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Original Research Article

A study on the prognostic value of the strong ion gap in acute pancreatitis

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ABSTRACT

Background: Severe acute pancreatitis (SAP) may range up to 20-30%. So, it is important to assess the disease severity in a timely and accurate manner to provide comprehensive treatment to Acute pancreatitis (AP) patients, which will allow the clinician to consider more aggressive interventions to prevent adverse outcomes and decrease the high mortality of SAP.
Methods: This is a prospective cohort study of 61 patients admitted to the KIMS, Hubli from December 2016 to June 2018 with Acute pancreatitis (AP). Blood gas and biochemical analysis for each patient was performed on admission and multiple metrics was calculated according to the Stewart's acid-base theory and their accuracy was used as predictors of AP severity and mortality. A p value of <0.05 was considered statistically significant.
Results: Of the 61 patients presenting with AP, 6 developed severe AP and 5 died during hospitalization. Patients with severe AP had significantly higher median strong ion gap (SIG) than patients with mild or moderate AP respectively with $p<0.001$ making SIG strong predictor of severity, mortality and good prognostic indicator.
Conclusions: SIG is a strong independent predictor of severity and mortality. It helps in better triaging, risk stratification, management and prognosis of such patients in the future.

Keywords: Acute pancreatitis, Strong ion gap, Outcome prediction, Anion gap

INTRODUCTION

Acute pancreatitis (AP) is an inflammatory condition of the pancreas with a clinical course that varies from mild to severe, leading to activation of pancreatic enzyme and causing self-digestion of the pancreas. Acute pancreatitis is a common indication for hospital admission, increasing in incidence, including in children, pregnancy and the elderly.[1] Mild AP is characterized by a lack of organ failure and no local or systemic complications. Moderately severe AP is indicated by transient organ failure (resolves within 48 h) and/or local or systemic complications. Lastly, severe AP is characterized by persistent organ failure that may involve one or more organs.[2] The mild acute pancreatitis is a self-limiting disease that ranges about 80-90% of patients with only minimal or transitional systemic manifestations, but about 20-30% of patients develop a severe disease that can progress to systemic inflammation and cause pancreatic necrosis, multi-organ failure, and potentially death.[3] The overall mortality rate of AP is 2-5% , but the mortality of severe acute pancreatitis(SAP) may range upto 20-30%. It is important to assess the disease severity in a timely and accurate manner to provide comprehensive treatment to AP patients, which will allow the clinician to consider more aggressive interventions to prevent adverse outcomes and decrease the high mortality of SAP. Reliable markers or score systems predicting the severity of AP is of clinical importance for the management of AP.[4]

METHODS

Study design

It is a Prospective cohort study.

Source of data

Patients with a primary diagnosis of AP admitted to Department of Surgery, Karnataka Institute of Medical Science (KIMS), Hubli from December 2016 to June 2018 were screened for potential inclusion. Diagnosis of AP required two of the three following criteria: abdominal pain consistent with the disease; serum amylase greater than three times the upper limit of normal or raised serum lipase or characteristic findings from abdominal ultrasonography, contrast-enhanced computed tomography (CECT) and/or Magnetic resonance imaging (MRI). A heparinized arterial blood sample was collected on admission for all the study patients and analyzed in the ICU blood-gas analyser.

Table 1: Classification of severity of acute pancreatitis based on Atlanta classification.

Severity category	Local complications	Systemic complications
Mild	No local complications	No systemic complications
Moderate	Sterile peripancreatic collection	Transient organ failure that resolves in 48 h
Severe	Infectious peripancreatic collection	Persistent organ failure >48 h (single or multiple organ failure)

Inclusion criteria

Adult patient with abdomen pain. Admission to our centre within 72 h of onset of abdomen pain. Available blood gas and laboratory assessments on admission to our centre.

Exclusion criteria

Patients with co-morbidities that might affect their blood gas results (e.g. diabetic ketoacidosis, chronic renal failure). Patients who had been previously treated in another hospital prior to transfer to our centre. Those who had received ≥400 ml intravenous fluids before admission to our centre.

Data collection

Demographic information, arterial blood gases, and biochemical data were collected. Blood gas and biochemical analysis for each patient was performed on admission and multiple metrics was calculated according to the Stewart's acid-base severity of AP was defined according to the 2012 revision of the Atlanta classification. Briefly, mild, moderate and severe types of AP were classified based on the presence of organ failure and complications.

Statistical analysis

Statistical analyses were performed using the SPSS 22.0 statistical software package (IBM Analytics, Armonk, NY). A p value of <0.05 was considered statistically significant.

Table 2: Definition of organ failure based on the modified Marshall scoring system.

Organ system	Score				
	0	**1**	**2**	**3**	**4**
Respiratory (PAO_2/FIO_2) (mm Hg)	>400	301-400	201-300	101-200	<101
Renal (serum creatinine)	<1.4 mg/dl	1.4-1.8 mg/dl	1.9-3.6 mg/dl	3.6-4.9 mg/dl	>4.9 mg/dl
Cardiovascular (systolic blood pressure)	>90 mm Hg	<90 mm Hg Fluid responsive	<90 mm Hg Not fluid responsive	<90 mm Hg Ph<7.3	<90 mm Hg Ph<7.2

Table 3: Estimation of FIO_2 in non-ventilated patients.

Supplemental oxygen (l/min)	FIO_2 (%)
Room air	21
2	25
4	30
6-8	40
9-10	50

RESULTS

Demographic data

Age distribution

The study included 61 patients. The age distribution was analysed and found that 59% of the patients were between 21-40 years old with mean age 35years and median age 36 years. 32% of patients were between the age 41-60 years.

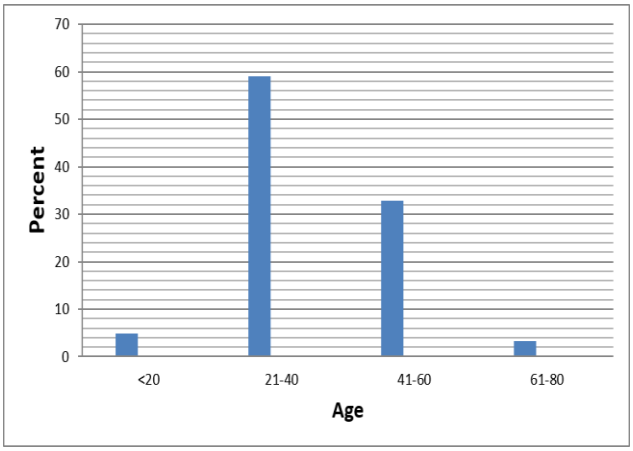


Figure 1: Age distribution.

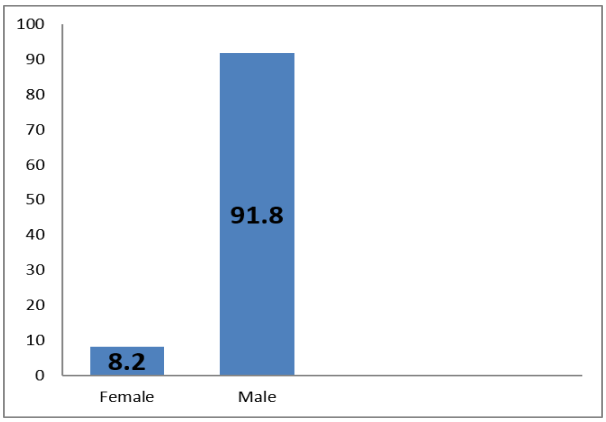


Figure 2: Gender distribution.

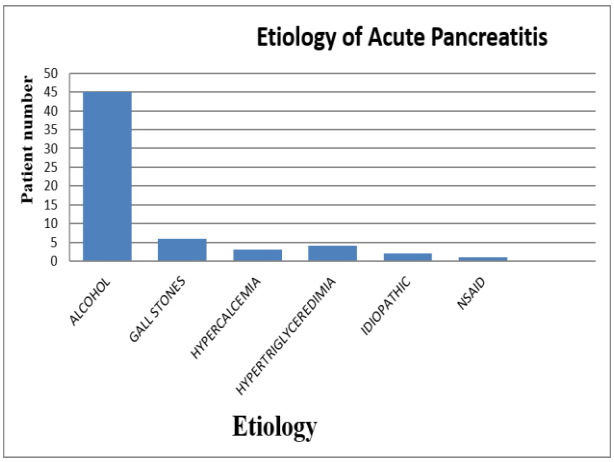


Figure 3: Etiology of acute pancreatitis.

Gender distribution

AP was more common in males with 91% being males (56 patients) compared to females which is 8% (5 patients). Distribution of severity of AP patients based on Atlanta classification during the study period, 61 patients with acute pancreatitis were screened. Out of 61 patients, 28 patients belonged to moderate group, 27 patients belonged to mild group and 6 patients belonged to severe group based on Atlanta classification.

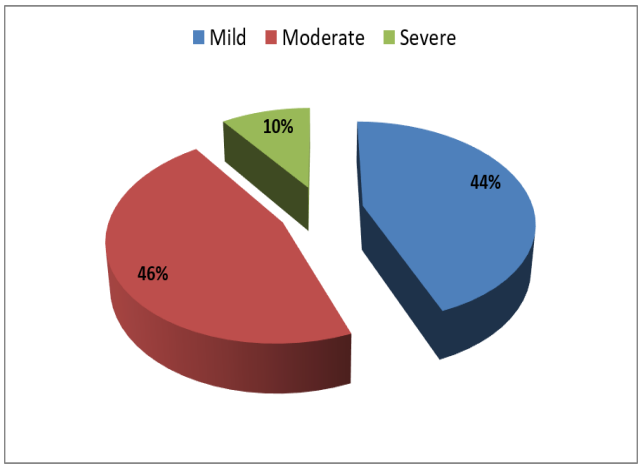


Figure 4: Distribution of severity of AP patients based on Atlanta classification.

Mean SIG score in different severity groups

Patients in the severe group showed significant higher median SIG of 28.27 meq/l, than those in mild and moderate group where median SIG was 8.8 meq/l and 12.53 meq/l respectively with $p<0.001$.

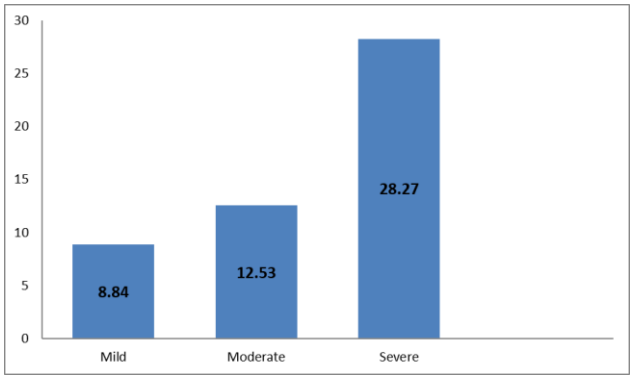


Figure 5: Mean SIG in different severity groups.

DISCUSSION

A prospective cohort study was conducted to identify predictors of severity and outcome in a cohort of AP patients admitted in Department of surgery, KIMS Hubli.

It was aimed to evaluate whether the Stewart analysis might help predict severity, mortality in adult AP patients with simple and routine clinical tests. The results suggested that SIG was an accurate predictor of severity of acute pancreatitis and a moderate predictor of mortality. For both severity and mortality, SIG was proved to be the strongest predictor and outperformed many other traditionally used markers.

AG and base excess (BE) are commonly used to assess acid-base disturbances in clinical practice. The predictive power of AG and BE for mortality had been evaluated in the literature in different subsets of patients with controversial results.[5] The main reason might be that AG lacks sensitivity and specificity due to over simplification not taking into account the influence of albumin and phosphate. In this way, albumin and lactate-corrected AG (AGcorr) might be more appropriate for the detection of unmeasured anions in critically ill patients.

Table 4: Comparison study with Shen et al on severity based on SIG.

Group	Present study	Xiao Shen and co.
Mild-moderate AP	10.4	2.41
Severe AP	25.65	7.69

Study by Moviat et al, demonstrated that Stewart's acid-base analysis was able to uncover underlying mixed metabolic acid-base disorders in an ICU population with otherwise no apparent acid-base abnormalities.[6]

The study conducted by Story et al, suggested that the Stewart approach had predictive power for mortality.[7] Antonini et al, compared the AG and Stewart's variables in 136 ICU patients and demonstrated that metabolic acidosis induced by unmeasured anions was closely correlated with late mortality.[8] In general, the predictive power of SIG was not clearly identified in these critically ill patients due to the heterogeneity of the population in those studies. However, in other more homogeneous populations, such as patients with trauma and cardiac disease, SIG was a strong and accurate predictor of outcome.

Sharma et al, evaluated the predictive power of arterial blood gas parameters using conventional methodology in 205 AP patients with a mortality rate of 14.6%, similar to our study.[9] The authors found that lower arterial pH, bicarbonate level and higher base deficit on admission predicted an adverse outcome in patients with acute pancreatitis and the area under ROC curve was 0.77 (95% confidence interval (CI): 0.66-0.88), 0.71 (95% CI:0.62-0.79) and 0.78 (95% CI:0.69-0.87) for the three parameters. However, many patients presented with hypoalbuminemia and hyperlactatemia in the early stage of acute pancreatitis and these variables were not taken into consideration.

Shen et al, evaluated 186 patients presenting with AP in which 85 (45.7%) developed severe AP and 33 (17.7%) died during hospitalization. Patients with severe AP had significantly higher median strong ion gap (SIG) than patients with mild or moderate AP (7.88 vs. 2.11 meq/l, $p<0.001$).[10] In multivariate logistic regression analysis, SIG had an odds ratio (OR) of 1.56 ($p<0.001$). They concluded that SIG was good predictor of severity and mortality. SIG could be easily calculated with simple and inexpensive blood tests right after hospital admission, its clinical use is of significant potential. In the case of acute pancreatitis, hypoperfusion and microcirculation disturbance might be the main reasons for elevated unmeasured anions. Moreover, the most commonly involved organs are lung and kidney, not liver.[11] The significantly elevated levels of BUN and creatinine, suggest that failed renal excretion of unmeasured anions may, at least in part, explain such SIG.[12] This hypothesis is partly supported by data from Moviat et al, showing that increased creatinine levels were independently related to a high SIG.

My study provides evidence that the SIG can be used to estimate the likely subsequent severity of pancreatitis with an excellent level of accuracy. Given the importance of estimating likely subsequent severity in the triage and treatment of these patients and their referral to appropriate centers, my findings imply that patients presenting with pancreatitis should be evaluated by calculation of their SIG. The finding that SIG also predicts mortality provides further justification for its early measurement in these patients for the purpose of prognosis and risk stratification.

Limitations

SIG calculation is limited to homogenous population only. Patients with other comorbid conditions are excluded. My study is also limited to patients who haven't visited any other hospital or taken first aid before reaching my hospital.

CONCLUSION

SIG can be used as a triaging and prognostic tool for acute pancreatitis within 24 hours of admission. It can predicit the early severity and complication associated and help in better and early management of the same.

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