PREVALENCE AND FACTORS ASSOCIATED WITH *STAPHYLOCOCCUS AUREUS* NASAL COLONISATION IN ORTHOPAEDIC PATIENTS

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A dissertation submitted in part fulfilment of the requirements of the University of Nairobi for the award of the Degree of Master of Medicine in Orthopaedic Surgery (M. Med. Orthopaedic Surgery).

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DEDICATION

I dedicate this study to my family for their continued love and support and to the lecturers at the Department of Orthopaedic Surgery, University of Nairobi.

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LIST OF ABBREVIATIONS

BMI	Body Mass Index
CA-MRSA	Community Acquired Methicillin Resistant *Staphylococcus aureus*
CHG	Chlorhexidine gluconate
CLSI	Clinical and Laboratory Standards Institute
HC-MRSA	Healthcare acquired Methicillin Resistant *Staphylococcus aureus*
KNH	Kenyatta National Hospital
MCS	Microscopy, Culture and Sensitivity
MRSA	Methicillin Resistant *Staphylococcus aureus*
MSSA	Methicillin Sensitive *Staphylococcus aureus*
S. aureus	*Staphylococcus aureus*
SCCmec IV	Staphylococcal Cassette Chromosome Mobile Element-Carrying type IV
SHEA	The Society for Healthcare Epidemiology of America
SPSS	Statistical Package for the Social Sciences
SSIs	Surgical site infections
THA	Total Hip Arthroplasty
TKA	Total Knee Arthroplasty
WHO	World Health Organisation

ABSTRACT

Background: *Staphylococcus aureus* (*S. aureus*) is a Gram-positive aerobic bacterium. It can be found as part of a person's normal bacterial flora i.e. these individuals (carriers) are asymptomatically colonised without evidence of staphylococcal disease. *S. aureus* is an important organism in orthopaedic practice as it is the most common cause of orthopaedic infections including surgical site infections (SSIs), osteomyelitis and septic arthritis.
Carriers of *S. aureus* are predisposed to developing invasive staphylococcal infections. This is of concern as *S. aureus* has developed mechanisms of evading the immune system and resisting antimicrobials.
Knowledge of a patient's carrier status before surgery together with interventions to eliminate the carrier state have been shown to reduce post-operative infections by both methicillin sensitive *Staphylococcus aureus* (MSSA) and methicillin resistant *Staphylococcus aureus* (MRSA)

Study Objective: To determine the prevalence and factors associated with colonisation by *Staphylococcus aureus* among patients who have been admitted to the orthopaedic wards at Kenyatta National Hospital (KNH) to undergo surgery and to determine the antibiotic susceptibility of *Staphylococcal aureus* found to be colonizing the anterior nares of patients

Study Design: Cross-sectional study

Study Setting: Kenyatta National Hospital orthopaedic clinics and wards as well as accident and emergency department from 1 June 2019 – 30 September 2019.

Methodology: Consecutive sampling of patients based on the defined inclusion criteria was done until the required sample size was achieved. Nasal swabs were taken from patients at admission for culture and sensitivity. Data concerning comorbid conditions as well as healthcare associated risk factors was collected.
Demographic characteristics were summarized and presented as frequencies and proportions for categorical variables, and as means with standard deviations for continuous variables. The prevalence of nasal colonisation by *Staphylococcus aureus* (both MRSA and MSSA) among orthopaedic patients was analysed and presented as a proportion of the sample size. The antibiotic susceptibility pattern of *Staphylococcus aureus* strains was analysed and presented as frequencies and proportions. The risk factors and socio demographic characteristics were analysed at univariate and multivariate with the use of Chi square tests. Odds ratio as well as 95% confidence intervals were calculated. A p-value < 0.05 was considered significant.

Data Processing: The collected data was analysed using the Statistical Package for the Social Sciences version 25.

Results: The overall prevalence of colonisation by *Staphylococcus aureus* at admission was found to be 24.7% whereas the overall prevalence of colonisation by Methicillin Resistant *Staphylococcus aureus* (MRSA) was found to be 3.03%.

Conclusion: The prevalence of colonisation by *Staphylococcus aureus* is high amongst patients being admitted to orthopaedic wards at Kenyatta National Hospital when compared to previous studies and amongst these are those who are colonised by MRSA. The prevalence of MRSA, its resistance to commonly used antibiotics and the association of colonisation by *Staphylococcus aureus* predisposing to infection call for the need of screening programmes to curtail spread within hospital and community settings.

CHAPTER 1: INTRODUCTION

Staphylococcus aureus is a Gram-positive aerobic coccus that is a human pathogen however it also exists as a skin commensal (1). *S. aureus* is the most frequent organism isolated from surgical sites that get infected after orthopaedic surgery (2–4). Patients who are carriers of methicillin-sensitive *S. aureus* (MSSA) or methicillin-resistant *S. aureus* (MRSA) have a higher likelihood of acquiring staphylococcal infections after undergoing surgery (1).

SSIs due to *S. aureus* in orthopaedic patients are a challenge to treat because *S. aureus* forms a biofilm on implants which complicates the eradication of infection in patients with *S. aureus* SSIs.

In patients who develop *S. aureus* infections bacteria cultured from the site match (by phage typing) those from the nares in 85% of the cases suggesting an endogenous source of infection (5).Kalmeijer et al. identified nasal carriage of *S. aureus* as the only independent risk factor for *S. aureus* SSI after orthopaedic implant surgery (6). Staphylococcal infections after orthopaedic operations are associated with greater mortality rates and increased healthcare expenditure as a result of the need for revision procedures and greater length of stay in hospital (7).

Knowledge of a patient's *S. aureus* carrier status and subsequent decolonisation has been shown to decrease the occurrence of infective complications after orthopaedic surgery with between 56-75% reduction of *S. aureus* SSIs, 29-100% reduction of SSIs due to MRSA and 29-81% reduction in all SSIs (8–10).

CHAPTER 2: LITERATURE REVIEW AND OBJECTIVES

LITERATURE REVIEW

S. aureus is an aerobic Gram-positive bacterium. *S. aureus* is a medically important bacteria that forms part of the human normal flora. Prevalence studies done among different populations show varying carriage rates but on average a third of the population is asymptomatically colonised at any time (1). Various parts of the body may be colonised by *S. aureus* however the anterior nares predominate as the carriage site for *S. aureus*. It is the site from which MRSA and MSSA are most consistently cultured. The groin, pharynx, perineum, and the axillae are other areas that may be colonised by *S. aureus* (11). Molecular typing of bacteria from the nares and other body sites of the same individual has shown that bacteria cultured from the nares are identical to those found in other body sites (5).

Nasal colonisation by *S. aureus* is asymptomatic. These carriers function as a reservoir spreading *S. aureus* to more individuals in the community. At the same time nasal colonisation predisposes the host to Staphylococcal infection (12).

MRSA is a pathogen of increasing medical importance due to its antibiotic resistance. The mecA gene (methicillin resistance gene) on staphylococcal cassette chromosome mobile element-carrying IV (SCCmec type IV) found in MRSA strains confers cross resistance to β-lactam antibiotics. The mecA gene locus encodes for a penicillin-binding protein (PBP2a). MRSA was initially isolated from and confined to healthcare settings however it has become more common in the community. MRSA may be broadly grouped as Community Acquired MRSA (CA-MRSA) or Healthcare Acquired MRSA (HC-MRSA).

CA-MRSA is believed to result when there is transfer of mecA gene to community *Staphylococcus aureus*. HC-MRSA has a larger SCCmec which confers resistance against multiple antibiotics ("superbugs") whereas CA-MRSA has a smaller SCCmec conferring less drug resistance. Almost all CA-MRSA have Panton-Valentine leucocidin (PVL) cytotoxin, the locus of which is found on the mecA gene. CA-MRSA commonly causes soft tissue infections presenting as an abscess or cellulitis frequently in athletes and otherwise healthy young individuals (13).

The prevalence of MRSA in hospital and community settings has been shown to be increasing (14). The increasing prevalence of MRSA is a matter of concern due to the increased healthcare costs associated with treating resistant bacterial infections as well as increased mortality.

PREVALENCE OF STAPHYLOCOCCUS AUREUS CARRIAGE

The general population, healthcare workers and patients can at one time, or another be carriers of *S. aureus*. Different rates of *S. aureus* carriage have been found depending on the population being investigated. Kluytman et al. reviewed carriage rates of different populations and found a mean of 33.2% among the general population (1). However, the range of carriage rates reported in their paper is large and was presumed to be due to differences in the quality of the sampling and of the culture techniques used in these studies. Antri et al. found a carriage rate of 54.7% among healthy adults in Algiers whereas Ateba Ngoa found a carriage rate of 37% amongst a rural population and 21% in a semi urban population in Gabon (15,16).

Kolawole et al. in Nigeria found a carriage rate of 32% among patients on admission to the surgical ward whereas the MRSA carriage rate was 3.6% (17). Egyir in Ghana found a carriage rate of 14% among inpatients in a paediatric and surgical ward with an MRSA carriage rate of 1.4% (18). Joachim et al. found a carriage rate of 34.5% when screening patients on admission to hospital in Tanzania (19). In this study the overall MRSA carriage rate was 8.9%. Aiken et al. found a carriage rate of 8.9 % while doing cross sectional surveys of inpatients at Thika Level 5 hospital (20).

Hospitalization has been found to influence nasal carriage of *S. aureus*. Healthy individuals' nasal mucosa has been found to be predominantly colonised by anaerobic *Actinobacteria* such as *Propionibacterium* and *Corynebacterium spp*. whereas patients were predominantly colonised by *S. aureus* and *S. epidermidis* (21). Lamikanra et al. found that increased length of hospital stay led to higher rates of nasal carriage (22). Increased rates of colonisation among patients is thought to be due to transmission from other patients and healthcare workers as well as contact with contaminated items in the hospital environment.

Hospital wards in developing countries are likely to have increased chances of nosocomial transmission of *S. aureus* due to overcrowding, bed sharing, understaffing, irregular water supply for hand washing, and a lack of training and expertise in infection control (23).

FACTORS ASSOCIATED WITH STAPHYLOCOCCUS AUREUS COLONISATION

Various host factors predispose to nasal colonisation by *S. aureus*. Nasal carriage is more prevalent among HIV infected individuals, diabetics and among obese patients (24,25). Amir et al. in 1995 in a study Kilifi found that HIV positive individuals have a significantly higher carriage rate of antibiotic resistant strains of *S aureus* when compared to HIV negative individuals (27% vs 17%) (26). Other diseases such as atopic dermatitis, Wegener's granulomatosis, skin and soft tissue infections and rheumatoid arthritis have been associated with an increased carriage rate (27–29). Age and households with more than 5 members have also been found to be risk factors (30). Smoking has been found to be protective against colonisation (12).

Liu et al. investigated the influence of sex on nasal carriage found men to have higher bacterial loads, but nasal colonisation rates were the same for men and women (31). A systematic review by Forster et al. found males to have a higher prevalence (32).

Additional risk factors for colonisation by MRSA include previous antibiotic use within the past 3 months, length of hospital stay, recent admission in a hospital or stay at a nursing home within the past year, open wounds and treatment administration by injection (33). Clements et al. also showed that overcrowding and understaffing play a key role in the transmission of MRSA (23). The presence of healthcare workers in the home and degree of education have been found to increase carriage rates of MRSA (30).

MAGNITUDE OF SSIs DUE TO STAPHYLOCOCCUS AUREUS

Surgical site infections are a common but preventable complication of surgery; they constitute approximately 30% of healthcare associated infections (34). *S. aureus* predominates as the cause of SSIs in orthopaedic surgery (2,3). *S. aureus* and *S. epidermidis* are the most common bacteria isolated in cases of prosthetic joint infection (35). *S. aureus* also predominates as the cause of SSI after the use of implants for internal fixation of fractures. A systematic review of surgical site infections in Africa by Ngaroua et al. found an overall high incidence of SSIs in sub Saharan Africa (36). Similar results were found by Bercion et al. in the Central African Republic where they had an overall SSI rate of 18% following orthopaedic surgery with methicillin sensitive *S. aureus* causing the majority of SSIs (37).The French Institute of Public Health Surveillance in 2014 found that 51.9% of orthopaedic SSIs were caused by *S. aureus(38)*. Locally, Ondari et al. found *S. aureus* to cause 50% of infections after Gustilo II open fractures of the tibia after debridement and antibiotic prophylaxis (39). A study by Dinda et al. in 2013 at Aga Khan University Hospital found an SSI incidence rate of 7% with *S. aureus* causing most infections at 30.8% of all SSIs (40).

SSIs in orthopaedics have certain unique aspects due to the use of implants which are foreign bodies. In orthopaedic SSIs by *S. aureus* associated with implants bacteria grow in biofilms on the implant surface making the infection difficult to treat and eradicate as the bacteria within the

biofilm are several hundred times more resistant to the effect of antibiotics due to being in a slow growing state. The biofilm also sequesters the bacteria from the immune system and releases planktonic bacteria that colonise other surfaces of the implant.

Orthopaedic surgeries frequently involve the use of implants which are foreign bodies thus predisposing the host to infection. Host immune cells and antibiotics cannot access the space occupied by the implant in large numbers/quantities because implants lack a micro circulation. In addition, foreign bodies also affect the phagocytic and bactericidal (e.g. generation of superoxide) function of neutrophils (41). Also, neutrophils that activate on foreign bodies release defensins that inactivate other granulocytes in the area (42). Due to this localized immune deficit infection can still develop in the presence of an orthopaedic implant despite antimicrobial prophylaxis as a bacterial load of 10^5 is required in a normal host to cause infection however this is reduced to 100 if a foreign object is present (41).

A retrospective database analysis done by Schmidt on the cost of Staphylococcal surgical infections in France showed that SSIs by *S. aureus* on average added €13,389 in cost per patient as well as leading to 1.4 more additional admissions per year per patient (7). McGarry et al. showed that *Staphylococcus aureus* SSIs among elderly patients were associated with a 5 times greater risk of mortality and 2.5 times increase in length of stay (43). Patients with an SSI secondary to MRSA have a greater than 10-fold risk of mortality with 77% of deaths being directly attributable to the SSI (44).

The low infective dose of *S aureus* required to cause infection in orthopaedic patients in whom implants are inserted as well as the increased morbidity and healthcare costs associated with orthopaedic *S. aureus* SSIs emphasize the need for adequate prevention strategies.

COLONISATION BY STAPHYLOCOCCUS AUREUS AS A RISK FACTOR FOR ORTHOPAEDIC SSI

Identification of preoperative risk factors for SSI and taking steps to mitigate them is an important part of the strategy to prevent SSIs (45). Nasal colonisation by *S. aureus* has long been known to predispose to infection after surgery (6).

S. aureus nasal colonisation is thought to lead to SSI through the induction of bacteraemia following intubation (46). Bacteraemia is thought to occur when there's trauma to an already colonised airway thus allowing the bacteria vascular access. In patients who develop staphylococcal bacteraemia the risk of an implant becoming infected by haematogenous seeding is higher for prosthetic joints (34%) when compared to other orthopaedic implants which get infected 7% of the time there's bacteraemia (47). Alternatively, there can be airborne spread from the patient's anterior nares to the surgical wound contaminating it during the operative procedure (34).

The risk of developing an SSI due to *S aureus* is estimated to be 2-9 times greater in carriers when compared to non-carriers (1,48). Kalmeijer et al. showed that nasal carriage was the only independent risk factor not only for *S. aureus* SSIs but also for SSIs by other bacteria in patients undergoing orthopaedic surgery where implants are to be used (6). Berthelot et al. conducted a prospective multicentre cohort study that showed that *S. aureus* nasal carriage is a risk factor for *S. aureus* SSI in orthopaedic surgery (49). An endogenous source of *S aureus* infection is suggested by the fact that bacteria isolated from infected wounds are identical to those in the nares in 85% of the cases (5).

The Centres for Disease Control and Prevention (CDC) describes "Preoperative nasal colonisation with *S. aureus* as a risk factor for SSI" (45). □

MRSA carriers have a 3-fold greater risk for infection compared to non-carriers (50). When comparing SSI rates in MRSA carriers versus MSSA carriers Kim et al. found MRSA carriers are 4 times more likely to acquire SSIs (51).

BENEFITS OF PREOPERATIVE DETECTION OF STAPHYLOCOCCUS AUREUS IN REDUCING ORTHOPAEDIC SSI

For patients undergoing orthopaedic surgery preoperative screening for colonisation by *S. aureus* (both MRSA and MSSA) and subsequent decolonisation has proved to be effective in decreasing the occurrence of SSIs.

A systematic review by Chen et al. showed a 56-75% reduction of *S. aureus* SSIs, 29-100% reduction of SSIs due to MRSA and 29-81% reduction in all SSIs in trauma and elective orthopaedic surgery when patients were screened preoperatively for *S. aureus* nasal carriage and decolonised (8). Pre-operative screening was also found to be a cost-effective method to reduce SSIs. Kim et al. also showed that screening for *S. aureus* carriage (both MRSA and MSSA) leads to a significant decrease in SSIs (51).
Jeans et al. showed a reduction of infection in cases undergoing arthroplasty when patients were screened preoperatively for colonisation by *S. aureus* (9).
Dancer et al. in 2016 showed that screening for methicillin sensitive *S. aureus* in elective orthopaedic and trauma surgery resulted in decreased staphylococcal infections after surgery (52).

In light of the increased risk posed by colonisation by *S. aureus* various bodies have issued recommendations aimed at reducing SSIs associated with S. aureus. The Society for Healthcare Epidemiology of America (SHEA) recommends screening for MSSA and MRSA for patients set to undergo orthopaedic and cardiothoracic procedures (53).
The Institute for Healthcare Improvement recommends screening for *S. aureus* (both MSSA and MRSA) among patients set to undergo hip or knee arthroplasty (54).
Current World Health Organisation guidelines on prevention of surgical site infections recommend "that patients undergoing cardiothoracic and orthopaedic surgery with known nasal carriage of *S. aureus* should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash" (55). National Health Service (NHS) guidelines recommend mandatory screening for MRSA in all acute and elective admissions to orthopaedic wards as orthopaedics is considered a high risk speciality (i.e. a speciality in which MRSA colonisation carries the greatest risk of infection/poor outcome) (56).

Routine decolonisation of all patients undergoing orthopaedic surgery results in a decrease in SSIs. Bebko et al. studied the effect of routine decolonisation in patients undergoing orthopaedic surgery. For patients undergoing surgery in which implants will be used Bebko et al. found a significant reduction (69.2%) in SSIs due to any cause (57). However, routine decolonisation is linked to the development of mupirocin and chlorhexidine resistant bacteria therefore active screening and selective decolonisation is preferred though it is associated with a higher cost (58,59).

Information on *S. aureus* colonisation status will be helpful in reducing SSIs after surgery. Data on antibiotic susceptibility pattern of isolated *S. aureus* strains will be useful for determining preoperative prophylactic antibiotics as well as influencing choice of empiric antibiotics for orthopaedic patients.

STUDY QUESTION

What is the prevalence and factors associated with *Staphylococcus aureus* nasal colonisation at admission among patients scheduled for orthopaedic surgery at KNH?

STUDY JUSTIFICATION

S. aureus is the most common cause of orthopaedic SSI and nasal colonisation results in increased risk of SSI. Less than ideal conditions locally and in the African setting translate to higher rates of SSI among patients. Orthopaedic SSIs by *S aureus* are difficult to eradicate and result in increased morbidity and mortality and considerable incremental healthcare costs either through increased length of stay or the need for revision surgery thus emphasizing the need to prevent SSIs through the identification of risk factors that may be modified preoperatively.

Results from this study will
1. Provide updated baseline data on the magnitude of *Staphylococcus. aureus* colonisation in orthopaedic patients.
Colonisation rates differ within the African continent and also differ to carriage rates in the west. This is compounded by the fact that rates of carriage of MSSA and MRSA are rising (14) also, increased use of antibiotics by outpatients has resulted in an increased number of patients harbouring antibiotic resistant bacteria. The above emphasize the need for current data on local trends not only on rates of nasal carriage but also on current antibiotic susceptibility trends.

Current practice guidelines such as from the NHS and SHEA recommend screening of all orthopaedic patients for carriage of Staphylococcus aureus on admission for purposes of improving patient outcomes (through reduction of infective complications) as well as infection control (reducing spread to non-colonised individuals within a hospital setting). Knowledge on our burden (prevalence) of asymptomatic colonisation would therefore help to inform on whether policy in mandatory screening is necessary so as to improve patient outcomes and service provision at KNH.

Knowledge of preoperative colonisation status has important implications due to the possibility of reducing orthopaedic SSIs through preoperative decolonisation. Decreased SSIs translate to reduced morbidity and a reduction in healthcare costs.

2. Provide data on the antibiotic susceptibility of colonizing *S. aureus* which could be used to guide treatment of orthopaedic infections as well as guiding prescription of preoperative prophylactic antibiotics for orthopaedic patients. This has the advantage of improving patient care, reducing the development of drug resistant strains and guiding policy on appropriate allocation of resources.

3. Factors identified through the study to be predictive of nasal colonisation may be used to formulate a focused decolonisation protocol thus helping reduce the rates of orthopaedic SSIs. Focused decolonisation protocols are necessary as routine decolonisation of patients has been shown to lead to the development of mupirocin resistant strains of bacteria.

STUDY OBJECTIVES

Broad Objective

To determine the prevalence and factors associated with colonisation by *Staphylococcus aureus* among orthopaedic patients admitted to KNH to undergo orthopaedic surgery.

Specific Objectives

1. To determine the prevalence of nasal colonisation by *Staphylococcus aureus* (both MRSA and MSSA) among orthopaedic patients being admitted for surgery.

2. To determine the antibiotic susceptibility pattern of *Staphylococcus aureus* strains found to be colonizing the anterior nares of patients.

3. To determine the risk factors associated with nasal colonisation by MSSA and MRSA.

CHAPTER 3: MATERIALS AND METHODS

STUDY DESIGN

The study will be a cross sectional study.

STUDY SETTING

This cross-sectional study was conducted at Kenyatta National Hospital Orthopaedic Wards. KNH is a metropolitan, tertiary, teaching and referral hospital situated at Upper Hill area, along Hospital Road about 5km from Nairobi city centre. KNH has a 2000 bed capacity with the orthopaedic wards having a capacity of approximately 300 patients. KNH is a major referral hospital serving East and Central Africa.

STUDY DURATION

1 June 2019 – 30 September 2019.

STUDY POPULATION

Patients being admitted to the orthopaedic wards at Kenyatta National Hospital and are assigned for surgery in which orthopaedic implants are to be used (including fracture fixation devices, arthroplasty, or spine implants).

Inclusion criteria

1.Patients being admitted to the orthopaedic ward for surgery from clinics or casualty.

Exclusion criteria

1. Patients who are currently receiving antibiotics or had been on antibiotics during the preceding two weeks.
2. Patients in whom nasal manipulation is contraindicated.
3. Patients with active MRSA or MSSA infections.
4. Patients with upper respiratory tract infections.
5. Patients less than 18 years.

SAMPLING

All eligible patients were enrolled until the required sample size was obtained.

SAMPLE SIZE

Kenyatta National Hospital has 3 orthopaedic wards that each have a theatre list with approximately 3 patients per day. Going by previous ward records the study envisages a population of 500 patients within the study period (assuming a recruitment success rate of 2 patients per ward per day). The sample size was calculated using Krejcie (60) formula as follows;

$$s = \frac{Z^2(1-\infty/2) \times NP(1-P)}{d^2 (N-1) + Z^2(1-\infty/2) P(1-P)}$$

where;
s = sample size to be determined
Z^2 (1-∞/2) =is the standard error of the mean corresponding to a 95% confidence interval and the corresponding value from a t-table is 1.96.
N = Estimated population size
P =is the expected prevalence of the event to occur. Value of P was 0.3.
d = is the target margin of error which will be 5 % (0.05) to increase precision.

Therefore, the sample size becomes:

$$s = \frac{1.96^2 \times 500 \times 0.3 (1 - 0.3)}{0.05^2 \times 499 + 1.96^2 \times 0.3 \times 0.7}$$

Hence s = 198.

DATA COLLECTION AND ANALYSIS

Patient Recruitment

Patients were recruited into the study within 24 hours of their admission to the orthopaedic wards.

DATA COLLECTION

Following participant recruitment, data was collected from enrolled patients using a questionnaire administered by the interviewer. Names were not recorded instead a study number was assigned. A research assistant was trained on data collection.

PARTICIPANT INTERVIEW AND QUESTIONNAIRE

All enrolled patients were interviewed using a questionnaire, which assessed the following

- Patient biodata and socio demographic information.
- Information on comorbid conditions (Diabetes, HIV)
- Risk factors for colonisation by *Staphylococcus aureus.*

Participants were then examined for wounds (such as abrasions, lacerations, draining sinuses etc.) and signs of soft tissue infection as evidenced by redness or a purulent discharge.

Specimen Collection

Nasal swabs were collected from orthopaedic patients that consented to participate in the study within 24 hours of admission to the orthopaedic ward by well-trained healthcare personnel. Swabs were collected using sterile cotton swabs moistened with sterile water for patient comfort.

Nasal swab collection: adapted from CDC guidelines for collection of specimens (61)

- The swab was removed from its packaging and pre moistened with sterile water.
- The swab was advanced 1-2 centimetres into the anterior nares then gentle external pressure was applied. The swab was then rotated against the nasal septum and anterior nares for 3-5 seconds.
- The procedure was repeated with the same swab for the second nares.
- The swab was then returned to its sleeve, labelled and transported to the laboratory.

The swabs were then inoculated onto sheep blood agar (Oxoid Ltd. Hampshire, UK) within one hour of sample collection. Plates were incubated at 37^0C and examined for growth after 24-48 hours. Isolates were confirmed as *S. aureus* based on colonial morphology, gram staining, coagulase and catalase tests.

Antimicrobial susceptibility testing was done by Kirby Bauer Disc diffusion testing for isolated *S. aureus* strains following clinical and laboratory standards institute guidelines (62). The following standard antibiotic discs (HIMEDIA) were used ciprofloxacin (5µg), clindamycin (2µg), erythromycin (15µg), gentamicin (10µg), cotrimoxazole (25µg), rifampin (5µg), penicillin G (10 units), ceftriaxone (30 µg) and cefuroxime (30 µg).
Isolates were determined to be MRSA on the basis of resistance to oxacillin (1µg) and cefoxitin (30µg).

Microscopy, culture and sensitivity were done at University of Nairobi, Paediatrics Laboratory.

DATA ANALYSIS

Data was entered and analysed using Statistical Package for the Social Sciences (SPSS) version 25. Demographic characteristics were summarized and presented as frequencies and proportions for categorical data, and as means with standard deviations for continuous data. The prevalence of nasal colonisation by *Staphylococcus aureus* (both MRSA and MSSA) among orthopaedic patients was analysed and presented as a proportion of the sample size. The antibiotic susceptibility pattern of *Staphylococcus aureus* strains was analysed and presented as frequencies and proportions. The risk

factors and sociodemographic characteristics were analysed at univariate and multivariate levels with the use of Chi square tests. Odds ratio as well as 95% confidence intervals were calculated. A p-value < 0.05 was considered significant

QUALITY CONTROL

1. Data collection and recording was done by the principal investigator and trained research assistants.
2. The research assistants were adequately trained and supervised.
3. The questionnaire was pretested to improve on clarity.
4. The data form was cross-checked to ensure completeness before the principal investigator and research assistants left the study site.
5. The principal investigator edited the questionnaires daily checking for completeness and storing them safely.
6. Analysis of results was done with the help of a statistician.
7. The Laboratory used was the Paediatrics Laboratory, University of Nairobi. Located within the School of Medicine, University of Nairobi. The lab is subject to external control tests to ensure that results are reliable.

ETHICAL CONSIDERATIONS

WHO International ethical guidelines for biomedical research involving human subjects were followed throughout the study.

Ethical approval was sought prior to commencing the study from the KNH/UON Ethics, Research and Standards Committee and the Department of Orthopaedic Surgery

The purpose of the study was carefully explained to the participants in order to obtain written, informed consent prior to participant enrolment. It was emphasized to patients that participation in the study would be at their own discretion. Patients were also alerted to the fact that refusal to participate or withdrawal from the study at any stage would not affect their treatment or management in any way.

No costs were incurred by the patients. Costs for performing all laboratory procedures were met by the principal investigator.

Participants who were unwilling to divulge their HIV status or who found some of the questions intrusive were free to decline to answer the questions.

Strict confidentiality was observed throughout the period of the study by the participating investigators, research assistants and study institution. Participants were given study identification numbers and no unique personal identifiers will be used.

STUDY LIMITATIONS

1. Patient self-reporting of HIV status. No further probing was done to ascertain the authenticity of the information.
2. Single site swabbing was done. Multisite swabbing has been shown to improve the accuracy of detection of colonisation status by picking up bacteria colonising other sites such as the axilla, groin and perineum.

DELIMITATIONS

1. Samples were taken by qualified personnel.

CHAPTER 4: RESULTS

A. Patient Characteristics

A total of 198 patients were recruited into the study during the study period from 1 June 2019 – 30 September 2019. Of these 167 were male and 31 were female. The male to female ratio was 5.4:1. The mean age was 35, ranging from 18 to 88 years.

Forty-three (21.7%) patients were smokers, eight (4%) were diabetic and 12 (6.1%) were HIV positive. Of the 198 patients 20 (20.1%) had been admitted to a healthcare facility in the past year, 44 had attended a form of outpatient clinic in the past year and 75 (37.9%) had used antibiotics in the preceding 3 months prior to admission. Majority of patients (49%) had attained at least secondary school level education and were of normal BMI.

Table 1 shows a summary of the characteristics (i.e. biodata, social and demographic information, comorbid conditions, risk factors for colonisation by MRSA and MSSA as well as number of patients positive for *S. aureus* carriage) of the study participants by sex.

Table 1: Characteristics of the Study Participants

Characteristic[1]	Males	Females	Total
Population size, *S. aureus* carriage and age			
Number of Participants	167 (84.3)	31 (15.7)	198 (100)
S. aureus carriage	42 (25.1)	7 (22.6)	49 (24.7)
Age, years, mean (range)	34 (18–88)	39(19–68)	35 (18–88)
Education			
Primary	61 (36.5)	10 (32.3)	71 (35.9)
Secondary	82 (49.1)	14 (45.2)	96 (48.4)
Tertiary	24 (14.4)	7 (22.6)	31 (15.7)
BMI			
Underweight	37 (22)	2 (6)	39 (20)
Normal	106 (63)	12 (39)	118 (60)
Overweight	19 (11)	9 (29)	28 (14)
Obese	5 (3)	8 (26)	13 (7)
Risk factors for *S. aureus* (MRSA and MSSA) colonisation			
Smoking	42 (25.1)	1 (3.2)	43 (21.7)
Diabetes	4 (2.4)	4 (12.9)	8 (4)
HIV	6 (3.6)	6 (19.4)	12 (6.1)
Admitted to a healthcare facility in the past one year	16 (9.6)	4 (12.9)	20 (10.1)
Used any antibiotics in the past 3 months	59 (35.3)	16 (51.6)	75 (37.9)
Skin or soft tissue infections in the past one year	12 (7.2)	5 (16.1)	17 (8.6)
Previously admitted to ICU	1 (0.6)	0	1 (0.5)
Open wounds	64 (38.3)	11 (35.5)	75 (37.9)
Outpatient clinic in the past one year	29 (17.4)	15 (48.4)	44 (22.2)
Household members ≤ 4	121 (72.5)	20 (64.5)	141 (71.2)
Household members > 5	46 (27.5)	11 (35.50	57 (28.8)
Soft tissue infection	14 (8.4)	5 (16.1)	19 (9.6)

[1]Unless otherwise indicated, data are no. (%) of participants by gender.

The following table summarises the characteristics of those colonised with MRSA and MSSA.

Table 2: Characteristics of Study Participants with MRSA and MSSA

		Colonised n (%)	
	N	**MRSA**	**MSSA**
Age			
18-30	19	2 (33.3)	17 (39.5)
31-60	29	4 (66.7)	25 (58.1)
>60	1	0 (0.0)	1 (2.3)
Sex			
Male	42	5 (83.3)	37 (86)
Female	7	1 (16.7)	6 (14)
Education			
Primary	19	2 (33.3)	17 (39.5)
Secondary	22	2 (33.3)	20 (46.5)
Tertiary	8	2 (33.3)	6 (14.0)
BMI			
<17.5	4	3 (75.0)	1 (25.0)
17.5 - <20.0	10	8 (80.0)	2 (20.0)
20.0 - <22.5	17	15 (88.2)	2 (11.8)
22.5 - <25.0	5	5 (100.0)	0 (0.0)
25.0 - <27.5	5	4 (80.0)	1 (20.0)
27.5 - <30.0	3	3 (100.0)	0 (0.0)
≥30.0	5	5 (100.0)	0 (0.0)
Risk factors for colonisation			
Smoking			
Yes	13	13 (100.0)	0 (0.0)
No	36	30 (83.3)	6 (16.7)
Diabetes			
Yes	1	1 (100.0)	0 (0.0)
No	48	42 (87.5)	6 (12.5)
HIV			
Yes	2	1 (50.0)	1 (50.0)
No	47	42 (89.4)	5 (10.6)
Admitted to a healthcare facility in the past one year			
Yes	5	5 (100.0)	0 (0.0)
No	44	38 (86.4)	3 (13.6)

Used any antibiotics in the past 3 months			
Yes	20	16 (80.0)	4 (20.0)
No	29	27 (93.1)	2 (6.9)
Skin or soft tissue infections in the past one year			
Yes	3	2 (66.7)	1 (33.3)
No	46	41 (89.1)	5 (10.9)
Previously admitted to ICU			
Yes	0	(0.0)	0 (0.0)
No	49	43 (87.8)	6 (12.2)
Open wound			
Yes	18	16 (88.9)	2 (11.1)
No	31	27 (87.1)	4 (12.9)
Outpatient clinic in the past one year			
Yes	12	8 (66.7)	4 (33.3)
No	37	35 (94.6)	2 (5.4)
Household members			
≤ 4	37	32 (86.5)	5 (13.5)
> 4	12	11 (91.7)	1 (8.3)
Soft tissue infection			
Yes	3	2 (66.7)	1 (33.3)
No	46	41 (89.1)	5 (10.9)

B. Nasal Carriage of *Staphylococcus aureus*

A total of 49/198 patients had *S. aureus* isolated from the nasal swab samples collected on admission to the hospital. Of the 49, 43 (87.8%) were methicillin susceptible *staphylococcus aureus* and 6 were (11.9%) were methicillin resistant *staphylococcus aureus*. The overall prevalence of MRSA among the study participants was 6/198 (3.03%) whereas the overall prevalence of S*taphylococcus aureus* nasal colonisation was 49/198 (24.7%). The mean age for the patients colonised by *S. aureus* was 34.8 (SD=9.7) years, those colonised with MRSA was 32.0 (SD=9.1) years, while those colonised with MSSA was 35.2 (SD=9.8). Majority of those colonised by MSSA had heavy growth of the bacteria whereas those colonised by MRSA predominantly had light growth of bacteria (See Table 3 below).

Of the patients colonised by MRSA one was female and 5 were male. Only one had no risk factors, 4 had previously visited an outpatient clinic and had antibiotics in the past 3 months. None of the patients colonised by MRSA had been admitted in the past year.

Table 3: Prevalence of *S aureus* and Growth levels

	Males	Females	Total
***Total S. aureus* carriage, MSSA & MRSA**			
Number of Participants	167 (53.6)	31 (46.3)	198 (100)
S. aureus carriage total	42 (25.1)	7 (22.6)	49 (24.7)
MSSA	37 (88.1)	6(85.7)	43 (87.8)
MSSA Growth level			
Heavy	26 (70.3)	3 (50)	29 (67.4)
Light	11 (29.7)	3 (50)	14 (32.6)
MRSA	5 (12.2)	1 (14.3)	6 (11.9)
MRSA Growth level			
Heavy	2 (40)	0	2 (33.3)
Light	3 (60)	1 (100)	4 (66.7)

C. Antibiotic Susceptibility Patterns

Five (83.3%) of the MRSA isolates were sensitive to ciprofloxacin, 3 (50%) of MRSA isolates were sensitive to gentamicin and rifampin.

Of the MSSA isolates there was extensive susceptibility to ciprofloxacin (97.7%), ceftriaxone (97.7%), cefuroxime (97.7%), gentamicin (95.3%) and rifampin (90.7%). There was widespread resistance to Penicillin G (93%) and Cotrimoxazole (86%) among the *S. aureus* strains that were isolated.

Table 4 summarises the antibiotic susceptibility patterns of the *S. aureus* strains isolated.

Table 4: *S. aureus* Antibiotic Susceptibility Patterns

	MRSA (N=6)				MSSA (N=43)			
	Susceptible		Resistant		Susceptible		Resistant	
Antibiotics	**Yes**	**Percentage**	**Yes**	**Percentage**	**Yes**	**Percentage**	**Yes**	**Percentage**
Ciprofloxacin	5	83.3	1	16.7	42	97.7	1	2.3
Clindamycin	1	16.7	5	83.3	26	60.5	17	39.5
Erythromycin	0	0.0	6	100.0	9	23.3	34	79.1
Gentamicin	3	50.0	3	50.0	41	95.3	2	4.7
Cotrimoxazole	1	16.7	5	83.3	6	13.9	37	86.0
Rifampin	3	50.0	3	50.0	39	90.7	4	9.3
Penicillin G	0	0.0	6	100.0	3	7.0	40	93.0
Ceftriaxone	0	0.0	6	100.0	42	97.7	1	2.3
Cefuroxime	0	0.0	6	100.0	42	97.7	1	2.3

D. Risk Factors Associated with *Staphylococcus aureus* Colonisation

Univariate and multivariate analysis of risk factors for nasal carriage was done. Statistically significant findings were found on multivariate analysis as pertains to BMI whereby patients who were underweight (BMI <18.5) were less likely to be colonised than obese patients (BMI ≥ 30) (OR 0.2 [95% CI 0.0-0.9]). None of the other risk factors for colonization were found to be significant in the study.

Male patients were slightly more likely to be carriers of *S. aureus* than female patients (OR 1.2 [95% CI 0.5-2.9]). Non-smokers were less likely to be carriers when compared to smokers (OR 0.7 [95% CI 0.7-3.0]). Persons from households with less than 4 persons were also more likely to be colonised compared with persons from houses with more than 4 persons (OR 1.3 [95% CI 0.6 – 2.8]).

In contrast to currently available literature patients who were HIV positive, diabetic, had open wounds or soft tissue infections were less likely to be colonised however these findings did not reach statistical significance.

Patients who had no history of antibiotic use in the prior 3 months or had not visited an outpatient facility in the past year were less likely to be colonised (OR 0.8). There was no effect of prior admission to a healthcare facility (OR 1)

Table 5 below summarises the findings.

Table 5: Univariate and Multivariate Association between Colonisation and Risk Factors

Characteristic	N= 198	Colonization n (%)	Univariate p-value; OR (95% CI)	Multivariate p-value; OR (95% CI)
Age				
18-30	82	19 (23.2)	0.594; 1.8 (0.2 -16.0)	0.909; 1.2 (0.1 - 12.7)
31-60	109	29 (26.6)	0.481; 2.2 (0.3-18.8)	0.785; 1.4 (0.1 - 14.3)
>60	7	1 (14.3)	1.0	1.0
Sex				
Male	167	42 (25.1)	0.761; 1.2 (0.5-2.9)	0.711; 1.2 (0.4 -3.8)
Female	31	7 (22.6)	1.0	1.0
BMI				
<18.5	39	6 (15.4)	0.087; 0.3 (0.1 - 1.2)	0.037; 0.2 (0.0 -0.9)
18.5-24.9	118	30 (25.4)	0.319; 0.5 (0.2 - 1.8)	0.150; 0.3 (0.1 -1.5)
25-29.9	28	8 (28.6)	0.528; 0.6 (0.2 - 2.6)	0.312; 0.4 (0.1 -2.2)
>=30	13	5 (38.5)	1.0	1.0
Household Members				
≤4	141	37 (26.2)	0.445; 1.3 (0.6-2.8)	0.241; 1.6 (0.7 -3.6)
>4	57	12 (21.1)	1.0	1.0
Diabetes				
Yes	8	1 (12.5)	1.0	1.0
No	190	48 (25.3)	0.426; 2.4 (0.3 -19.7)	0.358; 3.3 (0.3 -41.5)
HIV				
Positive	12	2 (16.7)	1.0	1.0
Negative	186	47 (25.3)	0.508; 1.7 (0.4 -8.0)	0.213; 3.2 (0.5 -20.3)
Open wound				
Yes	75	18 (24.0)	1.0	1.0
No	123	31 (25.2)	0.849; 1.1 (0.5 -2.1)	0.678; 1.2 (0.6 -2.4)
Soft tissues infection				
Yes	19	3 (15.8)	1.0	1.0
No	179	46 (25.7)	0.481; 1.6 (0.4 -5.8)	0.406; 1.8 (0.4 -7.5)
Smoking				
Yes	43	13 (30.2)	1.0	1.0
No	155	36 (23.3)	0.348; 0.7 (0.3 -1.5)	0.381; 0.7 (0.3 -1.6)
Education				
Primary	71	19 (26.8)	0.92; 1.1 (0.4 -2.7)	0.849; 1.1 (0.4 -3.1)
Secondary	96	22 (22.9)	0.742; 0.9 (0.3 - 2.2)	0.723; 0.8 (0.3 -2.3)
Tertiary	31	8 (25.8)	1.0	1.0
Admitted to a healthcare facility in the past one year				
Yes	20	5 (25.0)	1.0	1.0
No	178	44 (24.7)	0.978; 1.0 (0.3 -2.9)	0.948; 1 (0.3 -3.5)
Used any antibiotics in the past 3 months				
Yes	75	20 (26.7)	1.0	1.0
No	123	29 (23.6)	0.625; 0.8 (0.4 -1.6)	0.405; 0.7 (0.3 -1.6)
Outpatient clinic in the past one year				
Yes	44	12 (27.3)	1.0	1.0
No	154	37 (24.0)	0.660; 0.8 (0.4 -1.8)	0.633; 0.8 (0.3 -2.1)
Previously admitted to ICU				
Yes	1	0 (0.0)	1.0	1.0
No	197	49 (24.9)	-	-

CHAPTER 5: DISCUSSION

A. Prevalence of *Staphylococcus aureus* Colonisation

The overall prevalence of colonisation by S*taphylococcus aureus* was 24.7% whereas the MRSA prevalence was 3.03%.

The overall carriage rate of 24.7% is in keeping with findings by Kluytman et al. who did a review of *S. aureus* carriage and found a mean carriage rate of 35.7% among patients on admission with a wide range of 10.2 – 85.0% however the difference can be explained by the differences in sampling and culture techniques used in the reviewed studies (1).

The carriage rate is higher compared to that found in some previous studies. Aiken et al. in 2014 reported a 10.1% carriage rate when screening inpatients at Thika Level 5, Nelwan et al. in Indonesia reported a 15.6% carriage rate when screening elective surgery patients whereas Egyir et al. found a 17% carriage rate among inpatients in paediatric and surgical wards in Ghana (18,20,63). The differences may be explained by the fact that Aiken et al used a different sampling technique in which he did repeated ward surveys of the inpatients whereas Egyir et al included paediatric patients in their study which differs from the present study in which we only recruited adult patients.

Joachim et al. in Tanzania found a higher overall nasal carriage rate of 34.5% whereas Kolawale et al. in Nigeria reported a higher carriage rate of 31.8% (17,19). The higher prevalence reported by Joachim et al. could be due to the collection of a second swab 48-72 hours after admission whereas Kolawale et al. utilised PCR (Polymerase Chain Reaction) to identify carriers. Both methods have been shown to increase detection rates of carrier status.

The overall MRSA prevalence matches that of Troillet et al. who found a carriage rate of 2.6% when nasal swabs were taken and 3.1% when nasal and wound swabs were taken for culture and sensitivity at admission (33).

Aiken et al. reported a low proportion of MRSA at 6.9% when compared to the 12% that we got in the current study (20). The difference may be explained by the fact that Aiken et al. used a different sampling technique in which he did repeated ward surveys of the inpatients. On the other hand, Joachim et al. in Tanzania found a MRSA carriage rate of 8.5% (19). The difference in MRSA carriage rates could be explained by the different populations studied, Joachim et al. was studying prevalence at admission among medical patients who are more likely to be chronically ill and therefore more likely to be colonised by MRSA as a result of repeated antibiotic exposure and visits to healthcare facilities which are both risk factors for colonisation by MRSA.

Egyir et al. in Ghana found a MRSA prevalence of 3.6% (18). The difference in results may be explained by the different populations studied as Egyir et al. included paediatric patients.

Kolawale et al. in Nigeria reported MRSA prevalence of 3.7% when testing patients on admission to surgical wards (17). The higher prevalence may be explained by the fact that nasal and cutaneous sites were tested on admission and extra nasal testing has been shown to increase detection rates of the carrier status.

While the MRSA prevalence stands at a 3.1% on admission there remains the possibility of spread of MRSA within the ward to other patients especially with the overcrowding, bed sharing, understaffing and poor infection control adherence sometimes witnessed in orthopaedic wards. Clements et al. showed that overcrowding and understaffing led to failure to control MRSA leading

to increased hospital stay, bed blocking hence worsening overcrowding and leading to a vicious cycle characterized by further infection control failure (23).

The carriage rate of 24.7% also represents an area at which interventions can be targeted so as to reduce orthopaedic surgical site infections through screening of patients at admission to determine their carriage status however, given the time and cost constraints routine decolonisation may be a more practical solution in our setup. Given the low level of mupirocin resistance in *S. aureus* isolates the use of intranasal mupirocin and chlorhexidine body washes preoperatively would help reduce orthopaedic surgical site infections and the extensive costs associated with their treatment (57,64).

B. Antibiotic Susceptibility Patterns

The antibiotic resistance pattern reported in this study shows that MRSA was resistant to a wide number of commonly used antibiotics. When compared to MSSA there was higher resistance to ciprofloxacin, clindamycin, gentamicin and rifampin.

Of the MSSA isolates there was extensive susceptibility to ciprofloxacin (97.7%), ceftriaxone (97.7%), cefuroxime (97.7%), gentamicin (95.3%) and rifampin (90.7%) however there was widespread resistance to penicillin G (93%).

Antibiotic susceptibility patterns for MSSA mirror those of Wangai et al. who looked at prevalence and antimicrobial sensitivity patterns of both MRSA and MSSA from clinical specimens (65). In their study they noted poor susceptibility to penicillin G and cotrimoxazole (17.7 -28.2%) with moderate susceptibility to clindamycin and good susceptibility to gentamicin and rifampin similar to MSSA isolates from this study. Antibiotic susceptibility of MRSA isolates between the two studies was also similar with only rifampin showing slightly higher susceptibility at approximately 80% (65).

Joachim et al reported similar results to those in our study. For MSSA isolates they reported 94% resistance to penicillin G whereas we found 93% resistance. In their study they also found 100% susceptibility to ceftriaxone, 95.5% susceptibility to gentamicin and 97% susceptibility to ciprofloxacin mirroring the 97.7%, 95.3% and 97.7% respective susceptibility we reported in our study (19). For MRSA isolates there was 45.5% resistance to gentamicin closely mirroring the 50% resistance we got in our study however 50% of their MRSA isolates were resistant to ciprofloxacin in contrast to the lower resistance we reported of 16.7% (19).

Aiken et al reported that MSSA isolates obtained were extensively resistant to penicillin and cotrimoxazole with good susceptibility to gentamicin, rifampin and ciprofloxacin similar to findings in our study (20).

Given the susceptibility pattern reported in this study the use of first, second and third generation cephalosporins for preoperative antibiotic prophylaxis as well as for empiric treatment of suspected *S. aureus* infections appears to be a prudent strategy for the vast majority of patients being treated at the hospital. The challenge would be in identifying those colonised or infected by MRSA making targeted screening and culture of clinical specimens important for this subset of the population.

C. Risk Factors Associated with Colonisation by *Staphylococcus aureus*

Statistically significant findings were found on multivariate analysis as pertains to BMI whereby patients who were underweight (BMI <18.5) were less likely to be colonised than obese patients (BMI ≥ 30) (OR 0.2 [95% CI 0.0-0.9]).

The other risk factors for colonisation by MSSA and MRSA did not reach significance. Joachim et

al in a similar study in Tanzania with 258 patients also found no association between risk factors and colonisation. Smoking was found to predispose to colonisation contrary to results by Sivaraman et al. (12). Diabetics, HIV positive patients, patients with soft tissue infections and patients with open wounds were found to be less likely to be colonised contrary to what is reported in the literature (26,28,33). Patients who had no history of antibiotic use in the prior 3 months or had not visited an outpatient facility in the past year were less likely to be colonised. This and the lack of significance of other findings in this study may be due to the smaller sample size and unique characteristics of the cohort i.e. predominantly young adult men with no comorbidities. This may also be due to poor recall on the part of the patients e.g. majority of respondents who said they had antibiotics prior to admission could not tell us which antibiotic they had been using. Additionally some of the risk factors such as diabetes, HIV, prior admission to ICU, admission to a nursing home or taking care of a bedridden patient had a small number of patients and in some cases no patients responding positively possibly contributing to the lack of association as some of these are important risk factors for colonisation by MSSA and MRSA.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

CONCLUSION

1. The prevalence of colonisation by *Staphylococcus aureus* is high amongst patients being admitted to the orthopaedic wards at KNH when compared to previous local studies and amongst these are patients who are already colonised by MRSA. Therefore, surgeons need to bear this in mind when evaluating patients preoperatively so as to maximise patient outcomes as well as have a high degree of suspicion when treating orthopaedic infections as these infections may be caused by antibiotic resistant strains of bacteria.
2. MRSA is resistant to commonly used antibiotics.

RECOMMENDATIONS

1. Routine decolonisation of orthopaedic patients prior to surgery with intranasal mupirocin or nasal povidone iodine and chlorhexidine body washes.

2. Due to the cost and time constraints of performing culture and sensitivity on patients targeted screening of patients for MRSA may be considered especially for patients with a long history of antibiotic use or those with prior exposure to healthcare facilities e.g. several prior admissions.

3. Need for more research to determine if those with MSSA and MRSA have higher infection rates.

DISCLAIMER

I, Dr David Githiomi Mwaura have not received any financial incentives from any party that may benefit from this study. I have no conflicts of interest to declare.

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CHAPTER 8: APPENDICES

APPENDIX I: DATA COLLECTION SHEET

PART 1: DEMOGRAPHIC DATA (To be filled in by Principal Investigator/Research Assistant)
DATE_____

STUDY ID_____

AGE_____

SEX MALE_____ FEMALE_____

BMI_____

PART 2: QUESTIONNAIRE TO BE ADMINISTERED TO STUDY PARTICIPANT

1. What is your level of education?
   Primary_____ Secondary_____ Tertiary_____

2. How many members are there in your household? _____

3. Are you a smoker?
   Yes_____ No_____

4. Do you suffer from any of the listed medical comorbidities?
   Diabetes Yes_____ No_____
   HIV Yes_____ No_____

5. Have you been admitted to a healthcare facility in the past one year?
   Yes_____ No_____

6. Have you attended an outpatient clinic in the past one year?
   Yes_____ No_____

7. Have you used any antibiotics in the past three (3) months?
   Yes_____ No_____

8. Have you had any skin or soft tissue infections in the past one year?
   Yes_____ No_____

9.Have you previously been admitted to ICU?
   Yes_____ No_____

10. Have you previously been admitted to a nursing home?
   Yes_____ No_____

11. Have you cared for a bedridden or previously hospitalized patient (or relative) in the past six (6) months?
   Yes_____ No_____

PART 3: PHYSICAL EXAM FINDINGS

1. Does the patient have any open wounds?

Yes_____ No_____

2. Does the patient have any signs of a soft tissue infection?

Yes_____ No_____

3. Does the patient have any signs of a chronic skin condition?

Yes_____ No_____

PART 3:SAMPLE COLLECTION

Take a nasal swab for MCS and label with participants Study ID

Study ID: _____

PART 4: MCS RESULTS

STUDY ID: _____

1. If culture is positive which bacteria has been grown_____

2. If bacteria grown is *Staphylococcus aureus* is it MSSA or MRSA

MSSA_____ MRSA_____

CULTURE RESULTS

Antimicrobial Agent	Result
Ciprofloxacin	
Clindamycin	
Erythromycin	
Gentamicin	
Cotrimoxazole	
Rifampin	
Penicillin G	
Cefuroxime	
Ceftriaxone	

APPENDIX II: (a) CONSENT FORM

TITLE: PREVALENCE AND FACTORS ASSOCIATED WITH STAPHYLOCOCCUS AUREUS COLONISATION AMONG ORTHOPAEDIC PATIENTS SCHEDULED FOR ELECTIVE SURGERY AT KNH

Principal Investigator: Dr David Githiomi Mwaura, Department of Orthopaedics, University of Nairobi

Introduction

My name is David Githiomi Mwaura, a doctor currently pursuing a postgraduate degree in Orthopaedic Surgery at the University of Nairobi.

I would like to tell you about a study that I am conducting. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear.

When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form.

You should understand the general principles which apply to all participants in a medical research:

i) Your decision to participate is entirely voluntary

ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal

iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No. _____

WHAT IS THE STUDY ABOUT?

I am carrying out a study on the prevalence of *Staphylococcus aureus* colonisation at Kenyatta National Hospital. This will involve me interviewing preoperative orthopaedic patients scheduled to undergo surgery. The purpose of the interview is to find out if you are willing to be enrolled in the study. Participants in this research study will be asked questions about predisposing factors to colonisation (such as medical comorbidities) as well as healthcare associated risk factors for colonisation by *Staphylococcus aureus*. Participants will also be asked to undergo collection of swabs from your nose for bacterial microscopy, culture and sensitivity testing.

There will be approximately 197 participants in this study randomly chosen. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately 10 minutes. The interview will cover topics such as level of education, smoking habits, presence of medical comorbidities, antibiotic use and visits to healthcare facilities.

After the interview has finished, we will collect a sample from your nostril using a swab that will be taken to the lab for microscopy, culture and sensitivity.

We will not require your telephone number or any personal information.

RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

It may be embarrassing for you to have a nasal swab specimen taken. We will do everything we can to ensure that this is done in private. Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews.

You may feel some discomfort during collection of the nasal swab. In case of an injury, illness or complications related to this study, contact the study staff right away at the number provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

ARE THERE ANY BENEFITS BEING IN THIS STUDY

Participation in this research has the benefit of identifying carrier state which is a known risk factor for postoperative infection. If found positive treatment will be offered to eradicate the bacteria.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

Participation in this study will not cost you anything. The cost of the lab tests will be met by me.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: Yes____ No____

I agree to have (define specimen) preserved for later study: Yes____ No_____

Participant printed name: _____

Participant signature / Thumb stamp _____ Date _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name: _____ Date: _____

Signature: _____

Role in the study: _____

For Any Enquiries, please contact:

1. David Githiomi Mwaura

Mobile: **0727234124**

E-mail: **githiomi@gmail.com**

2. Dr E. M. Gakuya

Consultant Orthopaedic and Trauma Surgeon,

Lecturer, Department of Orthopaedic Surgery,

University of Nairobi

E-mail: **kibaka62@gmail.com**

3. Dr. Sitati, F.C.

Consultant Orthopaedic and Trauma Surgeon,

Senior Lecturer Orthopaedic Surgery, University of Nairobi.

Email: **fredsitati@yahoo.com**

4. KNH/UON Ethics and Research Committee

P.O. Box 19676 - 00202

Nairobi

Email: **uonknh_erc@uonbi.ac.ke**

APPENDIX II: (b) FOMU YA IDHINI

FOMU YA IDHINI YA MSHIRIKA KWENYE UTAFITI

Jina langu ni Dkt. David Githiomi Mwaura, mwanafunzi wa shahada ya juu katika Upasuaji wa Mifupa katika chuo kikuu cha Nairobi.

Ninafanya utafiti kugundua idadi ya wagonjwa waliolazwa wanaobeba bacteria aina ya Staphylococcus aureus. Utafiti huu itahusisha kuchukua sampuli kutoka mapua. Sampuli itakayochukuliwa itapimwa kwenye maabara.

Ningependa ushiriki kwa huu utafiti na haki zako zitalindwa, habari utakayotoa au itakayopatikana kukuhusu itakuwa siri wakati wote na utatumika kwa huu utafiti pekee yake.

Ushiriki katika utafiti ni kwa hiari yako. Unaweza kukataa kushiriki katika huu utafiti, na pia unaweza kujitoa kwenye huu utafiti wakati wowote baada ya kupeana idhini yako. Kukataa kushiriki au kujitoa kwenye utafiti baadaye haitabadilisha huduma za afya zenye utapokea.

Nimeelewa kamili kuhusu utafiti na napea idhini yangu kushiriki

Sahihi.....

Tarehe.....

Ninathibitsha ya kwamba nimetoa maelezo sahihi kwa mhusika kuhusu pana ya utafiti na yale yote yaliyomo kwa ustadi, naye mhusika ametoa uamuzi wa kushiriki bila ya kushurutishwa.

Sahihi ya mchunguzi……. Tarehe……

Ukiwa na maswali yeyote kuhusu utafiti huu, wasiliana na:

1. Dr. David Githiomi Mwaura

Mobile number: **0727234124**

E-mail: **githiomi@gmail.com**

2. Dr E. M. Gakuya

Consultant Orthopaedic and Trauma Surgeon,

Senior Lecturer, Department of Orthopaedic Surgery,

University of Nairobi

E-mail: **kibaka62@gmail.com**

3. Dr. F. C. Sitati

Consultant Orthopaedic and Trauma Surgeon,

Senior Lecturer, University of Nairobi.

Email: **fredsitati@yahoo.com**

4. KNH/UON Ethics and Research Committee

College of Health Sciences

P.O. Box 19676-00202

Nairobi

APPENDIX III: TIMEFRAME

ACTIVITY	Nov ‘18 – Jan ‘19	Feb ‘19 – May ‘19	Jun ‘19 -Sep ‘19	Sep ‘19	Oct ‘19
Proposal Development and Presentation					
Submission for Ethical Approval					
Data Collection and Analysis					
Thesis Writing					
Thesis Submission					

APPENDIX IV: KNH-UON ETHICAL RESEARCH COMMITTEE APPROVAL

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KENYATTA NATIONAL HOSPITAL
APPROVED
21 MAY 2019
KNH/UoN-ERC
P. O. BOX 20723 - 00202 NAIROBI

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
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Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/188

21st May, 2019

Dr. David Githiomi Mwaura
Reg. No.H58/75339/2014
Dept.of Orthopaedic Surgery
College of Health Sciences
University of Nairobi

Dear Dr. Mwaura

RESEARCH PROPOSAL: PREVALENCE AND FACTORS ASSOCIATED WITH *STAPYLOCOCCUS AUREUS* COLONIZATION ORTHOPAEDIC PATIENTS (P130/02/2019)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 21st May 2019 – 20th May 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Orthopaedic Surgery, UON
Supervisors: Dr. Gakuya E.M, Dr.Sitati F.C.

APPENDIX V: KNH STUDY REGISTRATION CERTIFICATE

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   DAVID GITHIOMI MWAURA
2. Email address: githiomi@gmail.com Tel No. 0727234124
3. Contact person (if different from PI) N/A
4. Email address: N/A Tel No. N/A
5. Study Title
   PREVALENCE AND FACTORS ASSOCIATED WITH STAPHYLOCOCCUS AUREUS COLONIZATION IN ORTHOPAEDIC PATIENTS
6. Department where the study will be conducted DEPARTMENT OF ORTHOPAEDICS.
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of the KNH Department where the study will be conducted.
   Name: Dr David G. Kinyanjui Signature [signature] Date 16/07/2019
8. Endorsed by KNH Head of Department where study will be conducted.
   Name: Dr. David G. Kinyanjui Signature [signature] Date 16/07/19
9. KNH UoN Ethics Research Committee approved study number P130/02/2019
   (Please attach copy of ERC approval)
10. I DAVID GITHIOMI MWAURA commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Research and Programs.
    Signature [signature] Date 16/7/2019
11. Study Registration number (Dept/Number/Year) Orthopaedics / 22 / 2019
    (To be completed by Research and Programs Department)
12. Research and Program Stamp

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Research and Programs and investigators **must commit** to share results with the hospital.

Version 2: August. 2014