

Original Research Article

Total serum calcium and corrected calcium as a predictor of severity in acute pancreatitis

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ABSTRACT

Background: Acute pancreatitis is an acute inflammatory process of the pancreas. The Ranson and the modified Glasgow scores require 48 hours of data collection to assess severity. Hypocalcaemia is one of the components of Ranson's scoring system done to assess the severity of pancreatitis. Albumin-corrected calcium (ACC) has also been associated with severity, but no study has evaluated it as a prognostic severity factor within the first 24 h of the patient's hospital admission. This study tries to evaluate total calcium and albumin corrected calcium as prognostic severity markers in acute pancreatitis within first 24 hour of admission.

Methods: This prospective study was conducted in Bowring and Lady Curzon hospital, a tertiary care centre from June 2016 to May 2018. Inclusion criteria included all patients above 18 years of age, who presented within 72 hours of onset of epigastric pain. The clinical and demographic data with respect to gender, age, previous history of pancreatitis, total calcium taken 24 h after admission. In order to evaluate total calcium and albumin corrected calcium as prognostic factors of severity, the lowest total calcium values were collected within the first 24 h of hospital admission. These values were then corrected according to the serum albumin level.

Results: A total of ninety-four patients were included in the study. There was no significant difference in the age of patients in each severity grade (p value: 0.242). No difference was observed in gender distribution of three groups. (P >0.05). As compared to total calcium, mean values of albumin corrected calcium were 8.03, 7.18 and 6.28 for mild, moderate and severe acute pancreatitis respectively, which were also significant at 0.05.

Conclusions: Total calcium and albumin-corrected calcium obtained within the first 24 hours of hospital admission are useful predictors of severity in acute pancreatitis.

Keywords: Acute pancreatitis, Albumin corrected calcium, Predictor of severity, Serum total calcium

INTRODUCTION

Acute pancreatitis is an acute inflammatory process of the pancreas with varying involvement of other regional tissues or remote organ systems.¹ Histologically characterized by acinar cell necrosis and the presence of inflammatory infiltrate in the parenchyma.² Diagnosis of acute pancreatitis is established by two of the following three characteristics: abdominal pain consistent with

acute pancreatitis, serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal, characteristic findings of acute pancreatitis on imaging.³

Most patients with acute pancreatitis resolve spontaneously without complications. However, 10 to 20% of patients experience a severe attack with mortality increasing up to 25%.⁴ To decrease mortality rate in

severe acute pancreatitis, it is important to precisely evaluate the severity early in the disease process and initiate appropriate treatment as early as possible. The Ranson and the modified Glasgow scores require 48 hours of data collection to assess severity.⁵

Biochemical markers have also turned out to be useful predictors. Examples of some of them are: C-reactive protein, procalcitonin, interleukin-6, thioredoxin-1, and polymorphonuclear elastase.⁶ Hypocalcaemia is one of the components of Ranson's scoring system done to assess the severity of pancreatitis. Independently, hypocalcaemia has been evaluated as a mortality prognostic factor and it has also been evaluated as a predictor of severe acute pancreatitis with infection. Albumin-corrected calcium (ACC) has also been associated with severity, but no study has evaluated it as a prognostic severity factor within the first 24 h of the patient's hospital admission.⁷

This study tries to evaluate total calcium and albumin corrected calcium as prognostic severity markers in acute pancreatitis within first 24 hour of admission.

METHODS

This prospective study was conducted in Bowring and Lady Curzon hospital, a tertiary care centre from June 2016 to May 2018. Inclusion criteria included all patients above 18 years of age, who presented within 72 hours of onset of epigastric pain.

The diagnosis of acute pancreatitis was established based on the American College of Gastroenterology recommendations.

The clinical and demographic data with respect to gender, age, previous history of pancreatitis, total calcium taken 24 h after admission, serum albumin, amylase and lipase and imaging data in the cases of patients with severe or moderately severe acute pancreatitis were collected. Diagnosis of acute pancreatitis, its severity, and local and systemic complications were defined as per the Revised Atlanta Classification 2012.

The patients were classified into three groups in accordance with the revised Atlanta Classification severe acute pancreatitis (associated with persistent organ failure longer than 48 hrs with or without local or systemic complications), moderately severe acute pancreatitis (that presents with local or systemic complications, with no persistent organ failure), and mild acute pancreatitis (with no organ failure or local or systemic complications).

In order to evaluate total calcium and albumin corrected calcium as prognostic factors of severity, the lowest total calcium values were collected within the first 24 h of hospital admission. These values were then corrected according to the serum albumin level.

Data analysis

Data analysis was based on descriptive statistics to determine the general population characteristics. The one-way ANOVA, paired student 't' test and the chi-square test were employed to establish the statistical significance of the differences between groups.

Statistical significance was determined with a p < 0.05. Sensitivity (S), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) was calculated at various cut off levels of hypocalcaemia.

RESULTS

A total of ninety-four patients satisfying inclusion and exclusion criteria were included in the study. The age of the patients ranged from 18 to 62 years. The mean age of the patients with acute pancreatitis was 36.24 ± 14.64 years.

Table 1: Various etiological factors of acute pancreatitis.

Etiology	No. of patients (%)
Biliary Pancreatitis	36 (38.30)
Ethanol induced	30 (31.91)
Idiopathic	16 (17.02)
Hypertriglycerdemia	8 (8.51)
Drug induced	4 (4.26)

Table 2: Total serum calcium and albumin corrected calcium according to severity of acute pancreatitis.

Factor	Total population n=94	Mild pancreatitis n=66	Moderate pancreatitis n=16	Severe pancreatitis n=12	P value
Total serum calcium. (mg/dl) (Mean±SD)	8.32±1.24	8.15±0.98	7.36±1.04	6.43±1.71	< 0.05
Albumin corrected calcium (mg/dl) (Mean±SD)	8.14±0.95	8.03±0.76	7.18±0.74	6.28±1.59	< 0.05

There was no significant difference in the age of patients in each severity grade (p value: 0.242). Sixty patients

(63.83%) who presented with acute pancreatitis were males, whereas thirty-four (36.17%) were females. 66

patients (70.21%) had mild pancreatitis, 16 patients (17.02%) had moderately severe pancreatitis and 12 patients (12.27%) had severe pancreatitis. No difference

was observed in gender distribution of three groups. ($P > 0.05$).

Table 3: Sensitivity, specificity, predictive values analyzed for predicting progression to severe acute pancreatitis.

Factor	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Total serum calcium < 7.5mg/dl	72	80	30	91
Total serum calcium < 7.5mg/dl	54	92	54	94
Albumin corrected serum calcium < 7.5mg/dl	69	88	42	96
Albumin corrected serum calcium < 7.5mg/dl	58	97	85	98

Out of 94 patients, 36 patients (38.30%) had biliary pancreatitis, 30 patients (31.91%) had ethanol induced pancreatitis, while 28 patients (29.17%) had other etiological factors for pancreatitis. There was no significant association between etiology and severity of the disease (p value > 0.05). The mean duration of stay in severe pancreatitis was 12.76 ± 5.42 days (Table 1).

The mean total calcium was 8.15, 7.36 and 6.43 for mild, moderate and severe acute pancreatitis respectively, which was significant at 0.05. As compared to total serum calcium, mean values of albumin corrected calcium were 8.03, 7.18 and 6.28 for mild, moderate and severe acute pancreatitis respectively, which were also significant at 0.05 (Table 2).

DISCUSSION

Acute pancreatitis remains a common disease with mortality of severe attacks reaching as high as 30% to 50%.⁸ This vulnerable group of patients need emergent diagnosis and grading of severity to be treated aggressively to prevent morbidity and mortality. Also, early identification of mild disease avoids unnecessary overtreatment, thus reducing cost of treatment.

The first numeric system was proposed by Ranson et al. for acute alcohol-induced pancreatitis and remains the most commonly used system. A more recently, the Acute Physiological Assessment and Chronic Health Evaluation (APACHE II) assessment and monitoring system has become popular, because it is more reliable.^{9,10}

A shortcoming of biochemical markers and multivariable scoring systems, however, as noted earlier is their inability to assess the extent of injury to the pancreas and peripancreatic tissues.

Hypocalcemia is one of the components of Ranson's scoring system done to assess the severity of pancreatitis. Ammori et al reported that hypocalcaemia was more frequent during severe attack as compared to mild attack of pancreatitis (86% versus 39%).¹¹ Prevalence of

hypocalcaemia ranges between 15% and 88% in critically ill patients depending on the setting and cut-offs used.^{12,13} Proposed mechanisms for hypocalcaemia in early phase are autodigestion of mesenteric fat by pancreatic enzymes and release of free fatty acids, which form calcium salts, transient hypoparathyroidism, and hypomagnesaemia.¹⁴⁻¹⁶ Later stages of pancreatitis are frequently complicated by sepsis. Whitted et al proposed that increased circulating catecholamines in sepsis cause a shift of circulating calcium into the intracellular compartment, leading to relative hypocalcemia. This causes increased PTH secretion by negative feedback loop, leading to further increase in intracellular calcium overload, oxidative stress, and cell death.¹⁷ Hypomagnesaemia-induced impaired PTH secretion and action, relative PTH deficiency, and vitamin D deficiency are some of the other plausible causes.

The largest multicenter study conducted in four hospitals of Australia on a cohort of 7024 patients showed that $Ca < 0.8$ mmol/L was an independent predictor of mortality in intensive care unit (ICU) patients.¹⁸ Steele et al. in a retrospective single-centre observational study on 1038 critically ill patients found that 55.2% patients had hypocalcemia ($Ca < 1.1$ mmol/L) at admission. Serum calcium normalized by day 4 in most patients. Calcium level normalization was not different in patients who received and who did not receive calcium supplementation. Patients with severe hypocalcemia (0.9 mmol/L) who failed to normalize their calcium level by day 4 had increased mortality (38% vs. 19%); however, the values did not reach statistical significance. Authors suggested that hypocalcemia patients who fail to correct their level spontaneously might form the subgroup of patients likely to benefit from intervention.¹⁹

Present study demonstrated inverse relationship between total serum calcium, albumin corrected calcium within first 24 hour of admission.

With respect to the total serum calcium and albumin corrected calcium, in present study we found that the specificity and sensitivity values for Total Serum Calcium with a cut-off point of 7.5 mg/dl were 72% and

80% respectively. For total calcium with a cut off of 6.5mg/dl the sensitivity decreased to 54% however specificity was about 92%. A total serum calcium concentration lower than 7.5 mg/dl would identify patients with severe acute pancreatitis. When the total serum calcium falls below 6.5 mg/dl, the patients had a 60% probability of presenting with severe acute pancreatitis.

With regard to albumin corrected calcium, with the 7.5 mg/dl cut-off point, its sensitivity was 69% and specificity was 88 %. With the 6.5 mg/dl cut-off point, its PPV reached 85%. These high prediction levels and the ease in calculating them when the serum albumin level is known, make obtaining the albumin corrected calcium concentration worthwhile, since it considerably increases diagnostic accuracy.

CONCLUSION

Serum calcium and albumin-corrected calcium obtained within the first 24 hours of hospital admission are useful predictors of severity in acute pancreatitis. With an adequate interpretation of their cutoff points, they can be used routinely in every case of acute pancreatitis to assess its severity, predict complications, and identify the patients who require intensive care support even in primary and secondary care centres.

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