Original Article

Hypoalbuminemia and its Relation with Acute Respiratory Distress Syndrome and In-Hospital Mortality in Intensive Care Unit Patients

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ABSTRACT

Objective: To evaluate the association of hypoalbuminemia with acute respiratory distress syndrome (ARDS), in-hospital mortality and length of hospital stay in intensive care unit (ICU) patients and to determine the relation of ARDS with demographics and worst clinical outcomes.

Methodology: This cross-sectional study was done at the Federal Government Polyclinic Hospital, Islamabad after ethical approval. The study duration was 8 months from March 2024 to October 2024. After taking informed consent from patients or their attendants, 350 patients admitted to the medical ICU were included using non-probability convenience sampling technique. The demographic details of the patients, their co-morbidities and primary diagnoses were noted. The serum samples of the patients were sent to the laboratory for estimation of serum albumin levels. Patients were allocated to group I having serum albumin <3.5 mg/dl (n=210) and Group II with serum albumin levels >3.5 mg/dl (n=140). The outcomes assessed were the frequency of ARDS, length of ICU stay, and in-hospital mortality. The statistical analysis was done by the Statistical Package for the Social Sciences (SPSS) version 25.

Results: Out of 350 patients, 136(38.9%) developed ARDS; 34.3% had low albumin levels whereas, only 4.6% had normal serum albumin. In-hospital mortality occurred in 30% of the patients, out of which 20.3% and 9.7% of the patients had low and normal serum albumin, respectively. The mean length of ICU stay was 12.2±1.4 days and 8.9±2.5 days in group I and group II, respectively. These findings were statistically significant. Acute respiratory distress syndrome has a significant association with age, risk factors, serum albumin levels, length of ICU stay, and in-hospital mortality.

Conclusion: Acute respiratory distress syndrome, in-hospital mortality, and length of hospital stay have a significant relation with hypoalbuminemia in ICU patients. There was a significant association of acute respiratory distress syndrome with advanced age, risk factors, in-hospital mortality, and length of hospital stay.

Keywords: Hypoalbuminemia. Respiratory distress syndrome. Hospital mortality.

INTRODUCTION

Hypoalbuminemia is characterized by albumin below 3.5 mg/dL in the serum. Albumin has many important physiological roles in our body. It helps in the preservation of colloid osmotic pressure and the transport of various substances such as proteins & fatty acids. It modulates inflammatory response due to its antioxidant properties. It also acts as an anticoagulant by preventing the aggregation of platelets and inhibiting the synthesis of clotting factors by the liver.[1,2] Hypoalbuminemia is a very common and consequential abnormality in patients admitted to the intensive care unit. It can occur owing to reduced synthesis by the liver, increased breakdown, and leakage from capillaries due to systemic inflammation.[3] It is linked to unfavorable outcomes including increased morbidity, ARDS, prolonged hospital stay, and mortality.[4]

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Acute respiratory distress syndrome is a serious inflammatory pulmonary disorder characterized by diffuse alveolar damage and non-cardiogenic pulmonary edema. The condition is of serious concern owing to the high mortality rate and extrapulmonary multiorgan involvement with lethal outcomes.[5,6] The disease is a global health challenge with a variable prevalence ranging from 7.2 to 78.9 cases per 100,000 people annually. The disease contributes to around 45% of in-hospital deaths and 30% of deaths at 28 days.[7] Low levels of serum albumin levels aggravate the disease by decreasing plasma oncotic pressure. This facilitates leakage of fluid into the alveolar space, impairing gas exchange.[5,6] The disease has multiple predisposing factors such as sepsis, pneumonia, smoking, inhalation injury, etc.[8] The prevalence of ARDS has increased in the last few years. This may be attributed to the availability of advanced and better diagnostic modalities. It has been found in ICU and critically ill patients requiring mechanical ventilation.[9]

These findings underscore the clinical importance of monitoring albumin levels in ICU patients who are at high risk of developing ARDS. Hypoalbuminemia is emerging as a pathophysiological factor and a prognostic marker in ARDS, warranting further investigation and potential therapeutic

considerations. A study done in Pediatric ICU patients in Pakistan reported that hypoalbuminemia is linked to an increased risk of mortality.[10] So, this study was designed to determine the association of hypoalbuminemia in ICU patients with ARDS, in-hospital mortality and length of ICU stay. In addition, the study also determined the relation of ARDS with demographic variables, predisposing factors, length of hospital stay, and in-hospital mortality. As far as we know, there hasn't been any research done on adult ICU patients in Pakistan investigating the relation between hypoalbuminemia and ARDS, in-hospital mortality & length of hospital stay.

METHODOLOGY

This cross-sectional study was done at the Federal Government Polyclinic Hospital, Islamabad after ethical approval (Letter No. FGPC/1/12/2024/E-Committee, 16-01-2024). The study duration was 8 months from March 2024 to October 2024. The sample size of 295 was estimated using 95% confidence interval, 5% margin of error and 26% frequency of ARDS in ICU patients.[11] Three-hundred and fifty (350) patients admitted to the medical ICU were enrolled using non-probability convenience sampling after taking informed consent from patients or their attendants. The demographic details of the patients, their co-morbidities and primary diagnoses were noted. Blood samples of the patients were taken and their serum was sent to the laboratory for estimation of serum albumin levels. Patients were allocated to group I having serum albumin <3.5 mg/dl (n=210) and group II with serum albumin levels > 3.5 mg/dl (n=140). The primary outcomes assessed were the frequency of ARDS and in-hospital mortality in these patients. The secondary outcome was the length of ICU stay. Acute respiratory distress syndrome was diagnosed based on Berlin's definition.[12] The association of ARDS was also seen with age, risk factors, hypoalbuminemia, in-hospital mortality and length of ICU stay.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS) version 25 was used for data analysis. For categorical variables, frequency & percentage were used and for numeric variables, mean & standard deviation were used. Independent t-test, Chi-square test, and Fisher's exact test were used to determine the association of hypoalbuminemia and ARDS with categorical and numeric variables, respectively. The p-value of ≤0.05 was statistically significant.

RESULTS

The majority of the patients were 51-60 years old (34.3%) followed by 61-70 years of age (32.8%). Most of the patients were males (55.4%). However, no significant difference was seen in age and gender between the two groups. The majority of the ICU patients (81.4%) had a predisposing factor, whereas 18.6% had no predisposing factor. The most common predisposing factor was sepsis (29.2%) followed by pneumonia (16.6%) and smoking (15.7%), aspiration (11.4%), pancreatitis (3.1%), and multiple transfusions (2%). The other less common risk factors were decompensated chronic liver disease (DCLD) (1.7%) and drug overdose (1.7%).

Out of 350 ICU patients, 136(38.9%) developed ARDS. Most of the patients with ARDS (34.3%) had low albumin levels whereas, only 4.6% had normal serum albumin. In-hospital mortality occurred in 30% of the patients, out of which 20.3% and 9.7% of the patients had low and normal serum albumin, respectively. The mean duration of ICU stay was 12.2±1.4 days in group I and 8.9±2.5 days in group II. There was a significant difference in the frequency of ARDS, in-hospital mortality and length of ICU stay between patients in groups I and II (p-value ≤0.05). The outcomes of the patients are given in Table 1.

The association of ARDS was also seen with various variables. Acute respiratory distress syndrome has a significant association with age, the disease is most common in advanced age. The majority of the patients with ARDS had a predisposing factor, with statistical significance. The most frequent risk factors seen in ARDS patients were sepsis (18.6%) and pneumonia (8.6%) followed by aspiration (4.3%), smoking (3.7%), pancreatitis (1.4%), multiple transfusions (0.6%), drug overdose (0.6%) and DCLD (0.3%). In-hospital mortality occurred in 24% of the ARDS patients, with a significant p-value. The length of ICU stay was 15.3±1.2 days in ARDS and 8.4±2.1 days in patients without ARDS with a p-value <0.0001 (Table 2).

DISCUSSION

Acute respiratory distress syndrome (ARDS) is a life-threatening disorder with a high mortality rate. Hypoalbuminemia is a poor prognostic factor in ARDS and other critically ill patients. It decreases the plasma oncotic pressure further increasing the extravasation of fluid into pulmonary circulation and worsening hypoxia.[13]

Table 1: Comparison of Outcomes between Groups I and II

Outcomes		Group I	Group II	Total	p-value
ARDS (Frequency & Percentage)	Present	120(34.3%)	16(4.6%)	136(38.9%)	<0.00001*
	Absent	90(25.7%)	124(35.4%)	214(61.1%)	
In-Hospital Mortality (Frequency & Percentage)	Present	71(20.3%)	34(9.7%)	105(30%)	0.05*
	Absent	139(39.7%)	106(30.3%)	245(70%)	
Length of ICU Stay (Days)	Mean±SD	12.2±1.4	8.9±2.5	-	<0.0001*

*Significant p-value

Table 2: Association of ARDS with Various Variables

Variables		ARDS		Total	p-value
		Present	Absent		
Age Groups (Years) (Frequency & Percentage)	<40	2(2.3%)	43(10.6%)	45(12.9%)	<0.00001*
	41-50	3(3.4%)	37(8%)	40(11.4%)	
	51-60	62(18.3%)	58(16%)	120(34.3%)	
	61-70	58(14%)	57(18.8%)	115(32.8%)	
	71-80	11(6%)	19(2.6%)	30(8.6%)	
Gender (Frequency & Percentage)	Male	74(21.1%)	120(34.3%)	194(55.4%)	0.76
	Female	62(17.7%)	94(26.9%)	156(44.6%)	
Risk Factors for ARDS (Frequency & Percentage)	Present	133(38%)	152(43.4%)	285(81.4%)	0.05*
	Absent	3(0.9%)	62(17.7%)	65(18.6%)	
Serum Albumin (Frequency & Percentage)	Low	120(34.3%)	90(25.7%)	210(60%)	<0.00001*
	Normal	16(4.6%)	124(35.4%)	140(40%)	
In-Hospital Mortality (Frequency & Percentage)	Dead	84(24%)	21(6%)	105(30%)	<0.00001*
	Alive	52(14.9%)	193(55.1%)	245(70%)	
Length of ICU Stay (Days)	Mean±SD	15.3±1.2	8.4±2.1	-	<0.0001*

*Significant p-value

Our study showed that 60% of the patients had low albumin levels with no significant difference in age and gender between those with low and normal serum albumin. Similarly, McNeil et al. reported that 53.1% of patients had low albumin levels and no significant difference was found in age or gender between the groups.[11] Our results showed that 81.4% of the patients had a predisposing factor, sepsis being the most common (29.2%). Other factors were pneumonia (16.6%), smoking (15.7%), aspiration (11.4%), pancreatitis (3.1%), multiple transfusions (2%), DCLD (2%) and drug overdose (2%). Similar findings were reported in another study in which 84% of the patients had at least one risk factor. Their frequency was as follows: sepsis (39%) pneumonia (18%), multiple blood transfusions (10%), aspiration (9%), drug overdose (3%) and pancreatitis (2%).[11] Our results showed that 38.9% of the ICU patients developed ARDS. Another study revealed that 26% of the patients admitted to the ICU developed ARDS.[11] The albumin levels were much lower in most of the patients with ARDS (34.3%) in our study. Our study revealed a statistically significant association of ARDS with low albumin levels. In another study conducted by Kumar et al., 42.4% and

8.3% of the patients with low and normal albumin levels developed ARDS. The difference was significant with a p-value of <0.001.[14] Another study showed a significant link between low albumin levels and ARDS.[11]

Our study revealed in-hospital mortality in 30% of the patients with 20.3% of the patients having low albumin levels. This demonstrated a significant relation between low albumin levels with in-hospital mortality. In a study by Zhang et al., 28-day mortality occurred in 8.86% of the admitted ICU patients but this study recruited only dialysis patients and they also observed a significant association between low albumin levels and in-hospital mortality.[15] Ozgungor et al. studied albumin levels as prognostic markers in ICU mortality and found that 28-day mortality in ICU patients can be predicted by 48 hours post-admission serum albumin levels.[16] A study by Maemum et al. reported an increased number of deaths in hospitalized patients with low albumin levels.[17] A study determined the association between lactate-to-albumin ratio (LAR) and deaths in ARDS patients. The study reported that the incidence of deaths in hospitalized patients was significantly higher in patients with higher

LAR.[18] Another study determined the significant relation between hypoalbuminemia and 28-day mortality in trauma patients, which was statistically significant.[14] A retrospective cohort study reported that administration of albumin in ARDS patients resulted in reduced mortality at 28 days as compared to those patients who did not receive albumin.[19] The length of hospital stay was significantly greater in patients with low albumin levels (p-value <0.0001). Our results were in accordance with the results of another study.[11]

Our results revealed a significant association of ARDS with age, predisposing factors, hypoalbuminemia, in-hospital mortality and length of ICU stay. The disease was frequent in advanced age, similar to another study.[20] Most of the patients who developed ARDS had a predisposing factor, with sepsis and pneumonia being the most common. The result of a meta-analysis also revealed sepsis, pulmonary infection and pancreatitis as the most common significant risk factors for ARDS.[21] In-hospital mortality and length of ICU stay were significantly greater in patients with ARDS, similar to another study.[22]

CONCLUSION

Our findings showed ARDS in 38.9% of the ICU patients, being significant in patients with hypoalbuminemia (34.3%). In-hospital mortality occurred in 30% of the patients, 20.3% had low serum albumin and 24% of the patients had ARDS with statistical significance. The length of ICU stay was significantly higher in patients with hypoalbuminemia and ARDS. There was a significant association of acute respiratory distress syndrome with advanced age and risk factors.

LIMITATIONS & RECOMMENDATIONS

It was a single-centered study. The patients were assessed for in-hospital mortality. Follow-up was not done for hospital readmissions, 28-day mortality, and long-term mortality. Studies should be conducted assessing these outcomes in the future. Furthermore, multi-centered studies should also be done. Careful monitoring of serum albumin is recommended in ICU patients and its administration should be evaluated in the light of the findings of clinical trials.

Authors' Contributions:
S.G: Conceptualization of the study, development of methodology, and manuscript drafting.
M.T: Data collection from ICU records and laboratory coordination.
R.A.J: Literature review, referencing, and formatting of the manuscript.
H.A: Statistical analysis and interpretation of findings.
M.N: Ethical approval processing and technical editing.
M.M: Critical revision, proofreading, and final approval of the manuscript.

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