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NASAL METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* CARRIAGE IN PRE AND POST-OPERATIVE PATIENTS IN A TERTIARY HEALTH FACILITY IN UYO, SOUTH-SOUTH, NIGERIA

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* is responsible for a greater number of hospital acquired infections which are difficult to treat in humans. Infection increases when unsuspected patients with community-acquired strains are placed in situations that require long-term intensive nursing interventions and cross-infections spreading from patient to patient do occur. This study aimed to determine the nasal Methicillin-resistant *Staph. aureus* carriage in pre and post-surgical patients and also assess its multi-drug resistant pattern. Nasal swabs were collected from the anterior nares of patients on the same day of admission into the hospital wards, and 48-96 hours after surgery. Samples were analyzed using standard microbiological methods, while antimicrobial susceptibility testing was done using the improved Kirby-Bauer disc diffusion method. *Staph. aureus* isolates resistant to Cefoxitin and Oxacillin discs, were phenotypically regarded as Methicillin-resistant. Of the 130 samples, 26(40.0%) from pre-operative patients yielded *Staph. aureus* while additional 15(23.1%) from the erstwhile non-infected patients were detected after surgery. MRSA prevalence were 9.8% and 26.8% from pre-operative and post-operative patients, respectively. Four(15.4%) of the 26 pre-operative *Staph. aureus* isolates and 11(73.3%) of the 15 post-operative isolates were identified as MRSA. All the MRSA strains exhibited high resistance to Ciprofloxacin (80.0%), Trimethoprim/Sulphamethoxazole (73.3%), Tetracycline(66.7%), Erythromycin(66.7%) and Gentamycin(66.7%). Low resistance was observed with Vancomycin(6.7%) and

Clindamycin(26.7%). All the MRSA strains exhibited multi-drug resistance in the combination of 4-8 antibiotics. The high rate of nasal MRSA colonization among pre-operative and post-operative patients signifies serious public health concern and emphasizes the need for a regular surveillance to forestall spread of multidrug resistance and nosocomial infections.

KEYWORDS: Pre-and-post surgical patients, nasal colonization, MRSA strains.

INTRODUCTION

Staphylococcus aureus is one of the most common causes of surgical site infections among surgical patients.[1] The anterior nares are the most common ecological niches and can also be found on other non-nasal sites such as, throat, perineum, skin, hairline, groin and the axilla.[2] *Staph aureus* involvement in surgical infections has attracted public health attention due to its multi-drug resistant pattern, difficulty in infection control and high dissemination rate within the hospital environment.[3] A great deal of virulence from this organism occurs through cross-infection spread from patient to patient in hospitals and other institutional settings. In contrast, healthy individuals have a small risk of contracting an invasive infection caused by the organism, but they can be carriers of the organism, thereby posing threats to susceptible individuals.[4]

The Methicillin-resistant *Staph. aureus* is any strain of *Staph. aureus* that has developed resistance to beta-lactam antibiotics which include beta-lactam stable formulations such as Methicillin, Oxacillin, Cefoxitin, Naficillin, among others.[5,6] These strains are responsible for a number of hospital-acquired infections which are difficult to combat in humans. The propensity of hospital-acquired infections increases when patients with unidentified community colonization are placed in situations where long-term devices are used, surgical wounds are frequent, or patients require intensive nursing interventions.[7] Risk factors that facilitate infection spread in the hospitals include hospital equipment, fomites, healthcare workers, patient visitors and patient themselves in cases of cross-infection.[8]

The anterior nares have been implicated in most hospital and community-associated infections as supported by the findings of study which showed that relationship exist between nasal *Staph. aureus* carriage and infection where the nasal strain and the infecting strain shared the same genotype.[9] Colonizing strains may either serve as endogenous reservoirs for clinical infection or may spread to other patients. MRSA strains are not only a problem in

hospital as distinct strains have emerged in community too, and are referred to as community-acquired MRSA (CA-MRSA). CA-MRSA strains have spread in community settings and have also entered health care facilities.[10] Health care workers who are at interface between the hospital and the community may serve as agents of cross contamination of Hospital acquired-MRSA (HA-MRSA) and CA-MRSA.[8] Hospital acquired-Methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infections were first observed during the mid-1980 and their prevalence has continued to increase.[11] The emergence of Methicillin-resistant *Staphylococcus aureus* which is often multidrug resistant renders the treatment of its related infections extremely challenging.[12] In an active surveillance programme, a patient is usually screened for the nasal carriage of the organism, regardless of whether or not the patient is currently exhibiting signs and symptoms of infection. This process helps to reduce the possibility of cross-infection and spread within the hospital setting.[13]

In locality in Southern Nigeria, there is still a dearth of epidemiological information on the role of newly admitted surgical patients from the community in the spread of Methicillin-resistant *Staphylococcus aureus.* Also, information on the rate of colonization of MRSA among surgical patients (pre and post-operative) is scarce. Therefore, this study was conducted to determine the prevalence of nasal MRSA colonization in surgical patients before and after surgery at the University of Uyo Teaching Hospital, Uyo, which also serves as one of the referral health centres in the Niger Delta region of Nigeria.

MATERIALS AND METHODS

Study Design: This was a descriptive cross sectional study involving pre and post-surgical patients seen at the University of Uyo Teaching Hospital, Uyo-Nigeria.

Study Population: Study population included patients admitted in Surgical Wards, Orthopaedic Surgical Ward, Paediatric Surgical Ward, Obstetrics and Gynaecology Ward at the University of Uyo Teaching Hospital, Uyo for surgery. The study was conducted over a period of 6 months, from April to October 2016.

Ethical consideration: Ethical approval was obtained from the Ethical Review Board of the University of Uyo Teaching Hospital, Uyo before commencement of the study. Informed consent was obtained from patients before recruiting them into the study.

Sample Collection: A total of 130 nasal swabs were collected using a sterile swab stick. The swab stick was introduced 2-3cm into the anterior nares of the subjects and rotated clock and anti-clock wise for 3-5 times. Samples were obtained from pre-operative patients on the same day of admission into the hospital ward and 48-96 hours after surgery (post-operative), when the patient must have become stable.

Isolation and identification of *Staphylococcus aureus*

The nasal samples were inoculated onto mannitol salt agar and blood agar plates and incubated at 37^0C for 18-24hours. Growth colonies exhibiting beta haemolysis on blood agar and mannitol fermenting colonies appearing yellowish on mannitol salt agar plates were further identified by standard bacteriological procedures such as colony morphology, Gram reaction, catalase test, tube coagulase test and DNase test.[14]

Antimicrobial susceptibility assay: Antimicrobial susceptibility testing using Kirby-Bauer disc diffusion method was carried out on Mueller-Hinton Agar plates. The results were interpreted according to the CLSI guidelines (2014).[15] The antimicrobial agents used include Vancomycin (VA) 30µg, Tetracycline (TE) 30µg, Gentamycin (CN) 10µg, Clindamycin (DA) 2µg, Ciprofloxacin (CIP) 5µg, Erythromycin (E) 5µg and Trimethoprim/ Sulphamethoxazole (SXT) 1.25µg/23.75µg (Oxoid, UK). *Staphylococcus aureus* ATCC 25923 was used as reference strain for quality control.

Methicillin-resistance detection using Oxacillin and Cefoxitin discs

Overnight cultured colonies of *Staph. aureus* were transferred into peptone water and incubated for three hours. The broth growth was diluted to a 0.5 McFarland turbidity standard equivalent and then inoculated onto a Mueller Hinton agar plate using a sterile swab stick.[11] Oxacillin (1µg) and Cefoxitin (30µg) discs were placed apart on the plate. The plate was incubated at 37^0C for 18 hours and inhibition zone diameter measured using a micrometer. An inhibition zone of <11mm for Oxacillin and <22mm for Cefoxitin was reported as Methicillin resistant.[15] Methicillin-resistant isolates that exhibited resistance to three or more antimicrobial classes were regarded as multi-drug resistant strains.

Data Analysis: Descriptive statistics for demographic variables and frequency of *Staph. aureus* and MRSA occurrence in the patients were presented in frequency tables in percentages and analyzed using SPSS version 17.

RESULTS

The distribution of *Staphylococcus aureus* and MRSA among pre- and post-operative patients according to their ward is shown on Table 1 below. Of the 41 *Staph. aureus* isolated, 26(63.3%) were from pre-operative patients, while 15(36.6%) were from post-operative patients. Pre-operative patients at the Gynaecology ward had the highest *Staph. aureus* isolates, 6(100%) while Pediatric ward had the least *Staph. aureus* isolates, 1(33.3%). Post-operative patients in the Pediatric ward had the highest *Staph. aureus* isolates, 2(66.7%) while those in the Gynaecology ward had no *Staph. aureus* isolate.

A total of 4(15.4%) of the 41 *Staph. aureus* isolates were MRSA strains isolated from preoperative patients while 11(26.8%) were from post-operative patients. Of the 15 *Staph. aureus* isolates from post-operative patients, 11 (73.3%) were MRSA strains occurring mostly in male Surgical, Orthopaedics and Caesarian section wards.

Table 1: Distribution of *Staphylococcus aureus* and MRSA among Pre- and Post-Operative Patients according to their Wards

Ward	No. of *Staph aureus*	Pre-op *Staph. aureus*(%)	Post-op *Staph. aureus*(%)	Pre-op MRSA(%)	Post-op MRSA(%)
Male surgical ward	5	3(60)	2(40.0)	0	2(100.0)
Female surgical ward	9	5(55.6)	4(44.4)	1(20.0)	1(25.0)
Gynaecology ward	6	6(100)	0	1(16.7)	0
Orthopaedic male ward	6	3(50.0)	3(50)	1(33.3)	3(100.0)
Orthopaedic female ward	2	1(50.0)	1(50)	0	1(100.0)
Pediatric ward	3	1(33.3)	2(66.7)	0	1(50.0)
Caesarean section ward	10	7(70.0)	3(30.0)	1(14.3)	3(100.0)
Total	41	26(63.4)	15(36.6)	4(9.8)	11(26.8)

The antimicrobial resistance profile of the MRSA isolates from pre and post-operative patients is represented in Table 2. The highest resistance was exhibited by the MRSA strains to Ciprofloxacin (80.0%), while the least was Vancomycin (6.7%). All the isolates obtained from the pre-operative patients were susceptible to Vancomycin but highly resistant to Tetracycline (100%), Ciprofloxacin (75%), Gentamycin (75%) and Trimethoprim/ Sulphamethoxazole (75%). Only 1(9.1%) of the MRSA strains from the post-operative samples that was resistant to Vancomycin but most were highly resistant to Ciprofloxacin (81.8%), Trimethoprim/ Sulphamethoxazole (72.7%), Erythromycin (72.7%) and Gentamycin (63.6%).

Table 2: Antimicrobial resistance profile of the MRSA isolates from pre and Post-operative patients

Antimicrobial Agents (µg/ml)	Symbol	Inhibition Zone diameter(mm)	Overall MRSA N=15(%)	Pre-Op MRSA N=4(%)	Post-Op MRSA N=11(%)
Gentamycin(10)	CN	≤12	10(66.7)	3(75.0)	7(63.6)
Clindamycin(2)	DA	≤14	4(26.7)	1(25.0)	3(27.3)
Erythromycin(15)	E	≤13	10(66.7)	2(50.0)	8(72.7)
Tetracycline(30)	TE	≤14	10(66.7)	4(100.0)	6(54.5)
Ciprofloxacin(5)	CIP	≤15	12(80.0)	3(75.0)	9(81.8)
Trimethoprim/ Sulphamethoxazole (1.25/23.75)	SXT	≤10	11(73.3)	3(75.0)	8(72.7)
Vancomycin(30)	VA	≤15	1(6.7)	0	1(9.1)
Oxacillin(1)	OX	≤11	15(100.0)	4(100.0)	11(100.0)
Cefoxitin (30)	FOX	≤21	15(100.0)	4(100.0)	11(100.0)

Table 3 shows the multidrug resistant (MDR) MRSA strains among patients in the various hospital wards. An MRSA isolate from the pre-operative patient in the Gynaecology ward exhibited the highest MDR with 8 drug combinations (Vancomycin, Gentamycin, Trimethoprim/ Sulphamethoxazole, Erythromycin, Oxacillin, Clindamycin, Trimethoprim/Sulphamethoxazole and Cefoxitin). While MRSA isolate in the Female Surgical and Orthopaedic male wards exhibited the least multidrug resistant pattern, with 4 drug combinations. MRSA strains from 2 pairs of patients from the Caesarean Section Ward had similar drug (n=6) combinations (Gentamycin, Ciprofloxacin, Trimethoprim/ Sulphamethoxazole, Erythromycin, Oxacillin and Cefoxitin). MRSA strains from patients in the Male Surgical (MSW) and Orthopaedic Male Wards (ORMW) had similar drug (n=5) combinations (Gentamycin, Ciprofloxacin, Tetracycline, Oxacillin and Cefoxitin). Strains from two patients at the Orthopaedic Male Ward (ORMW) shared similar multidrug resistant (n=7) combinations (Erythromycin, Clindamycin, Tetracycline, Ciprofloxacin, Trimethoprim/Sulphamethoxazole, Oxacillin and Cefoxitin). Generally, MRSA strains from post-operative patients had more resistant drug combinations that the pre-operative patients.

Table 3: Multidrug Resistance MRSA Strains (N=18)

Hospital Wards	MRSA Strain	Surgical Status	Antimicrobial Resistance Profile	No. of Combinations
Female Surgical Ward	FSW1	Pre-op	CN, CIP, OX, FOX	4
Orthopaedic Male Ward	ORMW2	Post-op	E, SXT, OX, FOX	4
Orthopaedic Male Ward	ORMW1	Post-op	CN, CIP, TE, OX, FOX	5
Male Surgical Ward	MSW1	Post-op	CN, CIP, TE, OX, FOX	5
Pediatric Ward	PDW1	Post-op	DA,TE, SXT, OX, FOX	5
Orthopaedic Female Ward	ORFW1	Post-op	E, TE, CIP, OX, FOX	5
Male Surgical Ward	MSW2	Post-op	CN, E, CIP, SXT, OX FOX	6
Caesarean Section Ward	CSW4	Pre-op	CN, E, CIP, SXT, OX, FOX	6
Caesarean Section Ward	CSW3	Post-op	CN, E, CIP, SXT, OX, FOX	6
Caesarean Section Ward	CSW1	Post-op	CN, CIP, SXT, TE, OX, FOX	6
Caesarean Section Ward	CSW2	Post-op	CN, E, CIP, SXT, TE, OX,FOX	7
Female Surgical Ward	FSW2	Post-op	CN, E, CIP, SXT, TE, OX, FOX	7
Orthopaedic Male Ward	ORMW3	Pre-op	E, DA, TE, CIP, SXT, OX, FOX	7
Orthopaedic Male Ward	ORMW4	Post-op	E, DA, TE, CIP, SXT, OX, FOX	7
Gynaecology Ward	GW1	Pre-op	VA, E , CN, DA, TE, SXT, OX, FOX	8

DISCUSSION

The increasing prevalence of hospital acquired and community associated MRSA and their current antimicrobial-prescribing trends make MRSA a concern for surgeons in various hospitals.[16,17] There has been no general consensus concerning the optimal pre-operative decolonization and prophylaxis of patients who have been colonized by MRSA.[18] Surgical site infections among surgical patients are as a result of exposure to hospital beddings and hospital equipment which can serve as fomites in transmitting infections. Healthcare workers and patient visitors/relatives can also serve as potential source or route of infection especially in immune compromised patients, and patients themselves can be sources of infections through cross infection.[19]

In this study, the prevalence of *Staph. aureus* among the pre-operative patients was high (40.0%) compared to 25.2% obtained from pre-operative patients in a study in the United States by Kapoor *et al.*[20] The overall MRSA prevalence rate among the pre-operative patients in this study was also high (15.4%) compared to 6.3% and 4.2% reported by Walrath *et al.* [21] and Kapoor *et al.* [20], respectively. The high prevalence of *Staph aureus* and MRSA strains among pre-operative patients in this study could be as a result of crowded settlements with household members of MRSA-colonized persons, a unique characteristic of most cities in developing countries, and a risk factor in community acquired-MRSA.[22] In addition, indescriminate drug use, abuse, availability and continuous consumption of antibiotics in this locality without prescriptions could lead to the increased colonization rate of *Staph aureus* and MRSA strains in the community. The pre-operative MRSA obtained from surgical patients in this study may have been community acquired. It has been reported that increasing emergence of Community acquired-Methicillin resistant *Staph*ylococcus *aureus* (CA-MRSA) from nasal carriage can further increase the chances of infection in patients before they arrive the hospital for surgery.[23,24] In Europe and United States, routine nasal screening of patients before, during and after discharge from the hospital has formed part of routine infection control and intervention measures of Methicillin-resistant *Staphylococcus aureus* infection.[25]

The prevalence of *Staph. aureus* among the post-operative patients in this study was 23.1%, lower than 55.0% obtained from a study in Sudan among in-patients with wound infections.[26] The prevalence of MRSA among the post-operative patients with *Staph. aureus* infection in this study was very high (73.3%) compared to 43.0% obtained from a study in a Welsh hospital [27], and 23.9% from a study in the United States.[28] A much lower prevalence rate of 3.2% has been reported among post-surgical patients in a tertiary hospital in Nepal.[29] The high prevalence of MRSA obtained in this study could be attributed to inadequate infection control measures in the hospital. The infection may have been acquired from either hospital facilities, cross infection from infected to non-infected patients in the same wards, healthcare workers or patient relatives.[8] This can be attested by the pattern of antimicrobial resistance and Methicillin-resistant *Staphylococcus aureus* isolates obtained in this study, where similar resistant patterns among isolates from patients in the same wards and hospital were observed.

Studies have shown that relationships exist between Methicillin-resistance and cross-resistance with other antibiotics.[30,31] In sub-Saharan African countries, high resistance to

commonly prescribed and administered agents is a common norm, because these agents can easily be purchased over the counter, administered for variety of clinical conditions and taken by individuals without physician's prescription while some are substandard antibiotics.[32] Worthy of note, is the high resistance pattern to Ciprofloxacin (81.8%) observed in this study. This antimicrobial agent has been abused by individuals in our community, because of the speculated synergy with antimalarial drugs when taken together to combat malaria in *Plasmodium* infections, an endemic disease in this part of the world.[33] This perceived action may possibly account for the high Ciprofloxacin resistance observed among patients in this study. However, low resistance was recorded with Vancomycin (9.1%) and relatively with Clindamycin (27.3%). This is almost similar to the results obtained in a study by Adelowo *et al.* in Northern Nigeria [34] where 20% resistance to Vancomycin and Clindamycin were recorded. As observed in this study, all the MRSA isolates were resistant to more than three classes of antimicrobial agents signifying multi-drug resistance.

CONCLUSION

Findings in this study have shown that MRSA prevalence of 9.8% and 26.8% were recorded among pre-operative and post-operative patients, respectively. A very high proportion of *Staphylococcus aureus* isolates from the post-operative patients were MRSA strains (73.3%) occurring mostly in male Surgical, Orthopaedics and Caesarian section wards while preoperative patients accounted for 26.7%. Strains from the preoperative patients were likely to be CA-MRSA while those of post-operative patients were HA-MRSA. The high rate of nasal MRSA colonization in both pre and post-operative patients in this study is of serious public health concern. This emphasizes the need for active and regular surveillance of community and hospital-acquired infections including monitoring of antimicrobial susceptibility pattern of Methicillin-resistant *Staphylococcus aureus* to limit the introduction and transmission of MRSA in healthcare environments. Nasal screening should be carried out on patients before admission and before discharging them to avoid further spread of infection.

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