Available online at *www.ujpronline.com*
Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)

RESEARCH ARTICLE

PATTERNS OF ANTIMICROBIAL RESISTANCE AMONG MAJOR BACTERIAL PATHOGENS ISOLATED FROM CLINICAL SAMPLES IN TWO TERTIARY'S HOSPITALS, IN SANA'A, YEMEN

Huda Zaid Al-Shami[1], Muhamed Ahmed Al-Haimi[2], Omar Ahmed Esma'il Al-dossary[1], Abeer Abdulmahmood Mohamed Nasher[1], Mohammed Mohammed Ali Al-Najhi[3], Hassan Abdulwahab Al-Shamahy[1,4], Azhar Azher Mohammed Al-Ankoshy[5]

[1]*Medical Microbiology and Clinical Immunology Department, Faculty of Medicine and Health Sciences, Sana'a University.*
[2]*Depertement of Medicine, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen.*
[3]*Orthodontics, Pedodontics and Prevention Department Faculty of Dentistry, Genius University for Sciences & Technology, Dhamar city, Republic of Yemen.*
[4]*Medical Microbiology department, Faculty of Medicine, Genius University for Sciences & Technology, Dhamar city.*
[5]*Jabir Ibn Hayyan Medical University, Faculty of medicine, Department of Physiology, An-Najaf, Iraq.*

Article Info:

Article History:
Received: 3 August 2021
Reviewed: 7 September 2021
Accepted: 12 October 2021
Published: 15 November 2021

Cite this article:
Al-Shami HZ, Al-Haimi MA, Al-dossary OAE, Nasher AAM, Al-Najhi MMA, Al-Shamahy HA, Al-Ankoshy AAM. Patterns of antimicrobial resistance among major bacterial pathogens isolated from clinical samples in two tertiary's hospitals, in Sana'a, Yemen. Universal Journal of Pharmaceutical Research 2021; 6(5):60-67.
https://doi.org/10.22270/ujpr.v6i5.674

***Address for Correspondence:**
Dr. Hassan A. Al-Shamahy, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a, Yemen. Tel- +967-1-239551; E-mail: *shmahe@yemen.net.ye*

Abstract

Background and objectives: At the present time, antimicrobial resistance (AMR) is a major public health hazard, with antimicrobial resistance bacteria increasing exponentially. This study estimates the epidemiological profiles and antimicrobial resistance of Gram-positive bacteria (GPB) and Gram-negative bacteria (GNB) isolated from clinical samples among patients admitted to two University hospitals in Sana'a city for one year (2019).
Methods: This was a retrospective study of clinical samples of patients collected from January 1, 2019 to December 30, 2019. All samples were appraised to determine presence of infectious agents using standard methods for isolation and identification of bacteria and yeasts from clinical samples of patients admitted to Al-Gumhouri University Hospital and Al-Kuwait University Hospital in Sana'a city. Antibiotic resistance was done using Kirby-Bauer disc diffusion methods.
Results: 2,931 different pathogenic bacteria were detected from 24,690 different clinical specimens. The samples had an overall detection rate of 11.9% (2931/24,690). Among the bacterial pathogens isolated from clinical samples, 52.4% (n=1536) had GPB and 41.2% (n=1207) had GNB. The predominant GNB isolates were *E.coli* (22.04%), *Klebsiella* spp (6.03%), *Pseudomonas aeruginosa* (7.1%), *Acinetobacter baumannii* (1.46%), *Enterobacter* spp. (1.09%), *Citrobacter* spp. (1.16%), respectively. Among the GPB, *S.aureus* was the most common (26.3%), Coagulase-negative *Staphylococcus* (8.1%), Non-hemolytic *Streptococcus* (9.1%), Other alpha-hemolytic *Streptococcus* (3.9%), *Streptococcus pyogenes* (1.9%), and *Streptococcus pneumoniae* (0.5%). A high rate of antibiotic resistance was recorded for sulfamethoxazole/trimethoprim (85.5%), ceftazidime (81.07%), ampicillin (70.4%), cefuroxime (66.4%).
Conclusions: The current study results revealed that the rate of resistance between GNB and GPB is associated with the incidence of different infections in patients attending two major tertiary hospitals in Sana'a city is very high. These results indicate ongoing screening and follow-up programs to detect antibiotic resistance, and also suggest the development of antimicrobial stewardship programs in Sana'a, Yemen.
Keywords: Antimicrobial resistance, bacterial, infection, Gram-negative bacteria, Gram-positive bacteria, Yemen.

INTRODUCTION

Global resistance to antimicrobials is increasing for many reasons, the most important of which is the increase in prescriptions, dispensation in developing countries, and indiscriminate use. It is estimated that 700,000 to several million deaths occur annually and remain a major public health threat worldwide[1].

Millions of patients contract antibiotic-resistant bacteria, many more die, and billions of dollars are lost in health care costs and lost productivity[2,3]. According to estimates by the World Health Organization (WHO) and United Nations report, deaths due to antimicrobial resistance could increase with the time[4,5]. Nowadays, antimicrobial resistance (AMR) is a major public health threat[6,7] and antimicrobial resistance bacteria in different hospital departments are increasing dramatically all over the world and in Yemen this problem is more extensive and complex[8-20]. As for some details of the previous work in Yemen, these studies mostly focused on studying the sensitivity to antibiotics for each bacteria separately[8-20], while the current study studied the resistance to all bacterial isolates, and the current study also identified the temporal correlation of the rate of increase in the prevalence of resistance of bacterial isolates to the antibiotics used in the study area. It has been predicted that if appropriate control and prevention measures are not taken, antimicrobial resistance will become one of the leading causes of death among hospitalized or non-hospitalized patients in developing and developed countries. Proper use and administration of antibiotics are essential to treat bacterial infections[21]. Consequently, inappropriate prescription and abuse of antibiotics can be a factor in the emergence of pathogenic bacteria that are resistant to antibiotics, restriction of treatment options, increased hospitalization time, higher treatment costs and, finally, higher mortality[22].

According to the WHO Global Action Plan on Antimicrobial Resistance[23], it is essential to increase awareness of antimicrobial resistance throughout research and monitoring programs in all parts of the world. Monitoring antimicrobial resistance is critical and has many benefits including: 1). providing data on the rate of bacterial resistance, 2). helping to select appropriate antibiotics and thus reducing the rate of antimicrobial resistance, 3). lowering hospitalization rate and treatment costs, and 4). Low mortality rate[21]. Hence, the present study assesses the epidemiological profiles and antimicrobial resistance of GNB and GPB isolated from clinical samples among patients admitted to two tertiary hospitals in 2019 in Sana'a city.

MATERIALS AND METHODS

Study design and identification of microorganisms: This was a retrospective study of clinical samples of patients collected from January 1, 2019 to December 30, 2019 at the Microbiology Department of the National Center for Public Health Laboratories (NCPHL) Sana'a, Yemen. NCPHL is the reference laboratory for the whole country, in the microbiology department there are 6 benches with 12 bacteriologists working in the department at a rate of 6 samples per day per worker. Samples were provided by two major hospitals in Sana'a: Al-Gumhouri University Hospital and Al-Kuwait University Hospital. This research used microbiological laboratory data for 24690 different clinical samples (Table 1) collected from different inpatient hospital wards and different clinics of the same hospitals. Clinical samples were cultured in an appropriate medium according to standard methods for bacterial isolation and identification for different samples[23]. Using conventional biochemical assays including IMVIC assay (Indole, Methyl red, Voges Proskauer and Citrate), catalase and oxidase assay, growth on triglyceride Agar and Kligler Iron Agar, and Bile Esculin agar, H_2S production, motility test, growth on 6% NaCl and DNase assay; the isolation and identification of different bacterial strains from positive cultures was performed[23].

Antibiotic susceptibility testing: Antibiotic resistance was done using Kirby-Bauer disc diffusion methods and interpretation of antibiotic sensitivity results was done according to CLSI[24]. Antibiotic disks and media powders used in NCPHL are usually Sigma-Aldrich sources. GPB and GNB isolates consisting of *Pseudomonas aeruginosa* (ATCC 27853) *Escherichia coli* (ATCC 25922), and *Staphylococcus aureus* subsp *Aureus* ATCC 25923 was used as quality control for a routine DDM test recommended in the NCPHL Department of Microbiology. Antimicrobial susceptibility to Gram-positive bacteria and GNB was determined using the antibiotic disks mentioned in Table 3. The research results were documented as either sensitive (S), intermediate (I) or resistant (R).

RESULTS

Number and distribution of specimens and positive cultures: During this year, a total of 24690 different clinical cultures were collected from January 2019 until the end of December 2019. Among them, 2931 (11.9%) positive cultures were isolated from different types of bacteria. Among the GPB, about 52.4% and 41.2% of the total GNB cultures were positive and the remaining positive was *Candida albicans* (6.4%). The frequency of different clinical samples from which bacterial strains were isolated is shown in Table 1. The most common positive samples were as follows: urine (n=1043; 35.6%), pus (n=680; 23.2%), semen (337, 11.5%), sputum (n=203; 6.9%) and ear swab (n=163; 5.6%) (Table 1).

Pathogen distribution: GNB and GPB comprised 41.2% (n=1207) and 52.4% (n=1536) of the total bacteria, respectively. The most prevalent isolated GPB were *Staphylococcus aureus* (n=772; 26.3%), non-hemolytic *streptococcus* (n=266; 9.1%), coagulase negative *staphylococcus* (n=238; 8.1%) and alpha-hemolytic *streptococcus* (n=115 ; 3.9%) (Table 2). The most prevalent isolated GNB were *Escherichia coli* (n=646; 22.04%), *Pseudomonas aeruginosa* (n=209; 7.1%), *Klebsiella* spp (n=177; 6.03%) *Acinetobacter* spp (n=43; 1.46%) and *Citrobacter*. spp (n=34; 1.16%) (Table 2).

Antimicrobial susceptibility: The resistance rates of isolated bacteria to commonly used antimicrobials are shown in Table 3. In bacteria isolated from different samples, the highest rates of resistance belonged to sulphamethoxazole/trimethoprime (n=900; 85.5%), ceftazidime (n=1114; 81.07%), ampicillin (n=1055; 70.4%), ceftoroxime (n=886; 66.4%), and cefotaxime (n=597; 32.6%).

Table 1 : Characterization of collected samples.

Type of specimens	Inpatients		Outpatients		Total No (%)
	Al-Gumhori hospital	Al-Kuwait hospital	Al-Gumhori hospital	Al-Kuwait hospital	
Body fluid	3	0	20	5	28 (0.95)
Breast discharge	0	0	1	7	8(0.27)
CSF	3	0	30	2	35(1.2)
Ear swab	39	8	25	91	163(5.6)
Eye	1	0	3	0	4 (0.14)
Mouth swab	0	0	2	0	2 (0.07)
Nasal swab	1	1	7	2	11 (0.38)
Pus	113	41	231	295	680 (23.2)
Sputum	27	5	56	115	203 (6.9)
Stool	4	0	10	0	14 (0.48)
Throat swab	2	0	30	28	60 (2)
Tongue swab	0	0	0	6	6 (0.02)
Urethral discharge	1	0	5	1	7 (0.03)
Urine	104	65	793	81	1043 (35.6)
Prostatic discharge	0	0	3	0	3 (0.01)
Seminal fluid	10	0	292	35	337 (11.5)
Cervical swab	1	2	110	0	113 (3.9)
High vaginal swab	0	1	23	0	24 (0.81)
Vaginal swab	37	9	100	44	190 (6.5)
Total	346	132	1741	712	2931

Table 2: Frequency rate of isolated pathogens from inpatients and outpatients.

Name of isolated pathogens	Frequency	Percent %
Gram positive bacteria		
Staphylococcus aureus	772	26.3
Staphylococcus saprophyticus	8	0.3
Other Alpha hemolytic *Streptococcus*	115	3.9
Other Beta hemolytic *Streptococcus*	19	0.6
Streptococcus pneumonia	13	0.5
Streptococcus pyogenes	55	1.9
Non hemolytic *Streptococcus*	266	9.1
Streptococcus viridians	18	0.6
Enterococcous spp	32	1.1
Coagulasenegative Staphylococcus	238	8.1
Total	1536	52.4
Gram Negative Bacteria		
Neisseria gonorrhea	5	0.17
Neisseria meningitidis	1	0.03
Haemophilus influenzae	9	0.31
Escherichia coli	646	22.04
Klebsiella spp	177	6.03
Citrobacter spp	34	1.16
Enterobacter spp	32	1.09
Proteus mirabilis	26	0.88
Proteus vulgaris	15	0.5
Acinetobacter spp	43	1.46
Pseudomonas aeruginosa	209	7.1
Salmonella spp	7	0.2
Salmonella paratyphi	1	0.03
Salmonella typhi	1	0.03
Vibrio cholerae	1	0.03
Total	1207	41.2
Fungi		
Candida albicans	188	6.4
Total	2931	100.0

DISCUSSION

In the current study, the highest rates of resistance occurred to sulphamethoxazole/trimethoprime (85.5%), ceftazidime (81.07%), ampicillin (70.4%), cefturixime (66.4%), cefotaxime (32.6%) (Table 3). This generally high rate of resistance and can be explained by the fact that the rise in drug resistance is mainly attributable to the use of antimicrobials in humans and other animals, and the prevalence of resistant strains between the two. Increased resistance has too been associated to the release of insufficiently treated effluents from the industry pharmaceutical, particularly in countries everywhere bulk pharmaceuticals are manufactured.

Antibiotics increase the selective pressure in bacterial populations, causing the susceptible bacteria to die; this increases the rate of resistant bacteria that remain to grow. Even at very low levels of antibiotics, resistant bacteria can have the advantage of growing and growing faster than weak bacteria. As antibiotic resistance becomes more frequent, so does the need for alternative treatments. There have been calls for new antibiotic treatments, but new drug development is becoming scarce[25,26].The current study inspected the rate of antibiotic resistance among major pathogenic bacteria isolated from inpatient and outpatient settings in two tertiary hospitals, in Sana'a city, Yemen. Certain that these antibiotic resistance to GNB and GPB be able to cause serious infections in hospitalized patients, particularly in immunocompromised patients, the elderly, neonates and children, the occurrence and spreading of these agents is one of the most important concerns of clinicians[19,20,27].

The application of several classes of antibiotics is not permitted in neonates and children and because there are different patterns of antimicrobial resistance in different areas, selection and prescribing of appropriate antibiotics to treat different infections in immunocompromised, elderly, neonates and children is difficult. Moreover, knowing the patterns of antimicrobial resistance can help clinicians and policy makers to find solutions to resistance problems in their countries[28].

Table 3: Antibiotics susceptibility profile of isolated bacteria.

Antibiotic name	Antibiotics/classes	Resistant		Moderate		Sensitive		Total (n)
		No.	%	No.	%	No.	%	
Ampicillin	Penicillin/amino-penicillin	1055	70.4	19	1.2	359	23.9	1498
Ceftazidime	3rd Cephalosporins β-lactam	1114	81.07	26	1.8	415	30.2	1374
Cefdroxil	4th Cephalosporins β -lactam	173	6.49	4	0.15	92	3.45	2662
Cefepime	4th Cephalosporins β -lactam	36	1.25	2	0.06	15	0.52	2878
Cefurixime	2nd Cephalosporins β -lactam	886	66.4	26	1.9	685	51.3	1333
Ceftizoxime	3rd Cephalosporins β -lactam	46	1.62	0	0	58	2.05	2827
Cefaxime	4th Cephalosporins β -lactam	483	21.4	7	0.3	193	8.58	2247
Cefotaxime	3rd Cephalosporins β -lactam	597	32.6	34	1.8	468	25.5	1831
Cefoxtine	2nd Cephalosporins β -lactam	141	5.47	1	0.03	213	8.26	2576
Cefazoline	1st Cephalosporins β -lactam	50	1.75	0	0	34	1.19	2847
Cefatrixone	3rd Cephalosporins β -lactam	210	8.33	6	0.23	197	7.82	2518
Nitrofuranatoin	Nitrofurans	41	1.48	6	0.21	115	4.15	2769
Ciprofloxacin	Fluoroquinolones	307	15.8	31	1.2	652	33.3	1941
Ofloxacin	Fluoroquinolones	132	5.20	12	0.4	251	9.89	2536
Norfloxacin	Fluoroquinolones	353	15.5	18	0.7	282	12.3	2276
Sulphamethoxazole /Trimethoprime	Folate pathway inhibitors	900	85.5	29	2.7	949	90.2	1052
Azithromycin	Macroloides	409	18.5	19	0.8	299	13.5	2204
Doxycyclin	Tetracycline	356	20.3	60	3.4	762	43.4	1753
Tetracycline-	Tetracycline	273	11.6	25	1.06	294	12.5	2338
Ampicillin/ Sulbactam	B-lactamase inhibitor combinations	188	7.02	1	0.03	65	2.42	2677
Amoxicillin-Clavulanic Acid	B-lactamase inhibitor combinations	646	35.4	35	1.9	426	23.3	1824
Piperacillin/ Tazobactam	B-lactamase inhibitor combinations	28	0.99	4	0.1	77	2.72	2822
Fosfomycin	Fosfomycin	5	0.17	1	0.03	35	1.21	2890
Gentamicin	Aminogylcosides	121	4.86	10	0.4	312	12.5	2488
Amikacin	Aminogylcosides	203	9.26	29	1.3	509	23.2	2190
Chloramphenicol	Phenicols	50	1.82	3	0.1	143	5.23	2734
Imipenem	Carbapenems	54	2.08	7	0.2	277	10.6	2593
Piperacillin	Ureido- penicillin	40	1.39	3	0.1	27	0.94	2861
Aztroneome	Monobactams	102	3.77	7	0.2	117	4.32	2705
Mezlocillin	Ureido-penicillin	83	2.96	5	0.1	44	1.57	2799
Colistin Sulphate	Poly-peptide	96	3.45	0	0	54	1.94	2781
Nalidixic Acid	Quinolones	273	10.8	7	0.2	135	5.36	2516
Methicillin	Penicillin–stable penicillin	105	3.93	1	0.03	155	5.81	2666
Oxacillin	Penicillin -stable penicillin	462	20.3	5	0.2	192	8.45	2271
Cloxacillin	Penicillin -stable penicillin	171	6.40	8	0.2	82	3.07	2669
Erythromycin	Macroloides	476	23.5	26	1.28	402	19.8	2025
Penicillin-	Penicillin	511	22.6	5	0.2	154	6.81	2259
Clindamycin-	Lincosamides	77	2.75	0	0	62	2.22	2792
Vancomycin	Glycopeptides	132	7.80	24	1.4	1081	63.8	1692
Linzolid	Oxazolidinones	12	0.42	0	0	98	3.47	2821
Rifampicin	Ansamycins	1	0.03	0	0	6	0.20	2924

The lack of public surveillance programs for antimicrobial resistance in development such as Yemen and many developed countries will lead to inappropriate use among patients and health care personnel[29-31]. Therefore, investigation of antimicrobial resistance patterns is critical and important, especially in developing countries such as Yemen, where there are no systematic guidelines for antibiotic use. On the other hand, it is necessary to investigate the antibiotic resistance patterns of GPB and GNB in hospitals and clinics in Sana'a city, during 2019, which could be a precious model for both policy makers and clinicians in applying experimental treatment.

The results of the current study showed that among 24690 diverse clinical samples of patients, 2931 (11.9%) were positive cultures from which different bacteria were isolated. The minimal rate of positive culture in the current study could be as a result of: 1). The current study used different types of clinical specimens such as cerebrospinal fluid, pleural fluid, dialysis fluid and luminal fluid as the prevalence of pathogens varies in these samples, 2). efficient guidance for correct administration of antibiotics, 3). improved managing and control of infection, and 4). pre-hospitalization antibiotic use.

In the current study, the most prevalent isolated GPB were *Staphylococcus aureus* (26.3%), non-hemolytic *streptococci* (9.1%), coagulase-negative *staphylococci* (8.1%) and alpha-hemolytic *streptococcus* (3.9%). In addition, the most common GNB isolated were *Escherichia coli* (22.04%), *Pseudomonas aeruginosa* (7.1%), *Klebsiella* spp (6.03%) *Acinetobacter* spp (1.46%) and *Citrobacter* spp (1.16%) (Table 2), which is in agreement with two different studies conducted in Tehran, Iran[22,32]. Though, in investigations previously conducted in Yemen[19,20,33-35], Saudi Arabia[36] and Iran by Ibrahim Saray *et al.*,[37] and Alam *et al.*,[35], *Acinetobacter* spp. GNB was most common in positive culture samples. The result of published studies[18,38] revealed that *E. coli* was the most frequent Gram-negative pathogen in positive cultures of the specimens as in current study (22.04%) (Table 2). The detected differences in proportions of GNB and GPB could be due to the diversity of specimen type, specimen size and applied detecting methods. The results also showed that coagulase-negative *staphylococci* isolated from clinical samples may have been considered a common contaminant. Therefore, more effective measures such as hygiene of the hands of health care workers, regular disinfection of medical devices, and disinfection of the sampling site during sampling should be taken. However, although rare, CoNS can cause many infections including infections of the skin and soft tissues, and therefore should not be considered as contaminants at all times[20,39]. Persistent CoNS infection is likely to be associated with various serious complications such as embolic complications, metastatic seeding and septic thrombophlebitis[40]. For that reason, the evaluation the medical association of CoNS is a challenging problem. In medical diagnostic laboratories, as in the present findings, the main diagnostic challenge is to assess whether the expected CoNS sequestration represents: 1), common colonization of the skin, soft tissues, or mucous membranes, 2). sample contamination during sample collection, handling, and handling, or 3). clinically significant infection[16,19,20,40]. In the situation of co-infection of CoNS with further bacterial infections (multimicrobial infections by CoNS), different bacteria isolates showed different patterns of sensitivity and resistance, this difficult diagnostic situation becomes more complex[40,41]. Close cooperation between physicians and diagnostic laboratory specialists can resolve this medical and diagnostic dilemma. In the false positive CoNS situation, patients are treated with several antibiotics, and it is expected that in addition to the extra costs, extreme antibiotic selection pressures happen that can lead to the emergence of antibiotic resistance[42]. Consequently, it is essential to answer the question that CoNS isolated from a clinical sample is a true infection or just a common cutaneous colonization. Some of the key factors useful in predicting true infection are: 1). isolating similar strains repeatedly during infection after isolating a strain in pure culture from the infected site, 2). in bloodstream infection, patients must have clinical evidence of infection with a single positive blood culture or Only two positive blood cultures were in CoNS within 5 days, and 3). if CoNS was isolated from the skin or soft tissue bacterial culture of a suspected infectious lesion, the isolated organism should be suggested as the pathogen and appropriate treatment should be started[43-45].

Among the antibiotics tested differently, the results of current study showed that the rate of resistance to linezolid was very low (0.42%) (Table 3) making it highly efficient antibiotics against *Enterococcus* spp and *S. aureus* which it was in accord with the rates previously described by Al-Safani *et al.*,[20], by Azimi *et al.*, in Iran[32], Dharmapalan *et al.*, from India[46], He *et al.*, from China[47], Li Tian *et al.*, from China[48] and Al-Naqshbandi and others from Iraq[49]. Nevertheless, the findings of several studies were inconsistent with the current research and it has been reported that the resistance to linezolid is high[50,51]. In current vancomycin resistance in *Enterococcus* spp. was much higher (7/32); 21.8% of *Enterococcus* spp. were resistant to vancomycin. Even though the classification of *Enterococcus* spp. not completed at the species level, therefore, most vancomycin-resistant isolates are likely to be *Enterococcus faecium*. According to several published studies and reports, effective measures have been taken to reduce the risk of VRSA in many countries such as the USA, and some guidelines have been developed to control infections caused by these pathogenic microorganisms[52]. Thus, we suggest similar guidelines and programs designed for patients in Sana'a, Yemen. Current study also revealed that colistin (3.45% resistant rate), in comparison with ciprofloxacin (15.8% resistant rate). These finding were similar to the results of Mahmoudi *et al.*, from Iran[22] and Dharmapalan *et al.*, from India [46], but different from that reported by Azimi *et al.*, in which colistin has a higher rate of resistance than ciprofloxacin[32].

Overall, the results of the current study showed that sulfamethoxazole/trimethoprim, ceftazidime, ampici-

llin, ceftoreximе and cefotaximе are ineffective antibiotics against GPB or GNB. It is worth mentioning that these antibiotics in different hospitals in Sana'a are often used to control various infections especially sepsis and septicemia. It is well understood that resistance to these antibiotics is increasing daily, which is the result of the selective pressure that is secreted by bystander selection and the misuse or overuse of antibiotics[53]. Consistent with the high antibiotic resistance among bacteria, in an attempt to stop the unwanted consequence of sepsis and septicemia, as well as with the purpose of reduce the mortality rate because of these infections, accurate recognition and employ of efficient antibiotics for effective treatment is critical[54-57]. Thus, awareness of antibiotic resistance patterns among common pathogens, holding workshops to correct prescribing for empirical therapy and changes in antimicrobial use are necessary and highly recommended. Finally, the results of the DDM are of great importance, and individuals' free access to access to antibiotics should be prevented. In this study, we revealed that GNB and GPB are resistant to different groups of antibiotics. However, it should be noted that these bacteria have two types of antibiotic resistance: acquired resistance and endogenous resistance. For example, according to EUCAST guidelines, most GNB (*Enterobacteriaceae*, *Pseudomonas* spp.) are self-resistant to various antibiotics including penicillin G, oxacillin, macrolides (e.g., azithromycin, erythromycin, tylosin), lincosamides (e.g. lincomycin), streptogramins (e.g., Virginiamycin), glycopeptides (e.g., vancomycin) and bacitracin. Moreover, based on these guidelines, most GPB are intrinsically resistant to polymyxins and quinolones/fluoroquinolones (e.g., enrofloxacin, ciprofloxacin, difloxacin, marbofloxacin)[58]. Therefore, these resistances should be known by clinicians in order to avoid unsuitable and ineffective therapy.

CONCLUSIONS

To counter these threats there have been increasing public calls for global collective action, including a proposal for an international treaty on antimicrobial resistance. It must be recognized that more details and attention are still needed in order to identify and measure resistance trends at the international level; the idea of a global tracking system has been proposed but implementation has yet to take place. A system of this nature will provide insight into areas of high resistance as well as information needed to evaluate programs and other changes that have been made to combat or reverse antibiotic resistance. Moreover, based on the fact that we did not have full access to patients' information such as treatment outcomes, mortality rate, etc., no specific analysis was carried out, so this information should be provided and an additional study should be carried out to clarify the picture of this problem. According to this data, choosing the right antibiotic is vital in treating bacterial infections. Therefore, awareness of antibiotic resistance patterns in pathogenic bacteria can be helpful in making the right therapeutic choice.

ACKNOWLEDGEMENTS

The authors also would like to acknowledge the Microbiology Department of the National Center of Public Health Laboratories (NCPHL) Sana'a, Yemen for support.

AUTHOR'S CONTRIBUTIONS

Al-Shami HZ: writing original draft, literature survey. **Al-Haimi MA:** methodology, conceptualization. **Al-dossary OAE:** formal analysis, review. **Nasher AAM:** investigation, data interpretation. **Al-Najhi MMA:** data curation, investigation. **Al-Shamahy HA:** critical review, supervision. **Al-Ankoshy AAM:** data curation, investigation. All authors revised the article and approved the final version.

DATA AVAILABILITY

The data supporting the findings of this study are not currently available in a public repository but can be made available upon request to the corresponding author.

CONFLICT OF INTEREST

None to declare.

REFERENCES

1. 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*
2. WHO. Antimicrobial resistance: global report on surveillance 2014. WHO. WHO. Archived from the original on 15 May 2015. Retrieved 19 September 2021.
3. Dadgostar P. Antimicrobial Resistance: Implications and Costs. Infection and Drug Resistance 2019; 12:3903–3910. *https://doi.org/10.2147/IDR.S234610*
4. CDC. The biggest antibiotic-resistant threats in the U.S." Centers for Disease Control and Prevention. 6 November 2019. Retrieved 19 September 2021.
5. Samuel S. Our antibiotics are becoming useless. Vox 2019. Retrieved 19 September 2021.
6. 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.
7. Pormohammad A, Nasiri MJ, Azimi T. Prevalence of antibiotic resistance in Escherichia coli strains simultaneously 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*
8. 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*
9. 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*
10. 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

11. AL-Haddad KA, Ali Al-Najhi MM, Al-Shamahy HA, *et al*. Antimicrobial Susceptibility of Aggregatibacter Actinomycetemcomitans Isolated from Localized Aggressive Periodontitis (LAP) Cases. J Dent Ora Heal Ad 2021; 103. *https://doi.org/10.1111/j.1600-0463.2007.apm_630.x*
12. Al-Akwa AA, Zabara A, Al-Shamahy HA, 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*
13. 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). *https://doi.org/10.22270/ujpr.v6i4.633*
14. 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*
15. 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). *https://doi.org/10.22270/ujpr.v4i6.329*
16. 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). *https://doi.org/10.22270/ujpr.v6i4.643*
17. Al-Eryani SA, Alshamahi EYA, Al-Shamahy HA, Alfalahi GHA, Al-Rafiq AA. Bacterial conjunctivitis of adults: causes and ophthalmic antibiotic resistance patterns for the common bacterial isolates. Universal J Pharm Res 2021; 6, (1). *https://doi.org/10.22270/ujpr.v6i1.535*
18. AL-Magrami RTF, H. A. Al-Shamahy. *Pseudomonas aeruginosa* skin-nasopharyngeal colonization in the in-patients: prevalence, risk factors and antibiotic resistance in tertiary hospitals in Sana'a city-Yemen. Universal J Pharm Res 2019; 3(6). *https://doi.org/10.22270/ujpr.v3i6.219*
19. 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), July 2020. *https://doi.org/10.22270/ujpr.v5i3.409*
20. 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*
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. Cheesbrough M. District laboratory practice in tropical countries. Cambridge: Cambridge University Press; 2010. *https://doi.org/10.1017/CBO9780511581304*
24. 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.
25. Gullberg E, Cao S, Berg OG, Ilbäck C, Sandegren L, Hughes D, Andersson DI. Selection of resistant bacteria at very low antibiotic concentrations. PLOS Pathogens 2011; 7 (7):e1002158. *https://doi.org/10.1371/journal.ppat.1002158*
26. 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*
27. 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*
28. 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.
29. 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*
30. 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.
31. 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*
32. 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;12:2089-2102. *https://doi.org/10.2147/IDR.S215329*
33. Al-Khawlany RS, Edrees WH, AL-Jaufy AY, *et al*. Prevalence of methicillin-resistant *Staphylococcus aureus* and antibacterial susceptibility among patients with skin and soft tissue infection at Ibb City, Yemen. PSM Microbiol 2021; 6(1): 1-11.
34. Alhlale MF, Humaid A, Saleh AH, Alsweedi KS, Edrees WH. Effect of most common antibiotics against bacteria isolated from surgical wounds in Aden Governorate hospitals, Yemen. Universal J Pharm Res 2020; 5(1): 21-24. *https://doi.org/10.22270/ujpr.v5i1.358*
35. Alam M, Pillai P, Kapur P, Pillai K. Resistant patterns of bacteria isolated from bloodstream infections at a university hospital in Delhi. J Pharm Bioallied Sci 2011;3(4):525. *https://doi.org/10.4103/0975-7406.90106*
36. Alabdullatif M, Alrehaili J. Three Years of Evaluation to Determine Reduction of Antibiotic Resistance in Gram-Negative Bacteria by the Saudi National Action Plan. Infect Drug Resist 2020; 13:3657-3667. *https://doi.org/10.2147/IDR.S265000*
37. Ebrahim-Saraie SH, Motamedifar M, Mansury D, Halaji M, Hashemizadeh Z, Ali-Mohammadi Y. Bacterial etiology and antibacterial susceptibility patterns of pediatric bloodstream infections: a two year study from Nemazee Hospital, Shiraz, Iran. J Compr Pediatr. 2016;7 (1)):e29929. *https://doi.org/10.17795/compreped-29929*
38. Buetti N, Atkinson A, Kottanattu L, Bielicki J, Marschall J, Kronenberg A. Patterns and trends of pediatric bloodstream infections: a 7-year surveillance study. Eur J Clin Microbiol Infect Dis 2017; 36(3):537–544. *https://doi.org/10.1007/s10096-016-2830-6*
39. Natsis NE, Cohen PR. Coagulase-negative Staphylococcus skin and soft tissue infections. Am J Clin Dermatol. 2018; 19(5):671–677. *https://doi.org/10.1007/s40257-018-0362-9*
40. von Eiff C, Jansen B, Kohnen W, Becker K. Infections associated with medical devices. Drugs 2005;65(2):179–214. *https://doi.org/10.2165/ 00003495-200565020-00003*
41. Becker K, Heilmann C, Peters G. Coagulase-negative staphylococci. Clin Microbiol Rev 2014; 27(4):870–926. *https://doi.org/10.1128/CMR.00109-13*
42. Niederbracht Y, Idelevich E, Penner H, *et al*. Applicability of a commercial multiplex PCR test for identification of true blood stream infections with coagulase-negative

staphylococci in neutropenic hematological patients. Int J Med Microbiol 2013.
43. Becker K, Skov RL, von Eiff C. *Staphylococcus, micrococcus*, and other catalase-positive cocci. In Jorgensen J, Pfaller M, Carroll K, Funke G, Landry M, Richter S, Warnock D, editors: Manual ofClinical Microbiology. 11th ed. Washington, DC; American Society of Microbiology; 2015:354–382. *https://doi.org/10.1128/9781555817381.ch21*
44. Hall KK, Lyman JA. Updated review of blood culture contamination. Clin Microbiol Rev 2006; 19(4):788–802. *https://doi.org/10.1128/CMR.00062-05*
45. Favre B, Hugonnet S, Correa L, Sax H, Rohner P, Pittet D. Nosocomial bacteremia clinical significance of a single blood culture positive for coagulase-negative staphylococci. Infect Control Hosp Epidemiol 2005;26(8):697–702. *https://doi.org/10.1086/502605*
46. 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*
47. 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*
48. 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.
49. 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.
50. Gandapor AJ, Khan AM. Antibiotic Sensitivity pattern of bacterial isolates of neonatal septicemia in Peshawar, Pakistan. Arch Iran Med 2016;19(12):866.
51. Hui-min Y, Yan-ping W, Lin Liu Y, Shamsi BH, Bo H, Xu-chun 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*
52. 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*
53. 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*
54. 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*
55. 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*
56. 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*
57. 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*
58. Leclercq R, Canton R, Brown DF, *et al*. EUCAST expert rules in antimicrobial susceptibility testing. Clin Microbiol Infect 2013;19(2):141–160. *https://doi.org/10.1111/j.1469-0691.2011.03703.x*