IOSR Journal Of Pharmacy And Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 17, Issue 1 Ser. II (Jan. –Feb. 2022), PP 26-33
www.Iosrjournals.Org

Prevalence and antimicrobial resistance pattern of multi drug resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* isolated from clinical specimens obtained from King Abdulaziz University Hospital, Jeddah, Saudi Arabia

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Abstract
Multidrug-resistant bacterial infections are the world's greatest health threats, especially those caused by A. baumannii, and P. aeruginosa. Diseases caused by these pathogens most often are difficult to treat, and they contribute to nosocomial infections which result in high mortality and morbidity rates. This study aims to find the prevalence of multidrug-resistant pathogens in a health care setting and to determine their antimicrobial resistance pattern. In the current study, a total of 156 bacterial isolates were collected from various clinical specimens at a teaching hospital in Jeddah, Saudi Arabia. All isolates were identified at the clinical and molecular microbiology laboratory using the VITEK 2 system with ID-GN cards for Gram-negative fermenting and non-fermenting bacilli. Antimicrobial resistance patterns were determined by using VITEK 2 system. The obtained results revealed that 86 the identified isolates were A. baumannii (55.13%) and 70 isolates (44.8%) as P. aeruginosa. About 32.4% of the isolates were isolated from patients hospitalized in Medical Intensive Care Unit; (MIC). Multidrug resistance (MDR) was largely observed in all A. baumannii isolates. Most of these isolates (98-100 %) were resistant to nearly all tested antibiotic classes. On contrast, a total of 26.3% of P. aeruginosa isolates were MDR and the highest resistance was to cefotaxime, tigecycline, and trimethoprim/ sulfamethoxazole. For both pathogens colistin was the most active antibiotic agent. Epidemiological data can be help to implement better infection control strategies in healthcare settings.

Keywords*: Acinetobacter baumannii, Pseudomonas aeruginosa, Antibiotic, resistant, Multidrug*

Date of Submission: 24-01-2022 Date of Acceptance: 07-02-2022

I. Introduction:

The Prevalence of multidrug-resistant *A. baumannii* and *P. aeruginosa* in health care settings is considered a serious threat to public health. These pathogens are the important common cause of hospital-acquired infections worldwide (Karaiskos et al., 2019; Pachori et al., 2019; Nguyen and Joshi., 2021). Multidrug-resistant *A. baumannii* and *P. aeruginosa* can cause serious nosocomial infections such as ventilator-associated pneumonia; burn wound infections, bacteremia, and urinary tract infections. These infections were observed in patients in intensive care units, generally associated with high morbidity and mortality (Ayoub Moubareck and Halat, 2020; Labovská, 2021). Moreover, the increasing resistance rate among *A. baumannii* and *P. aeruginosa* present a complicated situation for antimicrobial therapy due to its natural and acquired resistance to nearly all major antibiotics classes, which compromise the ability to treat patients who are infected by this pathogen (World Health Organization, 2019; Nijsingh et al., 2020).

Numerous studies reported the prevalence of MDR *A. baumannii* and *P. aeruginosa* among clinical isolates in Saudi hospital settings. Alarge prospective study in 2020 to determine the distribution and resistance pathogens in surgical site infections (SSI) in Saudi Arabiareported that *A. baumannii* was the most identified pathogen among MDR- Gram-negative isolates (El-Saed et al., 2020). Another study reported Carbapenem-resistant *A. baumannii* is the most frequent pathogen associated with nosocomial infection, followed by *P. aeruginosa* (Alotaibi et al., 2017). Another study has identified the prevalence of P. aeruginosa to be the most frequent pathogen in KSA hospitals (Khan et al., 2018).

Study of prevalence, antibiotic resistance patterns and reliable, and accurate laboratory detection of the MDR *A. baumannii* and *P. aeruginosa* are essential for appropriate antibiotic treatment and improve infection control programs to control the spread of these pathogens (Thatrimontrichai and Apisarnthanarak, 2020). Considering these,this study was performed to find out the prevalence, and evaluate the antimicrobial resistance profile of *A. baumannii* and *P. aeruginosa* strains isolated from clinical specimens from a tertiaryhospital in Jeddah, the west region of Saudi Arabia.

II. Materials and Methods:

Ethics Statement

The study was approved by the unit of biomedical ethics - research committee- of King Abdulaziz University Hospital (KAUH) in Jeddah in December 2020 (reference no.: 693-20).

Bacterial isolates

A total of 156 bacterial isolates belong to *A. baumannii* and *P. aerugionsa* were obtained from 122 patients admitted to (KAUH). The isolates were recovered from different clinical specimens such as tracheal aspirate, sputum, wound swab, urine catheter, tissue, blood, ascitic fluid, and ear swab. The specimens were collected from October 2020 to June 2021 from all units of King Abdulaziz University Hospital (KAUH) at Jeddah.

Culture and Identification of bacterial isolates

The isolates were cultured on 5% Sheep blood agar, MacConkey's agar, and Tryptic Soy Agar (TSA) under aerobic conditions for 24 hours at 37˚C. Pseudomonas agar was used for the isolation and differentiation of *P. aerugionsa* from other Pseudomonas based on pigment formation. The strains were stored in Tryptic Soy Broth (TSB) with 30 % glycerol at -20°C until used.

Phenotypic identification of bacterial isolates was completed at the clinical and molecular microbiology laboratory using the VITEK 2 system with ID-GN cards for Gram-negative fermenting and non-fermenting bacilli (bioMérieux, Marcy IÉtoile France) as described by Funke et al. (1998). Matrix-Assisted Laser Desorption Ionization -Time of Flight Mass Spectrometry (MALDI-TOF MS) (Bruker Daltonik GmbH) was used to confirm the identification of *A. baumannii* isolates which identified by VITEK 2 as *Acinetobacter* complex (Romero-Gómez et al., 2012;Dahdouh et al., 2017).

Antimicrobial susceptibility test

Susceptibility to antimicrobial agents and Minimum Inhibitory Concentrations (MICs) were determined by using VITEK 2 with AST-N291 cards according to the manufacturer's instructions (BioMérieux Mercy l'Etoile, France). Bacterial isolates were sub-cultured on Muller Hinton agar for 18hr at 37ºC. A suspension was prepared by transfer a few colonies for each isolate into 3 mL of 0.45% sterile sodium chloride solutionthen the suspension was adjusted to 0.5 McFarland standards (Bobenchik et al., 2014). The susceptibility testing system was used, the antimicrobial agents with MIC reference ranges were piperacillin/tazobactam (4/4-128/4 µg/mL), cefepime (1-64 µg/mL), cefotaxime (1–64 µg/mL), ceftazidime (1-64 µg/mL), meropenem (0.25-16 µg/mL), imipenem (0.25-16 µg/mL), amikacin (2-64 µg/mL), gentamicin (1-16 µg/mL), ciprofloxacin (0.25-4 µg/mL), trimethoprim/sulfamethoxazole (1/19-16/304 µg/mL) and tigecycline (0.5–8 µg/mL). For colistin (MIC) was determined by E-test strips ((BioMérieux Mercy l'Etoile, France). These tests were applied according to the Clinical and Laboratory Standards Institute guidelines (CLSI, 2017), and the results were accordingly reported as resistant, intermediately resistant, or susceptible.

Data analysis

All statistical analyses were completed using the SPSS program version 22 statistical software. Chi-square test was usedto compare the prevalence of *A. baumannii*, and *P. aeruginosa* strains between specimen type and hospital units with P-values < 0.05 considered significant.

III. Results:

Demographic and clinical characteristics:

The bacterial samples were collected from 122 patients who included 73 patients infected with *A. baumannii* and 49 patients infected with *P. aeruginosa*. In addition, these patients comprised 68 (55.7%) males and 54 (44.3%) females, with an overall ratio of male to female 1:1. There was no significant difference in the isolation of *A baumannii* and *P. aeruginosa* according to p patient's gender ($P > 0.05$). The ages of patients ranged from 1 month to 93 years, with the mean of age 42.4 ± 0.5 years. According to age groups, the results showed that the prevalence of the tested isolates was significantly higher in the oldest age groups (51-70) and (71-90) years old; the number of patients in these age groups was 47 (38.5%) and 27 (22.13%) respectively for

both pathogens. The duration of hospital stay ranged from 1 day to 471 days with the mean of days 42.9 ±5 days. Patients during the study were diagnosed clinically with immunocompromised conditions such as diabetes mellitus (39.3%), kidney disease (22 %), Cardiovascular (20.5%), and Malignancy (13.9%). The overall mortality rate of the study population was considerably high, 61 (50%). Table 1 demonstrated the clinical distribution of *A. baumannii* and *P. aerugionsa* isolates.

Table 1: Distribution of *A. baumannii and P. aerugionsa* isolates according to gender, age, and clinical diagnose of the patients.

Demographic Characteristics		***A. baumannii***		***P. aeruginosa***		**Total**		**P-value**
		n	%	n	%	n	%	
Gender	Males	42	57.5	26	53.1	68	55.7	*P*=0.63
	Females	31	42.5	23	46.9	54	44.3	
Age (years)	≤10	1	1.4	12	24.5	13	10.7	*P*=0.002
	11-30	7	9.6	5	10.2	12	9.8	
	31-50	16	21.9	7	14.3	23	18.9	
	51-70	31	42.5	15	30.6	46	37.7	
	71-90	18	24.7	9	18.4	27	22.1	
	≥ 91	0	0.0	1	2.0	1	0.8	
Underlying Diseases	Cancer	8	8.1	9	15.0	17	13.9	*P*=0.38
	Heart disease	19	19.2	6	10.0	25	20.5	
	Kidney disease	18	18.2	9	15.0	27	22.1	
	Pulmonary disease	6	6.1	6	10.0	12	9.8	
	Liver diseases	2	2.0	0	0.0	2	1.6	
	Diabetes mellitus	29	29.3	19	31.7	48	39.3	
	Sepsis and meningitis	11	11.1	10	16.7	21	17.2	
	HIV infection	1	1.0	0	0.0	1	0.8	
	Neurological conditions	5	5.1	1	1.7	6	4.9	
Number of Deaths		40	54.8	21	42.8	61	50	

Out of 156 isolates were collected from various clinical samples from different units at KAUH, 86 isolates (55.13%) were identified as *A. baumannii*. Most of these isolates, thirty-eight (44.19%), were recovered from tracheal aspirate, followed by twelve (13.95%) from wound swab. The highest number of *A. baumannii* 37(43.02 %) isolates were collected from patients in Medical Intensive Care Unit (MICU) and 21 (24.41%) from Male Medical (MM).

Among the 156 isolates, 70 isolates (44.8%) were *P. aeruginosa*. 25 (35.71%) of these isolates were obtained from the tracheal aspirate, followed by ten isolates (14.28%) from each sputum and wound. Like *A. baumannii*, most *P. aeruginosa* isolates were 13 isolates (18.5%) from MICU, 10 isolates (14.28%) from each of the emergency room and Pediatric Medical unit (PMU). The distribution of *A. baumannii* and *P. aerugionsa* isolates according to the hospital ward and specimens type were illustrated in Table 2.

Table 2: Distribution of *A. baumannii* and *P. aerugionsa* isolates according to specimen type and Hospital Units .

Source of bacterial isolates		***A. baumannii***		***P. aeruginosa***		**Total**		***P*-value**
		n	%	n	%	n	%	
specimen type	Blood	8	9.30	3	4.29	11	7.05	*P=0.36*
	Wound Swab	12	13.95	10	14.29	22	14.10	
	Body fluid	4	4.65	1	1.43	5	3.21	
	Bronchial Washing	1	1.16	0	0	1	0.64	
	Ear Swab	1	1.16	2	2.86	3	1.92	
	Nasopharyngeal	0	0	3	4.29	3	1.92	
	Nostril	0	0	1	1.43	1	0.64	
	Pus	1	1.16	1	1.43	2	1.28	
	Sputum	8	9.30	10	14.29	18	11.54	
	Tissue	4	4.65	7	10	11	7.05	
	Tracheal Aspirate	38	44.19	25	35.71	63	40.38	
	Urine catheter	9	10.47	7	10	16	10.26	

Hospital Units	ER	7	8.14	10	14.29	17	10.90	*P=0.04*
	FS	1	1.16	3	4.29	4	2.56	
	ICU	3	3.49	2	2.86	5	3.21	
	ISO	1	1.16	0	0	1	0.64	
	MICU	37	43.02	13	18.57	50	32.05	
	MM	21	24.42	8	11.43	29	18.59	
	MS	9	10.47	5	7.14	14	8.97	
	PICU	1	1.16	8	11.43	9	5.77	
	PDE	0	0	10	14.29	10	6.41	
	PS	0	0	1	1.43	1	0.64	
	SIC	4	4.65	6	8.57	10	6.41	
	Other Units	2	2.33	4	5.71	6	3.85	

E.R: Emergency Room; FS: Female Surgical; ICU: Intensive Care Unit; ISO: Isolation Unit; MICU: Medical ICU; MM: Male Medical; MS: Male Surgical; PDE: Pediatric Medical; PICU: Pediatric ICU; PS: Pediatric Surgical; SIC: Surgical ICU.

All of *A. baumannii* isolates were resistant against ceftazidime, cefotaxime, ciprofloxacin, cefepime, and piperacillin/ tazobactam. Also, 98.8% of the isolates were highly resistant to carbapenems (imipenem and meropenem),and amikacin. Approximately, 67.4% of isolates were non-sensitive to gentamicin, respectively. More than 90% of the isolates wereresistant totrimethoprim/sulfamethoxazole. 69.76% of the tested isolates were sensitive tigecycline and 23.25% of isolates were intermediately resistantto this antimicrobial agent. Colistin was effective against the tested isolates; only two isolates 2.32% were resistant to colistin. Table 3 illustrates the susceptibility profiles of *A. baumannii* isolates for each antimicrobial agent.

Table 3: Antibiotic susceptibility profiles for *A. baumannii* isolates.

Antimicrobial agent												
	AK		**CAZ**		**CFM**		**CIP**		**CO**		**FEP**	
	n	%	n	%	n	%	n	%	n	%	n	%
Resistance	85	98.8	86	100	86	100	86	100	2	2.32	86	100
Intermediate	-	-	-	-	-	-	-	-	-	-	-	-
Sensitive	1	1.16	-	-	-	-	-	-	84	97.6	-	-
Antimicrobial agent												
	GEN		**IMP**		**MEM**		**TAZ**		**TGC**		**TRI**	
	n	%	n	%	n	%	n	%	n	%	n	%
Resistance	58	67.4	85	98.8	85	98.8	86	100	6	6.97	78	90.69
Intermediate	-	-	-	-	-	-	-	-	20	23.25	-	-
Sensitive	32	37.2	1	1.16	1	1.16	-	-	60	69.76	8	9.30

AK: Amikacin; CAZ: Ceftazidime; CFM: Cefotaxime; CIP: Ciprofloxacin; CO: Colistin; FEP: Cefepime; GEN: Gentamicin; IMP: Imipenem; MEM: Meropenem; TAZ: Piperacillin/ Tazobactam; TGC: Tigecycline; TRI: Trimethoprim/ Sulfamethoxazole.

All *P. aeruginosa* isolates showed full resistance to cefotaxime, tigecycline, and trimethoprim/ sulfamethoxazole. The resistance rates for carbapenems ranged from 98.5% for imipenem to 95.7% for meropenem. The percentage of resistance *P. aeruginosa* isolates was 75.7% for cefotaxime, and piperacillin/tazobactam, and about 65% for ceftazidime, and 51% for ciprofloxacin. The highest susceptibility rates were observed for gentamicin (72%) and amikacin (52%) while all *P. aeruginosa* isolates were sensitive to colistin. The results in Table 4 showed the susceptibility profiles of *P. aeruginosa* isolates for each antimicrobial agent.

Table 4: Antibiotic susceptibility profiles for *P. aeruginosa* isolates

Antimicrobial agent												
	AK		CAZ		CFM		CIP		CO		FEP	
	n	%	n	%	n	%	n	%	n	%	n	%
Resistance	33	47.14	46	65.7	70	100	36	51.4	-	-	53	75.7
Intermediate	-	-	2	2.8	-	-	-	-	-	-	-	-
Sensitive	37	52.8	22	31.4	-	-	34	48.5	70	100	17	24.2
Antimicrobial agent												
	GEN		IMP		MEM		TAZ		TGC		TRI	
	n	%	n	%	n	%	n	%	n	%	n	%
Resistance	18	25.7	69	98.5	67	95.7	53	75.7	70	100	70	100
Intermediate	1	1.42	-	-	-	-	-	-	-	-	-	-
Sensitive	51	72.8	1	1.42	3	4.28	17	24.2	-	-	-	-

AK: Amikacin; CAZ: Ceftazidime; CFM: Cefotaxime; CIP: Ciprofloxacin; CO: Colistin; FEP: Cefepime; GEN: Gentamicin; IMP: Imipenem; MEM: Meropenem; TAZ: Piperacillin/ Tazobactam; TGC: Tigecycline; TRI: Trimethoprim/ Sulfamethoxazole.

According to the US Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC) MDROs definition, bacteria are classified as MDR if they have acquired non-susceptibility to at least one agent in each of three or more antibiotic categories (Magiorakos et al., 2012), in this study, the antibiotic susceptibility results revealed that among 156 bacterial isolates all *A. baumannii* isolates were classified as MDR strains (55.1%), while (26.3%) of isolates were multidrug-resistant *P. aeruginosas*trains and (12.2%) of themwere carbapenem-resistant *P. aeruginosa* (CARP). (Figure1) demonstrates the prevalence of bacterial isolates according to their susceptibility patterns.

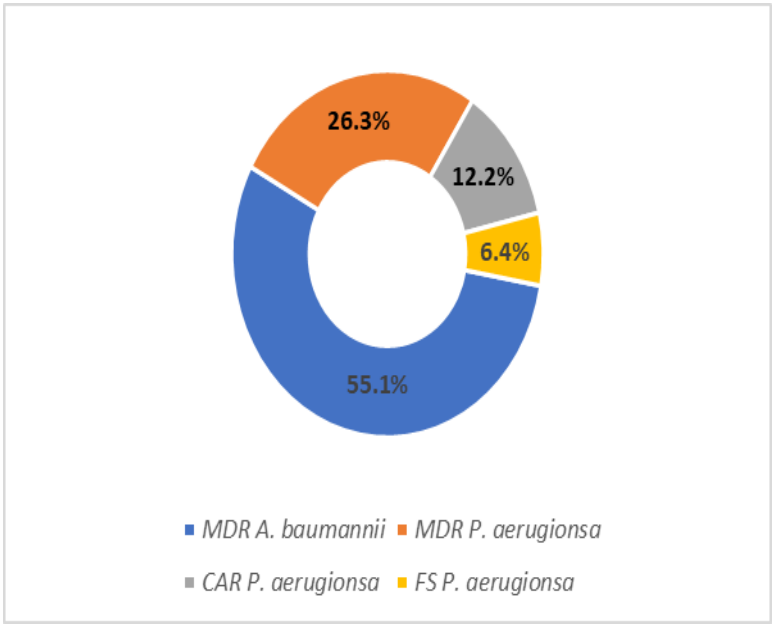

Figure1: The prevalence of the studied multidrug resistant *A. baumannii* and *P. aeruginosa* bacterial isolates, obtained from KAUH Hospital

IV. Discussion:

This study investigates the prevalence and distribution of *A. baumannii* and *P. aeruginosa* and their resistance patterns in a large tertiary care hospital in the Western region of Saudi Arabia. According to our results, the prevalence of *A baumannii* was reported (55.13%) while the prevalence of *P. aeruginosa* was (44.8%). These observations agreed with the reported findings in a previous study conducted at King Abdullah Hospital (Ibrahim, 2018). In this study (Ibrahim, 2018), the *A. baumannii* was the most secluded pathogen with

a prevalence of 27.2% followed by *P. aeruginosa* (23.8%) and *K. pneumoniae* (18.6%) while WHO (2017) report pointed to the rapid spread of MDR *A. baumannii* and *P. aeruginosa* in hospitals around the world.

Although the results have not shown a significant difference in the isolation of *A. baumannii* and *P. aeruginosa* according to patient's gender or the specimen type, the infections caused by these pathogens are more frequent in males than females. This pattern of infections is similar to previousstudies conducted to investigate the associations between the pathogen types and patients' gender (Limoli et al., 2016; Al-Gethamy et al., 2017; Yuan et al., 2018). For the two types of bacteria under study, *A baumannii* and *P. aeruginosa*, most isolates were recovered from the respiratory specimens compared with other specimens'type. Thishigh number of respiratory specimens was probably because the bacterial isolates were collected from patients during the COVID-19 pandemic, as it was required to test all patients for COVID-19. Also, *A. baumannii* and *P. aeruginosa* are opportunistic pathogens that can be associated with viral respiratory tract infections in hospitalized patients (Sharifipour et al., 2020; Rangel et al., 2021; Pasero et al., 2021).

Furthermore, ourresults showed that the prevalence of the tested isolates was significantly higher (48.7%) in the oldest age group, above 61years, for both pathogens. This increase can be explained by the higherrisk associated with the elderly patients for antimicrobial resistance due to the lower efficiency of their immune system. This finding agrees with a recent study by Bandy and Almaeen, 2020,as this study showed that older patients are more likely to be affected by MDR bacteria. The study revealed a highly significant resultof 32.7% of the isolated strains collected from patients in a medical intensive care unit. Severalstudies conducted in different regions of Saudi Arabia confirmed similar observation. For instance, a study carried out in King Abdulaziz Medical City, in Riyadh found that the mostisolated Gram-negative bacteria in intensive care units was *A. baumannii* (Amer et al., 2017).Another study by Abdalhamid *et* al., 2016) examined the prevalence of carbapenem-resistant *P. aeruginosa* colonization in ICU patients in two hospitals in Dammam and Khobar.

Another interesting finding observed inthis study isthe highest resistance of *A. baumannii* isolates against ceftazidime, cefotaxime, ciprofloxacin, cefepime, and piperacillin/ tazobactam. Approximately, 98. % of isolates were resistant to imipenem, meropenem, and amikacin. Tigecycline reported a lower resistance (6.97%) compared with other antimicrobial agents. only two isolates 2.32% were resistant to colistin. All *A. baumannii* isolates were assigned as MDR strains. These results are consistent with the findings of several studies to determine the antimicrobial resistance pattern of *A. baumannii* (Shah et al., 2019; Tafreshi et al., 2019; Breijyeh et al., 2020; Thatrimontrichai and Apisarnthanarak., 2020; Said et al., 2021).

P. aeruginosa isolates were highly resistant against cefotaxime, tigecycline, and trimethoprim/ sulfamethoxazole. About 98 % of isolates were resistant to imipenem, and 95% for meropenem. The frequency of the cefotaxime, and piperacillin/tazobactam resistance by *P. aeruginosa* isolates were (75.7%). The lowest resistance rates were observed for gentamicin and amikacin. No resistance was observed against colistin. As a result of antibiotic susceptibility profiles, (26.3%) of *P. aeruginosa* isolates were categorized multidrug-resistant strains and (12.2%) of the isolates were carbapenem-resistant (CARP). Over the recent years, various studies reported the high level of intrinsic resistance of *P. aeruginosa* isolates to different antibiotics classes used for treatment in Saudi Arabia (Al-Agamy et al., 2017; Akbar Ali 2018; Ahmad et al., 2020; Bosaeed et al., 2020).

The continuously increasing resistance of *A. baumannii* and *P. aeruginosa* strains presents a complicated situation for antimicrobial therapy. This resistance to several antimicrobial agents is often caused by one or a combination of various resistance mechanisms, including aminoglycoside modifying enzymes, topoisomerase mutations, alterations of outer membrane proteins, the activities of efflux pumps, but the most common mechanism of resistance is enzymatic degradation of antimicrobial agents (Leite et al., 2016; Vrancianu et al.,2020).

V. Conclusion:

Reports on the emergence and rapid spread of multidrug-resistant *A. baumannii* and *P. aeruginosa* strains are increasing worldwide.As shown in this study, the prevalence of isolation of MDR *A baumannii* and MDR *P. aeruginosa* from clinical specimens were (55.1%), (26.3%), respectively. Antimicrobial susceptibility testing revealed high resistance rates among *A baumannii* isolates (90-100%) to nearly all major antibiotics classes including broad-spectrum penicillins, cephalosporins, carbapenems, fluoroquinolones, chloramphenicol, and carbapenems. Multidrug resistance was also observed among *P. aeruginosa* isolates which have the highestresistance to cefotaxime, tigecycline, and trimethoprim/ sulfamethoxazole. Hence, there is a need to improve infection control measures in healthcare settings by identifying the epidemiology, phenotypic, and molecular characteristics of clinical MDR *A. baumannii*, and *P. aeruginosa*.

Reference:

[1]. Abdalhamid, B., Elhadi, N., Alabdulqader, N., Alsamman, K. and Aljindan, R. (2016). Rates of gastrointestinal tract colonization of carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* in hospitals in Saudi Arabia. New microbes and new infections, 10, pp.77-83.

[2]. Ahmad, S., Alotaibi, M.A. and Alamri, M.S. (2020). Antibiotic Sensitivity Pattern of Clinical Isolates of Pseudomonas aeruginosa at a Tertiary Care Hospital in Saudi Arabia. Dhaka University Journal of Pharmaceutical Sciences, 19(1), pp.77-82.

[3]. Al-Agamy, M.H., Jeannot, K., El-Mahdy, T.S., Shibl, A.M., Kattan, W., Plésiat, P. and Courvalin, P. (2017). First detection of GES-5 carbapenemase-producing *Acinetobacter baumannii* isolate. Microbial Drug Resistance, 23(5), pp.556-562.

[4]. Al-Gethamy, M.M., Faidah, H.S., Adetunji, H.A., Haseeb, A., Ashgar, S.S., Mohanned, T.K., Mohammed, A.H., Khurram, M. and Hassali, M.A. (2017). Risk factors associated with multi-drug-resistant Acinetobacter baumannii nosocomial infections at a tertiary care hospital in Makkah, Saudi Arabia-a matched case–control study. Journal of International Medical Research, 45(3), pp.1181-1189.

[5]. Ali, A. (2018). Antimicrobial Resistance Pattern of Uropathogens Isolated from Rafha Central Hospital, Rafha, Kingdom of Saudi Arabia. Journal of Pure and applied Microbiology, 12(2), pp.577-586.

[6]. Amer, R. R., Alzomaili, B. T., AlTuwaijri, R. M., AlZahrani, R. S., AlHarbi, S. H., AlThubaiti, A. and Al Johani, S. M. (2017). Prevalence of Antimicrobial Resistance among Gram-Negative Isolates in an Adult Intensive Care Unit at a Tertiary Care Center in Saudi Arabia (2010-2014). Global Journal of Medical Research, 11: 339-345.

[7]. Ayoub Moubareck, C. and HammoudiHalat, D. (2020). Insights into *Acinetobacter baumannii*: a review of microbiological, virulence, and resistance traits in a threatening nosocomial pathogen. Antibiotics, 9 (3), p.119.

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

[9]. Bobenchik, A. M., Hindler, J. A., Giltner, C. L., Saeki, S., & Humphries, R. M. (2014). Performance of Vitek 2 for antimicrobial susceptibility testing of *Staphylococcus* spp. and *Enterococcus* spp. Journal of clinical microbiology, 52(2), 392-397.

[10]. Bosaeed, M., Ahmad, A., Alali, A., Mahmoud, E., Alswidan, L., Alsaedy, A., Aljuhani, S., Alalwan, B., Alshamrani, M. and Alothman, A. (2020). Experience With Ceftolozane-Tazobactam for the Treatment of Serious *Pseudomonas aeruginosa* Infections in Saudi Tertiary Care Center. Infectious Diseases: Research and Treatment, 13, p.1178633720905977.

[11]. Breijyeh, Z., Jubeh, B. and Karaman, R. (2020). Resistance of Gram-negative bacteria to current antibacterial agents and approaches to resolve it. Molecules, 25(6), p.1340.

[12]. CLSI (2020). Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; twenty fourth informational supplement. CLSI M100-S24. Accessed October8, 2020.

[13]. Dahdouh, E., Gómez-Gil, R., Pacho, S., Mingorance, J., Daoud, Z. and Suárez, M. (2017). Clonality, virulence determinants, and profiles of resistance of clinical Acinetobacter baumannii isolates obtained from a Spanish hospital. PloS one, 12(4), p.e0176824.

[14]. El-Badawy, M.F., Abdelwahab, S.F., Alghamdi, S.A. and Shohayeb, M.M. (2019). Characterization of phenotypic and genotypic traits of carbapenem-resistant Acinetobacter baumannii clinical isolates recovered from a tertiary care hospital in Taif, Saudi Arabia. Infection and drug resistance, 12, p.3113.

[15]. El-Saed, A., Balkhy, H.H., Alshamrani, M.M., Aljohani, S., Alsaedi, A., Al Nasser, W., El Gammal, A., Almohrij, S.A., Alyousef, Z., Almunif, S. and Alzahrani, M. (2020). High contribution and impact of resistant gram-negative pathogens causing surgical site infections at a multi-hospital healthcare system in Saudi Arabia, 2007–2016. BMC infectious diseases, 20, pp.1-9.

[16]. Funke, G., Monnet, D., deBernardis, C., von Graevenitz, A. and Freney, J. (1998). Evaluation of the VITEK 2 system for rapid identification of medically relevant gram-negative rods. Journal of clinical microbiology, 36(7), pp.1948-1952.

[17]. Ibrahim, M.E. (2018). High antimicrobial resistant rates among Gram-negative pathogens in intensive care units: A retrospective study at a tertiary care hospital in Southwest Saudi Arabia. Saudi medical journal, 39(10), p.1035.

[18]. Karaiskos, I., Lagou, S., Pontikis, K., Rapti, V. and Poulakou, G. (2019). The "old" and the "new" antibiotics for MDR gram-negative pathogens: for whom, when, and how. Frontiers in public health, 7, p.151.

[19]. Khan, M. A., Al-Motair, K., Alenezi, M. M., Altheban, A. S., Hammam, S. A., and Al-Mogbel, M. S. (2018). Nosocomial Pathogens-A Single Center Study in Saudi Arabia. Journal of Pure and Applied Microbiology, 12(3), pp.1411-1416.

[20]. Labovská, S. (2021). *Pseudomonas aeruginosa* as a Cause of Nosocomial Infections. In *Pseudomonas aeruginosa*-Biofilm Formation, Infections and Treatments. IntechOpen.

[21]. Leite, G.C., Oliveira, M.S., Perdigão-Neto, L.V., Rocha, C.K.D., Guimarães, T., Rizek, C., Levin, A.S. and Costa, S.F., 2016. Antimicrobial combinations against pan-resistant Acinetobacter baumannii isolates with different resistance mechanisms. PloS one, 11(3), p.e0151270.

[22]. Limoli, D.H., Yang, J., Khansaheb, M.K., Helfman, B., Peng, L., Stecenko, A.A. and Goldberg, J.B. (2016). *Staphylococcus aureus* and *Pseudomonas aeruginosa* co-infection is associated with cystic fibrosis-related diabetes and poor clinical outcomes. European Journal of Clinical Microbiology & Infectious Diseases, 35(6), pp.947-953.

[23]. Magiorakos, A.P., Srinivasan, A., Carey, R.B., Carmeli, Y., Falagas, M.E., Giske, C.G., Harbarth, S., Hindler, J.F., Kahlmeter, G., Olsson-Liljequist, B. and Paterson, D.L. (2012). Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical microbiology and infection, 1*8*(3), pp.268-281.

[24]. Nguyen, M. and Joshi, S.G., (2021). Carbapenem Resistance in Acinetobacter baumannii, and their Importance in Hospital acquired Infections: A Scientific Review. Journal of Applied Microbiology, 53: 112-119.

[25]. Nijsingh, N., Munthe, C., Lindblom, A., &Åhrén, C. (2020). Screening for multi-drug-resistant Gram-negative bacteria: what is effective and justifiable? Monash bioethics review, 38(1), pp.72-90.

[26]. Pachori, P., Gothalwal, R. and Gandhi, P. (2019). Emergence of antibiotic resistance *Pseudomonas aeruginosa* in intensive care unit; a critical review. Genes & diseases, 6(2), pp.109-119.

[27]. Pasero, D., Cossu, A.P. and Terragni, P. (2021). Multi-Drug Resistance Bacterial Infections in Critically Ill Patients Admitted with COVID-19. Microorganisms, 9(8), p.1773.

[28]. Rangel, K., Chagas, T.P.G. and De-Simone, S.G. (2021). *Acinetobacter baumannii* Infections in Times of COVID-19 Pandemic. Pathogens, 10(8), p.1006.

[29]. Romero-Gómez, M. P., Gómez-Gil, R., Paño-Pardo, J. R., and Mingorance, J. (2012). Identification and susceptibility testing of microorganism by direct inoculation from positive blood culture bottles by combining MALDI-TOF and Vitek-2 Compact is rapid and effective. The Journal of Infection, *65*(6), 513-520.

[30]. Said, D., Willrich, N., Ayobami, O., Noll, I., Eckmanns, T. and Markwart, R. (2021). The epidemiology of carbapenem resistance in Acinetobacter baumannii complex in Germany (2014–2018): an analysis of data from the national Antimicrobial Resistance Surveillance system. Antimicrobial Resistance & Infection Control, 10(1), pp.1-13.

[31]. Shah, M. W., Yasir, M., Farman, M., Jiman-Fatani, A. A., Almasaudi, S. B., Alawi, M., El-Hossary, D., and Azhar, E. I. (2019). Antimicrobial susceptibility and molecular characterization of clinical strains of *Acinetobacter baumannii* in Western Saudi Arabia. Microbial Drug Resistance, 25(9), pp.1297-1305.

[32]. Sharifipour, E., Shams, S., Esmkhani, M., Khodadadi, J., Fotouhi-Ardakani, R., Koohpaei, A., Doosti, Z. and Golzari, S.E. (2020). Evaluation of bacterial co-infections of the respiratory tract in COVID-19 patients admitted to ICU. BMC infectious diseases, 20(1), pp.1-7.
[33]. Tafreshi, N., Babaeekhou, L. and Ghane, M. (2019). Antibiotic resistance pattern of Acinetobacter baumannii from burns patients: increase in prevalence of blaOXA-24-like and blaOXA-58-like genes. Iranian journal of microbiology, 11(6), p.502.
[34]. Thatrimontrichai, A., &Apisarnthanarak, A. (2020). Active surveillance culture program in asymptomatic patients as a strategy to control multidrug-resistant gram-negative organisms: What should be considered? Journal of the Formosan Medical Association = Taiwan yizhi, 119(11), 1581–1585.
[35]. Vrancianu, C.O., Gheorghe, I., Czobor, I.B. and Chifiriuc, M.C. (2020). Antibiotic Resistance Profiles, Molecular Mechanisms and Innovative Treatment Strategies of Acinetobacter baumannii. Microorganisms, 8(6), p.935.
[36]. World Health Organization (2019). WHO publishes list of bacteria for which new antibiotics are urgently needed. 2017. URL: https://www. who. int/ru/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed.
[37]. World Health Organization (2017). Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in health care facilities.
[38]. Yuan, W. L., Shen, Y. J. and Deng, D. Y. (2018). Sex bias of *Acinetobacter baumannii* nosocomial infection. American journal of infection control, 46(8), 957-958.

Naheda Alshammari, et. al. "Prevalence and antimicrobial resistance pattern of multi drug resistant Acinetobacter baumannii and Pseudomonas aeruginosa isolated from clinical specimens obtained from King Abdulaziz University Hospital, Jeddah, Saudi Arabia." *IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)*, 17(1), (2022): pp. 26-33.