Original Article

Methicillin-Resistant *Staphylococcus aureus* in a Central Nigeria Tertiary Hospital

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Abstract

Background: Methicillin-resistant Staphylococcus aureus (MRSA) is a significant cause of both health care- and community- associated infections worldwide and do present therapeutic challenges to beta-lactam antibiotics and other antibiotics due to the development of multidrug resistance. **Aim:** This study was carried out to determine the prevalence and antibiotic susceptibility profile of MRSA among patients at National Hospital Abuja with a view to providing information that will guide rational choice of antimicrobial agents in the empirical therapy of its infections. **Materials and Methods:** Between April 2014 and August 2015, clinical samples of patients submitted to Medical Microbiology laboratory of the hospital were processed and all Staphylococcus aureus isolates recovered, using standard laboratory methods. They were subjected to antibiotic susceptibility testing using the modified Kirby Bauer disc diffusion technique with zones of inhibition interpreted according to the Clinical and Laboratory Standard Institute (CLSI) guidelines. Methicillin resistance was determined using cefoxitin disc diffusion. Other clinical data of the patients were gathered along for analysis. **Results:** Of the 360 S. aureus isolates recovered, 97 (26.9%) were MRSA. All (100%) the MRSA isolates were susceptible to vancomycin, 88 (90.7%) to imipenem and 71 (73.2%) to clindamycin. All (100%) the MRSA isolates were resistant to penicillin, 85(88.0%) to tetracycline, 61 (62.9%) to ciprofloxacin, 58 (60.0%) to erythromycin and 52 (53.6%) to gentamycin. The MRSA strains showed higher resistance rate than MSSA strains to all tested antibiotics. Multidrug resistance was found in 68.0% of the MRSA strains. **Conclusion:** There was high prevalence of MRSA with high rates of resistance to commonly used anti-staphylococcal antimicrobials, and a significant proportion of these MRSA isolates were multi-drug resistant. Vancomycin is the best choice for empiric treatment of suspected MRSA infections. Routine screening of clinical S. aureus isolates for methicillin resistance, regular surveillance studies as well as institution of infection control measures and antibiotic stewardship programme are recommended.

Keywords: Abuja, antibiotic susceptibility, methicillin-resistant *Staphylococcus aureus*, National Hospital Abuja, prevalence

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant cause of both healthcare-and community-associated infections globally with enormous clinical and economic impact.[1-3] MRSA is due to the acquisition of *mecA* that is carried on a large mobile genetic element, the staphylococcal cassette chromosome, and which encodes a low affinity penicillin-binding protein 2a (PBP2a) to β-lactam antibiotics (except the fifth-generation cephalosporins).[4] *mecC* when present may also mediate methicillin resistance. The *mecA* complex also contains insertion sites for plasmids and transposons that facilitate acquisition of resistance to other antibiotics (multidrug resistance [MDR]) such as erythromycin, clindamycin, gentamicin, cotrimoxazole, and ciprofloxacin.[5,6] Consequently, options left for therapy are very few, expensive, and of limited availability, thereby making MRSA infections associated with poor outcome, prolonged hospital stay, increased cost of treatment, and increased morbidity and mortality.[7-9] All these present a daunting challenge to virtually all healthcare institutions and policymakers in respect of the management of MRSA infections as well as its control.[10] Tackling these challenges and ensuring quality of care in any healthcare environment requires good knowledge of the burden of MRSA infections and their antibiotic susceptibility pattern. This study was, therefore, carried out to fill this gap

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in knowledge in Abuja where there was no previous reliable study on MRSA and its antibiotic susceptibility and resistance pattern.

Materials and Methods

The study was conducted at National Hospital Abuja (NHA), Nigeria, between April 2014 and August 2015. All *S. aureus* isolates from routine clinical samples submitted to the medical microbiology laboratory of NHA within this period were included in this study. Identification of all isolates both morphologically and biochemically was done using standard laboratory methods.[11] Briefly, all Gram-positive cocci in clusters that were positive to catalase, and coagulase tests were tentatively identified as *S. aureus*. They were confirmed by a positive result with mannitol fermentation and DNase tests.

Susceptibility testing was carried out on Mueller Hinton Agar (MHA) (Oxoid, Basingstoke, UK) plates using the modified Kirby–Bauer disc diffusion technique.[12] The following antibiotic discs from oxoid were used: cefoxitin (30 μg), penicillin G (10 units), augmentin (20/10 μg), erythromycin (15 μg), tetracycline (30 g), gentamicin (10 μg), clindamycin (2 μg), vancomycin (30 μg), ciprofloxacin (5 μg), cefazolin (30 μg), cefuroxime (30 μg), ceftriaxone (30 μg), and imipenem (10 μg). Following this technique, a sterile cotton swab stick was used to inoculate the test organism onto the entire surface of MHA plate with the suspension of the test isolates equivalent to a 0.5 McFarland standard and then incubated at 35°C in ambient air for 18–24 h. The diameter of the zone of inhibition of each isolate to the tested antibiotics was measured in millimeters with a ruler and compared to the Clinical Laboratory and Standards Institute guideline (M100-S21) for interpretation.[12,13] The isolates were considered methicillin resistant if the diameters of the zones of inhibition for cefoxitin were ≤21 mm and susceptible if ≥22 mm. *S. aureus* ATCC25923 (methicillin-susceptible *S. aureus* MSSA strain) and *S. aureus* ATCC 43300 (MRSA strain) were used as quality control strains. Collected data on patients' biodata, clinical sample type, point-of-care access/service units as well as the susceptibility and resistance profile of all the recovered *S. aureus* isolates were analyzed using the IBM-SPSS-version 18 (SPSS Inc., Chicago Inc I11, USA).

Results

Three hundred and sixty clinical strains of *S. aureus* were isolated from the various clinical specimens of patients submitted during the study. One hundred and eighty-one (50.3%) isolates were from males, while 179 (49.7%) were from females. One hundred and forty-one (39.2%) were from the age group of 0–14 years, 22 (6.1%) from the age group of 15–24 years and 197 (54.7%) from the age group of ≥25 years. Two hundred and thirteen (59.2%) of the *S. aureus* isolates were from inpatients, while 147 (40.8%) were from outpatients. One hundred and thirty-one (36.4%) of the isolates were from surgery units, 119 (33.1%) from pediatrics units, 53 (14.7%) from general outpatient department, 44 (12.2%) from internal medicine units, and 13 (14.7%) from other units [Table 1].

Table 1: Overall demographics and baseline characteristics of sample population

Demographics/baseline characteristics	MRSA (*n*=97), *n* (%)	MSSA (*n*=263), *n* (%)	Total (*n*=360), *n* (%)
Age (years)			
0-14	27 (28.0)	114 (43.4)	141 (39.2)
15-24	4 (4.0)	18 (6.8)	22 (6.1)
≥25	66 (68.0)	131 (49.8)	197 (54.7)
Total	97 (100)	263 (100)	360 (100)
Gender			
Male	44 (45.4)	137 (52.1)	181 (50.3)
Female	53 (54.6)	126 (47.9)	179 (49.7)
Total	97 (100)	263 (100)	360 (100)
Occupation			
Healthcare worker	10 (10.3)	35 (13.3)	45 (12.5)
Nonhealthcare worker	87 (89.7)	228 (86.7)	315 (87.5)
Total	97 (100)	263 (100)	360 (100)
Type of patient's specimen			
Wound swab	25 (25.8)	99 (37.6)	124 (34.4)
Blood culture	22 (22.7)	41 (15.6)	63 (17.5)
Urine	24 (24.7)	30 (11.4)	54 (15.0)
Throat swab	1 (1.0)	17 (6.5)	18 (5.0)
Aspirate	4 (4.1)	24 (9.1)	28 (7.8)
Eye swab	9 (9.3)	27 (10.3)	36 (10.0)
Ear swab	3 (3.1)	9 (3.4)	12 (3.3)
Endocervical swab	9 (9.3)	14 (5.3)	23 (6.4)
Sputum	0 (0.0)	2 (0.8)	2 (0.6)
Total	97 (100)	263 (100)	360 (100)
Point-of-care access/service units			
A. Inpatients			
Surgery	21 (21.7)	37 (14.1)	58 (16.1)
ICU	2 (2.0)	4 (1.5)	6 (1.7)
Internal medicine	13 (13.4)	25 (9.5)	38 (10.5)
Pediatrics	22 (22.7)	86 (32.7)	108 (30.0)
Oncology	3 (3.1)	1 (0.4)	4 (1.1)
Subtotal	61 (62.9)	153 (58.2)	214 (59.4)
B. Outpatients			
Surgery	15 (15.5)	58 (22.1)	73 (20.3)
Internal medicine	2 (2.1)	4 (1.5)	6 (1.7)
Pediatrics	2 (2.1)	9 (3.4)	11 (3.1)
Oncology	0 (0)	3 (1.1)	3 (0.8)
GOPD	17 (17.4)	36 (13.7)	53 (14.7)
Subtotal	36 (37.1)	110 (41.8)	146 (40.6)
Total (A+B)	97 (100)	263 (100)	360 (100)

Surgery units: All surgery units including trauma and gynecological unit, MRSA: Methicillin-resistant *Staphylococcus aureus*, MSSA: Methicillin-susceptible *Staphylococcus aureus*, GOPD: General outpatient department, ICU: Intensive Care Unit

All the 360 isolates were sensitive to vancomycin, 351 (97.5%) were susceptible to imipenem, 299 (83.1%) to cefazolin, 298 (82.8%) to clindamycin, and 281 (78.1%) to amoxicillin-clavulanic acid. Three hundred and thirty-one (91.9%) of the isolates were resistant to penicillin, 202 (56.1%) to tetracycline, and 163 (45.3%) to ceftriaxone [Table 2]. Ninety-seven (26.9%) of the 360 isolates were cefoxitin resistant (MRSA), while 263 (73.1%) were cefoxitin susceptible (MSSA) [Tables 1 and 2].

Table 2: Antibiotic sensitivity pattern of *Staphylococcus aureus* isolates

Antibiotics	MSSA (*n*=263), *n* (%)			MRSA (*n*=97), *n* (%)			Total (*n*=360), *n* (%)		
	Susceptibe	Intermediate	Resistant	Susceptibe	Intermediate	Resistant	Susceptibe	Intermediate	Resistant
Cefoxitin	263 (100)	-	0 (0)	0 (0)	-	97 (100)	263 (73.1)	-	97 (26.9)
Penicillin G	29 (11.0)	-	234 (89.0)	0 (0)	-	97 (100)	29 (8.1)	-	331 (91.9)
Augmentin	229 (87.1)	-	34 (12.9)	52 (53.6)	-	45 (46.4)	281 (78.1)	-	79 (21.9)
Erythromycin	176 (66.9)	26 (9.9)	61 (23.2)	31 (32.0)	8 (8.0)	58 (60.0)	208 (57.8)	33 (9.2)	119 (33.0)
Tetracycline	128 (48.7)	19 (7.2)	116 (44.1)	11 (11.0)	1 (1.0)	85 (88.0)	138 (38.3)	20 (5.6)	202 (56.1)
Gentamycin	201 (76.4)	11 (4.2)	51 (19.4)	38 (39.2)	7 (7.2)	52 (53.6)	238 (66.1)	18 (5.0)	104 (28.9)
Clindamycin	226 (85.9)	11 (4.2)	26 (9.9)	71 (73.2)	4 (7.2)	22 (22.7)	298 (82.8)	17 (4.7)	45 (12.5)
Vancomycin	263 (100)	-	0 (0)	97 (100)	-	0 (0)	360 (100)	-	0 (0)
Ciprofloxacin	192 (73.0)	36 (13.7)	35 (13.3)	31 (40.0)	5 (5.1)	61 (62.9)	223 (61.9)	41 (11.4)	96 (26.7)
Cefazolin	243 (92.4)	16 (6.1)	4 (1.5)	56 (57.7)	12 (12.4)	29 (29.9)	299 (83.1)	28 (7.8)	33 (9.1)
Cefuroxime	218 (83.0)	22 (8.4)	33 (12.6)	25 (25.8)	23 (23.7)	49 (50.5)	243 (67.5)	45 (12.5)	72 (20.0)
Ceftriaxone	130 (49.4)	62 (23.6)	71 (27.0)	4 (4.0)	1 (1.0)	92 (95.0)	135 (37.5)	62 (17.2)	163 (45.3)
Imipenem	263 (100)	-	0 (0)	88 (90.7)	-	9 (9.3)	351 (97.5)	-	9 (2.5)

MRSA: Methicillin-resistant *Staphylococcus aureus*, MSSA: Methicillin-sensitive *Staphylococcus aureus*

Table 3: Multidrug-resistant isolates among methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *Staphylococcus aureus*

Mutidrug-resistant isolates	MRSA	MSSA
MDR	66 (68.0)	79 (30.0)
NonMDR	31 (32.0)	184 (70.0)
Total	97 (100.0)	263 (100.0)

P<0.0001. MRSA: Methicillin-resistant *Staphylococcus aureus*, MSSA: Methicillin-susceptible *Staphylococcus aureus*, MDR: Multidrug resistance

Thirty-six (37.1%) of the MRSA isolates were from samples collected at the surgery units, 24 (24.7%) at the pediatrics units, and 15 (15.5%) at the internal medicine units. Sixty-one (62.9%) of the MRSA isolates were from inpatients, while 36 (37.1%) were from outpatients. Twenty-five (25.8%) of the MRSA isolates were from wound swabs, 24 (24.7%) from urine, and 22 (22.7%) from blood culture [Table 1]. All the 97 MRSA isolates were sensitive to vancomycin, 88 (90.7%) to imipenem, and 71 (73.2%) to clindamycin. All were resistant to penicillin, 92 (95.0%) to ceftriaxone, and 85 (88.0%) to tetracycline [Table 2]. Sixty-six (68.0%) of the MRSA isolates were MDR, while 34 (32.0%) were non-MDR [Table 3].

Discussions

The overall MRSA prevalence of 26.9% of *S. aureus* isolates in this study may be considered high although it falls within the range determined in a previous report of Gorwitz *et al*. which put the prevalence in Nigeria at the range of 21%–30%.[14] Similar proportions of 28.6% and 28% have been reported from studies done in Kano and Bauchi, respectively.[15,16] Some centers, however, had reported even higher rates of 34.7%, 43%, and 79% from Ilorin, Jos, and Benin, respectively.[17-19] The use of methicillin disc for MRSA detection in these studies might have been responsible for the higher prevalence recorded in them. This is because hyperproducing penicillinase strains of *S. aureus* phenotypically give false-positive result for MRSA even in the absence of *mecA* and might have been falsely characterized as MRSA using methicillin for detection of MRSA. However, when compared to studies that used polymerase chain reaction PCR for *mecA* detection in southwestern Nigeria and Ekiti in particular which recorded prevalence of 22.2% and 19.2%, respectively,[20,21] the prevalence in this study is higher, particularly as this is the first available information on this in the hospital. As in other kinds of resistance, this may be connected with inappropriate use of antibiotics in the hospital, lack of antibiotics policy and guidelines and poor infection control practices.

The finding that almost two-thirds of the MRSA isolates were from inpatients corroborates previous studies that had demonstrated the predominance of MRSA in hospital environments.[16,18,22,23] This may be due to higher antibiotic consumption among hospitalized patients as well as the undoubtable role that the hospital environment plays in aiding the spread of MRSA. The existence of MRSA in the community suggests spread from the hospital through patients, healthcare workers, and probably visitors and tends to blur the distinctive profile of hospital strains from community strains. This has negative implication in the management of infections.

Wound swabs yielded the highest proportion of MRSA, and this had been established in previous studies.[15,17,18,22,24] This was followed by urine and blood cultures in descending order. There is a breach in the skin epithelium in all wounds and is therefore more prone to infection than the intact skin. The expanding use of invasive procedures in tertiary hospital environment, including prosthetic devices, intravascular, and urinary catheterization, might have accounted for high yields from both blood culture and urine.

Although most of the MSSA isolates showed high susceptibility to amoxicillin/clavulanic acid in this study, the susceptibility to penicillin was low. Penicillin is cheap, commonly available

over-the-counter and has been misused over the years.[25] Motayo *et al.* and Fayomi *et al.* recorded similarly high rates in previous studies.[20,26] Excellent and very poor susceptibility of these isolates to amoxicillin/clavulanic acid and penicillin, respectively, implied that beta-lactamase production was the main means of resistance among the isolates. This in effect identifies amoxicillin/clavulanic acid as a possible good choice for therapy of MSSA infections.

The characteristic MDR feature of MRSA was well observed in this study with respect to penicillin, tetracycline, ceftriaxone, ciprofloxacin, erythromycin, gentamicin, and cefuroxime. Previous studies elsewhere have made similar observation.[27,28] The presence of insertion sites for plasmids and transposons in *mecA* complex of MRSA which often carry antibiotics resistance genes account for the resistance to several classes of antibiotics.

The high resistance of MRSA to ciprofloxacin, tetracycline, erythromycin, and gentamicin in this study has been confirmed by studies elsewhere[15,20,29] although studies in Kano, Ekiti, and Abeokuta have reported otherwise to ciprofloxacin and gentamycin. These drugs are commonly prescribed, available as over-the-counter antibiotics, and may have developed resistance due to selective pressure from inappropriate use.

Although MRSA displayed excellent susceptibility to imipenem, vancomycin, and clindamycin in this study, the nonutilization of MIC method to determine vancomycin susceptibility may have missed out some vancomycin intermediate *S. aureus* isolates among the 360 found susceptible using disc susceptibility testing method. Likewise, the nonperformance of D-test may have exaggerated the percentage susceptibility of the isolates to clindamycin, as some macrolide-induced clindamycin resistant strains might have been missed out. Elsewhere in Nigeria[30-32] and Michigan[33] similarly high susceptibility (88-100%) was reported for imipenem.The finding that all the MRSA isolates were susceptible to vancomycin have been reported by previous studies in Nigeria,[15,17,24,34] however, there are few reports of the emergence of vancomycin-resistant S. aureus in some centres in Nigeria.[35,36] In addition, while previous study in Ekiti has documented similarly high MRSA susceptibility (74.5%) to clindamycin,[24] reports from other studies still within the country recorded 92-94% sensitivity to the drug.[31,37] Notwithstanding the aforementioned observations with respect to vancomycin and clindamycin, the display of excellent susceptibility of these isolates to imipenem, vancomycin, and clindamycin (if inducible resistance is not found with D-test) is good for therapeutic purposes, even as further studies are suggested to clear expressed doubts with respect to the susceptibilities recorded against the latter two drugs. These three drugs are not commonly in use in the hospital and so do not contribute significantly to selective pressure. They are also not readily available across the counter. The finding of clindamycin susceptibility in this study can be exploited in the treatment of skin and soft tissue infections, pneumonia, septic arthritis, and osteomyelitis in children caused by CA-MRSA as recommended in the Infectious Disease Society of American guidelines.[38] This may be particularly useful in climes such as ours where vancomycin is not readily available.

Sixty-six (68.0%) of the MRSA isolates in this study were MDR-MRSA. This high prevalence of MDR-MRSA compares favorably with that recorded in Ido-Ekiti[24] but lower than that recorded in Benin and Zaria.[19,39] This phenotypic characteristics seriously impairs therapeutic options, enhances spread, and increases morbidity and mortality.

From the findings of this work, vancomycin which is the only antibiotic with 100% susceptibility, even with multidrug resistant strains of MRSA, remains the best therapeutic option in our setting. Imipenem and clindamycin (in the absence of inducible resistance on D-test) are the alternatives for therapy of MRSA infections considering the high susceptibility of MRSA to these agents.

Conclusion

The study has shown high prevalence of MRSA with high rates of resistance to commonly available and used antimicrobials. There is therefore needed for both routine screening of all clinical *S. aureus* isolates for methicillin resistance and trend monitoring through regular surveillance studies. All the *S. aureus* isolates (MRSA and MSSA) remain sensitive to vancomycin, while the MRSA isolates were also highly susceptible to imipenem and clindamycin, respectively. Vancomycin should be used as the first empirical choice of treatment for serious MRSA infections in this environment, and to preserve its value, its use should be limited to those cases where they are clearly needed and as determined by laboratory susceptibility testing and/or recommended by treatment guidelines. Where vancomycin is not available, imipenem or clindamycin should be empirically used as alternatives for MRSA infections in that order. Institution of infection control measures and antibiotic stewardship will help in curtailing the emergence and spread of this resistant strain.

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Conflicts of interest

There are no conflicts of interest.

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