

Drug resistant *Staphylococcus aureus* in Clinical Samples at Kampala International University-teaching Hospital, Bushenyi District, Uganda

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Abstract Background: *Staphylococcus aureus* that is resistant to methicillin is an important nosocomial pathogen that often causes infections that are hard to treat. This is due to the fact that the pathogen is usually resistant to other commonly used antibiotics. The presence of drug resistant MRSA among patients has previously been documented in various parts of Uganda. However no reports have been documented for Kampala International University-Teaching hospital in western Uganda. This study was therefore carried out to determine the prevalence and antibiotic resistance of MRSA strains in the patients hospitalized in the surgical ward. **Methods:** Wound swabs were collected from both male and female patients hospitalized in the surgical ward. Samples were then cultured in suitable media. The *Staphylococcus aureus* colonies that were obtained were tested for resistance to oxacillin to determine the strains that were MRSA. Further antibiotic resistance of the MRSA isolates was determined by the disc diffusion method using various antibiotics. **Results:** Out of the one hundred and fourteen isolates from the clinical samples, only seventy five isolates were clearly identified as *S. aureus* with 85.3% coagulase positive and 13.3% coagulase negative. Methicillin resistant staphylococcus aureus was prevalent at a rate of 56.1%. among the MRSA isolates, resistance to ciprofloxacin was observed to be the highest while resistance to ceftriaxone was observed to be the least. **Conclusion:** The high prevalence of MRSA amongst the surgical ward patients requires proper measures to be taken to prevent further spread of the pathogen. It is recommended that the source of this drug resistant strains of MRSA be determined so as to design appropriate interventions to prevent the future emergence of infections that are hard to treat.

Keywords: surgical site infections, methicillin resistant *Staphylococcus aureus*, surgical ward, Uganda, drug resistance

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1. Introduction

All over the world, methicillin-resistant *Staphylococcus aureus* (MRSA) has been reported to be a major pathogen. When compared with other infections caused by *Staphylococcus aureus*, infections caused by MRSA are associated with a higher rate of morbidity and mortality. Compounded with the changing pattern of resistance in *Staphylococcus aureus* in recent times, the need for newer and effective antimicrobial agents for treating MRSA has been augmented [1]. Currently, the situation has been worsened by the fact that most of the isolates found worldwide are multidrug resistant. It has previously been recommended that routine identification of *S. aureus* be performed using coagulase test or latex agglutination tests,

since use of the more powerful molecular tests for identification is impractical in many diagnostic laboratories [2]. This is especially true for resource limited settings, including sub-Saharan Africa. A wide variety of infections have been linked to MRSA, including some which are more superficial while others are deep rooted. Cases of life-threatening infections like neonatal sepsis and community-acquired pneumonia have in the past been attributed to MRSA [3,4]. MRSA infections have drawn increased attention because such infections are attributed to prolonged hospital stays, increased medical costs, and relatively limited therapeutic options for the patients suffering from such infections [5]. In developing countries for instance, the multidrug resistant hospital acquired strains of MRSA and their characteristic resistance to beta-lactam antibiotics limit the available treatment options, in which case the less costly antibiotics are often

used [6,7]. Estimates indicate that approximately 10% of surgical procedures in Uganda end up becoming septic, with *Staphylococcus aureus* being the most commonly isolated organism. However, no MRSA had been isolated from surgical site infections in Uganda by the year 1999 [8,9,10]. Data on MRSA prevalence in developing countries is still limited [11]. Data from Uganda in particular is very scanty, with most published reports emerging mainly from hospitals in the country's capital city. Laboratory services in the country are sparsely distributed, poorly equipped and in some instances, poorly financed. This scenario may therefore pose a great challenge and also a major risk factor in MRSA outbreaks in hospitals, more especially now that the world is witnessing an ever increasing occurrence of antibiotic resistance [12,13]. This study was therefore carried out to determine the drug resistance pattern of *Staphylococcus aureus* in clinical samples at Kampala International University-teaching hospital, Bushenyi District, Uganda. The western region of Uganda, where the study was carried out, has had extremely few reported studies on MRSA.

2. Materials and Methods

2.1. Study Setting

This study was cross sectional and descriptive in nature, carried out in the surgical ward of Kampala International University-Teaching Hospital, that is located in Ishaka, Bushenyi district, western Uganda. Both male and female patients that were hospitalized at the surgical wards of Kampala International University teaching hospital were enrolled in the study. Only patients who gave informed consent to participate in the study were enrolled for clinical sample collection.

2.2. Sample Collection and Culturing

Samples were collected from one hundred and fourteen patients hospitalized in the surgical wards. Samples were collected from the patients by swabbing their wounds using sterile cotton swabs. The swabs were transported to the microbiology laboratory of Kampala International University in tubes containing Amies transport medium (Biolab, Budapest, Hungary). The samples were then cultured on blood agar and Mannitol salt agar at 37°C for 24 hours, which ensured growth of distinct colonies. After selection of the predominant colony type for each sample, identification of *Staphylococcus aureus* to species level was done according to the protocol described elsewhere [14].

2.3. Antibiotic Susceptibility Testing

Identification of MRSA was done by the disc diffusion method with Mueller Hinton agar containing discs of oxacillin (1 µg). A zone of inhibition less than 10 mm was indicative of methicillin resistance. The *S. aureus* ATCC 25923 was used as a standard control strain. The susceptibility pattern of the methicillin resistant

Staphylococcus aureus isolates to other antibiotics was also determined by Kirby Bauer disc diffusion method according to the Clinical laboratory standard Institute (2012). In this procedure, the samples were incubated in medium with discs of erythromycin (15 µg), cloxacillin (10 µg), ciprofloxacin (5 µg) and vancomycin (30 µg), ceftriaxone (30 µg) for 18 hours at 37°C.

2.4. Ethical Approval for the Study

An approval to conduct the research was obtained from the Research and Ethics Committee of School of Pharmacy Kampala International University-Western Campus. Informed consent was sought from all patients before any procedure was carried out. All information obtained from the patients was kept confidentially.

3. Results

3.1. Growth of Microorganisms

Of the one hundred and fourteen isolates from the clinical samples, only seventy five isolates were clearly identified as *S. aureus* with 85.3% coagulase positive and 13.3% coagulase negative. Thirty of the isolates were *E.coli*. Other isolates were *Pseudomonas spp*, *Klebsiella spp*, *Proteus spp*, *Streptococcus spp* and *Enterobacteriaceae spp*. The prevalence of *Staphylococcus aureus* was 65.8%.

3.2. Prevalence of MRSA among the Isolates

The prevalence of MRSA was 56.1%. All MRSA isolates were susceptible to erythromycin. A total of fifty seven MRSA isolates (93.4%) were susceptible to vancomycin and four (6.6%) isolates were resistant to vancomycin. Out of the total MRSA isolates, fifty two (85.2%) were susceptible to ceftriaxone, eight (13.1%) had an intermediate sensitivity and only one (1.7%) isolate was resistant to ceftriaxone. Forty (65.6%) MRSA isolates were susceptible to cloxacillin, seventeen (27.9%) isolates had an intermediate sensitivity and four (6.5%) samples were resistant to the antibiotic. MRSA isolates that were resistant to ciprofloxacin were forty two (68.9%), seventeen isolates (27.9%) had an intermediate sensitivity and only one was susceptible to the antibiotic. The susceptibility profile of the isolates is as shown in Table 2. The percentage sensitivity is indicated in Figure 1.

Table 1. Microbial isolates from the clinical samples collected

Microorganisms yielded	Number of isolates
<i>Staphylococcus aureus</i>	75
<i>E. coli</i>	30
<i>Pseudomonas spp</i> ,	2
<i>Klebsiella spp</i>	1
<i>Proteus spp</i>	1
<i>Streptococcus spp</i>	1
<i>Enterobacteriaceae spp</i>	4

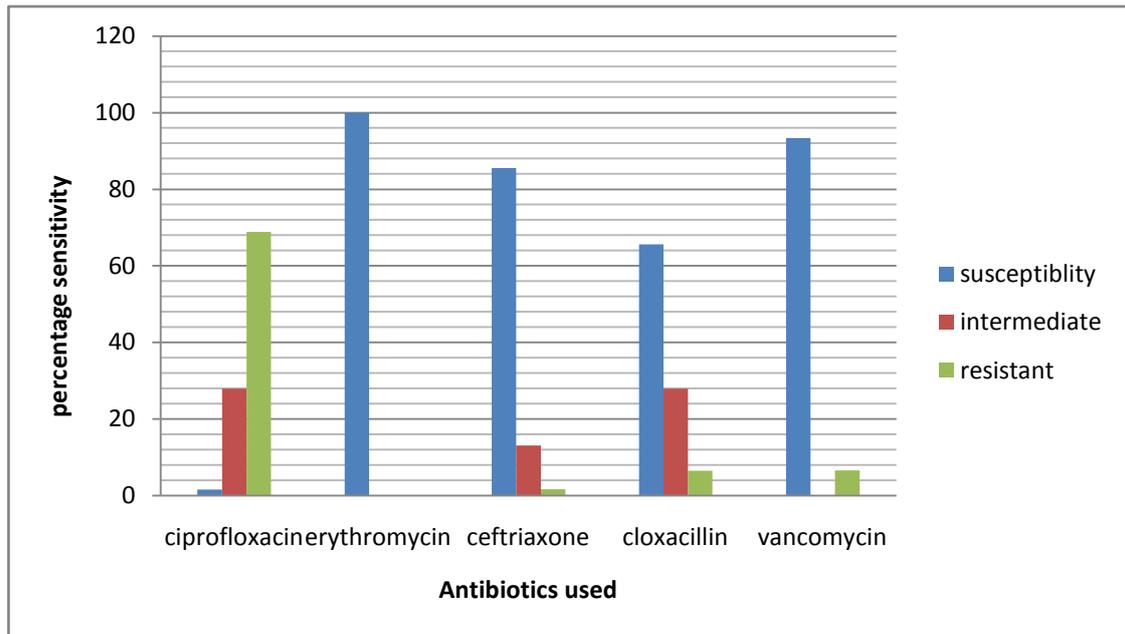


Figure 1. A graph showing the percentage of antibiotic sensitivity patterns

Table 2. Antibiotic susceptibility patterns of the MRSA isolates

Antibiotics used	Susceptible	Intermediate	Resistant
Ciprofloxacin	1 (1.6%)	17 (27.9%)	42 (68.9%)
Erythromycin	60 (100%)	0	0
Ceftriaxone	52(85.2%)	8(13.1%)	1 (1.7%)
Cloxacillin	40 (65.6%)	17 (27.9%)	4 (6.5%)
Vancomycin	57(93.4%)	0 (0%)	4(6.6%)

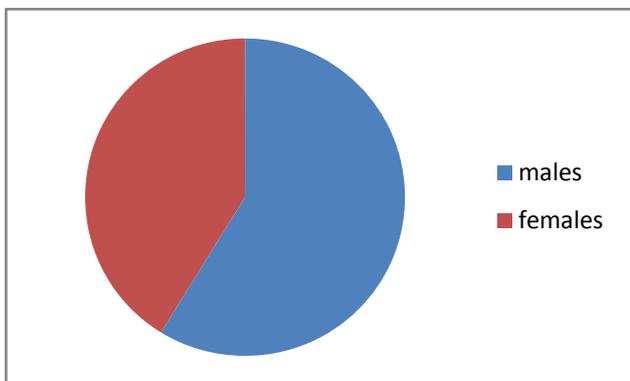


Figure 2. Distribution of MRSA among patients

3.3. Distribution of MRSA amongst Patients

Of the 65.8% *Staphylococcus aureus* samples isolated, sixty one isolates were identified as MRSA. Out of the sixty one MRSA samples isolated, 68.8 % were from males and 48.2% from females. Therefore males had a higher prevalence of MRSA than females, as shown in Figure 2.

4. Discussion

Findings from the current study indicate that *S. aureus* was the predominant microbe among the isolates. From this study, the prevalence of *Staphylococcus aureus* was

65.8%. These results are consistent with the findings of other studies conducted elsewhere, which showed a high prevalence of *Staphylococcus aureus* in clinical samples from surgical sites [15,16,17,18]. This study also found a higher level of prevalence of coagulase positive *S. aureus* (85.3%). A previous study conducted in India [31] also reported a high prevalence of coagulase positive *S. aureus* in clinical samples, which is consistent with the findings of our study. Our study also found a high prevalence of MRSA among the isolates, which is consistent with studies previously conducted in other places in Uganda [19,20]. The authors of one of the study settings in Uganda have recommended that surgical site infection therapies be guided by laboratory findings. They also recommended stronger infection control surveillance measures within the setting. However, our findings are contrary to findings of studies carried out in Libya and Australia, where lower prevalence rates of MRSA have been reported [21,22]. Our study found no MRSA strain that was resistant to erythromycin. This finding is contrary to other studies conducted in Uganda and Libya, where higher levels of resistance (46.9% and 46.8% respectively) to the antibiotic were reported [20,21]. Low level of vancomycin resistance (6.6%) was found in our study. A previous study conducted in China found MRSA isolates that were completely susceptible to vancomycin [23]. On the contrary, higher levels of vancomycin resistance have been reported from elsewhere [21]. This resistance to the drug could be attributable to prolonged use of the antibiotic in the setting, or even due to a possible presence in the hospital, of enterococci that are resistant to vancomycin. However our findings are contrary to another study, which found no resistance to the drug [20]. Authors of this previous study pointed out that the lack of vancomycin resistance in the isolates indicates that the drug was left as the last resort in cases of systemic infections resulting from MRSA in that particular setting. In this our study, it was found out that a higher proportion of the MRSA isolates (68.9%) were resistant to

Ciprofloxacin. This finding is contrary to another study that was carried out in Philippines that found lower percentage of resistance to the antibiotic among the MRSA isolates. However it is noteworthy to point out that the Philippine study was carried over a period of three years (2010-2012). This difference in time intervals could have influenced the findings of the study [24]. Findings from our study revealed that there were more MRSA isolates from male patients than female patients, which is contrary to findings from another recent study conducted in Nigeria that showed more MRSA isolates from female patients than their male counterparts [25]. The carriage of MRSA among healthcare workers has been pointed out as a dangerous factor that could increase the chances of transmission of such microbes to patients during patient care in hospitals. This can especially be a potential problem when the healthcare workers are predominantly from the surgical wards and operating rooms. A recent study has demonstrated a high proportion of nasal carriage of MRSA in healthcare workers in the surgical wards and operating rooms of a tertiary care hospital in Nepal [26]. Asymptomatic carriers of MRSA have been shown to be an important reservoir and source of spread of infections. For this reason, documenting risk profiles to identify patients who are at an increasingly high risk of carrying MRSA has been suggested as a mechanism that might improve prevention of MRSA infections [27]. This strategy can bring a big change in the trend of surgical site infections in resource limited settings. This can be especially true in settings like rural health facilities in Uganda, where proper surveillance of MRSA spread may be constrained by limited resources and unavailability of proper surveillance systems. High importance has been attached to the control of surgical site infections within hospitals, just as it is equally important to identify patients who are at a greater risk of being colonized and subsequently infected by multi-drug resistant microbes like MRSA. Reports have indicated that surveillance itself, even without any specific remedial intervention, is associated with a reduction in the reported incidences of surgical site infections. This on its own is another good enough reason to recommend implementation of surveillance systems for checking the spread of MRSA in hospital settings [28]. Surgical site infections due to MRSA have been shown to be very significant risk factors for adverse economic outcomes. A recent study has shown the risk-adjusted attributable increase in the duration of hospitalization to be approximately one day, and consequently, the cost of hospitalization was also increased by over \$1,000 [29]. There are other studies which have confirmed that patients with MRSA infections require more healthcare resources than patients with methicillin-sensitive *S. aureus* (MSSA) infections [30]. These adverse economic outcomes can have a great effect on households in economically underprivileged areas. For instance, households in rural Uganda may have to adjust their spending priorities in order to meet such higher hospitalization costs. Even in middle income households, the increased costs can have a significant impact, especially if the period of hospitalization is prolonged by several days. If such cases occur in settings that do not have medical expense subsidization programs, then the increased costs can easily drain the finances of households.

5. Conclusion

Our study has demonstrated an MRSA prevalence of more than fifty percent among the samples obtained from the patients. This is a relatively high prevalence and calls for measures to tame the spread of MRSA strains in the hospital. It is recommended that the antibiotics of choice for treating MRSA associated infections be adhered to by healthcare workers in this facility. Periodical screening of patients, especially in the surgical wards, for MRSA strains is also recommended so as to document the spread of MRSA, and design effective interventions for cases where the strains are causing serious infections. Plans are underway to determine the carriage of drug resistant MRSA among the healthcare workers in the hospital, since they have been noted to be a potential source of these resistant microbes in hospital setups.

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