SOUTH ASIAN JOURNAL OF SOCIAL SCIENCES & HUMANITIES

ISSN: 2582-7065 (Online) SAJSSH, VOL 6, ISSUE 4, PP. 75-85

# C-Reactive Protein/Albumin Ratio as Predictor of COVID-19 Severity and Mortality

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| **Received:** 15th April 2025 | **Accepted:** 22nd July 2025 | **Published:** 5th August 2025 |
|---|---|---|

## ABSTRACT

**Background:** Early detection of COVID-19 patients with a higher risk of infection advancement can help tailor treatment plans more specifically and ensure better allocation of healthcare resources. Both C-reactive protein also albumin serve as markers that are sensitive to inflammation. **Study objective:** evaluate the ability of CRP/ and Alb proportion in the prediction of cruelty and mortality of COVID-19 infection. **Method:** sample of 130 clients with COVID that confirmed outcomes entered the private nursing home \ medical city, Baghdad, Iraq, between January - October 2023. Patients are divided into mild, moderate and severe, and into dead and alive patients. To predict disease progression, CRP, albumin and CRP\Alb ratio were evaluated on admission. **Results:** A study of 130 patients with COVID-19 infection, mean age of (53.80 ± 16.33) years old, (48.5%) of patients are females, while (51.5%) of patients are males. (66.92%) of patients have severe infection, while (33.08%) of them have non-severe (mild and moderate) infection with COVID-19. High CRP\Alb ratio occurs more in severe COVID infection and those who died than in non-severe (mild and moderate) and those who were discharged alive, respectively. **Conclusion:** CRP/and albumin percentage may serve consider early indicator of the development of severe illness or death, offering a predictive biomarker to assess risk and guiding the clinical interventions of COVID-19 clients.

**Keywords:** CRP\Alb ratio, COVID-19, severity, mortality.



DOI: 10.48165/sajssh.2024.6405

## INTRODUCTION

Coronavirus disease 2019 (COVID-19), infectious virus caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Page et al., 2021). The disease has rapidly spread across the globe, resulting in the ongoing COVID-19 pandemic (Obaid et al., 2022). Although the clinical presentation of COVID19 varies, common symptoms include fever, cough, headache, fatigue, shortness of breath, and loss of smell or taste. Symptoms typically appear within 1 to 14 days after exposure. Notably, a significant proportion of infected individuals—at least one-third—remain asymptomatic, while older adults are more likely to develop severe symptoms (Islam et al., 2021).

COVID19 has been associated with organ damage, and some individuals continue to experience persistent symptoms for months after recovery, a condition known as "long COVID." Diagnosis is initially based on clinical symptoms but can be confirmed through reverse transcription polymerase chain reaction (RT-PCR) or other nucleic acid tests of respiratory secretions. Chest CT scans can support the diagnosis in cases with strong clinical suspicion, while serological testing can detect antibodies indicating past infection (Talib et al., 2022).

C-reactive protein (CRP) acute-phase reactant which increases in response to inflammatory process, whereas albumin (Alb) levels tend to decrease during such responses. Elevated CRP and reduced albumin levels are not only markers of disease severity but also predictors of mortality in patients with severe COVID-19, often indicating a cytokine storm—a hyperinflammatory state commonly seen in these patients. CRP levels correlate with the intensity of inflammation and are independent of demographic factors such as age, sex, or physical status. It is considered a crucial marker for identifying and evaluating severe pulmonary infections. High CRP concentrations have been associated with poor outcomes and increased mortality in critically ill patients (Saniasiaya, Islam, & Abdullah, 2021).

Under normal conditions, CRP levels in the blood are below 10 mg/L, but they begin to rise within 6–8 hours of disease onset, peaking at around 48 hours. CRP has a half-life of approximately 19 hours, and its levels decrease as the inflammatory process resolves and recovery begins (Agyeman et al., 2020).



DOI: 10.48165/sajssh.2024.6405

Albumin, which constitutes about 50% of total plasma protein in humans, accounts for nearly 80% of intravascular oncotic pressure due to its molecular properties and concentration. It is synthesized in the liver and has a serum half-life of around 21 days. Albumin metabolism becomes more complex in hospitalized patients, and the exact mechanisms linking low plasma albumin levels to poor health outcomes are not fully understood. Because of its extensive ligand-binding abilities, albumin also plays an antioxidant role, with the majority of extracellular albumin existing in a reduced state (Li et al., 2020).

In critically ill patients, hypoalbuminemia is typically a consequence of systemic inflammation. The release of cytokines and chemokines leads to increased capillary permeability, altering albumin distribution between intravascular and extravascular spaces. Importantly, albumin reduction in COVID-19 does not necessarily reflect liver dysfunction. Instead, serum albumin levels at admission may indicate the extent of systemic inflammation and can potentially serve as a prognostic marker for disease severity (Ai et al., 2020).

Given these properties, many clinical researchers view the CRP/albumin ratio (CRP/Alb) as a promising composite marker for patients experiencing cytokine storm syndromes. This ratio, derived by dividing CRP by albumin, is considered more reflective of the inflammatory burden than either marker alone (Salehi et al., 2020).

**Study objective:** assess the utility of CRP/ to Alb ratio in expecting illness development and severity among COVID19 people.

## METHODOLOGY

A retrospective study, and conducted at private nursing home \ medical city, Baghdad, Iraq, for a period of ten months from January 2023 to the end of October 2023. A convenient sample of patients who admitted to the private nursing home.130 patients with confirmed covid 19 infection included in this study, 67 of patients are male and 63 are females. Inclusion criteria: all patients included in this study had covid 19 infection confirmed by Real time RT–PCR and aged above 18 years. Data were collected retrospectively with review of medical records. A paper form prepared by researcher and supervisor to collect information from the medical records regarding selected variables. The form included questions about: age, gender, Spo2 with type of oxygenation, admission period, CRP and albumin level at time of admission, and the fate at discharge.



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CRP and albumin values were obtained from patients' medical records. Both parameters were measured using the ABBOTT C4000 automated biochemical analyzer. The reference ranges were 34–54 g/L (3.4–5.4 g/dL) for serum albumin and 0–10 mg/L for CRP. Statistical analysis was performed using SPSS software, version 27. Associations between categorical variables were assessed using Pearson's chi-square test or Fisher's exact test, as appropriate. A p-value of ≤ 0.05 was considered statistically significant.

## RESULTS

**Table 1:** *The Distribution of patients with COVID-19 according to socio demographic characteristics (N=130)*

| **Socio-demographic characteristics** | | |
|---|---|---|
| **Age (years)** | (53.80 ± 1.43) | (24-91) |
| **sex** | | |
| Male | 67 | 51.5% |
| Female | 63 | 48.5% |
| Total | 130 | 100.0% |

This table shows mean age of patients was (53.80 ± 16.33) with maximum age was (91.00) years and minimum age was (24.00) years. More than half of patients (N=67, 51.5%) were males.

**Table 2:** *The mean differences of CRP \ Albumin ratio according to severity of disease (N=130)*

| **Study variable** | **Severity of disease** | **N** | **Mean ± SE** | **F** | **P-value** |
|---|---|---|---|---|---|
| CRP \ Albumin ratio | Mild | 30 | 0.361 ± 0.062 | **35.945** | **<0.001*** |
| | Moderate | 13 | 0.602 ± 0.074 | | |
| | Severe | 87 | 4.220 ± 0.311 | | |

The mean differences of CRP to Albumin ratio according to severity of illness including (mild, moderate and severe).There were significant differences between means of CRP to Albumin ratio according to severity of illness.

**Table 3:** *Multiple comparisons (LSD)**



DOI: 10.48165/sajssh.2024.6405

| Study variables | Severity of disease | | P-value |
|---|---|---|---|
| CRP \ Albumin ratio | Mild | Moderate | 0.763 |
| | | Severe | **<0.001*** |
| | Moderate | Severe | **<0.001*** |

*LSD: least sign difference.

**Table 4:** *The mean differences of CRP \ Albumin ratio according to fate of patient (N=130)*

| Study variable | Fate of the patient | N | Mean ± SE | t-test | P-value |
|---|---|---|---|---|---|
| CRP \ Albumin ratio | Discharge well | 86 | 1.731 ± 0.238 | **-7.512** | **<0.001*** |
| | Death | 44 | 5.385 ± 0.424 | | |

The mean differences of CRP \ Albumin ratio according to the destiny of the client, including discharge well and demise, show significant differences between the means of the CRP to Albumin ratio according to the fate of the patient.

**Table 5:** *The mean differences of study variables according to severity of disease (N=130)*

| Study variable | Severity of disease | N | Mean ± SE | F | P-value |
|---|---|---|---|---|---|
| Age (years) | Mild | 30 | 35.27 ± 1.67 | **42.904** | **<0.001*** |
| | Moderate | 13 | 53.69 ± 3.44 | | |
| | Severe | 87 | 60.21 ± 1.47 | | |
| Hospital stay (days) | Mild | 30 | 2.30 ± 0.32 | **23.143** | **<0.001*** |
| | Moderate | 13 | 4.62 ± 0.45 | | |
| | Severe | 87 | 15.95 ± 1.33 | | |
| SPO2 (%) | Mild | 30 | 97.87 ± 0.16 | **91.239** | **<0.001*** |
| | Moderate | 13 | 96.38 ± 0.37 | | |
| | Severe | 87 | 85.46 ± 0.62 | | |



DOI: 10.48165/sajssh.2024.6405

The mean differences of study variables including (age), hospital stay (days) and SPO2 (%) according to severity of disease including (mild, moderate and severe).There were significant differences between means of study variables according to severity of disease.

**Table 6:** *Multiple comparisons (LSD)*

| Study variables | Severity of disease | | P-value |
|---|---|---|---|
| Age (years) | Mild | Moderate | **<0.001*** |
| | | Severe | **<0.001*** |
| | Moderate | Severe | 0.087 |
| Hospital stay (days) | Mild | Moderate | 0.498 |
| | | Severe | **<0.001*** |
| | Moderate | Severe | **<0.001*** |
| SPO2 (%) | Mild | Moderate | 0.35 |
| | | Severe | **<0.001*** |
| | Moderate | Severe | **<0.001*** |

**Table 7:** *The mean differences of study variables according to fate of patient (N=130)*

| Study variable | Fate of the patient | N | Mean ± SE | t-test | P-value |
|---|---|---|---|---|---|
| Age (years) | Discharge well | 86 | 49.35 ± 1.71 | **-4.683** | **<0.001*** |
| | Death | 44 | 62.50 ± 2.07 | | |
| Hospital stay (days) | Discharge well | 86 | 9.08 ± 1.03 | **-3.627** | **<0.001*** |
| | Death | 44 | 16.73 ± 2.16 | | |
| SPO2 (%) | Discharge well | 86 | 92.03 ± 0.68 | **6.507** | **<0.001*** |
| | Death | 44 | 84.30 ± 1.01 | | |



DOI: 10.48165/sajssh.2024.6405

The table above shows mean differences of variables (age), hospital stay (duration) and SPO2 level (%) according to destiny of ill person.significant differences among means of variables according to destiny of ill person.

**Table 8:** *Association between study variables and severity of disease (N=130)*

*P value ≤ 0.05 was significant.

| Study variables | Severity of disease | | | Total | P-value |
|---|---|---|---|---|---|
| | Mild | Moderate | Severe | | |
| **sex** | | | | | |
| Male | 11 (36.7) | 6 (46.2) | 50 (57.5) | 67 (51.5) | 0.133 |
| Female | 19 (63.3) | 7 (53.8) | 37 (42.5) | 63 (48.5) | |
| Total | 30 (100.0) | 13 (100.0) | 87 (100.0) | 130 (100.0) | |
| **Route of oxygenation** | | | | | |
| Room air | 30 (100.0) | 13 (100.0) | 30 (34.5) | 73 (56.2) | **<0.001*** |
| Nasal cannula | 0 (0.0) | 0 (0.0) | 1 (1.1) | 1 (0.8) | |
| Simple mask | 0 (0.0) | 0 (0.0) | 14 (16.1) | 14 (10.8) | |
| Non –rebreather mask | 0 (0.0) | 0 (0.0) | 32 (36.8) | 32 (24.6) | |
| Continuous positive airway pressure | 0 (0.0) | 0 (0.0) | 10 (11.5) | 10 (7.6) | |
| Total | 30 (100.0) | 13 (100.0) | 87 (100.0) | 130 (100.0) | |

The table shows the association between study variables, including sex and route of oxygenation, and severity of disease, including mild, moderate and severe.

**Table 9:** *Association between study variables and fate of patient (N=130)*

| Study variables | Fate of the patient | | Total | P-value |
|---|---|---|---|---|
| | Discharge well | Death | | |
| **Sex** | | | | |
| Male | 41 (47.7) | 26 (59.1) | 67 (51.5) | 0.218 |
| Female | 45 (52.3) | 18 (40.9) | 63 (48.5) | |
| Total | 86 (100.0) | 44 (100.0) | 130 (100.0) | |



DOI: 10.48165/sajssh.2024.6405

| | | | | |
|---|---|---|---|---|
| **Route of oxygenation** | | | | |
| Room air | | 11 (25.0) | | |
| Nasal cannula | | 1 (2.3) | | |
| Simple mask | | 6 (13.6) | | |
| Non – rebreather mask | | 19 (43.2) | | |
| Continuous positive airway pressure | 62 (72.1) | 7 (15.9) | 73 (56.2) | |
| Total | 0 (0.0) | | 1 (0.8) | |
| | 8 (9.3) | 44 (100.0) | 14 (10.8) | **<0.001*** |
| | 13 (15.1) | | 32 (24.6) | |
| | 3 (3.5) | | 10 (7.6) | |
| | 86 (100.0) | | 130 (100.0) | |

It shows the association between study variables including (sex and route of oxygenation) and fate of patient including (discharge well and death).There was significant association between type of breathing and fate of patient.

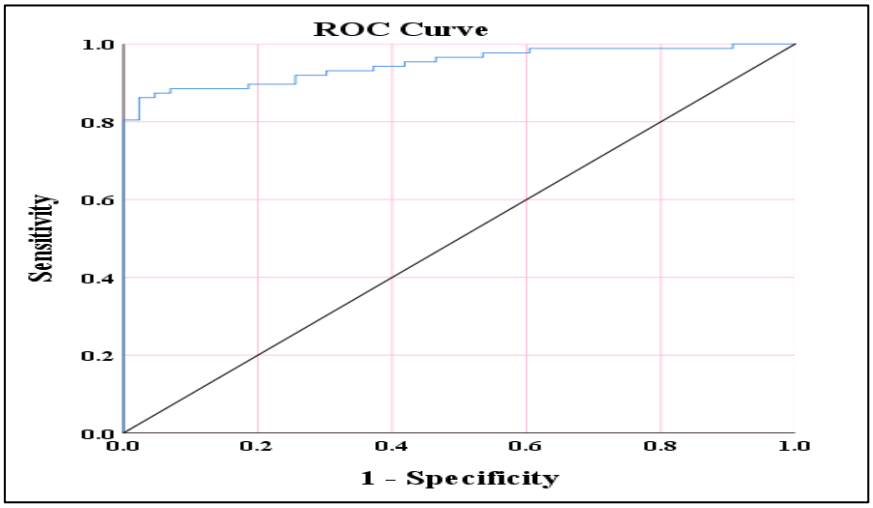


***Figure 1:*** ROC curve for the sensitivity of CRP/Albumin Ratio in prediction of severity of COVID-19 (N=130)



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## DISCUSSION

As demonstrated, CRP and albumin levels are each independently linked to adverse outcomes, regardless of patient age, sex, or the influence of the other marker. This suggests that their ratio warrants evaluation as a distinct parameter. The CRP/Albumin (CRP/Alb) ratio merges the inflammatory significance of CRP and the nutritional indicator of albumin, forming a novel scoring method based on both inflammatory and nutritional status. This parameter has gained increased attention recently. Initially, the ratio was searched as predictive marker in sepsis. In sepsis patients, it was shown to reflect disease severity and to predict 90-day mortality (Lucijanic et al., 2018). More recently, researchers have explored the CRP/Alb ratio as a prognostic indicator in oncology. Elevated ratios in cancer patients have been associated with poor clinical outcomes (Zhou et al., 2020).

In the present study, the average age of COVID-19 patients was 53.80 ± 16.33 years, with the youngest being 24.00 years and the oldest 91.00 years. Males made up a slightly higher proportion of the study population (N=67, 51.5%), although this difference was not statistically significant, which aligns with other studies (24.00) showing a male predominance. Moreover, consistent with findings from other investigations (24.00), older age was associated with increased risk of severe disease and mortality. Longer hospitalization durations were also observed in patients with severe COVID-19 and in those who did not survive.

Additionally, the current study identified a higher ratio in patients classified as very high in those who died. The mean CRP/Alb ratios across mild, moderate, and severe groups were 0.361, 0.602, and 4.220, respectively. When comparing patients based on outcomes, the mean CRP/Alb ratio was 1.731 in those who were discharged alive and 5.385 in those who died. At a cutoff point of ≥ 0.973, the CRP/Alb ratio demonstrated a sensitivity of 88.5%, specificity of 93.0%, and an overall accuracy of 90.0% for predicting COVID-19 severity (AUC = 0.948, P < 0.001, 95% CI: 0.912–0.983). For predicting patient mortality, a CRP/Alb cutoff of ≥ 2.212 yielded a sensitivity of 90.9%, specificity of 73.3%, and an overall accuracy of 79.23% (AUC = 0.862, P < 0.001, 95% CI: 0.794–0.929).

The CRP/Alb ratio showed strong predictive value for both disease severity and mortality in COVID-19 patients. Although its predictive strength was greater for severity, it remained a statistically significant marker in both contexts. When these results were compared with a study conducted by Aleksandr et al. in New York City (24.00), similar conclusions were drawn



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regarding the CRP/Alb ratio being a reliable marker of disease severity, though its role in predicting death was less definitive. Another investigation by Inanc Karakoyun et al. in Turkey supported the use of the CRP/Alb ratio as a helpful early marker for assessing severity among hospitalized COVID-19 patients. Other studies also concluded that the ratio is a superior predictor of adverse results.

Furthermore, as a tool for identifying disease progression in patients with severe COVID-19, the CRP/Alb ratio offers notable advantages. While several inflammatory markers such as ferritin, TNF-α, and IL-6 are known to rise during cytokine storm episodes in severe COVID-19, they are not commonly available in routine clinical practice, especially in primary hospitals or in resource-limited settings, where their use is mainly confined to research. In contrast, CRP and albumin tests are widely accessible, reliable, cost-effective, and commonly included in standard hospital admission panels, especially in intensive care units. Studies shown CRP levels increase significantly in primary phases of COVID19, often before lung abnormalities are visible on computed tomography scans (C-reactive protein correlates with computed tomographic findings and predicts.pdf, n.d.). Therefore, the ratio is an affordable, marker that reflects timely disease development and can serve as an effective tool for detecting worsening clinical status among severe COVID19 clients.

## CONCLUSION

This paper revealed, CRP/Albumin ratio was markedly higher among clients with severe COVID19 when compared with those with mild or moderate form of the illness. It was also significantly elevated in patients who died compared to survivors. Elevated CRP/Alb ratios at hospital admission were strongly associated with increased disease severity, clinical deterioration, and higher mortality. As a result, this ratio may serve as an important early prognostic tool, aiding in the timely identification of high-risk patients and enabling healthcare providers to implement closer monitoring and more individualized treatment strategies to improve patient outcomes.



DOI: 10.48165/sajssh.2024.6405

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DOI: 10.48165/sajssh.2024.6405