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RESEARCH ARTICLE

ANTIBIOTIC SENSITIVITY OF BACTERIAL BLOODSTREAM INFECTIONS IN THE INTENSIVE CARE UNIT PATIENTS OF UNIVERSITY HOSPITALS IN SANA'A CITY, YEMEN

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Abstract

Aim: High rates of morbidity and mortality are associated to bacterial bloodstream infections (B-BSI) in many hospitals, especially in the intensive care unit. This study investigated the prevalence of antibiotic- and multidrug-resistant bacteria isolated from blood samples of patients in intensive care units of university hospitals in the city of Sana'a, Yemen.
Subjects and methods: A cross-sectional study was conducted on sepsis patients admitted to intensive care units in four hospitals in Sana'a, Yemen, between January 1 and April 30, 2022. The blood cultures of patients suspected of suffering from sepsis were performed. The potential bacterial pathogens were isolated and identified using standard laboratory methods, and microbial susceptibility testing was performed using the disk diffusion technique.
Results: For all identified bacteria, the average resistance rate to a broad spectrum of antibiotics tested ranged from 22.5% to 98.1%, with cefazoline (98.1%) having the greatest resistance rates, followed by amoxicillin (87.2%) and cefixime (83%). Vancomycin had a resistance rate of 4.8% whereas erythromycin had a resistance rate of 75% for Gram-positive bacteria. For Gram-negative bacteria, the resistance rates to narrow spectrum antibiotics ranged from 2.3% for colistin sulphate to 84.8% for aztreonam. Our isolates' MDR rates for resistance to at least three classes of antibiotics were 52.2% and 8.7%, respectively, for resistance to 10 different classes of broad-spectrum antibiotics and their subclasses.
Conclusion: Gram positive bacteria are highly resistant to erythromycin and penicillin, while gram negative organisms are highly resistant to amoxcillin+clavulanic acid, ciprofloxacin, and all generations of cephalosporins. This study highlights the significance of prompt clinical and bacteriological monitoring among patients in critical care conditions, such as ICU patients, and also illustrates the establishment and rates of Multi Drug Resistance (MDR) pathogens.
Keywords: Antibiotic resistant, bacteria, Bloodstream infections (BSIs), ICUs, multi-drug resistant.

INTRODUCTION

Bacterial sepsis is a life-threatening condition that arises when the body's response to an infection injures its tissues and organs. A dysregulated host response to infection is now the new definition of sepsis, which is defined as life-threatening organ dysfunction. Since then, this disease entity has undergone numerous variations, with the late 19th century's advances laying the groundwork for our current understanding of sepsis. The general consensus that sepsis is a systemic infection caused by a harmful organism invading the host and spreading via the bloodstream (septicemia) was established as a result of the development of antiseptic measures, the germ theory of disease, and bacteriology. The pathogenesis of sepsis was not thought to be significantly more complex until the discovery of endotoxin and the continued widespread use of antibiotics[1]. One of the leading causes of illness and mortality worldwide continues to be bloodstream

infection (BSI). Geographical variables can affect the variety of organisms that have been documented to cause BSI. Clinical staff members in charge of intensive care unit (ICU) patients face some of the most challenging issues when it comes to BSI[2,3]. Antimicrobial resistance is spreading globally for a variety of causes, the most significant of which is the rise in prescriptions, distribution in poorer nations, and indiscriminate use. A significant concern for global public health continues to be the estimated 700,000–multiple million deaths that take place each year[4]. Antimicrobial resistance-related mortality may become more common over time, according to predictions made by the World Health Organization (WHO) and United Nations study[5-7]. Antimicrobial resistance (AMR) is a significant public health risk in the modern era. Antimicrobial resistance bacteria are growing rapidly in a variety of hospital departments around the globe, but the issue is particularly severe and complicated in Yemen[8-17]. Regarding some specifics of the earlier research in Yemen, these studies mainly concentrated on examining the sensitivity to antibiotics for each bacterial isolate separately[9-17], whereas the current study examined resistance to all bacterial isolates and also determined the temporal correlation of the rate of increase in the prevalence of bacterial isolate resistance to the studied antibiotics. Antimicrobial resistance is expected to become one of the major causes of death among hospitalized patients, especially immunocompromised patients such as ICU patients in developing countries including Yemen as well as even in developed countries, if appropriate control and prevention measures are not taken[18-20]. Antibiotics must be administered and used properly to treat bacterial infections[21]. Therefore, improper antibiotic prescribing and abuse may contribute to the development of pathogenic bacteria that are resistant to antibiotics, a limitation on available treatments, a lengthening of hospital stays, an increase in treatment expenses, and ultimately a rise in mortality[22].

There is growing worry around the globe regarding the incidence of antibiotic resistance in blood-borne isolates[23]. BSI must therefore be regularly monitored. The inappropriate and illogical use of antibiotics has contributed to an increase in the development of antibiotic resistance (AMR) in Yemen, where the burden of infectious disease is among the highest in the world[24]. A high disease burden, inadequate infra-structure, deficient economic conditions, and uncont-rolled over-the-counter sales of inexpensive antibiotics have all contributed to Yemen's AMR crisis [25,26]. Being aware of the baseline microbial resistance unique to a hospital helps prevent the unnecessary use of antibiotics. This might be referred to as appropriate antibiotic stewardship[27] and could help avoid the spread of antibiotic resistance.

The WHO Global Action Plan on antibiotic Resistance[28] states that raising awareness of antibiotic resistance in research and monitoring initiatives around the globe is crucial. Monitoring bacterial resistance is important and has many advantages, such as: 1) giving information about the prevalence of bacterial resistance; 2) helping to choose the right antibiotics to lower the rate of bacterial resistance; 3) lowering treatment expenses and hospitalization rates; and 4) producing low death rates[22]. Therefore, the goal of the current study is to ascertain the epidemiological profiles and antibiotic resistance of bacteria isolated from ICU sepsis patients admitted to 4 specialist hospitals in Sana'a city in 2022.

SUBJECTS AND METHODS

Study design and subjects: ICU patients admitted to Sana'a city's Al Kuwait, Al Gumhory, Al Sabeen, and Al-Thawra hospitals' ICUs between initial admission and first January 1 through April 30 in 2022 were the subjects of this cross-sectional study. Patients with suspected sepsis who were hospitalized for at least 72 hours during the study period were included.

Diagnosis of sepsis: Sepsis was suspected based on the presence of clinical indicators or risk factors and was confirmed as sepsis if a blood culture was positive, in accordance with international guidelines[1]. To record the clinical traits of sepsis patients, clinicians employed standardized tools. The guardians of all patients were informed of the study's goals before providing signed consent.

Ethical approval: All of the techniques employed in this study were authorized by the research and ethics committee of the Faculty of Medicine and Health Sciences at Sana'a University, Sana'a, Yemen (Approval No. UGR/SU-223).

Laboratory investigations:

Laboratory examinations were conducted in accordance with accepted microbiological practices[29]. Blood was added to a BacT/Alert PF plus culture bottle (BIOMERIEUX, France, LOT 4053532) with a minimum of 1 ml (typically 5 ml in adult patients), and the bottle was left to incubate until the BacT/Alert instrument (BACTEC 9050, Becton Dickinson) identified the culture as positive or negative. Then, after being sub-cultured on blood agar, MacConkey agar, and choclate agar, all positive samples were incubated at 37°C for 24-48 hours. Gram-staining was utilized to differentiate between gram-positive and gram-negative microorganisms. Enough pure culture colonies were used to suspend the bacteria in 3.0 ml of sterile saline in a test tube. Following the guidelines in the product information manuals (BIOMERIEUX), pure bacterial suspension was added to the bacterial specific identification and sensitivity testing kit device. The samples were then analyzed using the VITEK II system for bacterial bio-typing and antibiotic susceptibility. A VITEK ® GN ID identification card (lot 2410933203) was used to identify gram negative bacteria, and a VITEK ® GP ID identification card (lot 2420938203) was used to identify gram positive bacteria. Every treatment was administered for the usual therapeutic and diagnostic intents.

Antibiotic sensitivity test: Utilizing Kirby-Bauer disc diffusion techniques, antibiotic resistance was assessed, and CLSI was used to interpret antibiotic sensitivity data[30]. Typically, Sigma-Aldrich sources are used in NCPHL for antibiotic disks and medium powders. GPB and GNB isolates comprising *Pseudomonas*

aeruginosa (ATCC 27853), *Escherichia coli* (ATCC 25922), and *Staphylococcus aureus* subsp. *aureus* ATCC 25923 were used as quality control for a routine DDM test recommended in the NCPHL Department of Microbiology. The antibiotic disks were utilized to evaluate the antibiotic susceptibility of GNB and Gram-positive bacteria. The study's conclusions were categorized as resistant (R), intermediate (I), or sensitive (S).

RESULTS

Gram-negative bacteria were more common than Gram-positive bacteria overall, with frequencies of 50 (52.1%) and 42 (43.7%) respectively. *E. coli* had the highest frequency of identified Gram-negative bacteria at 20.8%, followed by *Klebsiella* spp. 11 (11.5%), *Burkholderia cepacia* 6, *H. influenzae* 5, *Acintobacter baumannii* 4, *Pseudomonas aeruginosa* 3, and *Chryseobacterium indologenes* 1. The highest frequency of isolated Gram-positive bacteria was coagulase negative *Staphylococci* 25 (26%) followed by *S. aureus* 9 (9.4%), *S. pneumoniae* 5 (5.2%), *Enterococci* 2 (2.1%) and *S. pyogenes* 1 (1.0%) respectively. For susceptibility to penicillin group antibiotics, the highest resistance rate was to piperacillin-tazobactam (76.1%) (Table 1).

Table 1: The susceptibility of bacterial isolates to penicillin's classes antibiotics.

Antibiotics	Classes	Sensitive No. (%)	Moderate No. (%)	Resistant No. (%)	Total No.
Amoxicillin-Clavulanate	Penicillin and β-lactamase inhibitor	41 (44.6)	2 (2.2)	49 (52.7)	92
Piperacillin- Tazobactam		11 (11.9)	11 (11.9)	70 (76.1)	92
Amoxicillin	Penicillin/amino-penicillin	5 (12.8)	0 (0)	34 (87.2)	39*
Ampicillin		9 (25.6)	1 (2.6)	29 (74.3)	39*

*=Expected *P. aeruginosa*, *Staphylococci*, *S. pneumoniae*, *S. pyogens*, *B.cepacia* and *A. baumannii*.

Table 2: The susceptibility of bacterial isolates to cephalosporins β-lactam classes antibiotics.

Antibiotics	Classes	Sensitive No. (%)	Moderate No. (%)	Resistant No. (%)	Total No.
Cefazoline	1st generation	0 (0)	1 (1.9)	52 (98.1)	53*
Cefadroxil		15 (28.3)	0 (0)	38 (71.7)	53*
Cephradin		20 (37.7)	5 (9.4)	28 (52.8)	53*
Cefoxitin	2nd generation	30 (34.5)	0 (0)	57 (65.5)	87***
Cefuroxime		25 (47.1)	4 (7.5)	24 (45.3)	53*
Cefotaxime	3rd generation	18 (34)	2 (3.8)	33 (62.2)	53*
Ceftriaxone		10 (18.9)	1 (1.9)	42 (79.2)	53*
Ceftazidime		20 (22.2)	2 (3.6)	34 (60.7)	56**
Cefoperazone		25 (35.7)	4 (7.5)	24 (45.3)	53*
Cefixime		8 (15.1)	1 (1.9)	44 (83)	53*
Cefepime	4th generation	16 (28.6)	0 (0)	40 (71.4)	56**

*=Excepted *Enterococci*, *P. aeruginosa* and *Staphylococcus spp*.,**=Excepted *Enterococci* and *Staphylococcus spp*., *** =Excepted *Enterococci* and *P. aeruginosa*.

For the beta-lactam classes of cephalosporins, the highest susceptibility rate was to cefuroxime (47.1%), for the first generation the highest resistance rate was to cefazolin (98.1%), and for the third generation beta-lactam cephalosporins the highest resistance rate was to ceftriaxone (79.2%). (Table 2). Meropenem (63%) and imipenem (34.8%) had the highest sensitivity rates among the different carbapenem classes. In addition, monobactams were tested only on Gram-negative bacteria, and the resistance rate was 84.8%, while glycopeptides were only tested on Gram-positive bacteria, and the highest sensitivity rate was to vancomycin (95.2%) (Table 3).

Table 3: The susceptibility of bacterial isolates to carbapenems, glycopeptides and monobactams classes antibiotics.

Antibiotics	Classes	Sensitive No. (%)	Moderate No. (%)	Resistant No. (%)	Total No.
Imipenem	Carbapenems	52 (56.5)	8 (8.7)	32 (34.8)	92
Meropenem		58 (63)	6 (6.5)	28 (30.4)	92
Vancomycin	Glycopeptides	40 (95.2)	0 (0)	2 (4.8)	42*
Aztreonam	Monobactams	14 (15.2)	0 (0)	36 (84.8)	50**

*=Tested only for Gram positive bacteria, **=Tested only for Gram negative bacteria

When it came to the poly-peptide classes of antibiotics, which were limited to testing for gram negative bacteria, the sensitivity rate for colistin sulphate was 90.9% (Table 4). We employed two varieties of each macrolide class azithromycin, which had a resistance rate of 77.8%, and erythromycin, which had a resistance rate of 75% for the classes of macrolides that were solely examined for isolated Gram-positive bacteria. Two types of aminoglycoside classes were also employed; they exhibited a 67.4% sensitivity rate to amikacin and a 41.8% resistance rate to gentamicin (none of which were tested against *Streptococcus*

pyogenes) (Table 5). The susceptibility to the antibiotic families of oxazolidinones, lincosamides, and tetracyclines is shown in Table 6. The sensitivity rate of doxycycline is 75.3%, while the resistance rate is 32.5%. The categories of fluoroquinolone susceptibility and folate pathway inhibitors are shown in Table 7. For the fluoroquinolone classes, ciprofloxacin had a 66.3% resistance rate and levofloxacin a 32.6% sensitivity rate. For folate pathway inhibitors, the co-trimoxazole sensitivity rate was 55.8% .

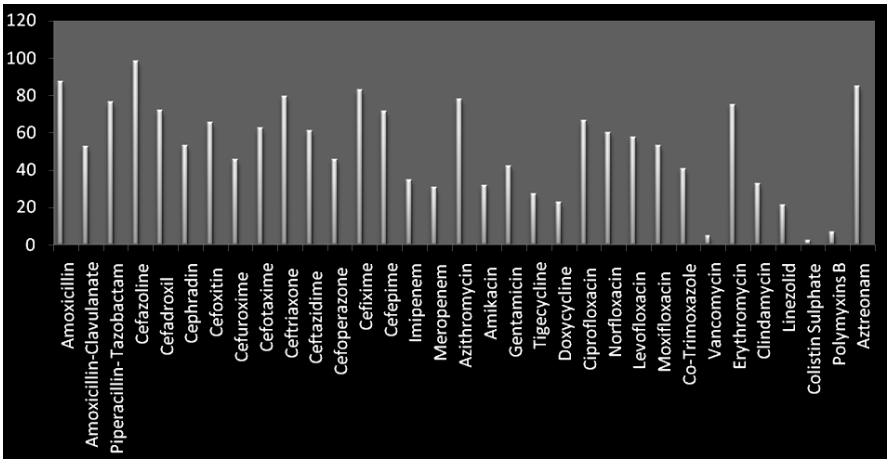

Figure 1: Antibiotics resistant rate for isolated bacteria from septicemia ICUs patients.

Figure 1 displays the range of antibiotic resistance rates for all identified bacteria, ranging from 22.5% to 98.1%, with cefazoline (98.1%) having the greatest resistance rates, followed by amoxicillin (87.2%) and cefixime (83%). For Gram-positive bacteria, the resistance rates to narrow spectrum antibiotics ranged from 4.8% for vancomycin to 75% for erythromycin. For Gram-negative bacteria, the resistance rates to narrow spectrum antibiotics ranged from 2.3% for colistin sulphate to 84.8% for aztreonam. Table 8 shows the prevalence of MDR among BSI isolates. The MDR that showed resistance to at least three classes of antibiotics for used isolates was 52.2%, and the MDR rate for resistance to 10 different classes of broad-spectrum antibiotics and their subclasses reached a rate equal to 8.7%.

Table 4: The susceptibility of bacterial isolates to polymyxins classes antibiotics.

Antibiotics	Classes	Sensitive No. (%)	Moderate No. (%)	Resistant No. (%)	Total No.
Colistin Sulphate	Polymyxins	40 (90.9)	3 (6.8)	1 (2.3)	44*
Polymyxins B		36 (81.8)	1 (2.3)	3 (6.8)	44*

*= Excepted *Burkhoderia cepacia*

DISCUSSION

The average proportion of resistance to broad-spectrum antibiotics evaluated for all identified bacteria in the current study ranged from 22.5% to 98.1%, with cefazoline having the greatest resistance rate at 98.1%, followed by amoxicillin at 87.2% and cefixime at 83%. This typically high incidence of resistance can be explained by the fact that antimicrobial usage in both humans and other animals, as well as the occurrence of resistant strains between the two, are primarily responsible for the rise in drug resistance[31]. The emission of inadequately treated effluents from the pharmaceutical industry, particularly in nations where bulk medicines are produced, has also been linked to an increase in resistance.

Antibiotics boost the rate at which the remaining resistant bacteria proliferate by increasing the selective pressure on bacterial populations, which causes the susceptible germs to perish. The advantage of resistant bacteria over weak microorganisms can exist even at relatively low levels of antibiotic use. Alternative therapies are becoming necessary as instances of antibiotic resistance increase. New antibiotic therapies have been demanded, but it is getting harder to produce new medications[31,32]. In tertiary hospitals in Sana'a, Yemen, the current study examined the prevalence of antibiotic resistance among the primary pathogenic bacteria isolated from ICU patients' blood.

Table 5: The susceptibility of bacterial isolates to macrolides and aminoglycosides classes antibiotics.

Antibiotics	Classes	Sensitive	Moderate	Resistant	Total
		No. (%)	No. (%)	No. (%)	No.
Azithromycin	Macrolides	9 (20)	1 (2.2)	35 (77.8)	45*
Erythromycin		8 (20)	2 (5)	30 (75)	40**
Amikacin	Aminoglycosides	62 (67.4)	1 (1.1)	29 (31.5)	92
Gentamicin		50 (54.9)	3 (3.3)	38 (41.8)	91***

*=Tested for *H. influenzae* and Gram-positive bacteria except *Enterococci.*, **=Tested for Gram-positive bacteria except *Enterococci.****=Excepted *Streptococcus pyogenes.*

Table 6: The susceptibility of bacterial isolates to tetracyclines, lincosamides and oxazolidinones classes antibiotics.

Antibiotics	Classes	Sensitive	Moderate	Resistant	Total
		No. (%)	No. (%)	No. (%)	No.
Tigecycline	Tetracyclines	60 (67.4)	5 (5.6)	24 (27)	89*
Doxycycline		67 (75.3)	2 (2.2)	20 (22.5)	89*
Clindamycin	Lincosamides	25 (62.5)	2 (5)	13 (32.5)	40**
Linezolid	Oxazolidinones	32 (76.2)	1 (2.4)	9 (21.4)	42***

*= Excepted *P. aeruginosa*,**=Tested only for Gram-positive bacteria except *Enterococci*, ***=Tested only for Gram positive bacteria

Table 7: The susceptibility of bacterial isolates to fluoroquinolones classes and folate pathway inhibitors antibiotics.

Antibiotics	Classes	Sensitive	Moderate	Resistant	Total
		No. (%)	No. (%)	No. (%)	No.
Ciprofloxacin	Fluoroquinolones	26 (28.3)	5 (5.4)	61 (66.3)	92
Norfloxacin		29 (31.5)	8 (8.7)	55 (59.8)	92
Levofloxacin		30 (32.6)	9 (9.8)	53 (57.6)	92
Moxifloxacin		27 (30.3)	15 (16.8)	47 (52.8)	89*
Co-Trimoxazole	Folate pathway inhibitors	48 (55.8)	3 (3.5)	35 (40.7)	86**

*= Excepted *P. aeruginosa*. **= Excepted *P. aeruginosa*, *S. pyogenes* and *Enterococci*.

One of the top concerns of clinicians worldwide is the occurrence and spread of these agents, which are certain to be capable of causing serious infections in ICU patients, particularly immunocompromised patients, the elderly, neonates, and children[26,33,34]. Because different patterns of antimicrobial resistance exist in different places, it is not permitted to administer multiple classes of antibiotics to neonates and children. It is also challenging to choose and prescribe the right antibiotics to treat various infections in immunocompromised, elderly, neonatal, and pediatric patients. Additionally, understanding the patterns of antibiotic resistance might assist physicians and policy officials in addressing the issues of resistance in their respective nations[35].

Table 8: Prevalence of MDR degree among BSI isolates (n = 92)

Broad spectrum Antimicrobial class used to define MDR	Degree	No (%)
Tetracycline (Tetercycline)	R 0	12 (13)
Imipenem (carbapenems)	R 1	25 (27.2)
Sulfonamides (Cotrimoxazole)	R 2	7 (7.6)
Gentamicin (Aminoglycoside)	R 3	5 (5.4)
Levofloxacin (fluoroquinolone	R 4	1 (1.1)
Cefoxitin (Cephalosporin)	R 5	15 (16.3)
Ciprofloxacin (Quinolone)	R 6	7 (7.6)
Piperacillin-Tazobactam (combination penicillin)	R 7	1 (1.1)
Azithromycin (macrolide)	R 8	9 (9.8)
Amoxicillin (Amino-penicillin)	R 9	2 (2.2)
	R 10	8 (8.7)
Resistant to at least three antibiotic class	MDR	48 (52.2)

R0: Sensitive against all selected antibiotic class; R1: Resistant to at least one antibiotic class; R2: Resistant to two antibiotic class; R3: Resistant to three antibiotic class; R4: Resistant to four antibiotic class; R5: Resistant to five antibiotic class; R6: Resistant to six antibiotic class; R7: Resistant to all seven antibiotic class; etc. MDR: Resistant to at least three antibiotic class.

Patients and healthcare professionals would use antibiotic resistance inappropriately as a result of the absence of public surveillance initiatives in the developing nations like Yemen and many industrialized nations[36-39]. Investigation of anti-microbial resistance trends is therefore crucial and significant, particularly in underdeveloped nations like Yemen where there are no formal recommendations for the use of antibiotics. On the other hand, it is vital to look at the patterns of GPB and GNB antibiotic resistance in Sana'a city hospitals' intensive care units (ICUs) in 2022. This research could serve as a valuable model for policymakers and physicians implementing experimental treatments to ICU sepsis patients. The findings of the current study revealed that linezolid had a rate of resistance of 21.4% (Table 8), making it ineffective against *Enterococcus* spp. and *S. aureus*. This rate differed from those previously reported by Al-Shami *et al.*,[25] (0.4%), Al-Huraibi *et al.*,[40] (0.0%), and Al-Safani *et al.*,[26] (<1%) in Yemen. The resistance to linezolid was also higher than that reported by Azimi *et al.*, in Iran[41], Dharmapalan *et al.*, in India[42], He *et al.*, in China[43], Li Tian *et al.*, in China[44], and Al-Naqshbandi and others in Iraq[45], where it was less than 2%. However, the results of other investigations were consistent with the current study, and it has been reported that linezolid resistance is widespread and may reach 20% or more[46,47].

As of right now, 4.8% of Gram-positive bacteria were resistant to a restricted range of antibiotics, including vancomycin (Table 8). In contrast to the rates of vancomycin resistance reported by Al-Huraibi *et al.*,[40] for *S. aureus* (0.0%) and total GPB by Al-Shami *et al.*, [25], which was 7.8%, the resistance rate observed in the current study was greater at 18.0%. Many nations, including the USA, have implemented successful VRSA risk reduction strategies, and certain guidelines have been produced to prevent infections brought on by these pathogenic bacteria, according to a number of published research studies and reports[48]. As a result, we recommend comparable policies and initiatives created for patients in Sana'a, Yemen. The current study also demonstrated that, in contrast to ciprofloxacin (66.3% resistant rate), a restricted spectrum of antibiotics targeting Gram-negative bacteria, such as colistin, exhibited a 2.3% resistance rate (Table 8). These findings contrasted with those published by Azimi *et al.*, who found that colistin has a higher rate of resistance than ciprofloxacin[41], but were similar to those of Mahmoudi *et al.*, from Iran[22] and Dharmapalan *et al.*, from India[5] .

Sulfamethoxazole/trimethoprim, ceftazidime, ampicillin, ceftorexime, cefazoline, cefadroxil, cefuroxime, cefixime, and cefotaxime are all ineffective antibiotics against GPB or GNB, according to the study's overall findings. It is important to note that these antibiotics are frequently used to treat various illnesses, particularly sepsis and septicemia, in Sana'a's hospitals. It is generally known that the misuse or overuse of antibiotics as well as bystander selection lead to the daily rise in antibiotic resistance, which is the cause of this[49]. So the following role must be followed in current situation: use antibiotics with caution if major pathogenic microorganisms have a resistance rate of > 40%. Drug sensitivity test findings must be utilized to choose which antibiotics to employ when major pathogenic bacteria have a resistance rate of > 50%. If the major pathogenic bacteria are more than 75% resistant to antibiotics, then antibiotic use must be discontinued. It is necessary to look into and assess feedback on bacterial resistance in order to decide if clinical usage of the medication can continue[50]. Given the high level of antibiotic resistance among bacteria, it is essential to accurately identify and use effective antibiotics for treatment in order to prevent the unintended consequences of sepsis and septicemia and to lower the mortality rate resulting from these infections[51-54]. Therefore, it is essential and strongly advised to be aware of the patterns of antibiotic resistance among common infections, to arrange workshops to rectify the prescribing of empirical therapy, and to make modifications in the usage of antibiotics.

The MDR rate in the current study was 52.2% (Table 8), which is higher than other reports that indicate MDR infections are common in patients admitted to the intensive care unit (ICU) and can have an incidence of up to 40%. These infections are typically linked to high mortality rates. Critically ill patients in intensive care units frequently have significant immune system failure as well as multiple organ dysfunctions. Patients' physiological barriers may be harmed by ventilators and invasive procedures, and ICU patients are more likely to become infected than patients in other departments[55]. ICU patients use antibiotics at a higher frequency, higher dose and longer duration, and infection with multiple drug-resistant bacteria (multidrug-resistant organisms; MDROs) is more severe compared with patients in other departments. Although bacteria have their own mechanisms for drug resistance, improper use of antibiotics, particularly abuse of third-generation cephalosporins, is the main cause of the high frequency of multidrug-resistant bacterial infection in ICUs[56-59]. According to studies, a significant cause of death for ICU patients is nosocomial infection. Improve the treatment effectiveness and prognosis of ICU patients by adopting clear, evidence-based prevention and control measures to drastically lower the incidence of nosocomial infection. To combat nosocomial infections and lower the risk of antibiotic resistance, lobbying efforts should be made.

Limitations of the study

The following were the study's limitations. First, we were unable to precisely identify the types of isolates and their patterns of antibiotic sensitivity in Yemen since the data only came from one place, Sana'a city. These isolates should be subjected to molecular studies in order to verify the presence of bacterial resistance genes.

CONCLUSIONS

The prevalence and antibiotic resistance of bacteria isolated from ICUs are briefly reviewed in this study's conclusion. In contrast to Erythromycin and Penicillin, which are extremely resistant to gram positive bacteria, *E. coli* was the most often isolated gram negative organism. It also exhibits strong resistance to amoxcillin+clavulanic acid, Ciprofloxacin, and all generations of cephalosporins. This study highlights the significance of timely clinical and bacteriological monitoring among patients in critical care conditions, such as ICU patients, and also demonstrates the appearance and rates of multi-drug resistant (MDR) pathogens. Antibiotics should also be administered with caution. ICUs and other critical care facilities should therefore establish antibiotic policies.

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AUTHOR'S CONTRIBUTIONS

Al-Yosaffi EA: conducted the fieldwork as part of her PhD studies. **Al-Shamahy HA:** supervision, review. **Othman AM:** data analysis, writing. **Al-Haddad AM:** methodology, investigation. **Al-Moyed KA:** data analysis and interpretations. The final manuscript was read and approved by all authors.

DATA AVAILABILITY

The data and material are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST

This work does not include any conflicts of interest.

REFERENCES

1. Funk DJ, Parrillo JE, Kumar A. Sepsis and septic shock: A history. Crit Care Clin 2009 Jan;25(1):83-101, viii. *https://www.ncbi.nlm.nih.gov/books/NBK537054*
2. Wasihun A, Wlekidan L, Gebremariam S, *et al*. Bacteriological profile and antimicrobial susceptibility patterns of blood culture isolates among febrile patients in Mekelle Hospital, Northern Ethiopia. Springerplus 2015; 4: 314.
3. Gohel K, Jojera A, Soni S, Gang S, Sabnis R, Desai M. Bacteriological profile and drug resistance patterns of blood culture isolates in a tertiary care nephrourology teaching institute. Biomed Res Int 2014. *https://doi.org/10.1155/2014/153747*
4. Dramé O, Leclair D, Parmley EJ, *et al*. Antimicrobial resistance of campylobacter in broiler chicken along the food chain in Canada. Food Borne Path Dis 2020; 17 (8): 512-20. *https://doi.org/10.1089/fpd.2019.2752*
5. CDC. The biggest antibiotic-resistant threats in the U.S." Centers for Disease Control and Prevention. 6 November 2019. Retrieved 19 September 2021.
6. Samuel S. Our antibiotics are becoming useless. Vox 2019. Retrieved 19 September 2021.
7. O'Brien TF, Clark A, Peters R, Stelling J. Why surveillance of antimicrobial resistance needs to be automated and comprehensive. J Glob Antimicrob Resist 2018; 17:8–15.
8. Pormohammad A, Nasiri MJ, Azimi T. Prevalence of antibiotic resistance in Escherichia coli strains simultaneo-usly isolated from humans, animals, food, and the environment: a systematic review and meta-analysis. Infect Drug Resist 2019; 12:1181. *https://doi.org/10.2147/IDR.S201324*
9. Tian L, Sun Z, Zhang Z. Antimicrobial resistance of pathogens causing nosocomial bloodstream infection in Hubei Province, China, from 2014 to 2016: a multicenter retrospective study. BMC Public Health 2018; 18(1):1121. *https://doi.org/10.1186/s12889-018-6013-5*
10. Alhasani AH, Ishag RA, Al Shamahy HA, *et al*. Association between the Streptococcus mutans biofilm formation and dental caries experience and antibiotics resistance in adult females. Universal J Pharm Res 2020; 5(6):1-3. *https://doi.org/10.22270/ujpr.v5i5.478*
11. Abbas AM, Al-Kibsi TAM, Al-Akwa AAY, *et al*. Characterization and antibiotic sensitivity of bacteria in orofacial abscesses of odontogenic origin. Universal J Pharm Res 2020; 5(6):36-42. *https://doi.org/10.22270/ujpr.v5i6.510*
12. AL-Haddad KA, Ali Al-Najhi MM, Al-Shamahy HA, *et al*. Antimicrobial susceptibility of Aggregatibacter Actinomycete mcomitans Isolated from Localized Aggressive Periodontitis (LAP) Cases. J Dent Ora Heal Ad 2021; 103. *https://doi.org/10.39127/2021/JDOHAR:1000103*
13. Al-Akwa AA, Zabara A, Al-Shamahy HA, *et al*. Actinomycete-mcomitans. Prevalence of *Staphylococcus aureus* in dental infections and the occurrence of MRSA in isolates. Universal J Pharm Res 2020; 5(2):1-6. *https://doi.org/10.22270/ujpr.v5i2.384*
14. Al-Deen HS, Al-Ankoshy AAM, Al-Shamahy HA, *et al*. Porphyromonas gingivalis: biofilm formation, antimicrobial susceptibility of isolates from cases of Localized Aggressive Periodontitis (LAP). Universal J Pharm Res 2021; 6(4):1-7. *https://doi.org/10.22270/ujpr.v6i4.633*
15. Alyahawi A, Alkaf A, Alnamer R, Alnosary T. Study of resistance for recently marketed carbapenem drug among hospitalised patients in Sana'a, Yemen. Universal J Pharm Res 2018; 3(5). *https://doi.org/10.22270/ujpr.v3i5.203*
16. Saleh AAM, Al-Shamahy HA, Al-Hrazi RMA, Jaadan BM, AL-Magrami RTF, Al-Sharani AA. Biofilm formation and antibiotic susceptibility of uropathogens in patients with catheter associated urinary tract infections in Ibb city - Yemen. Universal J Pharm Res 2020; 4(6):1-7. *https://doi.org/10.22270/ujpr.v4i6.329*
17. Ishak AA, Alhadi AM, Al-Moyed KAA, Al-Shamahy HA. Childhood urinary tract infection: Clinical signs, bacterial causes and antibiotic susceptibility. Universal J Pharm Res 2021; 6(4):58-64. *https://doi.org/10.22270/ujpr.v6i4.643*
18. Al-Hamzi, MA, Sharafuddin, AH, Al-Shameri BHH, *et al*. The effect of dental implants on aerobic bacteria colonization in the oral cavity and the antibiotic profile of common isolated aerobic bacteria. Universal J Pharm Res 2023; 8 (4):1-6. *https://doi.org/10.22270/ujpr.v8i4.969*
19. Al-Shehari, MM, Al-Khamesy, KSA, Al-Moyed, KA, *et al*. Distribution and antibacterial resistance of wound pathogenic bacteria in patients of Sana'a hospitals, Yemen. Universal J Pharm Res 2023; 8(3):1-8. *https://doi.org/10.22270/ujpr.v8i3.942*
20. Saleh, AAM, Al-Shamahy, HA, Al-Hrazi, RMA, *et al*. Biofilm formation and antibiotic susceptibility of uropathogens in patients with catheter associated urinary tract infections in Ibb city -Yemen. Universal J Pharm Res 2020; 4(6):1-8. *https://doi.org/10.22270/ujpr.v4i6.329*
21. Aslam B. Antibiotic resistance: a rundown of a global crisis. Infect Drug Resist 2018; 11:1645–1658. *https://doi.org/10.2147/IDR.S173867*
22. Mahmoudi S, Mahzari M, Banar M, *et al*. Antimicrobial resistance patterns of Gram-negative bacteria isolated from bloodstream infections in an Iranian referral paediatric hospital: a 5.5-year study. J Glob Antimicrob Resist 2017; 11:17–22. *https://doi.org/10.1016/j.jgar.2017.04.013*
23. Timsit J, Ruppe´ E, Barbier F, *et al*. Bloodstream infections in critically ill patients: an expert statement. Intens Care Med 2020; 46: 266–284.
24. Al-Hammadi, MA, Al-Shamahy, HA, Qaid AA. The prevalence and phenotypic characterization of extended-spectrum β-lactamases-producing Escherichia coli strains isolates recovered from tertiary hospitals in Sana'a city, Yemen. Universal J Pharm Res 2019; 3(6):1-6. *https://doi.org/10.22270/ujpr.v3i6.220*
25. Al-Shami HZ, Al-Haimi MA, Al-dossary OAE, *et al*. Patterns of antimicrobial resistance among major bacterial pathogens isolated from clinical samples in two tertiary's hospitals, in Sana'a, Yemen. Universal J Pharm Res 2021; 6(5):60-67. *https://doi.org/10.22270/ujpr.v6i5.674*
26. Al-Safani AA, Al-Shamahy H, Al-Moyed K. Prevalence, antimicrobial susceptibility pattern and risk factors of MRSA isolated from clinical specimens among military patients at 48 medical compound in Sana'a city-Yemen. Universal J Pharm Res 2018; 3(3):40-44. *https://doi.org/10.22270/ujpr.v3i3.165*
27. Al-Haifi, AY, Al Makdad, ASM, Salah MK, Al-Shamahy, HA, Al Shehari WAA. Epidemiology, bacterial profile, and antibiotic sensitivity of lower respiratory tract infections in Sana'a and Dhamar city, Yemen. Universal J Pharm Res 2020; 5(2):1-8. *https://doi.org/10.22270/ujpr.v5i2.386*
28. Cheesbrough M. District laboratory practice in tropical countries. Cambridge: Cambridge University Press; 2010. *https://doi.org/10.1017/CBO9780511581304*
29. Isenbergh HD. Clinical microbiology procedures handbook. 2nd ed. Washington: ASM Press; 2004.
30. CLSI. Performance Standards for Antimicrobial Disc Susceptibility Tests. (11th edn.), Approved standard M02-A11– Publication of Clinical and Laboratory Standards Institute [CLSI), 2012, USA, 32.
31. Gullberg E, Cao S, Berg OG, *et al*. Selection of resistant bacteria at very low antibiotic concentrations. PLOS Pathogens 2011; 7 (7):e1002158.

https://doi.org/10.1371/journal.ppat.1002158
32. Cassir N, Rolain JM, Brouqui P. A new strategy to fight antimicrobial resistance: the revival of old antibiotics. Frontiers Microbiol 2014; 5: 551. *https://doi.org/10. 3389/fmicb.2014.00551*
33. Alshamahi EYA, Al-Shamahy HA, Musawa YA, Al-Shami HZ. Bacterial causes and antimicrobial sensitivity pattern of external ocular infections in selected ophthalmology clinics in Sana'a city. Universal J Pharm Res 2020; 5(3):1-6. *https://doi.org/10.22270/ujpr.v5i3.409*
34. Folgori L, Bielicki J, Heath PT, Sharland M. Antimicrobial-resistant Gram-negative infections in neonates: burden of disease and challenges in treatment. Curr Opin Infect Dis. 2017; 30(3):281-288. *https://doi.org/10.1097/QCO.0000000000000371*
35. Gopalakrishnan R, Sureshkumar D. Changing trends in antimicrobial susceptibility and hospital acquired infections over an 8 year period in a tertiary care hospital in relation to introduction of an infection control programme. J Assoc Physicians India 2010; 58(Suppl):25–31.
36. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathog Glob Health. 2015; 109 (7):309–318. *https://doi.org/10.1179/2047773215Y.0000000030*
37. Edrees HW, Anbar AA. Prevalence and antibacterial susceptibility of bacterial uro-pathogens isolated from pregnant women in Sana'a, Yemen. PSM Biol Res 2020; 5(4): 157-165.
38. Edrees WH, Banafa MA. Antibacterial susceptibility of isolated bacteria from wound infection patients presenting at some government Hospitals at Sana'a city, Yemen. Al-Razi Univ J Med Sci 2021; 5(1):1-13. *https://doi.org/10.51610/rujms5.1.2021.99*
39. Al-Haifi AY, Al Makdad ASM, Salah MK, Al-Shamahy HA. Urinary tract infections in post operative patients: prevalence rate, bacterial profile, antibiotic sensitivity and specific risk factors. Universal J Pharm Res 2020; 5(3):1-6. *https://doi:10.22270/ujpr.v5i3.411*
40. Al-Huraibi BS, Al-Shehari M, Al-Moyed KA, Al-Shami HZ, Al-Hymia FM, Al-Shamahy HA. Comparison of antibiotic sensitivity of MRSA with mssa among Staphylococcus aureus isolates from patients in the 48 military hospital in Sana'a city, Yemen. Universal J Pharm Res 2023; 8(4):47-52. *https://doi.org/10.22270/ujpr.v8i4.974*
41. Azimi T, Maham S, Fallah F, Azimi L, Gholinejad Z. Evaluating the antimicrobial resistance patterns among major bacterial pathogens isolated from clinical specimens taken from patients in Mofid Children's Hospital, Tehran, Iran: 2013-2018. Infect Drug Resist 2019; 2:2089-2102. https://doi.org/10.2147/IDR.S215329
42. Dharmapalan D, Shet A, Yewale V, Sharland M. High reported rates of antimicrobial resistance in Indian neonatal and pediatric blood stream infections. J Pediatr Infect Dis Soc 2017; 6(3):e62–e68. *https://doi.org/10.1093/jpids/piw092*
43. He X, Xie M, Li S, *et al*. Antimicrobial resistance in bacterial pathogens among hospitalized children with community acquired lower respiratory tract infections in Dongguan, China (2011–2016). BMC Infect Dis 2017; 17(1):614. *https://doi.org/10.1186/s12879-017-2757-2*
44. Tian L, Sun Z, Zhang Z. Antimicrobial resistance of pathogens causing nosocomial bloodstream infection in Hubei Province, China, from 2014 to 2016: a multicenter retrospective study. BMC Public Health 2018; 18(1):1121.
45. Al-Naqshbandi AA, Chawsheen MA, Abdulqader HH. Prevalence and antimicrobial susceptibility of bacterial pathogens isolated from urine specimens received in Rizgary hospital – Erbil. J Infect Public Health 2018; 12(3):330–336.
46. Gandapor AJ, Khan AM. Antibiotic Sensitivity pattern of bacterial isolates of neonatal septicemia in Peshawar, Pakistan. Arch Iran Med 2016; 19(12):866.
47. Hui-min Y, Yan-ping W, Lin Liu Y, Shamsi BH, Bo H, Xuchun M. Analysis of distribution and antibiotic resistance of pathogens isolated from the paediatric population in Shenmu Hospital from 2011–2015. J Int Med Res 2018; 46(1):225–233. *https://doi.org/10.1177/0300060517716343*
48. Keihanian F, Saeidinia A, Abbasi K, Keihanian F. Epidemiology of antibiotic resistance of blood culture in educational hospitals in Rasht, North of Iran. Infect Drug Resist 2018; 11:1723. *https://doi.org/10.2147/IDR.S169176*
49. Moges F, Eshetie S, Yeshitela B, Abate E. Bacterial etiologic agents causing neonatal sepsis and associated risk factors in Gondar, Northwest Ethiopia. BMC Pediatr 2017; 17(1):137. *https://doi.org/10.1186/s12887-017-0969-7*
50. Han Y, Zhang J, Zhang HZ, Zhang XY, Wang YM. Multidrug-resistant organisms in intensive care units and logistic analysis of risk factors. World J Clin Cases. 2022 Feb 26; 10(6):1795-1805. *https://doi:10.12998/wjcc.v10.i6.1795*
51. Shariati A, Azimi T, Ardebili A, *et al*. Insertional inactivation of oprD in carbapenem-resistant Pseudomonas aeruginosa strains isolated from burn patients in Tehran, Iran. New Microbes New Infect 2018; 21:75–80. *https://doi.org/10.1016/j.nmni.2017.10.013*
52. Behmadi H, Borji A, Taghavi-Rad A, Soghandi L, Behmadi R. Prevalence and antibiotic resistance of neonatal sepsis pathogens in Neyshabour, Iran. Arch Pediatr Infec Dis. 2016; 4(2). *https://doi.org/10.5812/pedinfect*
53. Ardehali SH, Azimi T, Owrang M, Aghamohammadi N, Azimi L. Role of efflux pumps in reduced susceptibility to tigecycline in *Acinetobacter baumannii*. New Microbes New Infect 2019; 30:100547. *https://doi.org/10.1016/j.nmni.2019.100547*
54. Bahramian A, Shariati A, Azimi T, *et al*. First report of New Delhi metallo-beta-lactamase-6 (NDM-6) among Klebsiella pneumonia ST147 strains isolated from dialysis patients in Iran. Infect Genet Evol 2019; 69:142–145. *https://doi.org/10.1016/j.meegid.2019.01.030*
55. Christie J, Macmillan M, Currie C, Matthews-Smith G. Improving the experience of hip fracture care: A multidisciplinary collaborative approach to implementing evidence-based, person-centered practice. Int J Orthop Trauma Nurs 2015; 19: 24- 35. *https://doi.org/10.1016/j.ijotn.2014.03.003*
56. Yu M, Wang QY, Gu Q. Clinical study of tigecycline combined therapy in the treatment of multi drug resistant bacterial infections in NICU patients. Zhongguo Yiyuan Ganran Zazhi 2014; 24: 6086-6088. *https://doi.org/10.1164/ajrccm-conference.2012.185.1_meetingabstracts.a6085*
57. Morris S, Cerceo E. Trends, Epidemiology, and Management of Multi-Drug Resistant Gram-Negative Bacterial Infections in the Hospitalized Setting. Antibiotics (Basel) 2020; 9. *https://doi.org/10.3390/antibiotics9040196*
58. Tang LL, Zhang PJ, Qian LH, Li Y, Wu Q, Cai DZ. Meta-analysis of risk factors for carbapenem-resistant Klebsiella pneumoniae infection in China. Zhongguo Xiaodu Zazhi 2019; 036 (003): 199-205.
59. Alkubati SA, Saghir SAM, Alhariri A, Al-Areefi M, Al-Sayaghi KM, Alsabri M, Alnaimat SM, Albagawi BS. Prevalence of antibiotic resident bacteria in intensive care units at Hodeida City, Yemen. J Appl Pharm Sci, 2022; 12(09):139-145. *http://dx.doi.org/10.7324/JAPS.2022.120916*