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Original Article

Prevalence and drug resistance patterns of ESKAPE pathogens in Nigde, Türkiye

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Abstract

Introduction: The escalating burden of antimicrobial resistance (AMR) presents a significant global health challenge. ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species*), frequently exhibiting multidrug resistance (MDR), are especially alarming. This study evaluated the prevalence and antibiotic susceptibility profiles of ESKAPE infections in patients from Nigde, Türkiye.

Methodology: This descriptive cross-sectional study was performed at Nigde Ömer Halisdemir University Training and Research Hospital from September 2022 to June 2024. Clinical specimens were collected and evaluated for antimicrobial susceptibility with the VITEK®2 compact system.

Results: A total of 13,387 bacterial isolates were obtained from 7,438 patients. The majority of isolates were Gram-negative (9,671; 72.2%), of which 3,928 (39.6%) were ESKAPE. Gram-positive isolates accounted for 3,716 (27.8%), with 1,123 (30.2%) categorized as ESKAPE. *Klebsiella pneumoniae (K. pneumoniae*) was the most common Gram-negative ESKAPE pathogen (1,921; 19.9%), while *Escherichia coli (E. coli)* was the most frequent non-ESKAPE pathogen (4,747; 49.1%). Of the 5,051 ESKAPE isolates, 29.7% (1,501) were categorized as MDR and 30.9% (1,562) as extensively drug-resistant (XDR). MDR was widespread, with the highest prevalence observed in *Enterococcus faecium* (76.9%). *Acinetobacter baumannii* exhibited the highest prevalence of XDR isolates at 72.4%.

Conclusions: This study emphasizes the substantial AMR burden linked to ESKAPE infections in Nigde, Türkiye, highlighting the necessity for effective infection management, antibiotic stewardship, and continuous research to track resistance patterns.

Key words: ESKAPE pathogens, MDR, XDR.

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Introduction

Antimicrobial resistance (AMR) has arisen as a substantial danger to global public health, undermining our capacity to successfully combat infectious diseases [1]. In 2021, AMR accounted for 4.71 million deaths worldwide and 2.88 billion disability-adjusted life years (DALYs) connected with it. The absence of thorough data regarding the incidence and associated ramifications of AMR in various countries underscores the gravity of this pressing concern [2,3]. Globally, AMR is associated with approximately 4.95 million deaths each year, with low- and middle-income countries carrying the greatest burden of drug-resistant infections [4].

Numerous studies have clearly established a robust association between antibiotic-resistant bacterial infections and negative patient outcomes, such as extended hospitalizations, heightened morbidity rates, and increased fatality rates [5–7]. This escalating issue transcends hospitals, affecting community-acquired illnesses by the dissemination of multidrug-resistant (MDR) clones from healthcare environments [8–11].

AMR is escalating globally, complicating the treatment of bacterial illnesses, especially those induced by Gram-negative bacteria [9]. There are few treatment options available for MDR bacteria, such as

Enterococcus faecium (*E. faecium*), *Staphylococcus aureus* (*S. aureus*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Acinetobacter baumannii* (*A. baumannii*), *Pseudomonas aeruginosa* (*P. aeruginosa*), and *Enterobacter* spp (*E. cloacae*) (the ESKAPE group). These bacteria account for a substantial proportion of nosocomial infections and necessitate potent antibiotics for treatment [12,13]. The ESKAPE infections represent a significant risk to critically ill and immunocompromised individuals because of their capacity to circumvent drug efficacy [14].

A multitude of variables contributes to the emergence of AMR. The global utilization of antimicrobial agents in human medicine has risen, especially in low- and middle-income nations, but consumption rates remain inferior to those in affluent countries [15].

In 2015, the Organization for Economic Cooperation and Development disclosed that Türkiye exhibited one of the highest antibiotic resistance rates among its member nations, seven-fold greater than the lowest recorded rate. The emergence of resistance is frequently linked to improper utilization of antibiotics [16]. In 2015, the World Health Organization (WHO) reported that antibiotic consumption in Türkiye was 38.2 defined daily doses (DDD) per 1,000 persons per day. This represented the highest consumption documented in the WHO European region, encompassing 45 countries [16].

Comprehending the frequency and consequences of MDR infections, particularly those contracted in the community as a result of the dissemination of MDR clones from healthcare facilities, is essential for effectively addressing AMR. This study aimed to ascertain the prevalence and antibiotic susceptibility profiles of ESKAPE infections in patients in Nigde, Türkiye.

Methodology

Study design, data, and sample acquisition

This research was a descriptive cross-sectional study executed at Nigde Ömer Halisdemir University Training and Research Hospital in Nigde, Türkiye, from September 2022 to June 2024. The study encompassed individuals who were admitted to the hospital during this timeframe and were diagnosed with a bacterial infection based on clinical and microbiological evidence. No informed consent was acquired prior to sample collection, as it constituted a standard procedure for all patients admitted to the hospital.

Demographic information (age and gender) and clinical information (type of infection, preexisting medical conditions, length of hospitalization, antibiotic treatment received, and clinical outcomes) were gathered during the study period.

Patients with no or inadequately reported clinical data and incomplete bacterial culture findings were eliminated from the analysis. The study followed ethical guidelines and was performed in accordance with the Declaration of Helsinki. Patient anonymity was upheld during the course of the study, and all data were anonymized prior to analysis.

Bacteriological investigation

The Clinical and Laboratory Standards Institute (CLSI) recommendations and the hospital's microbiology unit's standard operating procedures (SOPs) were followed for all microbiological procedures during the investigation [17].

Clinical samples were grown in the appropriate media for the type of specimen according to standard microbiological methods. In summary, specimens were inoculated onto the appropriate isolation medium, such as blood agar, chocolate agar, and eosin-methylene blue (EMB) agar; and incubated at temperatures ranging from 35 °C to 37 °C.

The bacteria were identified based on the shape of the colonies and Gram stain. After that, the VITEK®2 compact system (bio-Mérieux, North Carolina 27712, USA) with GN and GP ID cards was used to automatically identify the bacteria, following CLSI recommendations [18]. Antimicrobial susceptibility testing (AST) was performed, both automatically and manually. The VITEK®2 compact system identified the antimicrobial susceptibility profiles of Gram-negative and Gram-positive bacteria in accordance with CLSI standards [14]. The Kirby-Bauer disk diffusion method was conducted in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations, and the zone widths were analyzed utilizing EUCAST clinical breakpoints version 4.

The standardized definitions for MDR and extensively drug-resistant (XDR) microorganisms as outlined by Magiorakos *et al*. [18] were utilized in this study. The focus was on the ESKAPE pathogens which are noted for their clinical relevance and resistance profiles. MDR implies that a pathogen is resistant to at least one drug in three or more groups of antimicrobial drugs. XDR implies that there is resistance to at least one agent in all but two or fewer categories. This means that these isolates are only vulnerable to one or two categories of antimicrobial drugs. These definitions help standardize the resistance terminology across labs and monitoring systems; thus making it easier to compare data to support worldwide efforts to prevent infections and use antibiotics wisely.

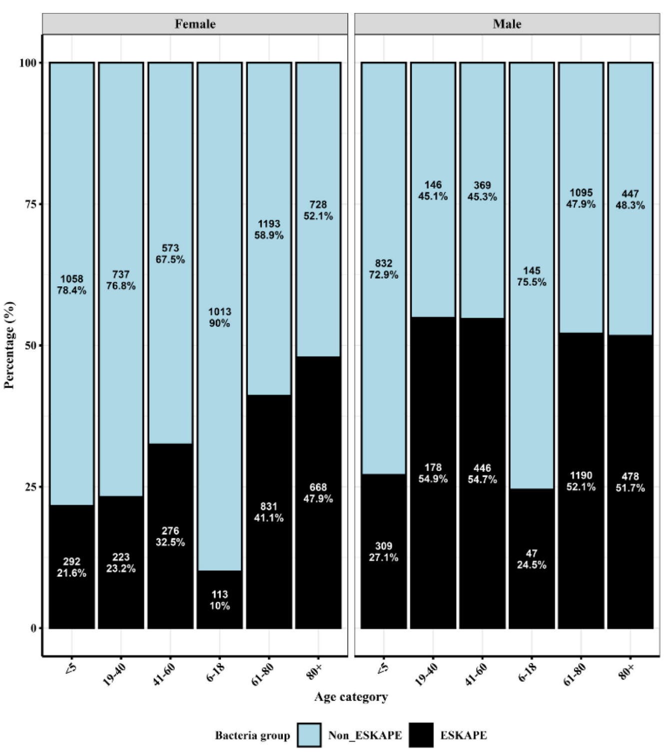
Statistical analyses

All statistical analyses were conducted utilizing R software (version 4.4.0, released 2024-04-24) within the RStudio integrated development environment (version 2024.04.0+735). Descriptive statistics including means, medians, ranges, and proportions were used to summarize the bacterial taxa, patient age groups, and AMR profiles of the clinical isolates.

The Anderson–Darling test for normality was used to analyze the distribution of the continuous age variable for the ESKAPE and non-ESKAPE groups individually. Both groups exhibited substantial deviations from normality ($p < 2.2 \times 1016$) [19], necessitating the application of non-parametric statistical approaches where relevant. The Chi-square test of independence was used to analyze the relationships between categorical variables, such as age group stratification and bacterial classification (ESKAPE versus non-ESKAPE). All tests were two-tailed, with a significance level established at $p < 0.05$.

Duplicate isolates were identified and excluded prior to analysis to ensure data integrity and minimize bias from repeated sampling. Each patient was tracked using a unique national identification number to enable accurate linkage across multiple specimens. When multiple isolates of the same bacterial species were obtained from the same specimen type, only one representative isolate was retained. Isolates obtained from different specimen types (e.g., urine and blood) were treated as independent and included separately.

Figure 1. Distribution of ESKAPE and Non-ESKAPE pathogens by age and gender.



Ethical approval and consent to participate

The Ethics Committee for Non-Interventional Clinical Research at Nigde Omer Halisdemir University in Nigde, Türkiye, gave approval for this study (decision number 2022/82, dated September 10, 2022), and determined that informed consent was not necessary for this study, as it pertained to regular clinical management of patients.

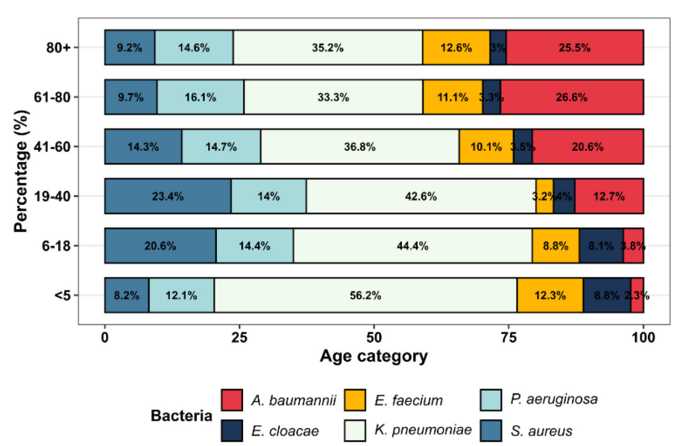
Results

General patients' demographics data

Data from a total of 7,438 patients were included in the study. There were 4,547 females (61%) and 2,891 males (39%) with ages ranging from 37.9 to 31.8 years. The two largest age groups were patients between the ages of 61 and 80 years (1,907; 25.6%) and children younger than 5 years (1,809; 24.4%). Out of all the patients, 1,004 (13.5%) were 80 years old or older. The next largest age groups were 6–17 years old (972, 13%), 41–60 years old (879, 11.8%), and 18–40 years old (867, 11.7%) (Figure 1).

Supplementary Figure 1 shows the distribution of ESKAPE and non-ESKAPE pathogens across the various age groups. The Chi-square test revealed a significant association between bacterial categories and age, as they were not evenly spread among the groups ($p < 0.001$). Additionally, particular bacterial species

Figure 2. Distribution of ESKAPE bacteria by age.



were more common in specific age groups and less common in others. Figure 2 shows the distribution of ESKAPE pathogens by age. A significant association was found between bacterial species and patient age groups ($\chi^2 = 307.63$, df = 25, and $p < 0.001$). The most commonly isolated pathogens across all ages were *K. pneumoniae* and *A. baumannii*. This was particularly true for elderly patients aged 61–80 and ≥ 80 years. *A. baumannii* accounted for 26.6–25.5% of isolates in these age groups, while *K. pneumoniae* constituted around 33.3–35.2%. Although the proportions were smaller, *E. cloacae* and *E. faecium* were likewise more common in the elderly. *S. aureus* was more prevalent in younger patients, especially those under the age of 18 years. *P. aeruginosa* was moderately dispersed throughout the middle-aged and older groups.

On the other hand, the distribution of non-ESKAPE bacteria (Supplementary Figure 2) followed a different pattern based on age. *E. coli* was the most common species in all age categories, making up most of the isolates in almost every category. It was especially common in pediatric patients (79.5% in the 6–18 years' group) and middle-aged adults (68.6% in the 19–40 years' group). *Proteus mirabilis* (*P. mirabilis*), *Streptococcus pneumoniae* (*S. pneumoniae*), *Streptococcus agalactiae* (*S. agalactiae*), *Staphylococcus epidermidis* (*S. epidermidis*), and *Enterococcus faecalis* (*E. faecalis*) were less common and more uniformly spaced out among the age groups. There was a significant association between non-ESKAPE bacterial species and the patient's age group, $\chi^2 = 295.6$, df = 20, $p < 0.001$. This indicated that the prevalence of non-ESKAPE pathogens varied remarkably across different age categories. This also indicated that ESKAPE pathogens were mostly associated with hospital acquired infections in older persons, but non-ESKAPE pathogens are more prevalent in community acquired cases affecting a broader age spectrum, particularly among the younger demographic.

Table 1. Distribution and frequency of pathogens isolated during the study period.

Bacteria isolate	No. isolates	Frequency %
Gram-negative		
ESKAPE		
K. pneumoniae	1921	19.9
A. baumannii	1049	10.8
P. aeruginosa	751	7.8
E. cloacae	207	2.1
SubTotal	**3928**	39.6%
Non-ESKAPE		
P. mirabilis	416	4.3
E. coli	4747	49.1
K. oxytoca	154	1.6
Others	426	4.4
SubTotal	5,743	59.4
Total	9671	72.2
Gram-positive		
ESKAPE		
E. faecium	542	14.6
S. aureus	581	15.6
SubTotal	1123	30.2
Non-ESKAPE		
E. faecalis	606	16.3
S. epidermidis	571	15.4
S. haemolyticus	254	6.8
S. hominis	566	15.2
S. agalactiae	78	2.1
S. pneumoniae	69	1.9
Others	449	12.1
SubTotal	2593	69.8
Total	3716	27.8
Total	**13387**	**100.0**

General distribution of bacterial isolates

A total of 13,387 bacterial isolates were recovered from various clinical specimens from the 7,438 patients included in this cross-sectional study. Among these patients, 66.0% had a single clinical sample that tested positive for bacterial isolates, 27.8 % had two clinical samples, and 6.2 % had three different clinical samples from which bacteria were isolated. The most common clinical samples were midstream urine or urinary catheter specimens, accounting for 6,142 (53.5%) of the total; followed by blood cultures (2,206; 19.2%), sputum (751; 6.5%), tracheal aspirates (784; 6.8%), wound or abscess samples (642; 5.6%), and rectal swabs/stool samples (257; 2.2%) (Supplementary Figure 3; Supplementary Figure 4).

There were 9,671 isolates in all, and 72.2% of them were Gram-negative; of those, 3,928 (39.6%) were ESKAPE pathogens and 5,743 (59.4%) were non-ESKAPE. The other 3,716 isolates (27.8%) were Gram-positive. Of these, 1,123 (30.2%) were ESKAPE pathogens and 2,593 (69.8%) were non-ESKAPE. *E. coli* was the most prevalent Gram-negative non-ESKAPE pathogen, with 1,123 (30.2%) isolates. *E. faecalis* (606; 16.3%), *S. epidermidis* (571; 15.4%), and *S. hominis* (566; 15.2%) were Gram-positive ESKAPE pathogens that were found at almost the same rate (Table 1).

An examination of the distribution of ESKAPE and non-ESKAPE pathogens by gender and age group revealed that ESKAPE pathogens were more frequently isolated from females aged 6–18 years compared to males in the same age group. On the other hand, ESKAPE pathogens were most often observed in men aged 61–80 years and older, followed by men aged 80+ years (Figure 1).

A statistical analysis of the distribution of ESKAPE and non-ESKAPE microorganisms across clinical departments showed a significant association ($p <$

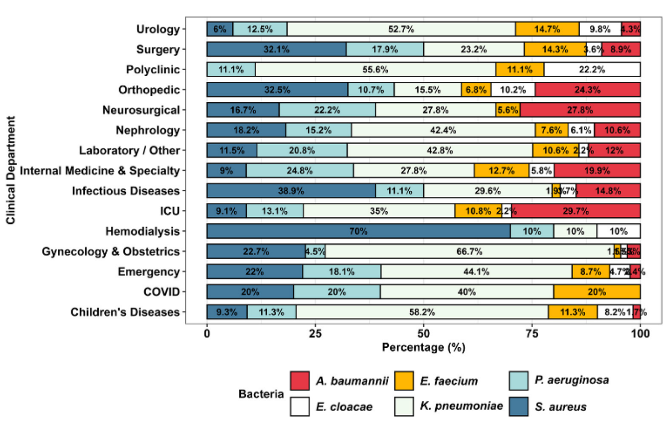
0.05). The intensive care unit (ICU) had the most ESKAPE isolates (2,647; 53.9%), followed by children's diseases (594; 20.5%), internal medicine (553; 37.7%), and orthopedic (206; 59.9%). Polyclinic had a lower proportion of ESKAPE pathogens (9; 37%), while most of the isolates (1,860; 80.3%) were non-ESKAPE. Departments such as the coronavirus disease (COVID) units had moderate levels of ESKAPE bacteria (32.3%). In general, these results show that some clinical areas, such the ICU and children's diseases, had a greater prevalence of ESKAPE pathogens (Figures 3 and 4).

Further analysis within the ICU revealed a significant presence of specific ESKAPE bacteria. *Acinetobacter baumannii* was identified in 29.7% of ICU cases, while *Klebsiella pneumoniae* was present in 35.0% of cases. Overall, ESKAPE pathogens constituted 53.7% of all detected microorganisms, emphasizing the critical need for continuous monitoring to ensure patient safety and to mitigate the spread of antimicrobial resistance. (Supplementary Figure 5).

Categorization of the ESKAPE pathogens according to the antibiotic susceptibility test

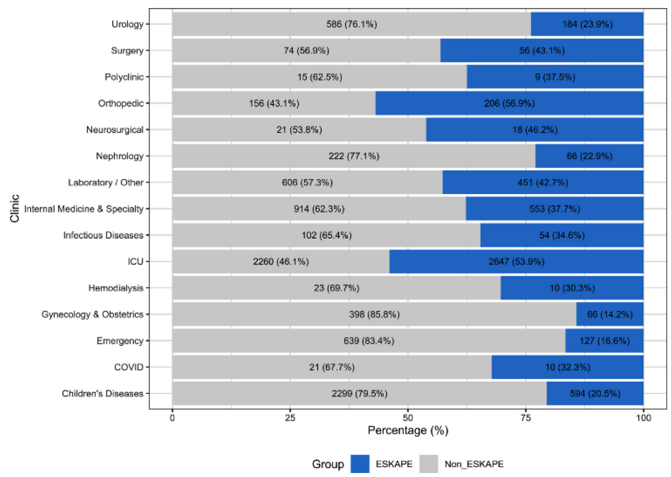
Among the ESKAPE isolates, 58.1% demonstrated resistance to a minimum of 1 antimicrobial agent across 3 separate antibiotic classes. Of these, 31.6% were identified as MDR and 26.5% as XDR. MDR was found in a wide range of ESKAPE infections, with *E. faecium* being the most common (76.9%). *A. baumannii* had the most (72.4%) XDR isolates. It was interesting to note that *E. cloacae* and *S. aureus* did not have any XDR isolates (Figure 5; Supplementary Figure 6, Supplementary Figure 7).

Figure 4. Distribution of ESKAPE bacteria by clinical departments.



ICU: intensive care unit; COVID: coronavirus disease.

Figure 3. Distribution of ESKAPE and Non-ESKAPE bacteria across clinical departments.

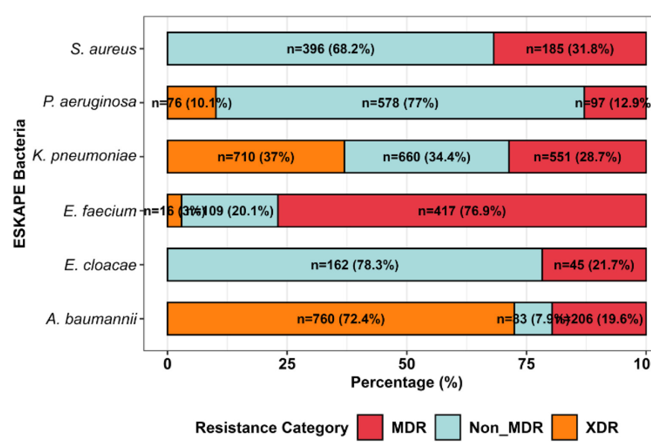


ICU: intensive care unit; COVID: coronavirus disease.

The antimicrobial resistance profiles of the 6 ESKAPE pathogens were analyzed against the antibiotics recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and categorized into non-MDR, MDR, and XDR groups (Figure 5). A pronounced heterogeneity in resistance patterns was observed. *A. baumannii* exhibited the most concerning profile, with the majority of isolates classified as XDR (72.4%, 760 of 1049). Similarly, *K. pneumoniae* demonstrated a high burden of XDR resistance, which constituted the largest single category at 37.0% (710 of 1921), followed by non-MDR (34.4%; 660) and MDR (28.7%; 551).

In contrast, *E. faecium* was dominated by MDR isolates, comprising 76.9% (417 of 542). The

Figure 5. Antibiotics profile categories of ESKAPE bacteria.

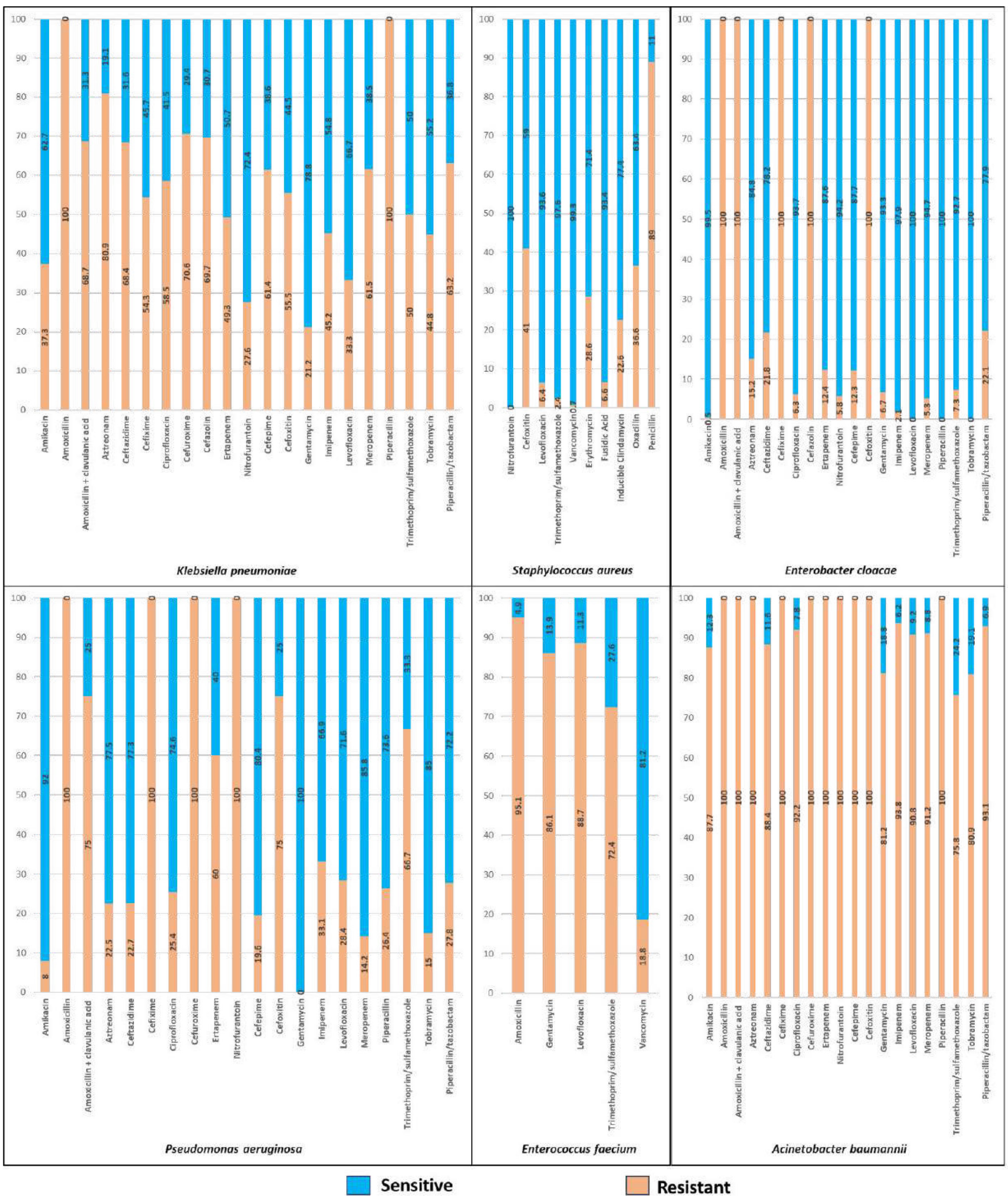


MDR: multi-drug resistant; XDR: extensively drug resistant.

proportion of non-MDR was higher in all remaining species. *E. cloacae* and *P. aeruginosa* were the species with the highest proportion of non-MDR; with 78.3% (162 of 207) and 77.0% (578 of 751), respectively. However, *P. aeruginosa* also presented a non-negligible proportion of XDR (10.1%, 76). *S. aureus* showed a significant proportion of MDR (31.8%; 185 of 581), whereas the majority were non-MDR (68.2%; 396). These data highlight that *A. baumannii* and *K. pneumoniae* represented the major XDR threats in this population, whereas *E. faecium* was the most prevalent MDR pathogen (Figure 5).

Consequently, *A. baumannii* demonstrated significant resistance to all evaluated antibacterial

Figure 6. Antibiotics resistance profiles of ESKAPE bacteria.



drugs, exhibiting total resistance (100%) to amoxicillin, amoxicillin-clavulanic acid, aztreonam, cefixime, cefuroxime, ertapenem, nitrofurantoin, cefepime, cefoxitin, and piperacillin. *P. aeruginosa* strains exhibited complete resistance to amoxicillin, cefixime, cefuroxime, and nitrofurantoin. *K. pneumoniae* isolates exhibited significant resistance to amoxicillin and piperacillin. *E. cloacae* isolates also showed a lot of resistance to amoxicillin, amoxicillin-clavulanic acid, cefazolin, and cefoxitin. It is interesting that none of the tested antibiotics were completely effective against *E. faecium* or *S. aureus* isolates (Figure 6).

Discussion

This study delineates the significant challenge posed by antimicrobial resistance (AMR) among ESKAPE pathogens within a clinical setting. ESKAPE organisms represented 37.7% of all clinical isolates, with *Klebsiella pneumoniae* and *Acinetobacter baumannii* being the most prevalent species. A notably significant finding is the elevated prevalence of extensively drug-resistant (XDR) *A. baumannii*, which exhibited resistance rates of 72.4% to most antimicrobial compounds evaluated, including carbapenems, cephalosporins, aminoglycosides, and fluoroquinolones. In a recent study conducted in Ankara, Türkiye (2024), researchers reported 47.4% XDR and 35.1% pan-drug-resistant (PDR) bacterial isolates [20]. Another study conducted in Türkiye demonstrated that all isolates exhibited multidrug-resistant (MDR) phenotypes, with 31.2% classified as XDR [21].

The resistance spanned several classes of antimicrobial agents, including first- to fourth-generation cephalosporins, carbapenems, aminoglycosides, and fluoroquinolones. The widespread occurrence of XDR *A. baumannii* presents considerable clinical and public health challenges, given this pathogen's reputation for causing nosocomial infections with limited therapeutic options [22]. The presence XDR pathogens indicates a possible excessive or inappropriate application of broad-spectrum antibiotics in clinical environments, which promotes the emergence of resistant strains [23]. These findings underscore the critical importance of implementing comprehensive antimicrobial stewardship programs, strengthening infection control protocols, and pursuing the development of alternative therapeutic approaches to address the proliferation of XDR *A. baumannii* and other MDR organisms [24].

This study also explored variations in AMR among ESKAPE pathogens across various patient age categories. Overall, the findings indicate that isolates from older patients demonstrated greater levels of antibiotic resistance relative to those from infants and younger adults. MDR and XDR strains were more commonly observed among older individuals. Conversely, the rates of MDR and XDR among children were markedly reduced. This increased prevalence of resistance among elderly individuals may be ascribed to various factors. Older patients are more prone to chronic illnesses and recurrent infections, resulting in extended and repetitive courses of antibiotic treatment over time. This prolonged use of antibiotics elevates the probability of selecting for resistant bacterial strains. Furthermore, elderly individuals are more commonly hospitalized or living in long-term care facilities, settings where antibiotic-resistant pathogens are more prevalent due to the extensive and often essential use of antimicrobial agents [25].

The observed MDR prevalence of 31.6% in this study signifies a significant rise relative to earlier national reports of 20.8% [26], indicating a swiftly changing AMR landscape. While earlier research emphasized MDR in *E. coli* and *K. pneumoniae* [27], the findings in this study indicate a shift, with *A. baumannii* emerging as the predominant XDR concern. The carbapenem resistance rate for *A. baumannii* has risen to 92.5%, surpassing prior national statistics [28] and reaffirming an ongoing trend of beta-lactam resistance. The complete resistance to multiple classes of antibiotics, including carbapenems and advanced-generation cephalosporins, corresponds with concerning international reports and underscores a significant therapeutic impasse [29].

Previous studies have reported remarkably high resistance rates in *A. baumannii*, notably for ceftriaxone (100%), ampicillin (100%), amoxicillin-clavulanate (100%), ertapenem (100%), cefuroxime (100%), and aztreonam (99.0%). Consistent with these reports, this investigation demonstrated that *A. baumannii* showed complete resistance (100%) to several antibiotics; including amoxicillin, amoxicillin-clavulanic acid, aztreonam, cefixime, cefuroxime, ertapenem, nitrofurantoin, cefepime, cefoxitin, and piperacillin. Notably, *E. cloacae* exhibited high resistance, with the majority of tested isolates resistant to ampicillin, co-amoxiclav, cefixime, and cefoxitin. Notably, the resistance patterns observed in this investigation for Enterobacterales diverged from those documented in prior research. Previous investigations indicated that 29% of *E. cloacae* isolates exhibited resistance to ceftazidime. Nonetheless, the results of this study demonstrate a reduced overall prevalence of *E. cloacae*, representing merely 1.6% of all bacterial isolates and 2.5% of ESKAPE pathogens. Among these, 21.7% demonstrated resistance to ceftazidime. Furthermore, the resistance of *E. cloacae* to imipenem observed in this study was lower than that reported in previous studies, which documented a resistance rate of 3% [19].

These findings highlight the dynamic and evolving nature of AMR, which is probably affected by factors such as regional antibiotic prescribing practices, infection control protocols, and healthcare-associated transmission.

On the flip side, MDR bacteria were also commonly observed among Gram-positive isolates. The maximum prevalence of MDR was observed in *E. faecium* (76.9%), which was significantly greater than that in *S. aureus* (31.8%). Furthermore, *E. faecium* exhibited the highest prevalence of XDR among Gram-positive bacteria, at 3.0%. Notably, no XDR cases were detected among any other Gram-positive ESKAPE isolates, including *S. aureus*. The comparatively reduced prevalence of *E. cloacae* observed in this study relative to prior reports indicates potential alterations in bacterial distribution or shifts in selection pressures attributable to antibiotic utilization. Nevertheless, the consistently elevated resistance rates, especially among *E. faecium*, raise concerns regarding the growing prevalence of MDR Gram-positive infections [30].

The incidence of vancomycin-resistant *E. faecium* (VRE) in this study was 27.2%, notably exceeding the European Union (EU) average vancomycin resistance rate in *E. faecium*, which is 17.3%.

Nevertheless, it aligns with the rate documented in 2018, indicating a sustained pattern of resistance. Conversely, the rate of vancomycin resistance among *E. faecium* isolates was significantly lower, at 10.4%, in 2014 across countries within the European Union (EU) and the European Economic Area (EEA). A hospital-based study conducted in Italy reported that, among 1,628 isolates from community-acquired infections, only 19 were identified as *E. faecium*, with vancomycin resistance observed in just 1 case (5.3%) [31]. Likewise, a recent study conducted in Germany reported no instances of VRE [32]. These findings underscore considerable geographic variation in VRE prevalence, which may be affected by local antimicrobial stewardship protocols, infection control strategies, and healthcare environments. Nevertheless, the significant prevalence of VRE identified in this investigation presents considerable clinical concerns, given that vancomycin is a primary treatment for *Enterococcus* infections [33]. The rising trend of resistance indicates that glycopeptide-resistant *E. faecium* must consistently be regarded in clinical contexts where this pathogen is suspected. The variation in resistance rates among various nations highlights the importance of region-specific surveillance and customized antimicrobial stewardship strategies. Fortunately, clinical success in treating *E. faecium* infections remains attainable with potent antibiotics such as linezolid, tigecycline, vancomycin, and trimethoprim/sulfamethoxazole, which have shown in vitro effectiveness. Nonetheless, the increasing resistance to last-resort antibiotics underscores the critical need to enforce stringent infection control protocols, encourage prudent antibiotic utilization, and advance the development of novel therapeutic strategies to combat VRE [34].

Yet, the findings provide an essential insight into infection control: targeted surveillance and monitoring within individual departments, which are integral to addressing antibiotic resistance [11]. The variations in susceptibility patterns among clinical departments highlight the importance of implementing infection control strategies customized to the data of each department. The data indicates considerable variation in susceptibility patterns among different clinical departments. For instance, the ICU department exhibited a concerning prevalence of XDR strains. Concurrently, the pediatric unit exhibited a higher incidence of non-MDR strains. This underscores the significance of implementing targeted interventions and surveillance strategies customized to address the unique risks and challenges faced by each department. Furthermore, the elevated prevalence of XDR strains in ICUs serves as a compelling indication that continuous proactive surveillance is essential in high-risk areas where MDR pathogens are more prevalent [35].

This underscores the significance of establishing comprehensive infection control protocols, antimicrobial stewardship initiatives, and surveillance systems to mitigate the dissemination of highly resistant organisms [36]. These findings highlight the critical importance of increased vigilance, prompt identification, and efficient containment strategies in managing novel and emergent infectious threats. Ultimately, the differences in susceptibility patterns across clinical departments highlight the importance of interdisciplinary collaboration among physicians, microbiologists, infection control specialists, and other healthcare professionals [37]. A multidisciplinary approach integrating clinical expertise with microbiological data is essential for the development of targeted therapies, the optimization of antibiotic utilization, and the reduction of AMR dissemination

[38].

The widespread occurrence of ESKAPE organisms and their resistance profiles have significant and immediate implications for empirical treatment in our region and comparable contexts within Türkiye:

1. Empiric treatment protocols for suspected Gram-negative infections, especially in the ICU or among patients with recent hospitalization, should incorporate an agent effective against XDR *A. baumannii*. This frequently requires the administration of colistin or tigecycline until susceptibility results are obtained.

2. The elevated prevalence of carbapenem resistance in *A. baumannii* and the significant rates observed in *K. pneumoniae* (37 % XDR) indicate that carbapenems can no longer be considered a universally reliable first-line empiric treatment for severe Gram-negative infections.

3. In cases of suspected enterococcal infections, the elevated prevalence of VRE warrants careful consideration when relying solely on vancomycin. Agents such as linezolid or daptomycin should be contemplated, particularly in high-risk patients.

These implications strongly support the establishment of comprehensive, hospital-specific antimicrobial stewardship programs (ASPs) that utilize local antibiograms to inform empiric therapy decisions and ensure de-escalation according to culture outcomes [39].

Clinical significance and suggested actions for clinicians in our region

These data have immediate implications for empirical treatment. In the case of severe nosocomial infections, particularly within the ICU, empirical treatment protocols must incorporate agents effective against XDR *A. baumannii* and MDR *K. pneumoniae*.

The elevated VRE prevalence also requires that this pathogen be taken into account in the management of severe enterococcal infections. The findings underscore the critical importance of implementing comprehensive ASPs aimed at optimizing the utilization of antibiotics, especially carbapenems and glycopeptides.

Enhanced infection control measures, encompassing rigorous contact precautions and comprehensive environmental cleansing within the ICU, are essential to effectively interrupt the transmission of these resistant clones.

Limitations of the study

Although informative, the findings of this study should be considered within the framework of several limitations. First, this was a single-center study, which may restrict the applicability of the findings to other regions with diverse patient populations and antibiotic usage protocols.

Second, the inclusion of multiple isolates from the same patient, although indicative of the clinical burden, may disproportionately represent specific resistant clones and distort prevalence estimates.

Third, the lack of molecular characterization (such as polymerase chain reaction (PCR) for carbapenemase genes or multi locus sequence typing (MLST) for strain typing hampers the ability to elucidate the underlying genetic mechanisms of resistance and to monitor specific outbreak strains. Future research employing genotypic methodologies is crucial for elucidating transmission dynamics and guiding effective containment strategies.

Conclusions

This study offers a stark overview of the AMR crisis within a Turkish hospital, emphasizing the prominent contribution of ESKAPE pathogens, which accounted for more than one-third of all isolates. The findings not only corroborate the national and regional trend of increasing resistance but also uncover species-specific and demographic differences that necessitate targeted interventions. The data necessitates prompt, coordinated measures encompassing antimicrobial stewardship, strengthened infection control protocols, and continuous surveillance to inform empirical treatment and prevent further dissemination of these highly resistant pathogens.

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Data availability

The data supporting the findings of this study are available from the authors; however, restrictions apply. These data were used under license from the Non-Interventional Clinical Research Ethics Committee at Nigde Omer Halisdemir University for the current study and are therefore not publicly available.

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Authors' contributions

MAS, SBD, AÖ, study design, statistical calculations, data interpretation; MAS, SBD, NSM, AÖ, manuscript draft; RK, bacterial isolates collection and testing with VITEK2; NMH, FP, NSM, revision of statistical calculations. All authors contributed to the manuscript by following the recommendations of the International Committee of Medical Journal Editors. All authors have read and agreed to the final draft before submission.

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Conflict of interest

No conflict of interest is declared.

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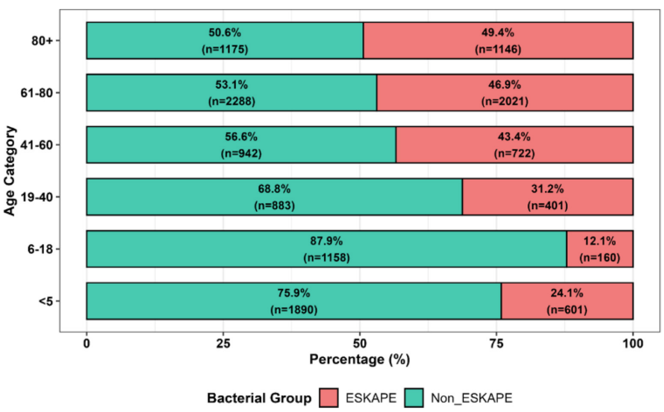
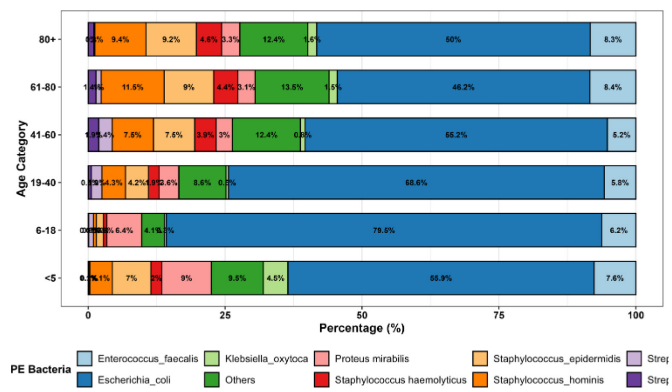
Annex – Supplementary Items

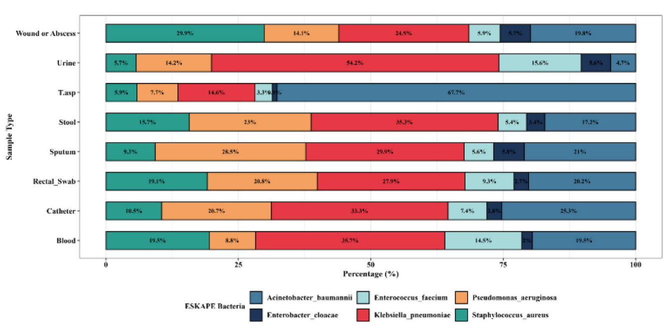
Supplementary Figure 1. Distribution of ESKAPE and Non-ESKAPE bacterial isolates across age groups.



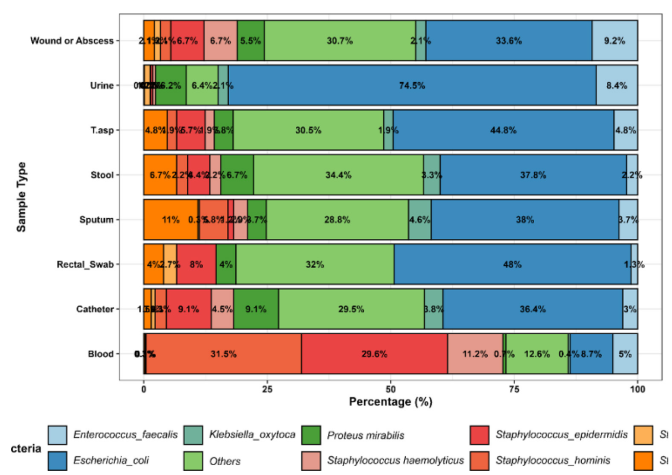
Supplementary Figure 2. Distribution of non-ESKAPE bacterial isolates across age groups.



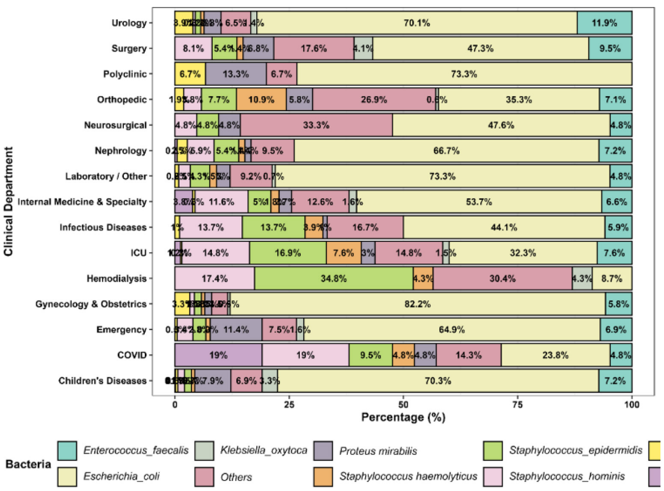
Supplementary Figure 3. Distribution of ESKAPE bacterial isolates across sample types.



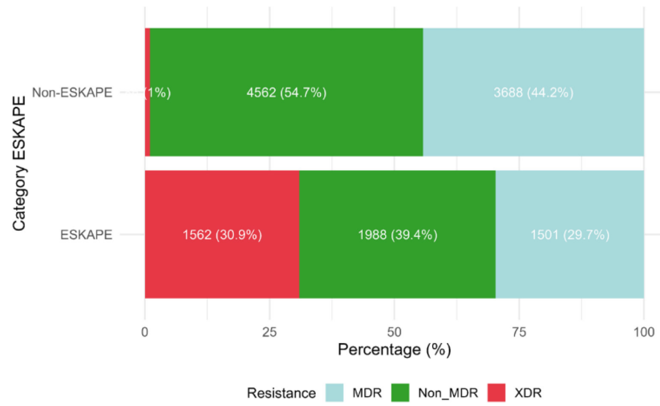
Supplementary Figure 4. Distribution of non-ESKAPE bacterial isolates across sample types.



Supplementary Figure 5. Distribution of non-ESKAPE bacterial isolates across clinical departments.

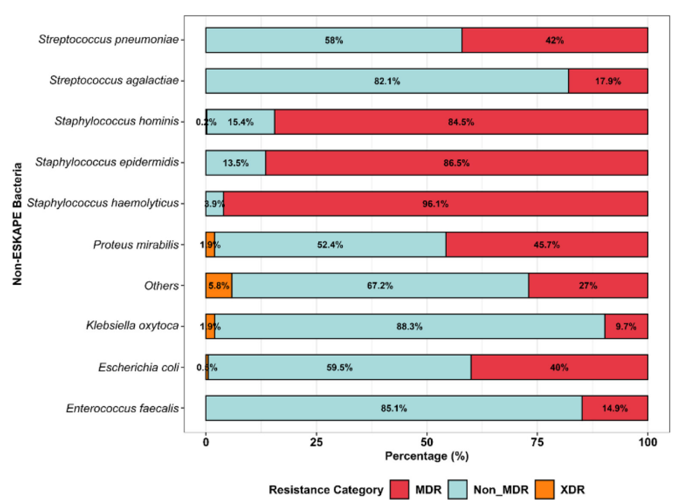


Supplementary Figure 6. Prevalence of ESKAPE and non-ESKAPE bacteria according to their antimicrobial resistance (AMR) category.



MDR: multi-drug resistant; XDR: extensively drug resistant.

Supplementary Figure 7. Prevalence of non-ESKAPE bacterial according to their AMR category.



MDR: multi-drug resistant; XDR: extensively drug resistant; AMR: antimicrobial resistance.