

## Prediction of Severity of Acute Pancreatitis Using Total Serum Calcium and Albumin Corrected Calcium: A Prospective Study in a Tertiary Care Hospital

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Conflict of interest: Nil

### Abstract:

**Background:** Acute pancreatitis (AP) is a major cause of mortality and morbidity worldwide. In approximately one-third of the patients, acute severe pancreatitis may develop, producing progressive organ dysfunction usually caused by a rapidly progressive inflammatory response, which is associated with a prolonged hospital stay and significant morbidity and mortality. Patients with mild Acute Pancreatitis have mortality rates of less than 1%, but it is rapidly increased up to 10–30% in cases with severe Acute Pancreatitis. We wanted to evaluate serum calcium and albumin corrected calcium as prognostic severity factors in acute pancreatitis.

**Methods:** This prospective study was conducted in a tertiary hospital from September 2023 to February 2024. 30 patients were enrolled for the study. All patients who were diagnosed as acute pancreatitis by clinical examination, laboratory, radiological and biochemical investigations were considered as subjects. Serum calcium & Albumin Corrected Calcium (ACC) were measured within 24 hrs of admission. Significance of Serum Calcium and Albumin Corrected Calcium in predicting outcome of acute pancreatitis was assessed and compared with BISAP score.

**Results:** Our study showed decreasing TC and ACC for increasing severity of the disease. Although this study failed to differentiate between moderate and mild AP, in our study cutoff of <7 mg/dL for TC predicted the occurrence of severe AP with Sensitivity of 100% and Specificity of 89%. Similarly, ACC of <7.5 mg/dL was computed for severity of AP we found Sensitivity of 100% and Specificity of 89%.

**Conclusion:** Total Serum Calcium and Albumin Corrected Calcium (ACC) can predict severity of acute pancreatitis, as with BISAP score but it is not superior to BISAP score.

**Keywords:** Total Serum Calcium, Albumin Corrected Calcium, Acute Pancreatitis, Hypocalcemia.

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### Introduction

Acute pancreatitis (AP) is a major cause of mortality and morbidity worldwide. In approximately one-third of the patients, Acute severe Pancreatitis may develop, producing progressive organ dysfunction usually caused by a rapidly progressive inflammatory response, which is associated with a prolonged hospital stay and significant morbidity and mortality. Patients with mild Acute Pancreatitis have mortality rates of less than 1%, but it is rapidly increased up to 10–30% in cases with severe Acute Pancreatitis. [1]

The global incidence of Acute Pancreatitis is 34 per 100,000 individuals. [11] Prevalence rate for Pancreatitis in India is 7.9 per 100,000. Prevalence rate for men and women 8.6 and 8.0 per 100,000 respectively in India. [12] Overall about 20% of patients with acute pancreatitis have a severe course and mortality rate is of 10% to 30% in severe pancreatitis patients. [12]

### Objectives of the Study

1. To measure and evaluate the Total Serum Calcium and Albumin Corrected Calcium levels in Acute Pancreatitis.
2. To compare the Total Serum Calcium and Albumin Corrected Calcium levels in Acute Pancreatitis with Revised Atlanta Classification of Acute Pancreatitis.

### Materials and Methods

A prospective case series study was done in a tertiary hospital for a period of 6 months from September 2023 to February 2024. Patients aged >18 yrs. who were admitted with clinical features and blood investigations suggestive of AP with following findings were included in study. 30 patients were enrolled using a re structural proforma and questionnaire.

Clinical and demographic data with respect to gender, age, clinical history, comorbidities was collected from medical records. Laboratory and radiological investigations were taken 24 hrs. after admission. Ethical approval was taken from respective ethical committee.

After taking consent from patient self-designed data collection form was used to collect data.

$$\text{Sample Size} = \frac{Z_{\alpha/2}^2 \times P(1-P)}{d^2}$$

$Z_{\alpha/2}$  = Std normal variant 1.96.

P = Expected proportion from population

d = Absolute error

Indian study reported prevalence rate for Pancreatitis in India is 7.9 per 100,000. Prevalence rate is very small 0.0009. Considering 0.0009% prevalence with 2% margin of error. Minimum sample needed to conduct this study will be less than 10 cases. 30 cases will be selected to conduct this study.

**Sampling Method:** Consecutive patients will be selected.

**Study Period:** 6 months from September 2023 to February 2024.

#### Inclusion Criteria

- All patients aged more than 18 years who are admitted with clinical features and blood investigations suggestive of acute pancreatitis with following findings.
- Upper abdominal pain of acute onset often radiating to back.
- Serum amylase or lipase greater than 3 times normal
- Findings on radiological imaging consistent with acute pancreatitis.

#### Exclusion Criteria

- Chronic kidney disease.
- On calcium supplements.

- Chemotherapy.

**Statistical Analysis:** Categorical data will be represented in the form of frequency and percentage. Association between variables will be assessed with Chi Square Test and Fisher's Exact test if the cell values were small. Quantitative data will be represented as Mean & Sd. ANOVA will be used to compare total calcium in mild, moderate, and severe cases. ROC curve will be used to establish the possible cutoff values for Total Serum Calcium and Albumin Corrected Calcium.

A P value of <0.05 will be considered statistically significant.

Data will be analyzed with IBM SPSS Version 28 for windows.

**Operational Definition:** To evaluate TC and ACC prognostic factors of severity the lowest TC values were collected within first 24 hours of hospital admission. These values were then corrected based on serum albumin level using formula  $ACC = TC + (0.8 * [4 - \text{serum albumin}])$ .

#### Results

Within the study period, a total of 30 patients were included in the study. Patients aged >18 yrs. were included in the study. AP was commonly observed between 25 to 45 years of age. In our study, severity of AP was not related to the age of the patient, there was no association between etiology and severity of AP. Out of 30 patients 17 of them had comorbidities like HTN, DM or both and 12 patients were found to have smoking habits. In our study alcohol consumption contributed to 96% of cases. Our study showed decreasing TC and ACC for increasing severity of the disease. Although this study failed to differentiate between moderate and mild AP, in our study cutoff of <7 mg/dL for TC predicted the occurrence of severe AP with Sensitivity of 100% and Specificity of 89%.

Similarly, ACC of <7.5 mg/dL was computed for severity of AP we found Sensitivity of 100% and Specificity of 89%.

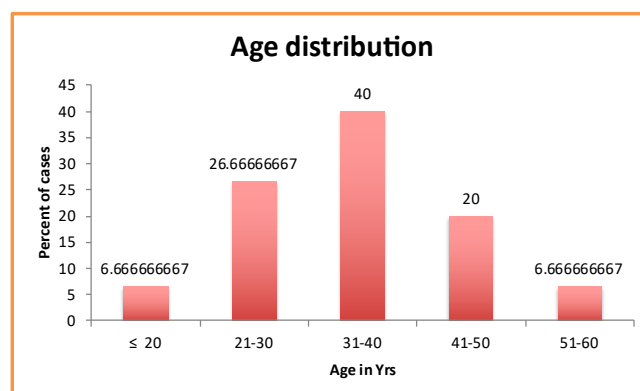


Figure 1: Age distribution

Above figure shows case distribution with respect to age. 40 percentage of cases were found in age group between 31-40 yrs. of age in our study.

In our study, severity of AP was not related to the age of the patient, there was no association between

etiology and severity of AP. In a review article by Meher et al [6], the total calcium and albumin corrected calcium were considered as emerging potential biomarkers for prediction of severity in AP.

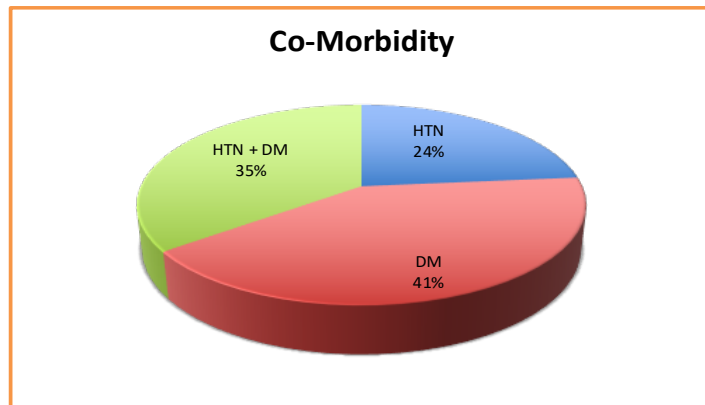


Figure 2: Co-Morbidity

Table 1

| Smoking | No of Cases | Percent |
|---------|-------------|---------|
| YES     | 18          | 60.0    |
| NO      | 12          | 40.0    |
| Total   | 30          | 100.0   |

In our study 60 percentage of cases had smoking habit and 40 percentage of cases didn't had smoking habit.

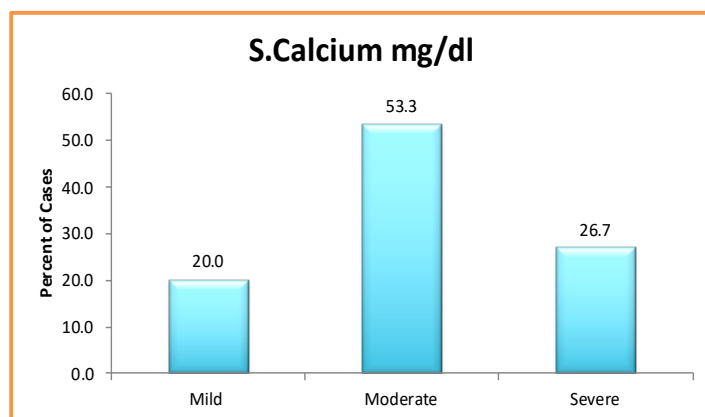


Figure 3: S. Calcium mg/dl

Table 2

| S. Calcium mg/dl   | BISAP-severity |        | Total |
|--------------------|----------------|--------|-------|
|                    | Mild -moderate | Severe |       |
| Mild - Moderate    | 21             | 1      | 22    |
| Severe             | 0              | 8      | 8     |
| Total              | 21             | 9      | 30    |
| Kappa P<0.001, Sig |                |        |       |
| Sensitivity        |                |        | 100%  |
| Specificity        |                |        | 89%   |
| PPV                |                |        | 95%   |
| NPV                |                |        | 100%  |
| Accuracy           |                |        | 97%   |

Our study showed decreasing TC and ACC for increasing severity of the disease. Although this

study failed to differentiate between moderate and mild AP, in our study cutoff of <7 mg/dL predicted

the occurrence of severe AP with sensitivity of 100%, specificity of 89%, positive predictive value of 95%, and negative predictive value of 100% and

was compared with the sensitivity 67%, specificity 82%, PPV 27% and NPV 96% of TC with that of the study done by Gutierrez-Jimenez et al.

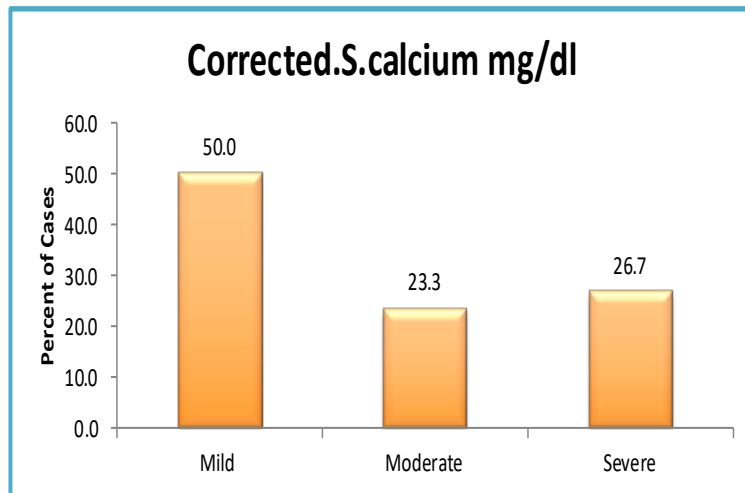


Figure 4: Corrected S. calcium mg/dl

**Table 3**

| Corrected. S. calcium mg/dl | BISAP-severity |        | Total |
|-----------------------------|----------------|--------|-------|
|                             | Mild -moderate | Severe |       |
| Mild - Moderate             | 21             | 1      | 22    |
| Severe                      | 0              | 8      | 8     |
| Total                       | 21             | 9      | 30    |
| Kappa P<0.001, Sig          |                |        |       |
| Sensitivity                 | 100%           |        |       |
| Specificity                 | 89%            |        |       |
| PPV                         | 95%            |        |       |
| NPV                         | 100%           |        |       |
| Accuracy                    | 97%            |        |       |

Similarly, ACC of <7.5 mg/dL was computed for severity of AP we found sensitivity of 100%, Sp 89%, PPV 95% and NPV 100% and was compared with the sensitivity 67%, specificity 90%, PPV 40% and NPV 96% of ACC with that of the study done by Gutierrez-Jimenez et al.

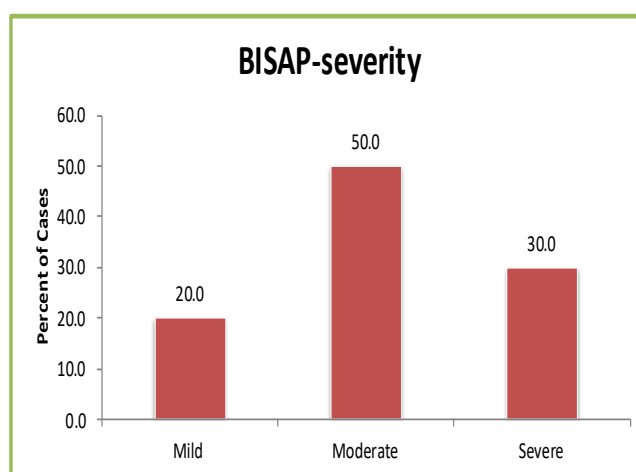


Figure 5: BISAP-severity

**Discussion**

Acute pancreatitis (AP) is a major cause of mortality and morbidity worldwide. In approximately one-third of the patients, Acute

severe Pancreatitis may develop, producing progressive organ dysfunction usually caused by a rapidly progressive inflammatory response, which is associated with a prolonged hospital stay and

significant morbidity and mortality. Patients with mild Acute Pancreatitis have mortality rates of less than 1%, but it is rapidly increased up to 10–30% in cases with severe Acute Pancreatitis. [1]

Severity assessment in Acute Pancreatitis was first started in 1974 by Ranson et al [2]. The Ranson, Glasgow, and APACHE II score are few of the commonly used scoring systems [3]. Limitations of these scoring systems include delay in complete scoring where it takes 48 hours to complete Ranson and Glasgow scoring systems to complete the assessment, while APACHE II score is cumbersome to calculate [3]. BISAP score largely replaced Ranson's and APACHE score. The modified Marshall score as a predictor of Organ dysfunction was determined at admission and at 48 hours and at any point of time during admission as per the need of the patient.

Early detection of severe Acute Pancreatitis is important so as to deliver proper care to the patient and to avoid its complications. Total Calcium and Albumin-corrected calcium are simplified markers that can be readily measured and can be easily calculated and interpreted by any health persons. It has been evaluated as a mortality prognostic factor and has also been evaluated as a predictor of severe Acute Pancreatitis with infection. [4]

Total Serum Calcium and Albumin Corrected Calcium measured within the first 24 hours, are useful severity predictors in acute pancreatitis [5]. In a review article by Meher et al. [6] the total calcium and albumin-corrected calcium were considered as emerging potential biomarkers for prediction of severity in Acute Pancreatitis.

Hypocalcaemia is a frequent finding in Acute Pancreatitis. Severe hypocalcaemia can present with neurological as well as cardiovascular manifestations. [7] Hypocalcaemia was significantly more frequent in patients with severe form of Acute Pancreatitis (AP). [8]

Proposed mechanisms for hypocalcemia in early phase are autodigestion of mesenteric fat by pancreatic enzymes and release of free fatty acids, which form calcium salts, transient hypoparathyroidism, and hypomagnesemia. Later stages of pancreatitis are frequently complicated by sepsis, increased circulating catecholamines in sepsis cause a shift of circulating calcium into the intracellular compartment, leading to relative hypocalcemia & it causes increased PTH secretion by negative feedback loop, leading to further increase in intracellular calcium overload, oxidative stress, and cell death.

A low serum albumin is regarded as the most common cause of low serum calcium in acute pancreatitis. [9] Hypoalbuminemia in early-stage

severe acute pancreatitis is significantly related to poor prognosis. [10]

The global incidence of Acute Pancreatitis is 34 per 100,000 individuals. [11] Prevalence rate for Pancreatitis in India is 7.9 per 100,000. Prevalence rate for men and women 8.6 and 8.0 per 100,000 respectively in India. [12] Overall about 20% of patients with acute pancreatitis have a severe course and mortality rate is of 10% to 30% in severe pancreatitis patients. [12]

There are many causes of Acute Pancreatitis gallstones, and alcohol accounts for 80-90%. Acute pancreatitis in 5-10% of patients following ERCP. Hypertriglyceridemia is the cause of AP in 1-4 % of cases. Most of patients with hypertriglyceridemia pancreatitis have undiagnosed or uncontrolled diabetes. Rest of the cases are contributed by drugs, trauma, idiopathic, connective tissue disorders, infection and autoimmune etc.

Diagnosis of AP is established by 2 out of 3 of following criteria.

- Typical abdominal pain in the epigastrium radiating to back.
- Threefold or greater elevation in serum lipase and/or amylase.
- Confirmatory finding of ap on cross sectional abdominal imaging.

Ultrasound helps to detect gallstones or sludge in gallbladder or CBD. CECT is used to detect peripancreatic collection and pancreatic parenchymal or peri pancreatic fat necrosis.

MRI or Ultrasound are the only modalities which can detect or absence of necrosis in such collections. The clinical course varies significantly from person to person. Use of prognostic scale enables us to detect severe cases and provide opportunity to treat them adequately.

Widely used are Ranson's, BISAP, APACHE II.

Treatment mainly consists of fluid resuscitation, imaging, prognostic scale to identify severity, amylase and lipase levels, supplemental oxygen and giving rest to gut and pancreas.

**BISAP (bedside index for severity in acute pancreatitis) score:** BISAP score allows for early identification of patients at increased risk for in hospital mortality. 5 variables measured within first 24 hours were found to be predictive of in hospital mortality.

BUN >25 mg/dl, Impaired mental status, SIRS, Age >60 years and presence of Pleural effusion.

According to present research study, in a total of 30 patients with, AP was commonly observed between 25 to 45 years of age. In western literature presence

of gallstones was found to be maximum causative factor for AP, but in INDIA alcoholism is the common etiological factor for developing acute pancreatitis.<sup>[13]</sup> In our study out of 30 patients 17 of them had comorbidities like HTN, DM or both and 12 patients were found to have smoking habits. In our study alcohol consumption contributed to 96% of cases. Serum Calcium, Albumin Corrected Serum Calcium and total BISAP were measured for all patients.

Three classes of severity have been defined according to Harrison's principles of internal medicine 21<sup>st</sup> edition. Mild AP is without local complications or organ failure. Moderately Severe AP is transient organ failure (resolves <48 hrs.) or local or systemic complications in the absence of persistent organ failure. Severe AP is characterised by persistent organ failure (>48 h) involving one or more organs. For mild, moderately severe, and severe cases total serum calcium 8.1-8.5, 7.1-8.0, and <7.0 was found to be significant. To measure organ failure, we used modified Marshall score and we calculated it at the time of admission and after 48 hours and compared with BISAP score.

### Conclusions

When we compare the sensitivity, specificity, and predictive values of TC and ACC, TC seems to better predict the severity of acute pancreatitis as the value of ACC varied with various other parameters including the nutritional status and chronic liver disease, and it also takes a little time for albumin to get depleted in diseases. Many health care centers have access to TC and ACC use their use as prognostic factors of severity in AP would be valuable for identifying those persons who require intensive care, even at the primary and secondary care center levels. Serum calcium and albumin-corrected calcium obtained within the first 24 hours of hospital admission are useful predictors of severity in acute pancreatitis. & it will not replace the currently accepted scoring systems, but these are simplified markers that can be readily measured and can be easily calculated and interpreted by any health staff.

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