Mechanism of Carbapenem Resistant among Multi-Drug-Resistant Gram-Negative Bacteria in Lower Respiratory Tract Infections in Kebbi State, Nigeria

BY
ZAHARADDIN MUHAMMAD KALGO
Department of Microbiology, Federal University Birnin Kebbi, Kebbi State, Nigeria

Background

Enterobacteriaceae are common pathogens causing a variety of severe infections, including bloodstream infections (BSIs), community-acquired pneumonia (CAP), hospital acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), complicated urinary tract infections (cUTIs), and complicated intra-abdominal infections (cIAIs). Therefore, antibiotic resistance in these bacteria has significant clinical and socioeconomic impacts (Lee *et al*., 2017; Rodriguez-Bano *et al*., 2018; Ting *et al*., 2018). As the prevalence of infections caused by extended-spectrum b-lactamase (ESBL)-producing Enterobacteriaceae is increasing, the medical community has been forced to use carbapenem as a first-line empirical treatment. The increasing use of carbapenem for possible ESBL infections has led to a more serious problem: the emergence of carbapenemase-producing Enterobacteriaceae (CPE) (Sheu *et al*., 2018).

Carbapenems possess broad spectrum antibacterial activity and have a unique structure that is defined by a carbapenem coupled to a B-lactam ring which confers protection against most B-lactamases such as metallo-β-lactamase (MBL) as well as extended spectrum β-lactamases (Knapp, 2001).

Consequently, carbapenems are considered one of the most reliable drugs for treating bacterial infections and the emergence and spread of resistance to these antibiotics constitute a major public health concern (Datta and Wattal, 2010; Livermore, 2012; Meletis, 2016).

The resistance of CRE to carbapenems is generally based on two mechanisms: carbapenemase production or the combination of structural mutations with the production of other β-lactamases, such as AmpC cephalosporinase (AmpC) and ESBL (Goodman *et al*., 2016; Tamma and Simner, 2018). The combination of porin loss and class c β-lactamase expression is an important cause of imipenem resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (katole and Laxmikant, 2020).

Table 2: Distribution of MDR among the isolates

S/N	Bacterial isolates	No. of Isolated bacteria	MDR (%)
1	*Staphylococcus aureus*	34	12(35.3)
2	*Klebsiella pneumoniae*	24	9(37.5)
3	*Klebsiella oxytoca*	15	5(41.7)
4	*Escherichia coli*	12	2(16.7)
5	*Aeromonas hydrophila*	6	5(83.3)
6	*Acinetobacter baumannii*	5	2(40.0)
7	*Pseudomonas aeruginosa*	6	5(83.3)
8	*B. pseudomallei*	3	3(100)
	TOTAL	**108(100)**	**43(39.8)**

Frequency of Occurrence of Carbapenem Resistant Bacteria among MDR Isolates of LRTI in Kebbi State.

S/N	Bacterial isolates	No. of isolates screened	Carbapenem Resistant Isolates (%)
1	*Klebsiella pneumoniae*	9	3(33)
2	*Klebsiella oxytoca*	5	2(40)
3	*Escherichia coli*	2	1(50)
4	*Aeromonas hydrophila*	5	4(80)
5	*Acinetobacter baumannii*	2	1(50)
6	*Pseudomonas aeruginosa*	5	4(80)
7	*B. pseudomallei*	3	2(67)
	TOTAL	31	17(55)

Mechanisms of Carbapenem Resistance among the MDR Isolates in some Hospitals, Kebbi State

S/N	Bacterial isolates	No. of isolates screened (%)	KPC (%)	MBL (%)	ESBL + Porin loss (%)	AmPc + Porin loss (%)
1	*Klebsiella pneumoniae*	9	0(0)	0(0)	2(22.2)	1(11.1)
2	*Klebsiella oxytoca*	5	0(0)	0(0)	2(40.0)	0(0)
3	*Escherichia coli*	2	0(0)	0(0)	1(50.0)	0(0)
4	*Aeromonas hydrophila*	5	0(0)	0(0)	4(80.0)	0(0)
5	*Acinetobacter baumannii*	2	0(0)	0(0)	0(0)	1(50.0)
6	*Pseudomonas aeruginosa*	5	0(0)	0(0)	4(80.0)	0(0)
7	*B. pseudomallei*	3	0(0)	0(0)	2(66.7)	0(0)
	TOTAL	31	0(0)	0(0)	15(48.3)	2(6.5)

Table 1: KPC, MBL and OXA-48 comfirm kit result interpretation table according to manufacturer's protocol.

		Meropenem + Phenylborinic acid	Meropenem + DPA	Meropenem + Cloxacillin	Temocillin
AmpC + Porin loss	Meropenem	> 4	< 3	>5	>14
ESBL + Porin loss	Meropenem	<3	<3	<3	>14
KPC	Meropenem	> 4	<3	<3	variable
	Meropenem +Cloxacillin (MRPCX)	> 4	-	-	-
MBL	Meropenem	< 4	>5	<3	Variable
OXA-48	Meropenem	<3	<3	<3	<=14
OXA-48 + ESBL	Meropenem	<3	<3	<3	<=14

Screening and Confirmatory Test for Carbapenem Resistant Bacteria

Isolates that were not susceptible to one or more Carbapenem were subjected to confirmatory test using KPC, MBL and OXA-48 Confirm Kit (Rosco) according to manufacturer's instruction. From a fresh, pure culture, the suspension of the organism to be tested were prepared equivalent to 0.5 McFarland standards. The suspension of the organism was swabbed on a dried surface of prepared Mueller Hinton agar using a sterile swap. Using a sterile forcep one of each tablet were placed on the inoculated agar plate. It was then incubated at 37^{o}C for 18 hours. The zones of inhibition were measured to the nearest millimetre including the diameter of the discs. The results for KPC, MBL and OXA-48 Confirm Kit were interpreted according to manufacturer's guidelines.

Conclusion

Antibiotics susceptibility profile of the isolated bacteria revealed high level of MDR of up to 39.8% rate. High level of MDR was observed among *Burkholderia pseudomallei* (100%), *Pseudomonas aeruginosa* (83.3%) and *Aeromonas hydrophila* (83.3%)., it was also found out that the highest level of carbapenem resistant were detected among *Pseudomonas aeruginosa* and *Aeromonas hydrophila* and the mechanism of resistant were found to be as a result of ESBL + Porin loss and AmPc + Porin loss.

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