Prevalence And Antibiotic Resistance Pattern Of Methicillin-Resistance Staphylococcus Aureus Among In-Patients At A Tertiary Health Facility In Ido-Ekiti, Nigeria
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Citation

Abstract
Aim: Methicillin-resistant Staphylococcus aureus (MRSA) is a known nosocomial pathogen associated with therapeutic difficulties as a result of intrinsic resistance to beta-lactam antibiotics and the development of multidrug resistance. This study aims at determining the prevalence and antibiotic resistance pattern of MRSA among in-patient at Federal Medical Centre, Ido-Ekiti, Nigeria.

Materials and method: Between January 2009 and December 2009, all specimens from in-patients submitted to Medical Microbiology laboratory of the hospital were processed and all Staphylococcus aureus isolates were included in the study, they were identified morphologically and biochemically by the standard laboratory procedures. Antibiotic susceptibility test was done using the Modified Kirby-Bauer disc diffusion technique with zones of inhibition evaluated according to the Clinical and Laboratory Standard Institute (CLSI) guidelines. Methicillin resistance was determined by the Cefoxitin disk diffusion test.

Results: Of the 158 S. aureus isolates, 49 (31%) were MRSA. All MRSA were resistant to penicillin and cephalexin while none was resistant to vancomycin. The MRSA strains showed higher resistance rate than methicillin-sensitive S. aureus (MSSA) strains to all tested antibiotics; ciprofloxacin (12.2% vs 9.2%), gentamicin (75.5% vs 50.5%), erythromycin (69.4% vs 13.8%), trimetoprim/sulphamethoxazole (91.8% vs 61.5%), clindamycin (24.5% vs 11.9%). Multidrug resistance was found in 63.3% of the MRSA strains.

Conclusion: There is high rate of MRSA and multidrug-resistant strains. Vancomycin is the drug of choice while ciprofloxacin can be considered in its absence. There is need for strict antibiotic policy, continuous monitoring of antibiotic susceptibility pattern of all S.aureus and observation of infection control measures to curtail the evolution of these resistant strains. Further molecular study on MRSA epidemiology in future is desirable.

INTRODUCTION
Methicillin resistant Staphylococcus aureus (MRSA) is an important nosocomial pathogen which evolved shortly after the introduction of methicillin, nafcillin and oxacillin antibiotics and was first reported in the United Kingdom 1961. It is a cause of serious public health problem worldwide and had been widely implicated in skin and soft tissue infections, ventilator associated pneumonia, catheter associated bacteraemia, and many other infections among hospital in-patients. Methicillin resistance, later called oxacillin-resistance (presence of the MecA gene responsible for methicillin resistance) is a predictor of resistance to all antibiotics belonging to the beta-lactam family. Infections due to MRSA are of special concern since they are always associated with prolonged hospital stay (as a result of few therapeutic options) and increased cost of treatment; in a prospective case-control study, the median hospital stay sequel to hospital acquired Methicillin Sensitive Staphylococcus aureus (MSSA) bacteraemia was four days compared to 12 days for MRSA and the overall costs were $9661 and $27,083 respectively. Also, infection with MRSA is associated with higher mortality compared to those due to MSSA and it has been found that methicillin-resistance was independently associated with death; in a prospective study of patients with ventilator associated pneumonia caused by MRSA and MSSA, there was a higher incidence of bacteraemia and septic shock among the MRSA group, and mortality directly due to pneumonia was significantly higher among patients with MRSA infections.

The emergence of these MRSA is a direct result of selective antibiotic pressure which once generated become extremely difficult to control and as a result the knowledge of
prevalence of MRSA with their antibiotic susceptibility pattern in any environment is of paramount importance in determining the best treatment options for patients infected with this strain of organism. This study aimed at determining the prevalence of MRSA infection among hospital in-patients at Federal Medical Centre (FMC), Ido-Ekiti, Ekiti State, a tertiary health facility in South-Western Nigeria, and to examine the resistance pattern of these strains to antibiotic commonly used to treat S. aureus infection for the purpose of generating a policy in management of these infections in our hospital.

MATERIAL AND METHODS

The study was carried out at FMC, Ido-Ekiti, Ekiti State, Nigeria, between January and December 2009. All Staphylococcus aureus isolates from all routine clinical specimens from in-patients submitted to the medical microbiology laboratory of FMC, Ido-Ekiti within this period were included in the study. All isolates were identified morphologically and biochemically by the standard laboratory methods.

Antibiotic susceptibility testing incorporating the following antibiotics: cefoxitin (10 µg, REMEL), penicillin (10U, REMEL), ciprofloxacin (5µg, REMEL), gentamicin (10µg, REMEL), erythromycin (15µg, REMEL), clindamycin (2µg, REMEL), cephalexin (30µg, REMEL), trimetoprim/sulphametoxazole (1.25/23.75µg, REMEL), and vancomycin (30µg, REMEL) was done using the modified Kirby-Bauer disc diffusion technique; a sterile cotton wool swab stick (Evans, UK) was used to inoculate the entire surface of Mueller-Hinton agar (MHA) plate (Oxoid, UK) with the inoculum of Staphylococcus aureus, turbidity matching 0.5 MacFarland standard, before antibiotic discs were laid on the surface. The plates were incubated overnight at 35°C. The zones of inhibition were evaluated according to the Clinical and Laboratory Standard Institute (CLSI) guidelines. Methicillin-resistance was determined by using the Cefoxitin Disk Diffusion Test; all Staphylococcus aureus isolates with zones of inhibition around cefoxitin disc less than or equal to 21mm diameter were considered MRSA. Staphylococcus aureus ATCC 29213 was used as methicillin-sensitive control strain while S. aureus ATCC 43300 was used as methicillin-resistant control strain. Data entry and processing was done using computer software SPSS version 15. Data was presented in tables and percentages.

RESULTS

A total of 158 strains of Staphylococcus aureus were isolated from various clinical specimens out of which 49 (31%) were methicillin resistant. The highest rate of isolation of MRSA was from wound swabs (19=38.8%), followed closely by pus/aspirates (17=34.7%), while majority of the rest were from sputum/throat swabs (8=16.3%). Nineteen out of 21 (90.5%) of S. aureus isolated from wound swab were MRSA. However, MSSA were mostly isolated from pus/aspirate (43=39.4%), sputum/throat swabs (35=32.1%), and urine (20=18.3%) Table I. The antibiotic resistant pattern of all isolated S. aureus strains is as shown in Table II. None of the S. aureus strain was resistant to vancomycin. All MRSA strains were resistant to penicillin and cephalexin while 72.5% and 47.7% of MSSA respectively were resistant to these antibiotics. Methicillin-resistant S. aureus also showed greater resistance to other tested antibiotics compared to MSSA; gentamicin (75.5% vs 50.5%), ciprofloxacin (12.2% vs 9.2%), erythromycin (69.4% vs 13.8%), trimetoprim/sulphametoxazole (91.8% vs 61.5%), and clindamycin (24.5% vs 11.9%) . Multidrug resistance was found in 63.3% of the MRSA isolates with 42.9% been resistant to more than three families of non-vancomycin antibiotics. Table III
Prevalence And Antibiotic Resistance Pattern Of Methicillin-Resistance Staphylococcus Aureus Among In-Patients At A Tertiary Health Facility In Ido-Ekiti, Nigeria

Figure 2
Table 2 Resistance pattern of MRSA and MSSA against commonly used anti-staphylococcal antibiotics tested.

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>MRSA n (%)</th>
<th>MSSA n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxim</td>
<td>49 (100.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Penicillin</td>
<td>49 (100.0)</td>
<td>79 (77.5)</td>
</tr>
<tr>
<td>Cephalaxin</td>
<td>49 (100.0)</td>
<td>52 (47.7)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>6 (12.2)</td>
<td>10 (0.2)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>37 (75.5)</td>
<td>55 (50.0)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>34 (69.4)</td>
<td>15 (13.8)</td>
</tr>
<tr>
<td>Trimethoprim/sulphamethoxazole</td>
<td>45 (91.8)</td>
<td>67 (61.5)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>12 (24.5)</td>
<td>13 (11.9)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Figure 3
Table 3 Multidrug resistance pattern in isolated MRSA

<table>
<thead>
<tr>
<th>Resistance to</th>
<th>MRSA n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than three vancomycin antibiotics</td>
<td>21 (42.9)</td>
</tr>
<tr>
<td>All antibiotics except vancomycin</td>
<td>3 (6.1)</td>
</tr>
<tr>
<td>All antibiotics except vancomycin and ciprofloxacin</td>
<td>9 (18.4)</td>
</tr>
<tr>
<td>All antibiotics</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total multidrug resistant</td>
<td>31 (63.3)</td>
</tr>
</tbody>
</table>

DISCUSSION

Methicillin-resistant S. aureus is an acclaimed nosocomial pathogen worldwide with varying prevalence rate ranging from 2% in the Netherlands and Switzerland to 70% in Japan and Hong-Kong.9,10 A prevalence rate of 31.3% detected in this study is comparable to report of Gowitz et al. which put the prevalence rate in Nigeria at the range of 21-30%.11 Similar high prevalence rates have been reported from different regions in Nigeria; 43% in Jos (of which 81% of this was from in-patients),12 28.6% in Kano (62% of this was from in-patient),13 and 34.7% in Ilorin (70.6% of this was from in-patients).14 However, in a study done involving eight African hospitals and Malta, a comparatively low prevalence rate of 15% was found.15 Also, comparable high prevalence rates have been reported in similar studies outside Nigeria; 31% in Tamil Nadu,16 34.8% in Assam17 and 38.6% in Delhi.18 Wide variability in MRSA prevalence had been reported in different countries; Pakistan (83%),19 France (6%), Ireland (5%), and United Kingdom (2%).20 There has been a progressive increase rate in methicillin resistance in United State of America from 5% in 1981 to 52% in 2005.21 The high prevalence of MRSA infection rate in this study might not be unconnected to the poor infection control program in our hospital where policy on antibiotic use is poorly documented or non-existent.

Methicillin-resistant S. aureus, as in previous studies,12,13,21 were mostly isolated from wound swabs in this study (38.8%) while MSSA were mostly isolated from pus/aspirates (39.4%). Up to 90.5% of S. aureus isolated from wound swabs were MRSA, the reason for this might not be unrelated to the chronic nature of most of the wounds from which swabs were taken, and as such the infecting S. aureus are expected to have been exposed to different antibiotics with subsequent development of varying resistance.

This study, like previous studies, had demonstrated that MRSA are more resistant to various group of antibiotics compared to MSSA.17,22,23 It is not surprising that all the MRSA tested in this study were resistant to penicillin and cephalaxin whereas only 72.4% and 48% of MSSA respectively were resistant to these antibiotics; the finding only substantiates the fact that resistance to methicillin predicts resistance to other beta-lactam drugs.1 All S. aureus (both MRSA and MSSA) in this work were sensitive to vancomycin, this finding is similar to those of some previous studies;13,14,15,24 although report of vancomycin resistance by some MRSA strains have been widely reported.25,26 The MRSA were highly resistant to trimetoprim/sulphamethoxazole (92.1%), gentamicin (76.2%), and erythromycin (70.2%) while a more encouraging pattern was seen against ciprofloxacin (12.2%) and clindamycin (24%). The high rate (63.3%) of multi-drug resistant MRSA (resistance to three or more families of antibiotic at a given point in time), with up to 42.9% of them being resistant to more than three non-vancomycin antibiotic families, found in this study is worrisome considering the ability of S. aureus to spread easily by direct or indirect person-to-person contact with resultant therapeutic difficulties. Vancomycin is the only antibiotic with 0% resistance even with multi-drug resistant strains and thus remain the best therapeutic option in our setting, however, the drug is widely unavailable and other available therapeutic options must be considered. Ciprofloxacin is favoured considering the lower rate of resistance (12.2%) to it by MRSA in this study. The MSSA are generally still of lower resistant rate (compared to MRSA) to commonly used antistaphylococcal agents tested in this study, however, only vancomycin (0%), ciprofloxacin (9.6%), and probably clindamycin (12%) and erythromycin (14%) were good enough to be considered for management of infections due to these MSSA.
CONCLUSION
The study had demonstrated a high prevalence rate of MRSA with high rate of resistance to commonly used antimicrobial agents. A large proportion of these MRSA were found to be multi-drug resistant. These findings call for urgent attention whereby strict antibiotic policy should be enforced to curtail irrational use of antibiotics with its attendant evolution of resistant strains of S. aureus. There is need for continuous monitoring of antibiotic susceptibility pattern of all S. aureus isolates for selection of appropriate therapy. Also, infection control measures such as handwashing and other aseptic techniques must be followed to avoid therapeutic difficulties associated with these resistant pathogens. Further molecular studies for studying and monitoring the epidemiology of MRSA and the multi-drug resistant MRSA in future is highly desirable.

References

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