CRP/albumin ratio as an early marker of mortality in acute pancreatitis
A retrospective analysis

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DOI: https://doi.org/10.36104/amc.2024.2976

Abstract

Acute pancreatitis is a rapidly progressive digestive disorder with a high degree of morbidity and mortality. The severity scales tend to be hard to measure, and thus a simple, rapid and accessible parameter is needed.

Objective: to establish the C-reactive protein/albumin (CRP/albumin) ratio as an early marker of mortality in patients with acute pancreatitis hospitalized at Hospital Luis Vernaza (2018-2019).

Design: an analytical retrospective case series.

Population: a total of 220 cases of adults with acute pancreatitis who had an albumin and C-reactive protein test on admission to the hospital were included.

Data analysis: to determine if the CRP/albumin ratio is an early predictor of mortality, univariate and bivariate analyses were run on the variables, a cutoff point was obtained and the predictive power was determined through logistic regression, according to the statistical significance ($p<0.05$).

Results: The median CRP/albumin ratio was 42.02, and a cutoff point ≥40 (95% CI 1.20-29.26) was found to be a predictor of mortality, with a p value of 0.029. The average age was 43.47 years, and the female sex predominated with 70% of the cases. The most frequent comorbidity was HTN, with 16.5% of the cases. The mean APACHE II was 6.26, the mean BISAP was 1.43, and the mortality rate was 4.50%. The median hospital stay was 25.2 days, and 15% were admitted to the ICU. There was a positive correlation between APACHE II and the CRP/albumin ratio, with $p<0.001$, with a similar significance for BISAP. **(Acta Med Colomb 2024; 49. DOI: https://doi.org/10.36104/amc.2024.2976).**

Keywords: *acute pancreatitis, CRP/albumin ratio, APACHE II, BISAP, mortality.*

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Received: 02/VII/2023 Accepted: 21/XII/2023

Introduction

Acute pancreatitis is an inflammatory disease of the pancreas characterized by abdominal pain and elevated pancreatic enzymes (1). It is the third cause of hospitalization for gastrointestinal disorders worldwide (2, 3). The most common etiology is gall stones (40-70%), followed by alcohol (25-35%) and hypertriglyceridemia >1,000 mg/dL (1-14%) (4, 5). It is mild in the absence of local or systemic complications or organ failure (80% of the cases); in the remaining 15-20% it is moderate or severe: moderate when there are local or systemic complications with transient organ failure (<48 hours) and severe when there is persistent failure (>48 hours) of at least one organ. Overall mortality is approximately 5% (6-9).

There are different models for determining severity and predicting early mortality in acute pancreatitis, based on clinical and radiological risk factors and serum markers. These approaches have led to the creation of several systems for classifying severity, which should be measured on hospital admission or within 48-72 hours. However, all of these models have low specificity (10). None of these systems can determine severity within an hour of admission (2, 7). They tend to be difficult to measure, and the immediate application of this prognostic information is complicated. These methods have low specificity, which leads to higher false positive rates. This, together with a low incidence of moderately severe and severe pancreatitis results in uncertain and low-quality predictive models (11-13).

The C-reactive protein (CRP)/albumin ratio has emerged as a new prognostic indicator determined by an inflammatory pattern (7). Both proteins change their plasma concentration by a minimum of 25% following cytokine stimulation (5). C-reactive protein is used as a severity marker in acute pancreatitis, with levels above 150 mg/L in the first 48 hours

helping differentiate between severe and mild illness (7). On the other hand, albumin falls during inflammatory processes and is directly related to the severity (2), thus being a useful marker for morbidity and mortality in several clinical settings, including severe acute pancreatitis. In light of this information, studies have begun on the CRP/albumin ratio as a premonitory marker for mortality (7).

Villacorta et al. showed that CRP is an independent predictor of cardiovascular mortality in patients with acute decompensated heart failure (7, 14). According to Kim et al., the CRP/albumin ratio on admission was positively correlated with the prognosis of patients with severe sepsis or septic shock (7, 15). Kaplan et al. found that the CRP/albumin ratio could predict mortality in patients with acute pancreatitis with 92.1% sensitivity and 58% specificity (16-18).

Previous studies have shown that both CRP and albumin are related to the severity and prognosis of acute pancreatitis. Their predictive value is limited when used individually, but combining them improves their predictive sensitivity. Given the high incidence of acute pancreatitis in Ecuador, these markers could be useful tools for determining the prognosis of patients admitted for acute pancreatitis.

In the following study, we focused on a simple, quick and accessible parameter for determining the short-term prognosis of acute pancreatitis, in order to make appropriate decisions during hospitalization and predict mortality early. The CRP/albumin ratio aspires to become a useful, easily applied marker in this setting. To accomplish this, we retrospectively studied patients with acute pancreatitis hospitalized at Hospital Luis Vernaza, a national referral center in Ecuador.

Materials and method

Study design: a retrospective analytical case study.

Population: patients with acute pancreatitis who were admitted to the emergency room or hospitalization wards at Hospital Luis Vernaza from 2018-2019.

Sample: census population.

Cases: research subjects over the age of 18 with confirmed acute pancreatitis and CRP and albumin ordered on hospital admission. Two hundred research subjects were collected and analyzed during the predetermined time period.

Case exclusion criteria: patients who received albumin therapy in the days prior to hospital admission were excluded, as were those with diseases that alter these markers, like lymphoproliferative diseases, heart failure, liver failure, chronic kidney disease and chronic rheumatological diseases.

Data analysis: for this study, the medical chart information on the hospital's SERVINTE system was analyzed. An Excel table was created to construct the database, and the SPSS program was used for statistical calculations. The analyses were run using RStudio and IBM SPSS version 25 programs, using descriptive statistics with tables and graphs showing absolute and relative values of the qualitative variables, as well as measures of central tendency and variability for quantitative variables. The assumption of normality for quantitative variables was verified using the Shapiro test, with the Mann Whitney test used for non-normal quantitative variables. Chi square or Fisher's exact test were used to compare proportions for the qualitative variables. The ROC curve was used to determine the cut-off point for the CRP/albumin ratio as a predictor of mortality. The predictive power of the cut-off point obtained was determined through logistic regression. Statistical significance was set at $p < 0.05$.

Ethical considerations

This retrospective, descriptive study with no interventions in the study population was carried out under the national ethical considerations, guaranteeing the principles of beneficence, non-maleficence, autonomy and justice, and with the approval of the research departments at Universidad de Especialidades Espíritu Santo and Hospital Luis Vernaza de Guayaquil.

Results

The study group was homogeneous. The mean age was 43.47 years, with a variability of 19.03 years. There were significant differences when comparing age by status at discharge (p: 0.007). Seventy percent of the patients were females, with no significant gender differences in the condition of non-survivors. The most common comorbidity was hypertension (16.5%), followed by obesity (13%) and diabetes mellitus (6.5%). The presence or absence of hypertension showed significant differences in the proportion of non-survivors ($p<0.001$), with 18.8% of hypertensive patients being non-survivors versus 1.80% of patients without hypertension (Table 1).

The mean APACHE II score was 6.26, with a variability of 4.08. Comparing the APACHE II score by status at discharge showed significant differences ($p<0.001$). The mean BISAP was 1.43, with a standard deviation of 1.20. There were significant differences in BISAP according to status at discharge ($p<0.001$). The mean hospital stay was 25.22 days. A comparison of hospital stay according to status at discharge yielded significant differences (p: 0.044). Fifteen percent of the patients were admitted to the intensive care unit (ICU); there were significant differences in the proportion of non-survivors between those who were admitted to the ICU and those who were not ($p<0.001$). Altogether, 12.50% of the patients received non-invasive mechanical ventilation (NIV); a comparison of the proportion of non-survivors between patients with or without NIV showed significant differences ($p<0.001$) (Table 1). Mortality in patients with acute pancreatitis was 4.5%.

A comparison of the CRP, albumin and CRP/albumin ratio parameters according to status at discharge showed the following: there were significant differences in CRP (p: 0.048), with a median of 211 mg/L in non-survivors versus

74 mg/L in survivors. There were significant differences in albumin (p: 0.001), with a median of 2 g/dL in non-survivors versus 4 g/dL in survivors. The CRP/albumin ratio was significantly different (p: 0.006), with a median of 94 in non-survivors versus 23 in survivors (Table 2).

The correlation between APACHE II, BISAP and the CRP/albumin ratio was determined and found to be significant (p<0.001), with Spearman correlation coefficients of 0.367 and 0.544, indicating a direct or positive linear relationship between APACHE II, BISAP and the CRP/albumin ratio. That is, if the APACHE or BISAP increases, the CRP/albumin ratio will also increase (Figure 1).

The ROC curve determined the cut-off point for the CRP/albumin ratio that would predict mortality in patients with acute pancreatitis. The area under the ROC curve was 0.774 (0.611-0.936) and the lower limit of the confidence interval was >0.5, indicating that the CRP/albumin ratio can predict mortality in patients with acute pancreatitis; the cut-off point was 40, with 89% sensitivity and 63% specificity (Figure 2). The mean CRP/albumin ratio was 42.02.

Table 1. *Clinical characteristics of patients with acute pancreatitis by discharge status.*

Clinical characteristics	Total	Discharge status		P value
		Non-survivor	Survivor	
Age (median (IQR))	38 (29-56)	66 (38-81)	38 (29-55)	0.007*
Sex (n (%))				
Female	140 (70)	5 (3.57)	135 (96.43)	0.456
Male	60 (30)	4 (6.67)	56 (93.33)	
Comorbidities (n (%))				
Diabetes mellitus				
Yes	13 (6.5)	0 (0)	13 (100)	1.000
No	187 (93.5)	9 (4.81)	178 (95.19)	
Hypertension				
Yes	33 (16.5)	6 (18.18)	27 (81.82)	<0.001*
No	167 (83.5)	3 (1.8)	164 (98.2)	
Inmunosuppression				
Yes	4 (2)	1 (25)	3 (75)	0.169
No	196 (98)	8 (4.08)	188 (95.92)	
Cardiovascular disease				
Yes	5 (2.5)	1 (20)	4 (80)	0.208
No	195 (97.5)	8 (4.1)	187 (95.9)	
Obesity				
Yes	26 (13)	1 (3.85)	25 (96.15)	1.000
No	174 (87)	8 (4.6)	166 (95.4)	
APACHE II (median (IQR))	5 (4-8)	11 (9-19)	5 (3-8)	<0.001*
BISAP (median (IQR))	1 (0-2)	4 (3-4)	1 (0-2)	<0.001*
ICU admission (n (%))				
Yes	30 (15)	8 (26.67)	22 (73.33)	<0.001*
No	170 (85)	1 (0.59)	169 (99.41)	
NIV (n (%))				
Yes	3 (1.5)	0 (0)	3 (100)	1.000
No	197 (98.5)	9 (4.57)	188 (95.43)	
NIV (n (%))				
Yes	25 (12.5)	9 (36)	16 (64)	<0.001*
No	175 (87.5)	0 (0)	175 (100)	
Hospital stay (median (IQR))	22 (13-33)	11 (2-29)	22 (14-33)	0.044*

HTN (hypertension). DM (diabetes mellitus). ICU (intensive care unit). NIV (non-invasive mechanical ventilation), * statistically significant.

Table 2. *Comparison between CRP, albumin and CRP/albumin ratio in patients with acute pancreatitis, by discharge status.*

Parameters	Discharge status		P value
	Non-survivor	Survivor	
	Median (IQR)	Median (IQR)	
CRP mg/L	211 (108-280)	74 (22-227)	0.048
Albumin g/dL	2 (2-3)	4 (3-4)	0.001
CRP/albumin ratio	94 (48-121)	23 (6-67)	0.006*
CRP: C-reactive protein			

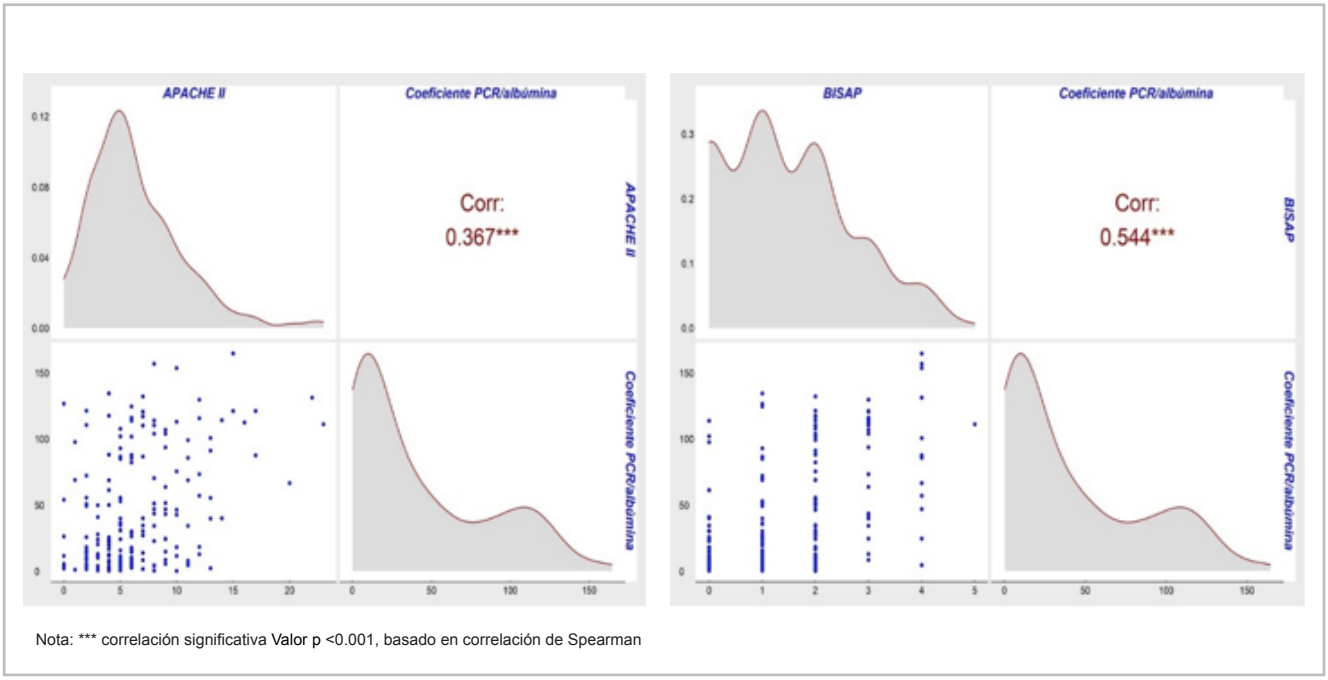

Figure 1. *Correlation between APACHE II, BISAP and the CRP/albumin ratio in patients with acute pancreatitis.*

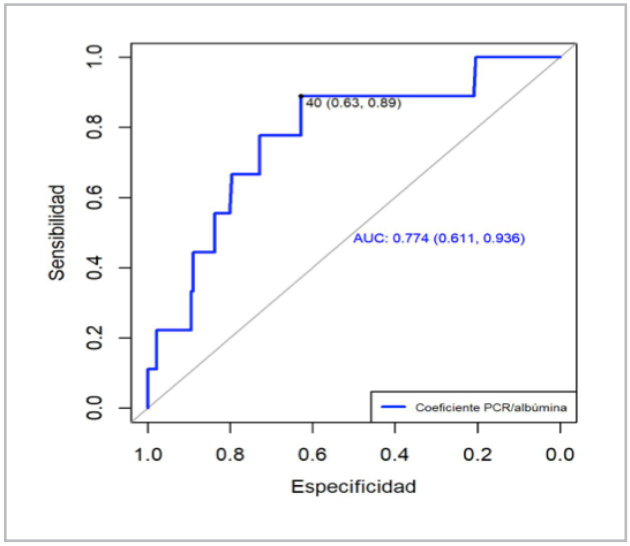

Figure 2. *ROC curve to predict mortality in patients with acute pancreatitis using the CRP/albumin ratio.*

Using the CRP/albumin ratio cut-off point, the predictive power for mortality was determined using logistic regression. The results showed that a CRP/albumin ratio ≥40 is a predictor of mortality (p 0.029), with patients having a CRP/albumin ratio ≥40 having a 5.92 times greater chance of dying compared to those with a level <40 (Table 3).

The CRP/albumin ratio cut-off point was used to compare APACHE II, BISAP and days of hospitalization, finding the following: APACHE II showed significant differences (p<0.001), with a median of 8 for a ratio ≥40 versus a median of 5 for a ratio <40. Also, BISAP showed significant differences (p<0.001), with a median of two for a ratio ≥40, versus a median of one for a ratio <40. Days of hospitalization showed significant differences (p<0.001), with a median of 27 days for a ratio ≥40 vs. 19 days for a ratio <40 (Table 4).

Discussion

The study compared the CRP/albumin ratio with the BISAP and APACHE II scales, based on its having been

Table 3. *Predictive model for mortality based on the CRP/albumin ratio in patients with acute pancreatitis.*

Variable	B	P value	OR	95% CI-OR	
				LL	UL
CRP/albumin ratio ≥40	1.78	0.029*	5.92**	1.20	29.26

Table 4. *Comparison between APACHE II, BISAP and hospital stay in patients with acute pancreatitis by CRP/albumin ratio cut-off point*

Parameters	CRP/Albumin Ratio		P value
	≥40	<40	
	Median (IQR)	Median (IQR)	
APACHE II	8 (5-11)	5 (3-6)	<0.001*
BISAP	2 (1-3)	1 (0-1)	<0.001*
Hospital stay	27 (19-40)	19 (11-29)	<0.001*

studied in various diseases. C-reactive protein and albumin abnormalities are associated with acute illness, sepsis and inflammatory diseases (15).

By themselves, CRP and albumin showed significant differences (CRP p: 0.008 and albumin p: 0001) when comparing survivors with non-survivors: the median CRP in non-survivors was 211 mg/L versus 74 mg/L in survivors; the median albumin in non-survivors was 2 g/dL versus 4 g/dL in survivors.

Villacorta et al. showed that CRP is a predictor of mortality in heart failure, but its isolated use is controversial. Silvestre et al. found no relationship between CRP levels and the severity of sepsis, organ failure and mortality in ICU patients. Hypoalbuminemia is associated with a poor prognosis in acute illnesses, but it can be caused by other factors like malnutrition or liver dysfunction, which are common in critically ill patients.

However, the combination of these markers has been associated with a more severe prognosis. In critically ill patients, Villalba et al. showed that the CRP/albumin ratio is the best indicator of mortality. Out of a total of 310 patients, 8% died, with a significant CRP/albumin ratio (r=0.959; p = 0.000), showing that it is an adequate indicator of mortality (7, 15, 19–21).

There was a 70% female predominance in the cases, similar to the national and Latin American trend, but contrary to the global setting where there is similarity between the genders, with greater mortality associated with the male gender. The female incidence varies according to the etiology of the disease; for example, having a higher proportion of biliary pancreatitis cases. In the Paraguayan study of the CRP/albumin ratio as a predictor of mortality, Aucejo et al. found that 69.7% of the patients were female. In a Peruvian study on pancreatitis, Sánchez et al. found that 82.6% of the cases were female. In Ecuador, according to the latest record in 2013 by the Instituto Nacional de Estadísticas y Censo (INEC) [National Statistics and Census Institute], out of a total of 4,061 hospital discharges for acute pancreatitis, 56% were females. In a study on pancreatitis in the city of Cuenca, Nivelo et al. reported that 64.9% of the patients with pancreatitis were women (7, 9, 22, 23).

The most common chronic diseases were hypertension (HTN) with 16.5%, obesity with 13%, diabetes mellitus (DM) with 6.5%, and cardiovascular disease with 2.5%. Hypertension showed a significant difference in patients who did not survive ($p < 0.001$) versus those who survived. Aucejo et al. reported a similar figure, where HTN occurred in 30.3% of the cases (7).

A cut-off point for the CRP/albumin ratio was established through the ROC curve, which was significant with a p value of 0.006. The area under the ROC curve was 0.774 (0.611-0.936), with a 95% CI reaching a lower limit >0.5, which indicates that the CRP/albumin ratio can predict mortality in patients with acute pancreatitis. With a cut-off point of 40 we obtain an 89% sensitivity with those who die and a 63% specificity with those who survive. Mortality at the >40 cut-off point was 1.69% and 9% in patients with a cut-off point <40, which was statistically significant. The predictive power for mortality when the CRP/albumin ratio is ≥40 was determined to indicate a 5.92 times greater likelihood of the patient dying, with a p = 0.029, compared to a ratio <40. This cut-off point is different from other studies of the CRP/albumin ratio, in which the cut-off point for mortality was lower. Kim et al. showed that the CRP/albumin ratio with a cut-off value of 5.09 was a poor prognostic indicator on hospital admission in patients with severe sepsis or septic shock. Ranzani et al. reported that, with a cut-off point of 8.7, the CRP/albumin ratio was an independent predictor of 90-day mortality in ICU patients with severe sepsis or septic shock. Aucejo et al. identified the CRP/albumin ratio as a better predictor of mortality than the indicators handled separately but did not determine a cut-off point per se (7, 15, 24, 25).

There was a positive correlation between APACHE II, BISAP and the CRP/albumin ratio, which was linear in both

cases; that is, an increase in either of the scores (APACHE II and BISAP) was associated with an increase in the CRP/albumin ratio, and vice versa.

The correlation between APACHE II and the CRP/albumin ratio was significant, with a $p < 0.001$, and a Spearman correlation coefficient of 0.367. When the CRP/albumin ratio is ≥ 40, the APACHE score is 8, and when the ratio is <40 the APACHE score is 5.

Likewise, the correlation between BISAP and the CRP/albumin ratio was significant, with a $p < 0.001$, and a Spearman correlation coefficient of 0.544. When the CRP/albumin ratio is 40, the BISAP score is two, with an interval ranging from one to three; when the ratio is <40 the BISAP score is one, with an interval ranging from zero to one.

Park et al. looked for a relationship between the CRP/albumin ratio and 28-day mortality in critically ill emergency patients and correlated it with the APACHE II score, using the ROC curve. They found that the CRP/albumin ratio was more prominent with a cut-off point of 34.3 for 28-day mortality (15).

Regarding the length of hospital stay, we found that when the CRP/albumin ratio was ≥40, the hospital length of stay was 27 days, and with a cut-off point of <40, the length of stay decreased to 19 days, with an approximate interval of eight days, which is statistically significant.

The study weaknesses and limitations are related to its retrospective, nonprobabilistic design, which could affect both the albumin and CRP values and, therefore, the accuracy of the results.

However, the study has some strengths, such as the fact that there are no prior studies comparing pancreatitis scales and the CRP/albumin ratio. The analysis of the relationship between the CRP/albumin ratio and the length of hospital stay is also a novel contribution.

Conclusion

In conclusion, the CRP/albumin ratio is an early predictor of mortality on hospital admission and improves the ability to predict the clinical course, indicating a 5.92 times greater risk of mortality in patients with a CRP/albumin ratio cut-off point ≥40. In addition, it predicts a prolonged hospital stay. Therefore, the CRP/albumin ratio can be used as an early indicator of mortality in patients with acute pancreatitis.

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