (91.7%) were male and 6 (8.3%) were female. Mean age of the study subjects was 38.47 + 11.01. Mean age of patients with SAP was slightly higher than with non-severe pancreatitis (41.89 vs. 37.33) but not statistically significant (p=0.55). 75% of the Pancreatitis was due to alcohol (54 out of 72), followed by gallstones in 13.88% (10/72) [Table 1].

18 out of 72 patients (25%) had persistent OF and classified as SAP, while 54 had non severe course. In SAP group 16 were due to alcohol and 2 due to gall stones.

Table 1: Demographic profile and outcomes

	Total (72)	Severe pancreatitis (18)	Non-severe pancreatitis(54)	p - value
Age in years (mean + SD)	38.47 + 11.01	41.89 + 12.68	37.33 + 10.41	0.55 (NS)
Sex (M:F)	33:3	9:0	27:3	0.55 (NS)
Alcohol	54	16	38	-
Gall stones	10	2	8	-
Post ERCP	2	0	1	-
Trauma	2	0	1	-
Hypertriglyceridimia	0	0	0	-
Drug induced	0	0	0	-
Malignancy	2	0	1	-
Idiopathic	2	0	1	-
Hospital stay in days	10.54 + 6.59	12.44 + 7.92	9.89 + 5.71	0.2996(NS)
ICU stay in days	2.36 + 2.79	5.67 + 3.91	1.26 +0.86	<0.0001
Mortality (%)	10 (13.89)	10 (55.55)	0 (0)	<0.0001
Necrotizing pancreatitis	28/58(48.27%)	10/10(100%)	18/48(37.5%)	0.0169

Table 2: Clinical, laboratory and imaging characteristics of cases

Units as Mean + SD	Total (72)	Severe pancreatitis (18)	Non severe pancreatitis (54)	p value
BISAP SCORE	1.44 + 1.18	3 + 1	0.93 + 0.68	<0.0001
BUN at admission mg/dl	18.88 + 18.19	39.88 + 26.54	11.88 + 5.02	<0.0001
BUN at 24 hours	21.61 + 19.80	46.05 + 27.26	13.28 + 4.86	<0.0001
BUN at 48 hours	21.13 + 20.27	47.70 + 25.78	11.91 + 4.93	<0.0001
Creatinine at admission	1.44 + 1.2	2.63 + 1.85	1.04 + 0.47	0.0002
Creatinine at 48 hours	1.47 + 1.23	3.13 + 1.46	0.92 + 0.35	<0.0001
CTSI	4.52 + 3.16	8 + 2	3.79 + 2.87	0.004
Hematocrit at admission	50.52 + 4.23	51 + 2.92	50.35 + 4.62	0.698
Hematocrit at 48 hours	46.82 + 5.11	45.11 + 4.57	47.38 + 5.2	0.25
Ranson score	3.56+ 2.58	7.11 + 2.37	2.37 + 1.18	<0.0001
SIRS at admission	56/72 (77.77%)	18/18 (100%)	38/54 (70.37%)	0.16 (NS)
SIRS at 48 hours	36/72 (50%)	18/18 (100%)	18/54 (33.33%)	0.001

Above [Table 2] showed the Different clinical, laboratory and imaging criteria as observed in both groups were presented.

[Table 3] showed the sensitivity, specificity, positive predictive value (PPV), negative predictive (NPV) value and diagnostic accuracy of different criteria for prediction of mortality.

Table 3: Sensitivity, specificity, positive & negative predictive value and diagnostic accuracy of different criteria for prediction of severe acute pancreatitis

Criteria used (critical value)	Sensitivity (percentage)	Specificity (percentage)	Positive predictive value (percentage)	Negative predictive value (percentage)	Accuracy of diagnostic test (percentage)
BISAP SCORE ≥3	77.77	96.29	87.48	92.86	91.66
BUN≥20 mg/dl at admission	89	93	80	96	91.66
BUN ≥25 mg/dl at 24&48 hours	89	100	100	96	97.22
BUN ≥20 mg/dl at 24 hours	100	75	89	100	91.66
BUN Rise ≥5 mg/dl at 48 hours	88.88	96.29	88.87	96.29	94.44
CTSI ≥ 5	100	63	36	100	68.96
RANSON SCORE ≥3	100	74.07	56.25	100	80.55

Table 4: Sensitivity, specificity, PPV, and NPV of different scoring systems in predicting mortality

Criteria used (critical value)	Sensitivity (percentage)	Specificity (percentage)	Positive predictive value (percentage)	Negative predictive value (percentage)	Accuracy of diagnostic test (percentage)
BISAP SCORE ≥3	100	90	63	100	91.66
BUN ≥25 mg/dl at 24 hours	100	90	63	100	91.66
BUN≥20 at admission	100	94	71	100	94.44
BUN ≥25 mg/dl at 48 hours	100	94	71	100	94.44
BUN rise ≥5mg/dl at 48 hours	100	94	71	100	94.44
RANSON SCORE≥3	100	42	22	100	50

[Table 4] showed, BUN at admission in non survivors is significantly higher than survivor group (40.13 + 17.13 vs 15.45 + 16.11 mg/dL; p=0.0034; PPV 71%, NPV 100%).

BUN at 24 hours was significantly higher among those who died. (Non survivors: 40.13 + 17.13 vs survivors: 15.45 + 16.11 mg/dL; p=0.0034; PPV 63%, NPV 100%).

All criteria have 100% NPV for predicting patients at risk of dying while specificity is better for BISAP (90%) and BUN ≥25 mg/dl at admission and at 24 or 48 hours (90 and 94%) and worse for Ranson score (42%).

DISCUSSION

In the present study, 72 patients with Acute Pancreatitis were included in the study, of these 66 (91.7%) were male and 6 (8.3%) were female. Mean age of the study subjects was 38.47 + 11.01. Mean age of patients with SAP was slightly higher than with non severe pancreatitis (41.89 vs. 37.33) but not statistically significant (p=0.55). 75% of the Pancreatitis was due to alcohol (54 out of 72), followed by gallstones in 13.88% (10/72). 18 out of 72 patients (25%) had persistent OF and classified as SAP, while 54 had non severe course. In SAP group 16 were due to alcohol and 2 due to gall stones.

In the present study patients were relatively younger compared to previous studies and majority of patients were male (91.7%) compared to previous studies where gender distribution was almost equal.[6-8] Alcohol was the most common cause of AP followed by gall stones in contrast to previous studies where gall stones were the most common cause of AP.[6-8]

10 out of 18 patients with SAP died during the course of illness while all patients with non severe course survived. 4 patients expired on 3rd day 6 patients expired after 9, 11, 13 days. Mean ICU stay was 5.67 + 3.91 days in SAP group while it is 1.26 +0.86 in non severe pancreatitis (p<0.0001).

Blood urea nitrogen is part of the long established Ranson and Glasgow scoring systems. Several studies have incorporated BUN as a part scoring systems such as “BALI”191 and “BISAP” to predict mortality in acute pancreatitis. Blood urea nitrogen was chosen because of its high predictive value because it is an integral marker of tissue necrosis, protein catabolism, and renal function.

In this study we evaluated BUN, because it serves as a surrogate of intravascular volume status and is also a physiological variable that changes in response to therapy. In addition it is simple and routinely used.

In a recent study by Wu et al, a BUN >20 mg/dl or any rise in BUN level at 24 hours was associated with increased risk for mortality.[7] They observed that, for every 5-mg/dl increase in BUN during the first 24 hours, odds ratio for mortality increased by 2.2 (95% confidence limits, 1.8, 2.7). The accuracy of serial BUN measurements to evaluate mortality risk was found to be comparable to APACHE II scores in the same patient population.[9]

Present study noted BUN ≥20 mg/dl at admission has PPV of 80% and NPV of 96% for predicting SAP with 89% sensitivity and 93% specificity. BUN ≥25 mg/dl at 24 hours is highly specific with PPV of 100% for prediction of SAP, and NPV of 89% and

may miss few cases which may require ICU care and aggressive management protocol. This can be overcome by reducing BUN threshold to ≥20 mg/dl, which identifies all the cases of SAP at the cost of specificity. BUN Rise ≥5 mg/dl at 48 hours has PPV of 88.87% and NPV of 96.29% for predicting SAP.

BUN ≥25 mg/dl at 24 or 48 hours has the best diagnostic accuracy (94.22%) for SAP with sensitivity and specificity of 89% and 100% respectively. Of all the criteria, BUN at 48 hours has the best predictive value for SAP with AUC of 0.996 with 24.27 as optimal cut off while BUN at admission and 24 hours has AUC of 0.949 and 0.992 respectively.

As compared to a Biliary Ranson score >3, a modified Imrie score >3 and an APACHE-II score >5, random blood sugar >150 mg/dL can be considered as an oversimplified and effective prognostic indicator at admission in patients with gallstone pancreatitis.

From our analysis, AUC of BISAP for prediction of SAP was 0.934 (0.799-0.99) with >2 as optimal discriminative value. Ranson score has better discriminative value with AUC of 0.975 (0.86-1.0) for prediction of SAP.

Thus BUN, BISAP and Ranson's in this study were found to be accurate for risk stratification and predicting mortality. In fact BUN performed better than more complex scoring systems such as Ranson's for identifying those at risk of organ failure and SAP. Increasing BUN and BISAP score correlated with increased SAP and mortality ($p<0.001$).

CONCLUSION

BUN serves as a simple, quick and accurate predictor of severity and mortality in AP. BISAP score within the first 24 hours of admission stratifies patients according to their risk of mortality and onset of organ failure. BUN is more elevated in etiology related to gall stone acute pancreatitis when compared to other etiologies like alcoholism, trauma, and malignancy, drug- induced and idiopathic.

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