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Impact of The COVID-19 Pandemic on Carbapenem and Colistin Resistance of Gram-Negative Bacteria Isolated from Laboratory-Confirmed Healthcare-Associated Infections in Intensive Care Units

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ABSTRACT

Introduction: The coronavirus disease 2019 (COVID-19) pandemic may have influenced antibiotic usage patterns. In particular, increased empirical use of broad-spectrum agents may have affected bacterial resistance profiles. This study aimed to evaluate the impact of the COVID-19 pandemic on carbapenem and colistin resistance in Gram-negative bacteria (GNB) isolated from laboratory-confirmed healthcare-associated infections (HAIs) in adult intensive care units (ICUs).

Methods: This retrospective study evaluated microbiological and antimicrobial resistance data across three consecutive time periods: Period 1 (March 2018–March 2020), Period 2 (March 2020–March 2022), and Period 3 (March 2022–March 2024). The carbapenem and colistin resistance profiles of GNB isolated from HAIs in ICU patients were assessed across these time frames.

Results: In Period 1, *Pseudomonas aeruginosa* was the most frequently isolated pathogen. In Period 2, *Acinetobacter baumannii* became predominant, while in the post-pandemic period, *Klebsiella pneumoniae* emerged as the leading pathogen. The rates of carbapenem-resistant *K. pneumoniae* (CRKP) (p=0.0007) and *P. aeruginosa* (CRPA) (p=0.0001) increased during the pandemic and remained elevated in Period 3. The rate of carbapenem-resistant *A. baumannii* remained unchanged across all periods. Colistin resistance in *A. baumannii* (p=0.0002) and *K. pneumoniae* (p=0.0063) increased significantly in Period 2. Colistin resistance in *P. aeruginosa* remained stable in Period 2, but increased in Period 3 (p=0.0019).

Conclusion: CRKP and CRPA became more prevalent during and after the COVID-19 pandemic, while colistin resistance among key ICU pathogens also increased. These findings suggest that pandemic-related changes in ICUs and antimicrobial use may have facilitated the persistence of highly resistant GNB. Continuous local surveillance and reinforcement of infection-control and stewardship programs are needed.

Keywords: COVID-19, Gram-negative bacteria, carbapenem resistance, colistin resistance

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has had a profound impact on healthcare systems worldwide. The sudden increase in hospitalization rates necessitated a rapid response to manage the increasing patient load in healthcare facilities (1). Intensive care units (ICUs) have been particularly affected by the frequent requirement for ventilatory support among patients with COVID-19. This situation has significantly increased demand for ICU beds and supplies, necessitating the reallocation of resources. However, the combination of increased demand and a shortage of healthcare professionals may have adversely affected certain operations and disrupted long-standing practices aimed at preventing healthcare-associated infections (HAIs). Considering factors, such as the rapid increase in ICU capacity, decreased staff-to-patient ratios, longer patient stays, and greater patient complexity, the risk of infection is likely to increase because of cross-contamination among patients (2). The COVID-19 pandemic may also have affected antibiotic consumption, contributing to increased antimicrobial resistance (AMR). Studies have shown that despite low rates of confirmed bacterial infections, the use of broad-spectrum antibiotics is common in patients with COVID-19 (3-5). Additionally, compliance with antibiotic stewardship programs has decreased during this period as healthcare providers struggle to save the lives of COVID-19 patients (6).

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Over the past decade, a notable rise in resistance to many antimicrobial agents has been observed among *Enterobacterales (CRE), Pseudomonas aeruginosa,* and *Acinetobacter baumannii*. This increase in AMR in ICUs is primarily due to the spread of high-risk clones, which play a crucial role in the global emergence of multidrug-resistant (MDR) bacteria. The increased empirical use of antibiotics during the COVID-19 pandemic and disruption of infection prevention and control practices in exhausted healthcare systems may have led to a further increase in AMR globally (5,7-9). Despite several reports on HAIs during the COVID-19 era, few studies have specifically tracked AMR among predominant Gram-negative bacteria (GNB) to evaluate the impact of COVID-19 in ICUs (10-12). Local data are essential to guide empirical therapy and infection-control policies. This study aims to assess the impact of the COVID-19 pandemic on carbapenem and colistin resistance in GNB isolated from laboratory-confirmed HAIs in adult ICUs.

Methods

This retrospective study was conducted at an academic tertiary care center comprising multiple ICUs with a total capacity of 80 beds. Data were analyzed across three distinct periods: Period 1 (March 2018–March 2020), Period 2 (March 2020–March 2022), and Period 3 (March 2022–March 2024). AMR to key antibiotics, including carbapenems and colistin, was evaluated among GNB isolated from HAIs in ICU patients.

Bacterial identification was performed using an automated VITEK 2 system (bioMérieux, France) and conventional microbiological methods. The Kirby-Bauer disk diffusion method and VITEK 2 system were employed to determine the AMR patterns of the isolated microorganisms. Extended-spectrum beta-lactamase positivity was assessed using a double-disk synergy test. Colistin susceptibility was determined based on the results of a broth microdilution test, in accordance with the recommendations of the European Committee on Antimicrobial Susceptibility Testing.

Standardized case definitions for HAIs. Inclusion criteria include adult patients aged 18 years and older who have been in hospital for 48 hours or more and are diagnosed with HAIs, such as ventilator-associated pneumonia (VAP), hospital-acquired pneumonia, urinary tract infection (UTI), and bloodstream infection (BSI) caused by GNB. Clinical samples included endotracheal aspirates, urine, and blood specimens. Exclusion criteria included patients under 18 years of age, those who had not been admitted to an adult hospital for at least 48 hours, and those without a diagnosis of HAI caused by GNB. Multiple ICU admissions for the same patient and cases identified as colonization without evidence of active infection were also excluded.

The study was approved by the Clinical Research Ethics Committee of Tekirdağ Namık Kemal University (research protocol number: 2025.147.07.17, dated: July 29, 2025) and conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Statistical Analysis

Data obtained in the study were analyzed using SPSS v. 15.0 for Windows. Categorical variables were expressed as frequencies (n) and percentages (%). The chi-square test for trend was used to compare categorical variables across the pre-pandemic, pandemic, and post-pandemic periods. A p value <0.05 was considered significant.

Results

During the study period (March 2018–March 2024), 804 bacteria were detected in the ICUs, of which 662 were Gram-negative. A total of 587 patients were included, of whom 327 (55.7%) were male. VAP was identified as the most common HAI across all periods, with 291 (43.9%) cases reported. Other HAIs, listed in order of frequency, included BSI with 229 (34.5%) cases and UTI with 83 (12.5%) cases.

Most isolated microorganisms were GNB (76.2%); of these, approximately two-thirds (61.8%) were non-fermentative. The most frequently isolated pathogens were *Acinetobacter baumannii* (33.9%), *Pseudomonas aeruginosa* (27.9%), and *Klebsiella pneumoniae* (23.0%). In Period 1, the most commonly isolated infectious agents in ICUs were *A. baumannii* and *P. aeruginosa*; in Period 2, *A. baumannii* remained the predominant agent. During Period 3, *K. pneumoniae* became the most frequently isolated agent. The distribution of GNB in HAIs in adult ICUs is shown in Table 1.

The prevalence of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) increased from 25% (9/36) in Period 1 to 53% (26/49) in Period 2 and to 62.5% (35/56) in Period 3 (p=0.0019). Similarly, carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) rose from 22% (16/73) to 46% (24/52) and to 65.2% (30/46) (p=0.0001). Carbapenem-resistant *Acinetobacter baumannii* (CRAB) showed 100% across all periods.

Colistin-resistant *K. pneumoniae* increased significantly in Period 2, with rates of 2.8%, 34%, and 32.1% across the three periods (p=0.0063). Colistin resistance in *A. baumannii* increased from 1.6% in Period 1 to 8% in Period 2 and 23.9% in Period 3 (p=0.0002), while *P. aeruginosa* showed a delayed increase, from 1.3% in Period 1 and 1.9% in Period 2 to 15.2% in Period 3 (p=0.0019). Carbapenem and colistin resistance rates of the predominant GNB are summarized in Table 2.

Discussion

HAIs are one of the most serious problems in medicine today, contributing to high mortality, prolonged hospital stays, and increased treatment costs. MDR bacteria are a significant cause of HAIs, especially in ICUs (13). Several studies have reported an increase in the prevalence of MDR bacteria and HAI rates, particularly in device-related infections, during the COVID-19 pandemic (8,9,14). In our study, *A. baumannii*, *P. aeruginosa,* and *K. pneumoniae* were the most frequently isolated GNB. Among them, A. baumannii consistently remained the predominant pathogen across all study periods. In Period 3, *K. pneumoniae* emerged as the most commonly isolated pathogen. CRPA and CRKP were higher during the pandemic than in the pre-pandemic period. During Period 3, CRPA and CRKP continued to increase. In this study, the proportion of resistant strains increased over the years. Possible reasons for this situation include overuse of antibiotics and reduced infection-control measures.

The impact of the COVID-19 pandemic on HAI rates and the AMR in microorganisms remains a topic of debate. Increasing resistance to carbapenems in GNB is particularly concerning due to the lack of safe

Table 1. Distribution of Gram-negative bacteria in healthcare-associated infections in adult intensive care units

	Period 1 (March 2018–March 2020)	Period 2 (March 2020–March 2022)	Period 3 (March 2022–March 2024)	Total	
	n	n	n	n	%
Acinetobacter baumannii	62	100	46	208	31.5
Pseudomonas aeruginosa	73	52	46	171	25.8
Klebsiella pneumoniae	36	49	56	141	21.3
Escherichia coli	22	24	7	53	8.1
Stenotrophomonas maltophilia	12	14	6	32	4.8
Enterobacter cloaceae complex	7	5	3	15	2.3
Enterobacter aerogenes	6	3	1	10	1.6
Proteus mirabilis	5	2	0	7	1.1
Serratia marcescens	3	3	1	7	1.1
Klebsiella oxytoca	3	2	1	6	0.9
Citrobacter spp.	1	1	1	3	0.5
Aeromonas sobria	1	0	0	1	0.1
Ochrobactrum anthropi	1	0	0	1	0.1
Delftia acidovorans	1	0	0	1	0.1
Sfingomonas paucimobilis	2	0	0	2	0.3
Morganella morganii	0	1	0	1	0.1
Pantoe agglomerans	0	1	0	1	0.1
Raoultella planticola	0	1	0	1	0.1
Acromobacter spp.	0	0	1	1	0.1
Total	235	258	169	662	100.0

Table 2. Carbapenem and colistin resistance of the most frequently isolated Gram-negative bacteria

Microorganism/resistance	Period 1 (March 2018–March 2020)		Period 2 (March 2020–March 2022)		Period 3 (March 2022–March 2024)		p value
	n	%	n	%	n	%	
Acinetobacter baumannii							
Carbapenem resistance	62	100.0	100	100.0	46	100.0	-
Colistin resistance	1	1.6	8	8.0	11	23.9	0.0002
Pseudomonas aeruginosa							
Carbapenem resistance	16	22.0	24	46.0	30	65.2	0.0001
Colistin resistance	1	1.3	1	1.9	7	15.2	0.0019
Klebsiella pneumoniae							
Carbapenem resistance	9	25.0	26	53.0	35	62.5	0.0007
Colistin resistance	1	2.8	17	34.0	18	32.1	0.0063

and effective alternative treatment options. In recent years, carbapenem-resistant *Enterobacterales* (CRE) have been reported worldwide, and their prevalence has dramatically increased in many countries. An increase in CRE infections in ICUs during the COVID-19 pandemic has also been reported (11,12). In a retrospective study, CRE colonization increased from 6.7% in 2019 to 50% in March–April 2020 (15). In a survey conducted in Wuhan, China, *A. baumannii* and *K. pneumoniae* were the most frequently isolated GNB. Carbapenem resistance rates for these bacteria were 91.2% and 75.5%, respectively (16). *Acinetobacter* species emerged as the predominant pathogens among COVID-19 patients who contracted HAIs, representing 22.3% of cases (17). A study from Brazil showed that *P. aeruginosa* (29.4%), *K. pneumoniae* (22.7%), and *A. baumannii* (15.9%) were the main MDR GNB isolated from patients in ICUs with COVID-19 (18). In a study from Türkiye, *A. baumannii* was the most common microorganism and *P. aeruginosa* the second most common, both before and during the COVID-19 pandemic; *A. baumannii* was an essential cause of HAIs in ICUs before and during the pandemic (10).

AMR is expected to remain a substantial threat to healthcare systems in the future. By 2050, an estimated 10 million people will die annually from antibiotic-resistant bacterial infections (19). Even before the COVID-19 pandemic, infections caused by MDR CREs, *P. aeruginosa,* and *A. baumannii* constituted a significant global public health concern because of limited effective antimicrobial options and the high lethality of these infections. This situation likely deteriorated during the pandemic, with hospitalized COVID-19 patients frequently

necessitating extended ICU stays and invasive procedures (16). In their study, Antunes et al. (20) reported that carbapenem resistance increased during the pandemic period. Although carbapenem resistance decreased after the pandemic, resistance rates remained higher than in the pre-pandemic period (20). According to our findings, carbapenem- and colistin-resistant GNB increased during the pandemic and in the post-pandemic period. During the pandemic and post-pandemic, there was an increase in infections caused by carbapenem and colistin-resistant GNB. It was thought that factors such as shortages of personnel in ICUs during the first year of the pandemic and personnel exhaustion due to long, demanding working hours adversely affected the rates of HAIs.

While the World Health Organization classified *P. aeruginosa* as a critical-priority pathogen in its 2017 list because of its carbapenem resistance, CRPA was reclassified into the high-priority group in the updated 2024 Bacterial Priority Pathogens List (21). However, we observed a continued increase in CRPA strains at our hospital during the study periods. This trend highlights a significant local concern that contrasts with the global reprioritization. The rising resistance in our setting may be attributed to local factors such as increased antibiotic pressure, prolonged ICU stays, and challenges in infection control. These findings underscore the importance of complementing global priority lists with local surveillance data to guide empiric therapy and infection control strategies effectively.

The increase in infections caused by resistant microorganisms, possibly related to a surge in antimicrobial use during the COVID-19 pandemic, highlights the seriousness of the AMR problem. Although the increase in carbapenem and colistin resistance during the pandemic and post-pandemic periods was notable, molecular typing was not performed in this study. However, based on the available data, there was no strong evidence to suggest clonal transmission, and the situation was therefore not considered an outbreak. While a rise in resistant isolates was observed within similar time frames, this increase did not appear to be linked to a single dominant strain. Instead, it is more likely attributable to various external factors, such as increased antibiotic pressure, lapses in infection control, or the introduction of resistant strains from different sources. The absence of clonal spread supports the hypothesis that the rise in resistance was multifactorial and system-driven, rather than due to in-hospital dissemination of a particular clone. From a public health perspective, these data support the reimplementation of strict hand-hygiene audits, environmental cleaning, and device-associated infection bundles in ICUs. Periodic feedback of unit-specific resistance rates to clinicians may improve empiric prescribing. Integration of antimicrobial stewardship with surge-capacity planning for future outbreaks is also recommended.

Study Limitations

This study has several limitations. First, its retrospective, single-center design inherently limits generalizability to other institutions or healthcare settings. Data reflect local epidemiology, which may differ significantly between regions and hospitals. Second, the analysis was limited to carbapenem and colistin resistance; susceptibilities to other clinically relevant antimicrobial agents such as ceftazidime-avibactam, tigecycline, or fosfomycin were not assessed. Third, molecular typing of resistant isolates was not performed; thus, clonal relatedness and potential in-hospital transmission dynamics could not be assessed. Although no outbreak was suspected based on phenotypic data, the absence of genotyping limits the ability to confirm or exclude clonal dissemination.

Conclusion

Carbapenem and colistin resistance among GNB in ICUs increased during the COVID-19 pandemic and remained high thereafter, especially in *K. pneumoniae* and *P. aeruginosa*, while CRAB was already highly prevalent. These findings indicate that pandemic-related pressure on ICUs may have accelerated the selection and transmission of highly resistant strains. Strengthening antimicrobial stewardship, restoring full infection-prevention bundles, and continuing local resistance surveillance are critical to limiting further spread.

Ethics

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Tekirdağ Namık Kemal University (research protocol number: 2025.147.07.17, dated: July 29, 2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions: Concept - M.N.Ö., İ.E.; Design - M.N.Ö., İ.E.; Data Collection or Processing - M.N.Ö., M.D., İ.Y., İ.E.; Analysis or Interpretation - M.N.Ö., İ.E.; Literature Search - M.N.Ö., M.D., İ.Y., İ.E.; Writing: M.N.Ö., M.D., İ.Y., İ.E.

Conflict of Interest: The authors declared that they have no conflict of interest.

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