Applied Nanoscience
https://doi.org/10.1007/s13204-021-02050-9

ORIGINAL ARTICLE

Totally antibiotic resistance *Pseudomonas aeruginosa* isolated from patients with blood stream infection

Ali M. Hussein[1] · Zhala B. Taha[2] · Ahmed G. Malik[3] · Dur K. Hazim[3] · Reman J. Ahmed[3] · Osama B. Mohammed[3] · Kamgar A. Rasul[3] · Safa Bazaz[4] · Dosti Rashid[4]

Received: 7 June 2021 / Accepted: 28 August 2021

Abstract
Pathogenic bacteria are the type of bacteria that is harmful to humans and can cause several diseases such as lung diseases, cholera, tuberculosis and syphilis. The multidrug-resistant bacteria that isolated from the patients were Klebsiella spp., *Escherichia coli*, *Pseudomonas aeruginosa*, that are known as the human pathogenic bacteria. The antibiotics that have been used against these bacteria were Meropenem MEM, Imipenem IPM, Gentamicin GNT, Co-AmoxiclavAMC and Ceftriaxone CRO. For the vial antibiotics, two different concentrations were prepared and Mueller Hinton agar used as the culture media. *Pseudomonas aeruginosa* was resistant against all vial and disk antibiotics. *Escherichia coli* was susceptible against all vial drugs and disks except ceftriaxone 10 mcg. Klebsiella spp. was susceptible against all vial and disk antibiotics. However, it was resistant against Ceftriaxone 10 mcg disk and Gentamicin 10 mcg. The most effective drug against all bacteria was Meropenem vial and disk. The most resistant bacteria against all antibiotic disks was *Pseudomonas aeruginosa.*

Keywords Multidrug resistance · *Pseudomonas aeruginosa* · Antibiotic · Pathogens

Introduction

Antimicrobial resistance is a significant and growing issue in the world of medicine (World Health Organization 2012). Since the advent of Penicillin, a significant number of bacteria have evolved and transmitted antimicrobial resistance to other organisms in response to antibiotic usage (Baum and Marre 2005). E. *coli* is a member of the Enterobacteriaceae bacterial family, it is the most common commensal inhabitant of humans and warm-blooded animals' gastrointestinal tracts, as well as one of the most significant pathogens (Kaper et al. 2004). *E. coli* was primarily identified based on the serologic detection of O (lipopolysaccharide, LPS) and H (flagellar) antigens prior to the identification of unique virulence factors in pathogenic strains (Kaper et al. 2004). E. *coli* as a human pathogen releases a virulence factor called Stx AB5-toxin (Steil et al. 2018). Because of its outer membrane barrier, E. *coli* is intrinsically immune to therapeutic levels of Penicillin G—the first lactam used in clinical practice. E. *coli* is also immune to a variety of antibiotic types, each with its own mechanism of action (Johnson et al. 2012; Erb et al. 2007). Most physicians are familiar with Klebsiella as a source of community-acquired bacterial pneumonia, which is more common in chronic alcoholics (Carpenter 1990). Human nosocomial infections are frequently caused by bacteria belonging to the genus Klebsiella. *Klebsiella pneumoniae* is the most medically important, because it is responsible for a large percentage of hospital-acquired urinary tract infections, pneumonia, septicemias, and soft tissue infections. The gastrointestinal tract and hospital personnel's hands are the main pathogenic reservoirs for Klebsiella transmission. These bacteria are known to cause nosocomial outbreaks due to their ability to spread quickly in a hospital setting (Podschun and Ullmann 1998). Treatment of Klebsiella spp. infection is very hard, because they are multi-drug resistant (Rossolini and Stone

✉ Ali M. Hussein
ali.m.hussein@cihanuniversity.edu.iq

[1] Department of Biomedical Sciences, Cihan University-Erbil, Erbil, Kurdistan Region, Iraq

[2] Department of Forestry, College of Agricultural Engineering Sciences, Salahaddin University, Erbil, Kurdistan, Iraq

[3] Department of Biology, Cihan University, Erbil, Kurdistan Region, Iraq

[4] Department of Laboratory Medicine, Clinical Research Center, Karolinska Institutet, Karolinska University Hospital Huddinge, 141 86 Huddinge, Sweden

Published online: 19 September 2021

2020). *Pseudomonas aeruginosa* has been a major pathogen for the past 2 decades. It is responsible for 10–20% of all diseases in most hospitals. Pseudomonas infection may occur in patients with burn wounds, cystic fibrosis, acute leukemia, organ transplants and intravenous opioid misuse. *P. aeruginosa* is a common nosocomial contaminant and microbial contamination has been related to outbreaks. In patients with bronchiectasis, *Pseudomonas aeruginosa* is one of the most common pathogens isolated from sputum, both when clinically stable and during exacerbation (Lin et al. 2016; Tunney et al. 2013). It has been widely stated to be a significant risk factor for bronchiectasis severity and prognosis (Loebinger et al. 2009; Wang et al. 2018). Multidrug-resistant *P. aeruginosa* (MDR-PA) isolates are well known as a rising health concern around the world. However, there is little evidence of a connection between MDR-PA isolates and bronchiectasis prognosis (Loebinger et al. 2009; Martínez-García et al. 2014; Chalmers et al. 2014). *P. aeruginosa* undergoes an evolutionary phase in chronic infection including loss of motility, reduced virulence factors and antibiotic resistance, both of which have been well studied in CF (Winstanley et al. 2016). There is a combination of vabomere and Meropenem which is used in the treatment of urinary tract infections and the combination is active against Gram-negative pathogenic bacteria (Griffith et al. 2019), also used as a routine prophylactic antibiotic in surgical procedures (Odabaş-Serin et al. 2020; Saleem and Malik 2019). Disk diffusion is a method of kirby-bauer's methods; it is a technique used to test rapidly growing pathogenic bacteria (Long et al. 2017).

Materials and methods

Disk diffusion method is a type of antibiotic susceptibility testing. There is more than one method for antibiotic susceptibility testing, each method has advantages and disadvantages, but the aim for all of them is the same, that is to determine the antibiotic sensitivity against isolated infectious bacteria. 80 mg of Gentamicin drug in 2 ml of sdH_2O, 1000 mg of Amoxicillin (as Amoxicillin sodium) and 200 mg of clavulanic acid (as potassium clavulanate), sterile Ceftriaxone sodium equivalent to 1 g of ceftriaxone, 500 mg of Imipenem (as imipenem monohydrate) and 500 mg of Cilastatin (as cilastatin sodium) and contains 77.1 mg of sodium, excipient: sodium bicarbonate, Meropenem trihydrate equivalent to 1 g Meropenem vial. In this study, two procedures have been explained: vial antibiotic drug testing and antibiotic disk testing. 38 g of Mueller Hinton agar dissolved in 1000 ml of dH_2O (first add 500 ml of dH_2O and mix the agar and dH_2O, then add the remaining of dH_2O to the flask and again mixing well until the agar dissolves in the dH_2O) then covered with a piece of aluminum. Filter paper disks prepared by cutting in a circle shape and putting in a small flask and cover. Sterilize by autoclave at 121 °C for 15 min. Imipenem, Meropenem, Ceftriaxone, Gentamicin, and Co-Amoxiclav vial solution: two solutions with different concentrations (1:2) and (1:4) prepared. First prepare (1:2) concentration by measuring (0.5 g) Amoxiclav powder then added to sterilized container and (1 ml) of normal saline added that is measured by syringe and mix. Later prepare (1:4) concentration by measuring (0.5 g) Amoxiclav powder then add (2 ml) of normal saline that is measured by syringe and mixed. For each bacterium such as *E. coli*, Klebsiella spp., *P. aeruginosa* different culture plates prepared for control and replications.

Results

Several drugs have been used against three types of bacteria, the effect of the drugs against these bacteria were different from one to another. *Pseudomonas aeruginosa* was resistant against all types of drugs. The most effective drugs of the study were Imipenem and Meropenem which showed an effective ratio against all types of bacteria. Ceftriaxone had an inhibition zone with a diameter of 33.25 mm in the 1:2 concentration and 24.93 mm in 1:4 concentration against *Pseudomonas aeruginosa*. Imipenem had an inhibition zone with a diameter of 27.82 mm in 1:2 concentration and 25.55 mm in 1:4 concentration against *Pseudomonas aeruginosa*. Meropenem had an inhibition zone with a diameter of 42.72 mm in 1:2 concentration and 38.28 mm in 1:4 concentration against *Pseudomonas aeruginosa* (Tables 1, 2, and 3; Figs. 1, 2, 3, 4, 5, 6, 7, 8, and 9).

Discussion

Pseudomonas aeruginosa was sensitive to Ceftriaxone 1 g, Imipenem (500 mg/500 mg) and Meropenem 1 g with a concentration of (0.5 mg/10 ml) (1:2) for all drugs, which had an inhibition zone with Ceftriaxone (33.25 mm) in compare to Ceftazidime of EUCAST (clinical society of antimicrobial susceptibility and infection disease) with ECOFF 8 mg in 1 l of sdH_2O and inhibition zone (17–50 mm) that means *Pseudomonas aeruginosa* is highly resistance to the used drugs. With Imipenem (500 mg), the inhibition zone was (27.82 mm) in compare with EUCAST with ECOFF 4 mg in 1 l of sdH_2O and inhibition zone (20–50 mm) shows resistant of the bacteria, same for Meropenem, the inhibition zone was (42.72 mm) in compare with EUCAST 2 mg/l, it was 18–24 mm. *Pseudomonas aeruginosa* was resistant to various antibiotic disks (AMC30mcg, MEM10 mcg, IPM10 mcg, CRO10 mcg and GNT10 mcg) that were used in this study. *Pseudomonas aeruginosa* was also resistant according to the previous studies

Table 1 The effect and inhibition zone against *Pseudomonas aeruginosa*

Pseudomonas aeruginosa						
	Imipenem		Meropenem		Ceftriaxone	
	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)
S1	26.69	30.84	46.6	58.77	36.24	31.02
S2	26.99	28.26	42.42	43.31	36.23	27.53
S3	23.71	29.58	36.09	36.61	28.9	28.09

Table 2 The effect and inhibition zone against *Escherichia coli*

Escherichia coli										
	Imipenem		Meropenem		Ceftriaxone		Co-Amoxiclav		Gentamycin	
	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)
S1	44.02	42.85	41.37	45.74	31.71	40.49	41.8	24.52	35.77	29.65
S2	45.12	41.08	45.91	43.43	38.66	35.37	25.25	21.98	37.76	30.07
S3	43.34	44.61	45.68	42.79	32.49	43.83	24.54	23.71	33.05	24.83

Table 3 The effect and inhibition zone against Klebsiella spp.

Klebsiella spp.										
	Imipenem		Meropenem		Ceftriaxone		Co-Amoxiclav		Gentamycin	
	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)	1:2 (mean SD ± 2)	1:4 (mean SD ± 2)
S1	44.62	40.8	44.9	43.12	31.7	34.88	29.27	32.22	22.01	36.85
S2	41.54	37.63	46	43.11	30.42	36.05	27.69	28.34	23.29	20.93
S3	41.05	44.91	48.47	43.83	28.51	35.84	28.77	28.68	20.24	24.26

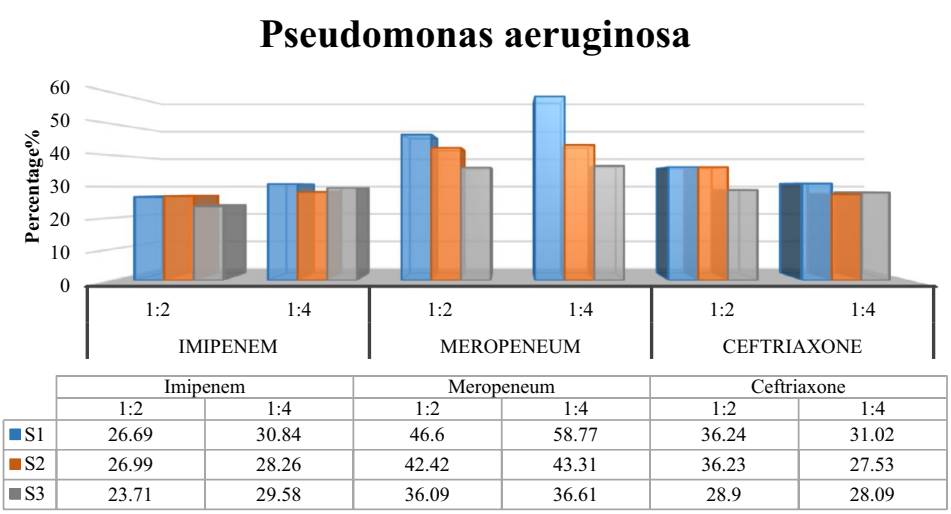


Fig. 1 The effect and inhibition zone against *Pseudomonas aeruginosa*

	Imipenem		Meropeneum		Ceftriaxone	
	1:2	1:4	1:2	1:4	1:2	1:4
S1	26.69	30.84	46.6	58.77	36.24	31.02
S2	26.99	28.26	42.42	43.31	36.23	27.53
S3	23.71	29.58	36.09	36.61	28.9	28.09

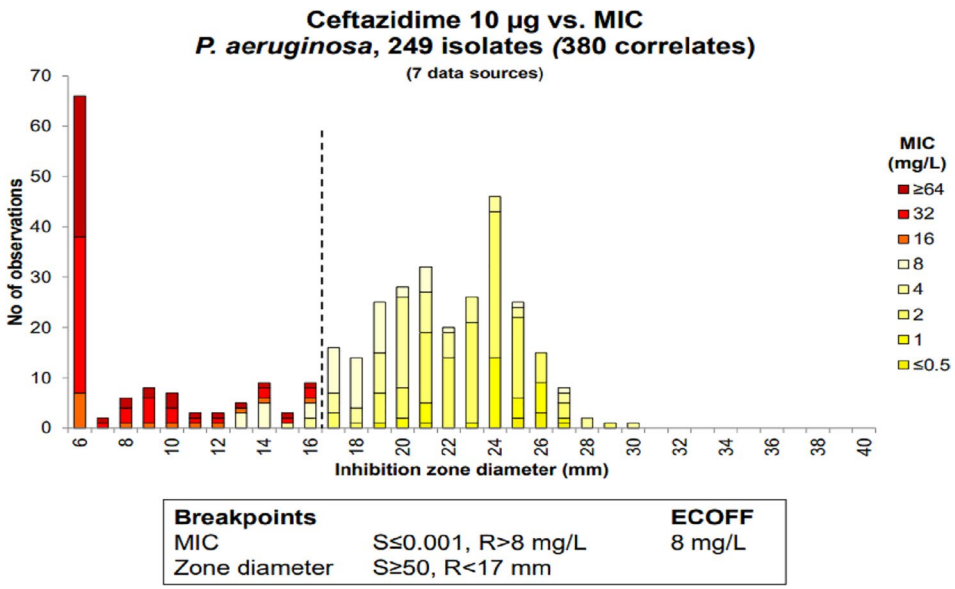


Fig. 2 The effect and inhibition zone of Ceftriaxone against *Pseudomonas aeruginosa.* The diameter of the inhibition zone of this study was 24.93–33.25, while the standard inhibition zone is 17–50

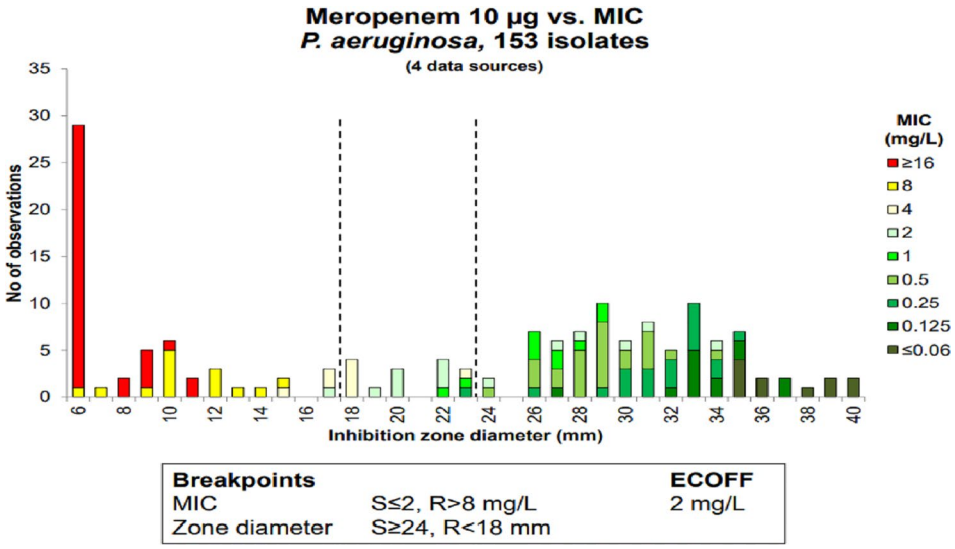


Fig. 3 The effect and inhibition zone of Meropenem against *Pseudomonas aeruginosa.* The diameter of the inhibition zone of this study was 38.28–42.72, while the standard inhibition zone is 18–24

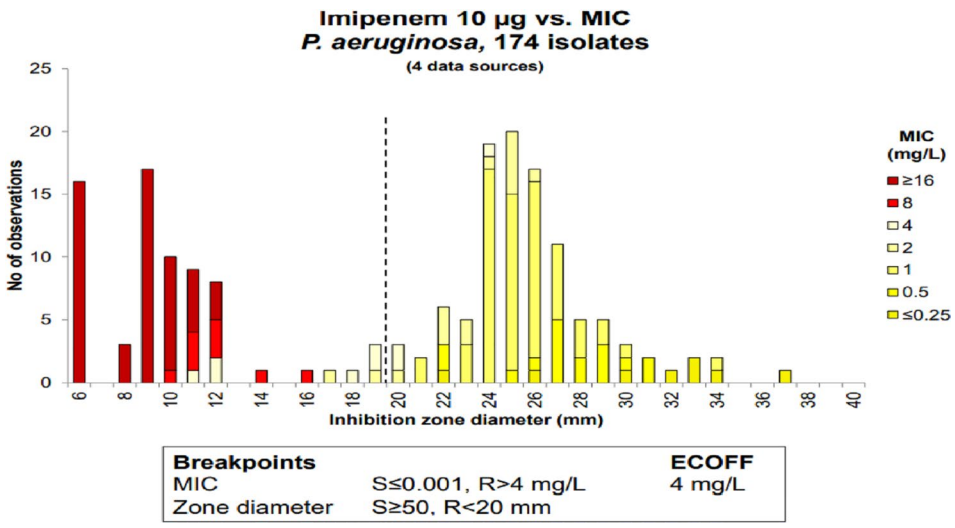


Fig. 4 The effect and inhibition zone of Imipenem against *Pseudomonas aeruginosa.* The diameter of the inhibition zone of this study was 25.5–27.82 while the standard inhibition zone is 20–50

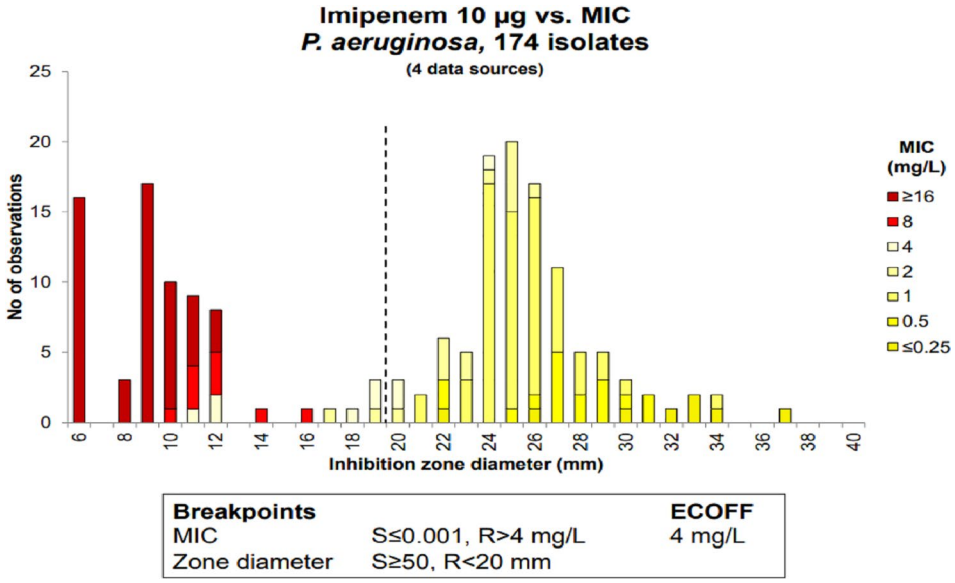


Fig. 5 The inhibition zone diameter of Imipenem (20–50) against *Pseudomonas aeruginosa*

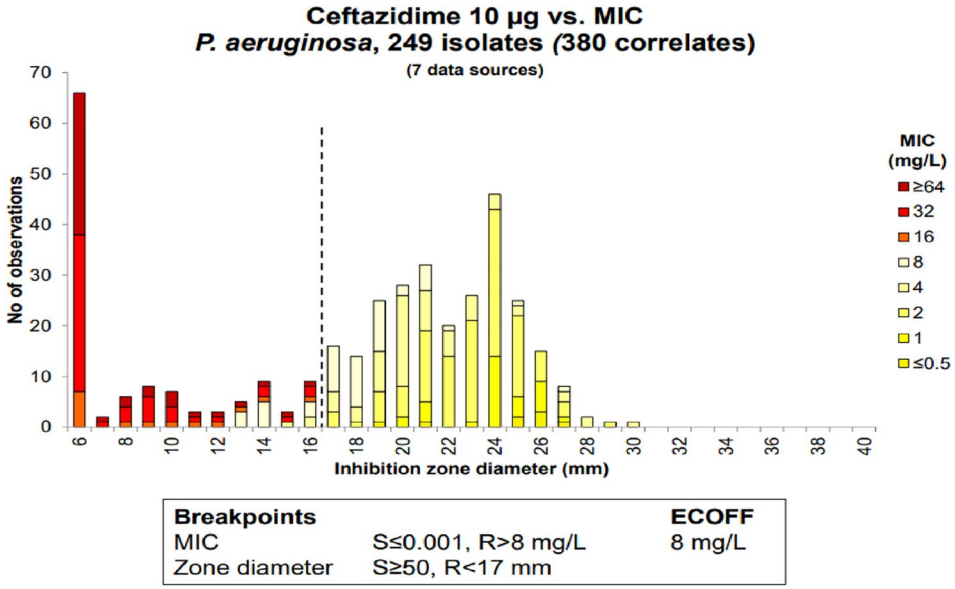


Fig. 6 The inhibition zone diameter of Ceftazidime (17–50) against *Pseudomonas aeruginosa*

(Odabaş-Serin et al. 2020; Hussein et al. 2021; Horcajada et al. 2019). The drugs that have been used for *Escherichia coli* were: Ceftriaxone 1 g, Imipenem (500 mg/500 mg), Meropenem 1 g with concentration of 0.5 mg/1 ml (1:2), Co-Amoxiclav (1000/200 mg) 0.6 mg/1.2 ml (1:2) and Gentamicin (80 mg/2 ml) with concentration 1 ml/2 ml (1:2). In Co-Amoxiclav (1000/200 mg), *Escherichia coli* showed sensitivity with an inhibition zone of 30.53 mm in diameter, while with EUCAST 2 mg in 1 l of sdH_2O, the inhibition zone was S > 19 mm < R in diameter, also it shows sensitivity against AMC 30mcg antibiotic which shows that *Escherichia coli* is resistant. Ceftriaxone (1 g) had an inhibition zone of 33.79 mm in diameter with CRO disk 10 mcg showed resistance. However, compared with EUCAST 0.125 mg in 1 l of sdH_2O the inhibition zone was 22–25 mm in diameter which means that the bacteria have resistance. In Imipenem (500 mg/500 mg), the inhibition zone was 44.16 mm in diameter and with IPM disk 10 mcg was 32.63 mm and is sensitive due to of EUCAST standard ECOFF 0.5 mg in 1 l of sdH_2O and zone diameter (17–22 mm). Meropenem 1 g had an inhibition zone of 44.32 mm in diameter and MEM antibiotic disk 10 mcg (31.71 mm), in comparison with EUCAST and ECOFF 0.125 mg in 1 l of sdH_2O, the inhibition zone was 16–22 mm in diameter which detects that the bacteria are sensitive to Meropenem. Gentamicin (80 mg/2 ml) had an inhibition zone of 35.53 mm in diameter and with GNT disc 10 mcg, it was 13.1 mm, while in comparison to EUCAST and ECOFF 2 mg in 1 l of sdH_2O, the inhibition zone was S ≥ 17 mm < R in diameter which shows that the bacteria is resistant to Gentamicin (Odabaş-Serin et al. 2020; Horcajada et al. 2019; Liao

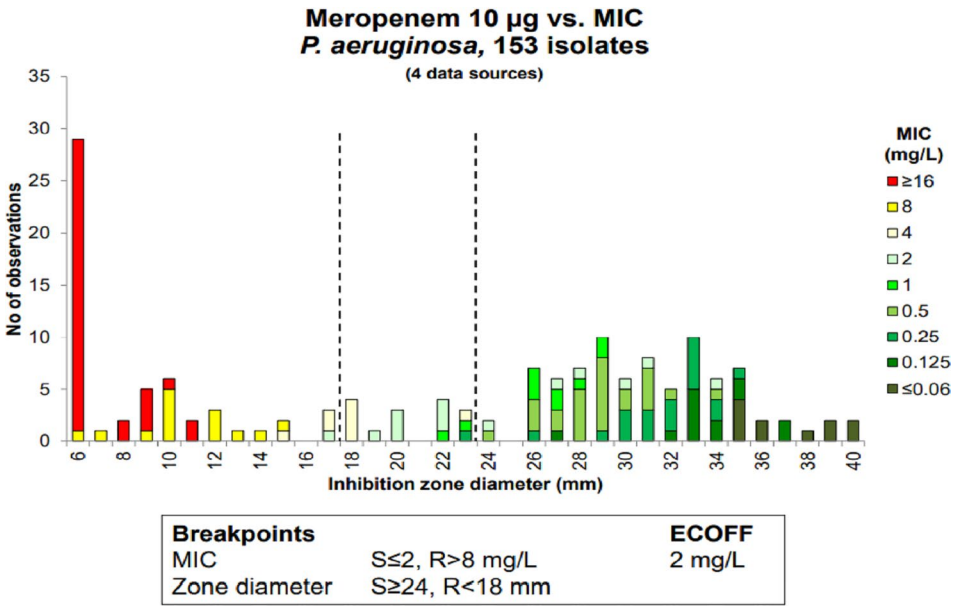
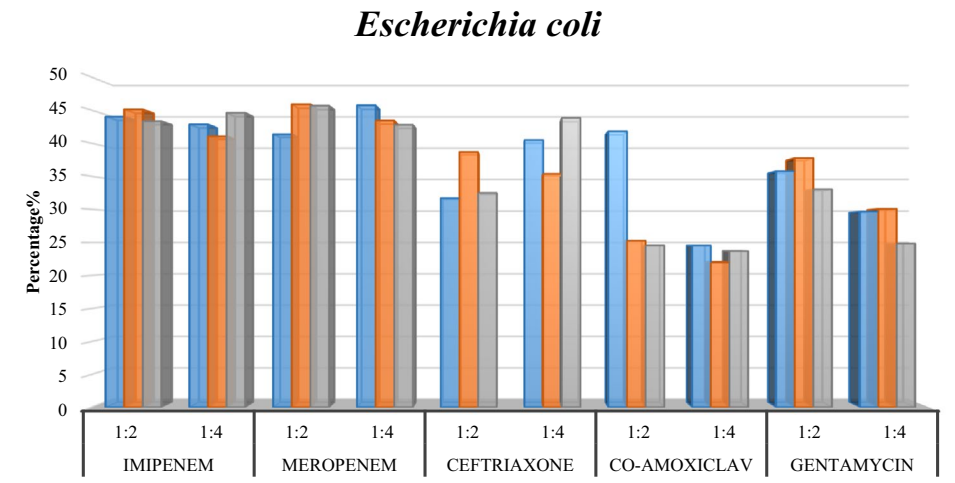


Fig. 7 The standard inhibition zone diameter of Meropenem (18–24) against *Pseudomonas aeruginosa*



	Imipenem		Meropenem		Ceftriaxone		Co-Amoxiclav		Gentamycin	
	1:2	1:4	1:2	1:4	1:2	1:4	1:2	1:4	1:2	1:4
S1	44.02	42.85	41.37	45.74	31.71	40.49	41.8	24.52	35.77	29.65
S2	45.12	41.08	45.91	43.43	38.66	35.37	25.25	21.98	37.76	30.07
S3	43.34	44.61	45.68	42.79	32.49	43.83	24.54	23.71	33.05	24.83

Fig. 8 The effect and inhibition zone against *Escherichia coli*

et al. 2019). *Escherichia coli* with various drugs either have sensitivity or resistance depending on the drug and bacterial strain as mentioned in Horcajada et al. (2019); Pogue et al. 2020). The drugs that have been used for Klebsiella spp. were Ceftriaxone 1 g, Imipenem (500 mg/500 mg) and Meropenem 1 g each with a concentration of 0.5 mg/1 ml (1:2). Co-Amoxiclav (1000/200 mg) 0.6 mg/1.2 ml (1:2) and Gentamicin (80 mg/2 ml) with concentration of (1:2). Co-Amoxiclav (1000/200 mg) had an inhibition zone of 28.21 mm in diameter and with AMC disc 30mcg had no inhibition zone (completely resistant), while in comparison to EUCAST of 2 mg in 1 l of sdH_2O, the inhibition zone was $S \geq 16$ mm $< R$. Ceftriaxone 1 g had an inhibition zone with a diameter of 30.64 mm which is sensitive and with CRO 10 mcg antibiotic disk had no inhibition zone (completely resistant), comparing with Ceftazidime of EUCAST and ECOFF 0.5 mg in 1 l of sdH_2O the inhibition zone was 19–22 mm in diameter. Gentamicin (80 mg/2 ml) had an inhibition zone of 21.85 mm in diameter which is sensitive and with the GNT antibiotic disc 10 mcg had no inhibition zone which is resistant. However, according to EUCAST and ECOFF 2 mg in 1 l of sdH_2O the inhibition zone was $S \geq 17$ mm $< R$. Imipenem (500 mg/500 mg) had inhibition zone of 42.40 mm in diameter and with IPM 10 mcg antibiotic disk (38.71 mm), in comparison with EUCAST and ECOFF 1 mg in 1 l of sdH_2O, the inhibition zone was 17–22 mm which detects that the bacteria is sensitive (Pogue

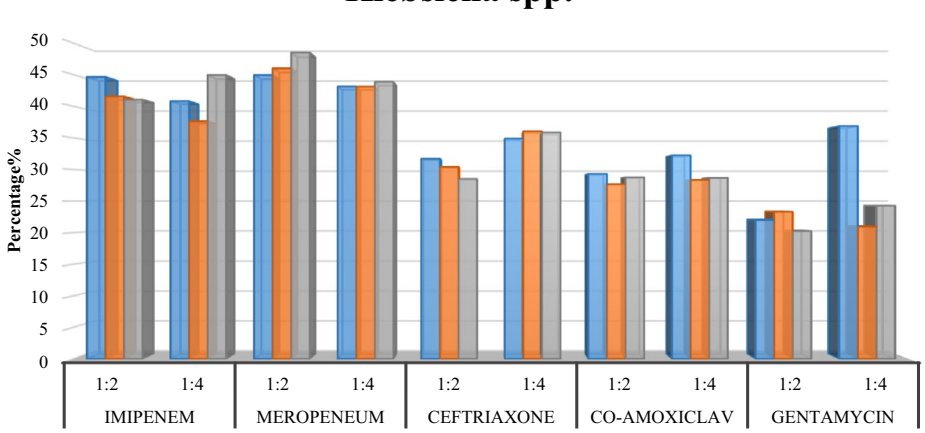


Fig. 9 The effect and inhibition zone against *Klebsiella spp.*

	Imipenem		Meropeneum		Ceftriaxone		Co-Amoxiclav		Gentamycin	
	1:2	1:4	1:2	1:4	1:2	1:4	1:2	1:4	1:2	1:4
S1	44.62	40.8	44.9	43.12	31.7	34.88	29.27	32.22	22.01	36.85
S2	41.54	37.63	46	43.11	30.42	36.05	27.69	28.34	23.29	20.93
S3	41.05	44.91	48.47	43.83	28.51	35.84	28.77	28.68	20.24	24.26

et al. 2020; Abd El-Baky et al. 2020; Jahangiri et al. 2021). Meropenem 1 g had an inhibition zone with a diameter of 46.46 mm which looks sensitive and MEM 10 mcg antibiotic disc had 29.02 mm, in comparison to EUCAST and ECOFF 0.125 mg in 1 l of sdH_2O, the inhibition zone was 16–22 mm which detects that the bacteria are resistant to the drugs (Odabaş-Serin et al. 2020; Horcajada et al. 2019).

Conclusion

The best result showed by Meropenem vial-drug; it has worked against all the three types of bacteria. The study examines the susceptibility of antibiotics to individual infectious bacteria.

Acknowledgements We would like to express our appreciation to Cihan University-Erbil for giving us the opportunity to do our research in the laboratory and fund the research and many thanks for Kalar Hospital for isolating the pathogens.

Funding This study was self-funded.

Declarations

Conflict of interest All authors declare, have no conflict of interest.

References

Abd El-Baky RM, Masoud SM, Mohamed DS, Waly NG, Shafik EA, Mohareb DA, Elkady A, El-Badr MM, Hetta HF (2020) Prevalence and some possible mechanisms of colistin resistance among multidrug-resistant and extensively drug-resistant *Pseudomonas aeruginosa*. Infect Drug Resist 13:323

Carpenter JL (1990) Klebsiella pulmonary infections: occurrence at one medical center and review. Rev Infect Dis 12(4):672–682

Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, Hill AT (2014) The bronchiectasis severity index. An international derivation and validation study. Am J Respir Crit Care Med 189(5):576–585

Erb A, Stürmer T, Marre R, Brenner H (2007) Prevalence of antibiotic resistance in *Escherichia coli*: overview of geographical, temporal, and methodological variations. Eur J Clin Microbiol Infect Dis 26(2):83–90

Griffith DC, Sabet M, Tarazi Z, Lomovskaya O, Dudley MN (2019) Pharmacokinetics/pharmacodynamics of vaborbactam, a novel beta-lactamase inhibitor, in combination with meropenem. Antimicrob Agents Chemother. https://doi.org/10.1128/AAC.01659-18

Horcajada JP, Montero M, Oliver A, Sorlí L, Luque S, Gómez-Zorrilla S, Benito N, Grau S (2019) Epidemiology and treatment of multidrug-resistant and extensively drug-resistant *Pseudomonas aeruginosa* infections. Clin Microbiol Rev. https://doi.org/10.1128/CMR.00031-19

Hussein AM, Taha ZB, Malek AG, Rasul KA, Hazim DQ, Ahmed RJ, Mohamed UB (2021) D-dimer and serum ferritin as an independent risk factor for severity in COVID-19 patients. Materials Today: Proceedings.

Jahangiri A, Neshani A, Mirhosseini SA, Ghazvini K, Zare H, Sedighian H (2021) Synergistic effect of two antimicrobial peptides, Nisin and P10 with conventional antibiotics against extensively drug-resistant Acinetobacter baumannii and colistin-resistant *Pseudomonas aeruginosa* isolates. Microb Pathog 150:104700

Johnson TJ, Logue CM, Johnson JR, Kuskowski MA, Sherwood JS, Barnes HJ, Nolan LK (2012) Associations between multidrug resistance, plasmid content, and virulence potential among extraintestinal pathogenic and commensal *Escherichia coli* from humans and poultry. Foodborne Pathog Dis 9(1):37–46

Kaper JB, Nataro JP, Mobley HL (2004) Pathogenic *Escherichia coli*. Nat Rev Microbiol 2(2):123–140

Liao S, Zhang Y, Pan X, Zhu F, Jiang C, Liu Q, Cheng Z, Dai G, Wu G, Wang L, Chen L (2019) Antibacterial activity and mechanism of silver nanoparticles against multidrug-resistant *Pseudomonas aeruginosa*. Int J Nanomed 14:1469

Lin JL, Xu JF, Qu JM (2016) Bronchiectasis in China. Ann Am Thorac Soc 13(5):609–616

Loebinger MR, Wells AU, Hansell DM, Chinyanganya N, Devaraj A, Meister M, Wilson R (2009) Mortality in bronchiectasis: a long-term study assessing the factors influencing survival. Eur Respir J 34(4):843–849

Long SS, Prober CG, Fischer M (2017) Principles and practice of pediatric infectious diseases E-book. Elsevier, Amsterdam

Martínez-García MÁ, De Gracia J, Relat MV, Girón RM, Carro LM, de la Rosa Carrillo D, Olveira C (2014) Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score. Eur Respir J 43(5):1357–1367

Odabaş-Serin Z, Hussein AM, Taha ZB (2020) Effect of Isatis spp. extraction on the growth of *Aspergillus niger* and *Candida albicans*. Cihan Univ Erbil Sci J 4(1):85–99

Podschun R, Ullmann U (1998) Klebsiella spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev 11(4):589–603

Pogue JM, Kaye KS, Veve MP, Patel TS, Gerlach AT, Davis SL, Puzniak LA, File TM, Olson S, Dhar S, Bonomo RA (2020) Ceftolozane/tazobactam vs polymyxin or aminoglycoside-based regimens for the treatment of drug-resistant *Pseudomonas aeruginosa*. Clin Infect Dis 71(2):304–310

Rossolini GM, Stone GG (2020) Assessment of the in vitro activity of ceftazidime/avibactam against a global collection of multidrug-resistant Klebsiella spp. from the INFORM surveillance programme (2015–2017). Int J Antimicrob Agents 56(3):106111

Saleem H, Malik SH (2019) Life threatening anaphylaxis with co-amoxiclav despite having a previous tolerant exposure to the antibiotic. J Ayub Med Coll Abbottabad JAMC 31(4):S680–S682

Steil D, Pohlentz G, Legros N, Mormann M, Mellmann A, Karch H, Müthing J (2018) Combining mass spectrometry, surface acoustic wave interaction analysis, and cell viability assays for characterization of Shiga toxin subtypes of pathogenic *Escherichia coli* bacteria. Anal Chem 90(15):8989–8997

Tunney MM, Einarsson GG, Wei L, Drain M, Klem ER, Cardwell C, Elborn JS (2013) Lung microbiota and bacterial abundance in patients with bronchiectasis when clinically stable and during exacerbation. Am J Respir Crit Care Med 187(10):1118–1126

Von Baum H, Marre R (2005) Antimicrobial resistance of *Escherichia coli* and therapeutic implications. Int J Med Microbiol 295(6–7):503–511

Wang H, Ji XB, Mao B, Li CW, Lu HW, Xu JF (2018) *Pseudomonas aeruginosa* isolation in patients with non-cystic fibrosis bronchiectasis: a retrospective study. BMJ Open 8(3):e014613

Winstanley C, O'Brien S, Brockhurst MA (2016) *Pseudomonas aeruginosa* evolutionary adaptation and diversification in cystic fibrosis chronic lung infections. Trends Microbiol 24(5):327–337

World Health Organization (2012) The evolving threat of antimicrobial resistance: options for action. World Health Organization, Geneva