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Association between hypoalbuminemia and pulmonary CT severity in COVID-19 ICU patients: A cohort study

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Abstract

English:

Background: *Hypoalbuminemia is recognised as a significant prognostic factor in critically ill coronavirus disease 2019 (COVID-19) patients. This study investigates the association between serum albumin levels and pulmonary computed tomography (CT) severity, as well as patient outcomes, including mortality, in intensive care unit (ICU)-admitted COVID-19 patients.*
Methods: *This cohort study was conducted between March 2020 and October 2021 at Imam Reza Hospital, Iran. ICU-admitted COVID-19 patients were evaluated for demographic characteristics, clinical and laboratory parameters, lung CT findings with severity scoring and outcomes. Data analysis was performed using SPSS version 25.*
Results: *Among 200 patients (mean age: 63.6 ± 16.1 years; 58% male), 80.0% (n = 160) presented with hypoalbuminemia. The average initial serum albumin level was 3.13 ± 0.49 g/dL. The overall mortality rate was 81% (n = 162). Survivors had significantly higher albumin levels (P = 0.003) compared to non-survivors. Based on multivariable logistic regression, higher serum albumin was associated with a 61% reduction in mortality odds (OR = 0.39, 95% CI: (0.18, 0.90), P = 0.027). However, no statistically significant correlation was found between serum albumin levels and pulmonary CT severity scores.*
Conclusion: *Hypoalbuminemia in ICU COVID-19 patients is strongly associated with poor clinical outcomes and increased mortality, but not with the radiological extent of lung involvement seen on CT imaging.*

Keywords

COVID-19 • ICU • albumin • CT scan • respiratory failure

Asocierea dintre hipoalbuminemie și severitatea leziunilor pe computer tomografiile pacienților cu Covid-19, internați în terapie intensivă: Un studiu de cohortă

Rezumat

Romanian:

Context: *Hipoalbuminemia este recunoscută ca un factor prognostic semnificativ la pacienții în stare critică cu boala coronavirus 2019 (COVID-19). Acest studiu investighează asocierea dintre nivelurile serice de albumină și severitatea la tomografia computerizată (CT) pulmonară, precum și outcome-urile pacienților, inclusiv mortalitatea, la pacienții cu COVID-19 internați în unitatea de terapie intensivă (UTI).*
Metode: *Acest studiu de cohortă a fost realizat între martie 2020 și octombrie 2021 la Spitalul Imam Reza, Iran. Pacienții cu COVID-19 internați în UTI au fost evaluați din punct de vedere al caracteristicilor demografice, parametrilor clinici și de laborator, constatărilor CT pulmonare cu scor de severitate și al outcome-urilor. Analiza datelor a fost efectuată utilizând SPSS versiunea 25.*

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Rezultate: *Dintre 200 de pacienți (vârsta medie: 63,6 ± 16,1 ani; 58% bărbați), 80,0% (n = 160) au prezentat hipoalbuminemie. Valoarea medie inițială a albuminei serice a fost 3,13 ± 0,49 g/dL. Rata globală a mortalității a fost 81% (n = 162). Supraviețuitorii au avut niveluri semnificativ mai mari ale albuminei (P = 0,003) comparativ cu non-supraviețuitorii. Pe baza regresiei logistice multivariate, o albumină serică mai mare s-a asociat cu o reducere cu 61% a șanselor de mortalitate (OR = 0,39; IC 95%: (0,18, 0,90); P = 0,027). Totuși, nu s-a identificat o corelație semnificativă statistic între nivelurile serice de albumină și scorurile de severitate CT pulmonară.*

Concluzie: *Hipoalbuminemia la pacienții cu COVID-19 din UTI se asociază puternic cu outcome-uri clinice nefavorabile și mortalitate crescută, dar nu și cu extinderea radiologică a afectării pulmonare evidențiate la CT.*

Cuvinte-cheie

COVID-19 • UTI • albumină • CT • insuficiență respiratorie

Introduction

Coronavirus disease 2019 (COVID-19) has emerged as the most widespread viral pandemic in recent history, with clinical outcomes ranging from mild illness to severe respiratory failure requiring intensive care unit (ICU) admission (1, 2). The heterogeneity of disease manifestations poses considerable diagnostic and therapeutic challenges, and identifying reliable prognostic markers remains a priority for clinicians (3). Serum albumin, a negative acute-phase reactant, has been proposed as a potential predictor of adverse outcomes in COVID-19. Reduced albumin levels have been associated with increased risk of ICU admission, mortality and more severe pulmonary involvement (4–7). Several studies have reported significant correlations between hypoalbuminemia and disease exacerbation, with markedly different albumin levels observed between deceased and discharged patients (1, 8). Xu et al. (7) demonstrated that hypoalbuminemia correlated with the severity of lung involvement and was proposed as a prognostic factor. Elevated inflammatory markers, such as IL-6 and IL-8, may impair liver function, contributing to disease progression and reduced albumin synthesis (9). Abdeen et al. (10) identified albumin as a strong predictor of mortality, whereas Acharya et al. (4) found no significant association between serum albumin and disease severity. Despite these observations, the relationship between hypoalbuminemia and radiological severity of pulmonary involvement in COVID-19 has not been fully clarified. Most prior studies have focused on clinical outcomes such as ICU admission or mortality, while fewer have examined the correlation between serum albumin levels and chest computed tomography (CT) findings (11). This gap limits our understanding of whether hypoalbuminemia can serve as a reliable biomarker for radiological severity and early risk stratification. This study aims to investigate the association between serum albumin levels at admission and chest CT severity in hospitalised COVID-19 patients. We hypothesised that lower albumin levels are correlated with more extensive pulmonary lesions and poorer clinical outcomes. By addressing this gap, our findings may contribute to the development of targeted, evidence-based strategies for risk assessment and intensive care management in patients with severe COVID-19.

Materials and methods

Study design

This cohort study was conducted at Imam Reza Hospital in Mashhad, Iran, among patients with PCR-confirmed COVID-19 admitted to the ICU. Exclusion criteria comprised severe renal insufficiency, nephrotic syndrome accompanied by hypoalbuminemia, liver disease or cirrhosis, severe malnutrition and incomplete medical records. Data collected included demographic characteristics (age and sex); comorbidities, such as diabetes mellitus, hypertension, cardiovascular and pulmonary diseases, malignancies, HIV infection, autoimmune disorders, history of organ transplantation, hematologic and rheumatologic conditions, obesity (defined as BMI ≥35) and infectious or neurologic diseases; substance use history including tobacco, alcohol and illicit drugs; medication history encompassing antihypertensive agents (e.g., ACE inhibitors and ARBs), antidiabetic drugs, chemotherapy, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) and immunosuppressants. Vital signs recorded were oxygen saturation, heart and respiratory rates and systolic and diastolic blood pressure. Clinical symptoms documented included fever, cough, fatigue, headache, haemoptysis, diarrhoea, vomiting, nausea and dyspnoea. Laboratory evaluations included measurement of serum albumin in the first week of hospitalization, and the initial CT scan was conducted

upon admission. Hypoalbuminemia was defined as serum albumin <3.5 g/dL and categorized as mild (3.0–3.5 g/dL), moderate (2.0–3.0 g/dL) or severe (<2.0 g/dL) (12). The variables of gender, age, albumin, CT score, C-reactive protein (CRP), intubation, diabetes, blood pressure, COPD and IHD were included in univariate logistic regression analysis. Variables with a significance level below 0.25 in the univariate model were included in the multivariate logistic regression model. Additional laboratory parameters included urea, creatinine, liver transaminases, complete blood count (CBC), quantitative CRP and peripheral oxygen saturation (SpO_2). Imaging findings were based on chest CT patterns, including ground-glass opacities, consolidation and nodules. A single specialist radiologist evaluated all CT scans independently, without access to clinical or biochemical information. Nevertheless, the pulmonologist and the lung radiologist reviewed all the CT results.

The CT severity score (total severity score [TSS]) was calculated by assigning each of the five lung lobes a score from 0 to 4 based on percentage involvement (0: 0%; 1: 1%–25%; 2: 26%–50%; 3: 51%–75% and 4: 76%–100%) (11), with the total score ranging from 0 to 20 (higher scores indicating greater lung involvement). Patient outcomes (recovery or death) were recorded.

Statistical analysis

Following data collection, the data were entered into SPSS version 25 (2017, IBM Corporation, USA) for statistical analysis, involved reporting continuous variables as means ± standard deviations (SD) and categorical variables as percentages, with comparisons using Student's *t*-test (normal distribution), Mann–Whitney *U* test (non-normal distribution), or Kruskal–Wallis test (>two groups) and multivariable logistic regression model was applied to assess predictors of mortality. The statistical significance was set at **P** < 0.05 using SPSS version 25.

Ethical considerations

Ethical approval was obtained from Mashhad University of Medical Sciences (IR.MUMS.MEDICAL.REC.1401.087; Approval No. 4001220), ensuring confidentiality through anonymisation and adherence to the Helsinki Declaration.

Results

This study included 200 patients with a mean age of 63.58 years (SD: ± 16.09). Among them, 116 (58%) were male, constituting the majority of the cohort. Diabetes mellitus and hypertension were the most commonly reported comorbidities, with frequencies of 88 (44%) and 87 (43.5%), respectively, followed by ischaemic heart disease with a frequency of 54 (27%). The patients presented with various comorbidities: chronic obstructive pulmonary disease (COPD) in 26 patients (13%), a history of tuberculosis in 4 patients (2%), cerebrovascular accident (CVA) in 7 patients (3.5%), Alzheimer's disease in 6 patients (3%), malignancy in 8 patients (4%), diabetes in 88 patients (44%), hypertension in 87 patients (43.5%) and ischaemic heart disease in 54 patients (27%). Upon admission, patients presented with a range of concerning symptoms: 88 (44%) had fever, 82 (41%) had cough and 82 (41%) had shortness of breath. Additionally, 75 (37.5%) suffered from myalgia, 52 (26%) showed respiratory distress and 20 (10%) exhibited a decreased level of consciousness. Other symptoms included gastroenteritis (14 patients, 7%), fatigue (13 patients, 6.5%), cyanosis (11 patients, 5.5%) and rare cases of a skin lesion and haemoptysis (1 patient each, 0.5%). Vital signs and laboratory findings for the patients are displayed in Table 1. It is important to note that all patients were admitted to the ICU during their treatment. At referral, the mean SpO_2 level was 82.44 ± 9.60, in the absence of oxygen therapy. Notably, 126 patients (64.6%) had SpO_2 levels below the critical threshold of 90%, and the average baseline albumin level was 3.13 ± 0.49 g/dL. Of 200 patients, 162 (81%) died. Out of 200 patients, a staggering 180 (90%) required intubation. Among those intubated, 145 patients (89.5%) did not survive. The comparison of albumin levels and TSS between the survivor and non-survivor groups is shown in Table 2.

One hundred sixty patients had hypoalbuminemia (albumin levels below 3.5 g/dL), while thirty-six had normal albumin

Table 1. Vital signs and laboratory findings.

Variable parameters	Mean ± SD	Min–Max
Systolic blood pressure (mmHg)	129.79 ± 22.07	90–250
Diastolic blood pressure (mmHg)	79.69 ± 12.33	58–130
Heart rate (per min)	99.23 ± 19.49	52–158
Respiratory rate (per min)	20.08 ± 3.89	14–45
Laboratory findings		
Albumin (g/dL)	3.13 ± 0.49	1.80–4.40
CRP (mg/dL)	127.02 ± 83.88	0.50–395
BUN (mg/dL)	45.33 ± 20.36	9–120
Creatinine (mg/dL)	0.99 ± 0.25	0.30–1.90
AST (u/L)	46.40 ± 22.69	8–174
ALT (µ/L)	37.16 ± 24.65	6–134
ALP (µ/L)	206.31 ± 95.64	29–657
WBC (109/L	10.43 ± 7.23	0.8–75
Haemoglobin (g/dL)	13.10 ± 2.22	5.50–19.50
Platelets	214.09 ± 89.54	3–486
Lymphocytes (%)	11.74 ± 6.91	0.80–40.80

CRP, C-reactive protein; SD, standard deviation.

levels. The results comparing TSS in patients with normal albumin and those with hypoalbuminemia are reported as follows (Table 3). Although the initial measurement revealed lower TSS levels in patients with normal albumin, this difference lacked statistical significance (Table 3).

TSS levels were compared among patients with varying degrees of hypoalbuminemia in Table 4. As shown, there was no significant difference in TSS levels between patients with varying degrees of hypoalbuminemia and normal individuals ($P > 0.05$), but TSS levels are significantly higher in living

Table 2. Comparison of serum albumin levels in survivors and non-survivors.

Parameters	Survivors (mean ± SD)	Non-survivors (mean ± SD)	95% CI for the difference between survivors and non-survivors	*P*-value	Cohen's *d*
First albumin (g/dL)	3.30 ± 0.35	3.09 ± 0.51	(0.07, 0.35)	0.003	0.43
Second albumin (g/dL)	3.17 ± 0.41	2.81 ± 0.53	(0.11, 0.77)	0.006	0.72
TSS on first CT	13.20 ± 5.24	13.11 ± 5.63	(−1.96, 0.63)	0.934	0.02

CT, computed tomography; TSS, total severity score; SD, standard deviation.
Albumin levels in the initial and subsequent measurements are significantly higher in living individuals compared to deceased individuals.

Table 3. Comparison of TSS and serum albumin.

Parameters	Hypoalbuminemia	Normal serum albumin	95% CI for the difference	*P*-value	Cohen's *d*
TSS on first CT scan (mean ± SD)	13.42 ± 5.24	11.71 ± 6.68	(−4.13,0.72)	0.163	−0.31

CT, computed tomography; SD, standard deviation; TSS, total severity score in lung CT.

Table 4. Comparison of TSS levels among degrees of hypoalbuminemia.

	Hypoalbuminemia						Normal Serum albumin (*n* = 36)		*P*-value	Eta squared
	Severe (*n* = 3)		Moderate (*n* = 71)		Mild (*n* = 86)					
TSS on first CT scan	15.67 ± 1.53		13.08 ± 5.76		13.62 ± 4.85		15.67 ± 1.53		0.312	0.02
Comparison between	Alive	Expired (*n* = 3)	Alive (*n* = 6)	Expired (*n* = 65)	Alive (*n* = 21)	Expired (*n* = 65)	Alive (*n* = 10)	Expired (*n* = 26)		
TSS on first CT scan	-	15.67 ± 1.53	16.83 ± 2.32	12.74 ± 5.87	12.29 ± 5.56	14.05 ± 4.57	12.56 ± 4.98	11.42 ± 7.23		
P-value	-		0.005		0.150		0.609			
Eta squared	-		0.720		−0.365		0168			

CT, computed tomography; TSS, total severity score.

Table 5. Logistic regression results.

Unadjusted logistic regression				Adjusted logistic regression				
Variables	Coefficient	OR	*P*-value	Variables	Coefficient	OR	95% CI	*P*-value
Gender (male)	−0.27	0.77	0.475	Age (years)	0.01	1.01	(0.99, 1.04)	0.262
Age (years)	0.02	1.02	0.060	Hypertension	0.53	1.69	(0.76, 3.79)	0.198
Diabetes	0.09	0.95	0.794	Albumin	−0.92	0.39	(0.18, 0.90)	0.027
COPD	0.29	1.10	0.615					
IHD	0.39	1.48	0.361					
Hypertension	0.62	1.86	0.103					
Intubation	−0.31	0.89	0.632					
Albumin	−0.95	0.39	0.020					
CT score	0.00	1.00	0.998					
CRP	0.002	1.002	0.481					

COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CT, computed tomography.

patients compared to deceased patients within the moderate albumin deficiency subgroup.

After adjusting for underlying diseases and potential confounders in the logistic regression model, each one-unit increase in serum albumin was associated with a 61% reduction in the odds of death (OR = 0.39, 95% CI: (0.18, 0.90) and *P* = 0.027) (Table 5).

Discussion

In this study, we investigated the prevalence of hypoalbuminemia among critically ill COVID-19 patients admitted to the ICU and its association with pulmonary involvement severity and patient outcomes. Hypoalbuminemia was highly prevalent, affecting nearly three-quarters of patients. While no significant correlation was found between serum albumin levels and chest CT severity scores, lower albumin concentrations were significantly associated with increased mortality. Logistic regression analysis confirmed that a 1-unit increase in serum albumin was associated with a 61% reduction in the odds of death.

Our findings align with prior studies reporting hypoalbuminemia as a predictor of poor outcomes in COVID-19 patients (8, 13, 14). Baig et al. (15) demonstrated that albumin levels measured during ICU admission were significantly lower in deceased patients, with stronger predictive value for mortality than CRP. Similarly, Huang et al. (8) reported hypoalbuminemia rates of 38%, 71% and 82% among patients with mild, severe and fatal disease, respectively, attributing this to cytokine storm-induced hepatic dysfunction. These results support the notion that hypoalbuminemia reflects systemic inflammation and physiological stress rather than direct pulmonary injury. Conversely, Acharya et al. (4) found no significant association between albumin and disease severity, highlighting heterogeneity across populations and study designs.

The absence of a significant correlation between albumin levels and CT severity in our cohort suggests that hypoalbuminemia may serve as a systemic biomarker of disease severity and mortality risk, rather than a direct indicator of radiological lung involvement. Albumin plays a critical role in maintaining oncotic pressure, modulating immune responses and preserving endothelial integrity (16–18). Severe COVID-19 may lead to endothelial dysfunction, capillary leakage and hepatic impairment, all contributing to decreased serum albumin levels. However, our data do not provide sufficient grounds for pathophysiological inferences beyond these associations, nor do they justify therapeutic recommendations such as albumin supplementation.

Several limitations should be acknowledged. First, this was a single-centre study with a relatively small sample size, which may limit generalizability. Second, all patients were admitted to the ICU, representing a severely ill population and potentially introducing selection bias. Third, albumin levels were measured only at baseline and the second week, without longitudinal follow-up. Another limitation of this study was the presence of only one radiologist. Finally, unmeasured confounding factors may have influenced the observed associations.

Conclusion

In summary, hypoalbuminemia was highly prevalent among ICU-admitted COVID-19 patients and independently associated with increased mortality, but not with radiological severity. These findings suggest that serum albumin may serve as a prognostic marker for mortality risk rather than a direct indicator of pulmonary involvement. Future multi-centre studies with larger cohorts and longitudinal measurements are warranted to clarify the role of albumin in COVID-19 outcomes.

Author Contributions

F.A: Literature Search, Design; MA.J.M: Data Collection, Writing Manuscript; F.R: Concept, Design, Critical Review; E.Sh.E: Analyzing and Processing, Writing Manuscript; All authors read and approved the final version of the article.

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Informed consent statement

This study used only patient information available in the records and is in line with the Declaration of Helsinki.

Conflicts of interest

The authors declare that they have no conflicts of interests.

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