Predominance of metallo-beta-lactamase *bla*VIM Genes in Clinical Isolates from Health Facilities in Nigeria: Role in Multidrug Resistance Surge

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Abstract

Background: The predominance of metallo-beta-lactamase (MBL) genes in Gram-negative bacteria (GNB) has been reported to contribute immensely in the emergence of multi-drug resistance (MDR) strains in hospital environments worldwide.

Aim: This study aimed to investigate the molecular characteristics of MBL genes in MDR-GNB in selected health facilities in Akwa Ibom State, Nigeria.

Materials and methods: A descriptive cross-sectional study was conducted in three health facilities in the State. One hundred and sixty (160) samples each of wound, urine and blood were collected aseptically from consented patients and analyzed using standard laboratory procedures. Identification, antibiotic susceptibility testing and phenotypic detection of MBL-producers were done using the VITEK®2 system, Kirby-Bauer disc diffusion and imipenem+EDTA CDT, respectively. Polymerase chain reaction was used to investigate the characteristics of MBL encoding genes: *bla*VIM, *bla*NDM and *bla*IMP.

Results: Out of 135 GNB identified, 60.7% exhibited MDR and 53(39.3%) were MBL-producers. Of the MBL genes screened, only the *bla*VIM was detected in 5(23.8%) of the 21 selected strains screened. The breakdown of *bla*VIM gene detection rate among isolates from wound, blood and urine samples were 20%, 11.1% and 3.4%, respectively. The GNB that harboured the *bla*VIM genes were *Serratia marcescens, Klebsiella pneumoniae and Escherichia coli* recovered from wounds as well as *Proteus mirabilis and Pseudomonas aeruginosa* recovered from blood and urine samples, respectively.

Conclusion: Findings of this study highlight the importance of the *bla*VIM gene in conferring multidrug among the Gram-negative bacteria, and the need to establish antimicrobial resistance surveillance network and policy to determine appropriate empirical treatment regimen among hospitals in the State.

Keywords: Metallo-beta-lactamase, Gram-negative bacteria, Multi-drug resistance, *bla*VIM genes

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Introduction

The emergence of multidrug resistance (MDR) in clinically important Gram-negative pathogens poses a serious public health threat in the treatment of related infections globally.[1] Antibiotics that belong to the beta-lactam class have been used successfully over the last 6 decades, and genes that code for the production of metallo-beta-lactamase

(MBL) enzymes have emerged in some strains of bacteria.[2,3] These resistance genes which are disseminated within a bacterial population through horizontal gene transfer (HGT) mechanisms have been implicated in delayed therapeutic outcomes, allowing infections to progress despite antibiotic administration.[4,5]

Metallo-beta-lactamases (MBLs) are class B group of beta-lactamases that catalyze the hydrolysis of a broad range of beta-lactam drugs (such as penicillins and their derivatives, cephalosporins including those with oxyimino side chain, cephamycins and oxapenems), and the cabapenems.[6,7] The MBL enzyme types, grouped on the basis of amino acid sequence homology include the Verona integron-encoded metallo-beta-lactamases (VIM), Imipenemase (IMP), Sau Paulo metallo-beta-lactamase (SPM), German Imipenemase (GIM), New Delhi metallo-beta-lactamase (NDM), Seoul Imipenemase (SIM) and Dutch Imipenemase (DIM).[8,9] The catalytic ability of these enzymes, which require zinc-ions, is not neutralized by commercially available beta-lactamase inhibitors such as clavulanate, tazobactam and sulbactam.[10] The genes that code for MBLs are carried on plasmids, transposons and gene cassettes which are the mobile genetic elements. This acquisition is responsible for the evolution and spread of multi-drug resistant (MDR) bacterial phenotypes through vertical or horizontal gene transfer mechanism.[11]

Among the MBLs, carbapenemases are of significant concern due to their increased efficacy against carbapenems, the broad-spectrum drugs often used for treating life-threatening infections, or as the empirical agents of last resort for treating infections caused by multi-drug resistant bacteria. This further limits the therapeutic option available in the management of infections caused by MDR Gram-negative bacteria pathogens.[2]

Currently, clinically active MBL inhibitors are readily not available and the easy spread of genes that encode them remains the most significant cause of multiple resistances seen in Gram-negative bacteria (GNB).[10] In view of the fact that, these MBL-borne pathogens are implicated in various hospital and community-acquired infections, application of molecular procedures to detect and characterize the different MBL genes and their MDR profiles becomes indispensable in providing useful epidemiological data that are necessary for the implementation of effective control policy and management of infections.[5]

Studies have reported a high incidence of metallo-beta-lactamases and their involvement in the widespread dissemination of multi-drug resistance globally, especially among Gram-negative clinical isolates.[5,12] The prevalent MBL genes vary in different countries and regions of the world. For instance, MBLs with blaVIM and *bla*NDM have been reported in Khartoum hospitals in Sudan as the prevalent MBL genes;[13] *bla*IMP in Bayelsa State, Nigeria[14] and in Nadu, India;[15] *bla*VIM in Abuja, Nigeria[7] as well as *bla*VIM and *bla*IMP in Italy[16] and Malaysia.[17] However, in Akwa Ibom State, Nigeria, information regarding the cause of multi-drug resistance surge in hospitals, the dominant MBL gene types in circulation as well as their transmission dynamics in clinical isolates still remains limited. Therefore, this study was carried out to investigate the molecular characteristics of the metallo-beta-lactamase genes in multi-drug resistant Gram-negative isolates from selected health facilities in Akwa Ibom State, Nigeria.

Materials and Methods
Study design and population
This was a descriptive cross-sectional study carried out in three health facilities namely: University of Uyo Teaching Hospital (UUTH), Uyo; General Hospital, Ikot Ekpene (GHIE) and Immanuel Hospital, Eket (IHE), located in 3 different senatorial districts in Akwa Ibom State from November 2021 to June 2023. The study population comprised 480 patients who had been previously diagnosed or suspected of bacteremia, wound infection and urinary tract infections. Clinical samples were collected from the subjects after obtaining informed consent.

Ethical considerations
Approval to conduct the study was obtained from Health Research Ethics Committees (HRECs) of the Akwa Ibom State Ministry of Health (AKSMH), with HREC assigned No: AKHREC/27/8/21/008 and University of Uyo Teaching Hospital (UUTH), Uyo with HREC assigned No: UUTH/AD/S/96/VOL.XXI/629. Written informed

consent was obtained from participants prior to their inclusion in the study.

Identification of bacterial isolates

Gram-negative bacteria were recovered from wound, urine and blood samples of patients in the selected hospitals. Bacterial cultures were grown in MacConkey agar, differentiated by Gram staining technique, identified using the conventional biochemical methods and validated by VITEK®2 automated biochemical system according to standard protocols.

Antibiotic susceptibility testing (AST)

The antibiotic susceptibility testing of the isolates was carried out using Kirby-Bauer disc diffusion method after overnight incubation at 37°C on Mueller-Hinton agar plates as recommended by the Clinical Laboratory Standard Institute.[18] The antibiotics with their concentrations included gentamicin (10µg), imipenem (10µg), amoxicillin-clavulanic acid (amoxicillin 20µg/clavulanate 10µg), ciprofloxacin (10µg), cefotaxime (30µg), ceftazidime (30µg), aztreonam (30µg), cefepime (30µg), trimethoprim-sulfamethoxazole (2.5µg), ceftriaxone (30µg) and ofloxacin (5µg) (Oxoid, UK). *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 700603 and *Pseudomonas aeruginosa* ATCC 27853 were used as reference strains for susceptibility testing, while AST results were interpreted in accordance with the CLSI guidelines and interpretive criteria.[18]

Phenotypic screening for MBL production

Gram-negative isolates that were resistant to imipenem at the initial screening test were selected for phenotypic confirmation of MBL production using the imipenem+EDTA combined disc test (IMP+EDTA CDT) according to previously described method.[19] Overnight culture of the test isolates adjusted to 0.5 McFarland turbidity standard and inoculated on a Mueller-Hinton agar plate was used to screen for MBL production. Two imipenem discs (10µg), of which one was supplemented with 10µl of 0.5M EDTA solution were placed at a distance of 5cm apart and the plates incubated at 35°C for 16-18 hrs. Isolates with enhanced zone size of ≥7mm towards IMP+EDTA disc compared to IMP disc alone was considered

and interpreted as MBL producers.[19]

Bacterial genomic DNA extraction and quantification

Extraction of bacterial DNA was done using a ZR fungal/bacterial DNA mini prep extraction kit supplied by Inqaba South Africa according to the manufacturer's instruction. The extracted genomic DNA was quantified using the Nanodrop 1000 spectrophotometer (Thermo Scientific, Inqaba Biotec).

Amplification of IMP gene

The blaIMP gene from the isolates was amplified using the forward (5'–GAAGGCGTTTATGTTCATAC–3') and reverse (5'–GTATGTTTCAAGAGTGATGC–3') primers on a nexus gradient Mastercycler (Eppendorf, Germany) at a final volume of 30 µL for 35 cycles. The PCR mixture included: The X2 Dream Taq Master Mix supplied by Inqaba, South Africa (Taq polymerase, DNTPs, buffer, MgCl2), the primers at a concentration of 0.5 µM, 2 µL of the extracted DNA as template and 11.8 µL of PCR water. The PCR conditions were as follows: Initial denaturation, 95°C for 5 min, denaturation, 95°C for 30 sec; annealing, touchdown of 55-49°C for 30 sec; extension, 72°C for 30 sec for 35 cycles, final extension, 72°C for 5. The amplicon was resolved on a 1% agarose gel at 200V for 15 min and visualized on a blue light trans-illuminator but there was no base pair of product size.

Amplification of NDM gene

The blaNDM gene from the isolates was amplified using the forward (5'–GGTTTGGCGATCTGGTTTTC – 3') and reverse (5'–CGGAATGGCTCATCACGATC – 3') primers on a nexus gradient Mastercycler (Eppendorf, Germany) at a final volume of 30 µL for 35 cycles. The PCR mixture included: The X2 Dream Taq Master Mix supplied by Inqaba, South Africa (Taq polymerase, DNTPs, buffer, MgCl2), the primers at a concentration of 0.5 µM, 2 µL of the extracted DNA as a template and 11.8 µL of PCR water. The PCR conditions were as follows: Initial denaturation, 95°C for 5 min, denaturation, 95°C for 40 sec, annealing, 56°C for 40 sec, extension, 68°C for 40 sec for 35 cycles, final extension, 68°C for 5

min and hold at 10min. The amplicon was resolved on a 1% agarose gel at 200V for 15 min and visualized on a blue light trans-illuminator but there was no base pair of product size.

Amplification of VIM gene

The *bla*VIM gene from the isolates was amplified using the forward (5' – GTTTGGTCGCATATCGCAAC – 3') and reverse (5' – CTACTCGGCGACTGAGCGAT – 3') primers on a nexus gradient Mastercycler (Eppendorf, Germany) at a final volume of 30 µL for 35 cycles. The PCR mixture included: The X2 Dream Taq Master Mix supplied by Inqaba, South Africa (Taq polymerase, DNTPs, buffer, MgCl2), the primers at a concentration of 0.5 µM, 2 µL of the extracted DNA as a template and 11.8 µL of PCR water. The PCR conditions were as follows: Initial denaturation, 95°C for 5 min, denaturation, 95°C for 30 sec, annealing, 57°C for 40 sec, extension, 72°C for 40 sec for 35 cycles, final extension, 72°C for 5 min and hold at 10 min. The amplicon was resolved on a 1% agarose gel at 200V for 15 min and visualized on a blue light trans-illuminator for a 265 base pair product size.

Statistical analysis

The statistical analysis was performed using SPSS software version 25.0 (IBM Corp., USA). Results obtained were presented as descriptive statistics in tables and percentages.

Results

The comparative in vitro antibiotic resistance patterns of MBL and non-MBL-producing Gram-

Table 1: *In vitro* antibiotic resistance patterns of MBL and non-MBL-producing clinical isolates in three health facilities in Akwa Ibom State

Antibiotics (disc conc.)	Number (%) of antibiotics resistant isolates		Total (%) (n=135)
	MBL-producers (n=53)	Non MBL-producers (n=82)	
SXT (2.5µg)	43(81.1)	63(76.8)	106(78.5)
IMP (10µg)	15(28.3)	26(31.7)	41(30.4)
OFX (5µg)	23(43.4)	38(46.3)	61(45.2)
FEP (30µg)	41(77.4)	36(43.9)	77(57.0)
AMC (20µg/10µg)	35(66.0)	17(20.7)	52(38.5)
CIP (10µg)	29(54.7)	55(67.1)	84(62.2)
CTX (30µg)	31(58.5)	49(59.8)	80(59.3)
CRO (30µg)	43(81.1)	57(69.5)	100(74.1)
ATM (30µg)	33(62.3)	57(69.5)	90(66.7)
CAZ (30µg)	42(79.2)	35(42.7)	77(57.0)
CN (10µg)	19(35.8)	30(36.6)	49(36.3)

Key: AMC=Amoxicillin-clavulanic acid; CIP=Ciprofloxacin; CTX Cefotaxime; CRO Ceftriaxone; ATM Aztreonam; CAZ=Ceftazidime; CN=Gentamicin; SXT=Trimethoprim-sulfamethoxazole; OFX Ofloxacin; FEP cefepime

negative clinical isolates in Akwa Ibom State is presented in Table 1. The results showed the highest level of resistance of MBL-producers against trimethoprim-sulfamethoxazole and ceftriaxone (81.1%), each. For the non MBL-producing isolates, in vitro resistance was observed against trimethoprim-sulfamethoxazole (76.8%), ceftriaxone (69.5%) and aztreonam (69.5%) antibiotics.

The percentage distribution of multidrug resistance (MDR) among MBL and non-MBL producing Gram-negative bacteria is presented in Figure 1. The results showed that all MBL-producing isolates (100%) were multidrug resistant while 35.4% of non-MBL producers were multidrug resistant. The overall prevalence of MDR Gram-negative bacteria in the three hospitals in Akwa Ibom State was 60.7%. An isolate was considered MDR if it resisted
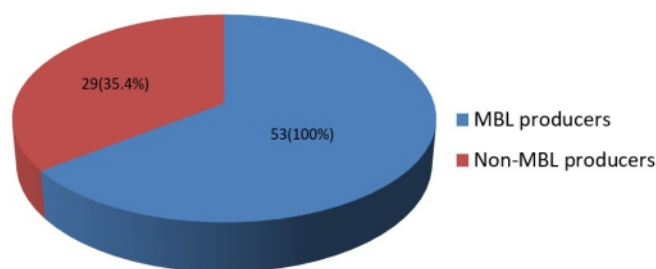

Figure 1: Percentage distribution of multidrug resistance (MDR) among MBL and non-MBL producers

Table 2: Distribution of MBL genes in Gram-negative bacteria isolated from the patients

Isolates	*bla*VIM	*bla*IMP	*bla*NDM
Serratia marcescens (n=2)	**+ve**	-ve	-ve
Klebsiella pneumoniae (n=2)	**+ve**	-ve	-ve
Klebsiella oxytoca (n=1)	-ve	-ve	-ve
Escherichia coli (n=5)	**+ve**	-ve	-ve
Proteus mirabilis (n=2)	**+ve**	-ve	-ve
Acinetobacter baumannii (n=2)	-ve	-ve	-ve
Burholderia cepacia (n=3)	-ve	-ve	-ve
Rhizobium radiobacter (n=1)	-ve	-ve	-ve
Pseudomonas aeruginosa (n 1)	**+ve**	-ve	-ve
Enterobacter aerogenes (n=1)	-ve	-ve	-ve
Enterobacter cloacae (n=1)	-ve	-ve	-ve
Total	**5**	**0**	**0**

Key: n=number of isolates tested; **+ve** = positive; -ve = negative

Table 3: Distribution of blaVIM MBL positive genes according to clinical samples

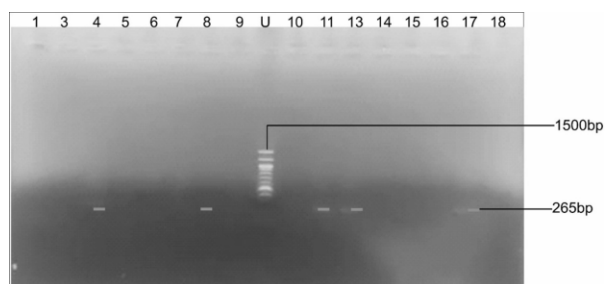| Sample	Number screened	MBL positive (%)	No. positive for *bla*VIM (%)
Urine	160	29(18.1)	1(3.4)
Blood	160	9(5.6)	1(11.1)
Wound	160	15(9.4)	3(20.0)
Total	**480**	**53(11.0)**	**5(23.8)**

Figure 2: Agarose gel micrograph of blaVIM gene from MBL-producing isolates

at least 3 different classes of antibiotics tested.

The distribution of MBL genes in Gram-negative bacteria isolated from the patients is indicated in Table 2. Out of the three MBL genes assayed in 21 clinical isolates of Gram-negative bacteria, only blaVIM was detected in 5 of the isolates. The following GNB harboured the *bla*VIM genes: *Serratia marcescens, Klebsiella pneumoniae, Proteus mirabilis, Escherichia coli and Pseudomonas aeruginosa.*

The distribution of *bla*VIM MBL positive genes in clinical samples in Akwa Ibom State is shown in Table 3. Of the 160 samples each of urine, blood and wound screened for the detection of MBL genes, the presence of *bla*VIM gene was in the rate of 3.4%, 11.1% and 20%, respectively. Hence, the overall prevalence of *bla*VIM gene detection in Akwa Ibom State was 23.8%.

The agarose gel micrograph of *bla*VIM gene in MBL-producing Gram-negative isolates is shown in Figure 2. Lanes 4, 8, 11, 13, and 17 revealed the 265 base pairs of amplified *bla*VIM genes in *S. marcescens, P. mirabilis, K. pneumoniae, E. coli* and *P. aeruginosa* isolates, respectively. Lane U represents the 100bp DNA ladder.

Discussion

The preponderance of multi-drug resistance (MDR) Gram-negative bacteria isolates in clinical samples is worrisome, especially in the area of therapeutic management of infections caused by these etiologic agents.[1,5] The predominance of *bla*VIM genes, among other MBL gene types in different parts of the world have been reported to contribute immensely in the widespread emergence of MDR strains in hospital environments.[12,20] The situation is even compounded by the absence of molecular diagnostic facilities for accurate detection of these

resistance genes, particularly in low-resource settings, including Nigeria. In this study, 15(28.3%) out of the 41 imipenem-resistant Gram-negative bacteria produced MBLs. Among the folate pathway antagonist group, resistance was highly detected in MBL-producing isolates against trimethoprim-sulfamethoxazole (SXT: 81.1%), while for the cephalosporin group, ceftriaxone (CRO: 81.1%) and ceftazidime (CAZ: 79.2%) showed high resistance rates. However, for the carbapenem group, a low resistance rate of 28.3% was obtained among MBL-positive isolates. These findings corroborate earlier reports from Emam Hossein and Loghman Hakim hospitals in Japan,[21] Immanuel Hospital, University of Uyo Teaching Hospital and General Hospital Ikot Ekpene in Akwa Ibom State, Nigeria[5] and a tertiary health facility in South India.[22] The production of these enzymes in certain Gram-negative clinical isolates has been reported in many studies to have contributed to the increased development of acquired resistance to both beta-lactam and non-beta-lactam antibiotics.[1,23,24]

Multidrug resistance (MDR) is a bane in many hospitals as it poses a significant therapeutic challenge in the management of infections.[1,25] This study revealed 60.7% overall prevalence of multidrug resistance Gram-negative bacteria in the three health facilities. All MBL-producing Gram-negative clinical isolates (100%) were multidrug resistance portraying the significant impact of MBL in the evolution of multidrug resistant strains. The prevalence of MDR obtained in this study is higher than that reported in previous studies.[25,26] The possible reason for this high prevalence may not be unconnected to irrational use of antibiotics, over-the-counter prescription by non clinicians and absence of antibiotic sensitivity testing of clinical isolates prior to antibiotics prescription by physicians.[5]

In this study, of the 21 selected MBL-producing Gram-negative isolates, 5 (23.8%) were found to harbor *bla*VIM gene while the other MBL genes, *bla*IMP and *bla*NDM were not detected in any of the clinical isolates tested. This contradicts the findings of Akereuke et al.[27] in which all the above mentioned 3 genes were detected among Gram-negative isolates recovered from inpatients with urinary tract infection (UTI) and wound infection in University

of Uyo Teaching Hospital, being one of the health facilities used in this study. The reason for this observed difference is not clear, but could be due to the primers used in studies. This report is also inconsistent with the findings of Abdu et al.[28] in which both NDM and VIM genes were detected among clinical isolates of *P. aeruginosa* and *K. pneumoniae*, while only IMP gene was not detected in Bayelsa State, Nigeria. However, it is consistent with the findings of Zubair et al.[7] in Abuja, in which only blaVIM gene was detected out of blaIMP, *bla*NDM, *bla*SPM, *bla*GIM and *bla*SIM among *Pseudomonas aeruginosa* isolates. A recent study in Bayelsa State, Nigeria by Alade et al.[14] did not detect NDM and VIM genes in clinical isolates of *P. aeruginosa* isolates and Davasena et al.[15] did not detect NDM-1 gene in *P. mirabilis* and *P. aeruginosa* isolates in a study conducted in Tamil, Nadu, India. Those bacterial isolate that resisted carbapenems but negative for any of the three MBL genes tested may have acquired other MBL genes which were not assayed in this study. Resistance may have been due to other mechanisms of antibiotic resistance such as outer membranes' impermeability, target sites' modification, efflux pump and possession of other carbapenemases.[14]

Also, it has been documented in literature that detection of MBL genes greatly vary among regions and countries of the world, due to differences in circulating strains, genetic variability and environmental factors.[29,30] Organism-specific gene variation may as well vary within country as observed in this study. MBL genes previously identified in a recent study among *E. coli* isolates in Anambra State University Teaching Hospital, Awka, Southeastern Nigeria include VIM, IMP, SPM, SIM and GIM-gene types.[31] The carbapenem resistant gene, *bla*IMP was detected among *P. aeruginosa* clinical isolates in Benin City, Nigeria,[32] NDM genes were detected in some *E. coli* isolates in Nnamdi Azikiwe University Teaching Hospital (NAUTH), Awka, Southeastern Nigeria and NDM-1 gene was responsible for the resistance of some *E. coli* and *K. pneumoniae* isolates to carbapenem in Kano, Northern Nigeria.[33] Higher detection rates for MBL genes for some organisms have also been reported in studies outside Nigeria. For instance, *bla*SIM (33%) in *E. coli* isolates from Indian hospital;[34] IMP-1, IMP-7, IMP-11 and VIM-1 genes

detected among *P. aeruginosa* isolates from Japanese hospital;[35] *bla*IMP (36.8%) and *bla*VIM (15.7%) genes among *E. coli* isolates from hospitals in Malaysia;[17] VIM (38.9%), IMP (26.4%) and NDM (4.2%) genes among clinical isolates of *Citrobacter* spp, *Escherichia coli, Enterobacter* spp, *Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Proteus vulgaris* from Khartoum hospitals in Sudan between 2015 and 2016;[13] *bla*IMP-1 (3.48%) and *bla*VIM-1 (17.44%) genes among *Acinetobacter baumannii* isolates from two hospitals in Tehran, Iran;[36] and VIM and IMP-type enzymes among MBL-producing *Pseudomonas aeruginosa, Pseudomonas putida* and *Enterobacter cloacae* isolates from a countrywide survey in Italy.[16]

According to Lauretti et al., the VIM, IMP and NDM-type genes are the most studied MBLs, first detected in the 1990s. The VIM gene was first isolated from *P. aeruginosa* strain in Verona Hospital, Italy in 1997.[37] It has now been recovered from many infections such as urinary tract infections, wound infections, blood-borne infections and device-associated infections.[7,34] Currently, these genes have been detected in more than 23 Gram negative bacterial species including *P. aeruginosa, Acinetobacter* spp. and members of Enterobacteriaceae family across 40 countries/regions of the world, largely in Europe, Asia, America and the Mediterranean region.[6,7] The predominance of the VIM gene in isolates obtained from this study may not be unconnected with cases of imported antibiotic resistance from Israel, Rome and Saudi Arabia by Nigerian travelers for pilgrimage and international travel for medical tourism and work as reported by Zubair et al.[7] There are presently 46 VIM variants (VIM-1 to -46) documented. While VIM-1 has 31.4% amino acid sequence identity with IMP-1, VIM-2 is the most widely distributed MBLs that have been implicated in multiple outbreaks of MBL-mediated antibiotic resistance globally.[38]

In this study, the *bla*VIM genes were detected in three Gram-negative bacterial strains recovered from wound infections (*Serratia marcescens, Klebsiella pneumoniae and Escherichia coli*) and one each from blood stream infection caused by Proteus mirabilis and UTI caused by *Pseudomonas aeruginosa*. Similarly, Abdu et al.[28] reportedly

detected 6 isolates of Gram-negative bacteria (GNB) habouring the VIM genes from patients with various infections in Bayelsa. Four (4) *P. aeruginosa* isolates were recovered from wound infection (66.7%) while one each of *E. coli* and *K. pneumoniae* were from UTI (33.3%). To the best of our knowledge, rarely is carbapenem-resistant *Serratia marcescens* reported in Nigeria and this is the first report on *bla*VIM gene detection in this bacterium in Akwa Ibom State. Most published studies on beta-lactamases detection among Gram negative clinical isolates in Akwa Ibom State were limited to ESBLs.[39,40,41] Only one study in UUTH reported on molecular detection of MBL genes in Gram-negative clinical isolates, in which the *bla*VIM gene was majorly detected in *P. mirabilis, K. pneumoniae, E. coli* and *P. aeruginosa* isolates.[27] This suggests that the *bla*VIM genes are probably the dominant MBL-gene type circulating in clinical isolates of Gram-negative bacteria in Akwa Ibom State.

Conclusion

The *bla*VIM MBL-positive Gram-negative bacteria are predominantly in circulation among bacteria causing multidrug resistant infections in patients seen in hospitals in Akwa Ibom State. This study is the first to report the detection of *bla*VIM gene in clinical isolates of carbapenem-resistant *Serratia marcescens* in wound samples. The high prevalence of *bla*VIM gene detection in this study (23.8%) is perturbing and calls for the establishment of systematic surveillance network and initiation of policies for monitoring of patients with multi-drug resistant Gram-negative bacteria infections (MDR-GNBIs) in the State. This is pertinent because the spread of these resistant genes in clinical isolates if left unchecked, could lead to widespread dissemination of uncontrollable epidemic clones for which efficient antimicrobial regimen may not be readily available.

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