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Diagnostic Accuracy of Albumin Levels in Predicting Colistin-Induced Nephrotoxicity in Critically ill Patients in the Intensive Care Unit

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ABSTRACT

Introduction: Colistin is an antibiotic utilized for the treatment of drug-resistant bacterial infections. Despite its efficacy, colistin is associated with significant nephrotoxicity, reported in up to 40% of cases. Hypoalbuminemia has been identified as a potential risk factor for acute kidney injury (AKI), but its predictive role in colistin-induced nephrotoxicity remains unclear. This study examines the relationship between hypoalbuminemia and the occurrence of AKI in critically ill patients undergoing colistin treatment.

Methods: This retrospective cohort study was conducted in a tertiary intensive care unit between 2020 and 2022. Patients aged 18 years or older who received colistin for at least 48 hours were included, excluding those with chronic kidney disease, high-dose vasopressor use, or advanced liver failure. Data on demographics, clinical characteristics, and laboratory findings were collected. AKI was diagnosed using KDIGO criteria, and hypoalbuminemia was defined as albumin <2.5 g/dL. Statistical analyses, including logistic regression, were performed using SPSS 26.0, with significance set at $p<0.05$.

Results: Among 104 patients, 49 (47.1%) developed AKI. Patients with AKI were older (mean age 66.7 vs. 59.1 years, $p=0.016$) and had longer durations of hypoalbuminemia (median 18 vs. 6 days, $p<0.001$). Hypoalbuminemia at the start of colistin therapy was significantly associated with AKI ($p<0.001$). Logistic regression identified low albumin levels as an independent predictor of AKI (odds ratio 0.14, $p=0.005$). Mortality was higher in the AKI group (57% vs. 43%, $p=0.003$).

Conclusion: Hypoalbuminemia is a significant predictor of colistin-induced AKI. Early identification and management of hypoalbuminemia may reduce nephrotoxicity and improve outcomes in critically ill patients receiving colistin therapy. Further multicenter studies are recommended to validate these findings.

Keywords: Hypoalbuminemia, colistin, nephrotoxicity

Introduction

Colistin, or polymyxin E, is an antibiotic first discovered in Japan in 1949 and produced by *Paenibacillus polymyxa*, a gram-positive bacterium. It disrupts gram-negative bacterial membranes by binding to lipid A in lipopolysaccharides and displacing calcium and magnesium ions, increasing membrane permeability and causing cell death. Among the five polymyxins (A-E), only polymyxin B and colistin are used clinically. Initially introduced for human and veterinary use in 1952, colistin was largely replaced by less toxic alternatives, but resurged as a last-resort treatment against multidrug-resistant gram-negative bacteria. The European Medicines Agency classifies colistin as a category B ("Restrict") antibiotic, recommended only when other treatments are ineffective (1).

Human albumin (albumin) is the principal protein in the blood of healthy individuals, with a concentration range of 3.5-5 g/dL. In healthy individuals, the liver synthesizes approximately 10-15 grams of albumin per day. The plasma half-life of albumin ranges from 12 to 19 days. Albumin plays a crucial role in maintaining plasma oncotic pressure, accounting for approximately 70-80% of the total oncotic pressure, thereby regulating fluid exchange between body compartments. This oncotic pressure is influenced by both the osmotic effect of the molecule's mass and its negative charge, which attracts sodium and, consequently, water (2).

The most notorious and feared side effect of colistin therapy is nephrotoxicity, which is reported in the literature, at rates approaching 40%.3 The exact mechanism underlying colistin-induced nephrotoxicity remains incompletely understood, but it is believed to involve direct proximal tubular cell damage and oxidative stress, ultimately leading to AKI. Various risk factors have been proposed to predict and prevent AKI during colistin therapy. Among patient-related risk factors, male sex, advanced age, obesity, diabetes mellitus, impaired liver function tests, and hyperbilirubinemia have been identified as contributors to increased susceptibility. Additionally, treatment-related factors such as septic

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shock, prolonged therapy duration, high-dose colistin administration, concurrent use of nephrotoxic agents, and multiple antibiotics or drugs use further elevate the risk (3,4). Additionally, hypoalbuminemia has been associated with deterioration in renal function (4,5).

Consequently, efforts have been made both to explore protective measures against nephrotoxicity and to develop new antibiotics (6). Although newly developed antibiotics like the combination of ceftazidime-avibactam are considered safer in terms of nephrotoxicity, their use in developing countries like ours is subject to stringent criteria (7). Therefore, colistin treatment remains a vital option (8). The aim of the study is to determine whether albumin levels and the duration of hypoalbuminemia can be used to predict colistin-induced nephrotoxicity.

Methods

This retrospective cohort study was conducted in a tertiary intensive care unit (ICU) between 2020 and 2022. Patients aged 18 years or older who received colistin therapy for at least 48 hours were included. Inclusion criteria were a baseline glomerular filtration rate (GFR) of ≥60 mL/min/1.73m² to ensure normal renal function before colistin initiation, AKI within the 48 hours prior to colistin therapy, and no history of chronic kidney disease (CKD) or prior renal replacement therapy (RRT). Exclusion criteria were as follows: pre-existing CKD with a baseline GFR below 60 mL/min/1.73 m², high-dose vasopressor use (greater than 0.25 mcg/kg/min norepinephrine or equivalent), advanced liver failure (Child-Pugh C), and patients already receiving RRT at baseline. The study was reviewed by the Non-Interventional Research Ethics Committee of University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital (approval no: 2011-KAEK-25 2023/02-09, date: 08.03.2023).

Demographic characteristics, clinical data, and laboratory values were retrieved from electronic medical records. Data included age, sex, comorbidities (diabetes, hypertension, cardiovascular disease, COPD), infection site (pulmonary, urinary, bloodstream), and mortality. Laboratory parameters included albumin levels, urea, creatinine, and inflammatory markers. GFR was calculated at baseline; however, it was not recalculated at the stage of AKI development due to the inability to obtain a stable creatinine level, which would result in inaccurate estimations (9).

Patients who developed AKI were identified based on their baseline creatinine levels, following the KDIGO recommendations. Accordingly, AKI was defined as an increase in serum creatinine of ≥0.3 mg/dL within 48 hours or an elevation to ≥1.5 times the baseline within the same period. The severity of AKI was determined based on the KDIGO staging system (9).

Hypoalbuminemia was defined as a serum albumin level <2.5 g/dL. The duration of hypoalbuminemia was calculated as the number of days the patient's albumin level remained below this threshold before the initiation of colistin therapy.

Antibiotics administered concomitantly with colistin were recorded. Patients who received a known nephrotoxic antibiotic (e.g., vancomycin) simultaneously with colistin initiation were excluded from the study. However, if such antibiotics had been administered at least 48 hours before colistin initiation, then their use was documented, and these patients were included in the study. Similarly, patients who had received nephrotoxic drugs such as angiotensin II receptor blockers, angiotensin-converting enzyme inhibitors, contrast agents, or calcineurin inhibitors within the last 48 hours were excluded from the study. However, those with a history of use of these drugs beyond this timeframe were included.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. Normally distributed data were reported as means with standard deviations and compared using the independent samples t-test. Non-normally distributed data were expressed as medians with interquartile ranges (IQR) and analyzed using the Mann-Whitney U-test. Categorical variables were presented as frequencies and percentages, and differences between groups were assessed using the chi-square test or Fisher's exact test. A binary logistic regression was performed to identify predictors of AKI, with AKI as the dependent variable (binary AKI present or absent). Independent variables included age, albumin levels at the start of colistin treatment, and the duration of hypoalbuminemia. Odds ratios (OR) with 95% confidence intervals were reported, with a p-value <0.05 considered statistically significant.

Results

As per the study, by AKI stages, 55 patients (52.9%) did not develop AKI, 7 patients (6.7%) were in stage 1 AKI, 19 patients (18.3%) were in stage 2 AKI, and 23 patients (22.1%) were in stage 3 AKI.

Patients who developed AKI were significantly older, with a mean age of 66.73±14.722 years, compared to patients who did not develop AKI, with a mean age of 59.09±16.798 years; p=0.016. There was no significant difference in the severity scores regarding SAPS, APACHE-II, and GKS, with p-values of 0.679, 0.424, and 0.194, respectively.

The albumin levels at admission, based on laboratory values, were not significantly different between the two groups (p=0.51). However, the AKI group had significant hypoalbuminemia at the start of therapy, 2.1 (IQR 2.000-2.400) g/dL compared to the non-AKI group of patients at 2 (1.680-2.200) g/dL, with a p-value of <0.001. The duration of hypoalbuminemia was longer in patients with AKI development compared to those without (median 18 days vs. 6 days, p<0.001). Among those who developed AKI, 37 (75.5%) did not receive RRT, 10 (20.4%) received continuous veno-venous hemodiafiltration (CVVHDF), and 2 (4.1%) received intermittent hemodialysis (IHD). After the discontinuation of colistin, 43 (87.7%) of the patients did not require RRT; 5 (10.2%) continued to require CVVHDF; and 1 (2.1%) was treated with IHD. During the treatment, 29 (27.9%) patients died. At the three-month follow-up, among all the patients, only 1 (1.0%) patient received IHD because of permanent kidney damage; 53 (51%) died, and 50 (48%) recovered sufficiently, not to require RRT. On the 14th day post-treatment, 35 (71.4%) of the patients who developed AKI recovered fully. Creatinine levels remained up to twice the baseline in 4 (6.5%) patients, between two to three times the

baseline in 7 (11.3%) patients, and more than three times the baseline in 6 (9.7%) patients. Table 1 provides a comparison of demographic characteristics, comorbidities, and infection sites.

Figure 1 shows the albumin level at the time of antibiotic initiation and the duration of hypoalbuminemia (in days) following the initiation of antibiotics. The best cut-off point for the duration of hypoalbuminemia, as determined by the receiver operating characteristic (ROC) curve analysis, was found to be 9.50 days. At this threshold, the sensitivity of the model is 73.5%, and the 1-specificity ratio is 36.4%.

The optimal cut-off value for the initial albumin level at the start of antibiotic treatment, as determined by the ROC curve analysis, was found to be 1.95 g/dL. At this threshold, the sensitivity of the model is 53.1%, and the 1-specificity is 14.5%.

The baseline demographic and clinical characteristics of the study population, including comorbidities and causes of ICU admission, are detailed in Table 1. The distribution of infection sites and isolated microorganisms is presented in Table 2. The distribution of concomitant medications potentially associated with nephrotoxicity between patients with and without AKI is presented in Table 3. Laboratory findings, including serum albumin, urea, creatinine, and inflammatory markers, are summarized in Table 4. As shown in Table 5, logistic regression analysis identified albumin level at the start of treatment as an independent predictor of AKI development.

Table 6 displays the proportion of patients across different AKI stages.

Table 1. Patient characteristics

Characteristics and risk factors	Not developed AKI	Developed AKI	p-value
Patient (%)	55 (52)	49 (48)	
Males n (%)	41 (40)	31 (30)	0.213
Females n (%)	14 (13)	18 (17)	0.213
Age, years, mean ± SD**	59.09±16.798	66.73±14.722	0.015
SAPS, mean ± SD**	42.42±14.004	43.48±14.732	0.679
APACHE-II, median (IQR)*	14 (11.00-25.90)	17 (17.00-31.20)	0.424
GKS, median (IQR)*	13 (0.00-15.00)	10 (0.00-15.00)	0.194
Comorbidity, n (% total case)*** Diabetes mellitus Hypertension Coronary artery disease COPD Cancer Stroke	 18 (17.3) 26 (25.0) 15 (14.5) 8 (7.7) 12 (11.5) 9 (8.7)	 17 (16.3) 25 (24.05) 14 (13.4) 7 (6.7) 11 (10.6) 8 (7.7)	 0.832 0.703 0.866 0.970 0.747 0.996
Cause of admission, n (% total case)*** Infection COVID-19 Other infection Medical Surgery	 37 (35.58) 22 (21.15) 15 (14.42) 4 (3.85) 14 (13.46)	 31 (29.81) 21 (20.19) 10 (9.62) 9 (8.65) 9 (8.65)	 0.668 0.768 0.413 0.088 0.358

p-values were determined using independent samples t-test for normally distributed continuous variables, Mann-Whitney U test for non-normally distributed continuous variables, and Fisher's exact test or chi-square test for categorical variables
*Non-normal distribution, mean value and the interquartile range (IQR) is provided
**Normal distribution,median value and standard deviation (SD) is provided, Mv: Mechanical ventilation
***Chi-square test was conducted
COPD: Chronic obstructive pulmonary disease, ACEI: Angiotensin-converting enzyme inhibitors, NSAID: Non-steroidal anti-inflammatory drugs, ARB: Angiotensin II receptor blockers, COVID-19: Coronavirus disease-19, AKI: Acute kidney injury. The percentages are calculated based on the total number of patients

Table 2. Infection site and microorganism

Characteristics and risk factors	Not developed AKI	Developed AKI	p-value
Site of infection, n (% total case)***			
Lung***	27 (26.0)	22 (21.2)	0.669
Urinary***	18 (17.3)	15 (14.4)	0.817
Cranial****	0 (0.0)	2 (1.9)	0.220
Bloodstream****	3 (2.9)	5 (4.8)	0.471
Other****	2 (1.9)	0 (0.0)	0.497
Unkown ****	5 (4.8)	5 (4.8)	>0.99
Patogen, n (% total case)			
Negative ****	6 (5.8)	4 (3.8)	0.746
*Acinetobacter baumannii****	30 (28.8)	22 (21.2)	0.326
*Klebsiella pneumonia****	15 (14.4)	22 (21.2)	0.061
*Pseudomonas aeruginosa*****	4 (3.8)	1 (1.0)	0.367

p-values were determined using independent samples t-test for normally distributed continuous variables, Mann-Whitney U test for non-normally distributed continuous variables, and Fisher's exact test or chi-square test for categorical variables
***Chi-square test was conducted
****Fisher's exact test was used due to the small sample size (n<5)
AKI: Acute kidney injury

Table 3. Drugs

Characteristics and risk factors	Not developed AKI	Developed AKI	p-value
Drugs***	42	49	0.672
ACEI	2 (1.92)	4 (3.85)	NE
Beta-lactam ***	23 (22.2)	22 (21.15)	>0.476
Quinolone	3 (2.88)	3 (2.88)	NE
Vancomycine	4 (3.85)	2 (1.92)	NE
Fosfomycin	4 (3.85)	0 (0.0)	NE
Aminoglycoside	2 (1.92)	0 (0.0)	NE
Amphotericin	1 (0.96)	0 (0.0)	NE
NSAID	0 (0.0)	1 (0.96)	NE
ARB	2 (1.92)	2 (1.92)	NE
Diuretic	3 (2.88)	2 (1.92)	NE
Contrast media	0 (0.0)	1 (0.96)	NE
Statin	2 (1.92)	2 (1.92)	NE
Antidepressant (fluoxetine)	1 (0.96)	1 (0.96)	NE
Immunosuppressant (calcineurin inhibitor)	1 (0.96)	0 (0.0)	NE
Steroid	1 (0.96)	1 (0.96)	NE
Clopidogrel	2 (1.92)	2 (1.92)	NE

p-values were determined using independent samples t-test for normally distributed continuous variables, Mann-Whitney U test for non-normally distributed continuous variables, and Fisher's exact test or chi-square test for categorical variables. Due to the small sample sizes, the chi-square test was applied generally to all drugs and specifically to the beta-lactam drug group, which had a sufficiently large sample size
***Chi-square test was conducted
NSAID: Non-steroidal anti-inflammatory drugs, ARB: Angiotensin II receptor blockers, ACEI: Angiotensin-converting enzyme inhibitors, AKI: Acute kidney injury, NE: Not evaluated

Table 4. Laboratory results

Characteristics and risk factors	Not developed AKI	Developed AKI	p-value
Admission albümin ± SD**	2.967±0.4941	2.743±0.6602	0.51
Albumin at the start of therapy median (IQR)*	2.1 (2.000-2.400)	2 (1.680-2.200)	<0.001
Hypoalbuminemia duration (days) (IQR)*	6 (1.00-10.00)	18 (6.00-22.70)	<0.001
Urea, median (IQR) (mg/dL)*	50.5 (39.25-50.50)	56 (35.00-85.00)	0.534
Creatinin, mean ± SD (mg/dL)**	0.7433±0.25655	0.8482±0.48588	0.165
GFR (mL/min/1.73 m^2)*	120 (87-120)	96.75 (73.75-120)	0.058
CRP, median (IQR) (mg/dL)*	127.5 (52.10-157.00)	138 (63.60-112.00)	0.062
WBC median (IQR) (10^3/µL*	11150 (7000.00-11150.00)	9700 (6000.00-9700.00)	0.300
LDH, median (IQR) (U/L)*	325.5(265.00-325.00)	358 (265.00-365.00)	0.817
Length of stay, median (IQR), (days)*	41 (85.00-20.1.00)	54 (63.60-142.00)	0.962
Length of stay at ICU, median (IQR), (days)*	34.5 (26-55.75)	34 (25-60)	0.922
Vasopressor n (%)	23 (50)	23 (50)	0.6
MV n (%)	46 (51)	44(49)	0.358
Duration of treatment, median (IQR), (days)*	10 (7-14)	11.5 (7-14)	0.745
ICU death n (%)	44 (48)	47 (52)	0.014
28 day mortality n (%)	31(43)	41 (57)	0.003

The percentages are calculated based on the total number of patients. p-values were determined using independent samples t-test for normally distributed continuous variables, Mann-Whitney U test for non-normally distributed continuous variables, and Fisher's exact test or chi-square test for categorical variables. Due to the small sample sizes, the chi-square test was applied generally to all drugs and specifically to the beta-lactam drug group, which was considered to have a sufficiently large sample size
*Non-normal Distribution, mean value and the interquartile range (IQR) is provided
**Normal distribution,median value and standard deviation (SD) is provided
Mv: Mechanical ventilation, AKI: Acute kidney injury, GFR: Glomerular filtration rate, CRP: C-reactive protein, WBC: White blood cell, LDH: Lactate dehydrogenase, ICU: Intensive care unit

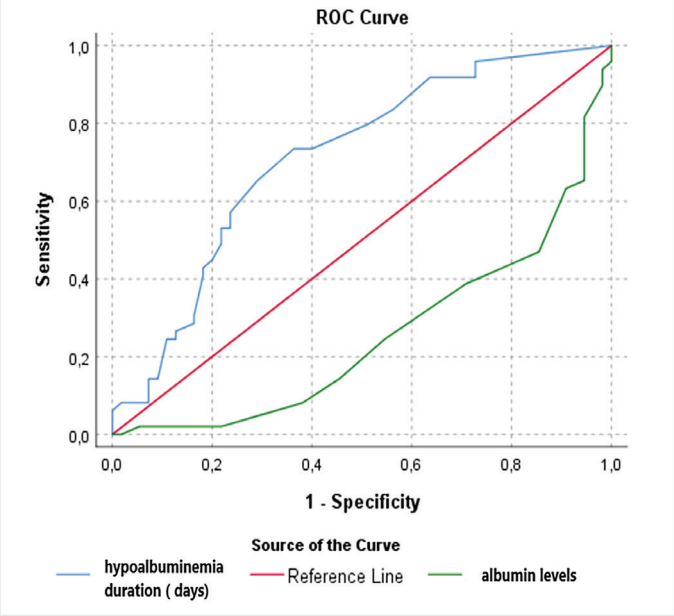

Figure 1. The albumin level at the time of antibiotic initiation and the duration of hypoalbuminemia
ROC: Receiver operating characteristic

Table 5. Binary logistic regression model

Factor	OR (CI 95%)	p-value*
Age	1.018 (0.987-1.050)	0.257
Duration of hypoalbuminemia	1.026 (0.995-1.058)	0.107
Albumin levels at treatment start	0.140 (0.035-0.556)	0.005

*The p-values were calculated using a binary logistic regression model to assess the independent impact of each factor on the development of AKI. Age, duration of hypoalbuminemia, and albumin levels at the start of treatment were included as independent variables in the model
AKI: Acute kidney injury, OR: Odds ratio, CI: Confidence interval

Table 6. AKI stages

AKI stage n (%) (total AKI patients)	Creatinin mean ± SD (mg/dL)
Stage 1 7 (14.29)	1.500±0.305
Stage 2 19 (38.78)	1.649±0.421
Stage 3 23 (46.94)	2.542±1.39

AKI: Acute kidney injury, SD: Standard deviation

Discussion

In our study, albumin levels were examined as a potential factor influencing colistin-induced nephrotoxicity in critically ill patients receiving colistin therapy in the ICU. Although albumin levels at admission were similar between the AKI and non-AKI groups, the AKI group had significantly lower albumin levels compared to the non-AKI group. The duration of hypoalbuminemia was also evaluated and found to be statistically significant; however, in logistic regression analysis, the duration of hypoalbuminemia did not contribute to the model. Another key finding of our study was that in the majority of patients who developed colistin-induced nephrotoxicity, kidney function returned to normal levels within 14 days after discontinuation of colistin. Among survivors, only one patient developed CKD requiring RRT.

Patients who received nephrotoxic agents such as vancomycin within 48 hours prior to colistin therapy initiation were excluded in order to isolate the nephrotoxic impact of colistin itself. However, patients who had received such agents more than 48 hours prior were included, and

their exposure was recorded. Despite this, due to the small number of patients who had previously received vancomycin (6), we could not perform a subgroup analysis to determine statistically its isolated impact on the development of AKI. Therefore, while we attempted to minimize the confounding effect of concomitant nephrotoxic agents, we acknowledge that prior exposure to such agents may still have contributed to the observed outcomes.

Colistin treatment is associated with nephrotoxicity rates of up to 40% (3). According to our results, AKI developed in 49 patients, accounting for 47.1% of the total study population. This highlights the critical need to identify nephrotoxicity risk factors early and implement preventive strategies to mitigate kidney damage. Several studies have investigated the development of AKI in patients receiving colistin therapy, and various colistin-associated AKI risk factors have been reported (10).

In our study, APACHE II scores did not predict AKI development. While this finding could be interpreted as an indication that there was no significant difference in disease severity and expected mortality between the AKI and non-AKI patient populations, another possible explanation could be incomplete or inaccurate patient records in a retrospective study design. The association between APACHE II scores and AKI prediction has been investigated in the literatüre (11). Moreover, it is important to note that the APACHE II score itself includes serum creatinine levels and the presence of AKI as a parameter.

Vasopressor use was not associated with an increased risk of AKI, as both AKI and non-AKI groups showed similar rates of vasopressor administration (50% in each group, p=0.6). This may be attributed to the exclusion of patients receiving high-dose vasopressors, potentially reducing the nephrotoxic hemodynamic burden. Nevertheless, the absence of an association in our study should be interpreted with caution, considering the relatively small sample size and the inability to analyze vasopressin-specific effects due to lack of dose-specific data.

This study highlights the association between colistin-induced AKI and hypoalbuminemia, demonstrating that lower serum albumin levels significantly increase the risk of nephrotoxicity. The relationship between AKI and hypoalbuminemia has been previously investigated in the literature (12). Colistin exerts nephrotoxic effects through oxidative stress, mitochondrial dysfunction, and direct tubular epithelial damage, particularly in the proximal tubules (6) albumin influences these mechanisms through three primary pathways. First, albumin is essential for maintaining plasma oncotic pressure, thereby supporting renal perfusion. Hypoalbuminemia reduces effective intravascular volume, predisposing patients to renal ischemia and further exacerbating tubular injury (13). In our cohort, this hemodynamic vulnerability likely contributed to the increased AKI rates observed in patients with prolonged hypoalbuminemia. Second, albumin possesses intrinsic antioxidant properties, acting as a buffer against ROS such as peroxynitrite and hypochlorous acid, which are central to colistin-induced tubular injury. Lower albumin levels may impair this protective mechanism, resulting in a more permissive environment for oxidative damage (14). Third, albumin binds to colistin in circulation. A reduction in serum albumin may theoretically increase the free, unbound colistin fraction, thereby amplifying its nephrotoxic potential (15,16). While our study did not measure serum colistin levels, this pharmacokinetic relationship is well supported in the literature. For instance, Sorlí et al. (15) reported that trough plasma levels of colistin correlated independently with nephrotoxicity, suggesting that free colistin is the key driver of renal injury. However, as Nation et al. (17) have pointed out, while hypoalbuminemia may lower total serum colistin concentrations (both bound and unbound), it may not significantly alter the concentration of unbound colistin, which is the toxic fraction responsible for nephrotoxicity. However, since hypoalbuminemia is also an acute-phase reactant, its association with AKI might reflect the overall severity of a patient's condition rather than a direct causal effect. Given this complexity, potential alternative explanations for the heightened risk of AKI in hypoalbuminemic patients should be explored (17). Furthermore, it remains unclear whether targeted albumin replacement in hypoalbuminemic patients can reduce nephrotoxic risk. While albumin supplementation is not routinely recommended for all ICU patients, individualized strategies in the context of high-risk nephrotoxic regimens like colistin may offer a renal-protective benefit worth investigating.

In our study, ROC analysis determined that an albumin level below 1.95 g/dL was the optimal cut-off value for predicting colistin-induced nephrotoxicity. Previous studies have established 3.2 g/dL and 2 g/dL as cut-off values for serum albumin levels (18,19). On the other hand, in a study with 102 colistin-treated patients, hypoalbuminemia was not associated with AKI (15).

To minimize confounding, patients who received nephrotoxic antibiotics concurrently with colistin were excluded, while those treated earlier were included and recorded. Given that colistin is a last-resort antibiotic, most patients receive multiple antimicrobial agents, making colistin monotherapy uncommon.

Furthermore, patients frequently receive nephrotoxic agents for various reasons before colistin initiation. ICU admissions typically involve prolonged hospital stays, making it unlikely for patients to avoid all nephrotoxic exposures before colistin therapy. To address this, a 48-hour exclusion window was established to ensure that patients who had received nephrotoxic agents within this timeframe were excluded. Patients with a history of nephrotoxic agent use prior to this period were included, with their medication history documented. This approach aimed to reduce confounding factors while maintaining the study's generalizability to real-world clinical scenarios.

Study Limitations

The retrospective nature of the design may introduce some bias connected with data collection and analysis. The small sample size might limit the generalization of our findings. Third, the study was carried out at one center and does not represent a broad population. Larger sample sizes and multicenter prospective studies are required to confirm our findings.

Conclusion

Our study highlights the critical role of hypoalbuminemia in colistin-induced nephrotoxicity, demonstrating that lower albumin levels at the initiation of therapy significantly increase the risk of AKI in critically ill patients. ROC analysis identified 1.95 g/dL as the optimal albumin threshold for predicting nephrotoxicity, and logistic regression confirmed albumin levels as an independent predictor of AKI.

Ethics

Ethics Committee Approval: The study was reviewed by the Non-Interventional Research Ethics Committee of University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital (approval no: 2011-KAEK-25 2023/02-09, date: 08.03.2023).

Informed Consent: Not required due to the retrospective design of the study.

Footnotes

Authorship Contributions: Concept – Y.Ö.; Design – Y.Ö., M.Y.Ç.; Data Collection or Processing – Y.Ö., Ş.B.; Analysis or Interpretation – Y.Ö., Ş.B.; Literature Search - Y.Ö., M.Y.Ç., Ş.B.; Writing - Y.Ö., M.Y.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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