To cite this article: Yildirim T, Savaci HS. Factors affecting colistin nephrotoxicity in intensive care units. Turk J Clin Lab 2026; 3: x-x.

Research Article

Factors affecting colistin nephrotoxicity in intensive care units

Yoğun bakımda kolistin nefrotoksisitesine etki eden faktörler

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Abstract

Aim: Colistin is frequently used for the treatment of multidrug-resistant gram-negative infections in intensive care units; however, nephrotoxicity remains a major limitation of its clinical use. The incidence and risk factors of colistin-associated renal toxicity vary across studies, particularly in critically ill populations. This study aimed to evaluate the incidence of renal toxicity and associated risk factors in intensive care unit patients receiving intravenous colistin therapy.

Material and Methods: This retrospective observational cohort study included 59 critically ill patients who received intravenous colistin therapy between 2013 and 2015. Nephrotoxicity was defined according to the Acute Kidney Injury Network criteria. Clinical and laboratory data were analyzed. Variables associated with nephrotoxicity were assessed using appropriate statistical tests, and multivariate analysis was performed to identify independent predictors.

Results: Nephrotoxicity developed in 67.8% of patients. Older age, coronary artery disease and higher baseline blood urea nitrogen were associated with toxicity in unadjusted analyses. After adjustment, only elevated baseline blood urea nitrogen remained independently associated with nephrotoxicity. Renal impairment most commonly occurred within the first week of therapy, and 8.5% of patients required renal replacement therapy. Colistin dose was not independently associated with nephrotoxicity.

Conclusion: Colistin-associated nephrotoxicity was common and typically developed early in critically ill patients. Reduced baseline renal functional reserve, particularly reflected by elevated blood urea nitrogen levels, appears to increase susceptibility to toxicity. Close renal monitoring and early risk assessment are essential during colistin therapy.

Keywords: colistin, nephrotoxicity, intensive care, risk factors, acute kidney injury

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Orcid: 0009-0008-8185-3246
Doi: 10.18663/tjcl.1811166
Received: xx.xx.2026 accepted: xx.xx.2026 Publication date: 08.05.2026

TJCL 2026; 1: 1849630

Öz

Amaç: Kolistin, yoğun bakım ünitelerinde çok ilaca dirençli gram-negatif enfeksiyonların tedavisinde sıklıkla kullanılmaktadır; ancak nefrotoksisite klinik kullanımının önemli bir sınırlılığıdır. Kolistine bağlı renal toksisitenin sıklığı ve risk faktörleri, özellikle kritik hastalarda, çalışmalar arasında değişkenlik göstermektedir. Bu çalışmada, intravenöz kolistin tedavisi alan yoğun bakım hastalarında renal toksisite insidansının ve ilişkili risk faktörlerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif gözlemsel kohort çalışmasına, 2013–2015 yılları arasında yoğun bakım ünitesinde intravenöz kolistin tedavisi alan 59 kritik hasta dahil edilmiştir. Nefrotoksisite, Acute Kidney Injury Network (AKIN) kriterlerine göre tanımlanmıştır. Klinik ve laboratuvar verileri analiz edilmiş; nefrotoksisite ile ilişkili değişkenler uygun istatistiksel testlerle değerlendirilmiş ve bağımsız belirleyicileri saptamak amacıyla çok değişkenli analiz uygulanmıştır.

Bulgular: Hastaların %67,8'inde nefrotoksisite gelişmiştir. Düzeltilmemiş analizlerde ileri yaş, koroner arter hastalığı varlığı ve yüksek başlangıç kan üre azotu (BUN) düzeyleri toksisite ile ilişkili bulunmuştur. Ancak çok değişkenli analiz sonrasında yalnızca yüksek başlangıç BUN düzeyinin nefrotoksisite ile bağımsız olarak ilişkili olduğu saptanmıştır. Renal bozulma en sık tedavinin ilk haftasında ortaya çıkmış ve hastaların %8,5'inde renal replasman tedavisi gereksinimi gelişmiştir. Kolistin dozu nefrotoksisite ile bağımsız olarak ilişkili bulunmamıştır.

Sonuçlar: Kolistine bağlı nefrotoksisite kritik hastalarda sık görülmekte ve genellikle tedavinin erken döneminde gelişmektedir. Özellikle yüksek başlangıç BUN düzeyi ile yansıyan azalmış renal fonksiyon rezervi, toksisite gelişimine yatkınlığı artırmaktadır. Kolistin tedavisi sırasında erken risk değerlendirmesi yapılması ve böbrek fonksiyonlarının yakından izlenmesi önemlidir.

Anahtar Kelimeler: kolistin, nefrotoksisite, yoğun bakım, risk faktörleri, akut böbrek hasarı

Introduction

Infection management in critical care has become increasingly complex due to the global rise of multi-drug resistant (MDR) gram-negative bacteria. Polymyxins, particularly polymyxin B and polymyxin E (colistin), discovered in 1947 and 1949 respectively, were initially sidelined due to neurotoxic and nephrotoxic effects but have re-emerged as key agents against MDR pathogens such as Acinetobacter baumannii, Pseudomonas aeruginosa, and Klebsiella pneumoniae [1,2].

Polymyxins are cationic polypeptides synthesized non-ribosomally by Paenibacillus polymyxa subsp. colistinus [3]. Although several derivatives exist, only polymyxin B and colistin are approved for clinical use due to lower toxicity profiles [4,5]. Colistin is now a last-resort antibiotic, particularly for nosocomial infections including pneumonia, bloodstream infections, and urinary tract infections [6]. It acts by binding lipopolysaccharides on the bacterial outer membrane, displacing divalent cations, and disrupting membrane integrity, ultimately causing cell death [7].

However, colistin's nephrotoxicity, especially in ICU (intensive care unit) patients, limits its clinical use, with incidence reported up to 40% [8]. Mechanisms include oxidative stress, mitochondrial dysfunction, and apoptosis in renal tubular cells [9]. Acute kidney injury (AKI) is the most frequent adverse effect, correlating with worse outcomes and a higher risk of chronic kidney disease [10,11]. Risk factors for colistin-induced nephrotoxicity include age, comorbidities, concurrent nephrotoxic agents, vasopressors, diuretics, dosing, and hypoalbuminemia [9]. A recent retrospective study of 103 ICU patients reported a 59.2% AKI incidence, with age, hypoalbuminemia, and use of vasopressors and furosemide as significant predictors [12]. Meta-analyses further support these findings [13].

This study aims to determine the incidence of AKI in colistin-treated ICU patients and identify demographic, clinical, and treatment-related risk factors to guide safer colistin use.

Material and Methods

This retrospective cohort study included adult patients who received intravenous colistimethate sodium in the Anesthesiology ICU of İzmir Katip Çelebi University Atatürk Training and Research Hospital between May 2013 and May 2015. Patients were identified via clinical information systems, pharmacy records, and archived files. Those with pre-existing kidney injury (per AKIN

criteria), chronic kidney disease, prior renal replacement therapy, or colistin treatment <48 hours were excluded. Of 96 patients treated with colistin, 59 met the inclusion criteria.

Demographic characteristics (age, gender, ICU admission type), comorbidities (e.g., diabetes, hypertension, chronic obstructive pulmonary disease [COPD], malignancy, trauma), Acute Physiology and Chronic Health Evaluation II (APACHE II) score II and Sequential Organ Failure Assessment (SOFA) scores, and ICU length of stay were recorded. Scores were based on the most abnormal values within the first 24 hours of ICU admission. Laboratory parameters on the day colistin was initiated including WBC, hematocrit, platelets, creatinine, bilirubin, electrolytes, albumin, C-reactive Protein (CRP), procalcitonin, and arterial blood gases were also evaluated.

Colistin-associated nephrotoxicity was assessed based on the AKIN criteria. Serum creatinine levels were monitored throughout the duration of colistin treatment and for 24–48 hours post-treatment. For patients who developed nephrotoxicity, the time of AKI onset, AKI stage, peak creatinine level, and need for renal replacement therapy were recorded.

Standard definitions were used for comorbid conditions such as diabetes mellitus, liver cirrhosis, sepsis, and CKD. AKI was defined according to the AKIN criteria as follows: an increase in serum creatinine by ≥0.3 mg/dL within 48 hours, or an increase of ≥50% from baseline, or urine output <0.5 mL/kg/hour for more than 6 consecutive hours. The severity of AKI was staged from AKIN stage 1 to stage 3.

The duration of colistin therapy, average daily dose, and concomitant use of other nephrotoxic agents (including antibiotics, antifungals, and antivirals) before and during the treatment were analyzed. The relationship between these treatments and the development of nephrotoxicity was evaluated.

Ethical approval was obtained from the İzmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee with approval date of 25 June 2015 and decision number 125. Due to the retrospective design, informed consent was not required. The study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as number and percentage, and continuous variables as mean ± standard deviation or median (minimum–maximum), as appropriate. Group comparisons were conducted using the Chi-square or Fisher's Exact test for categorical variables and the independent samples t-test or Mann–Whitney U test for continuous variables. Variables found to be significant in univariate analysis were included in a multivariate Cox proportional hazards regression model to identify independent predictors of nephrotoxicity. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated. A p-value < 0.05 was considered statistically significant.

Results

A total of 59 patients were included in the study, of whom 40 (67.8%) developed renal toxicity during colistin therapy. Renal toxicity was classified according to AKIN criteria as stage 1 in 19 patients (32.2%), stage 2 in 12 patients (20.3%), and stage 3 in 9 patients (15.3%). The median time to toxicity onset was 5 days (2–21 days), with most cases occurring within the first week (Figure 1). Renal replacement therapy was required in 5 of 9 patients (55.6%) with AKIN stage 3 injury.

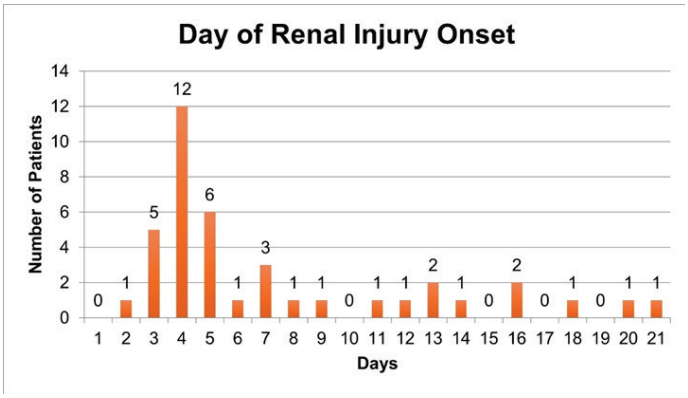

Figure 1. Distribution of Time to Onset of Renal Injury After Initiation of Colistin Therapy [Median time to renal toxicity, 5 days (2–21 days)].

Patients who developed nephrotoxicity were significantly older than those without toxicity (59.1 ± 18.2 vs. 46.9 ± 21.4 years, p = 0.028). Although male sex was more frequent in both groups (72.5% vs. 63.2%), no significant association was observed between sex and nephrotoxicity (p = 0.670). Surgical admission was more common in the toxicity group (62.5% vs. 36.8%), whereas medical admissions were more frequent in patients without toxicity; however, this difference did not

reach statistical significance (p = 0.117).

Median intensive care unit length of stay did not differ significantly between groups (32 [10–387] vs. 49 [12–396] days, p = 0.153). Follow-up duration was significantly shorter in patients who developed nephrotoxicity (5 [2–21] vs. 13 [2–24] days, p = 0.025), reflecting earlier onset of renal injury.

Regarding severity scores, SOFA scores were similar between groups (6.0 ± 2.1 vs. 6.6 ± 2.2, p = 0.317). APACHE II scores (22.9 ± 6.7 vs. 19.8 ± 5.8, p = 0.092) and predicted mortality percentages (42.8 ± 24.8 vs. 30.3 ± 18.9, p = 0.057) were numerically higher in the nephrotoxicity group but did not reach statistical significance.

Colistin dose was slightly higher in patients who developed nephrotoxicity (461 [231–550] vs. 450 [150–600] mg/day, p = 0.070), while duration of colistin therapy did not differ significantly (13.3 ± 6.7 vs. 11.8 ± 6.8 days, p = 0.416).

At the initiation of colistin therapy, baseline creatinine levels were significantly higher in the nephrotoxicity group (0.6 ± 0.2 vs. 0.5 ± 0.1 mg/dL, p = 0.023). Similarly, baseline blood urea nitrogen (BUN) levels were significantly elevated in patients who developed toxicity (21 [3–40] vs. 10 [4–24] mg/dL, p < 0.001). No significant differences were observed between groups regarding total bilirubin, sodium, potassium, magnesium, phosphorus, hematocrit, leukocyte count, platelet count, albumin, C-reactive protein, procalcitonin, or PaO_2/FiO_2 ratio (all p > 0.05).

Among comorbidities, CAD was significantly more frequent in patients who developed nephrotoxicity (30.0% vs. 5.3%, p = 0.044). Other comorbid conditions, including diabetes mellitus, hypertension, COPD, peripheral arterial disease (PAD), neurological disease, malignancy, hematological disease, immunological disease, and trauma history, were not significantly associated with nephrotoxicity.

The distribution of concomitant antimicrobial therapies administered within one week prior to colistin initiation did not differ significantly between groups. No association was found between nephrotoxicity and the use of cephalosporins, carbapenems, β-lactam/β-lactamase inhibitors, oxazolidinones, glycopeptides, aminoglycosides, quinolones, antifungal agents, antiviral agents, metronidazole, tigecycline, or trimethoprim–sulfamethoxazole (all p > 0.05).

The demographic, clinical, laboratory, and treatment-related characteristics of patients according to nephrotoxicity status are presented in Table 1.

Data are presented as mean ± standard deviation, n (%), or median (minimum–maximum). Column percentages are shown. [1] Student's t-test; [2] Yates-corrected chi-square test; [3] Mann–Whitney U test; [4] Fisher's Exact test. Abbreviations: Chronic Obstructive Pulmonary Disease (COPD); Coronary Artery Disease (CAD); Peripheral Arterial Disease (PAD); Trimethoprim–Sulfamethoxazole (TMP-SMX).

To identify independent predictors of nephrotoxicity, a multivariate Cox proportional hazards regression analysis was performed including age, coronary artery disease, and baseline BUN level. In the multivariate model, baseline BUN level remained independently associated with nephrotoxicity (HR: 1.050, 95% CI: 1.006–1.095), whereas age and coronary artery disease were not independently associated (Table 2).

Table 1. Baseline demographic and clinical characteristics of patients with and without renal toxicity (n = 59).

Variable	Total (n=59)	Renal Toxicity		p
		Present (n=40)	Absent (n=19)	
Age	55.2±20.0	59.1±18.2	46.9±21.4	0.0281
Gender				
Male	41 (69.5)	29 (72.5)	12 (63.2)	0.6702
Female	18 (30.5)	11 (27.5)	7 (36.8)	
Reason for ICU admission				
Medical	27 (45.8)	15 (37.5)	12 (63.2)	0.1172
Surgical	32 (54.2)	25 (62.5)	7 (36.8)	
ICU Length of Stay (days)	35 (10-396)	32 (10-387)	49 (12-396)	0.1533
Follow-up Duration (days)	6 (2-24)	5 (2-21)	13 (2-24)	0.0253
Mortality scores				
SOFA	6.2±2.2	6.0±2.1	6.6±2.2	0.3171
APACHE II	21.9±6.6	22.9±6.7	19.8±5.8	0.0921
APACHE % II	38.8±23.6	42.8±24.8	30.3±18.9	0.0571
Colistin Dose (mg/day)	450 (150-600)	461 (231-550)	450 (150-600)	0.0703
Duration of Colistin Therapy (days)	12.8±6.7	13.3±6.7	11.8±6.8	0.4161
Laboratory Parameters at Colistin Initiation				
Creatinine (mg/dL)	0.6±0.2	0.6±0.2	0.5±0.1	0.0231
Blood Urea Nitrogen (BUN) (mg/dL)	17 (3-40)	21 (3-40)	10 (4-24)	<0.0013
Total Bilirubin (mg/dL)	0.7 (0.3-6.0)	0.7 (0.3-4.2)	0.8 (0.3-6.0)	0.1913
Sodium (mmol/L)	142.0±7.7	143.2±8.3	139.5±5.8	0.0531
Potassium (mmol/L)	3.8±0.8	3.7±0.9	4.0±0.7	0.2831
Magnesium (mg/dL)	1.9±0.3	1.9±0.3	1.8±0.4	0.1301
Phosphorus (mg/dL)	3.1±1.3	2.9±0.9	3.6±1.7	0.1101
Hematocrit (%)	30.4±3.6	30.4±3.7	30.4±3.5	0.9901
Leukocyte Count ($\times 10^9$/L)	11.1 (2.0-43.1)	11.4 (2.0-2.8)	11.1 (2.7-43.1)	0.6853
Platelet Count ($\times 10^9$/L)	305.0±171.5	314.8±173.3	284.3±170.3	0.5281
Albumin (g/dL)	2.2±0.5	2.2±0.5	2.3±0.6	0.4421
C-reactive Protein (mg/L)	15.0±8.5	14.7±8.6	15.5±8.4	0.7661
Procalcitonin (ng/mL)	0.7 (0.1-127.9)	0.8 (0.1-127.9)	0.3 (0.1-25.2)	0.1723
PaO2/FiO2	199.8 (67.5-425.0)	177.8 (67.5-410.0)	220.0 (89.2-425.0)	0.1633
Comorbidities				
Diabetes Mellitus	7 (11.9)	6 (15.0)	1 (5.3)	0.4114
Hypertension	18 (30.5)	15 (37.5)	3 (15.8)	0.1652
COPD	10 (16.9)	8 (20.0)	2 (10.5)	0.4764
CAD	13 (22.0)	12 (30.0)	1 (5.3)	0.0444
PAD	1 (1.7)	1 (2.5)	0 (0.0)	1.0004
Neurological Disease	18 (30.5)	14 (35.0)	4 (21.1)	0.4332
Malignancy	17 (28.8)	11 (27.5)	6 (31.6)	0.9882
Hematological Disease	2 (3.4)	2 (5.0)	0 (0.0)	1.0004
Immunological Disease	1 (1.7)	1 (2.5)	0 (0.0)	1.0004
Trauma	10 (16.9)	7 (17.5)	3 (15.8)	1.0004
Concomitant Antimicrobial Therapy				
Cephalosporins	8 (13.6)	6 (15.0)	2 (10.5)	1.0004
Carbapenems	56 (94.9)	39 (97.5)	17 (89.5)	0.2404
β-lactam/β-lactamase inhibitors	26 (44.1)	15 (37.5)	11 (57.9)	0.2332
Oxazolidinones	16 (27.1)	12 (30.0)	4 (21.1)	0.6832
Glycopeptides	13 (22.0)	8 (20.0)	5 (26.3)	0.7384
Aminoglycosides	4 (6.8)	3 (7.5)	1 (5.3)	1.0004
Quinolones	6 (10.2)	3 (7.5)	3 (15.8)	0.3764
Antifungal Agents	18 (30.5)	12 (30.0)	6 (31.6)	1.0002
Antiviral Agents	2 (3.4)	0 (0.0)	2 (10.5)	0.1004
Other Antibiotics				
Metronidazole	15 (25.4)	11 (27.5)	4 (21.1)	0.7534
Tigecycline	6 (10.2)	5 (12.5)	1 (5.3)	0.6534
TMP-SMX	1 (1.7)	0 (0.0)	1 (5.3)	0.3224

Table 2. Multivariate Cox Proportional Hazards Regression Analysis for Predictors of Renal Toxicity.

Variable	HR	95% CI	p
Age	1.010	0.986-1.034	0.430
Male sex (reference: female)	1.054	0.484-2.296	0.894
Coronary artery disease	1.669	0.760-3.665	0.202
Carbapenem use	1.755	0.221-13.959	0.595
Magnesium (mg/dL)	1.226	0.406-3.702	0.718
Blood urea nitrogen (mg/dL)	**1.050**	**1.006-1.095**	**0.026**

Abbrev.: HR, Hazard Ratio; CI, Confidence Interval

Discussion

In this retrospective cohort of critically ill patients receiving colistin therapy, nephrotoxicity occurred in a substantial proportion of cases and frequently developed early during treatment. While older age, the presence of CAD and baseline BUN were initially associated with renal toxicity, only elevated baseline BUN remained independently related to nephrotoxicity after adjustment for confounding factors, highlighting the central role of reduced baseline renal reserve. Notably, a considerable number of patients progressed to advanced stages of kidney injury, and more than half of those with severe injury required renal replacement therapy. These findings suggest that colistin-associated nephrotoxicity in intensive care settings may be both common and clinically significant, underscoring the importance of early risk stratification and close renal monitoring.

Colistin nephrotoxicity was observed in 67.8%, aligning with the upper range of reported incidences (20–70%) [2, 8, 14]. The observed rate exceeds those in some meta-analyses, such as a 34.8% pooled incidence for ICU patients receiving polymyxins [13], likely reflecting differences in population characteristics and diagnostic criteria (AKIN vs. RIFLE/KDIGO). Ghafur et al. also noted higher nephrotoxicity rates in critically ill ICU patients [15]. Severe renal dysfunction corresponding to advanced AKIN stages was observed in a notable proportion of patients, and some (55.6% of AKIN Stage 3 cases) required renal replacement therapy. This finding suggests that colistin-associated nephrotoxicity may not be limited to mild or reversible injury but can progress to clinically significant renal impairment, particularly in vulnerable critically ill patient.

Consistent with the existing literature [16,17], older age and the presence of coronary artery disease were associated with nephrotoxicity in unadjusted analyses. Age-related vascular dysfunction, endothelial injury, and potential cardiorenal interactions may reduce renal tolerance to nephrotoxic agents. However, after adjustment for confounding variables, these factors did not remain independently associated with toxicity in our cohort.

Although baseline serum creatinine levels were within the normal range, relatively higher values in the toxicity group may reflect subtle reductions in renal reserve. In elderly or sarcopenic patients, normal-range creatinine levels may underestimate underlying renal vulnerability [18,19]. In parallel, elevated baseline blood urea nitrogen levels further support the presence of reduced renal functional reserve, suggesting that even mild preexisting impairment may predispose patients to colistin-associated nephrotoxicity.

Renal toxicity in our cohort most frequently developed during the first week of colistin therapy. This temporal pattern is consistent with previous reports describing a 5–7 day high-risk window for the onset of colistin-associated nephrotoxicity [16,17,20,21].

Colistin dose was not independently associated with nephrotoxicity in our cohort; however, previous studies have suggested a potential dose-dependent risk [21,22]. Therefore, cautious dosing strategies may still be considered, particularly in high-risk critically ill patients.

Despite previous reports suggesting a potential nephroprotective effect of magnesium supplementation [23,24], no significant association was found between serum magnesium levels and renal toxicity in our cohort. Therefore, our findings do not support a definitive protective role of magnesium in this setting. Further prospective studies are needed to better elucidate its role in colistin-associated nephrotoxicity.

Taken together, our findings emphasize that colistin-associated nephrotoxicity remains a clinically significant concern in critically ill patients. Baseline renal functional reserve appears to play a central role in susceptibility to toxicity, and renal impairment may develop early during treatment. Careful patient selection, early risk stratification, and close monitoring of renal function are essential to minimize adverse outcomes. Further prospective, multicenter studies are warranted to better define risk profiles and optimize preventive strategies in this vulnerable population.

Limitations of the study

Our study has several limitations. First, its retrospective and single-center design may limit generalizability. Second, the relatively small sample size may have reduced statistical power, particularly in multivariate analyses. Third, residual confounding cannot be fully excluded despite adjustment for selected variables. Finally, the observational nature of the study precludes establishing a causal relationship between identified risk factors and nephrotoxicity.

In conclusion, colistin-associated nephrotoxicity was common among critically ill patients and frequently occurred early during therapy. Reduced baseline renal functional reserve, particularly reflected by elevated blood urea nitrogen levels, appears to increase susceptibility to toxicity. Early identification of high-risk patients and close monitoring of renal function during treatment are essential to mitigate adverse renal outcomes.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

Ethics approval

Ethical approval was obtained from the İzmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee with approval date of 25 June 2015 and decision number 125. Due to the retrospective design, informed consent was not required. The study was conducted in accordance with the Declaration of Helsinki.

References

1. Ning Y, Chu Y, Wu Y, Huang Y, Wang C, Jiang L. Case Report: Respiratory paralysis associated with polymyxin B therapy. Front Pharmacol 2022; 13: 963140.
2. Falagas ME, Kasiakou SK. Colistin: the revival of polymyxins for the management of multidrug-resistant gram-negative bacterial infections. Clin Infect Dis 2005; 40: 1333-41.
3. Ayoub Moubareck C. Polymyxins and Bacterial Membranes: A Review of Antibacterial Activity and Mechanisms of Resistance. Membranes (Basel) 2020; 10: 181.
4. Niu B, Vater J, Rueckert C, Blom J, Lehmann M, Ru JJ et al. Polymyxin P is the active principle in suppressing phytopathogenic Erwinia spp. by the biocontrol rhizobacterium Paenibacillus polymyxa M-1. BMC Microbiol 2013; 13: 137.
5. Yang S, Wang H, Zhao D, Zhang S, Hu C. Polymyxins: recent advances and challenges. Front Pharmacol 2024; 15: 1424765.
6. El-Sayed Ahmed MAE, Zhong LL, Shen C, Yang Y, Doi Y, Tian GB. Colistin and its role in the Era of antibiotic resistance: an extended review (2000-2019). Emerg Microbes Infect 2020; 9: 868-85.
7. Nikaido H. Molecular basis of bacterial outer membrane permeability revisited. Microbiol Mol Biol Rev 2003; 67: 593-656.
8. Pogue JM, Lee J, Marchaim D, Yee V, Zhao JJ, Chopra T et al. Incidence of and risk factors for colistin-associated nephrotoxicity in a large academic health system. Clin Infect Dis 2011; 53: 879-84.
9. Nation RL, Rigatto MHP, Falci DR, Zavascki AP. Polymyxin Acute Kidney Injury: Dosing and Other Strategies to Reduce Toxicity. Antibiotics (Basel) 2019; 8: 24.
10. Baradaran S, Black DJ, Keyloun KR, Hansen RN, Gillard PJ, Devine B. The impact of acute kidney injury on the risk of mortality and health care utilization among patients treated with polymyxins for severe Gram-negative infections. Open Forum Infect Dis 2018; 5: ofy191.
11. Gomes EC, Falci DR, Bergo P, Zavascki AP, Rigatto MH. Impact of polymyxin-B-associated acute kidney injury in 1-year mortality and renal function recovery. Int J Antimicrob Agents 2018; 52:86–9.
12. Deniz M, Alişik M. Risk factors and prognosis for the development of acute kidney injury in patients using colistin in the intensive care unit: A retrospective cohort study. Medicine (Baltimore) 2024; 103: e36913.
13. Wang JL, Xiang BX, Song XL, Que RM, Zuo XC, Xie YL. Prevalence of polymyxin-induced nephrotoxicity and its predictors in critically ill adult patients: A meta-analysis. World J Clin Cases 2022; 10: 11466–85.

Gilliam BL. Higher incidence of acute kidney injury with intravenous colistimethate sodium compared with polymyxin B in critically ill patients at a tertiary care medical center. Clin Infect Dis. 2013; 57: 1300-3.

15. Ghafur A, Gohel S, Devarajan V, Raja T, Easow J, Raja MA et al. Colistin Nephrotoxicity in Adults: Single Centre Large Series from India. Indian J Crit Care Med 2017; 21: 350-4.
16. Moghnieh R, Husni R, Helou M, Abdallah D, Sinno L, Jadayel M et al. The Prevalence and Risk Factors of Acute Kidney Injury during Colistin Therapy: A Retrospective Cohort Study from Lebanon. Antibiotics (Basel) 2023; 12: 1183.
17. Alotaibi FM, Alshehail BM, Al Jamea ZAH, Joseph R, Alanazi AH, Alhamed NA et al. Incidence and Risk Factors of Colistin-Induced Nephrotoxicity Associated with The International Consensus Guidelines for the Optimal Use of the Polymyxins: A Retrospective Study in a Tertiary Care Hospital, Saudi Arabia. Antibiotics (Basel) 2022; 11: 1569.

18. Delanaye P, Cavalier E, Pottel H. Serum Creatinine: Not So Simple!. Nephron 2017; 136: 302-8.

19. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function--measured and estimated glomerular filtration rate. N Engl J Med 2006; 354: 2473-83.

20. Kwon JA, Lee JE, Huh W, Peck KR, Kim YG, Kim DJ, Oh HY. Predictors of acute kidney injury associated with intravenous colistin treatment. Int J Antimicrob Agents 2010; 35: 473-7.

21. Rattanaumpawan P, Ungprasert P, Thamlikitkul V. Risk factors for colistin-associated nephrotoxicity. J Infect 2011; 62: 187-90.

22. Arrayasillapatorn N, Promsen P, Kritmetapak K, Anunnatsiri S, Chotmongkol W, Anutrakulchai S. Colistin-Induced Acute Kidney Injury and the Effect on Survival in Patients with Multidrug-Resistant Gram-Negative Infections: Significance of Drug Doses Adjusted to Ideal Body Weight. Int J Nephrol 2021; 2021: 7795096.

23. Yavuz YC, Cetin N, Menevşe E, Cizmecioglu A, Celik E, Biyik Z, Sevinc C et al. Can magnesium sulfate prophylaxis reduce colistin nephrotoxicity?. Nefrologia (Engl Ed) 2021; 41: 661-9.

24. Hosseini S, Alavi Darzam I, Amirdosara M, Zangi M, Sahraei Z. Evaluating the effects of intravenous magnesium sulfate for prevention of colistin induced acute kidney injury: an open-label, placebo-controlled, block randomized clinical trial. Naunyn Schmiedebergs Arch Pharmacol 2025; 398: 4559-70.