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Research Article
Evaluation of Carrier of Methicillin Resistance/Sensitive *Staphylococcus aureus* producing Penicillinase from Health Workers

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Abstract

Background and Objective: Methicillin-Resistance *Staphylococcus aureus* (MRSA) usually colonizes the skin, respiratory tract and urinary tract. MRSA is considered an emerging disease because it's easily communicated from one person to another and its incidence is rising quickly. This study was undertaken to evaluate the carrier of methicillin resistance/sensitive *Staphylococcus aureus* producing penicillinase from health workers. **Materials and Methods:** Specimens were collected randomly from the health workers with a sterile swab stick from the nasal nares (nasal swab), skin swab and swab from the laboratory coat of workers (practitioners) in Irrua Specialist Teaching Hospital (ISTH), Irrua, Edo State, Nigeria. A total of 200 specimens (nasal swab, skin swab and laboratory coat swab) were randomly collected from apparently healthy male and female subjects. **Results:** This study, had 30 (15%) *Staphylococcus aureus* prevalence with the highest occurrence of 24 (30%) from skin swabs and 6 (7.5%) from nasal swabs. About 13 (43.3%) prevalence of MRSA was recorded with the highest occurrence seen in skin 9 (30%), 4 (13.3%) from nasal swabs while 17 (56.6%) of the *Staphylococcus aureus* isolates were Methicillin-Sensitive (MSSA). When the prevalence of MRSA and MSSA were analyzed, 7 (23%) were penicillinase negative (non-producing) and there was no significant difference. About 23 (77%) penicillinase-producing *Staphylococcus aureus*, 13 (57%) were methicillin/resistant and 10 (43%) were methicillin/sensitive *Staphylococcus aureus* with no significant difference between the two growth from penicillinase-producing. **Conclusion:** It was observed that methicillin-resistant/penicillinase-producing *Staphylococcus aureus* is significantly present in the skin and nasal nares of staff in ISTH and this may pose nosocomial infection prevalent in the hospital environment if not promptly detected and controlled.

Key words: *Staphylococcus*, penicillinase, MRSA, MSSA, methicillin, resistance, sensitive

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Staphylococcus aureus is ubiquitous and may be a part of human flora found in the axillae, the inguinal and perineal areas and the anterior nares. Baddour *et al.*[1] described three patterns of carriage: Those who always carry a strain, those who carry the organism intermittently with changing strains and a minority of people who never carry *Staphylococcus aureus*. Persistent carriage is more common in children than in adults[2]. Nasal carriers can be split into two categories: Persistent carriers who are at high risk of infection and intermittent or non-carriers who are at low risk of infection[3,4]. Persistent nasal carriage depends on host genetic determinants[4,5]. *Staphylococcus aureus* is a multipurpose bacteria that is a major hospital and community pathogen[6]. Surface local infections such as folliculitis, furuncles and abscesses are caused by direct invasion through breaks in the skin or mucus membrane. Multidrug resistance is a typical characteristic of *Staphylococcus aureus*, making antibiotic treatment of severe infections problematic[7,8]. The resistance to the penicillin category of antibiotics is caused by enzymes produced by *Staphylococcus aureus*, such as penicillinase[8,9]. Penicillinase-positive Penicillinase-resistant antibiotics like methicillin, oxacillin and nafcillin are currently used to treat *Staphylococcus aureus* infections. These drugs have also been proven to develop resistance in *Staphylococcus aureus*[8,10].

MRSA stands for methicillin-resistant *Staphylococcus aureus*, which is a type of *Staphylococcus aureus* that is resistant to the antibacterial activity of methicillin and other related antibiotics of the penicillin class[7,10,11]. Curiously, Methicillin-Resistant *Staphylococcus* aureus (MRSA) is less often found in the anterior nares than Methicillin-Sensitive *Staphylococcus aureus* (MSSA) and Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus* (HA-MRSA)[1,10]. With the development of the antibiotic penicillin, the management of infections caused by *Staphylococcus aureus* was transformed. However, most strains of *Staphylococcus aureus* are now resistant to penicillin, which is due to the ability of *Staphylococcus aureus* to produce a substance called β-lactamase (pronounced beta-lactamase), which degrades penicillin and destroys its antibacterial activity. This penicillin is mediated by penicillinase (a type of -lactamase) production, an enzyme that cleaves the β-lactam ring. Penicillinase-resistant β-lactam antibiotics, such as methicillin, nafcillin, oxacillin, cloxacillin, dicloxacillin and flucloxacillin, can resist degradation by staphylococcal penicillinase[10,12].

All this strain of drug-resistant *Staphylococcus aureus*, colonizes the skin, particularly in the perineal area and the rectum. It also colonizes the pharynx, gut and vagina[3,4,8]. Methicillin-Resistance *Staphylococcus aureus* (MRSA) usually colonizes the skin, respiratory tract and urinary tract. It's estimated that about 1% of the population carries MRSA[4,8]. Since the 1950s, MRSA has been a widespread nosocomial (hospital-based) infection, but in recent years, it has been found as a source in nursing homes, outpatient treatment centres, jails, athletic facilities and others, such as those who engage in daily activities like traders. Community-acquired infections[13] refers to the transmission of infections and outbreaks. MRSA is classified as an emerging illness because it is easily transmitted from one person to another and because its prevalence is rapidly increasing. It has been found in approximately 12% of all cultured boils outside of medical settings. *Staphylococcus aureus* is an important cause of Skin and Soft-Tissue Infections (SSTIs), endovascular infections, pneumonia, septic arthritis, endocarditis, osteomyelitis, foreign-body infections and sepsis[4].

Since the mid 1990s, however, there has been an explosion in the number of MRSA infections reported in populations lacking contamination risk factors for exposure to the health care system[14]. Methicillin-Resistant *Staphylococcus aureus* (MRSA) isolates are resistant to all available penicillins and other β-lactam antimicrobial drugs[8,10,15]. They were once confined largely to hospitals, other health care environments and patients frequenting these facilities[15]. Since the mid 1990s, however, there has been an explosion in the number of MRSA infections reported for populations lacking risk factors for exposure to health care[12].

This study was undertaken to evaluate the carrier of methicillin resistance/sensitive *Staphylococcus aureus* producing penicillinase from health workers in Irrua Specialist Teaching Hospital (ISTH). *Staphylococcus aureus* has been found frequently as an aetiological agent of a variety of human infections. Methicillin/resistance and penicillinase-producing strain are potential sources of nosocomial infections in patients and healthcare workers. Centre for Disease Control (CDC) reported MRSA as the primary source of nosocomial infections, which could be transferred from patients to patients, patients to health workers, health workers to health workers and health workers to patients[10]. Failure of antibiotics activities in the treatment of *Staphylococcus aureus* infections is increased due to resistance, a defining characteristic of penicillinase-producing *Staphylococcus aureus*. This study was set to determine the prevalence of MRSA in the skin, nasal nares and fomites of medical staff to validate the claims of CDC and other researchers in a different area of study.

MATERIALS AND METHODS

Study area and population: This study was carried out in Irrua Specialist Teaching Hospital (ISTH), located in Esan Central Local Government Area of Edo State. The study was carried out between January and August, 2019. Irrua is a rural area, geographically located at latitude 6°45'01"N. longitude: 6°15'48"E having a population of about 21,870 people whose major occupations were farming, trading, civil servant and students.

Research design: This project work was carried out within three months, with a total of two hundred samples from male and female health workers in Irrua Specialist Teaching Hospital.

Sample selection: Specimens were collected randomly from the health workers with a sterile swab stick from the nasal nares (nasal swab), skin swab and swab from laboratory coat (fomites) of workers (practitioners) in Irrua Specialist Teaching Hospital (ISTH) Irrua, Edo State, Nigeria.

Sample size: Thus, a total of 200 specimens (nasal swab, skin swab and laboratory coat swab) was randomly collected from apparently healthy male and female subject.

Materials: The following materials and apparatus were used for the bacteriological analysis: Mannitol salt agar (by HIMEDIA), Mueller Hinton agar (by HIMEDIA), swab sticks, Petri dishes, conical flask, distilled water, autoclave, bunsen burner, inoculating wire loop, binocular microscope, weighing balance, measuring cylinder, glass slides, human plasma, hydrogen peroxide, crystal violet Lugol's iodine, acetone, neutral red, Penicillinase reagent, sensitivity discs (Ampicillin, Methicillin, Gentamicin, Ciprofloxacin, Streptomycin, Erythromycin) (by Pfizer) and other reagents.

Media: The media used were nutrient agar, mannitol salt agar and Mueller Hinton agar (for sensitivity test of the isolates).

Sample collection: Two hundred specimens were collected randomly from health workers that were interested in the study at Irrua Specialist Teaching Hospital (ISTH) Irrua. The samples (nasal swabs, skin swabs and swabs from laboratory coats). Subjects' nasal swabs were collected in good light eyesight by leaning their heads backwards and using a sterile swab stick to capture the specimens deep into the anterior passageways. Nasal swabs, sex, code number and date of the collection were swabbed in both the right and left nostrils. The swab sticks were carefully placed back into their sterile containers, sealed with adhesive tape and labelled. Skin swabs, as well as samples from laboratory coats, were obtained aseptically by swabbing their skin (particularly their forearm) with a swab moistened with physiological saline and the swab sticks were carefully returned to their sterile containers. Collected specimens were taken to the laboratory where bacteriological analysis was carried out immediately.

Procedure for culture:

- The swab stick was used to make primary inoculated on each mannitol salt agar
- Spreading was done by streaking from the primary inoculum using a sterile inoculating wire loop to obtain discrete bacterial colonies
- The plates were then incubated at 37°C for 24 hrs
- Growth was observed after incubation and the colonial morphology was studied carefully, noting the size, shape, edge, colour consistency, elevation and opacity of the colonies
- This was followed by Gram staining

Biochemical test: The biochemical tests that were used for this work include:

- Catalase test
- Coagulase test
- Penicillinase test

Antibiotic sensitivity test: Antibiotic discs such as Erythromycin, Gentamicin, Streptomycin, Ciprofloxacin, Ampicillin, (manufactured by Abtek Biologicals Ltd.) and methicillin (oxacillin) disc included were used to test the susceptibility of *Staphylococci aureus* isolates obtained. The test isolates were inoculated into sterile peptone water broth. The antibiotic discs were placed aseptically on the seeded plate. They were incubated at 37°C for 24 hrs and examined for zones of inhibition. The zones of inhibition were measured in millimetres and recorded. Antibiotic zones less than 10 mm in diameter were recorded as being resistant (R) by the organism while those with diameters of 10 mm and above were recorded as sensitive (S).

Penicillinase test (beta-lactamase): A simple screening parameter for beta-lactamase production is resistance to penicillin and related drugs.

There are three methods or modifications employed for the testing:

- Chromogenic cephalosporin method
- Iodometric method
- Acidimetric method

These methods are all available for testing but the acidimetric method was described and used in this research because it is commercially and easily prepared in the laboratory.

Principle: The rapid acidimetric is carried out with a strip of Whatman No. filter paper, When the enzyme, beta-lactamase (penicillinase) hydrolyses penicillin, penicilloic acid is produced. This reaction between the enzyme and the penicillin cause a drop in pH of the medium and a change in colour from purple to yellow indicates the production of the penicillinase enzyme[16].

Procedures:

- A strip of Whatman No. 1 filter paper was placed in a Petri dish
- A few drops of the reagents were placed on the filter paper to obtain saturation
- With a sterile wire loop, colonies of the methicillin/resistance and methicillin/sensitive *Staphylococcus aureus* were smeared on saturated filter paper inside the petri dish with positive and negative control
- Petri dish was covered and incubated at 36°C for 30 min
- It was observed for a spot of the colour change of the reagent from purple to yellow
- Reported as beta-lactamase-producing or non-beta-lactamase-producing *Staphylococcus aureus*[16].

Statistical analysis: The collected data were expressed as frequency and percentage. A comparison of qualitative variables was made using the Chi-square test. In all cases studied, the difference having $p<0.05$ were considered statistically significant using interactive calculation Chi-square tool software (version 18).

RESULTS

Based on standard bacteriological method, after proper investigation, from 200 samples [nasal swab (80), skin swab (80) and swab from Laboratory coat ie fomites (40)] of health workers/medical practitioners in Irrua Specialist Teaching Hospital (ISTH). This study had Chi-square 30 (15%) *Staphylococcus aureus* prevalence with the highest occurrence of 24 (30%) from skin swabs and 6 (7.5%) from nasal swabs. Other growths of non-*Staphylococcus aureus* were excluded from this study. When the isolate was analysed statistically among the samples used for this study, there was a statistically significant difference ($p<0.05$) with $X^2cal = 24.7$ and $p = 0.000$ (Table 1).

The distribution of Methicillin/Oxacillin Resistance *Staphylococcus aureus* (MRSA/ORSA) and Methicillin/ Sensitive *Staphylococcus aureus* (MSSA) among the studied population and fomites was shown in Table 2. From this study, 13 (43.3%) prevalence of MRSA was recorded with the highest occurrence seen in skin 9 (30%), 4 (13.3%) from nasal swabs while 17 (56.6%) of the *Staphylococcus aureus* isolates were Methicillin-Sensitive (MSSA). When the prevalence of MRSA and MSSA were statistically analyzed, there was no statistical difference $p>0.05$.

The frequency and distribution of penicillinase-producing/positive *Staphylococcus aureus* and penicillinase negative/not producing *Staphylococcus aureus* among the studied population was shown in Table 3. About 23 (77%), while 7 (23%) were penicillinase negative (non-producing). Statistically, there was no significant difference with ($p>0.05$). The frequency and distribution of penicillinase-producing of methicillin/resistance and methicillin/sensitive *Staphylococcus aureus* were shown in Table 4. From this research 23 (77%) penicillinase-producing *Staphylococcus aureus*, 13 (57%) were methicillin/resistance, 10 (43 %) were methicillin/sensitive *Staphylococcus aureus* with $p>0.05$ no significant difference within the two growth ($p>0.05$), $X^2cal = 1.405$ and $p = 0.235$ from penicillinase-producing.

Table 1: Distribution of *Staphylococcus aureus* among studied samples and fomites

Samples	No examined	(Positive) culture (%)	*S. aureus* (%)	No growth (%)	Other bacteria (%)
Skin	80	48 (60)	24 (30)	32 (40)	24 (50)
Nasal	80	20 (25)	6 (7.5)	60 (75)	14 (70)
Lab coat	40	0 (0)	0 (0)	40 (100)	0
Total	200	68 (34)	30 (15)	132 (66)	38 (55.9)

$X^2cal = 24.7$, Degree of freedom = 2, $p = 0.0000$, $p<0.05$, N: Number and *S. aureus*: *Staphylococcus aureus*

Table 2: Distribution of MRSA and MSSA among studied samples and fomites

Samples	*S. aureus*	MSSA (%)	MRSA (%)
Skin	24	9 (37.5)	15 (62.5)
Nasal	6	4 (67)	2 (33.3)
Lab coat	0	0	0
Total	30	13 (43.3)	17 (56.6)

X^2cal = 1.663, Degree of freedom = 1, p = 0.197, (p>0.05), MRSA: Methicillin-Resistance *Staphylococcus aureus*, MSSA: Methicillin-Sensitive *Staphylococcus aureus*, N: Number and *S. aureus*: *Staphylococcus aureus*

Table 3: Show distribution of penicillinase producing positive/*Staphylococcus aureus* and penicillinase not producing negative/*Staphylococcus aureus*

Samples	*S. aureus* (%)	Penicillinase positive (%)	Penicillinase negative (%)
Skin	24 (30)	19 (79)	5 (21)
Nasal	6 (7.5)	4 (67)	2 (33)
Lab coat	0	0	0
Total	30	23 (77)	7 (23)

X^2cal = 0.419, Degree of freedom = 1, p = 0.517 and (p>0.05)

Table 4: Show frequency and distribution of penicillinase producing of methicillin resistance and methicillin sensitive *Staphylococcus aureus*

Samples	Penicillinase[a] positive (%)	MRSA[b] (%)	MSSA[c] (%)
Skin	19 (79)	9 (47.3)	10 (53)
Nasal	4 (67)	4 (100)	0
Lab coat	0	0	0
Total	23 (100)	13 (57)	10 (43)

X^2cal = 2.118, Degree of freedom 2 and p = 0.346, (p>0.05), [a]: Penicillinase positive, [b]: MRSA (Methicillin-Resistance *Staphylococcus aureus*), [c]: MSSA (Methicillin-Sensitive *Staphylococcus aureus*), a vs. b = X^2cal = 0.385, p = 0.562, (p>0.05), a vs c = X^2cal = 1.405, p = 0.235 and (p>0.05)

DISCUSSION

Despite recognising *Staphylococcus* species as regional flora of the skin and mucus membrane, certain species have been found frequently as the aetiological agent of a variety of human infections[4]. The most common among these infections is the superficial supportive infection caused by *Staphylococcus aureus*. Under minding the introduction of chemotherapy and recent improvement in medical services, the Methicillin-Resistant *Staphylococcus aureus* (MRSA) strain emerge and has posed a major threat to public health in the treatment and management of *Staphylococcus aureus* infection. The increasing prevalence of MRSA among *Staphylococcus aureus* strains resulted in a significant increase in the utilization of vancomycin. Methicillin-Resistant *Staphylococcus aureus* (MRSA) has been recognized as a major strain of *Staphylococcus aureus* prevalent as a cause of nosocomial infection which often results in to increase in morbidity and mortality[10]. Penicillinase-producing *Staphylococcus aureus*, however, has become a major concern with their extraordinary ability and ingenuity to adapt to antibiotics stress with specific enzymatic activity.

From this study, 15% prevalence of *Staphylococcus aureus* was recorded from 200 samples collected from the skin, nasal nares and laboratory coat of health workers in Irrua Specialist Teaching Hospital (ISTH), with the highest occurrence, was from the skin at 30 and 7.5% from nasal nares with no isolates from laboratory coat (fomites). The highest prevalence of *Staphylococcus aureus* from the skin may be connected with the skin as a carrier of *Staphylococcus aureus* as well as the first contact when predispose. The prevalence and distribution of *Staphylococcus aureus* among samples and fomites were statistically significant (p<0.05). There was no reported comparison in the area of study.

The prevalence of Methicillin-Resistance *Staphylococcus aureus* (MRSA) and Methicillin-Sensitive *Staphylococcus aureus* (MSSA) among the studied population and fomites was 43.3%, which differs from previous research done in different regions of Nigeria, where Taiwo *et al.*[17] reported a prevalence of 34.7% in Ilorin, Kwara State. In terms of differences, the study area, sample size, sample type and application of standard operating procedures in the workplace may all have a role. MRSA was found most frequently on the skin (30%) and in the nasal nares (13.3%), while 56.6% of the *Staphylococcus aureus* isolated in our research group were Methicillin-Resistant *Staphylococcus aureus* (MRSA). There was no reported comparison in the area of study.

Beta-lactamase (penicillinase) distribution of *Staphylococcus aureus* was significant (p<0.05) and had an occurrence of 77% penicillinase-producing *Staphylococcus aureus* while 23% were penicillinase not producing. The variation in penicillinase-producing *Staphylococcus aureus* and penicillinase not producing *Staphylococcus aureus* was statistically not significant (p>0.05).

This study revealed the frequency and distribution of penicillinase-producing methicillin/resistance *Staphylococcus aureus* and methicillin/sensitive *Staphylococcus aureus*. From 100% penicillinase-producing *Staphylococcus aureus* isolated, 57% were methicillin-resistant while 43% were methicillin-sensitive *Staphylococcus aureus* with no statistical significant difference (p>0.05) observed between penicillinase-producing *Staphylococcus aureus* and Methicillin-Resistance *Staphylococcus aureus* (MRSA). As regards, the relationship between methicillin resistance and beta-lactamase (penicillinase) producing *Staphylococcus aureus*, it was observed that all methicillin-resistant *Staphylococcus aureus* in this study were relatively penicillinase-producing. The MRSA's ability to produce penicillinase as reported by Harkins *et al.*[18], states that in fact, it has been hypothesized that it was the extensive use of penicillin rather than the

introduction of methicillin that drove the emergence of MRSA. This implies that *Staphylococcus aureus* that produces the enzyme penicillinase equally possesses the *mecA* gene that encodes methicillin resistance. There was no significant difference ($p>0.05$) observed comparatively with Methicillin-Sensitive *Staphylococcus aureus* (MSSA) 57% and penicillinase-producing isolates 23 (77%).

This study has established the prevalence of MRSA and penicillinase-producing *Staphylococcus aureus* in the skin and nasal nares of medical workers, it is necessary for medical personnel, especially those involved in routine care, monitoring and prescription of commonly used antibiotics to pay attention to the prevalence of Methicillin-Resistance *Staphylococcus aureus* (MRSA), Methicillin-Sensitive *Staphylococcus aureus* (MSSA) and penicillinase-producing *Staphylococcus aureus* in treatment of *Staphylococcus aureus* infections. Individuals who used IV drugs, participants in close contact sports and people living together in crowded situations, such as inmates, military recruits and disabled individuals in group homes, were all linked to these epidemics.

Regular surveillance of both nosocomial, Hospital Acquired Methicillin-Resistance *Staphylococcus aureus* (HA-MRSA) and Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) infection is necessary to succumb its prevalence in the hospital settings and community at large. Regular monitoring of antibiotic sensitivity pattern of *Staphylococcus aureus* must be made mandatory, to control the further spread of its infections. Proper hygiene should be maintained at all times by all health workers to reduce its spread and infection by contact. Hand-washing, particularly is very important for all health workers after each procedure with a patient before touching the next patient. This will stop the transmission of MRSA. The use of disposable aprons and gloves by hospital staff should be practised thereby reducing the risk of transmission in the hospital.

CONCLUSION

In conclusion from this research, it was observed that methicillin-resistant/penicillinase-producing *Staphylococcus aureus* is significantly present in the skin and nasal nares of staff in Irrua Specialist Teaching hospital and this may pose nosocomial infection prevalent in the hospital environment if not promptly detected and controlled. This research also showed that penicillinase-producing *Staphylococcus aureus* are relatively methicillin-resistant and has an increased resistance pattern of *Staphylococcus aureus* to antibiotics use, which has relatively increases resistance and failure of antibiotics used in conventional treatment and management of *Staphylococcus aureus* infections.

SIGNIFICANCE STATEMENT

This study has established the prevalence of MRSA and penicillinase-producing *Staphylococcus aureus* in the skin and nasal nares of medical workers, it is necessary for medical personnel, especially those involved in routine care, monitoring and prescription of commonly used antibiotics to pay attention to the prevalence of Methicillin-Resistance *Staphylococcus aureus* (MRSA), Methicillin-Sensitive *Staphylococcus aureus* (MSSA) and penicillinase-producing *Staphylococcus aureus* in treatment of *Staphylococcus aureus* infections.

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