Anaesthesia Section

Impact of Albumin Therapy in Critically III COVID-19 Patients: A Retrospective Cohort Study

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ABSTRACT

Introduction: Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Due to the limited understanding of this disease, research has quickly extended towards identifying biomarkers to predict its prognosis and progression.

Aim: To explore the impact of albumin infusion on critically ill COVID-19 patients.

Materials and Methods: In this retrospective cohort study, a total of 150 severe COVID-19 patients aged 18 to 65 years were enrolled. These patients were categorised into the no albumin infusion group (n=61), consisting of those who did not undergo albumin transfusion during their treatment, and the albumin infusion group (n=89), comprising patients who received albumin transfusion as part of their treatment protocol. Assessments of hospitalisation included the Sequential Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation (APACHE-II) scores obtained at baseline and day 5. Unpaired t-tests, Chi-square tests, and paired t-tests were used for analysis.

Results: The mean values of Haemoglobin (Hb), eosinophils, Random Blood Sugar (RBS), Mean Corpuscular Volume (MCV), total protein, serum urea, serum bilirubin, Prothrombin Time (PT), International Normalised Ratio (INR), Interleukin 6 (IL-6), Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), and D-dimer exhibited significant differences between the two groups. The average duration of vasopressor usage and Intensive Care Unit (ICU) stay were significantly reduced in the albumin infusion group (3.50±1.55 days and 8.70±4.20 days, respectively) compared to no albumin infusion group (4.33±1.05 days and 12.80±3.43 days, respectively). The albumin infusion group also displayed a lower incidence of Renal Replacement Therapy (RRT) and poorer ICU outcomes.

Conclusion: The intravenous administration of albumin did not exhibit a significant impact on mortality. However, albumin transfusion in patients with severe COVID-19 who initially had albumin levels <3 g/dL demonstrated a notable reduction in the requirement for vasopressors, RRT, and the length of ICU stay.

Keywords: Albumin infusion, Hypoalbuminemia, Intensive care unit stay, Mortality, Vasopressor

INTRODUCTION

The SARS-CoV-2 serves as the causal agent of COVID-19. The initial recorded case was identified in Wuhan, China, in December 2019. Subsequently, the disease rapidly disseminated worldwide, giving rise to an ongoing pandemic [1]. Among affected individuals, a minority of 14% experienced severe symptoms, marked by dyspnoea, hypoxia, or extensive lung involvement, while 5% faced more critical symptoms, including respiratory failure, shock, or multiorgan dysfunction. Conversely, a substantial majority (81%) showcased mild to moderate symptoms, often characterised as mild pneumonia. Notably, advanced age correlated with heightened symptom severity. Increased mortality and morbidity risks are associated with COVID-19 [2]. COVID-19's complications encompass a spectrum that spans Acute Respiratory Distress Syndrome (ARDS), multiple organ failure, septic shock, and fatality. Cardiovascular implications involve heart failure, arrhythmias (notably atrial fibrillation), cardiac inflammation, and thrombosis, particularly venous thromboembolism [3]. Additionally, 20-30% of COVID-19 patients exhibit elevated liver enzyme levels, indicative of liver injury [4]. Neurological manifestations encompass fainting, stroke, encephalitis, and Guillain-Barré syndrome, characterised by muscle function loss. In paediatric cases, a severe systemic inflammation akin to Kawasaki disease can emerge postinfection . Remarkably rare, acute encephalopathy may arise in diagnosed COVID-19 individuals. Severe disease correlates with elevated D-dimers, CRP, troponin levels, and diminished albumin concentrations [5]. Albumin, a reactive product of the acute phase, exhibits antioxidant properties. Under usual conditions, plasma albumin serves as a rich reservoir of free thiols, acting as scavengers for Reactive Oxygen Species (ROS) [6]. In situations of oxidative stress, Cys34 in human serum albumin undergoes irreversible oxidation, resulting in decreased antioxidant capacity and potential cellular and tissue damage. Detecting albumin levels in blood offers another approach for early identification of patients at heightened risk of mortality [2]. SARS-CoV-2 employs the Angiotensin-Converting Enzyme (ACE-2) as a host cell receptor. The virus is proficient in infecting a wide array of cells and systems. Extensive documentation reveals COVID-19's impact on the upper and lower respiratory tracts, encompassing sinuses, nose, throat, and lungs [7]. Cytokine storms, often emerging in the advanced stages of severe COVID-19, involve a lethal immune response characterised by an abrupt release of numerous cytokines and chemokines, leading to inflammatory processes. Consequently, cytokine storms are linked to multiple organ failure and ARDS [8]. Given that COVID-19's cellular entry involves the ACE-2 receptor, which is highly concentrated in alveolar type II cells within the lungs, the virus primarily affects lung function. The virus utilises a characteristic glycoprotein "spike" to interact with the ACE-2 receptor, facilitating cell invasion. Sommerstein's theory postulates that the upregulation of ACE-2 receptors renders individuals taking Angiotensin Receptor Blockers (ARB) or ACE-1 more susceptible to severe infections. Notably, albumin's role in inhibiting ACE-2 receptors and enhancing the ratio of arterial partial pressure of oxygen to inspired oxygen fraction is underscored in ARDS patients [9]. COVID-19 has been associated with changes in a number of acute phase proteins, including albumin. In fact, a higher mortality rate in COVID-19 has been associated with lower albumin levels on hospital admission [10-14]. In light of the COVID-19 pandemic, the role of albumin infusion in critically ill patients remains unclear. While some studies suggest potential benefits in the treatment of severe cases, there is a lack of comprehensive studies specifically for COVID-19 patients [14-16]. This new study, which focuses on COVID-19 patients, could fill this gap by investigating the effects of albumin on mortality, inflammation, and organ dysfunction. Therefore, the aim of this study was to investigate the effects of albumin infusion in critically ill COVID-19 patients.

MATERIALS AND METHODS

This retrospective cohort study was conducted in the Department of Anaesthesiology and Critical Care at Era's Lucknow Medical College and Hospital, Lucknow, India, from September 2022 to July 2023. A total of 150 patients were purposefully selected from the database from June 1, 2020, to December 31, 2020. The study protocol received ethical approval from the Institutional Ethics Committee (ref. no ELMC&H/R-cell/EC/2021/102).

Inclusion criteria: Patients aged between 18 and 65 years, meeting the critically ill COVID-19 criteria set by the World Health Organisation (WHO) [17] and confirmed through real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR) testing, who were admitted to the ICU for more than 24 hours and exhibited an albumin level <3 g/dL during the period from June 1, 2020, to December 31, 2020, were included in the study.

Exclusion criteria: Patients with an ICU stay having duration of fewer more than 24 hours, individuals with terminal illnesses, and those with documented albumin allergies were excluded from the study.

Study Procedure

The 150 patients were randomly allocated to two groups based on whether they received albumin transfusion during their treatment. The first group, labeled as the 'No Albumin Infusion Group (n=61),' consisted of patients who did not undergo albumin transfusion, while the second group, the 'Albumin Infusion Group (n=89),' encompassed patients who received 60 g albumin 20% over 3 hours transfusion as part of their treatment regimen.

Patient data was extracted from the electronic hospital information system, focusing on critically ill COVID-19 patients with a respiratory rate of more than 30 breaths per minute and an Oxygen Saturation (SpO₂) below 90% on room air. This included demographic details such as age, gender, home medications, smoking and/or drinking habits, and occupation, as well as information about co-morbidities, initial symptoms, and vital signs. Subsequently, patients were categorised into their respective groups based on whether albumin transfusion was administered or not. Additionally, key outcome metrics including 90-day mortality, length of ICU stay, ICU and in-hospital mortality rates, requirement for vasopressors, and necessity for RRT were recorded.

SOFA and APACHE-II scores were determined at baseline. The SOFA score took into account variables such as arterial oxygen pressure (PaO $_2$)/fraction of inspired oxygen (FiO $_2$) ratio, platelet count, total bilirubin, mean arterial pressure, Glasgow Coma Scale, creatinine level, and daily urine output. The APACHE-II score included the Glasgow Coma Scale, white blood cell count, mean arterial blood pressure, heart rate, respiratory rate, oxygenation status, arterial pH, serum sodium and potassium levels, serum creatinine level, hematocrit, and serum bicarbonate level (HCO $_3$) [11]. The primary study outcomes for the COVID-19 patients were the mortality rate and the number of ICU hospitalisations.

STATISTICAL ANALYSIS

The statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 23.0 statistical analysis software. An unpaired t-test was used to determine the significance between the two groups for continuous variables, and a paired t-test was

used for intra group comparisons. The Chi-square test was used to assess the significance of study parameters on a categorical scale. Data were presented as mean±standard deviation, and a p-value <0.05 was considered statistically significant.

RESULTS

The distribution of patients according to age, sex, habits, home medication, and symptoms did not differ significantly between the no albumin infusion group and the albumin infusion group [Table/Fig-1]. It is notable that the majority of patients were in the age range of 40 to 59 years. The mean age was 56.67±13.87 in the no albumin infusion group and 56.09±14.37 in the albumin infusion group. In terms of gender, there were more men in the albumin infusion group {50 (67.42%)}, while there were more women in the group without albumin infusion {32 (52.46%)}, although there was no significant difference (p=0.298). The frequency of co-morbidities was significantly higher in the no albumin infusion group (98.36%) compared to the albumin infusion group (61.80%) (p-value <0.001) [Table/Fig-1].

Parameters		No albumin infusion group (n=61) n (%)	Albumin infusion group (n=89) n (%)	p- value	
Farameters	0-19	0		value	
		-	1 (1.12)		
	20-39	6 (9.84)	11 (12.36)	0.000	
Age (years)	40-59	29 (47.54)	38 (42.70)	0.832	
	60-79	22 (36.07)	35 (39.33)		
	80-99	4 (6.56)	4 (4.49)		
	Mean±SD	56.67±13.87	56.09±14.37	0.809	
Gender	Female	32 (52.46)	39 (32.58)	0.298	
	Male	29 (47.54)	50 (67.42)		
	Housewife	33 (54.10)	25 (28.09)		
	Private Job	8 (13.11)	14 (15.73)		
	Retired	4 (6.56)	1 (1.12)	0.002	
Occupation	Student	0	1 (1.12)		
Occupation	Teacher	0	1 (1.12)		
	Business	9 (14.75)	18 (20.22)		
	Gov. Job	7 (11.48)	13 (14.61)		
	Unemployed	0	16 (17.98)		
	Drinking habit	13 (21.31)	11 (12.36)	0.240	
Habit	Smoking	19 (31.15)	29 (32.58)		
Home	No	23 (37.70)	41 (46.07)	0.309	
medications	Yes	38 (62.30)	48 (53.93)		
	Fever	61 (100)	89 (100)		
	Cough	41 (67.21)	57 (64.04)		
	Sore throat	26 (42.62)	27 (30.34)		
_	Fatigue	51 (83.61)	80 (89.89)		
Symptoms	Runny nose	4 (6.56)	6 (6.74)	0.838	
	Headache	38 (62.30)	59 (66.29)		
	Diarrhoea	5 (8.20)	14 (15.73)		
	Dyspnoea	51 (83.61)	74 (83.15)		
	Yes	60 (98.36)	55 (61.80)	<0.001	
Co-morbidities	No	1 (1.64)	34 (38.20)		
	Diabetes Mellitus (DM)	25 (41.67)	21 (23.60)	0037	
	Hypertension (HTN)	30 (50)	29 (32.58)	0.061	
	Coronary Artery Disease (CAD)	5 (8.33)	5 (5.62)	0.774	

[Table/Fig-1]: Comparison of baseline characteristics between no albumin infusion group and albumin infusion group.

Mean Hb, RBS, total protein, IL-6, CRP, D-dimer, and S.ferritin were significantly lower in the no albumin infusion group compared

to the albumin infusion group (p-value <0.05). In contrast, the mean values for eosinophils, MCV, S. urea, S. bilirubin, PT, INR, and ESR were significantly higher in the no albumin infusion group. Moreover, the albumin level was comparable between groups before therapy and at day 0, but it was significantly lower in the no albumin infusion group (1.70 ± 0.15) compared to the albumin infusion group (2.11 ± 0.37) at day 7 [Table/Fig-2].

No albumin Albumin infusion group infusion group (n=89)(n=61)Haematological value parameters Mean±SD Mean±SD t 10.34±2.12 Hb (gm/dL) 12.07+1.92 5.195 < 0.001 TLC (/mm cubic) 9388.52±4722.92 10033.71±5179.43 0.439 0.776 Neutrophils (%) 78.97±12.64 79.16±12.92 0.089 0.929 Lymphocytes (%) 15.97±9.90 16.80±11.87 0.449 0.654 Eosinophils (%) 2.64±2.81 1.86±1.47 2.216 0.028 Monocytes (%) 2.30 ± 1.59 2.14±1.30 0.676 0.500 2.07±0.80 0.811 Platelets counts (lakh) 2.04±0.68 0.240 134.11±63.85 162.88±80.41 2.334 0.021 RBS (ma/dL) RBC (/mmcube) 11.58±60.48 4.35±0.72 1.129 0.261 27.46±4.24 28.33±6.01 0.976 MCH (pg/cells) 0.331 MCV (micro mili 85 91+11 41 81 74+9 75 2 400 0.018 meter cube) MCHC (hb/cell) 32.75±6.40 34.27±5.33 1.580 0.116 Total protein (gm/dL) 6.15±0.62 6.46±0.67 2.868 0.005 84.67±79.01 52.49±38.79 3.308 S. Urea (mg/dL) 0.001 S. Creatinine (mg/dL) 5.50±20.84 1.78±1.92 1.676 0.096 S. Sodium (mmol/L) 137.47±18.11 138.09±5.29 0.305 0.761 S. Potassium (mmol/L) 6.45±17.25 4.19±0.54 1.237 0.218 0.800 S. Calcium (mg/dL) 8.69+2.48 8.76+0.65 0.254 SGOT (u/L) 78.83+122.25 79.34+117.87 0.026 0.980 ALP (u/L) 135.48±92.46 129.20±139.04 0.309 0.758 SGPT (u/L) 69.01±115.24 49.88±63.62 1.304 0.194 S. Bilirubin (mg/dL) 0.85±1.04 0.62 + 0.291.980 0.050 S. LDH (u/L) 595.21±474.50 672.15±533.14 0.907 0.366 PT (seconds) 14.59±3.49 13.54±2.78 2.046 0.043 INR 1.29±0.29 1.19±0.25 2.254 0.026 Troponin (ng/mL) 1.01±0.98 0.98±0.81 0.204 0.838 IL-6 (ng/mL) 30.75±22.95 54.44±51.82 3 350 0.001 ESR (mm/hr) 34.00±7.49 27.90±8.18 4.641 < 0.001 Pao₂/Fio₂ 245.04±42.79 0.099 258.36±55.18 1.663 CRP (gm/litre) 69.76+36.20 86.22+17.52 3.707 < 0.001 D-Dimer (mg/L) 2.44+0.87 7.00 + 2.4513.930 < 0.001 250.13±101.80 331.12±241.75 2.469 0.015 S. Ferritin (mg/dL) S. Albumin before 2.47±0.38 2.41±0.25 1.167 0.245 therapy (gm/dL) S. Albumin at day-0 2.23±0.14 2.21±0.27 0.531 0.596 (gm/dL) S. Albumin at day-7 1.70±0.15 2.11±0.37 8.198 (gm/dL)

[Table/Fig-2]: Comparison of biochemical parameters of patients between no albumin infusion group and albumin infusion group.

Hb: Haaemoglobin; TLC: Total leukocyte count; RBS: Random blood sugar; RBC: Red blood cells; MCH: Mean corpuscular haemoglobin; MCV: Mean corpuscular volume; MCHC: Mean corpuscular haemoglobin concentration; S: Serum; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamate pyruvate transaminase; ALP: Alkaline phosphatase; PT: Prothrombin time; INR: International normalised ratio; IL: Interleukin; ESR: Erythrocyte sedimentation rate; CRP: C-reative protein

The average albumin level demonstrated a statistically significant elevation in the albumin infusion group compared to the no albumin infusion group, evident at baseline, day 1, and day 2. The average duration of vasopressor usage and ICU stay were significantly

reduced in the albumin infusion group (3.50 ± 1.55 days and 8.70 ± 4.20 days, respectively) compared to the no albumin infusion group (4.33 ± 1.05 days and 12.80 ± 3.43 days, respectively) (p-value <0.001). The albumin infusion group also showed a lower incidence of RRT and poorer ICU outcomes compared to the no albumin infusion group (p-value <0.001) [Table/Fig-3].

		No albumin infusion group (n=61)	Albumin infusion group (n=89)		
Parameters		M±SD/n (%)	M±SD/n (%)	p-value	
APACHE score at day 1	Mean±SD	29.33 (20.37)	29.95 (18.86)	0.849	
SOFA score at day 1	Mean±SD	0.59 (0.89)	0.53 (0.72)	0.650	
GCS score at day 1	Mean±SD	12.52 (1.00)	12.51 (1.07)	0.954	
Albumin level (gm/dL)	Baseline	2.47 (0.38)	2.61 (0.23)	0.006	
	Before therapy	2.47 (0.38)	2.41 (0.25)	0.245	
	Day 0	2.23 (0.14)	2.21 (0.27)	0.596	
	Day 1	1.89 (0.37)	2.12 (0.42)	0.001	
	Day 2	1.99 (0. 37)	2.24 (0.34)	<0.001	
Mortality (n, %)	Mortality at 28 days	11 (18.03)	4 (4.49)		
	Mortality at 90 days	2 (3.28)	0	0.580	
	Mortality in ICU	11 (18.03)	2 (2.25)		
Use of	Yes	9 (14.75)	12 (13.48)	0.943	
vasopressors (n,%)	No	52 (85.25)	77 (86.52)		
No. of days on vasopressor	Mean±SD	4.33 (1.05)	3.50 (1.55)	<0.001	
ICU stay (days)	Mean±SD	12.80 (3.43)	8.70 (4.20)	<0.001	
ICU Outcome	Improved	45 (73.77)	85 (95.51)	<0.001	
(n,%)	Poor	16 (26.23)	4 (4.49)	<0.001	

[Table/Fig-3]: Comparative analysis of different parameters between the no albumin infusion group and albumin infusion group.

In the multivariate logistic regression analysis, the pretherapy serum albumin level, serum albumin at day 0, serum albumin at day 7, INR, SOFA score, and the utilisation of vasopressors demonstrated significant associations with the risk of non survival (p-value <0.05) [Table/Fig-4].

		95% CI		
	Odds ratio	Lower	Upper	p-value
Co-morbidities	1.56	0.32	7.73	0.585
Sr. Albumin before therapy	25.33	1.98	118.74	0.009
Sr. Albumin at day-0	0.03	0.00	0.31	0.003
Serum albumin at Day-7	2.29	0.02	3.59	0.033
CRP	3.71	0.00	6.31E3	0.730
D-Dimer	1.12	0.08	14.91	0.934
НВ	0.80	0.06	10.09	0.866
RBC	1.34	0.12	15.32	0.812
MCV	0.14	0.01	1.62	0.116
MCHC	0.71	0.11	4.47	0.714
Sr. Sodium	4.42	0.64	30.46	0.131
Sr. Calcium	1.06	0.15	7.77	0.953
PT	0.05	0.00	7.28	0.240
INR	293.30	1.56	5.534	0.034
IL-6	0.41	0.08	2.15	0.293
ESR	0.44	0.06	3.25	0.423

APACHE	1.62	0.13	3.03	0.077
SOFA	8.13	1.69	39.18	0.009
GCS	0.15	0.01	2.73	0.200
Use of vasopressors	14.36	1.83	113.04	0.011
Duration of ICU stay	4.61	0.27	78.53	0.291

[Table/Fig-4]: Multivariate logistic regression analysis in both groups to determine the risk factors for non survival (mortality) patients.

DISCUSSION

In this study, the mean age of the patients was comparable in both the no albumin infusion group and albumin infusion group and consisted of patients aged 40 to 59 years. Similarly, Zhang L et al., observed no significant age-associated difference between the no albumin infusion group (68.4±12.3) and the albumin infusion group (69.34.5±12.4) [14]. However, Huang J et al., found a significantly higher mean age in patients with hypoalbuminemia (62.9±13.1 years) compared to the normal albumin group (48.2±16.1 years) [18]. Additionally, Kheir M et al., demonstrated a significant association between age and hypoalbuminemia (Albumin <3.3) [19].

In present study, the majority of patients in the no albumin infusion group were female (52.46%) and the majority in the albumin infusion group were male (67.42%). However, this difference was statistically non-significant (p=0.298). Zhang L et al., Huang J et al., and Kheir M et al., also reported that gender was not significantly linked to hypoalbuminemia [14,16,19]. Wang X et al., noted that 61.29% of male patients were and 8.16% female patients in clinically diagnosed and confirmed SARS-CoV-2 patients [20]. Furthermore, only 6.12% of males and 22.58% of females had hypertension. Notably, there were comparable clinical characteristics between genders in other aspects.

In present study, co-morbidities were significantly more common in the no albumin infusion group (98.36%) compared to the albumin infusion group (61.80%). Out of a total of 150 patients, 46 (30.67%) had diabetes, 59 (39.33%) had hypertension, and 10 (6.67%) had CAD. Moreover, diabetics were significantly more prevalent in the no albumin infusion group compared to the albumin infusion group, while hypertension and CAD rates were comparable in both groups. Similarly, Zhang L et al., reported that the distribution of patients with diabetes, hypertension, and coronary heart disease was similar in both the no albumin infusion group and the albumin infusion group [14]. They also noted that out of 114 patients, a total of 24 (21.05%) had diabetes, 39 (34.21%) had hypertension, and 16 (14.04%) had coronary artery disease. This result was consistent with a study that highlighted different regional trends in the prevalence of comorbidities [21].

In present study, Hb, RBS, total protein, IL-6, CRP, D-Dimer, serum ferritin, and serum albumin at Day-7 were significantly higher, whereas eosinophils (%), MCV, serum urea, PT, INR, and ESR were decreased in the albumin infusion group compared to the no albumin infusion group. Zhang L et al., [14] reported that lymphocytes and CRP were significantly higher, and IL-6 was significantly lower in the albumin infusion group than in the no albumin infusion group.

Several processes could lead to a reduction in serum albumin as a result of COVID-19 infection. Additionally, albumin may help protect host cells from the oxidative burst that occurs as a consequence of viral infection [14]. In present study, albumin levels were similar in both groups pretherapy and at day zero; however, the group that did not receive albumin infusion had significantly lower albumin levels (1.70±0.15 gm/dL) than the group that received albumin infusion (2.11±0.37 gm/dL). According to Ramadori G, serum albumin levels in the albumin group reached a mean of 3.6 g/dL [22]. In the first week of hospitalisation, albumin serum levels, which were already lower in the control group at the beginning of treatment, decreased significantly more. According to the study by Zhang L et al., the albumin level after treatment showed a strong negative correlation [14].

Multivariate logistic regression analysis identified various factors associated with non survival. Parameters such as INR, serum albumin levels before therapy, the use of vasopressors, and SOFA score exhibited significant associations with non survival. Similarly, Zerbato V et al., reported that serum albumin was significantly lower in COVID-19 patients who died within 90 days of hospital admission (3.1 g/dL; IQR 2.8-3.4; p-value <0.001) than in those who survived (3.4 g/dL; IQR 3.1-3.7). Additionally, a serum albumin level of <3.23 g/dL appeared to be an independent risk factor for 90-day mortality [23]. The correlations between albumin levels, inflammatory markers, and clinical parameters further support the importance of albumin in influencing disease progression and outcomes [24-26].

Hypoalbuminemia in COVID-19 patients appears to be linked to disease severity and prognosis. Albumin infusion shows a potential positive impact on improving ICU outcomes and mortality rates. While this study contributes valuable insights into the association between albumin levels, clinical parameters, and patient outcomes, further research is necessary to comprehend the underlying mechanisms and potential therapeutic interventions for managing COVID-19 cases with hypoalbuminemia.

Limitation(s)

One of the main limitations was that the administration protocol could not be blinded in both groups. The results are limited to a single tertiary care centre and may not be generalisable to all areas. Therefore, they cannot be generalised to a larger population. Additionally, the limited experience and small sample size make it difficult to assess risk factors for disease severity and mortality using multivariable-adjusted methods.

CONCLUSION(S)

This study revealed that intravenous administration of albumin did not have a significant impact on mortality. However, in severely ill COVID-19 patients with albumin levels below 3 g/dL, albumin transfusion was associated with reduced requirements for vasopressors, RRT, and length of ICU stay. Further research is warranted to ascertain whether albumin evaluation can aid healthcare practitioners in identifying patients at a heightened risk of adverse outcomes at an early stage. Additionally, investigating whether this parameter can serve as an indicator of treatment response in the early phases is also essential.

REFERENCES

- [1] Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. Glob Health Res Policy. 2020;5:6.
- [2] Violi F, Cangemi R, Romiti GF, Ceccarelli G, Oliva A, Alessandri F, et al. Is albumin predictor of mortality in COVID-19? Antioxid Redox Signal. 2021;35(2):139-42.
- [3] Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and multiorgan response. Curr Probl Cardiol. 2020;45(8):100618.
- [4] Moon AM, Barritt AS 4th. Elevated liver enzymes in patients with COVID-19: Look, but not too hard. Dig Dis Sci. 2021;66(6):1767-69.
- [5] Liu BC, Gao J, Li Q, Xu LM. Albumin caused the increasing production of angiotensin two due to the dysregulation of ACE/ACE2 expression inHK2 cells. Clin Chim Acta. 2009;403(1-2):23-30.
- [6] Belinskaia DA, Voronina PA, Shmurak VI, Jenkins RO, Goncharov NV. Serum albumin in health and disease: Esterase, antioxidant, transporting and signaling properties. Int J Mol Sci. 2021;22(19):10318.
- [7] Ni W, Yang X, Yang D, Bao J, Li R, Xiao Y, et al. Role of Angiotensin-Converting Enzyme 2 (ACE2) in COVID-19. Crit Care. 2020;24:422.
- [8] Ragab D, Salah Eldin H, Taeimah M, Khattab R, Salem R. The COVID-19 cytokine storm; what we know so far. Front Immunol. 2020;11:1446.
- [9] Sommerstein R, Gräni C. Rapid response: Re: Preventing a COVID-19 pandemic: ACE inhibitors as a potential risk factor for fatal COVID-19. BMJ 2020. Available from: https://www.bmj.com/content/368/bmj.m810/rr-2. (8 March 2020).
- [10] Uhlig C, Silva PL, Deckert S, Schmitt J, De Abreu MG. Albumin versus crystalloid solutions in patients with the acute respiratory distress syndrome: A systematic review and meta-analysis. Crit Care. 2014;18(1):R10.
- [11] Asmarawati TP, Suryantoro SD, Rosyid AN, Marfiani E, Windradi C, Mahdi BA, et al. Predictive value of sequential organ failure assessment, quick sequential organ failure assessment, acute physiology and Chronic Health Evaluation II, and new early warning signs scores estimate mortality of COVID-19 patients requiring intensive care unit. Indian J Crit Care Med. 2022;26(4):464-71. Doi: 10.5005/ip-journals-10071-24170.

- [12] Bassoli C, Oreni L, Ballone E, Foschi A, Perotti A, Mainini A, et al. Role of serum albumin and proteinuria in patients with SARS-CoV-2 pneumonia. Int J Clin Pract. 2021;75(4):e13946.
- Li T, Zhang Y, Gong C, Wang J, Liu B, Shi L, et al. Prevalence of malnutrition and analysis of related factors in elderly patients with COVID-19 in Wuhan, China. Eur J Clin Nutr. 2020;74(6):871-75.
- [14] Zhang L, Yu W, Zhao Y, Chen X, Wang P, Fan X, et al. Albumin infusion may improve the prognosis of critical COVID-19 patients with albumin infusion group in the Intensive Care Unit: A retrospective cohort study. Infect Drug Resist. 2022;15:6039-50.
- [15] Hajiar LA, Costa IBS, Rizk SI, Biselli B, Gomes BR, Bittar CS, et al. Intensive care management of patients with COVID-19: A practical approach. Ann Intensive Care. 2021;11(1):36. Available from: https://doi.org/10.1186/s13613-
- Minatoguchi S, Nomura A, Imaizumi T, Sasaki S, Ozeki T, Uchida D, et al. Low serum albumin as a risk factor for infection-related in-hospital death among hemodialysis patients hospitalized on suspicion of infectious disease: A Japanese multicenter retrospective cohort study. Ren Replace Ther. 2018;4:30.
- World Health Organization-Health Topics [Internet]. https://www.who.int/healthtopics/coronavirus#tab=tab_1. Accessed on 2020.
- Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y, et al. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. J Med Virol. 2020;92(10):2152-58. Doi: 10.1002/jmv.26003. Epub 2020 May 25.

- [19] Kheir M, Saleem F, Wang C, Mann A, Chua J. Higher albumin levels on admission predict better prognosis in patients with confirmed COVID-19. PLOS ONE. 2021:16(3):e0248358.
- Wang X, Liu W, Zhao J, Lu Y, Wang X, Yu C, et al. Clinical characteristics of 80 hospitalized frontline medical workers infected with COVID-19 in Wuhan, China. J Hosp Infect. 2020;105(3):399-403. Doi: 10.1016/j.jhin.2020.04.019.
- [21] Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: Retrospective case series. BMJ. 2020;368:m606. Doi: 10.1136/ bmj.m606.
- Ramadori G. Albumin infusion in critically ill COVID-19 patients: Hemodilution and anticoagulation. Int J Mol Sci. 2021;22(13):7126.
- Zerbato V. Sanson G. De Luca M. Di Bella S. di Masi A. Caironi P. et al. The impact of serum albumin levels on COVID-19 mortality. Infect Dis Rep. 2022;14(3):278-86.
- [24] Huang W, Li C, Wang Z, Wang H, Zhou N, Jiang J, et al. Decreased serum albumin level indicates poor prognosis of COVID-19 patients: Hepatic injury analysis from 2,623 hospitalized cases. Sci China Life Sci. 2020;63(11):1678-87.
- [25] Chi G. Gibson CM, Liu Y. Hernandez AF, Hull RD, Cohen AT, et al. Inverse relationship of serum albumin to the risk of venous thromboembolism among acutely ill hospitalized patients: Analysis from the APEX trial. Am J Hematol. 2019;94(1):21-28.
- [26] Xu Y, Yang H, Wang J, Li X, Xue C, Niu C, et al. Serum albumin levels are a predictor of COVID-19 patient prognosis: Evidence from a single cohort in Chongging, China. Int J Gen Med. 2021;14:2785-97.

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