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## Trends in Antimicrobial Resistance of *Staphylococcus aureus* Isolated from Clinical Samples at Mbarara Regional Referral Hospital in Rural Uganda

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### Authors' contributions

This work was carried out in collaboration with all the authors. Authors JB, YB, NS and DN contributed substantially to the conception, design and interpretation of the study. Authors JB, JI, JS and DN contributed to the data collection and statistical analysis. Author JB drafted the manuscript. All authors reviewed and approved the manuscript for publication.

Short Research Article

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### ABSTRACT

**Aim:** This study aimed at describing the antibiotic susceptibility patterns of *S. aureus* isolated from clinical samples at Mbarara Regional Referral Hospital from 2003 to 2012.

**Methods:** This was a retrospective study that included clinical specimens cultured at the Microbiology laboratory of Mbarara Regional referral hospital between 2003 and 2012. Cultures and sensitivity data were abstracted from the laboratory registers using a data abstraction form. Among the positive culture reports, the antibiotic sensitivity of the common bacteria isolated were also recorded. Analysis of susceptibility data was limited to *Staphylococcus aureus*, the commonest organism identified. The data were entered into Epi info and exported to Stata Version 12.1 for analysis.

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**Results:** A total of 36,080 cultures were performed over a period of 10 years. Of these 7,744 (21.5%) specimens grew an organism. *S. aureus* was the most prevalent organism isolated. Fifty nine percent of the *S. aureus* was isolated from blood samples followed by 22% from pus samples, urine (8%) and HVS (5%). During the study period, resistance of *S. aureus* to chloramphenicol, amoxicillin, penicillin, tetracycline, and cotrimoxazole ranged from 50-90% while *S. aureus* resistance to Gentamicin and ceftriaxone ranged from 10-20%.

**Conclusion:** Over the last decade, *S. aureus* isolates showed up to 90% resistance to commonly prescribed oral antibiotics. We recommend regular review of antibiotic resistance patterns to inform hospitals' on guidelines on empirical antibiotic prescription, especially in resource-limited settings where susceptibility testing may not be feasible.

*Keywords: Antibiotics; resistance patterns; sensitivity patterns; Staphylococcus aureus; hospital; oral; parenteral, empirical antibiotic prescriptions.*

## 1. INTRODUCTION

*Staphylococcus aureus* is an important pathogen in human infections and is implicated in a wide variety of infections, ranging from mild skin infections to more severe and invasive infections [1-3], associated with significant morbidity and mortality [4-6]. *S. aureus* is the most common cause of hospital acquired infections among new-born babies, surgical patients, malnourished persons, patients with diabetes and chronic diseases [7,8]. *S. aureus* rapidly acquires resistance to new drugs, which has contributed to the global pandemic of antimicrobial resistance to *S. aureus* [9-11]. The recent extension of resistance to *S. aureus* from health-care to the community has important clinical and pharmacological implications for health care providers and public health programs [12].

Empirical and often inappropriate use of antibiotics, combined with crowding, multiple pathology and frequent use of invasive devices, contribute to high levels of resistance. Resistance to the most available, most frequently-prescribed and affordable antibiotics poses a major concern in the management of bacterial infections, especially in resource poor countries [13], where a minimum essential drug list is used for most of the infections encountered by clinicians. Indeed, the emergence of drug resistance contributes to more clinically complex infections, requiring longer hospitalization times, often unaffordable alternative antibiotics, and subsequently higher mortality rates [14].

Due to lack of routine bacterial cultures, surveillance of antibiotic resistance in developing countries has been lacking and data regarding trends of antimicrobial resistance remain scarce throughout Africa. In Uganda, the resistance of *S. aureus* in patients remains unknown. This is mainly because the laboratory services of the country are scanty, ill equipped or poorly financed yet increasing drug availability has led to the possibility of drug abuse and eruption of drug resistance. Availability of this data is important to document trends and magnitude of drug resistance as well as inform the regulation of local public health policies and guidelines for antibiotic use and infection control efforts.

This study described antibiotic susceptibility patterns of *S. aureus* isolated from clinical samples at Mbarara Regional Referral Hospital from 2003 to 2012.

## 2. MATERIALS AND METHODS

This investigation was a retrospective review of culture records from the Mbarara Regional Referral Hospital, the main hospital in South-Western Uganda that serves up to 3 million people. We examined the results from all bacterial cultures taken from clinical specimens (blood, urine, pus, nasopharyngeal swabs, high vaginal swabs (HVS), stool, cerebral spinal fluid (CSF) and sputum) performed in the Microbiology laboratory of Mbarara University of science and Technology during the period 2003-2012 and identified *S. aureus* as the commonest isolate. We then examined the sensitivity/resistance patterns of *S. aureus* isolates to the commonly prescribed antibiotics within the hospital.

### 2.1 Study Setting

The retrospective review of *S. aureus* antibiotic sensitivity patterns was conducted within the microbiology laboratory for Mbarara hospital. Routinely in the microbiology laboratory at Mbarara University clinical specimens are plated out on media depending on the type of specimen. Characteristic colonies were picked for analysis by Gram staining and confirmed by Biochemical tests. *S. aureus* was isolated based on the colonial characteristics and confirmed by catalase and tube coagulase tests.

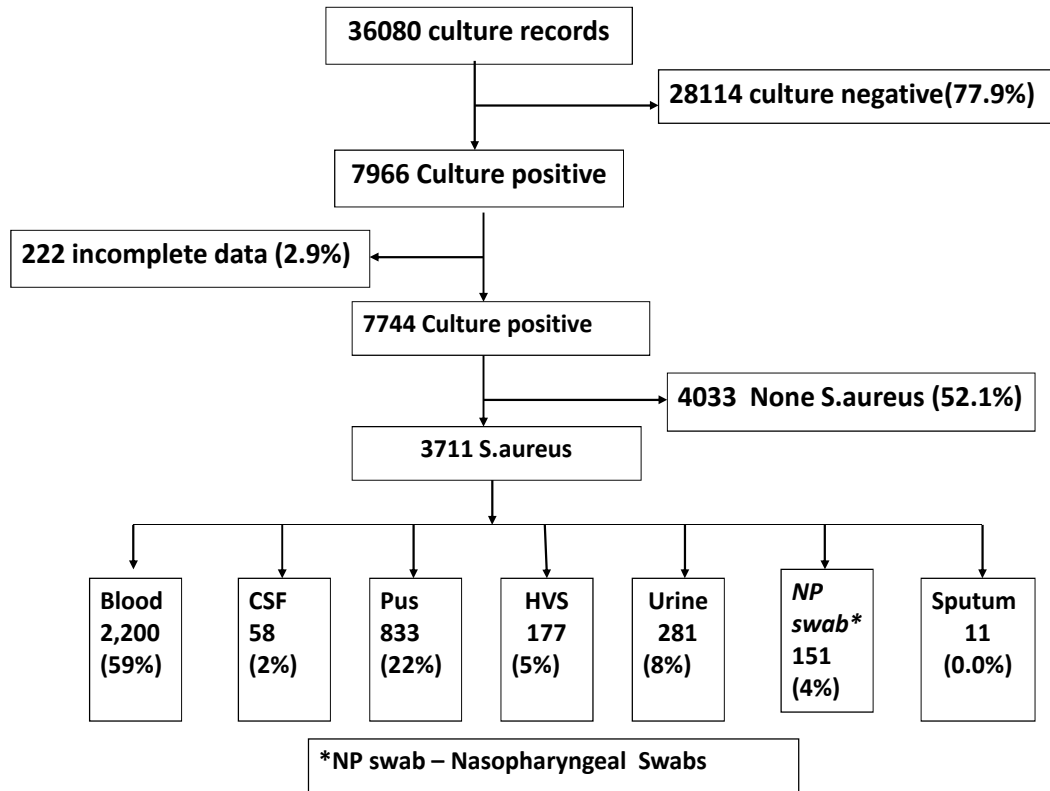
Antibiotic susceptibility is determined using the Kirby Bauer disc diffusion method for the following drugs: Gentamicin (10µg), Cloxacillin (5µg), Erythromycin (15µg), Chloramphenicol (30µg), Cotrimoxazole (25µg), Tetracycline (30µg), Penicillin (10µg) Ceftriaxone (30µg) Amoxicilin 10µg, and incubated at 37°C for 18-24hrs. The breakpoints used were defined by the Clinical Laboratory Standards Institute (CLSI) on antimicrobial susceptibility testing. Drug Sensitivity data was abstracted from the laboratory registers at the Microbiology laboratory of Mbarara University using a data abstraction form. The abstracted data included laboratory number, type of specimen, date of collection, age and sex of the patient, organism isolated and its susceptibility pattern.

### 2.2 Statistical Analyses

Analysis of susceptibility data was limited to one isolate per patient specimen. We created an antibiogram describing the proportion of isolates susceptible to commonly used antibacterials per organism. We performed data analysis using Stata Version 12.1 (Stata Corp., College station Texas). Percentages and proportions were calculated and trends were drawn over the 10 year analysis period.

## 3. RESULTS AND DISCUSSION

This study included 36080 culture records performed over a 10 year period from 2003-2012. As shown in the flow chart below [Fig. 1], *S. aureus* was isolated from 3711 specimens (47.9%) and the majority was isolated from blood (59%). Laboratory records indicated that majority of the blood cultures that grew *S. aureus* were drawn from children and to rule out possible contamination we consulted the pediatricians who informed us that most of the children who had *S. aureus* in their blood cultures also had skin infections implying that the *S. aureus* isolated from these cultures is actually not merely a contaminant but an actual cause of systemic infections in the children. This finding is similar to a findings in a study in Eritrea [15].

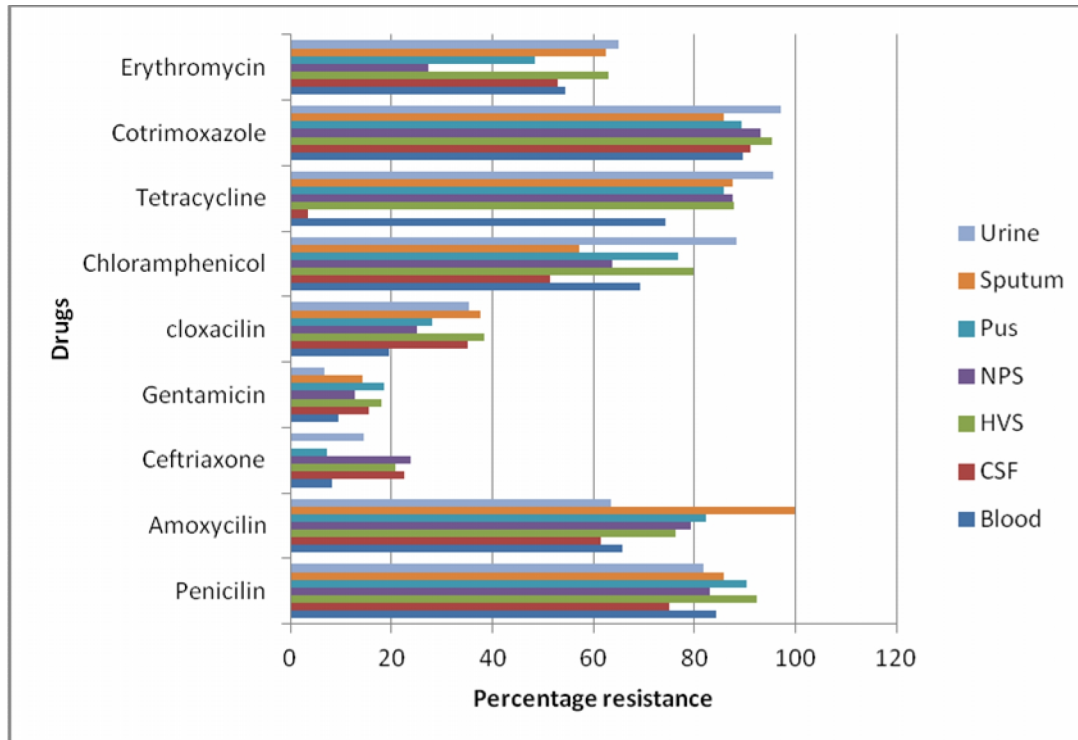


**Fig. 1. Flow Chart of clinical specimens cultured at Mbarara Regional Referral Hospital for the period of 2003-2012**

Over the ten year period there was very high resistance of *S. aureus* to Cotrimoxazole, Tetracycline, Penicillin, Amoxycillin and Chloramphenicol and low resistance to ceftriaxone, Gentamicin and Cloxacillin over the time period. The high resistance of *S. aureus* observed in the present study against Tetracycline, Chloramphenicol, Penicillin and Cotrimoxazole was in agreement with the reports published by some workers [16-18] from Nigeria and Eritrea [15].

This high rate of resistance to commonly used drugs is probably related to the prevailing availability and prescription patterns, use and abuse of the drugs in Mbarara, South western Uganda. Indiscriminate use of antibiotics without prescriptions and the judicious use of antibiotics by health workers in developing countries such as Uganda, have rendered the commonly used antibiotics completely ineffective in the treatment of *S. aureus* infections.

The resistance pattern of the *S. aureus* was the same irrespective of the specimen of origin (Fig. 2). This may indicate that the source of the organism does not influence its response to any particular drug and therefore the same drug can be used to treat a staphylococcal infection from any site of the body



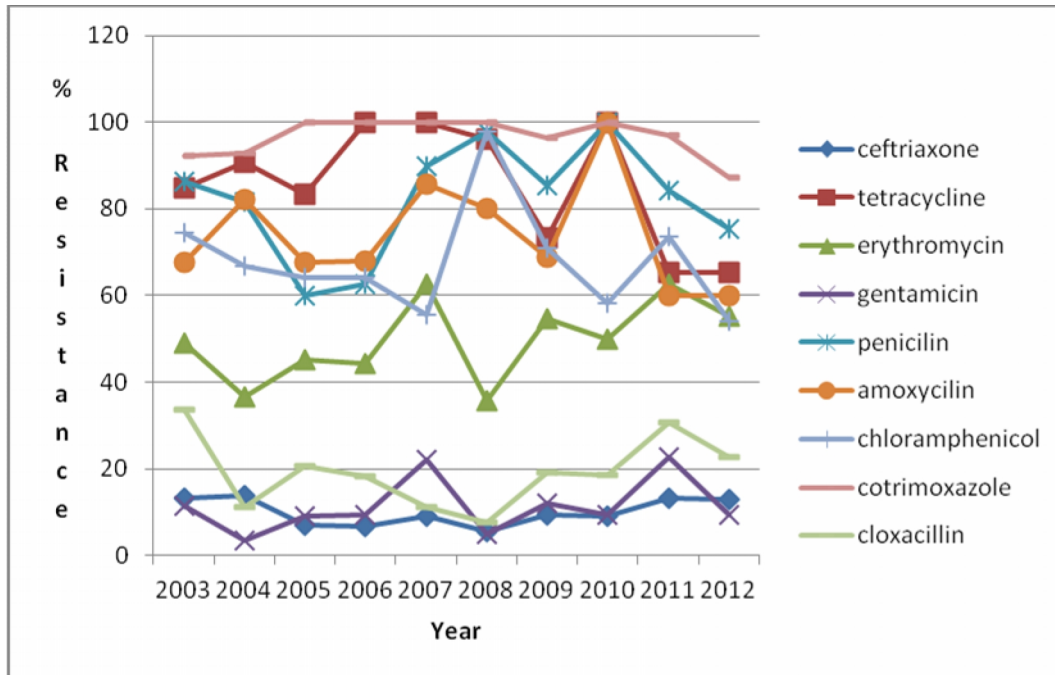
**Fig. 2. Resistance pattern of *Staphylococcus aureus* from different clinical specimens for the period of 2003-2012**

Over the 10 year period, two trends of drug resistance were exhibited by the *S. aureus*. Resistance to Penicillin, Tetracycline, Amoxycilin, and Erythromycin remained high whereas resistance to ceftriaxone, Gentamicin and cloxacilin remained relatively low (Fig. 3).

However resistance to ceftriaxone has been on the rise and could be explained by the injudicious use of this drug in the hospital in the recent past, when it was included on the hospitals' essential drug list. Pharmacy reports at this hospital indicate that there has been a sharp increase in the consumption of Ceftriaxone in the last three years (unpublished data).

We also noticed that since 2010 there was a decrease in the resistance of penicilin, ampicilin, and amoxycilin while resistance to ceftriazone, Gentamicin and cloxacilin has slightly increased and might be related to changing prescription patterns of the medical practioners. The recent surge in the widespread use of ceftriaxone, and gentamicin in the hospital for empirical and prophylactic treatment could explain the increase in resistance levels observed in this study.

Generally, inadequate antimicrobial treatment defined as ineffective treatment of infection was an important factor in emergence of antibiotic resistant bacteria. Factors that contribute to inadequate antimicrobial treatment of hospitalized patients include: prior use of antibiotic, broad spectrum antibiotics, prolonged hospital stay and the presence of invasive medical devices. Other factors include the spread of resistant organisms through overcrowding and inadequate hospital infection control practices [19].



**Fig. 3. Trends of antimicrobial resistance of *Staphylococcus aureus* to commonly used drugs**

The strength of this review is the large sample size, however a prospective surveillance of antimicrobial resistance is highly recommended as a follow of this study. This study provides one-time information about the antibiotic sensitivity which is not sufficient, as the periodic revision of the sensitivity pattern is very essential in order to compare results with similar studies.

#### 4. CONCLUSION

Over the last decade, *S. aureus* isolates showed up to 90% resistance to commonly prescribed oral antibiotics. We recommend regular review of antibiotic resistance patterns to inform the hospitals' guidelines on empirical antibiotic prescription, especially in resource-limited settings where susceptibility testing may not be feasible.

#### ETHICAL APPROVAL

This study was approved by the Institutional Ethics review committee of Mbarara University of Science and technology and the Uganda National Council for Science and Technology.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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