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Prevalence of Multidrug Resistant Bacterial Infection of Healthcare Associated Bloodstream Infections at King Fahd Spaecilast Hospital in Qasssim Saudi Arabia

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Abstract

This study conducted at King Fahd specialist Hospital in Qassim, Saudi Arabia, from January 2019 to December 2023, investigated the prevalence and antimicrobial resistance of bloodstream infections (BSIs) across various age groups and genders. Utilizing the BD PhoenixTM system and microscan walkway for bacterial identification and antibiotic susceptibility testing, the research highlights the challenges posed by gram-negative and gram-positive bacterial infections in a hospital setting. The study found a near-equal gender distribution among the patients, with a significant portion of infections originating from the Intensive Care Unit (ICU), emphasizing the critical issue of multidrug-resistant infections among the severely ill. Gram-positive bacteria, making up 67.6% of the isolates, include prevalent strains such as *Coagulase-negative Staphylococci* and *Enterococcus Fecalis*, with *Methicillin-Resistant Staphylococcus Aureus (MRSA)* presenting significant resistance challenges. On the other hand, gram-negative bacteria, accounting for 32.4% of isolates, feature *Klebsiella Pneumoniae* and *Escherichia Coli* as common strains, with notable resistance in Acinetobacter species. The results revealed high morbidity rates associated with specific bacterial strains, indicating an increased risk linked to these pathogens. Multidrug resistance (MDR) is alarmingly present in both gram-positive (30.4%) and gram-negative (25.9%) bacteria, with a significant presence of Extended-Spectrum Beta-Lactamase (ESBL) resistance, particularly among gram-negative isolates.

Keywords: MDR, ESBL, Infection, Bloodstream, Saudi Arabia

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1. Introduction

The prevalence of healthcare-associated bloodstream infections (HABSI) poses a grave danger to public health, influencing morbidity and mortality, especially within the confines of hospital environments. Healthcare-associated bloodstream infections (HABSI), often stemming from medical procedures, affect millions of individuals worldwide each year, contributing significantly to elevated mortality rates influenced by a multitude of factors [1]. One of the alarming developments in recent years has been the emergence of multidrug-resistant strains, notably *Methicillin-resistant Staphylococcus aureus (MRSA)* and *Extended-Spectrum Beta-Lactamase (ESBL)*-producing bacteria, which have complicated the already challenging landscape of treatment approaches [2, 3]. Both gram-positive and gram-negative pathogens play a substantial role in hospital-acquired bloodstream infections, leading to heightened mortality rates, especially among patients with compromised immune systems [2]. The indiscriminate use of broad-spectrum antibiotics has inadvertently exacerbated antimicrobial resistance, impairing mortality rates and imposing substantial burdens on society. Consequently, preventive measures have become paramount. Rigorous infection control practices, robust surveillance programs, and timely interventions have proven instrumental in curbing the spread of these infections [4]. Additionally, managing bloodstream infections requires precise identification of pathogens and the implementation of targeted antimicrobial therapy. This approach is crucial in mitigating the challenges posed by drug-resistant bacterial infections, ensuring that patients receive appropriate treatment tailored to the specific strains they are battling. Addressing the complexities of

HABSI demands a multifaceted approach that integrates prevention, surveillance, and strategic interventions. By adopting stringent infection control protocols and vigilant monitoring, healthcare facilities can significantly reduce the incidence of these infections. Furthermore, advancements in diagnostic techniques and the development of novel antimicrobial therapies are essential in the ongoing battle against drug-resistant bacterial strains, offering a glimmer of hope in the pursuit of improved patient outcomes and reduced mortality rates. On the other hand, the escalating prevalence of multidrug-resistant bacterial infections within healthcare settings has emerged as a pressing concern in Saudi Arabia. Recent studies conducted in Riyadh, the capital city, have revealed alarming rates of multidrug-resistant bacteria among hospitalized patients, painting a concerning picture of the situation. Gram-positive bacteria, particularly *Staphylococcus epidermidis* and *Klebsiella pneumoniae*, have been notably prevalent, exhibiting diverse resistance patterns [5]. Another study focused on the distribution of pathogens responsible for healthcare-associated infections (HAIs), emphasizing the dominance of gram-negative bacteria such as *Escherichia coli* and *Klebsiella species*. Although antimicrobial susceptibility patterns displayed stability, specific changes in resistance rates over time were observed. In-depth investigations, including a case-control study, identified risk factors contributing to multidrug-resistant Gram-negative bacteria (GNB) infections. These factors included prior antibiotic use and admission to intensive care units, shedding light on the complexities of the issue [6]. Saudi Arabia is grappling with a significant challenge posed by diverse multidrug-resistant organisms, leading to elevated mortality rates. Various research papers have underscored this concern, focusing on a range of pathogens, including *Acinetobacter baumannii, E. coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. The gravity of these findings cannot be overstated, highlighting the urgent necessity for tailored treatment strategies and comprehensive approaches to tackle the growing threat of multidrug-resistant bacterial infections in the country [6]. Addressing this challenge demands a multifaceted approach encompassing stringent infection control measures, judicious use of antibiotics, continuous surveillance, and research to inform evidence-based policies. Collaborative efforts among healthcare professionals, researchers, and policymakers are essential to develop effective strategies, ensuring the safety of patients and the sustainability of healthcare systems in the face of this escalating crisis. The primary objective of this study is to ascertain the prevalence of multidrug-resistant (MDR) bacteria within the bloodstream of patients in the Qassim region of Saudi Arabia. Specifically, the research aims to investigate the prevalence of MDR strains in various critical healthcare units, including Intensive Care Units (ICUs), burn units, and critical care units situated within King Fahd Specialist Hospital. Additionally, the study attempts to assess the antibiotic resistance profiles of diverse MDR bacterial strains identified within the premises of King Fahd Specialist Hospital.

2. Materials and Methods

2.1. Sample collection

This study was conducted between January 2019 and December 2023 in Qassim region, Saudi Arabia. The collected sample size was 2051 specimens from the patients and was collected by the Department of Microbiology, King Fahd specialist Hospital in Qassim, Saudi Arabia. Blood samples from patients admitted to ICU, including adults and children, were taken. Different age group samples were also collected. The procedure for acquiring and conserving blood samples from patients has been established in accordance with global protocols. The King Fahd specialist Hospital employed an electronic system to record patient details. Clinicians were responsible for gathering information such as age, ethnicity, tribe, place of residence, level of education, and medical history. Blood samples were obtained from patients only after obtaining their informed consent. The steps performed include isolating and identifying bacteria, followed by antimicrobial susceptibility.

2.2. Isolation and BD Phoenix™ system identification of bacteria

In isolating and identifying bacterial pathogens from blood samples, Automated Blood Culture Equipment was employed to pretest the samples for bacterial growth signals [7]. Those samples indicating microbial growth signals were subjected to cultivation on blood agar, chocolate agar, McConkey agar, and mannitol salt agar plates at 37°C under aerobic conditions for 18 hours. After this incubation period, bacterial cultures were purified on blood agar plates to ensure the acquisition of pure cultures [8]. Subsequently, the isolated bacteria were subjected to Gram staining to distinguish between gram-negative and gram-positive strains. Following the manufacturer's instructions, gram-negative and gram-positive isolates were further identified using the Microscan Walkaway 96 instrument. Specifically, gram-negative organisms were cultured on MacConkey agar, which exhibited a distinct crystal blue hue. Further gram-negative and gram-positive isolates were identified using the BD Phoenix™ system, which involved rapid identification and antimicrobial susceptibility research. The system utilized modified traditional, fluorogenic, and chromogenic substrates as redox indicators to detect bacterial growth in the presence of antimicrobial agents [9]. Valid identification of isolates required a score exceeding 90%, failing which no identification was recorded. These meticulous procedures ensured the study's accurate isolation and identification of bacterial pathogens.

2.3. Antimicrobial susceptibility of clinical isolates

In the comprehensive assessment of antimicrobial susceptibility for clinical isolates, a multiple antibiotic resistance index (MAR) was calculated to determine the number of resistant antibiotics, with a MAR value exceeding 0.2, indicating a high-risk source of infection. This assessment integrated various methods, including disk diffusion, Minimum Inhibitory Concentration (MIC), broth micro-dilution, agar dilution, and the ETEST gradient strip test. Blood cultures, which typically require 24 hours to 5 days to display positive results based on microorganism

growth, now benefit from automated techniques such as VITEK2, enabling swift Antimicrobial Susceptibility Testing (AST) outcomes. Treatment strategies were tailored based on the patient's condition, with the administration of broad-spectrum antibiotics every 6 to 8 hours, followed by targeted de-escalation against the causal infection. Notably, adjustments to antibiotic regimens were made before the second dose to prevent unnecessary use of broad-spectrum variants. Furthermore, the antimicrobial susceptibility of all clinical isolates was rigorously evaluated using the BD Phoenix™ system, encompassing a wide array of antimicrobials ranging from oxacillin to ceftolozane-tazobactam. This thorough analysis provided invaluable insights into bacterial resistance patterns, guiding clinicians toward informed and effective treatment decisions, thereby enhancing the overall management of antimicrobial therapies in clinical settings.

2.4. Data analysis

Data were analyzed using version 28.0 of the IBM SPSS software package (Armonk, NY: IBM Corp). Qualitative data were described using numbers and percentages (%). Values less than 0.05 were considered statistically significant.

2.5. Ethical consideration

This study was approved by the Research Committee of King Fahad specialist hospital in Qassim, Saudi Arabia. IRB Log No. (~~21-002E~~).

3. Results and discussion

3.1. Demographic and clinical characteristics of the patients in the study

Table 1 shows the demographic and clinical characteristics of the patients in the study, including gender, age, sample type, and mortality. The gender distribution in the study is fairly balanced, comprising 879 females (42.9%) and 1172 males (57.1%). Regarding sample types, the results reveal a significant prevalence of BL.C/S 1st - AEROBIC samples at 37.8%, closely followed by BL.C/S 2nd - ANAEROBIC at 32.5%. This variety in sample types underscores the thoroughness of the study, allowing it to comprehensively explore different aspects of the patient's conditions. A critical aspect examined in this study is the mortality rate. The findings show a balanced yet concerning statistic, with 52.8% of patients unfortunately succumbing to their conditions while 47.2% managed to survive. Lastly, the breakdown of age groups provides valuable insights. A significant portion of the patients (60.6%) falls within the 41-80 age range, indicating that a majority of the patients in the study are middle-aged to elderly. Additionally, 26.2% of patients are 81 years or older. A significant portion of cases, 51.3%, was reported from the Intensive Care Unit (ICU). Surprisingly, the Emergency department accounted for 21.7% of the cases. The results also revealed infections in specialized units like Critical Care, Intermediate Unit, CCU, and AhO, Table 1.

3.2. Isolation and identification of clinical bacterial from the targeted patients

A total of 1125 bacterial isolates were identified. The gram-positive accounts for 67.6% of all isolates, indicating a significant challenge within the healthcare sector. Predominant strains such as *coagulase-negative Staphylococcus*, *Staphylococcus hominis*, and *Enterococcus Fecalis* highlight their prevalence among the studied patients. Particularly noteworthy is the remarkably high number of *Staphylococcus Epidermidis* cases (409), Table 3. Thirty six casese were identified as MRSA. On the other hand, the percentage of the gram-negative bacteria isolated was 32.4%. Among these isolated gram-negative bacteria, *Klebsiella Pneumoniae* stands out as the most common strain, appearing in 244 cases, underscoring its significant presence in these infections. *Escherichia Coli (E. Coli)* closely follows with 138 cases, emphasizing its role as a prevalent pathogen in healthcare-associated contexts. Multidrug-resistant strains like *Acinetobacter baumannii, haemolyticus* (34 cases), and *Acinetobacter boumannii* (103 cases) were also identified. The emergence of *Providencia rettgeri*, *Providencia Stuartii*, and *Burkholderia Cepacia* was recognized. It is noteworthy that the study identifies less common strains like *Serratia Marcescens*, *Serratia Odorifera*, and *Pseudomonas fluorescens*.

3.3. Morbidity distributions in the study

For the Gram-positive bacteria, The results reveal a range of morbidity rates across different bacterial strains. Notably, *Staphylococcus lugdunensis* stands out with a significantly lower morbidity rate, indicating a higher survival rate among patients (76.9%). Conversely, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, and *Staphylococcus Epidermidis* exhibited relatively higher morbidity rates (Tables 4). Furthermore, the varying morbidity rates observed across different Staphylococcus species, including *Coagulase-negative Staphylococcus* and different Enterococcus species. Among the gram-negative bacteria, *Klebsiella Pneumoniae* and *E. Coli* stand out as the most prevalent strains. However, their morbidity rates, 66.8% and 49.3%, respectively. Acinetobacter species, including *Acinetobacter baumannii/haemolyticus* and *Acinetobacter boumannii*, also exhibit alarmingly high morbidity rates, 70.6%, and 72.8%, respectively (Tables 5).

3.4. Multidrug resistance distribution in the study

A staggering 30.4% of the isolated gram-positive bacteria exhibited multidrug resistance (MDR), Figure 2. Methicillin-Resistant Staphylococcus Aureus (MRSA) was demonstrated in 3.9% of cases adds a layer of complexity. MRSA and MDR coexisted in (0.3%). A substantial portion of the isolated gram-negative bacteria (25.9%) displayed multidrug resistance (MDR), Figure 2. Extended-Spectrum Beta-Lactamase (ESBL) resistance was recognized in 32.1% of cases. ESBL and MDR coexisted (2.0%).

3.5. Distribution of isolated clinical bacteria regarding the multidrug-resistant

Regarding Gram-positive bacteria, within *coagulase-negative Staphylococcus* isolates, a staggering 60% exhibited multidrug resistance (MDR), signifying the complexities in treating infections caused by these bacteria. *Enterococcus Faecium* displayed a significant resistance rate of 17.9%, underscoring the need for meticulous antibiotic selection. Staphylococcus aureus - MRSA exhibited substantial resistance at 69.4%, emphasizing the formidable challenge in managing infections arising from this strain. Additionally, varying resistance levels were noted within *Staphylococcus haemolyticus*, *Staphylococcus sciuri*, *Staphylococus capitis*, and *Staphylococcus epidermidis*, highlighting the diverse antibiotic resistance profiles even within the same species (Tables 6 and 7). Regarding Gram-negative bacteria, the results illuminate significant disparities in multidrug resistance patterns among different bacterial species. *Acinetobacter baumannii/haemolyticus* and *Acinetobacter boumannii* exhibit alarming multidrug resistance rates, at 91.2% and 83.5% respectively, emphasizing the urgent need for targeted interventions against these strains. *Klebsiella Pneumoniae* and *E. coli*, significant contributors to healthcare-associated infections, showcase varied resistance profiles. *Klebsiella Pneumoniae* presents a concerning 50.4% ESBL resistance rate, while *E. coli*, though relatively lower, still demonstrates worrying levels of multidrug resistance (2.2%) and ESBL resistance (35.5%). In addition, *Enterobacter Cloacae*, *Proteus Mirabilis*, and *Serratia Marcescens* display diverse resistance levels, highlighting the multifaceted challenges in treating infections caused by these bacteria. Additionally, the presence of multidrug-resistant strains among less common species like *Serratia Odorifera* underscores the significance of acknowledging the potential impact of these lesser-known pathogens. This study meticulously investigated the prevalence and characteristics of multidrug-resistant bacterial infections within healthcare-associated bloodstream infections in the Qassim region of Saudi Arabia. Our research delves deeply into the clinical implications of multidrug-resistant infections, analyzing patient records meticulously. This study explored how antimicrobial resistance affects treatment outcomes, the association with the patient's location in the hospital, and overall morbidity and mortality rates. Our findings highlight the pressing need for personalized therapeutic approaches, emphasizing the urgency of developing specific antimicrobial strategies to tackle the distinct resistance patterns observed in Qassim. Our findings show that 67.6 % of gram-positive bacteria and 32.4 % of gram-negative bacteria were isolated from 2051 patients in the study. These results are consistent with a previous Saudi Arabian study by Banawas et al. who found that gram-positive bacteria were significantly more abundant than gram-negative bacteria from 1039 patients in the Qassim region of Saudi Arabia [5]. Also, Bhadauria et al., showed that Gram-positive organisms were more than Gram-negative organisms, constituting about 57.69% of total isolates versus 42.74% of Gram-negative organisms [10]. Furthermore, other Pakistanian study agreed with our findings and detected that 62% of the blood culture bacteria isolated were gram-positive, whereas 38% were gram-negative [11]. However, these findings conflicted with the previous Chinese study by (Zhuo et al., 2020), which detected that 71.8% of the blood specimen isolates were gram-negative bacilli and 28.2% were gram-positive cocci. In addition, Gong et al. found that the isolation rates of Gram-negative bacteria and Gram-positive bacteria were 68.4% and 24.5%, respectively [12]. Also, another recent Saudian study observed that 62.2% of bloodstream infections are caused by gram-negative bacteria versus 36.4% caused by gram-positive bacteria [13]. Also, Oza et al. recently found that Gram-Negative Bacteria represent 70.90% and Gram-Positive Bacteria represent only 29.09% of the total 574 positive blood cultures [14]. Moreover, different studies detected a varying degree of bacterial distribution in bloodstream infections. For instance, Run-xiang, found that Gram-positive and Gram-negative bacteria accounted for 48.9% and 43.8%, respectively. Besides, fungi account for 7.3% of 252 strains isolated from blood specimens [15]. Further, Ejaz et al. found that the percentage of gram-negative bacilli and gram-positive cocci was almost the same (49.52%), while candida spp. was recovered from the remaining (1.41%) isolates [16]. In our study, the most common gram-negative bacterial isolates were *K. pneumoniae*, *E. coli*, and *A. baumannii*. The most common gram-positive bacterial isolates were *S. epidermidis*, *E. faecalis*, *S. haemolyticus*, *S. aureus*, and *S. capitis.* These results align with a previous Chinese study by Tian et al. [17], who isolated various clinical bacterial strains, including *S. aureus*, *E. coli*, *K. pneumoniae*, and *S. typhi*. Moreover, Hani, [18], demonstrated that Staphylococcus aureus and coagulase negative staphylococci (CoNS) were the most common Gram-positive pathogens, while Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa were the most Gram-negative in Saudi Arabia. Moreover, Della Rocca et al. recently found that *S. aureus* and *Enterococci* were the most common Gram-positive causative pathogens, while *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii* were the most common Gram-positive causative pathogens in the Southern Italian hospital [19]. Another recent study by Foglia et al. found that the most frequent bacteria pathogens identified among Bloodstream infections are coagulase-negative Staphylococci (CoNS), Klebsiella pneumoniae, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, and enterococci [20]. However, Licata et al. found that Italy's most common pathogens were Coagulase-negative Staphylococcus (CoNS), Staphylococcus aureus, and Escherichia coli [21]. In addition, the present study focused particularly on the prevalence rates and morbidity associated with various gram-positive and gram-negative bacterial strains. Among these, *S. lugdunensis* characterized by its notably low morbidity rate (76.9%), offers a glimmer of hope, suggesting a higher survival rate among afflicted patients. This observation prompts further exploration into potential factors such as lower virulence or enhanced susceptibility to available treatments, providing valuable avenues for future research. In contrast, *S. haemolyticus*, *S. hominis*, and *S. Epidermidis* present relatively higher morbidity rates, indicating an elevated risk associated with these specific strains.

Table 2. Demographic and clinical characteristics of the patients

	Frequency	Percent
Gender		
Female	879	42.9
Male	1172	57.1
Sample types		
BL.C/S 1st - AEROBIC	776	37.8
BL.C/S 2nd - ANAEROBIC	666	32.5
BL.C/S 3rd - AEROBIC	321	15.7
BL.C/S 4th - ANAEROBIC	288	14.0
Mortality		
Alive	969	47.2
Died	1082	52.8
AGE in years		
≤ 40	269	13.1
41-80	1243	60.6
≥ 81	538	26.2

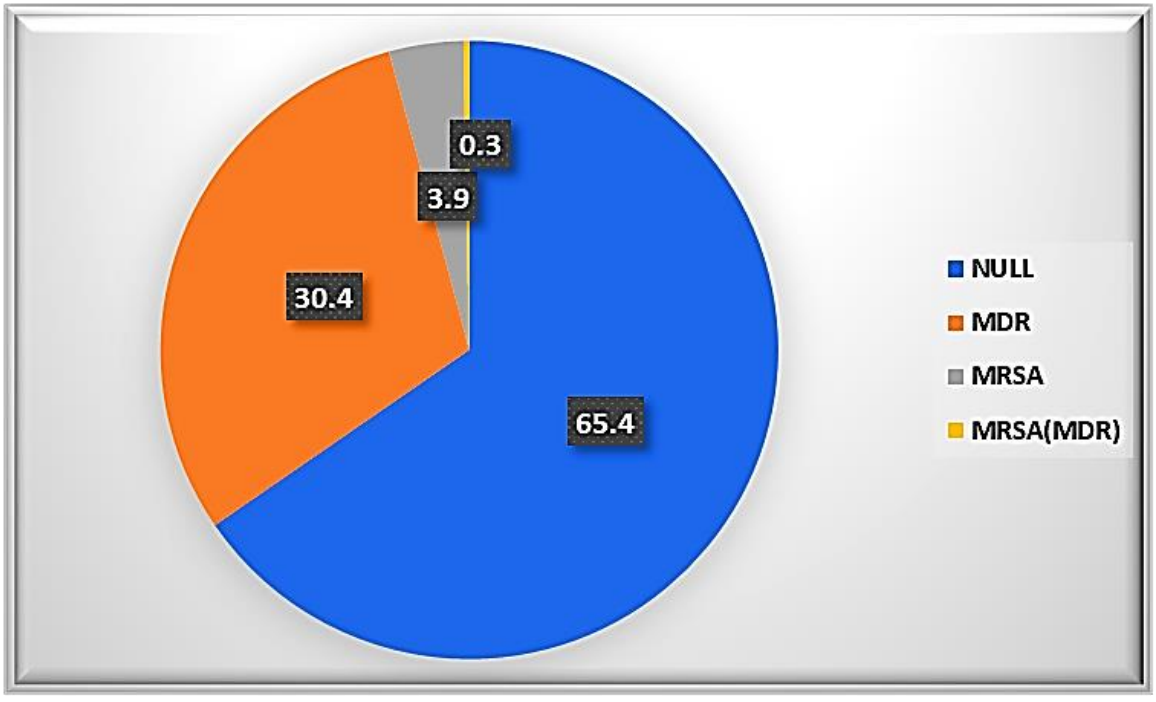

Figure 1. Multidrug resistant distributions among the gram +ve bacteria isolated in the study

Table 3. Different patient's locations in the study

Locations	Frequency	Percent
ICU	1053	51.3
Emergency	445	21.7
Critical Care	154	7.5
INTERMEDIATE UNIT	85	4.1
CCU	61	3.0
AhO	51	2.5
Stroke Unit	26	1.3
BURN UNIT	25	1.2
Trauma Room	23	1.1
CARDIO WARD	17	0.8
Isolation Ward	10	0.5
SICU	10	0.5
MCHU	9	0.4
AJGH	6	0.3
FCHU	6	0.3
CSU	3	0.1
CARDIOLOGY CLINIC	2	0.1
Total	2051	100.0

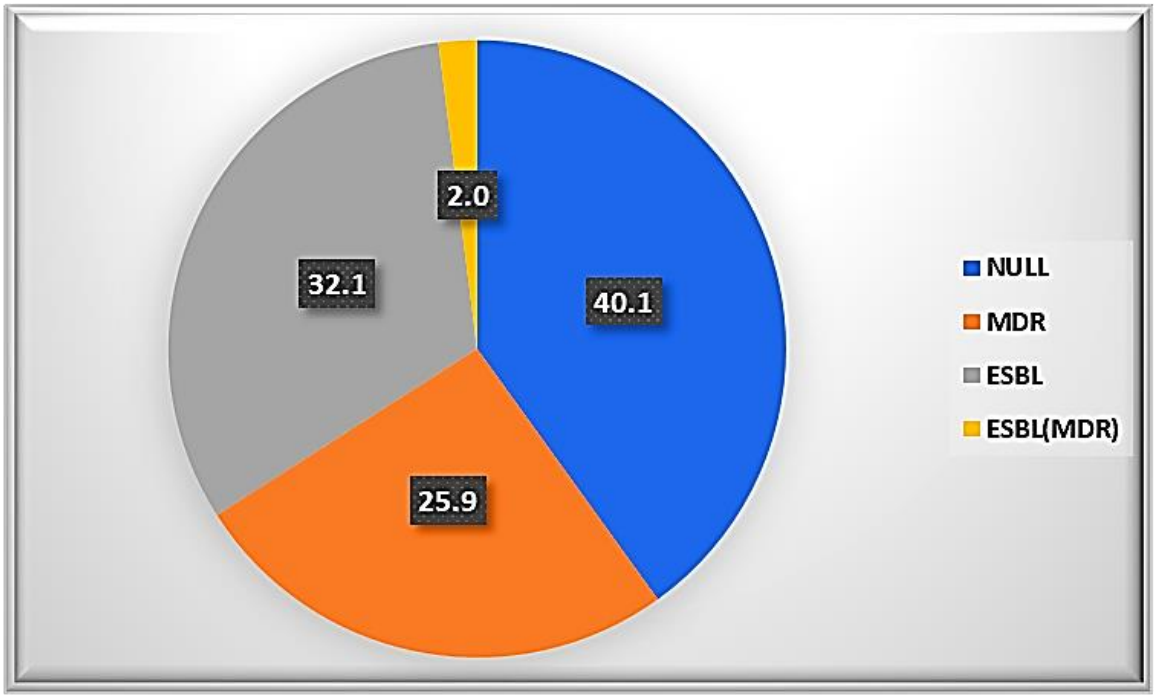

Figure 2. Multidrug resistant distributions among the gram -ve bacteria isolated in the study.

Table 4. Names, numbers, and total percentage of clinical gram-positive and gram-negative bacteria isolated from targeted patients.

gram+ve, total n= 1387 (67.6%)	*Coagulase Negative Staphylococcus* (**5**)	*Staphylococcus hominis* **(285)**	*Streptococcus pyogenes* **(3)**
	Enterococcus Faeceum **(39)**	*Staphylococcus sciuri* **(12)**	*Streptococcus viridans* **(10)**
	Enterococcus Fecalis **(197)**	*Staphylococus aureus* **(129)**	
	Staphylococcus aureus - MRSA **(36)**	*Staphylococus capitis* **(104)**	
	Staphylococcus cohnii **(5)**	*Staphylococus Epidermidis* **(409)**	
	Staphylococcus haemolyticus **(140)**	*Staphylococus lugdunensis* **(13)**	
gram-ve, total n= 664 (32.4%)	*Acinetobacter baumannii / haemolyticus* **(34)**	*Klebsiella Pneumoniae* **(244)**	*Pseudomonas putida* **(1)**
	Acinetobacter boumannii **(103)**	*Proteus Mirabilis* **(48)**	*Pseudomonas stutzeri* **(2)**
	Burkholderia Cepacia **(9)**	*Providencia rettgeri* **(1)**	*Serratia Marcescens Isolated* **(17)**
	E. COLI **(138)**	*Providencia Stuartii* **(13)**	*Serratia Odorifera* **(2)**
	Enterobacter Aerogenes Isolated **(10)**	*Pseudomonas Aeruginosa Isolated* **(9)**	
	Enterobacter Cloacae **(30)**	*Pseudomonas fluorescens* **(3)**	

G +ve, gram-positive bacteria; G –ve, gram-negative bacteria; total n, the total number of isolates in each gram group; % mean percentage of bacterial isolates number in the patients, the total number of patients was 2051.

Table 5. Morbidity frequencies and percentage among the gram +ve bacteria isolated

Bacteria isolated	alive	died	Total
Coagulase -ve Staphylococcus	2 (40.0%)	3 (60.0%)	5 (100.0%)
Enterococcus faeceum	14 (35.9%)	25 (64.1%)	39 (100.0%)
Enterococcus fecalis	84 (42.6%)	113 (57.4%)	197 (100.0%)
Staphylococcus aureus - MRSA	17 (47.2%)	19 (52.8%)	36 (100.0%)
Staphylococcus cohnii	2 (40.0%)	3 (60.0%)	5 (100.0%)
Staphylococcus haemolyticus	73 (52.1%)	67 (47.9%)	140 (100.0%)
Staphylococcus hominis	153 (53.7%)	132 (46.3%)	285 (100.0%)
Staphylococcus sciuri	5 (41.7%)	7 (58.3%)	12 (100.0%)
Staphylococus aureus	73 (56.6%)	56 (43.4%)	129 (100.0%)
Staphylococus capitis	54 (51.9%)	50 (48.1%)	104 (100.0%)
Staphylococus Epidermidis	213 (52.1%)	196 (47.9%)	409 (100.0%)
Staphylococus lugdunensis	10 (76.9%)	3 (23.1%)	13 (100.0%)
Streptococcus pyogenes	2 (66.7%)	1 (33.3%)	3 (100.0%)
Streptococcus viridans	4 (40.0%)	6 (60.0%)	10 (100.0%)
Total	706 (50.9%)	681 (49.1%)	1387 (100.0%)

Table 6. Morbidity frequencies and percentage among the gram +ve bacteria isolated

Bacteria isolated	alive	died	Total
Acinetobacter baumannii / haemolyticus	10 (29.4%)	24 (70.6%)	34 (100.0%)
Acinetobacter boumannii	28 (27.2%)	75 (72.8%)	103 (100.0%)
Burkholderia Cepacia	5 (55.6%)	4 (44.4%)	9 (100.0%)
E. COLI	70 (50.7%)	68 (49.3%)	138 (100.0%)
Enterobacter Aerogenes	6 (60.0%)	4 (40.0%)	10 (100.0%)
Enterobacter Cloacae	20 (66.7%)	10 (33.3%)	30 (100.0%)
Klebsiella Pneumoniae	81 (33.2%)	163 (66.8%)	244 (100.0%)
Proteus Mirabilis	22 (45.8%)	26 (54.2%)	48 (100.0%)
Providencia rettgeri	1 (100.0%)	0 (0.0%)	1 (100.0%)
Providencia Stuartii	7 (53.8%)	6 (46.2%)	13 (100.0%)
Pseudomonas Aeruginosa	2 (22.2%)	7 (77.8%)	9 (100.0%)
Pseudomonas fluorescens	2 (66.7%)	1 (33.3%)	3 (100.0%)
Pseudomonas putida	0 (0.0%)	1 (100.0%)	1 (100.0%)
Pseudomonas stutzeri	0 (0.0%)	2 (100.0%)	2 (100.0%)
Serratia Marcescens	8 (47.1%)	9 (52.9%)	17 (100.0%)
Serratia Odorifera	1 (50.0%)	1 (50.0%)	2 (100.0%)
Total	263 (39.6%)	401 (60.4%)	664 (100.0%)

Table 6. The percentage of prevalent gram +ve bacteria isolated among different multidrug-resistant groups in the study.

Gram-positive bacterial isolate	NULL	MDR	MRSA	MRSA(MDR)
Coagulase -ve Staphylococcus	2 (40.0%)	3 (60.0%)	0 (0.0%)	0 (0.0%)
Enterococcus Faeceum	32 (82.1%)	7 (17.9%)	0 (0.0%)	0 (0.0%)
Enterococcus Fecalis	193 (98.0%)	4 (2.0%)	0 (0.0%)	0 (0.0%)
Staphylococcus aureus - MRSA	8 (22.2%)	1 (2.8%)	25 (69.4%)	2 (5.6%)
Staphylococcus cohnii	5 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Staphylococcus haemolyticus	67 (47.9%)	73 (52.1%)	0 (0.0%)	0 (0.0%)
Staphylococcus hominis	192 (67.4%)	93 (32.6%)	0 (0.0%)	0 (0.0%)
Staphylococcus sciuri	5 (41.7%)	7 (58.3%)	0 (0.0%)	0 (0.0%)
Staphylococus aureus	89 (69.0%)	10 (7.8%)	28 (21.7%)	2 (1.6%)
Staphylococus capitis	60 (57.7%)	44 (42.3%)	0 (0.0%)	0 (0.0%)
Staphylococus Epidermidis	231 (56.5%)	177 (43.3%)	1 (0.2%)	0 (0.0%)
Staphylococus lugdunensis	10 (76.9%)	3 (23.1%)	0 (0.0%)	0 (0.0%)
Streptococcus pyogenes	3 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Streptococcus viridans	10 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 7. The percentage of prevalent gram -ve bacteria isolated among different multidrug-resistant groups in the study.

Gram-negative bacterial isolate	NULL	MDR	ESBL	ESBL(MDR)
Acinetobacter baumannii / haemolyticus	2 (5.9%)	31 (91.2%)	0 (0.0%)	1 (2.9%)
Acinetobacter boumannii	14 (13.6%)	86 (83.5%)	0 (0.0%)	3 (2.9%)
Burkholderia Cepacia	9 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
E. COLI	85 (61.6%)	3 (2.2%)	49 (35.5%)	1 (0.7%)
Enterobacter Aerogenes Isolated.	3 (30.0%)	0 (0.0%)	6 (60.0%)	1 (10.0%)
Enterobacter Cloacae	21 (70.0%)	2 (6.7%)	7 (23.3%)	0 (0.0%)
Klebsiella Pneumoniae	77 (31.6%)	38 (15.6%)	123 (50.4%)	6 (2.5%)
Proteus Mirabilis	26 (54.2%)	4 (8.3%)	17 (35.4%)	1 (2.1%)
Providencia rettgeri	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Providencia Stuartii	6 (46.2%)	2 (15.4%)	5 (38.5%)	0 (0.0%)
Pseudomonas Aeruginosa	5 (55.6%)	4 (44.4%)	0 (0.0%)	0 (0.0%)
Pseudomonas fluorescens	2 (66.7%)	1 (33.3%)	0 (0.0%)	0 (0.0%)
Pseudomonas putida	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pseudomonas stutzeri	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serratia Marcescens Isolated.	12 (70.6%)	1 (5.9%)	4 (23.5%)	0 (0.0%)
Serratia Odorifera	0 (0.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)

This disparity underscores the imperative for tailored therapeutic approaches and heightened vigilance in the clinical management of infections caused by these bacteria. Further, the presence of *Methicillin-Resistant Staphylococcus Aureus (MRSA)* among the isolates adds a concerning dimension to the discussion. The alarmingly high mortality rate among patients affected by MRSA emphasizes the critical nature of multidrug-resistant strains. The challenges these strains pose, in terms of both limited treatment options and adverse patient outcomes, necessitate urgent attention. Effective infection control measures, judicious antibiotic use, and ongoing research to develop new antimicrobial agents are pivotal in mitigating the impact of MRSA infections and improving patient survival rates. On the other hand, *K. Pneumoniae* and *E. Coli* have surfaced as significant pathogens in the Gram-negative bacteria isolated, With morbidity rates of 66.8% and 49.3%, respectively. These strains pose formidable challenges in clinical management, necessitating precise and tailored therapeutic approaches. Equally concerning are the discoveries related to Acinetobacter species, especially *Acinetobacter baumannii/haemolyticus* and *Acinetobacter boumannii*, displaying remarkably high morbidity rates of 70.6% and 72.8%, respectively. This result underscores a critical concern in healthcare settings, where infections caused by Acinetobacter species have become exceedingly challenging due to their elevated morbidity rates. The presence of multidrug-resistant strains within Acinetobacter species further complicates treatment options, emphasizing the importance of stringent infection control practices to curb their spread. The morbidity rate finding in this study was consistent with the global mortality rate. For example, in a large recent systematic review study by Ikuta et al. out of an estimated 13.7 million deaths caused by infections, 7.7 million were attributed to 33 bacterial pathogens, regardless of their susceptibility to antimicrobials [22]. These bacterial infections accounted for 13.6% of all global deaths and 56.2% of all sepsis-related deaths. Notably, five key pathogens—*Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*—were responsible for nearly 55% of deaths linked to these bacterial infections. Moreover, the mortality rate within the Gram-negative bacteria group in bacterial bloodstream infection in liver transplant recipients undergoing immunosuppression reduction was significantly higher compared to the Gram-positive bacteria group. All deaths were attributed to worsening infections following Immunosuppressive (IS) withdrawal. In contrast, within the Gram-positive bacteria group, all deaths were caused by graft-versus-host disease. Additionally, the Gram-negative bacteria group exhibited a significantly higher incidence of intra-abdominal infections, reductions in Immunosuppressive therapy, and complete withdrawals of Immunosuppressive medications compared to the GPB group [23]. Regarding multidrug resistance (MDR), 30.4% of the isolated gram-positive bacteria displayed MDR, signifying resistance to multiple antibiotic classes. Particularly worrisome was the presence of Methicillin-Resistant Staphylococcus Aureus (MRSA) in 3.9% of cases. MRSA strains, notorious for their resistance to a wide array of antibiotics, pose significant challenges in management and treatment. The coexistence of MRSA and MDR (0.3%) emphasizes the emergence of strains resistant not only to methicillin but also to other vital antibiotics, posing a severe threat to patient outcomes. Regarding gram-negative bacteria, a substantial 25.9% of the isolated gram-negative bacteria exhibited MDR, indicating resistance to multiple antibiotic classes. Even more concerning was the presence of Extended-Spectrum Beta-Lactamase (ESBL) resistance in 32.1% of cases. ESBL-producing bacteria, resistant to a broad spectrum of antibiotics, including most penicillins and cephalosporins, present a formidable challenge in clinical settings. The coexistence of ESBL and MDR (2.0%) signifies the emergence of strains resistant to beta-lactam antibiotics and other crucial antibiotic classes, complicating treatment strategies further. The percentage of multidrug-resistant distributions among the gram-positive and gram-negative bacteria in bloodstream infections varies depending on the location and time of the study. For instance, Kong et al. found that among the multidrug-resistant bacteria in their hospital, 62.16% were Gram-negative, and 25.68% were Gram-positive, which does not agree with the current study findings [24]. Golli et al. found that high rates of MDR were found for *A. baumannii* (97.77%), *P. aeruginosa* (65%), *K. pneumoniae* (50%), *E. faecalis* (47.61%) and MRSA (46.55%) [25]. Another study in Saudi Arabia found that the most prevalent gram-negative bacterial isolates in healthcare-associated bloodstream infections were *E. cloacae*, *E. coli (non-ESBL)*, *E. coli (ESBL)*, *K. pneumoniae (non-ESBL)*, and *K. pneumoniae (ESBL)* [5]. Another study in Spain found that 28.7% of patients with bloodstream infections had infections caused by multidrug-resistant gram-negative bacteria, which was aligned with our results. The authors also found that *K. pneumoniae* was the most frequently observed causative agent and had the highest resistance level [26]. Furthermore, the prevalence of multidrug-resistant gram-negative bacteria cases at admission in a multispecialty hospital in India was found to have increased throughout 2012–2014 from 26.16% to 33.33%. The most MDR-Gram-negative bacteria were *Escherichia coli, Klebsiella, Acinetobacter, Pseudomonas* and *Enterobacter* [27]. On the other hand, Zhang et al. found that *methicillin-resistant Staphylococci (MRS)* exhibited significantly higher drug resistance rates compared to *methicillin-sensitive Staphylococci* ($p<0.05$) in a Chinese population. Further, *E. faecalis* displayed a higher rate of multidrug resistance in comparison to *E. faecium* ($p<0.01$) [28].

4. Conclusions

The present study revealed high morbidity rates associated with specific bacterial strains, indicating an increased risk linked to these pathogens. Multidrug resistance (MDR) is alarmingly present in both gram-positive (30.4%) and gram-negative (25.9%) bacteria, with a significant presence of Extended-Spectrum Beta-Lactamase (ESBL) resistance, particularly among gram-negative isolates.

References

[1] C. Fleischmann, A. Scherag, N.K. Adhikari, C.S. Hartog, T. Tsaganos, P. Schlattmann, K. Reinhart. (2016). Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. American journal of

respiratory and critical care medicine. 193 (3) 259-272.

[2] F. Hu, L. Yuan, Y. Yang, Y. Xu, Y. Huang, Y. Hu, Y. Zhang. (2022). A multicenter investigation of 2,773 cases of bloodstream infections based on China antimicrobial surveillance network (CHINET). Frontiers in cellular and infection microbiology. 12 1075185.

[3] F. Perez, A.M. Hujer, K.M. Hujer, B.K. Decker, P.N. Rather, R.A. Bonomo. (2007). Global challenge of multidrug-resistant Acinetobacter baumannii. Antimicrobial agents and chemotherapy. 51 (10) 3471-3484.

[4] C.L. Ventola. (2015). The antibiotic resistance crisis: part 1: causes and threats. Pharmacy and therapeutics. 40 (4) 277.

[5] S.S. Banawas, A.S. Alobaidi, T.M. Dawoud, A. AlDehaimi, F.M. Alsubaie, A. Abdel-Hadi, P. Manikandan. (2023). Prevalence of Multidrug-Resistant Bacteria in Healthcare-Associated Bloodstream Infections at Hospitals in Riyadh, Saudi Arabia. Pathogens. 12 (9) 1075.

[6] S. Alhumaid, A. Al Mutair, Z. Al Alawi, A.J. Alzahrani, M. Tobaiqy, A.M. Alresasi, A. Al-Omari. (2021). Antimicrobial susceptibility of gram-positive and gram-negative bacteria: a 5-year retrospective analysis at a multi-hospital healthcare system in Saudi Arabia. Annals of clinical microbiology and antimicrobials. 20 (1) 43.

[7] A. Peretz, A. On, H. Koiefman, D. Brodsky, N. Isakovich, T. Glyatman, M. Paritsky. (2013). BACTEC™ FX system as a tool for culturing gastric biopsies and Helicobacter pylori diagnosis. European journal of clinical microbiology & infectious diseases. 32 1541-1543.

[8] J.L. Donay, D. Mathieu, P. Fernandes, C. Pregermain, P. Bruel, A. Wargnier, J.L. Herrmann. (2004). Evaluation of the automated Phoenix system for potential routine use in the clinical microbiology laboratory. Journal of clinical microbiology. 42 (4) 1542-1546.

[9] R.T. Saffert, S.A. Cunningham, S.M. Ihde, K.E. Monson Jobe, J. Mandrekar, R. Patel. (2011). Comparison of Bruker Biotyper matrix-assisted laser desorption ionization–time of flight mass spectrometer to BD Phoenix automated microbiology system for identification of gram-negative bacilli. Journal of clinical microbiology. 49 (3) 887-892.

[10] B. Bhadauria, U. Farooq, S. Singh, N. Dayal, S. Mashkoor, D. Sridhar. (2017). Bacteriological profile and antibiogram of gram negative bacteria isolated from blood culture. International Archives of BioMedical and Clinical Research. 3 (2) 91-95.

[11] A. Fatima, H. Gohar, K. Dawood, M. Sajjad, F. Fasih, Z. Hussain. (2022). Distribution of the invasive pathogenic isolates in blood culture with their antimicrobial susceptibility pattern in a diagnostic laboratory in Karachi. JPMA.

[12] Y.L. Gong, Z.C. Yang, S.P. Yin, M.X. Liu, C. Zhang, X.Q. Luo, Y.Z. Peng. (2016). Analysis of the pathogenic characteristics of 162 severely burned patients with bloodstream infection. Zhonghua Shao Shang za zhi= Zhonghua Shaoshang Zazhi= Chinese Journal of Burns. 32 (9) 529-535.

[13] A. Bandy, A.H. Almaeen. (2020). Pathogenic spectrum of blood stream infections and resistance pattern in Gram-negative bacteria from Aljouf region of Saudi Arabia. PLOS one. 15 (6) e0233704.

[14] M. Oza, B. Jagad, S. Patel, R. Jadeja, P. Dholakiya, K. Desai. (2023). Characterization and Antibiotic Susceptibility Pattern of Gram-Negative Bacteria Isolates from Bloodstream infection at Sir Takhtsinhji Hospital, Bhavnagar. BJKines National Journal of Basic & Applied Sciences. 15 (01) 49–55.

[15] W. Run-xiang. (2011). Common pathogens isolated from blood culture specimens and their distribution and drug resistance. Medicine, Biology.

[16] A. Ejaz, A. Khawaja, F. Arshad, A. Tauseef, R. Ullah, I. Ahmad. (2020). Etiological profile and antimicrobial patterns in blood culture specimens in a tertiary care setting. Cureus. 12 (10).

[17] L. Tian, Z. Sun, Z. Zhang. (2018). Antimicrobial resistance of pathogens causing nosocomial bloodstream infection in Hubei Province, China, from 2014 to 2016: a multicenter retrospective study. BMC public health. 18 1-8.

[18] A.O. Hani. (2018). Epidemiology of bloodstream infection in Saudi Arabia. African Journal of Microbiology Research. 12 (43) 973-987.

[19] M.T. Della Rocca, V. Panetta, A. Durante, L. Bucci, A. Matano, A. Annecchiarico, R. Greco. (2023). Pathogens distribution and antimicrobial resistance pattern of blood stream infections in Southern Italian hospital, 2016-2021 surveillance. New Microbiol. 46 (1) 29-36.

[20] F. Foglia, M.T. Della Rocca, C. Melardo, B.M. Nastri, M. Manfredini, F. Montella, M. Galdiero. (2023). Bloodstream infections and antibiotic resistance patterns: a six-year surveillance study from southern Italy. Pathogens and Global Health. 117 (4) 381-391.

[21] F. Licata, A. Quirino, D. Pepe, G. Matera, A. Bianco, Collaborative Group. (2020). Antimicrobial resistance in pathogens isolated from blood cultures: a two-year multicenter hospital surveillance study in Italy. Antibiotics. 10 (1) 10.

[22] K.S. Ikuta, L.R. Swetschinski, G.R. Aguilar, F. Sharara, T. Mestrovic, A.P. Gray, S. Dhingra. (2022). Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 400 (10369) 2221-2248.

[23] F. Chen, X.Y. Pang, C. Shen, L.Z. Han, Y.X. Deng, X.S. Chen, Y.B. Qian. (2020). High mortality associated with gram-negative bacterial bloodstream infection in liver transplant recipients undergoing immunosuppression reduction. World Journal of Gastroenterology. 26 (45) 7191.

[24] Q. Kong, C. Kang, H. Liu. (2018). Distribution and drug resistance analysis of multi-drug resistant bacteria in hospital. Int J Clin Exp Med. 11 (3) 2648-2653.

[25] A.L. Golli, O.M. Cristea, O. Zlatian, A.D. Glodeanu, A.T. Balasoiu, M. Ionescu, S. Popa. (2022). Prevalence of multidrug-resistant pathogens

causing bloodstream infections in an intensive care unit. Infection and Drug Resistance. 5981-5992.

[26] H.F. Leal, J. Azevedo, G.E.O. Silva, A.M.L. Amorim, L.R.C. de Roma, A.C.P. Arraes, J.N. Reis. (2019). Bloodstream infections caused by multidrug-resistant gram-negative bacteria: epidemiological, clinical and microbiological features. BMC infectious diseases. 19 1-11.

[27] V. Nagvekar, S. Sawant, S. Amey. (2020). Prevalence of multidrug-resistant Gram-negative bacteria cases at admission in a multispeciality hospital. Journal of global antimicrobial resistance. 22 457-461.

[28] R. Zhang, F. Wang, J. Kang, X. Wang, D. Yin, W. Dang, J. Duan. (2015). Prevalence of multidrug resistant Gram-positive cocci in a Chinese hospital over an 8-year period. International journal of clinical and experimental medicine. 8 (6) 9462.