JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Does C reactive protein/Albumin ratio have prognostic value in patients with COVID-19

Aleksandr Kalabin[1 #], Vishnu Raj Kumar Mani[1,2 #], Sebastian Cristobal Valdivieso[1], Brian Donaldson[1]

[1] Columbia University College of Physicians and Surgeons at Harlem Hospital, New York City, NY, United States
[2] Duke University Medical Center, Durham, NC, United States

# These Authors contributed equally.

Abstract

Introduction: There is paucity of data regarding C reactive protein/Albumin (CRP/Alb) ratio in patients with SARS-CoV-2 infection. We aimed to evaluate the significance of CRP/Alb ratio in COVID-19 patients.

Methodology: Patients hospitalized between March – April 2020 with COVID-19, who had CRP and Albumin levels documented within 24 hours from admission were retrospectively analyzed. Unpaired Student's t-test was used for continuous and Pearson Chi-square (χ^2) test for categorical variables. Univariate and multivariate logistic regression models were developed to assess the relationship between CRP/Alb and mortality. Nonparametric correlations were calculated using Spearman's Rho correlation coefficient.

Results: 75 patients were included. Mean age was 62.92, 26 females (34.67%) and 49 males (65.33%), mean Body Mass Index (BMI) 29.86, mean body temperature 101.3 and mean length of stay (LOS) was 14.80 days. 24 (32%) patients required invasive mechanical ventilation and 51 (68%) did not, mean CRP/Alb ratio was 6.89 and 4.7 respectively ($p = 0.036$). 15 (20%) patients died, 60 (80%) survived and the mean CRP/Alb difference between these groups was also statistically significant (7.74 vs 4.83, $p = 0.02$). LOS (OR 0.71, 95% CI 0.57.-0.88, $p < 0.001$) and BUN (OR 1.04, 95% CI 1.01.-1.07, $p = 0.006$) were independent predictors of mortality by multivariate logistic regression, whereas CRP/Alb (OR 1.21, 95% CI 0.96.-1.51, $p = 0.06$) was not.

Conclusions: CRP/Alb ratio could be useful as a prognostic indicator of disease severity in COVID-19, but we could not corroborate its potential to predict mortality. The work was conducted at Columbia University College of Physicians and Surgeons at Harlem Hospital.

Key words: SARS-CoV-2; COVID-19; C reactive protein/Albumin ratio; pandemic.

J Infect Dev Ctries 2021; 15(8):1086-1093. doi:10.3855/jidc.14826

(Received 01 February 2021 – Accepted 19 May 2021)

Introduction

Current outbreak of SARS-CoV-2 infection resulted in catastrophic global public health crisis. The United States emerged as the epicenter of this pandemic with global numbers steadily on the rise. Despite significant advances in management of COVID-19 patients, there are no reliable diagnostic and prognostic markers of disease severity to guide therapy. The role of systemic inflammatory response has been increasingly appreciated in pathophysiology of COVID-19 infection. Studies have suggested that uncontrolled inflammation is a predominant contributor to the disease severity as higher levels of inflammatory markers, including C reactive protein (CRP), are correlated with disease severity in patients with SARS-CoV-2 [1,2], (Table 1). On the other hand, patient's nutritional status impacts the host immune system and poor nutrition is associated with altered immunocompetence and increased risks of infections [3]. Albumin has been used for decades as an indicator of nutritional status and it was recently shown that hypoalbuminemia is associated with severe COVID-19 disease [4]. CRP/Albumin (CRP/Alb) ratio represents a fraction of a positive acute phase inflammatory reactant to a negative acute phase reactant and has a potential to concurrently represents host's inflammatory state and nutritional status. It was recently identified as a prognostic biomarker in various inflammatory states and disorders [5,6]. However, data regarding its role in SARS-CoV-2 infection is lacking. We postulated that CRP/Alb ratio has a potential to predict disease seveirty in COVID-19 patients and in this study we aimed to evaluate if it could be utilized as a prognostic biomarker in SARS-CoV-2 infection.

Methodology

Study design

Ethical approval from the hospital Institutional Review Board (IRB) for Health Sciences Research was expeditiously sought and approved. This retrospective

study entails the clinical and laboratory characteristics of hospitalized patients with confirmed SARS-CoV-2 infection between March and April 2020.

Data collection

Data collection was done through review of electronic medical records (EMR) for all parameters included in the study of patients confirmed with SARS-Cov2 infection.

Inclusion and Exclusion criteria

184 patients confirmed with SARS-CoV-2 infection admitted to our facility during the study period were originally included in data collection. 109 cases were subsequently excluded from the final analysis because they did not undergo CRP or Albumin testing within 24 hours of admission.

Outcomes

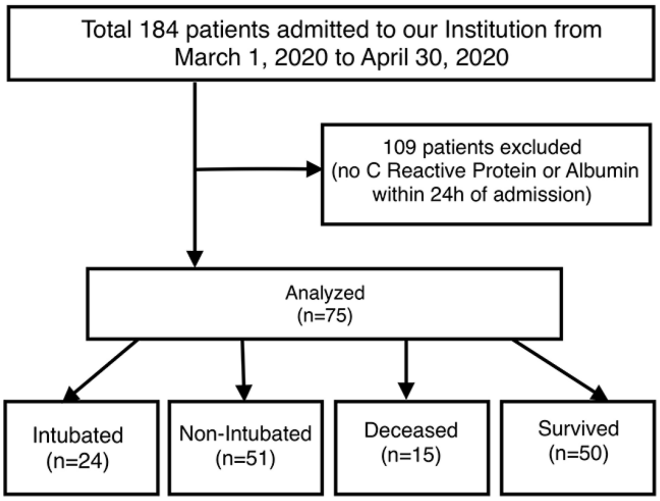
The primary outcome of interest was to determine if CRP/Alb ratio obtained within 24 hours of admission in patients diagnosed with COVID-19 could serve as a clinical predictor of disease severity.

Secondary outcomes aimed to evaluate the association of CRP/Alb with other clinical parameters as well as to determine the prognostic value of the ratio in predicting mortality in patients with SARS-CoV-2 infection.

Statistical analysis /Methods

Continuous variables were reported as means values and standard deviation (SD), while categorical variables were expressed as counts and percentages. The statistical significance of intergroup differences was compared through unpaired Student's t-test for continuous and Pearson Chi-square (χ^2) test for categorical variables. Univariate logistic regression analyses were performed to separately examine the association between unfavorable outcomes and each of the included variables. Multivariate logistic regression models were conducted to determine independent predictors adjusted for previously specified baseline covariates. Criteria of p <0.05 for entry and p > 0.10 for removal were imposed in this analysis. Nonparametric correlations between multiple continuous variables were calculated using Spearman's Rho correlation coefficient. Two-sided p value < 0.05 was considered to represent statistically significant difference. Microsoft Excel spreadsheet was used to display extrapolated data. JMP®, Version 15. SAS Institute Inc., Cary, NC, 1989-2019 was used for statistical analysis.

Figure 1. Flow chart of patient selection process.



Results

Patient Characteristics

184 patients with confirmed SARS-CoV-2 infection were admitted to our facility between first of

Table 1. Biomarker abnormalities in COVID-19 patients with severe systemic disease.

Hematologic biomarkers		Biochemical biomarkers		Coagulation biomarkers	Inflammatory biomarkers
Elevated	**Decreased**	**Elevated**	**Decreased**	**Elevated**	**Elevated**
White blood cell (WBC) count	Lymphocyte count	Alanine aminotransferase (ALT)	Albumin	Prothrombin time	Erythrocyte sedimentation rate (ESR)
Neutrophil count	Platelet count	Aspartate aminotransferase (AST)		D-dimer	C Reactive protein (CRP)
	Eosinophil count	Total bilirubin			Serum ferritin
	T cell count	Blood urea nitrogen (BUN)			Procalcitonin
	B cell count	Creatinine kinase (CK)			Interleukin-2 (Il-2)
	Natural killer (NK) cell count	Lactate dehydrogenase (LDH)			Inerleukin-6 (Il-6)
		Myoglobin			Interleukin-8 (IL-8)
		Creatinine kinase (CK)-MB			Interleukin-10 (Il-10)
		Troponin I			
		Creatinine			

March and thirtieth of April 2020, 109 cases were excluded from the final analysis because laboratory values for CRP or Albumin within the first 24h of admission were not available (Figure 1).

75 patients were included in the final analysis. Mean age for our cohort was 62.92 (SD 14.27, range 59.64-66.20). There were 26 females (34.67%) and 49 males (65.33%). 38 (50.67%) patients identified themselves as African American, 33 (44%) as Hispanic and 4 (5.33%) as Asians. Mean Body Mass Index (BMI) was 29.86 (SD 7.02, range 28.21-31.51), mean body temperature - 101.3 (SD 1.69) and mean length of stay (LOS) 14.80 (SD 6.64).

Comprehensive laboratory evaluation was done for all patients and the results included in Table 2. Of note mean CRP and albumin were 18.82 (SD 14.26), and 3.61 (SD 0.50) respectively.

The distribution of comorbidities among included patients were as follows – Hypertension (HTN) - 50 (66.67%), Diabetes Mellitus (DM) - 30 (40.00%), Chronic Kidney Disease (CKD) - 11 (14.67%), Coronary Artery Disease (CAD) - 15 (20.00%), Bronchial Asthma (BA) - 8 (10.67%) and Chronic Obstructive Pulmonary Disease (COPD) - 6 (8.00%) respectively. The average comorbidity number was 1.60 (SD 1.27) for all patients admitted with SARS-CoV-2 infection (Table 2).

Table 2. Baseline clinical and laboratory characteristics.

Parameter	Results
Age, Years, Mean (SD)	62.92 (14.27)
Males, n (%)	49 (65.33%)
Females, n (%)	26 (34.67%)
African-Americans, n (%)	38 (50.67%)
Hispanics, n (%)	33 (44%)
Asians, n (%)	4 (5.33%)
Body-Mass-Index, kg/m^2, Mean (SD)	29.86 (7.02)
Body Temperature, Fahrenheit, Mean (SD)	101.3 (1.69)
Length of Stay, Days, Mean (SD)	14.80 (6.64)
Albumin, g/dL, Mean (SD)	3.61 (0.50)
Total Bilirubin, mg/dL, Mean (SD)	0.66 (0.41)
Blood Urea Nitrogen, mg/dL, Mean (SD)	53 (45.17)
C Reactive Protein, mg/L, Mean (SD)	18.82 (14.26)
Creatinine, mg/L, Mean (SD)	2.96 (3.09)
D-dimer, ng/ml, Mean (SD)	7363.73 (14314.43)
Ferritin, ng/dL, Mean (SD)	6.46 (3.34)
Glucose, mg/ml, Mean, (SD)	248.69 (191.45)
Lactate Dehydrogenase (U/L), Mean (SD)	642.16 (242.98)
Lactic Acid, mmol/l, Mean (SD)	2.26 (1.70)
Lymphocytes %, Mean (SD)	13.82 (6.98)
Monocytes %, Mean (SD)	6.46 (3.34)
Neutrophils %, Mean (SD)	78.02 (8.48)
Platelets, x10(3)/mcl, Mean (SD)	217.64 (76.48)
Procalcitonin, ng/dL, Mean (SD)	3.36 (8.85)
Prothrombin Time, seconds, Mean (SD)	14.87 (4.33)
Hypertension, n (%)	50 (66.67%)
Diabetes Mellitus, n (%)	30 (40.00%)
Chronic Kidney Disease, n (%)	11 (14.67%)
Coronary Artery Disease, n (%)	15 (20.00%)
Bronchial Asthma, n (%)	8 (10.67%)
Chronic Obstructive Pulmonary Disease, n (%)	6 (8.00%)

SD: Standard deviation.

Primary Outcomes

The primary outcome of interest was to elucidate if CRP/Alb ratio would provide a correlation with disease severity or have a clinical meaningful association. In order to investigate this, we grouped our patients into 4 major categories – Intubated, Non-Intubated, Deceased and Survived.

Patients defined as survived were alive at the time of data accrual.

Mean CRP/Alb ratio was 5.4 (SD 4.2, range 4.44-6.38). 24 (32.00%) patients got intubated and 51 (68.00%) patients did not require mechanical ventilation (Non-Intubated). There was no statistically significant difference between these two groups for Age, Gender, Ethnical representation or comorbidities, albeit intubated patients had higher BMI (32.31 vs 28.64, $p = 0.04$). Our analysis revealed that body temperature was higher in Intubated patients compared to Non-intubated (102.1 vs 100.92, $p = 0.007$). Similar trend was observed with respect to conventional markers of inflammation such as CRP (24.06 vs 16.35, $p = 0.02$) and Lactate (2.91 vs 1.87, $p = 0.046$). Although albumin values were negligibly different between the two groups, the CRP/Alb ratio for intubated was 6.89 (SD 3.51) whereas for Non-intubated it was significantly lower - 4.7 (SD 4.36), $p = 0.036$ (Table 3). Mortality was derived from deceased - 15 (20.00%) and survived - 60 (80.00%) patients, there were no intergroup differences for mortality when accounting for Age, BMI and Ethnicity. 14 male patients deceased compared to 1 female, 35 males and 25 females survived ($p = 0.01$). Diabetic patients were more likely to succumb to the disease and Diabetes Mellitus was the only comorbidity significantly associated with mortality - 20 (13.33%) patients in Survived group vs 10 (66.67%) in Deceased, ($p = 0.02$). Albumin, lactate and core temperature did not make statistically significant difference for mortality. CRP was significantly elevated in Deceased patients compared to the Survived group (27.09 vs 16.75, $p = 0.01$) as well as the CRP/Alb ratio with mean of 7.74 (SD 6.16) for the Deceased group vs 4.83 (SD 3.39) for the Survived, $p = 0.02$ (Table 4).

Table 3. Clinical and laboratory characteristics of Intubated and Non-Intubated patients.

	Total N = 75	Intubated N = 24	Non-Intubated N = 51	p-value/Chi square (Pearson)
Age	62.92	60	64.29	0.23
SD	14.27	10.43	15.66	
Gender				
Males	49 (65.33%)	17 (70.83%)	32 (62.75%)	0.49
Females	26 (34.67%)	7 (29.17%)	19 (37.25%)	
BMI	29.86	32.31	28.64	0.04*
SD	7.02	9.29	5.25	
Ethnicity				
African-American	38 (50.67%)	9 (37.50%)	29 (56.86%)	
Hispanics	33 (44%)	13 (54.17%)	20 (39.22%)	0.27
Asians	4 (5.33%)	2 (8.33%)	2 (3.92%)	
Temperature	101.3	102.1	100.92	0.004*
SD	1.69	1.79	1.52	
CRP	18.82	24.06	16.35	0.03*
SD	14.26	11.60	14.83	
Lactate	2.26	2.91	1.87	0.02*
SD	1.70	2.24	1.14	
Albumin	3.61	3.57	3.63	0.66
SD	0.50	0.56	0.48	
CRP/Alb ratio	5.4	6.90	4.71	0.04*
SD	4.2	3.51	4.36	
Comorbidities				
HTN	50 (66.67%)	16 (66.7%)	34 (66.67%)	1.00
DM	30 (40.00%)	9 (37.50%)	21 (41.18%)	0.76
CKD	11 (14.67%)	2 (8.33%)	9 (17.65%)	0.29
CAD	15 (20.00%)	4 (16.67%)	11 (21.57%)	0.62
BA	8 (10.67%)	3 (12.50%)	5 (9.80%)	0.72
COPD	6 (8.00%)	3 (12.5%)	5 (5.88%)	0.32

BMI: Body Mass Index; CRP: C Reactive Protein; CRP/Alb: C Reactive Protein to Albumin Ratio; HTN: Hypertension; DM: Diabetes Mellitus; CKD: Chronic Kidney Disease; CAD: Coronary Artery Disease; BA: Bronchial Asthma; COPD: Chronic Obstructive Pulmonary Disease; SD: Standard Deviation; *-statistically significant value (P<0.05).

Table 4. Clinical and laboratory characteristics of Deceased vs Survived patients.

	Total N = 75	Deceased N = 15	Survived N = 60	p-value/Chi square (Pearson)
Age	62.92	66.07	62.13	0.34
SD	14.27	10.79	14.99	
Gender				
Males	49 (65.33%)	14 (93.33%)	35 (58.33%)	0.01*
Females	26 (34.67%)	1 (6.67%)	25 (41.67%)	
BMI	29.86	28.44	30.24	0.38
SD	7.02	5.28	7.40	
Ethnicity				
African-American	38 (50.67%)	6 (40.00%)	32 (53.33%)	
Hispanics	33 (44%)	8 (53.33%)	25 (41.67%)	0.65
Asians	4 (5.33%)	1 (6.67%)	3 (5.00%)	
Temperature	101.3	101.44	101.27	0.72
SD	1.69	1.88	1.66	
CRP	18.82	27.09	16.75	0.01*
SD	14.26	21.49	11.13	
Lactate	2.26	2.84	2.09	0.15
SD	1.70	2.37	1.43	
Albumin	3.61	3.50	3.64	0.35
SD	0.50	0.45	0.51	
CRP/Alb ratio	5.4	7.74	4.83	0.02*
SD	4.2	6.17	3.39	
Comorbidities				
HTN	50 (66.67%)	13 (86.67%)	37 (61.67%)	0.07
DM	30 (40.00%)	10 (66.67%)	20 (33.33%)	0.02*
CKD	11 (14.67%)	2 (13.33%)	9 (15.00%)	0.87
CAD	15 (20.00%)	1 (6.67%)	14 (23.33%)	0.15
BA	8 (10.67%)	2 (13.33%)	6 (10.00%)	0.71
COPD	6 (8.00%)	0	6 (10.00%)	0.20

BMI: Body Mass Index; CRP: C Reactive Protein; CRP/Alb: C Reactive Protein to Albumin ratio; HTN: Hypertension; DM: Diabetes Mellitus; CKD: Chronic Kidney Disease; CAD: Coronary Artery Disease; BA: Bronchial Asthma; COPD: Chronic Obstructive Pulmonary Disease; SD: Standard Deviation; *-statistically significant value (p < 0.05).

Secondary Outcomes

CRP/Alb ratio was positively correlated with CRP values (r = 0.985, $p < 0.0001$), Ferritin (r = 0.391, $p = 0.003$), Glucose (r = 0.231, $p = 0.05$) and Procalcitonin (r = 0.114, $p < 0.0001$), and negatively correlated with Age (r = -0.314, $p = 0.006$), Albumin (r = -0.432, $p = 0.0001$) and percentage of Monocytes in peripheral blood (r = -0.290, $p = 0.01$). No significant correlation between CRP/Alb and other variables was observed (Table 5). Univariate logistic regression analysis for the association of each variable with mortality was used to calculate R square and the odds ratio (Table 6). LOS ($p = 0.004$, R square 0.114), Blood Urea Nitrogen (BUN) ($p = 0.01$, R square 0.083), CRP ($p = 0.02$, R square 0.078), Procalcitonin ($p = 0.009$, R square 0.101) and CRP/Alb ($p = 0.02$, R square 0.070) were statistically significant indicative of predicting mortality in patients with COVID-19. Multivariate logistic regression analysis revealed only LOS (OR 0.71, 95% CI 0.57.-0.88, $p < 0.001$) and BUN (OR 1.04, 95% CI 1.01.-1.07, $p = 0.006$) as significant covariables to predict mortality. Even though CRP/Alb ratio was included in the model, it was not statistically significant (OR 1.21, 95% CI 0.96.-1.51, $p = 0.06$) and thus could not independently predict mortality in patients with COVID-19 (Table 7).

Discussion

C Reactive Protein is well known as a positive acute phase reactant and for its clinical applicability to reflect a host's inflammatory response. Serum albumin reflects nutritional status [7], it is considered to be a negative acute phase reactant and is usually downregulated during inflammation. Both have been utilized as biomarkers to predict mortality in patients with infectious diseases and sepsis [8,9]. In COVID-19 patients increased CRP was reportedly associated with severe disease and increased mortality [10,11,12]. In contrast, decreased levels of albumin is a common feature in patients with SARS-CoV-2 infection [13] and studies showed that hypoalbuminemia was correlated with increased mortality [4,14]. CRP/Alb ratio concurrently reflecting host's inflammatory response and nutritional state could serve as an indirect surrogate of the disease severity and has been lately recognized as a useful prognostic factor in predicting mortality in patients with sepsis [15,16], septic shock [16] and critically ill patients [17]. However, there is paucity of data regarding clinical utilization of the ratio in COVID-19 patients and hence, we aimed to retrospectively evaluate Northern American population who were admitted to our institution during the first wave of pandemic and appraise the role of CRP/Alb in predicting disease severity in patients with SARS-CoV-2 infection.

Consistent with previous reports of hyper-inflammatory response to SARS-CoV-2 infection [1], mean CRP for our cohort was markedly elevated. Furthermore, mean CRP was significantly higher for intubated and deceased patients compared to non-intubated and survived. Our results consistently demonstrate the association between the degree of pathogenic inflammation and disease severity and thus reinforce applicability of CRP as a biomarker to predict disease severity and to help guide rational therapeutic measures. On the other hand, decreased levels of albumin in COVID-19 patients has been reported in recent studies [14,18]. As expected, patients in all groups were noted to have low-to-normal albumin values, and no statistically significant inter-group variation was observed. As suggested lately, low albumin phenomenon should not be explained by liver dysfunction secondary to hepatocellular injury alone [14]. In patients with SARS-CoV-2 infection hypoalbuminemia is the result of complex interplay of the systemic inflammation with subsequent increased capillary permeability and redistribution of albumin to interstitial fluids.

Cut-off values of CRP/Albumin ratio diverge significantly in patients with acute and chronic inflammatory conditions [16,19,20], for 75 patients included in our study with confirmed COVID-19 infection mean CRP/Alb ratio was 5.4. More importantly, we demonstrated that CRP/Alb ratio was significantly higher in patients with more severe disease, who required mechanical ventilation (intubated) as compared to non-intubated patients. Moreover, CRR/Alb ratio was markedly elevated in deceased group of patients in contrast to those who survived and we believe the ratio could be used a prognostic indicator for patients with COVID-19. Multivariate analysis from our study cohort did not reveal significant effect of CRP/Alb ratio on mortality. Hence, based on our findings CRP/Albumin ratio can be used as a predictor of disease severity, but not mortality in COVID-19 patients. Our study significantly adds to the emerging scant literature on CRP/Alb ratio and its utility in patients with SARS-CoV-2 infection, to our knowledge there only few studies and their results do not necessarily corroborate with our findings [21,22,23]. This could be secondary to varying methods in differentiating disease severity, ethnicity, population differences and most importantly small sample sizes.

Table 5. Nonparametric correlations between CRP/Albumin ratio and other variables in COVID-19 patients.

	r	p-value
Age, Years	-0.314	0.006*
Body-Mass-Index, kg/m2	0.183	0.12
Body Temperature, Fahrenheit	0.208	0.07
Length of Stay, Days	0.143	0.22
Albumin, g/dL	-0.432	0.0001*
Total Bilirubin, mg/dL	0.168	0.15
Blood Urea Nitrogen, mg/dL	0.272	0.02*
C Reactive Protein, mg/L	0.985	< 0.0001*
Creatinine, mg/L	0.211	0.07
D-dimer, ng/ml	0.291	0.06
Ferritin, ng/dL	0.391	0.003*
Glucose, mg/ml	0.231	0.05*
Lactate Dehydrogenase (U/L)	0.267	0.06
Lactic Acid, mmol/l	0.142	0.28
Lymphocytes %, Mean	-0.208	0.07
Monocytes %, Mean	-0.290	0.01*
Neutrophils %, Mean	0.225	0.052
Platelets, x10(3)/mcl, Mean	0.186	0.11
Procalcitonin, ng/dL, Mean	0.489	< 0.0001*
Prothrombin Time, seconds,	0.114	0.54

r- Spearman's Rho correlation coefficient; *-statistically significant value ($p < 0.05$).

Table 6. Results of univariate logistic regression analysis for predicting mortality.

Factors	R square (U)	Odds ratio (OD)	95 confidence interval (CI)	P value
Age, Years	0.013	1.02	0.98-1.06	0.33
Body-Mass-Index, kg/m2	0.012	0.96	0.86-1.06	0.35
Body Temperature, Fahrenheit	0.002	1.06	0.76-1.49	0.72
Length of Stay, Days	0.114	0.86	0.77-0.96	0.004*
Albumin, g/dL	0.012	0.58	0.18-1.83	0.35
Total bilirubin, mg/dL	0.017	0.40	0.07-2.30	0.27
Blood Urea Nitrogen, mg/dL	0.083	1.02	1.00-1.03	0.01*
C Reactive Protein, mg/L	0.078	1.05	1.00-1.10	0.02*
Creatinine, mg/L	0.038	1.16	0.98-1.37	0.09
Creatinine/Alb	0.070	1.17	1.01-1.35	0.02*
D-Dimer, ng/ml	0.010	1.00	1.00-1.00	0.55
Ferritin, ng/dL	0.015	1.00	1.00-1.00	0.35
Glucose, mg/ml	0.036	1.00	1.00-1.01	0.10
Lactate Dehydrogenase (U/L)	0.061	1.00	1.00-1.01	0.07
Lactic Acid, mmol/l	0.028	1.25	0.91-1.71	0.17
Lymphocytes %, Mean	0.007	0.97	0.89-1.06	0.46
Monocytes %, Mean	0.028	0.85	0.67-1.08	0.15
Neutrophils %, Mean	0.019	1.04	0.97-1.12	0.24
Platelets, x10(3)/mcl, Mean	0.0001	1.00	0.99-1.01	0.93
Procalcitonin, ng/dL, Mean	0.101	1.09	1.00-1.19	0.009*
Prothrombin Time, seconds,	0.030	1.09	0.91-1.31	0.34
Comorbidity Index	0.011	1.22	0.79-1.89	0.37

CRP/Alb: C Reactive Protein to Albumin ratio; *-statistically significant value ($P<0.05$).

Table 7. Results of multivariate logistic regression analysis for predicting mortality.

Factors	Odds ratio (OD)	95 confidence interval (CI)	p-value
Length of Stay, Days	0.71	0.54-0.93	0.0003*
Blood Urea Nitrogen, mg/dL	1.03	1.00-1.06	0.006*
C Reactive Protein, mg/L	0.98	0.67-1.43	0.93
Creatinine/Alb	1.30	0.40-4.27	0.66
Procalcitonin, ng/dL, Mean	1.02	0.92-1.14	0.69

CRP/Alb: C Reactive Protein to Albumin ratio; *-statistically significant value ($p < 0.05$).

Further evaluation with large cohort will help guide its prognostic significance for patients with SARS-CoV-2 infection. Our study has some limitations. It is a retrospective cohort study conducted in a single institution. Only 75 patients were included in the final analysis and the mean age for the cohort was above 60 years old, and thus our study may be underpowered and findings may not be representative across all age groups. These limitations should be taken into consideration when interpreting results. Results of our study should be further validated on a multi-institutional basis with larger samples and broad age groups. We advise the readers to make a note that while these inflammatory markers were taken at a set point in time, each individual patient could have been at different stages of the disease spectrum.

Conclusions

Our study indicates that CRP/Alb ratio could be useful as a prognostic indicator of disease severity in SARS-CoV-2 infection. However, our results could not establish the value of CRP/Albumin ratio in predicting mortality in COVID-19 patients and more studies are needed to validate our results.

Acknowledgements

We would like to acknowledge and thank Clinical Laboratory Director Helen Richards, MD and other staff of the laboratory at Columbia University College of Physicians and Surgeons at Harlem Hospital.

References

1. Del Valle DM, Kim-Schulze S, Huang HH, Beckmann ND, Nirenberg S, Wang B, Lavin Y, Swartz TH, Madduri D, Stock A, Marron TU, Xie H, Patel M, Tuballes K, Oekelen OV, Rahman A, Kovatch P, Aberg JA, Schadt E, Jagannath S, Mazumdar M, Charney AW, Firpo-Betancourt A, Mendu DR, Jhang J, Reich D, Sigel K, Cordon-Cardo C, Feldmann M, Parekh S, Merad M, Gnjatic S (2020) An inflammatory cytokine signature predicts COVID-19 severity and survival. Nat Med 26: 1636–1643.
2. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T (2020) Biomarkers associated with COVID-19 disease progression. Crit Rev Clin Lab Sci 57: 389-399.
3. Chandra RK (1997) Nutrition and the immune system: an introduction. Am J Clin Nutr 66: 460S-463S.
4. Aziz M, Fatima R, Lee-Smith W, Assaly R (2020) The association of low serum albumin level with severe COVID-19: a systematic review and meta-analysis. Crit Care 24: 255.
5. Moon JS, Ahn SS, Park YB, Lee SK, Lee SW (2018) C-Reactive Protein to Serum Albumin Ratio Is an Independent Predictor of All-Cause Mortality in Patients with ANCA-Associated Vasculitis. Yonsei Med J 59: 865-871.
6. Oh TK, Song IA, Lee JH (2018) Clinical usefulness of C-reactive protein to albumin ratio in predicting 30-day mortality in critically ill patients: A retrospective analysis. Sci Rep 8: 14977.
7. Carriere I, Dupuy AM, Lacroux A, Cristol JP, Delcourt C, Pathologies Oculaires Liées à l'Age Study Group (2008) Biomarkers of inflammation and malnutrition associated with early death in healthy elderly people. J Am Geriatr Soc 56: 840-846.
8. Devran O, Karakut Z, Adiguzel N, Gungor G, Mocin OY, Balci MK, Celik E, Salturk C, Takir BH, Kargin F, Yilmaz A (2012) C-reactive protein as a predictor of mortality in patients affected with severe sepsis in intensive care unit. Multidiscip Respir Med 7: 47.
9. Povoa P (2002) C-reactive protein: a valuable marker of sepsis. Intensive Care Med 28: 235–243.
10. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, Jiang X, Li X (2020) C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol 92: 856-862.
11. Ruan Q, Yang K, Wang W, jiang L, Song J (2020) Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 46: 846-848.
12. Mani VR, Kalabin A, Valdivieso SC, Donaldson B (2020) New York Inner City Hospital COVID-19 Experience and Current Data: Retrospective Analysis at the Epicenter of the American Coronavirus Outbreak. J Med Internet Res 22: e20548.
13. Zhang Y, Zheng L, Liu L, Zhao M, Xiao J, Zhao Q (2020) Liver impairment in COVID-19 patients: a retrospective analysis of 115 cases from a single center in Wuhan city, China. Liver Int 40: 2095-2103.
14. Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y, Lin S (2020) Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. J Med Virol 92: 2152-2158. doi: 10.1002/jmv.26003. Epub 2020 May 25.
15. Kaplan M, Duzenli T, Tanoglu A, Guney BC, Tastan YO, Bicer HS (2020) Presepsin: albumin ratio and C-reactive protein:albumin ratio as novel sepsis-based prognostic scores: A retrospective study. Wien Klin Wochenschr 132: 182-187.

16. Ranzani OT, Zampieri FG, Forte DN, Pontes Azevedo LC, Park M (2013) C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. PLoS One 8: e59321.
17. Llop-Talaveron J, Badia-Tahull MB, Leiva-Badosa E (2018) An inflammation-based prognostic score, the C-reactive protein/albumin ratio predicts the morbidity and mortality of patients on parenteral nutrition. Clin Nutr 37: 1575-1583.
18. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 395: 1054-1062.
19. Kim MH, Ahn JY, Song JE (2015) The C-Reactive Protein/Albumin Ratio as an Independent Predictor of Mortality in Patients with Severe Sepsis or Septic Shock Treated with Early Goal-Directed Therapy. PLoS One 10: e0132109.
20. Li N, Tian GW, Wang Y, Zhang H, Wang ZH, Li G (2017) Prognostic role of the pretreatment C-reactive protein/albumin ratio in solid cancers: A meta-analysis. Sci Rep 7: 41298.
21. Karakoyun I, Colak A, Turken M, Altin Z, Arslan FD, Iyilikci V, Yilmaz N, Kose S (2021) Diagnostic utility of C-reactive protein to albumin ratio as an early warning sign in hospitalized severe COVID-19 patients. Int Immunopharmacol 91: 107285.
22. Feketea GM, Vlacha V (2020) The Diagnostic Significance of Usual Biochemical Parameters in Coronavirus Disease 19 (COVID-19): Albumin to Globulin Ratio and CRP to Albumin Ratio. Front Med (Lausanne) 7: 566591.
23. El-Shabrawy M, Alsadik ME, El-Shafei M, Abdelmoaty AA, Alazzouni AS, Esawy MM, Shabana MA (2021) Interleukin-6 and C-reactive protein/albumin ratio as predictors of COVID-19 severity and mortality. Egypt J Bronchol 15: 5.

Corresponding author

Aleksandr Kalabin, MD
Department of SurgeryColumbia University College of Physicians and Surgeons at Harlem Hospital
506 Lenox Avenue, MLK11.101, New York, NY - 10037, USA
Phone: 001-646-270-5089
FAX: 001-212-939-3536
Email: kalabin.al@gmail.com

Conflict of interests: No conflict of interests is declared.