NASAL CARRIAGE OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* AMONG HEALTHCARE WORKERS IN HIGH-RISK UNITS OF A TERTIARY HOSPITAL IN NORTHWEST NIGERIA

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ABSTRACT

Carriage of Methicillin resistant *Staphylococcus aureus* (MRSA) by individuals has been the means by which it perseveres in the environment. Healthcare workers get colonized due to their close contact to patients and poor adherence to infection control. The study aimed at evaluating the nasal carriage of MRSA among healthcare workers in high-risk units of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria and evaluate the antibiotic susceptibility pattern of the isolates. A descriptive cross-sectional study was conducted over a period of 10 months (between January to November). Stratified sampling was used to collect a total of 427 nasal swabs, screened for MRSA using cefoxitin disk diffusion, then confirmed by testing for the *mec*A gene product using latex agglutination test for PBP2a. From the 427 healthcare workers swabbed, 81 (19%) isolates were identified as *S. aureus* using Staphaurex®, among which 10(12.3%) screened positive for methicillin resistance using cefoxitin disk, and all were confirmed by Oxoid latex agglutination test for PBP2'to be MRSA, given an overall nasal carriage of 2.3% for MRSA from the total population studied. Nurses accounted for 6(60%) while doctors accounted for the rest (40%), with the highest proportions of MRSA recovery from oncology (50%) and orthopaedic (25%) units. There was no significant difference in carriage between the ages (P=0.702), and length of stay in the units (P=0.89). The highest percentage resistance was to penicillin (90.1%), then sulphamethoxazole-trimethoprim (28.4%), however, there was almost universal (98.8%) susceptibility to genticin and complete susceptibility to rifampicin (100%). Most 6(60%) of the MRSA isolates were multidrug resistant. The carriage from this study was low compared to what was reported from other parts of Nigeria. The pattern of resistance to other antibiotics tallies with reports from other centers in Africa. Continuous vigilance, improved infection control practices and antibiotic stewardship program is necessary to maintain this low prevalence.

Keywords: Carriage, Healthcare workers, High-risk units, MRSA.
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INTRODUCTION

Methicillin resistant *Staphylococcus aureus* (MRSA) is one of the Multidrug Resistant (MDR) organisms that have threatened global health security [1, 2]. It is a common cause of healthcare associated infections (HAI), with such infections being very difficult to treat. As such MRSA infections are associated with poor outcome, prolonged hospital stays, higher cost of treatment [3] and increased mortality because options left for therapy are few [3, 4]. *Staphylococcus aureus* (whether methicillin susceptible or resistant) are ubiquitous colonizers of the skin and mucosa of patients and healthcare workers from where they pose risk to their carriers, or can be transmitted to other susceptible patients and close contacts [5, 6]. The transmission of MRSA and the risk of MRSA infection (including MRSA bacteraemia) can only be addressed effectively if measures are taken to identify MRSA carriers as potential sources and decolonizing them to reduce the risk of transmission [7].

S. aureus demonstrates a niche preference for the anterior nares, especially in adult humans. Other sites of colonization include the skin - especially the hands, axillae and perineum - rectum, vagina, gastrointestinal tract, as well as the pharynx [8]. Studies have presented clear molecular and epidemiological evidence of MRSA transmission from healthcare workers – who are the population with the closest contact – to patients [8, 9]. Chronic nasal carriage may put certain populations of patients at increased risk for infection, such as patients with recurring furunculosis (as in diabetes), cancer patients, patients with central venous lines, burns or skin ulcers, patients with depressed immunity (infants, elderly, HIV-infected individuals) and patients who are subject to medical interventions including chronic haemodialysis or peritoneal dialysis or undergoing surgery [10].

Mean nasal carriage of *S. aureus* worldwide is about 37.2% in the general population [10], with a very wide range depending on population studied. The range is particularly wide among health-care workers (16.8%-56.1%), probably due to the quality of sampling or culture techniques [10]. Meanwhile, the mean nasal carriage of MRSA amongst healthcare workers was 4.1% from a review of 104 studies worldwide (range 0 – 59%) [8]. In Zaria, a nasal MRSA carriage of 14.9% was gotten from a study on healthy primary school pupils [11].

The extent of MRSA carriage among healthcare workers who are at the centre of the problem should be investigated because, they (colonized healthcare workers) are at risk of

developing clinical MRSA infections, and have been implicated by several reports in transmission from patient to patient [12, 13], as sources of outbreaks [14, 15], as reservoirs for re-infection and they have also been implicated in transmitting infection to family members [16]. Low staff to patient ratio which is obtainable in most hospitals in Nigeria, increases workload, and results in high staff-patient contact, as well as poor attention to infection control practices. These have been implicated in both acquisition and transmission of MRSA by healthcare workers [8]. In view of these and the problems with the development of new antibiotics for therapy, it became necessary to study the nasal MRSA carriage among this population in Zaria. We aimed to determine the nasal carriage of MRSA among health care workers in high-risk units in Ahmadu Bello University Teaching Hospital, Zaria and to evaluate the antibiotic susceptibility pattern of the *Staphylococcus aureus* isolates from this carriage site among these individuals.

MATERIALS AND METHODS

Study area

The study area was Ahmadu Bello University Teaching Hospital, Zaria, a tertiary hospital in North-western Nigeria, which is a referral centre for several contiguous States in the region. The hospital provides general and specialist care in various units.

Study design

A descriptive cross-sectional study was conducted over a period of ten (10) months (January to November). Our study population were healthcare workers in high-risk units - the intensive care unit, special care baby unit, dialysis, radio-oncology, diabetic unit, HIV unit, delivery suite, orthopaedic, burns, and all the other surgical subunits. We included doctors, nurses, technicians and ward attendants who had been working in these high-risk units for at least two (2) weeks (including temporary staff) and we excluded doctors on external postings, nurses who are out on courses, medical and nursing students. Staff who were on leave, or having upper respiratory tract infections, or who had taken beta-lactam antibiotics within the previous two (2) weeks were also excluded.

Ethical considerations

Ethical approval was given by the Ahmadu Bello University Teaching Hospital, Zaria ethical committee (ABUTH/HREC/TRG/36). A written informed consent was also sought from each subject that participated in the study. Confidentiality of participants was ensured.

Data collection

Stratified sampling technique with proportionate allocation was used to select subjects from the different categories of staff from the various units. Then a self-administered questionnaire was used to collect information on demographics, individual and professional risk factors, knowledge of MRSA and self-admitted practice of infection control. We used sterile rayon tip swabs that comes together with Amies transport medium, (Transwab® MW170 from MWE, United Kingdom) moistened with sterile physiological saline to collect nasal swab specimen by rubbing the inside of the ala and septum of each nostril and rotating evenly about 3-4 times. A single swab was used for both nostrils of one subject. The swabs were inoculated onto Mannitol Salt Agar (MSA), and *S. aureus* (yellow colonies) were further identified using Gram stain, catalase, coagulase production (using Staphaurex® latex agglutination test kit from Remel, Europe) and DNAse production. We carried out antibiotic susceptibility testing by disk diffusion method following the Kirby-Bauer technique as modified by the Clinical and Laboratory Standards Institute (CLSI) [M02-A10] [17], using Oxoid® disks. The following antibiotics were tested penicillin (10 units), cefoxitin (30µg), genticin (10µg), erythromycin (15µg), ciprofloxacin (5µg), cotrimoxazole (1.25/23.75µg), chloramphenicol (30 µg), clindamycin (2µg), vancomycin (30 µg), on two 100mm plates. *Staphylococcus aureus* ATCC 25923 and 43300 were used as quality control strains and were subjected to the same procedures as the test isolates for each batch of testing.

Using the CLSI chart (M100-S23) [18], a zone diameter of less than 21mm and greater than 22mm was considered resistant (and thus MRSA) and susceptible (MSSA) respectively for cefoxitin. Other antibiotics tested were also interpreted similarly and documented. We confirmed MRSA using Oxoid Penicillin Binding Protein latex agglutination test, Oxoid-United Kingdom (DR0900) which detects the *mecA* gene product (PBP2').

Data analysis

We cleaned and analysed data obtained using the software statistical package for social sciences (SPSS) version 20 and EPI INFO 7.2. Results were presented using tables and charts while association between variables was determined using odds-ratio. Statistical significance was taken at $P < 0.05$.

RESULTS AND DISCUSSION

Results

Of the four hundred and twenty-seven (427) subjects that participated in the study, 220 (51.5%) were females. The age group most represented was 30 – 34 years age group with 107 (25.1 %) of the participants, while the least was 55 – 59 years age group, accounting for just 5 (1.2%) participants, though the

mean age was 36.6 years with a standard deviation SD of 7.96. Doctors and nurses accounted for 182 (42.6%) and 172 (40.3%) of the participants, respectively. A little above a third of the participants 151 (35.4%) were from surgical wards being the highest, followed by labour ward with 65 (15.2%) participants, while 24 (5.6%) and 20 (4.7%) were from oncology and dialysis units respectively, in proportion to the sizes of the respective units.

From the 427 health workers swabbed, 81 (19%) *S. aureus* isolates were identified using Staphaurex®, among which 10 (12.3%) screened MRSA positive using cefoxitin disk, all of which were confirmed by Oxoid latex agglutination test for PBP2' to be *mecA* carrying MRSA, giving an overall nasal carriage of 2.3% for MRSA from the total population studied.

Specifically, 23.1% of doctors were colonized by *S. aureus* followed by nurses (18%), with ward attendants having 11% of them being colonized. Of the 10 MRSA carriers, 50% were females, MRSA carriage was found mainly among nurses 6(60%) and doctors 4(40%), while no MRSA carriage was detected among ward attendants and technicians (figure 1). Among the high-risk units and wards, the highest proportions came from oncology (50%) and orthopaedic (25%) units, while SCBU and dialysis had no carriers detected (fig 2).

Carriage of MRSA was higher among the older age group 40 – 59 (15%) but on bivariate analysis this difference was not statistically significant (P = 0.702). Those who had stayed longer (> 5 years) in the relevant units were more likely to carry MRSA than those who had stayed less, but this finding was not statistically significant (OR = 1.72, 95% CI = 0.32-5.86). Meanwhile, good practice of infection control was found to be highest among ward attendants (75%) and nurses (74.2%), though following bivariate analysis, poor practice of infection control was not significantly associated with MRSA carriage (OR = 0.79, 95% CI = 0.15-4.10).

The *S. aureus* isolates recovered from these colonized individuals were generally (90.1 %) resistant to penicillin, while on the other hand, they were almost universally (98.8%) susceptible to genticin. A little more than a quarter (28.4%) of the isolates were resistant to sulphamethoxazole – trimethoprim. Ciprofloxacin was the next most resistant (11.1%), followed closely by erythromycin (9.9%), while chloramphenicol and clindamycin each had 2.5% of the *S. aureus* isolates resistant to them (figure 3).

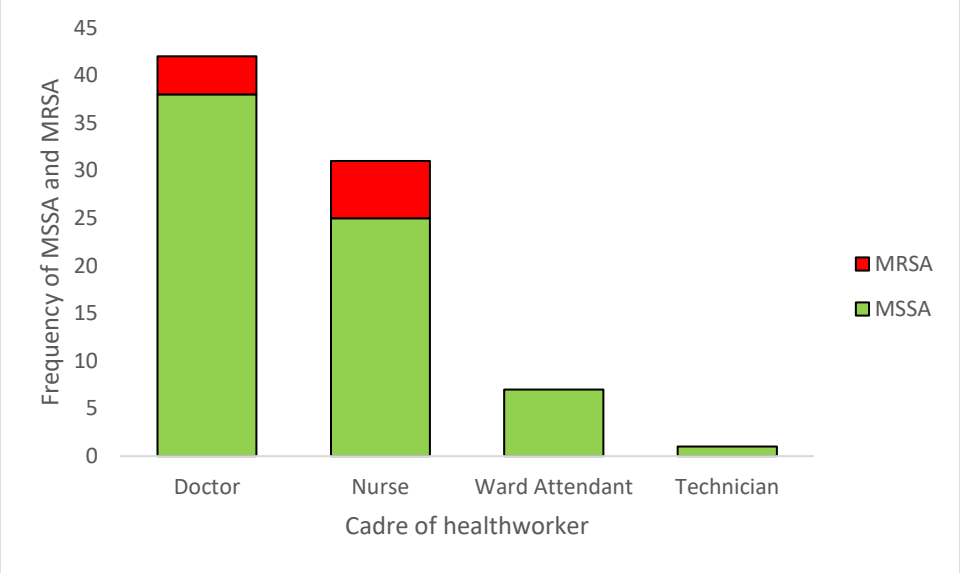

Figure 1: Nasal carriage of MSSA and MRSA by cadre of healthcare workers in high-risk units of a tertiary hospital in North-western Nigeria

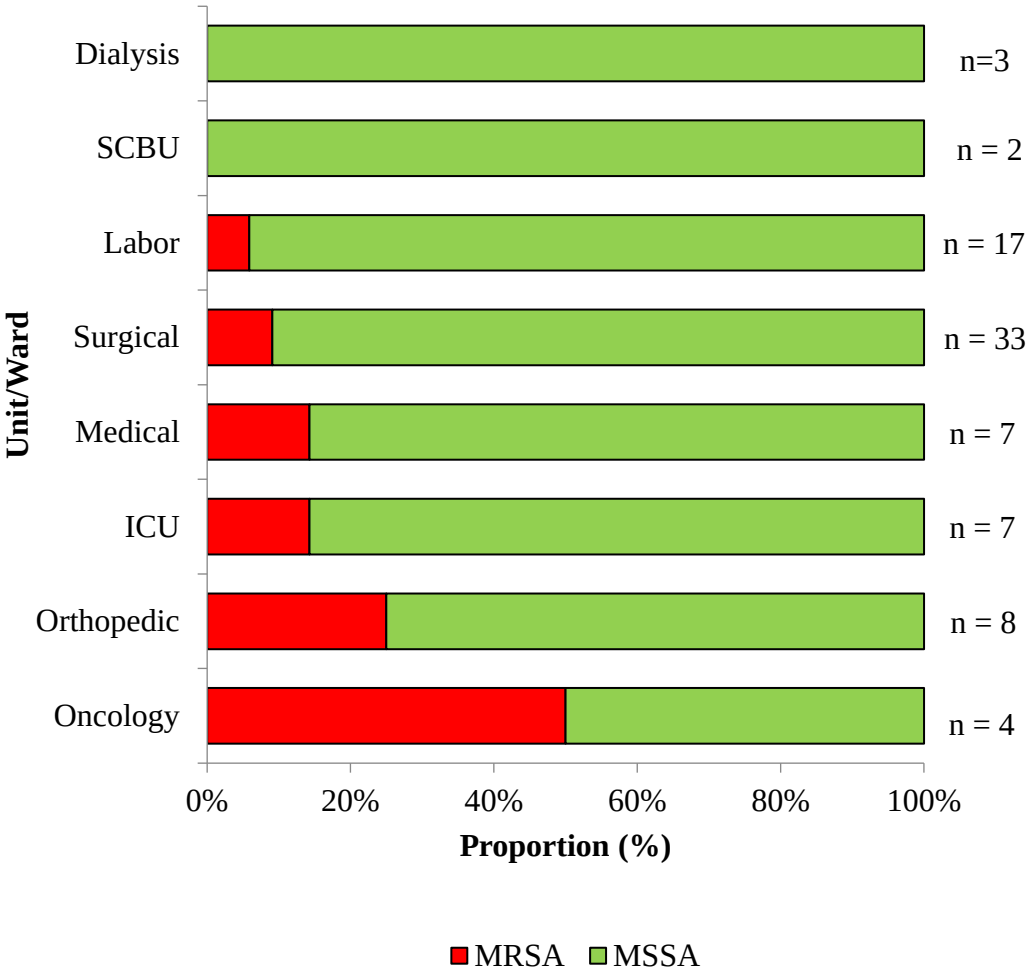

Figure 2: Proportion of *S. aureus* colonizing healthcare workers that are MRSA by high risk unit/ward in a tertiary hospital in North-western Nigeria

Table 1: Factors associated with nasal carriage of MRSA among healthcare workers in high risk units in a tertiary hospital in North western Nigeria

	MRSA (%)	MSSA (%)	Total (%)	Odds ratio (95% CI)	P - value
Age group (years)					
40 -59	3(15.0)	17(85.0)	20(100.0)	1.36 (0.32-5.85)	P = 0.702
20 - 39	7(11.5)	54(88.5)	61(100.0)		
HCW Length of stay in unit					
> 5 Years	2 (18.1)	9(81.8)	11 (100.0)	1.72 (0.31-9.43)	P = 0.889
≤ 5 Years	8 (11.4)	62(88.6)	70 (100.0)		
Practice of infection control (Reported)					
Poor	2 (10.5)	17 (89.5)	19 (100.0)	0.79 (0.15-4.10)	P = 0.570
Good	8 (12.9)	54 (87.1)	62 (100.0)		

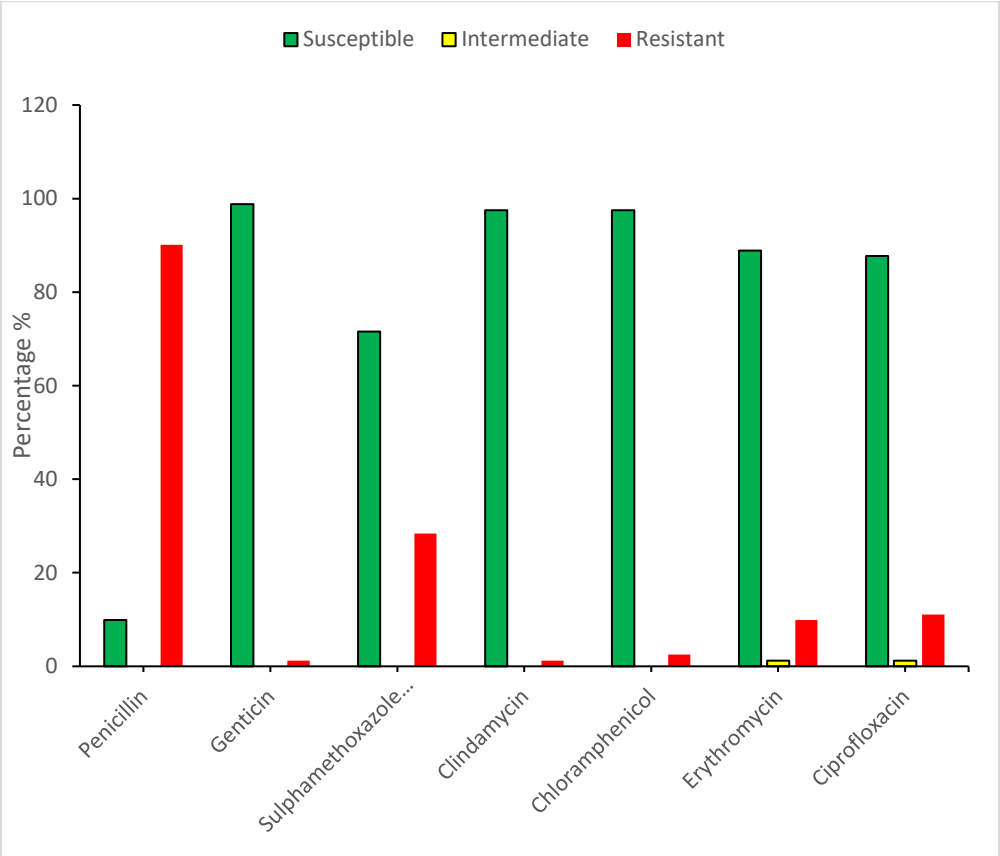

Figure 3: Antimicrobial susceptibility pattern of S. aureus isolates from colonized healthcare workers in a tertiary institution in North-western Nigeria.

DISCUSSION

A nasal carriage of MRSA of 2.3% was found among healthcare workers in this study. This prevalence is low and a possible explanation is the fact that there had been several trainings on infection prevention and control (IPC) in this hospital starting from 2009, including several hand hygiene campaigns. This eventually culminated in the introduction of the use of alcohol hand rub in 2011 which has now been made available in all wards and in certain cases at patients' bedside. This is in keeping with the findings that IPC measures help reduce carriage of and infections with MRSA [19, 20, 21].

The carriage is lower than that observed by Egwuatu *et al.* [22] working in Lagos, south western Nigeria got a prevalence of 13.6% from healthcare workers, while Akujobi *et al.* [23] obtained a nasal carriage of 30% from healthcare workers in Anambra, south eastern, Nigeria. Furthermore, Edem *et al.* [24] in Uyo, south southern Nigeria got an MRSA carriage of 40% from healthcare workers colonized by *S. aureus.*

Studies from other African countries gave 4% in São Tomé and Principe, 12.7% in Dessie, Ethiopia, 21.4% in Benghazi, Libya and 41.3% in Cameroon as reported by Conceição *et al.* [25], Shibabaw *et al* [26], Al-Abdi *et al* [27] and Gonsu *et al.* [28] respectively.

A common feature of these studies (except that by Conceição *et al* which used similar methods) is the use of traditional biochemical methods for *S. aureus* identification using tube coagulase (for which Kateete *et al.* [29] gave a low specificity of 11%) as confirmatory test for *S. aureus*. This may have led to the misclassification of coagulase negative staphylococci which is known to have a higher prevalence of methicillin resistance as *S. aureus*. In a 2014 study in Kenya, Omuse and colleagues [30] argued that the prevalence of MRSA may have being previously overstated. Using the automated Vitek-2 machine, they got an MRSA prevalence of 3.7 % against prevalence reported by previous studies in the same country of between 20% and 84.1% as cited in their work. This assertion has previously been documented by Olayinka *et al.* [31] working in Zaria, where they compared multiplex PCR using 16 primers for typing for 5 different Staphylococcal cassette chromosome *mec* (SCC*mec*) and *mec*A gene detection as well as latex agglutination test for PBP2a against traditional oxacillin disk diffusion method on isolates that have previously been identified as MRSA. None of the isolates was positive for *mec*A gene or PBP2a but demonstrated phenotypic oxacillin resistance and were rather hyperproducers of betalactamase. However, this study used Staphaurex latex agglutination test for *S. aureus* identification, after screening with mannitol salt agar and deoxyribonuclease agar plates, while cefoxitin disk

diffusion and Oxoid latex agglutination test for PBP2a were used for screening and confirmation of MRSA respectively, this may partly be responsible for the low prevalence obtained.

Around the world, a carriage of 60.5% was gotten from Iran by Alireza *et al.* [31], while Zer *et al.* [32] using real time PCR got 14.3 % from intensive care unit (ICU) staff in Turkey. Rongpharpi *et al.* [33] on the other hand working in India got an MRSA carriage of 11.43% from healthcare workers colonized by *S. aureus*. Eveillard *et al.* [16] however had reported a prevalence of 6.2% from healthcare workers in France, Western Europe.

The variability of this study from other studies is in keeping with the high variability of reported prevalence of nasal carriage all over the world [34, 35] as seen in the works cited earlier. Status of implementation of infection control strategies, differences in use of antibiotics, methods of *S. aureus* and MRSA detection could all contribute to this variability.

The fact that nurses and doctors have closest contact to patients predisposes them to be the most colonized as this study shows. This is consistent with other studies like those by Eguwatu *et al.* [22] and Gonsu *et al.* [28]. Doctors seem to carry *S. aureus* more than other cadre of staff, which is consistent with work by Al-Abdi *et al.* [27], this is also consistent with their being the least compliant with infection control practices as seen in this work. On the other hand, nurses were the ones more colonized by the multidrug-resistant MRSA, this corroborates the work by Shibabaw *et al.* [26]. In this work, healthcare workers in oncology and orthopaedic wards had the highest carriage for MRSA, this is similar to what was observed by Rongharpi *et al.* in India, while other works have variably noted the ICU [33.34], and the surgical wards [23, 26]. The few numbers of MRSA positive isolates do not provide enough statistical power to be able to comment on factors such as length of hospital stay and infection control practice.

Most of the MRSA isolates in this work were resistant to at least three to four different classes of antibiotics and this is of significance, because the healthcare workers may transmit these multidrug resistant strains to other colleagues and to patients during healthcare delivery. More than 90% of *S. aureus* isolates and all the MRSA isolates were resistant to penicillin (representing beta lactams) which was expected and consistent with the report by Al-Abdi *et al.* [27], while the high resistance seen with sulphamethoxazole-trimethoprim (90%) for MRSA isolates was similar to that obtained by Fadeyi *et al* [35] and Gonsu *et al.* [28]. The MRSA isolates showed low resistance to genticin, similar to findings by Al-Abdi *et al.* [27], while some other studies had variable results - Gonsu *et al.* reported a resistance of 53.5%, while Askarian *et al.* [36] working in Iran obtained 69%. Ciprofloxacin and erythromycin also had low resistance, but the lowest resistance was seen against clindamycin and chloramphenicol, probably because they are not commonly used drugs.

CONCLUSION

This study found a low carriage of MRSA among healthcare workers in high-risk units in ABUTH, following screening with cefoxitin and confirmation with latex agglutination test for PBP2a. The carriage was highest in oncology and orthopedic units, mainly among doctors and nurses. The isolates were multidrug resistant especially to penicillin, sulphamethoxazole-trimethoprim and ciprofloxacin, but retained significant susceptibility to antibiotics like genticin, clindamycin, erythromycin and chloramphenicol. Continuous vigilance, improved infection control practices and antibiotic stewardship program is necessary to maintain this low prevalence.

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