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Coronavirus Pandemic

Distribution and antibiotic resistance of Gram-negative bacteria from blood cultures before and during the COVID-19 pandemic

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Abstract

Introduction: Antimicrobial resistance in bloodstream infections is an important clinical challenge. The impact of the coronavirus disease 2019 (COVID-19) pandemic on antimicrobial resistance remains a subject of ongoing debate. This single-center study aimed to analyze Gram-negative bacteria (GNB) isolated from blood cultures and evaluate changes in antimicrobial resistance between the pre-pandemic (March 2018–February 2020) and pandemic (March 2020–February 2022) periods.

Methodology: Blood culture data collected over 4 years were retrospectively analyzed using the BACT/ALERT 3D system. Bacterial identification was conducted with the VITEK® 2 compact system, and antimicrobial susceptibility testing was performed according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria.

Results: Of 1,668 positive blood cultures, 38.3% yielded GNB. There was an increase in Gram-negative isolates during the pandemic, compared to the pre-pandemic period (55.9% vs. 44.1%). Resistance changes were detected in extensive antibiogram analyses in which 18 different antibiotics were studied for the 4 most frequently isolated species, *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. During the pandemic period, resistance to amoxicillin/clavulanic acid, ampicillin, ampicillin-sulbactam, ceftriaxone, and cefuroxime decreased; while resistance to amikacin, levofloxacin, and cefepime increased; except in *Escherichia coli*.

Conclusions: *K. pneumoniae* remained the most frequently isolated bacterium in both periods, while *A. baumannii* showed a significant increase during the pandemic. The 2.6-fold increase in *A. baumannii* may have been caused by the increased use of broad-spectrum antibiotics during the pandemic. These findings reflect data from a single hospital and should be validated by further multicenter studies.

Key words: COVID-19; bacteremia; Gram-negative; resistance.

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Introduction

Bacteremia is a serious health concern that may lead to hospitalization and is associated with increased morbidity and mortality. Therefore, rapid diagnosis and treatment are critical for improving patient prognosis. Prompt identification of causative microorganisms through blood cultures and initiation of targeted antimicrobial therapy based on susceptibility results play a crucial role in reducing hospital stay and morbidity, while increasing survival rates [1]. Gram-negative bacteria (GNB) are among the most frequently isolated pathogens in cases of bacteremia. The management of GNB infections is becoming increasingly challenging due to the resistance mechanisms these organisms have developed. Treatment is typically initiated empirically [1]. It is essential for centers to regularly monitor the distribution of bacteremia-causing microorganisms and their antibiotic susceptibility to guide empirical treatment, enable more appropriate antibiotic use, and help prevent resistance [2].

Antimicrobial resistance (AMR) has emerged as one of the most pressing global health challenges in recent years due to its economic burden and impact on public health. Currently, AMR is estimated to cause approximately 700,000 deaths annually. If effective measures are not implemented and resistance rates continue to rise, AMR-related deaths could reach 10 million per year by 2050 [3].

In line with these data, the World Health Organization (WHO) described AMR as an “invisible pandemic” in 2019. Shortly thereafter, the emergence of the coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), reshaped global healthcare dramatically. The WHO declared COVID-19 a pandemic on 11 March 2020, and on the same day, the Ministry of Health in Turkey reported the first COVID-19 case in the country [3].

The prolongation of hospital stays due to COVID-19 and the use of various drugs, particularly high-dose steroids, suggested that the distribution and antibiotic

susceptibility of microorganisms likely to cause secondary infections might have changed [2]. Therefore, data demonstrating the impact of the COVID-19 pandemic on AMR are needed.

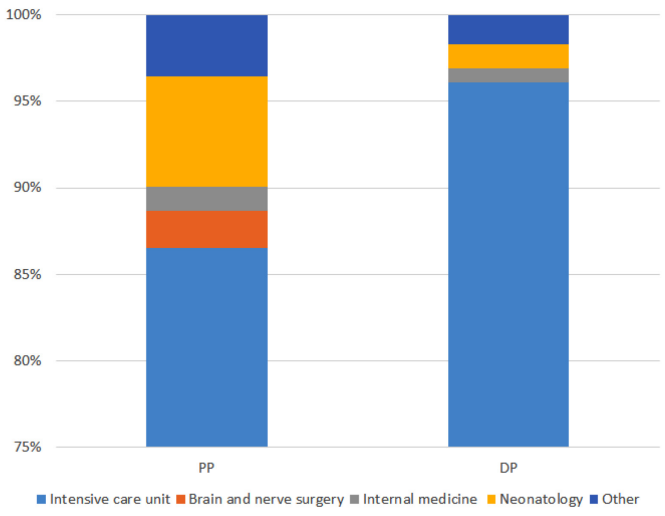
In this regard, this study aimed to determine the distribution of GNB isolated from blood culture samples before and during the COVID-19 pandemic, as well as the changes in AMR patterns potentially associated with the pandemic. The findings provide important insights into the potential impact of the COVID-19 pandemic on AMR, which are valuable for guiding necessary interventions.

Methodology

In this retrospective study, data from the Medical Microbiology Laboratory were evaluated over 4 years. Two timeframes were compared: the pre-pandemic period (PP), from March 2018 to February 2020; and the during-pandemic period (DP), from March 2020 to February 2022.

Blood culture bottles submitted to the laboratory from intensive care units (ICUs) and various clinical wards were included if they met the laboratory's acceptance criteria. The cultures were monitored using the BacT/ALERT 3D system (bioMérieux, Marcy-l'Etoile, France). GNB identified by Gram staining and demonstrating consistent morphology were included in the analysis. In cases of repeated isolates from the same patient, only the first isolate was considered.

Figure 1. Distribution of isolated Gram-negative bacteria (GNB) by hospital unit during pre-pandemic (PP) and during-pandemic (DP) periods.



The number of Gram-negative bacterial isolates identified in various hospital units (e.g., intensive care unit (ICU), internal medicine, surgery, etc.) is shown for both the PP and DP periods. The bars represent the total count of isolates per unit for each period.

Samples from the same blood culture bottles were inoculated onto 5% sheep blood agar, MacConkey agar, and chocolate agar. The VITEK® 2 Compact system (bioMérieux Clinical Diagnostics, Marcy-l'Etoile, France) was used for species-level identification and antimicrobial susceptibility testing of the isolates obtained after 18–24 hours of incubation under appropriate conditions. The antimicrobial susceptibility results were interpreted according to the breakpoints recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [4].

Demographic data, including patient age, gender, and the clinical units from which the samples were submitted, were retrieved from the hospital information management system.

Sample selection

Blood culture samples were included in the study if they met the following criteria: they were collected from hospitalized patients (including those in intensive care units and other clinics) between March 2018 and February 2022; the blood cultures were positive and yielded GNB confirmed by Gram staining; and only the first isolate from each patient during the study period was considered, to avoid duplication. Samples were excluded if they exhibited polymicrobial growth; represented repeated isolates from the same patient within the same infection episode; were considered contaminated or did not meet laboratory quality standards; or if the isolates lacked complete demographic or clinical data.

Statistical analysis

Statistical analyses were performed using the SPSS software (IBM SPSS Statistics 22, IBM Corp, Armonk, NY, USA). In addition to descriptive statistical methods (standard deviation, frequency, and percentage values), the Chi-square test (χ^2) was used for independent two-group comparisons of categorical variables, while Fisher's exact test (FET) was applied when the assumptions for the Chi-square test were not met. A p value of < 0.05 was considered statistically significant.

Ethical approvals

This single-center retrospective study was approved by the Non-Interventional Clinical Research Ethics Committee of Çukurova University Faculty of Medicine (Date: 10 May 2024; Decision No: 144/2) and was conducted following the principles of the Declaration of Helsinki.

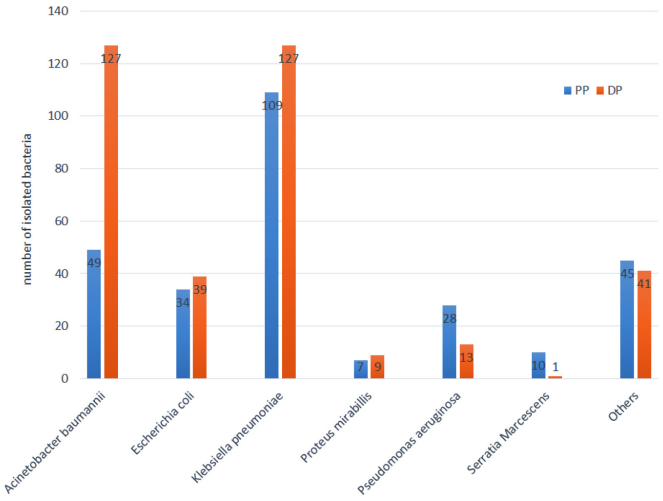
Results

A total of 1,668 blood culture samples sent to the laboratory between March 2018 and February 2022 showed microbial growth. GNB were detected in 639 (38.3%) of the positive cultures. Of these, 282 (44.1%) were isolated during the PP and 357 (55.9%) during the DP. The mean age of the patients was 65.5 ± 23 years in the PP and 71.3 ± 17.3 years in the DP. The male-to-female ratio was 3:2 in the PP and 6:5 in the DP. A total of 91.9% of the isolates were obtained from samples submitted from the ICU. The distribution of isolates by hospital units for both the PP and DP is shown in Figure 1.

The species distribution of the isolates in the PP and DP is presented in Figure 2. Antibiotic resistance rates of the isolated GNB according to the two time periods are shown in Table 1. The AMR profiles of the first four isolates most frequently isolated in this study were statistically examined. The resistance trends were assessed through extensive antibiogram evaluations involving 18 antibiotics for *Acinetobacter baumannii (A. baumannii)*, *Escherichia coli (E. coli)*, *Klebsiella pneumoniae (K. pneumoniae)*, and *Pseudomonas aeruginosa (P. aeruginosa)*.

The AMR profile of *A. baumannii* showed no statistically significant difference between the PP and DP periods in resistance to ciprofloxacin, meropenem, netilmicin, tigecycline, trimethoprim/sulfamethoxazole, cefepime, and ampicillin/sulbactam ($p > 0.05$). During the DP, *A. baumannii* isolates demonstrated a significant increase in resistance to amikacin (PP: 31/49 vs. DP: 115/127, $p < 0.001$, χ^2), ceftazidime (12/49 vs. 115/127, $p < 0.001$, χ^2), levofloxacin (28/49 vs. 116/127, $p < 0.001$, χ^2), and piperacillin/tazobactam (13/49 vs. 117/127, $p < 0.001$, χ^2). Conversely, a significant decrease in resistance was observed for colistin (8/49 vs. 4/127, $p = 0.005$, χ^2), gentamicin (46/49 vs. 93/127, $p = 0.005$, χ^2), imipenem (48/49 vs. 108/127, $p = 0.031$, χ^2), cefuroxime (43/49 vs. 13/127, $p < 0.001$, χ^2), amoxicillin/clavulanate (43/49 vs. 16/127, $p < 0.001$, χ^2), ceftriaxone (37/49 vs.

Figure 2. Distribution of Gram-negative bacteria (GNB) isolated from blood cultures during pre-pandemic (PP) and during-pandemic (DP) periods.



This figure presents the frequency of Gram-negative bacterial isolates obtained from blood cultures in the PP and DP periods. Each bar indicates the number of isolates detected per bacterial species across the two-time frames.

Table 1. Antimicrobial resistance rates (%) of isolated Gram-negative bacteria during pre-pandemic (PP) and during-pandemic (DP) periods.

	Acinetobacter baumannii		***Escherichia coli***		***Klebsiella pneumoniae***		***Pseudomonas aeruginosa***	
	PP	**DP**	**PP**	**DP**	**PP**	**DP**	**PP**	**DP**
	49	**127**	**34**	**39**	**109**	**127**	**28**	**13**
	%	**%**	**%**	**%**	**%**	**%**	**%**	**%**
Amikacin	63.3	90.6	11.8	0.0	67.9	81.9	35.7	46.2
Amoxicillin / Clavulonic acid	87.8	12.6	85.3	0.0	91.7	0.0	82.1	7.7
Ampicillin-Sulbactam	2.0	0.0	41.2	0.0	11.9	0.0	14.3	0.0
Ampicillin	75.5	0.0	88.2	64.1	99.1	67.7	82.1	0.0
Ceftazidime	24.5	90.6	70.6	59.0	94.5	85.8	46.4	69.2
Ceftriaxone	75.5	0.0	70.6	2.6	91.7	58.3	78.6	0.0
Colistin	16.3	3.1	2.9	0.0	47.7	52.8	3.6	23.1
Gentamicin	93.9	73.2	41.2	17.9	76.1	80.3	46.4	53.8
Imipenem	98.0	85.0	14.7	7.7	59.6	24.4	5.6	69.2
Levofloxacin	57.1	91.3	47.1	12.8	17.4	29.9	17.9	61.5
Meropenem	95.9	90.6	23.5	10.3	73.4	82.7	60.7	69.2
Netilmicin	65.3	74.8	23.5	10.3	46.8	29.1	39.3	84.6
Piperacillin-Tazobactam	26.5	92.1	50.0	15.4	89.0	86.6	57.1	69.2
Cefepime	2.0	3.1	70.6	51.3	85.3	90.6	50.0	61.5
Cefuroxime	87.8	10.2	76.5	61.5	86.2	60.6	71.4	7.7
Ciprofloxacin	98.0	94.5	76.5	56.4	90.8	90.6	50.0	61.5
Tigecycline	26.5	25.2	11.8	0.0	67.0	74.8	85.7	7.7
Trimethoprim-Sulfamethoxazole	95.9	95.3	38.2	59.0	81.7	82.7	17.9	7.7

Antimicrobial resistance percentages of *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* isolates against selected antibiotics. The data are categorized based on two time periods: PP and DP. The number of isolates (n) for each species and period is indicated. Resistance was determined using standard clinical laboratory methods. Values are given as percentages (%).

0/127, $p < 0.001$, FET), and ampicillin (37/49 vs. 0/127, $p < 0.001$, FET).

No statistically significant difference was observed in the AMR profiles of *E. coli* strains from the PP and DP for ceftazidime, ciprofloxacin, colistin, gentamicin, imipenem, meropenem, netilmicin, trimethoprim/sulfamethoxazole, cefuroxime, and cefepime ($p > 0.05$). During the pandemic (DP), *E. coli* isolates exhibited a statistically significant decrease in resistance to amikacin (PP: 4/34 vs. DP: 0/39, $p = 0.042$, FET), levofloxacin (16/34 vs. 5/39, $p = 0.003$, χ^2), piperacillin/tazobactam (17/34 vs. 6/39, $p = 0.003$, χ^2), tigecycline (4/34 vs. 0/39, $p = 0.042$, FET), amoxicillin/clavulanate (29/34 vs. 0/39, $p < 0.001$, FET), ceftriaxone (24/34 vs. 1/39, $p < 0.001$, χ^2), ampicillin (30/34 vs. 25/39, $p = 0.034$, χ^2), and ampicillin/sulbactam (14/34 vs. 0/39, $p < 0.001$, FET). No statistically significant increase in resistance to any antibiotic was observed in the DP period compared to the PP period.

No statistically significant difference was observed in the resistance profiles of *K. pneumoniae* strains between the PP and DP periods against ciprofloxacin, colistin, gentamicin, meropenem, piperacillin/tazobactam, tigecycline, trimethoprim/sulfamethoxazole, and cefepime ($p > 0.05$). During the DP period, *K. pneumoniae* isolates demonstrated a statistically significant decrease in resistance to imipenem (PP: 65/109 vs. DP: 31/127, $p < 0.001$, χ^2), netilmicin (51/109 vs. 37/127, $p = 0.007$, χ^2), cefuroxime (94/109 vs. 77/127, $p < 0.001$, χ^2), amoxicillin/clavulanate (100/109 vs. 0/127, $p < 0.001$, FET), ceftriaxone (100/109 vs. 74/127, $p < 0.001$, χ^2), ampicillin (108/109 vs. 86/127, $p < 0.001$, χ^2), ampicillin/sulbactam (13/109 vs. 0/127, $p < 0.001$, FET), and ceftazidime (103/109 vs. 109/127, $p = 0.047$, χ^2). Resistance to amikacin (74/109 vs. 104/127, $p = 0.019$, χ^2) and levofloxacin (19/109 vs. 38/127, $p = 0.037$, χ^2) significantly increased during the DP.

No statistically significant difference was observed in the resistance profiles of *P. aeruginosa* strains between the PP and DP against amikacin, ceftazidime, ciprofloxacin, colistin, gentamicin, imipenem, meropenem, piperacillin/tazobactam, trimethoprim/sulfamethoxazole, cefepime, and ampicillin/sulbactam antibiotics ($p > 0.05$). During the DP period, *P. aeruginosa* isolates demonstrated a statistically significant increase in resistance to levofloxacin (PP: 5/28 vs. DP: 8/13, $p = 0.014$, χ^2) and netilmicin (11/28 vs. 11/13, $p = 0.017$, χ^2). Conversely, a significant decrease in resistance was observed for tigecycline (24/28 vs. 1/13, $p < 0.001$, χ^2), cefuroxime (20/28 vs. 1/13, $p < 0.001$, χ^2), amoxicillin/clavulanate (23/28 vs. 1/13, $p < 0.001$, χ^2), ceftriaxone (22/28 vs. 0/13, $p < 0.001$, FET), and ampicillin (23/28 vs. 0/13, $p < 0.001$, FET).

Discussion

Bloodstream infections have high mortality rates and are among the most life-threatening infections for patients in ICUs and other hospital wards. The incidence of bloodstream infections caused by bacteria resistant to commonly used antimicrobial agents has been increasing in recent years [5,6].

Today, the impact of the COVID-19 pandemic, whose effects are still not entirely resolved, on AMR rates remains a topic of debate. AMR is already a major global concern, and the issue has been further exacerbated by the increased use of antibiotics during the pandemic, largely due to disruptions in diagnostic processes and attempts to prevent superinfections in infected patients [5]. In this study, the distribution of GNB isolated from blood culture samples before and during the COVID-19 pandemic, as well as the changes in AMR patterns potentially associated with the pandemic, were evaluated. Several studies from different parts of the world, including Europe [7,8], the United States [9], and Asia [10], have reported an increase in antimicrobial use during the COVID-19 pandemic [5].

An international cohort study reported that GNBs were isolated more frequently in ICUs, with a rate of 58.3% [11,12]. In a multicenter study conducted in Canada, the rates of Gram-positive bacteria (GPB) and GNB isolated from ICU patients were found to be 58.6% and 21.2%, respectively [11,13]. In studies conducted in Türkiye, the most frequently isolated microorganisms in ICUs were Gram-positive cocci, particularly coagulase-negative *Staphylococci* [2,14,15]. Şirin *et al*. reported the isolation rates of GPB and GNB as 44.9% and 40.3%, respectively [11,14]. Similarly, Aytaç *et al.* found that 60.7% of pathogens isolated from blood cultures during the PP were GPB, while 35% were GNB [2,11]. Çeken *et al.* reported the GNB isolation rate in blood cultures as 27.5% [1]. In various studies, the frequency of GNB isolation from blood cultures has been reported to range between 17% and 59.3% [1,16]. In this study, the frequency of GNB isolation from blood cultures was found to be 38.5%, which falls within the range reported in the literature. The increasing rates of Gram-negative bacteremia in recent years have been attributed to several factors, including the lack of newly developed and effective antibiotics, despite the rise in multidrug resistance

among GNBs; the occurrence of Gram-negative bacteremia secondary to urinary and pulmonary tract infections; and the growing prevalence of nosocomial pathogens such as *P. aeruginosa* and *A. baumannii* [17].

In the study by Çekin *et al.*, the majority of patient samples originated from the ICU (39%), internal medicine departments (32%), and the emergency department (17%) [17]. Çelik *et al*. reported that 34% of the bacterial isolates were from ICU patients, while 66% were from patients in other hospital wards [5]. In this study, the majority of isolates (91.9%) were obtained from samples submitted from the ICU. This may be related to the ICU bed capacity and the relative distribution of patient admissions across departments in the study center. Additionally, patients in ICUs often require invasive procedures, prolonged hospitalization, and are more likely to be immunocompromised; all of which are well-established risk factors for bloodstream infections and colonization by multidrug-resistant organisms [18]. The high rate of bacteremia in ICUs may be attributed to the high prevalence of comorbidities, immunodeficiency, and the generally poor condition of patients. Therefore, strict adherence to infection control measures, minimizing unnecessary invasive procedures, and promptly transferring patients who no longer require intensive care are essential for preventing bloodstream infections in these settings [17].

According to the 2023 report by the WHO and the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR), *Acinetobacter* spp. and *Enterococcus faecium* were more frequently detected in many countries in 2021 compared to previous years. A comparison of 2020 and 2021 data from 13 countries that submitted reports to CAESAR revealed a higher overall number of microorganisms reported in 2021. This increase was attributed to a greater number of isolates submitted for all pathogens. Although these general trends were not consistently observed at the national level, all countries reported an increase in *Acinetobacter* spp. isolates in 2021, relative to 2020. Among the isolates submitted by 16 countries to CAESAR in 2021, the majority of isolates (70.0%) consisted of *E. coli* (37.9%), *Staphylococcus aureus* (17.2%), and *K. pneumoniae* (14.9%) [19].

Some studies have indicated that *E. coli*, *Klebsiella* spp., *Pseudomonas* spp., and *Acinetobacter* spp. are the most frequently isolated GNBs in patients monitored in ICUs [2,11,14,13,20,21]. Arslan *et al.* reported that the most commonly isolated GNBs were *Klebsiella* spp., *Acinetobacter* spp., and *E. coli*. A significant increase in the isolation rate of *Klebsiella* spp. was observed during the DP compared to the PP (3.9% vs. 10.8%, $p = 0.006$). In this study, *K. pneumoniae* was the most frequently isolated GNB in both the PP and DP; however, *A. baumannii* showed the greatest increase in isolation rate during DP [11]. This notable increase in *A. baumannii* isolation during the pandemic may be attributed to its intrinsic resistance mechanisms, its ability to survive on environmental surfaces for extended periods, and potential lapses in infection control measures due to the strain on healthcare systems during the COVID-19 pandemic [18,22,23]. COVID-19 is known to be more common and severe in immunocompromised patients. *Klebsiella* spp. may have been frequently isolated during the DP period, as it is capable of causing infections in surgical wounds, pneumonia, bacteremia, as well as urinary and respiratory tract infections, particularly in individuals with weakened immune systems. Bacteremias caused by *P. aeruginosa* and *Acinetobacter* spp. have been reported to be difficult to treat. Şirin *et al.* reported that *Acinetobacter* spp. and *P. aeruginosa* were isolated from blood culture samples at rates of 13.1% and 4.8%, respectively [14]. In the study by Arslan *et al., Acinetobacter* spp. was detected in 8.4% of the cases during the PP and in 4.4% during the DP period. *Pseudomonas* spp. was isolated at a rate of 1% in the PP and 1.6% in the DP [11]. Arslan *et al.* reported that *Acinetobacter* spp. isolates exhibited resistance rates of 76.5% to gentamicin and 71.6% to amikacin during the PP, with a non-significant decrease in susceptibility observed during the DP [11]. In this study, *A. baumannii* strains demonstrated significantly higher resistance rates to amikacin, ceftazidime, levofloxacin, and piperacillin/tazobactam during the DP compared to the PP ($p < 0.001$). These findings highlight that *A. baumannii* infections remain a significant concern for hospitalized patients, particularly those in ICUs, due to both their high incidence and elevated resistance rates [1]. Although colistin has long been regarded as the most effective antimicrobial agent against *A. baumannii*, increasing resistance to this agent has been reported in recent years [2]. Petrakis *et al.* identified a declining trend in colistin non-susceptibility among ICU isolates during the PP (from 43.6% to 41.4%, $p = 0.05$), followed by a marked increase during the DP (from 42.5% to 59.6%, $p < 0.001$) [24]. In contrast to these findings, this study demonstrated a statistically significant decrease in colistin resistance during the DP compared to the PP. This divergence may be attributed to more judicious use of colistin during the pandemic, potentially due to heightened awareness of its

nephrotoxicity, implementation of antimicrobial stewardship efforts, or a shift in empiric therapy choices based on local resistance trends [25,26].

Studies evaluating changes in antimicrobial susceptibility rates of *E. coli* isolates during the pandemic have yielded varying results. A study conducted by Wardoyo *et al.* in Indonesia examined *E. coli* susceptibility before and during the pandemic and emphasized that susceptibility rates increased during the DP period [3,27]. Yılmaz *et al.* conducted a study in Türkiye and reported an increase in cefotaxime and ceftazidime susceptibility rates in *E. coli* isolates from ICU patients, whereas no change was detected in the susceptibility of isolates obtained from patients in other inpatient clinics [3]. Carbapenems are the first-line treatment for ESBL-producing bacteria, and the emergence of carbapenem-resistant isolates significantly limits therapeutic options [5,28]. In the study by Gürbüz *et al*., *E. coli* strains, which accounted for 10.5% of the total isolates in both the PP and DP, demonstrated a susceptibility rate above 85%, although limited resistance to meropenem was reported in both periods [29]. Aytaç *et al*. did not detect carbapenem resistance in *E. coli* during either period, consistent with the CAESAR data [2]. Similarly, Çelik *et al.* did not find a significant difference in *E. coli* resistance rates between the two periods; however, they reported a significant difference in amikacin and meropenem susceptibility in *K. pneumoniae* ($p < 0.05$) [5]. A study presenting data from the Greek national surveillance system reported an increase in the resistance rates of *K. pneumoniae* isolates obtained from blood and lower respiratory tract samples in ICUs. It was emphasized that AMR poses a global threat comparable to COVID-19, and therefore, urgent measures are needed [3,30]. In this study, when the PP and DP were compared, no statistically significant difference was observed in the overall resistance rates of *E. coli*. However, consistent with the findings of Yılmaz *et al*., a significant decrease in resistance to cefotaxime was detected. The resistance rates in *K. pneumoniae* were found to have increased against amikacin, an aminoglycoside antibiotic, and levofloxacin, a fluoroquinolone antibiotic ($p < 0.05$). These increases may reflect the increased and potentially inappropriate use of these agents as empiric treatment options during the pandemic. Overuse may have contributed to the emergence and spread of resistant *K. pneumoniae* clones [31]. It was reported that, during the DP, a rapid increase in resistance was observed in GNB, particularly in *K. pneumoniae* strains carrying various resistance genes [32].

In recent years, increased carbapenemase production in *Pseudomonas* spp. has led to heightened resistance to carbapenem antibiotics. Imipenem susceptibility in *P. aeruginosa* has been reported to range from 51% to 82% [11]. In the study by Arslan *et al*., *Pseudomonas* spp. showed 100% susceptibility to imipenem during PP, which decreased to 20% during DP. However, they emphasized that the decrease in susceptibility during DP was not statistically significant [11]. Similarly, in the study by Aytaç *et al*., the changes in antibiotic susceptibility of *Pseudomonas* spp. between PP and DP were not found to be statistically significant ($p > 0.05$). The susceptibility of *Pseudomonas* spp. to imipenem in blood cultures was reported as 100% in PP [2]. In this study, no statistically significant difference was observed in the imipenem resistance profile of *P. aeruginosa* between the two periods ($p > 0.05$). However, resistance rates of *P. aeruginosa* strains to levofloxacin and netilmicin were found to be significantly higher during DP compared to PP ($p < 0.05$). This could be a consequence of selective antimicrobial pressure or clonal expansion of resistant *P. aeruginosa* strains in ICUs during the pandemic. Additionally, infections related to invasive medical devices and compromised immunity may have facilitated the persistence of more resistant strains [33].

Hamidi *et al.* reported an increased use of meropenem, piperacillin/tazobactam, teicoplanin, and fluoroquinolones during DP [34]. A common finding across studies regarding the rise in AMR rates during DP was the inappropriate and excessive use of antibiotics [3].

One of the limitations of this study is its retrospective design. Further studies involving larger patient populations and simultaneous data analysis from multiple hospitals are needed to better elucidate the impact of the COVID-19 pandemic on AMR. Additional limitations include the inability to investigate resistance genes and enzymes, as well as the lack of data on antibiotic consumption in the study center. More comprehensive, multicenter studies are required to evaluate the long-term impact of the pandemic on AMR.

Conclusions

The COVID-19 pandemic may have played a significant role in the emergence and transmission of resistant pathogens, particularly GNB, in hospital settings. Although the pandemic has left a profound mark on the 21st century, AMR persists as a parallel, "invisible pandemic," as described by the WHO. Data on AMR prevalence before and after the pandemic,

especially from developing countries, are crucial to understanding the spread of resistant pathogens. To achieve this, reliable microbiological surveillance should be established, rapid diagnostic tests for infectious diseases must be developed, rational antibiotic use should be promoted, antimicrobial stewardship programs should be promptly restructured, and vaccination strategies significantly enhanced. Considerable heterogeneity exists in resistance rates across different studies. Our findings underscore the urgent need to reinforce infection prevention and control measures, implement comprehensive antimicrobial stewardship, and ensure robust and standardized AMR surveillance as part of the global pandemic response and recovery efforts [3].

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Conflict of interest

No conflict of interest is declared.

References

1. Çeken N, Duran H, Kula Atik T (2022) Distribution of Gram negative bacteria isolated from blood culture and antibiotic resistance rates. Turk Hij Den Biyol Derg 79: 451–46010. [Article in Turkish]. doi: 10.5505/TurkHijyen.2022.57983.
2. Aytaç Ö, Şenol FF, Şenol A, Öner P, Aşçı Toraman Z (2022) A comparison of the species distribution and antibiotic susceptibility profiles of blood culture isolates from intensive care unit patients before and during COVID-19 pandemic. Turk Mikrobiyol Cemiy Derg 52: 39–47. [Article in Turkish]. doi: 10.54453/TMCD.2022.42103.
3. Yılmaz N, Altınkanat Gelmez G, Söyletir G (2023) The change in antimicrobial resistance during the COVID-19 pandemic in Türkiye. Mikrobiyol Bul 57: 507–534. [Article in Turkish]. doi: 10.5578/mb.20239943.
4. The European Committee on Antimicrobial Susceptibility Testing (2019) Breakpoint tables for interpretation of MICs and zone diameters. Version 9.0. Available; http://www.eucast.org. Accessed: 29 June 2024.
5. Çelik C, Özden M, Karahan H, Hasbek M, Tutar U (2022) Resistance of *Escherichia coli* and *Klebsiella pneumoniae* isolates grown from blood samples at a university hospital: a six-year evaluation comparative to the COVID-19 pandemic period. ANKEM Derg 36: 74–82. [Article in Turkish]. doi: 10.54962/ankemderg.1166737.
6. Karpuz T, Yazısız H, Koyuncu Özyurt Ö, Çetinkaya Ö, Özhak B, Öngüt G, Çolak D, Ögünç D (2022) Evaluation of positivity times of isolates growing in blood cultures. FLORA 27: 218–226. [Article in Turkish]. doi: 10.5578/flora.20229805.
7. Friedli O, Gasser M, Cusini A, Fulchini R, Vuichard-Gysin D, Halder Tobler R, Wassilew N, Plüss-Suard C, Kronenberg A (2022) Impact of the COVID-19 pandemic on inpatient antibiotic consumption in Switzerland. Antibiotics 11: 792. doi: 10.3390/antibiotics11060792.
8. Giacomelli A, Ridolfo AL, Oreni L, Vimercati S, Albrecht M, Cattaneo D, Rimoldi SG, Rizzardini G, Galli M, Antinori S (2021) Consumption of antibiotics at an Italian university hospital during the early months of the COVID-19 pandemic: were all antibiotic prescriptions appropriate? Pharmacol Res 164: 105403. doi: 10.1016/j.phrs.2020.105403.
9. Dieringer TD, Furukawa D, Graber CJ, Stevens VW, Jones MM, Rubin MA, Goetz MB (2021) Inpatient antibiotic utilization in the veterans' health administration during the coronavirus disease 2019 (COVID-19) pandemic. Infect Control Hosp Epidemiol 42: 751–753. doi: 10.1017/ice.2020.1277.
10. UI Mustafa Z, Salman M, Aldeyab M, Kow CS, Hasan SS (2021) Antimicrobial consumption among hospitalized patients with COVID-19 in Pakistan. SN Compr Clin Med 3: 1691–1695. doi: 10.1007/s42399-021-00966-5.
11. Arslan K, Şahin AS (2023) Evaluation of species distribution and antibiotic susceptibility of blood culture isolates of patients followed in the intensive care unit before and during the COVID-19 pandemic: retrospective, single-center analysis. Phnx Med J 5: 71–77. doi: 10.38175/phnx.1222179.
12. Tabah A, Koulenti D, Laupland K, Misset B, Valles J, Bruzzi de Carvalho F, Paiva J, Çakar N, Ma X, Eggimann P, Antonelli M, M JM, Csomos B, Krueger W, Mikstacki A, Lipman J, Depuydt P, Vesin A, Garrouste-Orgeas M, Zahar JR, Blot S, Carlet J, Brun-Buisson C, Martin C, Rello J, Dimopoulos G, Timsit JF (2012) Characteristics and determinants of outcome of hospital-acquired bloodstream infections in intensive care units: the EUROBACT International Cohort Study. Intensive Care Med 38: 1930–1945. doi: 10.1007/s00134-012-2695-9.
13. Zhanel GG, DeCorby M, Laing N, Weshnoweski B, Vashisht R, Tailor F, Nichol KA, Wierzbowski A, Baudry PJ, Karlowsky JA, Lagacé-Wiens P, Walkty A, McCracken M, Mulvey MR, Johnson J; Canadian Antimicrobial Resistance Alliance (CARA); Hoban DJ (2008) Antimicrobial-resistant pathogens in intensive care units in Canada: results of the Canadian National Intensive Care Unit (CAN-ICU) study, 2005–2006. Antimicrob Agents Chemother 52: 1430–1437. doi: 10.1128/AAC.01538-07.
14. Şirin MC, Ağuş N, Yılmaz N, Bayram A, Yılmaz-Hancı S, Şamlıoğlu P, Karaca Derici Y, Doğan G (2017) Microorganisms isolated from blood cultures of the patients in intensive care units and their antibiotic susceptibilities. Turk Hij Den Biyol Derg 74: 269–278. doi: 10.5505/TurkHijyen.2017.94899.
15. Küçükateş E, Gültekin N (2016) Antimicrobial susceptibility and microorganisms isolated from blood cultures of hospitalized patients in intensive care units. Haseki Tip Bul 54: 97–102. doi: 10.4274/haseki.2872.
16. Müderris T, Yurtsever SG, Baran N, Özdemir R, Er H, Güngör S, Aksoy-Gökmen A, Kaya S (2019) Microorganisms isolated from blood cultures and the change of their antimicrobial susceptibility patterns in the last five years. Turk Hij Den Biyol Derg 76: 231–242. [Article in Turkish]. doi: 10.5505/TurkHijyen.2019.65902.
17. Kalaycı Çekin Z, Behçet M, Avcıoğlu F, Afşar Y, Şentürk E, Kurtoğlu M (2023) Investigation of antibiotic resistance profiles of Gram negative bacteria isolated from blood culture samples. Value Health Sci 13: 80–86. [Article in Turkish]. doi: 10.33631/sabd.1133713.

18. Boral J, Genç Z, Pınarlık F, Ekinci G, Kuskucu M.A, İrkören P, Kapmaz M, Tekin S, Çakar N, Şentürk E, Yurdakul F, Dikenelli B, Can F, Ergönül Ö (2022) The association between *Acinetobacter baumannii* infections and the COVID-19 pandemic in an intensive care unit. Scientific Reports 12: 20808. doi: 10.1038/s41598-022-25493-8.
19. European Centre for Disease Prevention and Control (2023) Antimicrobial resistance surveillance in Europe 2023 (2021 data). Available: https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-surveillance-europe-2023-2021-data. Accessed: 24 May 2024.
20. Karlowsky JA, Jones ME, Draghi DC, Thornsberry C, Sahm DF, Volturo GA (2004) Prevalence and antimicrobial susceptibilities of bacteria isolated from blood cultures of hospitalized patients in the United States in 2002. Ann Clin Microbiol Antimicrob 3: 7. doi: 10.1186/1476-0711-3-7.
21. Köck R, Becker K, Cookson B, van Gemert-Pijnen JE, Harbarth S, Kluytmans J, Mielke M, Peters G, Skov RL, Struelens MJ, Tacconelli E, Navarro Torné A, Witte W, Friedrich AW (2010) Methicillin-resistant *Staphylococcus aureus* (MRSA): burden of disease and control challenges in Europe. Euro Surveill 15: 19688. doi: 10.2807/ese.15.41.19688-en.
22. Lee KH, Kim J, Lee JA, Kim CH, Kwon OM, You EJ, Lee HM, Kim JH, Jeong SJ, Ku NS, Yeom JS, Ahn JY, Choi JY (2024) Carbapenem-resistant *Acinetobacter baumannii* outbreak in a COVID-19 isolation ward and successful outbreak control with infection control measures. Infect Chemother 56: 222–229. doi: 10.3947/ic.2023.0091.
23. Pustijanac E, Hrenović J, Vranić-Ladavac M, Močenić M, Karčić N, Lazarić Stefanović L, Hrstić I, Lončarić J, Šeruga Musić M, Drčelić M, Majstorović D, Kovačić I (2023) Dissemination of clinical *Acinetobacter baumannii* isolate to hospital environment during the COVID-19 pandemic. Pathogens 12: 410. doi: 10.3390/pathogens12030410.
24. Petrakis V, Panopoulou M, Rafailidis P, Lemonakis N, Lazaridis G, Terzi I, Papazoglou D, Panagopoulos P (2023) The impact of the COVID-19 pandemic on antimicrobial resistance and management of bloodstream infections. Pathogens 12: 780. doi: 10.3390/pathogens12060780.
25. Costantino M, Giudice V, Campana F, Iannelli AA, Scala P, Longanella W, Marongiu F, Vozzella EA, Elberti MG, Alfieri M, Boccia G, Conti V, De Caro F, Filippell, A (2024) Pre- and post-COVID-19 antibiotic consumption and stewardship program in a southern Italian hospital. Antibiotics 13: 1128. doi: 10.3390/antibiotics13121128.
26. Fahmy AM, Elgendy MO, Mohamed AA, Imam MS, Alharbi AN, Al-Anezi MH, Aldhafeeri OM, Aldhafeeri SM, Ajeebi JA, Kamal M, Osama H (2025) The efficacy and tolerability of colistin versus non-colistin antimicrobial regimens among hospitalized COVID-19 patients with multidrug-resistant bacterial superinfection: an observational multicenter study. Medicina 61: 884. doi: 10.3390/medicina61050884.
27. Wardoyo EH, Suardana IW, Yasa I, Sukrama IDM (2021) Antibiotics susceptibility of *Escherichia coli* isolates from clinical specimens before and during COVID-19 pandemic. Iran J Microbiol 13: 156–160. doi: 10.18502/ijm.v13i2.5974.
28. Polemis M, Tryfinopoulou K, Giakkoupi P, WHONET-Greece study group, Vatopoulos A (2020) Eight-year trends in the relative isolation frequency and antimicrobial susceptibility among bloodstream isolates from Greek hospitals: data from the Greek electronic system for the surveillance of antimicrobial resistance-WHONET-Greece, 2010 to 2017. Euro Surveill. 25: 1900516. doi: 10.2807/1560-7917.ES.2020.25.34.1900516.
29. Gürbüz M, Şen Türkekul E, Esen B (2024) Evaluation of bacterial and fungal agents isolated from patients admitted to intensive care units before and during the COVID-19 pandemic and comparison of antibiotic susceptibilities. Kocatepe Medical Journal 25: 86–93. [Article in Turkish]. doi: 10.18229/kocatepetip.1235556.
30. Polemis M, Mandilara G, Pappa O, Argyropoulou A, Perivolioti E, Koudoumnakis N, Pournaras S, Vasilakopoulou A, Vourli S, Katsifa H, Karampatakis T, Papavasiliou A, Petinaki E, Xitsas S, Skoura L, Protonotariou E, Mantzana P, Gartzonika K, Priavali E, Kallinteri A, Giannopoulou P, Charalampaki N, Memezas M, Calina Oana Z, Papadogianni M, Panopoulou M, Koutsidou A, Vatopoulos A, Tryfinopoulou K (2021) COVID-19 and antimicrobial resistance: data from the Greek electronic system for the surveillance of antimicrobial resistance- WHONET-Greece (January 2018–March 2021). Life 11: 996. doi: 10.3390/life11100996.
31. Ristori MV, Scarpa F, Sanna D, Casu M, Petrosillo N, Longo UG, Lucia DF, Spoto S, Chiantia RM, Caserta A, Vescio RR, Davini F, Bani L, Riva E, Ciccozzi M, Angeletti S (2024) Multidrug-resistant *Klebsiella pneumoniae* strains in a hospital: phylogenetic analysis to investigate local epidemiology. Microorganisms 12: 2541. doi: 10.3390/microorganisms12122541.
32. Lai CC, Chen SY, Ko WC, Hsueh PR (2021) Increased antimicrobial resistance during the COVID-19 pandemic. Int J Antimicrob Agents 57: 106324. doi: 10.1016/j.ijantimicag.2021.106324.
33. Ng QX, Ong NY, Lee DYX, Yau CE, Lim YL, Kwa ALH, Tan BH (2023) Trends in *Pseudomonas aeruginosa* (*P. aeruginosa*) bacteremia during the COVID-19 pandemic: a systematic review. Antibiotics 12: 409. doi: 10.3390/antibiotics12020409.
34. Hamidi AH, Yılmaz Ş (2021) Antibiotic consumption in the hospital during COVID-19 pandemic, distribution of bacterial agents and antimicrobial resistance: a single-center study. J Surg Med 5: 124–127. doi: 10.28982/josam.834535.