Research Article

The effect of CRP/albumin ratio on prognosis of hospitalized patients due to COVID-19

COVID-19 nedeniyle hastanede yatan hastaların CRP/albümin oranının prognoz üzerine etkisi

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Abstract

Introduction: COVID-19 disease caused by the SARS-Cov-2 virus is characterized by clinical spectra of varying severity. Coagulopathy and inflammation are the most important factors associated with COVID-19 severity. The use of a biomarker of inflammation and coagulation factors has not yet been clarified. The present study aimed to examine the role of CRP/Albumin, an inflammation marker, in predicting the course of COVID-19 disease.

Methods: The Demographic, laboratory, and prognosis of 457 patients who were hospitalized during the COVID-19 pandemic service between April and May 2020 were analyzed retrospectively. The relationship between the patients' CRP/Albumin ratio and disease severity, length of hospital stays, and prognosis were analyzed.

Results: The rate of hospitalization in the intensive care unit was 10.5% (n=48), mechanical ventilation was 8.1% (n=37), and death was 1.3% (n=6). The CRP/albumin ratio was statistically higher in those with lung infiltration (p=0.005), those who were taken to the intensive care unit (p<0.001), and those who needed mechanical ventilation (p<0.001). A positive significant correlation was found between the length of hospital stay and the CRP/albumin ratio(r=0.412, p < 0.001).

Conclusion: The CRP/Albumin ratio is thought to be an auxiliary marker for doctors in the early transfer of patients to the intensive care unit, the early detection of those in need of MV, and the determination of lung infiltration.

Keywords: COVID-19, CRP/albumin ratio, prognosis

Öz

Giriş: SARS-Cov-2 virüsünün neden olduğu COVID-19 hastalığı farklı şiddette klinik spektrumlar ile karakterize edilmiştir. Koagülopati ve inflamasyon COVID-19 şiddeti ile ilişkili en önemli faktörlerdir. Enflamasyon ve pıhtılaşma faktörlerinin biyobelirteç kullanımı henüz netleştirilememiştir. Mevcut çalışma inflamasyon belirteci olan CRP/Albümin düzeyinin COVID-19 hastalık seyrinin tahminindeki rolünü incelemeyi amaçlamıştır.

Yöntem: Pandemi servisinde Nisan-Mayıs 2020 tarihleri arasında yatarak tedavi gören 457 COVID-19 hastasının demografik, laboratuvar ve hastalık seyirleri retrospektif olarak analiz edildi. Hastaların CRP/Albümin oranı ile hastalık şiddeti, hastanede kalış süresi ve prognoz arasındaki ilişki analiz edildi.

Bulgular: Hastaların yoğun bakıma yatış oranı %10,5 (n=48), mekanik ventilasyon ihtiyacı %8,1 (n=37) ve ölüm oranı %1,3 (n=6) idi. Akciğer infiltrasyonu olanlarda (p=0,005), yoğun bakıma alınanlarda (p<0,001) ve mekanik ventilasyon ihtiyacı olanlarda (p<0,001) CRP/albümin oranı istatistiksel olarak yüksekti. Hastanede kalış süresi ile CRP/albümin oranı arasında pozitif anlamlı korelasyon saptandı (r=0,412, p < 0,001)

Sonuç: CRP/Albümin oranının hastaların yoğun bakım ünitesine erken transferinde, MV ihtiyacı olanların erken tespitinde ve akciğer infiltrasyonun tespitinde doktorlara yardımcı bir belirteç olabileceği düşünülmektedir.

Anahtar kelimeler: COVID-19, CRP/albümin oranı, prognoz

Key Points

1. The CRP/Albumin ratio is a fast, cheap, repeatable test.
2. The CRP/Albumin ratio can be effective method to predict the prognosis of patients with COVID-19.

Introduction

COVID-19 is a systemic infectious disease caused by the SARS-CoV-2 virus [1]. On January 30, 2020, the World Health Organization Emergency Committee declared a global health emergency based on increased case notification rates [2]. From the first report of patients infected with SARS-CoV-2 in Wuhan, China in December 2019, until February 25, 2022, the number of cases has exceeded 430 million and the number of deaths has exceeded five million [3]. Patients with SARS-CoV-2 infection may have symptoms of varying severity. Hence, early isolation and effective treatment of infected patients is of great importance in terms of reducing mortality and morbidity. Prediction of patients' prognosis and appropriate triage are key issues for the functioning of healthcare systems. The diagnosis of COVID-19 is based on clinical symptoms, positive viral genome by reverse transcription polymerase chain reaction (RT-PCR) for SARS-Cov2, lung screening, and blood tests [4-5].

The rapidly progressing type of COVID-19 disease, which causes serious and fatal complications, has led studies to focus on predicting the clinical course. Despite advances in the management of the disease, there are no reliable diagnostic and prognostic markers to guide the treatment. When discussing the clinical features and imaging manifestations of COVID-19 in published articles, few studies have addressed the diagnostic and prognostic value of abnormal laboratory findings [6]. Abnormalities in haematological, biochemical, coagulation and inflammatory parameters have been demonstrated in COVID-19 patients with severe and mild systemic disease [7]. Complete blood count; coagulation and fibrinolysis parameters (PT, aPTT and D-dimer); acute phase reactants such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin and procalcitonin are laboratory tests commonly used in the follow-up of COVID-19 patients [8]. CRP is one of the most used acute phase reactants produced by hepatocytes after stimulation by various cytokines in response to infection, ischemia, trauma, and other inflammatory conditions [9-10].

Albumin is the main protein in the blood. It is one of the negative acute phase reactants whose level decreases in case of inflammation [11]. Also, since low albumin is associated with poor prognosis, it can be used as a parameter for early diagnosis and risk stratification [12]. The CRP/Albumin ratio has been studied extensively as an independent prognostic marker in patients with infections, malignancies and other comorbidities [13]. The CRP/Albumin ratio has been found to be an independent predictor of 1-year mortality in patients with Chronic Obstructive Pulmonary Disease (COPD) [14]. In addition, the CRP/albumin ratio is an independent risk factor for 90-day mortality in sepsis patients [15]. Also, the CRP/Albumin ratio can be used as a disease activity parameter in many non-infectious inflammatory patients [16]. In conclusion, the CRP/Albumin ratio is a new and useful indicator that is used in critically ill patients with sepsis, septic shock, and malignancy [13,17]. Currently, the CRP/Albumin ratio is believed to be a more reliable prognostic indicator than the separate evaluation of CRP and albumin in inflammatory conditions [18].

Predicting the course of COVID-19 can assist clinicians in determining the treatment of patients and can also reduce the burden of the disease on the healthcare system through effective triage of patients. In this study, it is aimed to determine whether the CRP/Albumin ratio can be a predictor of prognosis in COVID-19 patients and to investigate its predictive role on the length of hospital stay.

Methods

Patients and study design

This is a retrospective cross-sectional study. All COVID-19 patients over the age of 18 hospitalized in the pandemic ward of a tertiary medical facility between April and May 2020 were included in the study. Pregnancy, lactation and having a malignancy were exclusion criterias. A total of 457 patients who were hospitalized in the COVID-19 service between April and May 2020 and met the study criteria were included in the study. In addition, the treatments of the patients were determined according to the COVID-19 guideline of the Turkish Ministry of Health, which was valid at that time [19]. The data of all the patients included in the study were obtained retrospectively.

The diagnosis of COVID-19 was accepted based on clinical sign and symptoms, specific findings on thorax CT [20] and positive RT-PCR test. All study parameters including demographic data and laboratory results, detailed physical examination findings, length of hospital stay, admission to the intensive care unit and the need for endotracheal intubation were recorded retrospectively from the hospital databases and patients' hospital files. CRP (mg/L) and albumin (mg/L) values used in the study are easy and accessible tests that are routinely looked at in COVID-19 patients. The CRP/Albumin levels of the patients at the time of hospitalization were calculated by dividing the CRP level by the albumin level. According to the primary study parameters, the study was death, length of hospitalization, presence of lung infiltration, need for ICU and/or MV.

Ethical approval, informed consent and permissions

This study was approved by the Ethics Committee of Kartal Dr. Lütfi Kirdar City Hospital, dated 14/10/2020 (Decision No: 2020/514/187/12). The study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using the SPSS Version 21.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to evaluate the distribution of the continuous variables. It was observed that continuous variables did not meet the parametric test criteria. Descriptive data was given as, median (IQR) for continuous data, and number (n) and percentage (%) for categorical variables. For comparison of two independent groups, we used Mann Whitney-U test for non-normal distributed continuous data. Pearson Chi-square test was used to analyze categorical data. Spearman correlation analysis was used to examine the relationship between continuous variables. A value of $p<0.05$ was considered statistically significant.

Results

A total of 457 patients hospitalized in the pandemic ward were included in the study. Most of the patients in our cohort were male. Here, the most common comorbid disease was hypertension, followed by diabetes mellitus. In addition, approximately three quarters of the patients had PCR positivity. The most common symptoms of the patients were cough, fever, and shortness of breath. Meanwhile, hypoxemia was found in more than two-thirds of patients. In addition, approximately three quarters of the patients had PCR positivity. The demographic, clinical and laboratory characteristics of the patients and the drugs used to treat COVID-19 are shown in Table 1.

Table 1. Demographic, clinical and laboratory characteristics of the patients and the agents used in the treatment of COVID-19

Demographics		Symptoms	
Age, year	54.93± 16.09	Fever	184 (40.3%)
Female gender	219 (47.9%)	Shortness of breath	169 (37%)
Comorbidities		Cough	280 (61.3%)
Hypertension	152 (33.3%)	Weakness/fatigue	114 (24.9%)
Diabetes mellitus	107 (23.4%)	Joint complaint	61 (13.3%)
CAD/CF	56 (12.3%)	Throat ache	34 (7.4%)
Asthma	34 (7.4%)	Nausea/vomiting	34 (7.4%)
COPD	17 (3.7%)	Headache	32(7.0%)
Malignancy	15 (3.3%)	Loss of Appetite	26 (5.7%)
Obesity	14 (3.1%)	Loss of smell/taste	19 (4.2%)
CKF	10 (2.2%)	Diarrhea	19 (4.2%)
Laboratory		Nose flow	5 (1.1%)
CRP, mg/L	26.9±11.29	**Drugs used**	
Albumin, g/L	37±6.88	Favipravir	124 (27.1%)
CRP/Albumin	0.737	Hydroxychloroquine	449 (98.2%)
PCR positivity	336 (73.5%)	Azithromycin	409 (89.5%)
Vital Findings		Additional antibiotics	337 (73.7%)
Sp02<92	182 (39.8%)		
Fever ≥37.5	153 (33.5%)		

CAD/CHF: Coronary artery disease/coronary failure, **COPD:** Chronic obstructive pulmonary disease, **CRP:** C-reactive protein.

All patients in the study were hospitalized due to COVID-19. However, only 10.5% of the patients were transferred to the intensive care unit and 8.1% of the patients required mechanical ventilation. Also, the mortality rate in our cohort was 1.3%. The median length of hospitalization of patients was 6 (IR: 5.5) days. There were 419 (91.7%) patients with lung infiltration, 48 (10.5%) patients with intensive care unit (ICU) needs and 37 (8.1%) patients with mechanical ventilation (MV) needs. 6 (1.3%) of the patients died due to COVID-19 (Table 2).

Table 2. COVID-19 related prognostic parameters

Duration of hospitalization, days	8.1±7.6*6 (5.5) **
Lung infiltration	419 (91.7%)
Need for an intensive care unit	48 (10.5%)
Need for mechanical ventilation	37 (8.1%)
Death	6 (1.3%)

IR: Interquartile range. Number of the patient was 457. * Mean±standard deviation**: Median IR

The CRP/albumin ratio was found to be significantly higher in patients with pulmonary infiltration, who needed intensive care or MV, when compared to patients without those. In addition, the CRP/albumin ratio did not change with respect to survival. (Table 3). A positive linear correlation was found between the duration of hospitalization and CRP/Albumin (Rho: 0.412, p < 0.001).

Table 3. CRP/Albumin ratios in patients hospitalized due to COVID-19 compared to COVID-19-related adverse outcomes

COVID-19 related consequences	N	Age	p	CRP/Albumin ratio	p
Death					
Yes	6	57.5 (32.0)		0.56 (2.3)	
No	456	55.0 (23.0)	0.79	0.74 (1.7)	0.76
Lung infiltration					
Yes	419	55.0 (21.0)		0.76 (1.9)	
No	38	59.5 (28.5)	0.21	0.17 (1.2)	**0.005**
Need for ICU					
Yes	48	70.0 (17.2)		2.4 (2.6)	
No	409	54.0 (20.5)	**<0.001**	0.5 (1.6)	**<0.001**
Need for MV					
Yes	37	71.0 (17.0)		2.4 (2.5)	
No	426	54.0 (20.0)	**<0.001**	0.6 (1.6)	**<0.001**

CRP: C-reactive protein, **ICU:** intensive care unit, **MV:** mechanical ventilation

Discussion

The COVID-19 pandemic is placing a serious burden on healthcare systems around the world. It is critically important to examine the prognosis of patients with easy and accessible medical tests. The use of CRP/Albumin ratio compared to CT, in the prognostic follow-up of COVID-19 patients, may be an advantage, especially for developing countries. In the International Federation of Clinical Chemistry (IFCC) guidelines on biochemical/haematological monitoring of COVID-19 patients, routine biochemical and haematological tests have been reported to be useful in the classification and prognosis of paediatric and adult patients diagnosed with coronavirus disease. Here, some laboratory parameters are shown to be associated with poor outcomes such as need for mechanical ventilation or intensive care, progression to multi-system organ failure, or death [21].

Comorbidities may increase the mortality rate in COVID-19. In our cohort the most common comorbidity was hypertension followed by diabetes mellitus. Inflammatory markers such as CRP are important prognostic indicators in COVID-19 patients especially with comorbidities [22]. In the former studies, it has been stated that the CRP/Albumin ratio in COVID-19 patients gives more reliable results than the CRP or albumin alone [23-24]. Likewise, our study shows that CRP/Albumin ratio is significantly related to the lung infiltration, the need for ICU and/or MV. Additionally, prognostic parameter to predict the increasing risk for poor prognosis may be useful for reducing the burden of the disease on functioning of health systems [25].

In former studies, the effect of CRP/Albumin ratio on determining the need for ICU in COVID-19 patients is consistent with our study [26]. In a study, it was emphasized that the CRP/Albumin ratio had been associated with the severity of pneumonia and might be an independent and easily accessible prognostic marker for this disease [27]. Our study presents similar findings with the studies evaluating the relationship between CRP/Albumin ratio and MV need in COVID-19 patients [24]. While it has been stated in the literature that a higher CRP/Albumin ratio increases mortality, in our study, the CRP/Albumin ratio is found similar in deceased and survived patients [25]. In another study evaluating mortality in COVID-19 patients with hypertension, it was found that the CRP/Albumin ratio was significantly associated with the length of hospitalization [28]. In our study, a positive linear correlation is found between CRP/Albumin and length of hospital stay, similar to the literature.

The course of COVID-19 has individual variability. Some patients may progress rapidly to serious clinical complications and death. Identifying these patients will be crucial for determining the initial treatment plan. We think that our study results will be clinically important in terms of the follow-up of COVID-19 patients and determining the treatment plans.

Limitations

The limitation of our study is that it was applied in a single hospital and designed retrospectively. Furthermore, we did not evaluate the predictive usefulness of the test in different COVID-19 subgroups with different prognostic risk factors.

Conclusion

In conclusion, the CRP/Albumin ratio may be an indicator of poor prognosis in COVID-19. In addition, the CRP/Albumin ratio can be a helpful marker that guides clinicians for early transfer of patients to the intensive care unit and early detection of those in need of MV.

	Author Contributions	Author Initials
SCD	Study Conception and Design	NS, GDG, NZK, SAK, AB
AD	Acquisition of Data	NS, GDG, NZK, AB
AID	Analysis and Interpretation of Data	NS, MET, GDG, NZK, SAK, AB
DM	Drafting of Manuscript	NS, MET, SAK
CR	Critical Revision	NS, MET

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