REVIEW ARTICLE

Phenotyphic Identification and Distribution of Methicillin Resistant *Staphylococcus aureus* from Clinical Samples in Some Selected Hospital Laboratories in Sokoto, Sokoto State, Nigeria.

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ABSTRACT

Methicillin- resistant *Staphylococcus aureus* (MRSA) is one of the most successful modern pathogens, and is transmitted in both health- care and community settings as a leading cause of bacteraemia, endocarditis, skin and soft tissue infections. This study was undertaken to identify and determine the distribution of MRSA from clinical samples in Sokoto. A total of 95 non repetitive *S. aureus* isolates were collected and screened for confirmation using standard microbiological techniques. Antibiotic sensitivity testing was carried out by disc diffusion using Cefoxitin. Of the 95 isolates, 42(44.2%) were methicillin resistant. The most potent antibiotic was quinupristin/dalfopristin with 83.3% followed by rifampicin with 81.0%. The least activity was shown to be in ciprofloxacin with 78.6% followed by tetracycline with 64.3%. Based on distribution of the MRSA, the highest prevalence of MRSA seen was by study centers Specialist Hospital (57.1%), females (48.9%), by age 21-30 years (56.5%), by samples pus, nasal and urethral swabs (100%) and patient admission status, inpatients (51.9%). With MRSA being a nosocomial pathogen, our findings highlight the need to pursue infection control measures in the hospitals while implementing antibiotic stewardship programs to reduce antibiotics misuse.

INTRODUCTION

Staphylococcus aureus is a bacterial pathogen that has been linked to a variety of infections in humans, ranging from minor skin infections to serious systemic disorders including pneumonia and endocarditis. MRSA has been recognized as a pathogen of global concern since the first report of methicillin-resistant *S. aureus* (MRSA) in the 1960s. MRSA was first isolated in the early 1960s (Turner *et al.*, 2019), and for the majority of the past five decades, MRSA infections have been predominantly connected with hospital environments and referred to as hospital-acquired MRSA (HA-MRSA).Community-acquired MRSA (CA-MRSA) infections began to develop in apparently healthy patients with no recognized risk factors for hospital-acquired infections in the early 1990s (Stefani *et al.*, 2012). This bacteria has quickly established itself as the bacterium of the twentieth century, causing substantial infections in both health care settings and the general public (Li *et al.*, 2019).Institutional environments, patient groups, and close physical contact are the three subcategories of risk factors for MRSA infection. Hospitalization in healthcare facilities and long-term care facilities such as nursing homes and institutions for the elderly are both conducive to transmission. Patients with a history of antibiotic use or abuse, extended hospitalization, indwelling catheters and other indwelling medical devices, dialysis, and being treated with enteral nutrition are all at a greater risk of colonisation and infection. Close physical contact transmission is most common among athletes, military personnel, inmates and residents of penal facilities, homosexuals, and infants in day care centres (Sassmannshausen *et al.*, 2016).

Several researches were carried out and some are still going on Multidrug-Resistant Methicillin-Resistant *Staphylococcus aureus* (MRSA) globally as the circulating gene is on rise in different hospital settings (Al-Trad *et al.*, 2023; Dierikx *et al.*, 2023; Nwabuife *et al.*, 2023; Rox

et al., 2023; Sarwar *et al.*, 2023). Ajayi *et al.*, (2023) from Ekiti State Nigeria who worked on the distribution of *lasI* and *rhlR* virulent gene among *Staphylococcus aureus* isolates in clinical samples of Ekiti State University Teaching Hospital, in Ado Ekiti-Nigeria, outlined that infection with *Staphylococcus aureus* has been considered a major problem in hospitals and the clinical importance of *S. aureus* is attributed to notable virulence factors and genetic diversity. Therefore identification of the distribution of MRSA within Sokoto metropolis will give baseline information on the phenotyphic and distribution of the circulating methicillin resistant genes of *S. aureus* within this region. This study was aimed to identify and determine the distribution of MRSA from some clinical samples in Sokoto metropolis, Sokoto State, Nigeria.

MATERIALS AND METHODS

Bacterial isolates

Isolates used in this study were obtained from UsmanuDanfodiyo University Teaching Hospital, Specialist Hospital and Maryam Abacha Women and Children Hospital all in Sokoto, North Western Nigeria. All isolates were identified by their colony morphology, Gram staining, catalase test, coagulase test using both slide and tube methods and deoxyribonuclease test (Garcia and Isenberg, 2010; UKSMI, 2014). All isolates were examined for methicillin resistance by: Cefoxitin disk (30µg) diffusion test (CDD).Inoculum for Antibiotic Susceptibility Testing was prepared by the direct colony suspension method as the method recommended by the Clinical Laboratory Standards Institute for testing *Staphylococci* for potential methicillin resistance (CLSI, 2012) and all MRSA isolates were subjected to antibiotic susceptibility testing to different antibiotics

Cefoxitin Disk Diffusion Test

Cefoxitin disk 30µg (Oxoid, UK) was used on Mueller Hinton agar (Oxoid, UK). The inoculumturbidity was adjusted to 0.5 McFarland and the agar plates inoculated, inverted and incubated at 35°C for 24h. After the prescribed period of incubation the zone of inhibition was measured using a metre rule (against transmitted light) and the results (zones ≤21mm indicate resistance) interpreted using the CLSI 2014 guidelines.

Inoculum for Antibiotic Susceptibility Testing was prepared by the direct colony suspension method as the method recommended by the Clinical Laboratory Standards Institute for testing *Staphylococci* for potential methicillin resistance (CLSI, 2012).

Antibiotic Susceptibility Testing

Standard inoculum was prepared by making a direct saline suspension of isolated colonies selected from an 18-hour agar plate incubated at 37°C. The suspension was adjusted to achieve a turbidity equivalent to a 0.5 McFarland (1-2 x 10^8 CFU/ml). It was then observed, using adequate light to visually compare the inoculum tube and the 0.5 McFarland standards against a card with a white background and contrasting black lines. Antibiogram was done in accordance to Clinical and Laboratory Standard Institute (CLSI). Commercially prepared antibiotic discs were placed on the inoculated Mueller Hinton agar 25mm away from each other. The plate was then incubated at 35°C for 18-24 hours after which the zones were read using the interpretation chart provide by clinical laboratory standard institute (CLSI, 2020).

RESULTS

During the period of this study a total of 95 isolates were collected from the two hospitals medical microbiology laboratories.

The results of the prevalence of MRSA among the isolates collected from the two hospitals are presented in Table 1. Out of the 35 confirmed *S. aureus* isolates from Specialists Hospital 20 (57.1) were confirmed as MRSA using Cefoxitin disc diffusion of the isolates confirmed as *S.aureus* from UDUTH only 22(36.7%) were identified as strains of MRSA.

The results of the antibiogram pattern of the MRSA isolates to the different antibiotics are presented in Table 2. The most potent antibiotic was quinupristin/dalfopristin with 83.3% of all the tested isolates being sensitive and an inhibition zone of ≥19mm, it is followed by Rifampicin with 81.0% inhibition zone of ≥20mm. The least activity was shown to be in ciprofloxacin for which 78.6% of the isolates demonstrated phenotypic resistance with an inhibition zone of ≤15mm, followed by erythromycin inhibition zone of ≤13mm.

The results of the distribution of the Methicillin resistant isolates based on the age groups of the study subjects are presented in Table 3. The highest prevalence was observed in the age group of 21-30 years where 13(56.5%) of the 23 isolates were found to be MRSA the age group with the least prevalence is 41-50 years age group only 1(14.3%) out of 7 isolates being MRSA. Also the results of the distribution of the MRSA isolates between male and female gender are presented in Table 4. Of the 48 *Staphylococcus aureus* isolated from male subjects, only 19(39.6%) were MRSA, however, the prevalence of MRSA in the female gender is 48.9% (23/47).

The results of the prevalence of the methicillin-resistant isolates by patient admission status are presented in Table 5. The highest prevalence of MRSA was seen in in-patients with 28 (51.9%) while the out-patients recorded a prevalence of 14 (34.1%) out of the 42 isolates. Also the results of the prevalence of the resistant isolates in

the different types of the isolates collected are presented in Table 6. The prevalence of the resistant isolates in the different types of the isolates collected had 100% prevalence seen in Nasal swab, Urethral swab, and Pus followed by Urine where the prevalence is 53.8%.

Catheter tip yielded a prevalence of 20% while no resistant isolate was recovered from Ear swab.

Table 1: Prevalence of MRSA among the *S. aureus* isolates collected from Specialist Hospital Sokoto and Usmanu Danfodiyo University Teaching Hospital Sokoto (UDUTH)

Hospital	MSSA	MRSA	TOTAL
Specialist Hospital	15(42.9)	20(57.1)	35
UDUTH	38(63.3)	22(36.7)	60
Total	53(55.8)	42(44.2)	95(100)

P-value = 0.053, χ^2 = 3.758

Table 2: Susceptibility pattern of the Methicillin resistant *Staphylococcus aureus* isolates to different antibiotics

Antibiotic	Disc content (µg)	Antibiogram of the isolates (mean zone of inhibition)		
		Sensitive	Intermediate	Resistant
Rifampicin	5	34(81.0)	-	8(19.0)
Ciprofloxacin	5	7(16.7)	2(4.8)	33(78.6)
Clindamycin	2	30(71.4)	5(11.9)	7(16.7)
Teicoplanin	2	27(64.3)	6(14.3)	9(21.4)
Tetracycline	30	11(26.2)	5(11.9)	26(61.9)
QD	15	35(83.3)	1(2.4)	6(14.3)
Erythromycin	15	11(26.2)	4(9.5)	27(64.3)
Gentamycin	30	10(23.8)	6(14.3)	26(61.9)

Plate 1: Antibiogram patterns of the *S. aureus* isolates to different antibiotics on Mueller Hinton agar

Table 3: Distribution and prevalence of MRSA based on age groups from Specialist Hospital Sokoto and Usmanu Danfodiyo University Teaching Hospital Sokoto (UDUTH)

Age Groups	MSSA	MRSA	Total
1 – 10	9 (52.9)	8(47.1)	17
11 – 20	13(59.1)	9(40.9)	22
21 – 30	10(43.5)	13(56.5)	23
31 – 40	8(57.1)	6(42.9)	14
41 – 50	6(85.7)	1(14.3)	7
>50	7(58.3)	5(41.7)	12
Total	53(55.8)	42(44.2)	95(100)

P-value = 0.528, χ^2 = 4.150

Table 4: Distribution of MRSA according to the gender of study subjects from Specialist Hospital Sokoto and Usmanu Danfodiyo University Teaching Hospital Sokoto (UDUTH)

Gender	MSSA	MRSA	Total
Male	29(60.4)	19(39.6)	48
Female	24(51.1)	23(48.9)	47
Total	53(55.8)	42(44.2)	95(100)

P-value = 0.359, χ^2 = 0.842

Table 5: Distribution of MRSA between hospital in-patients and out-patients from Specialist Hospital Sokoto and Usmanu Danfodiyo University Teaching Hospital Sokoto (UDUTH)

Category	MSSA	MRSA	TOTAL
In-Patients	26(48.1)	28(51.9)	54
Out-Patients	27(65.9)	14(34.1)	41
Total	53(55.8)	42(44.2)	95

P-value = 0.085, χ^2 = 2.962

Table 6: Prevalence of MRSA according to the specimen type used in the study from Specialist Hospital Sokoto and Usmanu Danfodiyo University Teaching Hospital Sokoto (UDUTH)

Specimen	MSSA	MRSA	TOTAL
Urine	18(46.2)	21(53.8)	39
Wound Swab	9(53.3)	7(46.7)	16
HVS	11(57.9)	8(42.1)	19
ECS	3(75.0)	1(25.0)	4
Catheter Tip	4(80.0)	1(20.0)	5
Wound Aspirate	3(75.0)	1(25.0)	4
Ear Swab	5(100.0)	0(0.0)	5
Nasal Swab	0(0.0)	1(100.0)	1
Urethral Swab	0(0.0)	1(100.0)	1
Pus	0(0.0)	1(100.0)	1
Total	53(55.8)	42(44.2)	95(100)

P-value = 0.289, χ^2 = 13.073

DISCUSSION

As a global health concern, the importance of *S. aureus* as a persistent nosocomial and community acquired pathogen cannot be over estimated. Oxacillin or methicillin-resistant (MRSA) isolates are among the major pathogens causing infections in the world, leading to the emergence of and disseminating increasingly virulent and multiresistant strains. This study showed that 42(44.2%) of the isolates obtained were methicillin resistant by the cefoxitin disc diffusion method. This finding is higher than findings of Adetayo *et al.,* (2014), Abdullahi and Iregbu (2018), Angela *et al.,* (2015), who reported a prevalence of 30.4% in Ibadan, 26.9% in Abuja and 31.4% in Brazil respectively. The rate 44.2% from this study is however similar to what was reported by Adeiza *et al.,* (2020) in Sokoto with 46.9%, Ariom *et al.,* (2019) in Abakaliki with 43.4% and Onemu and Ophori (2013) in Benin City with 79%, indicating that MRSA is ever increasing. This is further corroborated by findings of Abubakar and Sulaiman (2018), who in a systematic review of MRSA infections in Nigeria

reported an increase from 18.3% (2009) to 42.3% (2013). It is clear that MRSA has become a global nosocomial pathogen with attendant therapeutic problems and warrant urgent infection awareness, considering the common practice of unregulated sale of antimicrobial agents and movement of people which may result in rapid dissemination.

The prevalence rate of MRSA by study centre differs, Specialists Hospital has the highest MRSA prevalence of 57.1% (20 of 35) while UDUTH has a prevalence of 36.7% (22 of 60). The variations in the prevalence rates between the centres has been shown to be statistically significant (P>0.05). UDUTH has a relatively lower prevalence rate when compared with the other centre apparently because it has better infection control measures and has a clean hospital environment than Specialists Hospital This is an indication that, its prevalence varies from one region to another and even among hospitals in the same city. The antibiogram pattern of the MRSA isolates showed that 39 (92.9%) were multi drug resistant and only 3(7.1%) were to 2 or

less antibiotics. The pattern showed a 78.6%, 64.3% and 61.9% resistance to ciprofloxacin, erythromycin and tetracycline respectively, while the most potent of the antibiotics tested were quinopristin/dalfostrin with 83.3%, rifampin with 81.0% and clindamycin with 71.4%. However, Mofolorunsho et al. (2015) in Anyingba reported 54% resistance to erythromycin and augmentine, and sensitivity to gentamicin, ofloxacin and ciprofloxacin as 100%, 81.8% and 72.7% respectively, while Ariom et al., (2019) in Abakaliki reported that the clinical isolates were completely resistant (100 %) to ceftazidime, tetracycline and penicillin and that gentamicin and ciprofloxacin were the most effective antibiotics. Another research conducted by Asiya et al., (2018) in Sokoto showed showed a 100% resistance to ceftazidime, cloxacillin and augmentine, while the most potent of the antibiotics tested were nitrofurantoin, quinopristin/dalfostrin and chlorampenicol with 96.7%, 95.7% and 86% respectively. Bunza et al., (2019) also in Sokoto reported that 40% of the S. aureus isolates were susceptible to clindamycin, 64% to ciprofloxacin, 57% to erythromycin, 71% to gentamicin, 34% to Cefoxitin, 46% to quinopristin/dalfostrin, 58% to tetracycline and sulphamethaxazole. The pattern of resistance shown by S. aureus to many groups of antimicrobial agents in this research represents a serious concern in therapeutic option available to the clinician in managing such infections and further confirms various literatures that S. aureus is a multidrug resistant bacterium. However, the potency of quinopristin/dalfostrin, rifampin and clindamycin seen in this study is an indication that physicians can still prescribe this antibiotic based on empirical therapy when needed, especially for urgent infections.

The distribution of MRSA within different age groups was demonstrated in this study, the highest prevalence was found in 21-30 years age group with 56.5% and the least in 41-50 years with 14.3%. This is in agreement with findings of Adelowo et al., (2014) in Nigeria, Kalyani et al., (2012) in India who reported a higher prevalence in 20-29 years, Abdullahi and Iregbu (2018) in Abuja with the highest rate of 68% in 25 years and above and Adeiza et al., (2020) in Sokoto with the highest rate of 36.8% between the ages of 21-25 and the least rate of 2.6% in 41 years and above. However, there was no statistical significant difference in MRSA carriage by age (P>0.005).

The study also demonstrates a relatively higher rate of MRSA in females (48.9%) than males (39.6%). This finding corroborates many other studies conducted across the country (Onemu and Ophori, 2013, Adelowo et al., 2014, Asiya et al., 2018, Abdullahi and Iregbu 2018 and Adeiza et al,. 2020). However, Kalyani et al., (2012) reported a higher prevalence in males in India. It's natural for women to visit the hospital more than men do, for the obvious reasons associated with pregnancy (for antenatal care) and complications that may arise from childbirth. However statistical analysis has shown that no significant difference exist (P>0.05), indicating that sex is not a factor in colonization with MRSA.

Taking a cursory look at the rates of infection between the two patient groups in this study (the in-patients and out-patients) findings in this study show that in-patients are more prone to colonization by MRSA because they are more at risk than patients who only visit the hospital once in a while and in most cases for only a few hours. In-patients (51.9%) are more infected than out-patients (34.1%) even though the difference is not statistically significant (P>0.05). Most studies involving these two groups have reported similar findings within (Abdullahi and Iregbu, 2018 with in-patients accounting for 62.9%: Asiya et al., 2018 with in-patients recording 62.5%: Adeiza et al., 2020 with in-patients accounting for 21%) and outside the country (Maina et al., 2013 in Kenya with 40.6% in in-patients: Prosperi et al., 2013 in Florida with 42.4% in in-patients: Tsige et al., 2020 in Ethiopia with 30.8% in in-patients).

When the prevalence was analysed based on the type of specimen collected using the Chi-square test, it was found that there was no statistical significant difference in samples more likely to yield MRSA (P>0.05). Samples with highest prevalence include urethral swab, nasal swab and pus with 100% prevalence. When examined closely the highest prevalence seen in relation to these specimen types, can be associated with the relatively lower sample size of these specimens. Thus, urine (53.8%), wound swab (46.7%) and HVS (42.1%) are the most infected of the specimens collected, as demonstrated in other studies in Nigeria (Nsofor et al., 2016, Abdullahi and Iregbu 2018, Asiya et al., 2018, Ariom et al., 2019).

CONCLUSION

It can be concluded that Specialists Hospital Sokoto has the highest MRSA prevalence rate of 57.1% (20 of 35) while UDUTH has a prevalence of 36.7% (22 of 60) and this revealed that methicillin resistant S. aureus infections are on the increase in Sokoto metropolis and becoming increasingly more resistant to other antibiotics. The study also demonstrates a relatively higher rate of MRSA in females (48.9%) than males (39.6%) and the highest prevalence was found in 21-30 years age group with 56.5% and the least in 41-50 years with 14.3%. It has also demonstrated that patients on admission are more at risk necessitating the need for infection control programmes in the hospitals.

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