

A Thorough Study and Meta-Analysis of The Prognostic Relevance of the C-Reactive Protein-Albumin Ratio in Acute Pancreatitis.

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Abstract

Background: Although most cases of acute pancreatitis (AP) are minor, severe cases are associated with a substantial risk of death. Acute pancreatitis (AP) is a common illness. Therefore, it is critical to assess AP severity as soon as possible. This review aimed to ascertain the predictive significance of the CRP to albumin ratio in individuals with AP.

Methods: We searched PubMed, Science Direct, and Cochrane Library electronic databases Until January 2023. Studies that reported the CRP/alb ratio at admission and its relationship to the severity or death of patients with AP were included. Using a random-effects model, we computed the pooled mean difference (MD) and 95% confidence interval (CI). The quality of the included studies was evaluated using the Newcastle-Ottawa scale.

Results: This meta-analysis combined data from six trials with a total of 2244 patients. Upon admission, the CRP/alb ratio was higher in patients with severe AP than in those with mild to moderate AP (pooled MD:3.59; 95% CI:2.51-4.68; $p < 0.00001$). Additionally, non-survivor AP patients had a substantially higher CRP/alb ratio than survivor AP patients (pooled MD:2.12; 95% CI:0.43-3.8; $p < 0.01$).

In conclusion, individuals with AP may benefit from a high CRP/ALB ratio as a preliminary indicator of poor prognosis.

Keywords: CRP albumin ratio, Severity of pancreatitis, systemic review, risk of death

1. Introduction

Gallstones are the most common cause of acute pancreatitis in Southern Europe and alcohol consumption in Eastern Europe, with documented incidences ranging from 4.6 to 100 per 100,000 population in 17 European nations [1]. A better understanding of this illness can lead to higher mortality and morbidity, even with recent advancements in medicine [2]. Over the years, several grading systems have been employed to help physicians accurately estimate the mortality rates and determine their severity. A few popular scoring systems that are utilized are the Glasgow, Atlanta classification, Ranson, acute physiological assessment and chronic health evaluation (APACHE), and bedside index for severity in acute pancreatitis (BISAP) [3, 4].

Sudden and severe abdominal discomfort, together with high pancreatic enzyme levels, is a symptom of acute pancreatitis (AP), a pancreatic inflammation [5]. The two leading causes of this illness. Regarding severe AP, the mortality risk is elevated,

even though the majority of instances are moderate. In 2019, the global incidence of AP, a common gastrointestinal ailment, was reported to be 34.8 per 100,000 people [6]. While AP generally has a mortality rate of 3–10%, in cases of severe AP, the mortality rate can reach 36–50% [7,8]. Therefore, it is crucial to assess disease severity early in order to select the best treatment course. The severity and prognosis of acute pancreatitis (AP) are often assessed using several scoring systems, including the Atlanta classification, bedside index for severity in acute (BISAP), sensitive physiological assessment and chronic health evaluation (APACHE II), and Ranson scores. [9,10]. Most of these scoring systems require further blood tests 48 h after admission to improve their accuracy in predicting AP severity. They also considered numerous blood tests and clinical indicators. Instruments that can predict the prognosis of AP during the first hour of admission are required. C-reactive protein (CRP), an inflammatory measure, is frequently used in clinical practice to assess the severity of several inflammatory and infectious disorders. The acute-phase reactant

generated by the liver is enhanced by inflammation and infection. Conversely, albumin is a negative acute-phase reactant produced by the liver, which decreases with inflammation. Additionally, albumin levels, illness severity, and death were related. Although the expected levels of the CRP/albumin ratio are still under debate, a new predictive score linked to mortality and the degree of inflammation was recently identified as the CRP-to-albumin (CRP/albumin) ratio. Most of the earlier studies that attempted to link the CRP/alb ratio to AP severity and mortality produced encouraging findings. Nevertheless, to the best of our knowledge, no meta-analysis has compiled the results of these investigations. This study examined the predictive significance of the CRP/ALB ratio in AP through a systematic review and meta-analysis

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed for this systematic review and meta-analysis. We conducted a thorough literature search using PubMed, Science Direct, and the Cochrane Library to identify relevant papers published through January 31, 2023. PANCREATIS AND ("CRP albumin ratio" OR "C-reactive protein/albumin" OR "C-reactive protein albumin" OR "CRP/albumin" OR "CRP alb ratio" OR "CRP/alb") were the keywords we used. We also looked at the references of relevant publications. Duplicate results were removed after the first search.

Study Choice

The study selection was carried out separately by two authors (HAS, and MIF). A review process was used to weigh unrelated research by reviewing paper titles and abstracts. Studies that passed the first screening were subjected to inclusion and exclusion criteria for this evaluation. Studies that satisfied each of the following requirements were included: (1) observational studies describing acute pancreatitis patients, (2) admission CRP/alb ratio, (3) adult patients, (4) documenting the severity of AP and patient death, and (5) papers written in Indonesian or English. Studies that satisfied any of the following criteria were also disqualified: (1) no full text available, (2) case reports, (3) conference papers, (4) review articles, (5) non-research letters, (6) commentaries, and (7) did not supply the information required to perform a meta-analysis.

Extraction of Data.

The name of the first author, year of publication, nation, type of study, number of patients, age, mean or median value of the CRP/ALB ratio, and outcomes (severity or mortality) are among the

data taken from the included studies. AP severity of AP is the primary outcome examined in this systematic review and meta-analysis. The secondary result was the death rate of patients with secondary result. The authors used an electronic data collection form with gather the required data from each article and analysed in Zagazig University Egypt.

Bias Risk

The Newcastle-Ottawa scale (NOS) was used to evaluate the risk of bias in each included study. This procedure was performed separately by three authors (IKM, CPS, and DAS). Three categories were used to categorize the assessment results: low risk (7-9), moderate risk (4-6), and high risk (0-3).

Statistical Analysis

The statistical analysis program used was Stata 17 together with Review Manager 5.4. Using the mean difference (MD) and standard deviation (SD) from each trial, we calculated the pooled mean difference (MD) with 95% confidence intervals (CI). In cases where the data were given as medians with Q1 and Q3 or ranges, we used a calculator developed by Luo et al. and Wan et al. to calculate the mean. 8, 9 The I2 statistic was used to evaluate heterogeneity; values > 60% indicated significant heterogeneity. This shows the proportion of variation in observed impacts across research linked to the variation in genuine effects. P values were all two-tailed, with a less than 0.05 considered statistically significant. A forest plot was created to visually represent the estimated effects and the degree of study heterogeneity. Sensitivity analysis used the leave-one-out strategy, which involves redoing the analysis after removing one study at a time.

Results

Examining choices and attributes. A total of 21 publications were identified using a keyword search. After removing duplicates, 18 journals were extracted. Eleven potential papers remained after we eliminated seven based on our analysis of the abstracts and titles. Subsequently, the entire texts of all possible studies were acquired and examined to determine whether they could be included in the meta-analysis. Publications that did not meet all inclusion criteria and those that did not provide all the data required for this meta-analysis were excluded. Consequently, six studies were included in the current investigation. Figure 1 shows exclusion and inclusion criteria .

PRISMA flow schematic, Figure 1

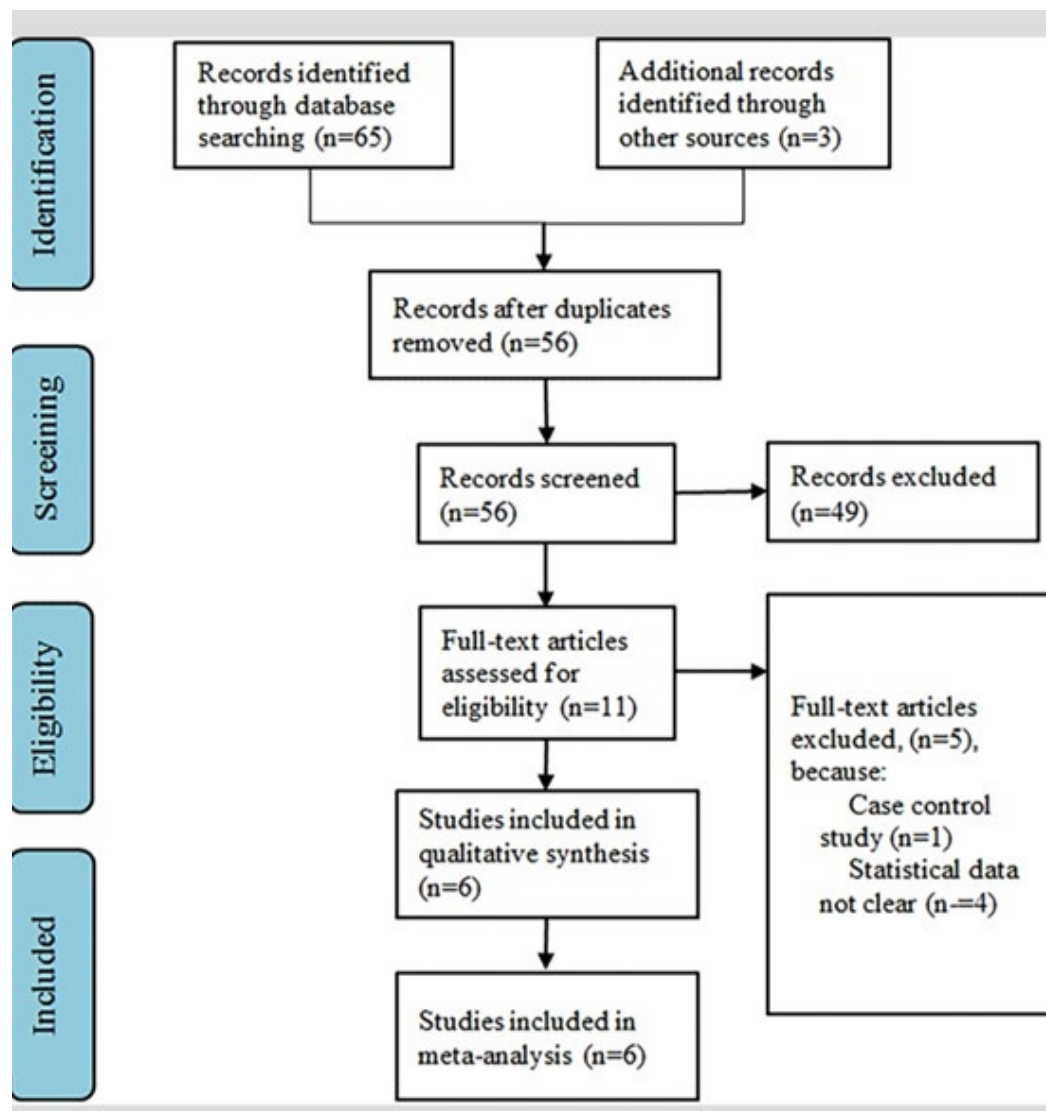


Figure 1: flowchart of study patients

All six included studies comprised 2244 patients and were retrospective cohorts. Each study will be conducted between 2017 and 2022. Owing to the location of the study, two were in China and four were in Turkey. The association between AP severity and CRP/ALB was examined in five studies. Two investigations reviewed the connection between AP mortality and the CRP/alb ratio. The features of the included studies are shown in Table 1.

Study	Country	Study design	Assessment of severity	Sample	Mean/median age	Non-severe/severe	Survivors/non-survivors	Cut-off severe	Cut-off mortality
Karabuga 2022	Turkey	retrospective observational study	BISAP score	female 253 (50.6%) male 247 (49.4%)	55.68 ± 18.30	mild 388 severe 112	survivor 473 death 23	>0.0015	
Kiyak 2022	Turkey	retrospective observational study	Balthazar and Ranson score	female 173 (52.6%) male 156 (47.5%)	male 50.3 ± 15.7 female 54.3 ± 17.4	mild 238 severe 91		>5.34	Mortality (-) 3.3 ± 2.6 (+) 6.5 ± 1.2
Ugurlyu 2022	Turkey	retrospective observational study	contrast-enhanced abdominal computed tomography (CECT) and Revised Atlanta Classification	582 female 344 (59.1%) male 238 (40.8%)	male 58.06 ± 17.34 female 57.9 ± 21.05	AEP 525 ANP 57	survivor 541 death 41	> 0.878	
Yilmaz 2018	Turkey	retrospective observational study	Ranson score	264 female 159 (60.2%) male 105 (39.8%)	59.97 ± 17.47	moderate 204 severe 60	no mortality	>8.51	
Zhao 2020	China	retrospective observational study		140 female 42 (30%) male 98 (70%)	49.88 ± 13.94		survivor 124 death 16		>7.69
Zhao 2023	China	retrospective observational study	severe AP defined as persistent single or multiple organ failure (>48 h)	284	59.50 (IQR 39.00–70.00)	non severe 249 severe 35	survivor 273 death 11	>5.03	>5.33

Table 1: Features of the research that were part of the meta-analysis

Quality evaluation

Five studies were deemed to be at low risk, and one study was considered to be at moderate risk when the NOS was used to assess the risk of bias. The assessment of the bias risk is presented in Table 2.

Study	Selection				Comparability	Outcome				
	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of Cohorts	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	SCORE	Evidence quality
Karabuga 2022	*	*	*		*	*	*	*	7	Low risk of bias
Kiyak 2022	*	*	*			*	*	*	6	Low risk of bias
Ugurlyu 2022	*	*	*	*	*	*	*	*	8	Low risk of bias
Yilmaz 2018		*		*		*	*	*	5	Moderate risk of bias
Zhao 2020	*	*	*	*		*	*	*	7	Low risk of bias
Zhao 2023	*	*	*		*	*	*	*	7	Low risk of bias

Table 2. The NOS of research was part of the meta-analysis.

AP severity and the CRP/alb ratio A total of 1960 participants from five studies were used to examine the connection between AP severity and the CRP/alb ratio. Patients with severe AP had a higher CRP/alb ratio than those with mild-to-moderate AP (pooled MD, 3.59; 95% CI:2.51-4.68; $p < 0.00001$ (figure 2.). Sensitivity analysis using the leave-one-out technique was also conducted because of the extreme heterogeneity ($I^2 = 89\%$). After removing one study at a time, the leave-one-out analysis revealed no discernible changes in the results (Figure 3).

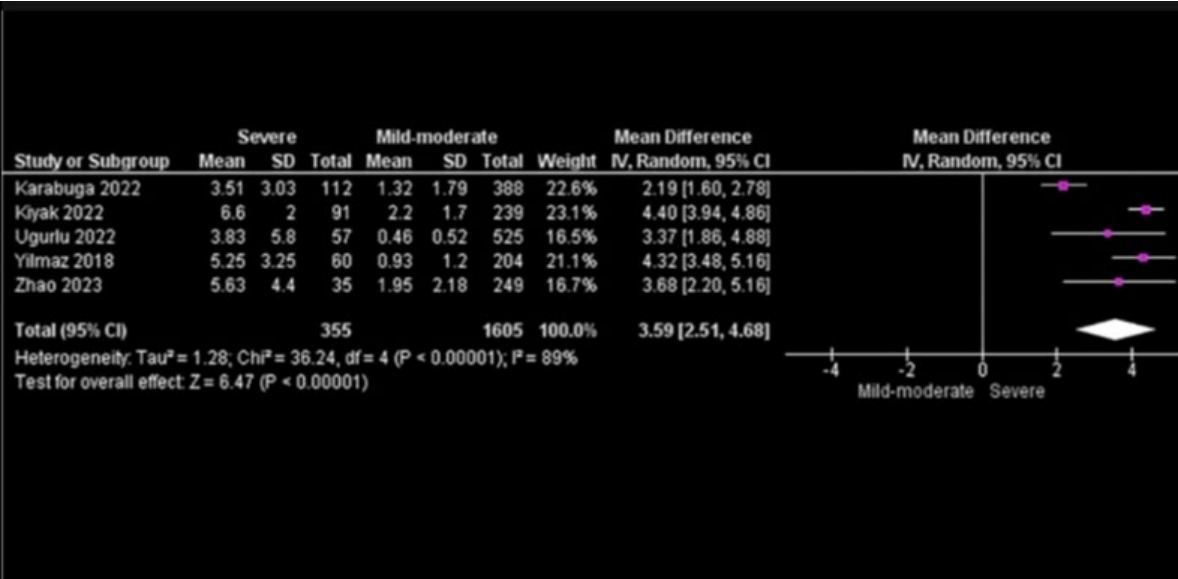


Figure 2: A forest plot of research contrasting the CRP/alb ratio in patients with severe AP with mild-to-moderate AP

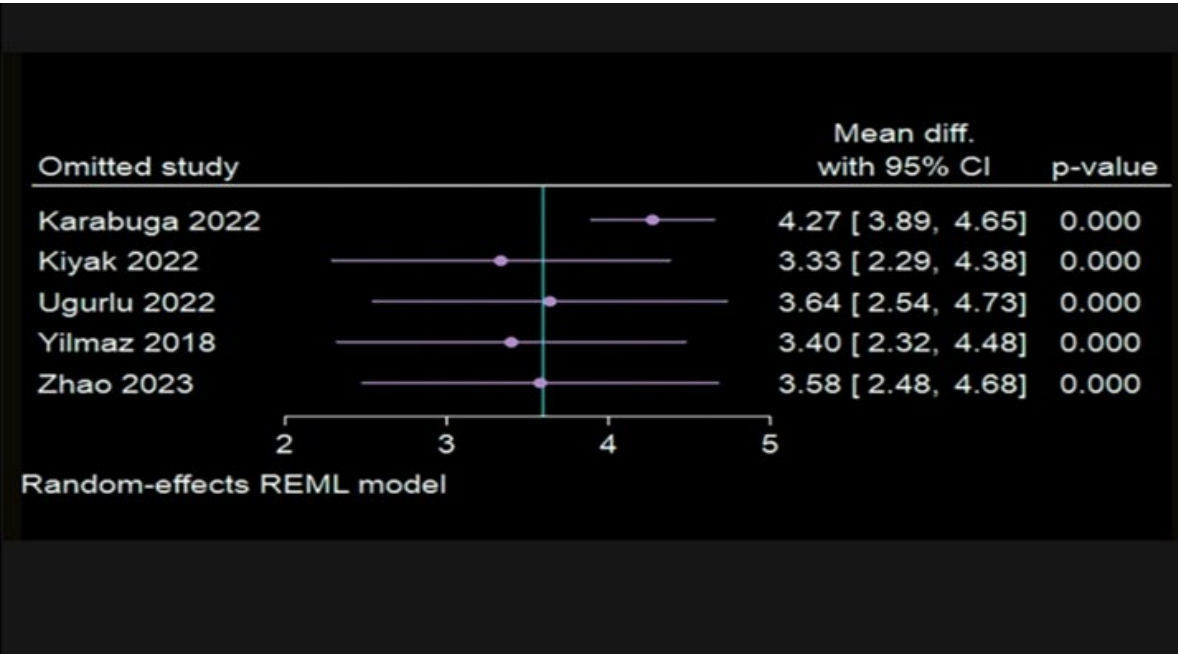


Figure 3: compares the CRP/alb ratios of patients with severe and mild-to-moderate AP using a leave-one-out approach.

Only two studies that assessed the CRP/ALB ratio and AP mortality met the inclusion criteria. Because the heterogeneity of these studies was regarded as low ($I^2 = 0\%$), fixed-effects models were used in this analysis. These analyses showed that the CRP/ALB ratio was higher in non-survivors than in survivors (pooled MD,2.12; 95% CI:0.43-3.8; $p < 0.01$). (Fig. 4)

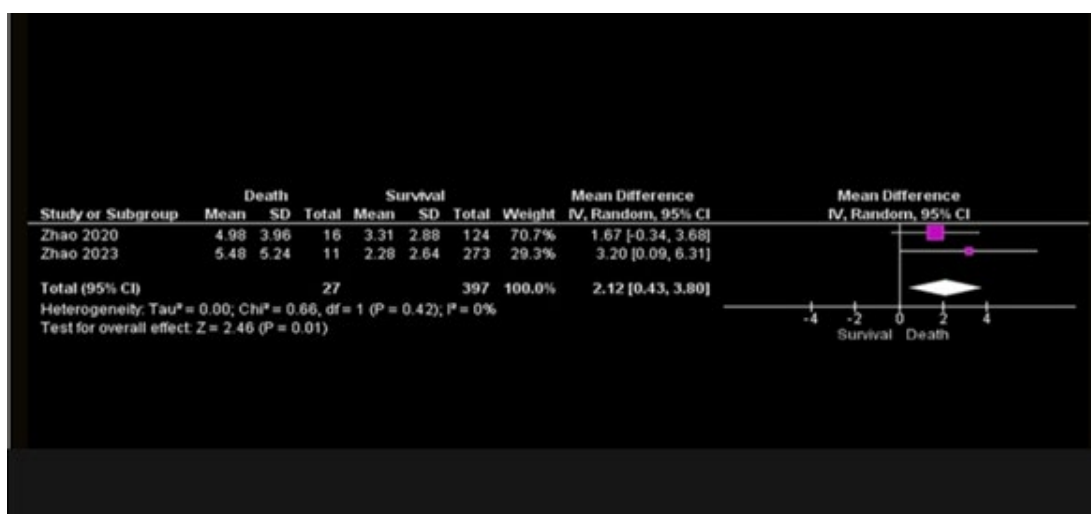


Figure 4: A forest plot of research comparing the CRP/alb ratio in AP patients who survived against those who did not.

Discussion

Localized inflammation can have systemic implications in patients with AP. The development of systemic organ malfunction, and ultimately organ failure, predisposes patients to systemic inflammation. Sixteen organ failures and the existence of systemic consequences were used to classify the severity of AP. Sustained organ failure was defined as severe AP. Organ failure or systemic consequences were absent in patients with moderate AP [10,17]. Inflammation markers are hypothesized to predict the prognosis of AP, because the degree of inflammation determines the severity of AP. One of the most widely used biomarkers, CRP, has been demonstrated to be strongly correlated with AP severity. The issue was that, when measured 48 hours after admission, the connection was only significant, and CRP levels alone upon admission had a low predictive value. Globally, the threshold for predicting severe acute pneumonia (AP) was established as $CRP > 150$ mg/L within 48 h. Numerous investigations have shown that albumin and CRP levels can help determine the prognosis of different diseases. It is anticipated that combining these two markers will result in a better prediction value than utilizing either marker alone, which is a potentially useful prognostic score for predicting the severity and death of patients with AP, according to our meta-analysis. Six studies met the inclusion criteria and were included. Two studies were from China and four were from Turkey. Several studies employed different CRP and albumin measurement units, whereas others did not state the measurement units used. As none of the corresponding authors of relevant studies responded when we attempted to contact them to address this issue, we estimated the measurement units based on other pertinent information from each study. All the data were converted into the same measurement units. Some of the studies met the inclusion criteria and completed the screening procedure [18,19]. However, they were ultimately disqualified owing to unclear statistical data, and compared to non-severe and survivor AP patients, we discovered that admission

CRP/ALB ratios were greater in severe and non-survivor AP patients. These results are consistent with those of other recent studies that demonstrated the usefulness of the CRP/ALB ratio as a prognostic indicator in a range of illnesses. As inflammation and carcinogenesis are related, several systematic studies have demonstrated the usefulness of the CRP/alb ratio as a predictor of various cancer types.[20, 21]. Several studies focusing on sick individuals have attempted to ascertain this association. In their single-center retrospective analysis, Park et al. discovered a correlation between a greater CRP/Alb ratio and higher ICU patient mortality[21], Wang et al. found that patients with acute renal injury who were critically unwell and had higher CRP/Alb ratios also had higher 2-year all-cause mortality and in-hospital mortality [22]. According to the findings of the present meta-analysis, the CRP/Alb ratio in AP patients may also be a valid prognostic indicator. When AP becomes severe, hospitalization to the critical care unit is common. This could account for the findings of this study, which is focused on critically sick patients, and another study that is comparable to this one. To our knowledge, this is the first meta-analysis assessing the CRP/alb ratio in AP patients as a predictive indicator. The predictive significance of the CRP/ALB ratio in patients with AP was evaluated in a systematic review by Tarar et al. However, that study only performed a qualitative analysis based on three retrospective cohort studies, and did not perform a meta-analysis.

Other quality of studies was further evaluated using the MINORS (methodological index by other reviews for non-randomized studies) assessment tool (Table 3. Data were assessed using Microsoft Excel (Microsoft Corporation, Redmond, WA, the data were), and tables were created as needed to carry out pertinent statistical analyses [21]. The authors have not yet registered any protocol for this study. Fewer than five cases were disqualified.

Articles included	Kaplan et al. [9]	Karabuga et al. [10]	Yilmaz et al. [11]	Zhao et al. [12]
Aim clearly stated	2	2	2	2
Inclusion of consecutive patients	2	2	2	2
Prospective collection of data	0	0	0	0
Endpoints appropriate to the aim of the study	2	2	2	2
Unbiased assessment of the study endpoint	0	0	0	0
Follow-up period appropriate to the aim of the study	2	0	0	0
Loss to follow up less than 5%	2	0	0	0
Prospective calculation of the study size	0	0	0	0
Total score (out of 16)	8	6	6	6

Table3: The MINORS evaluation instrument

Using the MINOR methodological index for non-randomized research, the included articles were rated. The scores for the items are either 2 (reported and adequate), 1 (registered but inadequate), or 0 (not reported). In non-comparative investigations, a score of 16 is considered excellent. However, none of these studies were comparable.

Some items for meta-Analyses and Systematic Reviews had nine hundred fifty-six participants with acute pancreatitis who were recruited in studies that looked at the link between the CRP/albumin ratio and the severity of acute pancreatitis their found in

our research across three studies (Table 4),. Of these, 478 (478; 50%) were male and 478 (50%) were female. Of the patients, 201 (215) had severe pancreatitis and 750 (755; 79%) had nonsevere pancreatitis [20]. The performance of the CRP/albumin ratio was assessed using the established scoring systems in all three investigations. These scoring systems include the Ranson, Atlanta, and BISAP scoring systems. These investigations revealed a strong connection between the CRP/albumin ratio at admission and the subsequent development of severe acute pancreatitis (Tables 4) and (Table 5) present assessment of ratio as a tool CRP: C-reactive protein; NLR: neutrophil-to-lymphocyte ratio

Study Name	Year Published	Retro/ Prospective	Study type (Case series, cohort, RCT)	Age, mean (range)/SD	Sex, M:F	Severity of cases by number
Kaplan et al. [9]	2017	Retrospective	Cohort	61.9 ± 18.0	72:120	Ranson "0": 29(15.1%); "1": 36 (18.8%); "2": 44 (22.9%); "3": 31 (16.1%); "4": 17 (8.9%); "5": 25 (13%); Atlanta "mild": 127 (66.1) "moderately severe": 36 (18.8); "severe": 29 (15.1%)
Karabuga et al. [10]	2022	Retrospective	Cohort study	50.19 ± 16.01	247:253	BISAP <3, mild AP: 388 (77.6%); BISAP ≥ 3, severe AP: 112 (22.4%)
Yilmaz et al. [11]	2018	Retrospective	Cohort study	59.97 (21-95) ±17.47	105:159	Defined as the Ranson score >3, N=60 (22.8%)
Zhao et al. [12]	2020	Retrospective	Cohort study	49.88 ± 13.94	98:42	Defined using the Atlanta score 46 (32.86%)

Table 4: Research Population

Study Name	Year conducted	Number of patients	CRP/albumin ratio values, mean mg/L (range)	Mortality	Complications	Follow-up, median	Study's recommendation
Kaplan et al. [9]	Jan 2002 - June 2015	192	The ratio of 16.28 had a 19.3x change in death	38 (19.8%)	Acute renal failure: 17 (8.9%); Abscess: 8 (4.2%); Sepsis: 10 (5.2%); Pseudocyst: 9 (4.7%); Ascites: 3 (1.6%); Haematoma: 5 (2.6%); Cholangitis: 6 (3.1%); Oedematous: 153 (79.7%); Necrotizing pancreatitis: 38 (19.8%)	63 months (1-126)	CRP/albumin ratio could be used to predict prognosis in patients with acute pancreatitis.
Karabuga et al. [10]	Feb 2019 – March 2020	500	0.0181 ± 0.00232; Median: 0.00083	Mild AP: 2 out of 388 (0.52%); Severe AP: 21 out of 112 (18.75%); Total: 23 out of 500 (4.6%)	N/A	N/A	NLR and CRP/albumin values were found most reliable in determining the severity of acute pancreatitis. Recommends usability of these inexpensive parameters.
Yılmaz et al. [11]	Jan 2014 – Nov 2017	264	19.16 (0.05-114.94) ± 26.09	0	22 (8.3%)	N/A	Highlight the CRP/albumin ratio promising a potential marker for use in determining prognosis in acute pancreatitis cases
Zhao et al. [12]	Jan 2008 – Nov 2019	140	Single-operation: 2.90±3.02; Re-operation: 4.63±2.8; Survival: 3.32 ±2.88	16 (11.43%)	90 (64.29%)	N/A	The creatinine/albumin showed better performance than CRP/albumin

Table 5 : Assessment of ratio as a tool CRP: C-reactive protein; NLR: neutrophil-to-lymphocyte ratio

Since Pinilla et al. found a substantial link between CRP/PALB and severe organ failure in patients with sepsis in 1998, the inflammatory ratio, including CRP and albumin (PALB), has been used for predictive purposes [13]. In 2009, Fairclough et al. reported the first study to utilize CRP/albumin to predict patient outcomes. They compared the effectiveness of the marker with the modified early warning score (MEWS) [14]. They discovered that the MEWS performed better than the CRP/albumin ratio for patients admitted to the acute medical unit; however, if this ratio increased from <2 to >4, mortality increased from 5% to 25%. Additionally, Ranzani et al. discovered that in patients with sepsis, the CRP/albumin ratio was an independent risk factor for 90-day mortality (Table 5) [15].

Hepatocytes release CRP, a positive acute-phase reactant, in response to interleukin 6 (IL-6), a systemic inflammatory marker. Conversely, these signals cause albumin, a negative acute-phase reactant, to decrease. Hypoalbuminemia has been demonstrated to be a strong and dose-dependent independent predictor of unfavorable results [16]. Given the biology of acute pancreatitis, using this ratio to predict severity is promising. Particularly in its severe form, acute pancreatitis causes systemic and localized

inflammatory reactions that would unavoidably impact these liver indicators.

The CRP/albumin ratio measures the outcomes in cancer patients owing to the role of inflammation in neoplastic diseases. When Kinoshita et al. initially investigated this relationship, they discovered that the ratio may predict tumor growth and a decline in liver functional reserve in patients (HCC) patients [17]. In HCC, a cut-off value of >0.037 was considered an early indicator of poor outcomes. Zhou et al. examined the relationship between CRP and albumin in patients with small-cell lung cancer patients and found that patients with a ratio greater than 0.441 had a 1.34 times higher risk of dying than those with a CRP level < 0.441. Therefore, this ratio was identified as an independent prognostic factor in patients with SCLC [18]. Additional research has further confirmed the function of the CRP/albumin ratio as a prognostic indicator in colorectal and esophageal squamous cell cancers (Table (Table 5) [19, 20].

Kaplan et al. first evaluated the relationship between this ratio and pancreatitis severity in 2015 [9]. The researchers discovered a positive correlation ($p < 0.001$) between the CRP/albumin ratio and

length of hospital stay, Atlanta classification of disease severity, and Ranson score. Balance was an independent risk factor for mortality in this study. A CRP/albumin ratio of >16.28 , with 92.1% sensitivity and 58% specificity, was linked to death. They found that a percentage larger than 16.28 was associated with a mortality rate 19.271 times higher than a ratio lower than 16.28. Moreover, the median survival was 55 months, as indicated by the area under the curve (AUC), with a ratio of >16.28 (Table 5).

Yilmaz et al. [10] also examined the association between severe acute pancreatitis and CRP/albumin ratio. Using Ranson scoring, they discovered that if the balance was > 8.51 , severity could be predicted with 66% sensitivity and 90% specificity. Additionally, they found that this ratio indicated longer stay in the ICU and hospitals. When Karabuga et al. used the BISAP score to evaluate the association of severity, they arrived at similar conclusions [11]. They discovered that the ratio was 71.43% sensitive and 70.88% specific for predicting severe acute pancreatitis at a cut-off of 0.0015.

It has been proposed that the various scoring systems and threshold values of hepatic parameters cause disparities in the cut-offs between these two investigations. Zhao et al. investigated the predictive value of the CRP/albumin ratio in patients requiring surgical debridement for acute pancreatitis [20]. They discovered that this ratio was substantially linked to longer ICU stays ($p = 0.003$) and an increased likelihood of reoperation following initial debridement ($p < 0.05$).

The CRP/albumin ratio has become a powerful prognostic marker in several medical fields in the past 20 years. Our assessment of the literature on this ratio revealed a generally positive link between the development of severe acute pancreatitis and CRP/albumin ratio upon admission. The primary usefulness of this ratio stems from the ease with which these characteristics can be regularly measured and computed. Because it is straightforward and uncomplicated, it is a priceless tool for healthcare evaluation. In acute pancreatitis, early patient categorization based on possible severity is critical; therefore, additional research is required to evaluate the usefulness of the CRP/albumin ratio as a predictive tool.

This study found a positive overall correlation between the admission CRP/ALB ratio and the incidence of severe AP along with an extended hospital stay [21]. These results are in line with the results of our study. However, our research has some limitations. First, only two nations, China and Turkey, were included in the six studies included in this meta-analysis. Although the lack of diversity in the study area is beyond our ability to explain, we can state that this poses a challenge to the current investigation. Second, there is a chance that the comparisons drawn in this study will not be correct because of variations in the units of measurement utilized in each study. Finally, to distinguish between severe and non-severe AP, nearly all the studies employed distinct methodologies and criteria. These variations were anticipated given that the studies were conducted in various nations and

locations. Usually, one center uses the acute pancreatitis severity criterion more frequently than the other. Nonetheless, we believe that this distinction had no appreciable impact on the outcomes [20,21], because all standards were well-accepted standards that had previously been examined in a small number of investigations and revealed no appreciable variations in predictive value.

In conclusion, the CRP/Alb ratios were associated with severe AP and patient mortality. Therefore, in individuals with AP, the CRP/ALB ratio can be used as an early predictor of a poor prognosis. However, large-scale trials including patients of different ethnicities are required to corroborate the results we obtained because of the study's limitations. According to our systematic review, The CRP/albumin ratio upon admission was positively correlated with the development of severe acute pancreatitis, extended hospital stays, and a higher mortality rate in these studies. We believe that it is simple to compute the CRP/albumin ratio and use it to determine disease severity.

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Author contributions

HAS, ME: contributed to the conception and design of ME, AKE organised the database and performed the statistical analysis.

HAS, KS, MR: wrote sections of the manuscript and prepared tables.

MIF : contributed to the manuscript revision.

HAS, MIF : selection proecssing

All authors approved and equally shared the submitted version

References

1. Roberts, S. E., Morrison-Rees, S., John, A., Williams, J. G., Brown, T. H., & Samuel, D. G. (2017). The incidence and aetiology of acute pancreatitis across Europe. *Pancreatology*, 17(2), 155-165.
2. Greenberg, J. A., Hsu, J., Bawazeer, M., Marshall, J., Friedrich, J. O., Nathens, A., ... & McLeod, R. S. (2016). Clinical practice guideline: management of acute pancreatitis. *Canadian journal of surgery*, 59(2), 128.
3. Venkatesh, N. R., Vijayakumar, C., Balasubramaniyan, G., Kandhasamy, S. C., Sundaramurthi, S., Sreenath, G. S., ... & Balasubramanian, G. (2020). Comparison of different scoring systems in predicting the severity of acute pancreatitis: a prospective observational study. *Cureus*, 12(2).
4. Mederos, M. A., Reber, H. A., & Girgis, M. D. (2021). Acute pancreatitis: a review. *Jama*, 325(4), 382-390.
5. Sproston, N. R., & Ashworth, J. J. (2018). Role of C-reactive protein at sites of inflammation and infection. *Frontiers in immunology*, 9, 754.
6. Wilson, C., Heads, A., Shenkin, A., & Imrie, C. W. (1989). C-reactive protein, antiproteases and complement factors as objective markers of severity in acute pancreatitis. *British Journal of Surgery*, 76(2), 177-181.
7. Braamskamp, M. J., Dolman, K. M., & Tabbers, M. M. (2010).

- Clinical practice: protein-losing enteropathy in children. *European journal of pediatrics*, 169, 1179-1185.
8. Hong, W., Lin, S., Zippi, M., Geng, W., Stock, S., Basharat, Z., ... & Zhou, M. (2017). Serum albumin is independently associated with persistent organ failure in acute pancreatitis. *Canadian Journal of Gastroenterology and Hepatology*, 2017.
 9. Kaplan, M., Ates, I., Akpınar, M. Y., Yuksel, M., Kuzu, U. B., Kacar, S., ... & Kayacetin, E. (2017). Predictive value of C-reactive protein/albumin ratio in acute pancreatitis. *Hepatobiliary & Pancreatic Diseases International*, 16(4), 424-430.
 10. Yılmaz, E. M., & Kandemir, A. (2018). Significance of red blood cell distribution width and C-reactive protein/albumin levels in predicting prognosis of acute pancreatitis. *Ulus Travma Acil Cerrahi Derg*, 24(6), 528-531.
 11. KARABUĞA, B., Gemcioglu, E., Karabuga, E., BAŞER, S., & ERSOY, O. (2022). Comparison of the predictive values of CRP, CRP/albumin, RDW, neutrophil/lymphocyte, and platelet/lymphocyte levels in determining the severity of acute pancreatitis in patients with acute pancreatitis according to the BISAP score. *Bratislava Medical Journal*, 123(2).
 12. Zhao, Z., Yu, Y., Xie, R., Yang, K., Xu, D., Li, L., ... & Fei, J. (2020). Prognostic value of the creatinine-albumin ratio in acute pancreatitis debridement. *BMC surgery*, 20(1), 1-10.
 13. Pinilla, J. C., Hayes, P., Lavery, W., Arnold, C., & Laxdal, V. (1998). The C-reactive protein to prealbumin ratio correlates with the severity of multiple organ dysfunction. *Surgery*, 124(4), 799-806.
 14. Fairclough, E., Cairns, E., Hamilton, J., & Kelly, C. (2009). Evaluation of a modified early warning system for acute medical admissions and comparison with C-reactive protein/albumin ratio as a predictor of patient outcome. *Clinical medicine*, 9(1), 30.
 15. Ranzani, O. T., Zampieri, F. G., Forte, D. N., Azevedo, L. C. P., & Park, M. (2013). C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. *PloS one*, 8(3), e59321.
 16. Vincent, J. L., Dubois, M. J., Navickis, R. J., & Wilkes, M. M. (2003). Hypoalbuminemia in acute illness: is there a rationale for intervention?: a meta-analysis of cohort studies and controlled trials. *Annals of surgery*, 237(3), 319-334.
 17. Kinoshita, A., Onoda, H., Imai, N., Iwaku, A., Oishi, M., Tanaka, K., ... & Matsushima, M. (2015). The C-reactive protein/albumin ratio, a novel inflammation-based prognostic score, predicts outcomes in patients with hepatocellular carcinoma. *Annals of surgical oncology*, 22, 803-810.
 18. Zhou, T., Zhan, J., Hong, S., Hu, Z., Fang, W., Qin, T., ... & Zhang, L. (2015). Ratio of C-reactive protein/albumin is an inflammatory prognostic score for predicting overall survival of patients with small-cell lung cancer. *Scientific reports*, 5(1), 10481.
 19. Kunizaki, M., Tominaga, T., Wakata, K., Miyazaki, T., Matsumoto, K., Sumida, Y., ... & Nagayasu, T. (2018). Clinical significance of the C reactive protein to albumin ratio for the prognosis of patients with esophageal squamous cell carcinoma. *Molecular and Clinical Oncology*, 8(2), 370-374.
 20. Ishizuka, M., Nagata, H., Takagi, K., Iwasaki, Y., Shibuya, N., & Kubota, K. (2016). Clinical significance of the C-reactive protein to albumin ratio for survival after surgery for colorectal cancer. *Annals of surgical oncology*, 23, 900-907.
 21. Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... & Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *International journal of surgery*, 88, 105906.