



## RESEARCH ARTICLE

## Role of Total Calcium and Albumin-Corrected Calcium as Early Predictors of Severe Acute Pancreatitis: A Prospective Observational Study

Charu Gunjal<sup>1</sup>, Ankita Sharma<sup>2</sup>, Santosh Sharma<sup>3</sup>, Deepa Thadani<sup>4</sup>, G.G. Kaushik<sup>5</sup>

### ABSTRACT

**Background:** Early identification of patients at risk of developing severe acute pancreatitis (SAP) remains a major clinical challenge. Although several prognostic scoring systems such as Ranson, APACHE-II, BISAP, and Modified CT Severity Index are available, many require multiple clinical variables or imaging studies that are not immediately available at admission. Serum total calcium (TC) and albumin-corrected calcium (ACC) are inexpensive, routinely available biochemical parameters that may facilitate early severity prediction.

**Objectives:** To evaluate the role of serum total calcium and albumin-corrected calcium as early predictors of severe acute pancreatitis and to compare their predictive performance with disease severity assessed by the Ranson score.

**Materials and Methods:** A prospective observational study was conducted in the Department of Biochemistry in collaboration with the Department of General Surgery from May 2022 to May 2024. Adult patients diagnosed with acute pancreatitis according to the Revised Atlanta Classification were enrolled consecutively after obtaining informed consent. Serum total calcium and albumin concentrations were measured within 24 hours of hospital admission. Albumin-corrected calcium was calculated using the formula: Corrected Calcium = Total Calcium +  $0.8 \times (4.0 - \text{Serum Albumin})$ . Disease severity was assessed using the Ranson scoring system. Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean  $\pm$  standard deviation, while categorical variables were expressed as frequencies and percentages. One-way ANOVA, Pearson's correlation analysis, ROC curve analysis, and multivariate regression were used wherever appropriate. A p-value  $<0.05$  was considered statistically significant.

**Results:** Both total calcium and albumin-corrected calcium showed a significant progressive decline with increasing disease severity. Total calcium demonstrated a stronger inverse correlation with Ranson score than albumin-corrected calcium, while both biomarkers exhibited excellent discriminatory ability for predicting severe acute pancreatitis. Their rapid availability and low cost make them clinically valuable tools for early risk stratification.

**Conclusion:** Serum total calcium and albumin-corrected calcium are reliable, inexpensive, and readily available early biomarkers for predicting severe acute pancreatitis. Their incorporation into routine admission investigations may facilitate early identification of high-risk patients and timely intensive management, particularly in resource-limited healthcare settings.

**Keywords:** Acute pancreatitis; Total calcium; Albumin-corrected calcium; Hypocalcaemia; Severity prediction; Biomarkers.

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### INTRODUCTION

One of the most frequent gastrointestinal conditions that necessitate hospitalisation globally is acute pancreatitis (AP). It is typified by a varied degree of local and systemic inflammatory response, autodigestion of pancreatic tissue, and acute inflammation of the pancreas brought on by early activation of pancreatic digestive enzymes. Severe acute pancreatitis (SAP), which is linked to long-term organ failure, pancreatic necrosis, systemic inflammatory response syndrome (SIRS), multiorgan dysfunction syndrome (MODS), extended hospital stays, and high mortality, can present clinically as anything from a mild, self-limiting illness (1).

Over the past 20 years, there has been a steady rise in the incidence of acute pancreatitis due to improved

diagnostic facilities, obesity, metabolic problems, rising alcohol intake, and changing lifestyle variables. Although hypertriglyceridemia, medications, trauma, infections, autoimmune illnesses, and post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis are increasingly recognised causes, gallstone disease and alcohol consumption continue to be the most common etiological variables. The death rate from severe acute pancreatitis is still between 20 and 30 percent, despite improvements in critical care therapy. This highlights the significance of early detection of patients at risk for developing severe illness (2).

It is still difficult to accurately forecast the severity of the illness within the first 24 hours of arrival. To anticipate the severity of an illness, a number of clinical

<sup>1</sup>Ph.D. scholar, Department of Biochemistry, J.L.N. Medical College, Ajmer, Rajasthan, India

<sup>2</sup>Associate Professor, Department of Biochemistry, J.L.N. Medical College, Ajmer, Rajasthan, India

<sup>3</sup>Assistant Professor, Department of Biochemistry, Government Medical College, Kota, Rajasthan, India

<sup>4</sup>Senior Professor, Department of Biochemistry, J.L.N. Medical College, Ajmer, Rajasthan, India

<sup>5</sup>Retired Senior Professor, Department of Biochemistry, J.L.N. Medical College, Ajmer, Rajasthan, India

**Corresponding Author:** Charu Gunjal, Ph.D. scholar, Department of Biochemistry, J.L.N. Medical College, Ajmer, Rajasthan, India .

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scoring systems have been established, including as the Ranson score, APACHE-II, BISAP score, Glasgow score, and Modified CT Severity Index. However, these scoring systems are limited in their applicability during the first hours of hospitalisation, especially in healthcare settings with limited resources, because they need several clinical and laboratory indicators, serial assessments, or contrast-enhanced computed tomography (3).

The Ranson and Glasgow scoring systems include hypocalcaemia, which has long been acknowledged as a distinctive biochemical anomaly in acute pancreatitis. Fat saponification in regions of pancreatic necrosis, hypoalbuminemia, temporary hypoparathyroidism, poor vitamin D metabolism, cytokine-mediated calcium redistribution, and elevated calcitonin activity are all contributing factors to the multifactorial decrease in serum calcium. Serum calcium levels gradually drop as pancreatic

necrosis and disease severity increase (4).

About half of the calcium in circulation is physiologically active ionised calcium, and the other 40–45% is linked to albumin. Total blood calcium alone may underestimate the physiologically active calcium concentration since hypoalbuminemia often coexists with severe acute pancreatitis due to systemic inflammation, increased vascular permeability, and decreased hepatic albumin production. Therefore, albumin-corrected calcium (ACC), which is determined by adjusting total calcium for serum albumin concentration, offers a more precise assessment of calcium homeostasis and may enhance predictive accuracy (5).

Numerous studies have shown a strong correlation between the severity of the disease, pancreatic necrosis, the need for intensive care, and death with both total calcium and albumin-corrected calcium measured during the first 24 hours. They are appealing prognostic biomarkers since their evaluation merely necessitates standard biochemical tests, particularly in underdeveloped nations where sophisticated prognostic scoring systems and cutting-edge imaging facilities might not be easily accessible. In order to assess the predictive value of serum total calcium and albumin-corrected calcium measured at hospital admission for early detection of severe acute pancreatitis and to compare their performance with disease severity as determined by the Ranson scoring system, the current prospective study was conducted. The study also seeks to ascertain if these straightforward biochemical markers might function as useful, affordable substitutes for early risk assessment in standard clinical practice (6).

## MATERIALS AND METHODS

### Study Design

Prospective observational hospital-based study.

### Study Duration

May 2022 to May 2024 (24 months).

**Table No. 1:** Biochemical Variables in Study Population (Severity-wise Comparison)

| Biochemical/Hormonal Parameter    | Control (n=56) Mean<br>± SD | Mild AP (n=38) Mean<br>± SD | Moderate AP (n=52)<br>Mean ± SD | Severe AP (n=22)<br>Mean ± SD |
|-----------------------------------|-----------------------------|-----------------------------|---------------------------------|-------------------------------|
| Age (Years)                       | 42.54 ± 14.90               | 49.29 ± 16.36               | 49.35 ± 14.52                   | 50.23 ± 16.92                 |
| Serum Total Calcium (mg/dL)       | 9.61 ± 0.33                 | 8.36 ± 0.27                 | 7.63 ± 0.43                     | 6.12 ± 0.21                   |
| Serum Albumin (g/dL)              | 4.14 ± 0.16                 | 3.23 ± 0.33                 | 3.22 ± 0.33                     | 3.27 ± 0.35                   |
| Albumin Corrected Calcium (mg/dL) | 9.51 ± 0.37                 | 8.98 ± 0.33                 | 8.25 ± 0.50                     | 6.71 ± 0.36                   |

**Table No. 2:** Comparison of Serum Total Calcium in Various Groups of Subjects

| One Way Analysis Of Variance For Serum Total Calcium |                |                    |                        |          |        |                          |
|------------------------------------------------------|----------------|--------------------|------------------------|----------|--------|--------------------------|
| Variation                                            | Sum of Squares | Degrees of Freedom | Variance (Mean Square) | F        | p      | Statistical Significance |
| Between Groups                                       | 69.82          | 2                  | 34.9077                | 286.8475 | 0.0001 | HS                       |
| Within Groups                                        | 13.26          | 109                | 0.1217                 |          |        |                          |
| Total                                                | 83.08          | 111                |                        |          |        |                          |

The p values by post-hoc test are in the following table:

| Between Groups               | p value  | Inference |
|------------------------------|----------|-----------|
| 1 and 2 (Mild vs Moderate)   | < 0.0001 | HS        |
| 2 and 3 (Moderate vs Severe) | < 0.0001 | HS        |
| 3 and 1 (Severe vs Mild)     | < 0.0001 | HS        |

1- Mild AP subjects

2- Moderate AP subjects

3- Severe AP subjects

HS – Highly Significant ( $p < 0.001$ )

Patients unwilling to participate.

### Study Setting

Department of Biochemistry in collaboration with the Department of General Surgery at a tertiary care teaching hospital.

### Study Population

Patients presenting with acute pancreatitis during the study period.

### Sample Size

A total of 112 patients diagnosed with acute pancreatitis were included in the study after fulfilling the eligibility criteria. Disease severity was categorized according to the Revised Atlanta Classification into mild, moderately severe, and severe acute pancreatitis.

### Inclusion Criteria

Patients aged  $\geq 18$  years.

*Diagnosis of acute pancreatitis based on at least two of the following*

- Characteristic upper abdominal pain.
- Serum amylase or lipase levels  $\geq 3$  times the upper limit of normal.
- Radiological evidence of acute pancreatitis on ultrasonography or contrast-enhanced CT.
- Patients admitted within 24 hours of symptom onset.
- Patients providing written informed consent.

### Exclusion Criteria

- Chronic pancreatitis.
- Pancreatic malignancy.
- Chronic liver disease.
- Chronic kidney disease.
- Primary hyperparathyroidism or known calcium metabolism disorders.
- Patients receiving calcium or vitamin D supplementation before admission.
- Pregnancy.

### Data Collection

A detailed history including demographic profile, alcohol consumption, gallstone disease, comorbidities, presenting symptoms, and duration of illness was recorded. Clinical examination findings and laboratory investigations were documented at admission.

### Laboratory Investigations

Venous blood samples were collected within 24 hours of admission before initiation of definitive treatment.

*The following investigations were performed*

- Serum total calcium
- Serum albumin
- Serum amylase
- Serum lipase
- Other routine biochemical investigations

### Estimation of Total Calcium

Serum total calcium was estimated by the Arsenazo III colorimetric method using an automated chemistry analyzer.

### Estimation of Serum Albumin

Serum albumin was estimated by the Bromocresol Green (BCG) method.

Calculation of Albumin-Corrected Calcium

Table No. 3: Comparison of Albumin Corrected Calcium (ACC) in Various Groups of Subjects

| One Way Analysis Of Variance For Albumin Corrected Calcium (Acc) |                |                    |                        |          |        |                          |
|------------------------------------------------------------------|----------------|--------------------|------------------------|----------|--------|--------------------------|
| Variation                                                        | Sum of Squares | Degrees of Freedom | Variance (Mean Square) | F        | p      | Statistical Significance |
| Between Groups                                                   | 71.86          | 2                  | 35.9322                | 202.0323 | 0.0001 | HS                       |
| Within Groups                                                    | 19.39          | 109                | 0.1779                 |          |        |                          |
| Total                                                            | 91.25          | 111                |                        |          |        |                          |

The p values by post-hoc test are in the following table:

| Between Groups               | p value  | Inference |
|------------------------------|----------|-----------|
| 1 and 2 (Mild vs Moderate)   | < 0.0001 | HS        |
| 2 and 3 (Moderate vs Severe) | < 0.0001 | HS        |
| 3 and 1 (Severe vs Mild)     | < 0.0001 | HS        |

1- Mild AP subjects

2- Moderate AP subjects

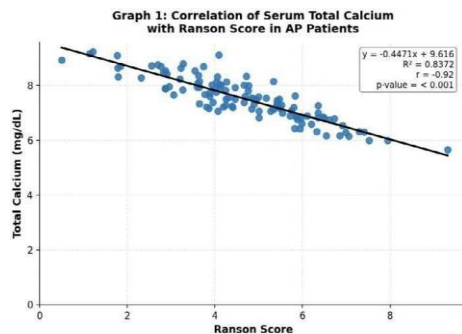
3- Severe AP subjects

HS – Highly Significant ( $p < 0.001$ )

Albumin-corrected calcium was calculated using the standard formula

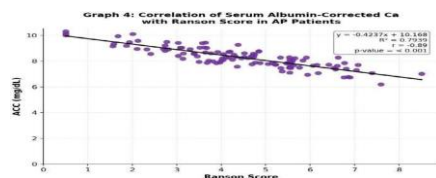
Corrected Calcium (mg/dL) = Total Calcium +  $0.8 \times (4.0 - \text{Serum Albumin})$

where serum albumin is expressed in g/dL.



**Graphs 1:** Correlation of Serum Total Calcium with Ranson Score in AP Patients

Negative correlation ( $r = -0.915$ ,  $p < 0.001$ ) — Strong inverse relationship



**Graph 2:** Correlation of Albumin-Corrected Calcium with Ranson Score in AP Patients

Negative correlation ( $r = -0.891$ ,  $p < 0.001$ ) — Strong inverse relationship

## Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0.

Continuous variables were expressed as mean  $\pm$  standard deviation, while categorical variables were expressed as frequency and percentage.

Comparisons among severity groups were performed using one-way Analysis of Variance (ANOVA) followed by Tukey's post hoc test. Pearson's correlation coefficient was used to determine the association between biochemical parameters and Ranson score. Receiver Operating Characteristic (ROC) curve analysis was performed to determine sensitivity, specificity, area under the curve (AUC), and optimal cut-off values of total calcium and albumin-corrected calcium for predicting severe acute pancreatitis. A p-value  $< 0.05$  was considered statistically significant.

## Ethical Considerations

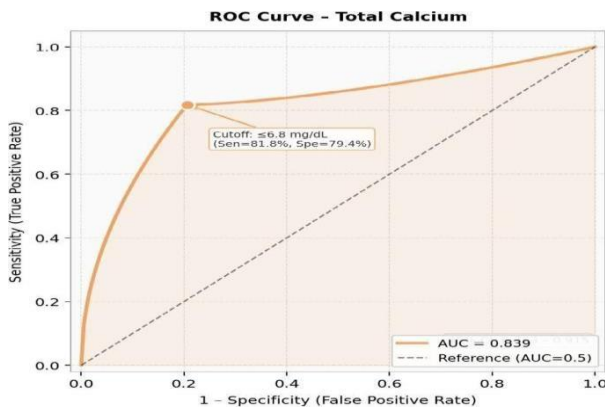
The study protocol was reviewed and approved by the Institutional Ethics Committee before commencement of the study. Written informed consent was obtained from all participants.

## RESULTS

### Disease Severity Distribution

A total of 112 patients with acute pancreatitis were included in the study. According to the Revised Atlanta Classification, 38 (33.9%) patients had mild acute pancreatitis, 52 (46.4%) had moderately severe acute pancreatitis, and 22 (19.6%)

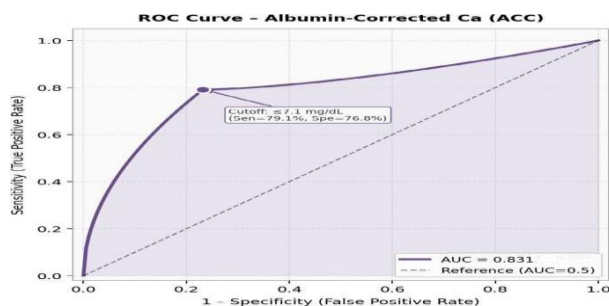
parameters can further improve early risk stratification in routine clinical practice.



**Graph 3:** Total Calcium: ROC curve of Serum Total Calcium for predicting severe acute pancreatitis

had severe acute pancreatitis. Thus, moderately severe acute pancreatitis constituted the largest proportion of cases, followed by mild and severe disease.

Both serum total calcium and albumin-corrected calcium demonstrated significant utility as early biochemical markers for predicting the severity of acute pancreatitis. However, serum total calcium exhibited slightly superior



**Graph 4:** ACC: ROC curve of Albumin-Corrected Calcium (ACC) for predicting severe acute pancreatitis

predictive performance compared with albumin-corrected calcium. Total calcium showed a higher AUC (0.839 vs. 0.831), greater sensitivity (81.8% vs. 79.1%), and higher specificity (79.4% vs. 76.8%) for predicting severe acute pancreatitis. Furthermore, total calcium demonstrated a stronger inverse correlation with the Ranson score ( $r = -0.915$ ) than albumin-corrected calcium ( $r = -0.891$ ). These findings indicate that although both biomarkers are clinically valuable, serum total calcium may serve as the preferred initial biochemical predictor, while albumin-corrected calcium provides additional prognostic value, particularly in patients with hypoalbuminemia. The combined assessment of both

## DISCUSSION

The usefulness of serum total calcium (TC) and albumin-corrected calcium (ACC) measured within 24 hours of hospital admission as early indicators of disease severity in patients with acute pancreatitis was assessed in the current prospective observational study. Of the 112 patients who were included, 33.9% had mild acute pancreatitis, 46.4% had moderately severe pancreatitis, and 19.6% had severe acute pancreatitis. This means that over one-fifth of the patients acquired severe disease that needed close observation and urgent care (7).

The progressive decrease in albumin-corrected calcium and total calcium with increasing disease severity was one of the study's key findings. In mild disease, mean serum total calcium was  $8.36 \pm 0.27$  mg/dL; in moderately severe disease, it was  $7.63 \pm 0.43$  mg/dL; in severe acute pancreatitis, it was  $6.12 \pm 0.21$  mg/dL. Similarly, albumin-corrected calcium decreased from  $8.98 \pm 0.33$  mg/dL to  $6.71 \pm 0.36$  mg/dL and  $8.25 \pm 0.50$  mg/dL, respectively. Post-hoc analysis verified statistically significant differences between each severity category, and one-way ANOVA showed extremely significant differences between severity groups for both biomarkers ( $p < 0.0001$ ). These results suggest that increased pancreatic inflammation and disease severity are correlated with worsening hypocalcaemia (8).

Fat saponification in regions of pancreatic necrosis, where released free fatty acids bind circulating calcium to create insoluble soaps, is the main cause of the multifactorial hypocalcaemia associated with acute pancreatitis. Systemic inflammatory response, cytokine-mediated calcium redistribution, hypoalbuminemia, compromised vitamin D metabolism, and temporary parathyroid dysfunction are other causes. Calcium is therefore a biologically plausible prognostic diagnostic because lower calcium values indicate more extensive pancreatic damage and systemic involvement (9). Additionally, the current investigation showed a significant inverse association between the Ranson score and serum calcium values. Declining calcium levels closely correspond with increasing disease severity, as evidenced by the higher negative correlation between serum total calcium ( $r = -0.915$ ,  $p < 0.001$ ) and albumin-corrected calcium ( $r = -0.891$ ,  $p < 0.001$ ). Serum calcium measurement at admission offers a quick and convenient substitute for early risk

assessment because the Ranson score necessitates the collection of several clinical and laboratory parameters over a 48-hour period (10). The prognostic value of both biomarkers was further validated by receiver operating characteristic analysis. While albumin-corrected calcium obtained an AUC of 0.831, sensitivity of 79.1%, and specificity of 76.8% at a cut-off value of  $\leq 7.1$  mg/dL, serum total calcium showed an AUC of 0.839 with 81.8% sensitivity and 79.4% specificity at a cut-off value of  $\leq 6.8$  mg/dL. Both indicators performed well in terms of diagnosis, however total calcium consistently shown somewhat higher predictive accuracy. However, because adjusting for serum albumin reduces the impact of hypoalbuminemia and more accurately represents physiologically active calcium in certain patients, albumin-corrected calcium is still clinically significant (11). Overall, the results are in favour of routinely measuring serum total calcium and albumin-corrected calcium when diagnosing acute pancreatitis. They are useful supplements to well-established prognostic scoring systems because of their low cost, widespread availability, quick turnaround times, and high predictive accuracy. This is especially true in healthcare settings with limited resources where complex scoring systems and advanced imaging may not be readily available (12).

## CONCLUSION

The current study shows that albumin-corrected calcium and serum total calcium are useful early biochemical markers for predicting the severity of acute pancreatitis in patients. Both metrics had substantial inverse relationships with the Ranson score and considerable decreases with increasing disease severity, demonstrating their usefulness in early prognostic evaluation. Both biomarkers showed good diagnostic performance according to ROC analysis; however, serum total calcium consistently showed somewhat greater predictive ability than albumin-corrected calcium, with a higher AUC, sensitivity, specificity, and stronger correlation with disease severity. Because albumin correction enhances the estimation of physiologically active calcium, albumin-corrected calcium is nevertheless a valuable supplementary marker, especially in individuals with hypoalbuminemia. Thus, routinely measuring both parameters within the first 24 hours of hospital admission can help identify high-risk patients early, allow for prompt intensive management, enhance risk stratification, and possibly lower morbidity and mortality, particularly in healthcare settings with

limited resources.

## REFERENCES

1. Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, et al. Acute pancreatitis. *Lancet*. 2020;396(10252):726-34.
2. Mederos MA, Reber HA, Girgis MD. Acute pancreatitis: a review. *JAMA*. 2021;325(4):382-90.
3. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102-11.
4. Boxhoorn L, Voermans RP, Bruno MJ. Management of acute pancreatitis. *Best Pract Res Clin Gastroenterol*. 2022; 58:101782.
5. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN. American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. *Gastroenterology*. 2018;154(4):1096-101.
6. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. WSES guidelines for the management of severe acute pancreatitis. *World J Emerg Surg*. 2019; 14:27.
7. Silva-Vaz P, Abrantes AM, Castelo-Branco M, Gouveia A, Botelho MF, Tralhão JG. Multifactorial scores and biomarkers of prognosis of acute pancreatitis: applications to research and practice. *Int J Mol Sci*. 2020;21(1):338.
8. Sternby H, Verdonk RC, Aguilar G, Olesen SS, Thorlacius H, Dimcevski G, et al. Determinants of severity in acute pancreatitis: a nationwide prospective cohort study. *United European Gastroenterol J*. 2019;7(6):822-30.
9. Hines OJ, Pandol SJ. Management of severe acute pancreatitis. *BMJ*. 2019;367: l6227.
10. Xiao AY, Tan ML, Wu LM, Asrani VM, Windsor JA, Yadav D, et al. Global incidence and mortality of pancreatic diseases: systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2016;14(10):1466-76.
11. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. *Lancet*. 2015;386(9988):85-96.
12. Vege SS, DiMagno MJ, Forsmark CE, Martel M, Barkun AN. Initial medical treatment of acute pancreatitis: American Gastroenterological Association Institute technical review. *Gastroenterology*. 2018;154(4):1103-39.