

**CARRIAGE RATE OF METHICILLIN RESISTANT
STAPHYLOCOCCUS AUREUS AMONG HEALTH
CARE WORKERS AT THE KENYATTA NATIONAL
HOSPITAL**

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**A THESIS SUBMITTED IN PART-FULFILMENT OF THE
REQUIREMENT FOR THE AWARD OF THE DEGREE OF MASTER
OF MEDICINE IN INTERNAL MEDICINE, UNIVERSITY OF
NAIROBI.**

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I Dr. Alex Wagucu Mogere declare that this thesis is my original work carried out in partial fulfilment for the requirement of the award of degree in Master of Medicine in Clinical Medicine and therapeutics at the University of Nairobi.I have not submitted the same to any other university or for the award of any other degree or diploma.

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LIST OF ABBREVIATIONS

AKUH -Aga Khan University Hospital

CA - Community associated

CA-MRSA -Community associated methicillin resistant *staphylococcus aureus*

CDC -Centres for Disease Control

CLSI -Clinical Laboratory Standards International

GISA -Glycopeptide-intermediate staphylococcus aureus

HCW -Health care worker

HA - Hospital Associated

HA-MRSA - Hospital acquired methicillin resistant *staphylococcus aureus*

ICU -Intensive Care Unit

KNH -Kenyatta National Hospital

MIC -Minimum Inhibition Concentration

MILST - Multilocus sequence typing

MRSA -Methicillin resistant *staphylococcus aureus*

MSSA -Methicillin sensitive *staphylococcus aureus*

ORSA -Oxacillin resistant *staphylococcus aureus*

PFGE -Pulsed-field gel electrophoresis

PPS -Probability Proportional to size

PVL -Panton-Valentine Leukocidin

S. aureus -*Staphylococcus aureus*

SCC -Staphylococcal chromosome cassette

TMP-SMZ -Trimethoprim Sulfamethaxazole

VISA -Vancomycin Intermediate *staphylococcus aureus*

VRSA -Vancomycin resistant *staphylococcus aureus*

VRE - Vancomycin resistant enterococcus

ABSTRACT

Background: *S.aureus* is associated with many community and hospital acquired infections. Nasal carriage among HCWs is an important source of staphylococci that results in nosocomial infections. Infections caused by Methicillin resistant *S.aureus* are associated with longer hospital stay, prolonged antibiotic administration, greater costs than infections caused by methicillin susceptible *S.aureus*. In hospital settings, drug resistant strains especially MRSA have emerged leading to severe and fatal infections. There's currently no data on carriage of MRSA among HCWs in Kenyan public hospitals.

Objectives: This study sought to determine the prevalence and the risk factors associated with MRSA colonization among HCWs at Kenyatta National Hospital and also the antibiotic susceptibility profile of the isolates.

Design: A cross sectional study

Methodology: The study was conducted on a total of 180 health care HCWs at Kenyatta National hospital's ICU, renal and Burns units and medical ward from 4th February 2015 to 3rd March 2015. Nasal and hand swabs were collected and cultured on Mannitol Salt Agar. Slide coagulase test was then performed, followed by an oxacillin susceptibility test on Mueller Hinton Agar using Kirby-Bauer disc diffusion method.

Results: *S.aureus* was isolated in 40% of HCWs. Nasal and hand carriage was 25% and 15% respectively, while 5.6% had both nasal and hand carriage leaving an overall carriage rate of 34.4%. The *S. aureus* isolates showed high sensitivity to linezolid (98.4%), and gentamycin (96.8%). They showed high resistance to vancomycin (53.2%). Penicillin and ampicillin were the most resistant, (80.6% and 66.1%) respectively. Methicillin resistance was seen in 59.7% of the *S.aureus* isolates, both by the disc diffusion test and by the Oxacillin Resistance Screen Agar (ORSA) test ,but 4.8% of these represented both nasal and hand carriage, therefore, giving an overall carriage of 54.8% of the *S.aureus* isolates. This represented 18.9% of all the HCWs. There was a slightly higher preponderance for MRSA in the females (19.1%). The males had (18.5%). The highest carriage was in the medical ward (29.4%) while the lowest was in the renal unit (8.8%)

Conclusions: There was a high rate of carriage of MRSA carriage among HCWs. Among the 4 units studied the carriage rate was highest in the medical ward. The *S.aureus* were most susceptible to Linezolid. In view of these findings we recommend enhanced periodic training of HCWs on control and prevention of infectious diseases, and also regular monitoring and review of antibiotics in order to ensure appropriate and rational use.

1.0 INTRODUCTION

S.aureus is both a human commensal and a frequent cause of clinically important infections. It is frequently found on the human respiratory tract and on the skin. Strains that are associated with disease often result in infections by producing potent protein toxins, and expressing cell-surface proteins that bind and inactivate antibodies. The emergence of antibiotic-resistant forms of pathogenic *S. aureus* (e.g. MRSA) is a worldwide problem in clinical medicine. *S. aureus* screening, today, is mainly done to identify MRSA carriers. The prevalence of MRSA is still quite low in some parts of the world, such as Northern European countries, but there is a worldwide increase in the number of infections caused by MRSA. Almost 25% of the HCWs are stable nasal carriers, and 30% to 50% of them also possess the bacteria on their hands. HCWs that carry *S. aureus* in their nares can occasionally cause outbreaks of surgical-site infections (1). Most of the invasive *S. aureus* infections are assumed to arise from nasal carriage (2).

Colonized patients and health care workers who are asymptomatic are the major sources of MRSA in the hospital environment, with the latter being more commonly identified as links in the transmission of MRSA between patients. Screening for MRSA carriers among this population is necessary for nosocomial infection control.

Data on carriage of MRSA among medical staff is limited in both public and private hospitals in Kenya. We deemed it of great importance to carry out this study to enable health policy makers develop and implement an effective MRSA control policy in hospitals in Kenya.

1.1 LITERATURE REVIEW

1.1.1 *S. aureus*

S. aureus is a facultative anaerobic gram positive cocci bacterium. It is catalase positive, so is able to convert hydrogen peroxide to water and oxygen. This can be used to distinguish staphylococci from enterococci and streptococci. They are non-motile and non-spore forming.

The nose is the main ecological niche where *S.aureus* resides in human beings, but the determinants of the carrier state are incompletely understood (3). 20% of the human population are estimated to be long-term carriers of *S.aureus* (4) which can be found as part of the normal skin flora and in anterior nares of the nasal passages (4).

S.aureus can cause a range of illnesses that include impetigo, furuncles, cellulitis, folliculitis, carbuncles, scalded skin syndrome, and abscesses, to life-threatening diseases

such as meningitis, pneumonia, toxic shock syndrome, osteomyelitis, endocarditis, bacteremia, and sepsis.

It is still one of the five most common causes of nosocomial infections and is the cause of postsurgical wound infections in many instances. Every year, about 500,000 patients in American hospitals contract a staphylococcal infection (5).

1.1.2 Evolution and antibiotic susceptibility pattern in *S. aureus*

The antibiotic Methicillin was first introduced in 1960 for the treatment of penicillin-resistant microbial infections and a year later, MRSA isolates resistant to all β -lactam antibiotics were isolated (6).

MRSA

Two kinds of MRSA have been described: Hospital-associated MRSA (HA-MRSA) and Community-associated MRSA (CA-MRSA). Naturally occurring strains of MRSA were first reported from England in 1961 (6, 7), shortly after the introduction of semi synthetic penicillins. Within ten years, MRSA was reported in the United States, with 22 such strains isolated from 18 patients at Boston City Hospitals (8). Data gathered between July 2004 and December 2005 by the Active Bacterial Core surveillance network (the laboratory surveillance component of the Emerging Infections Program of the US Centres for Disease Control and Prevention (CDC) showed an estimated rate of invasive MRSA infection (bloodstream or other sterile sites) of 31.8 case per 100,000 population(9).

HA-MRSA and CA-MRSA isolates have been found to be distinct microbiologically, implying that CA-MRSA did not originate from HA isolates that escaped from the hospital setting (10); rather, CA-MRSA seems to have emerged de novo from established CA-MSSA isolates (11). A typing scheme established at the CDC showed that the majority of CA-MRSA infections are caused by 2 pulsed-field gel electrophoresis types (USA300 and USA400), whereas the predominant genotypes endemic in hospitals are USA100 and USA200 (12).

Additionally, the infections caused by HA-MRSA and CA-MRSA are generally different; the CA pathogen is most frequently associated with skin and soft tissue (abscesses, boils, and folliculitis), whereas HA pathogen is more likely to infect the respiratory tract, blood stream, urinary tract, and surgical sites. CA-MRSA is more frequently susceptible to non B-lactam antibiotics (e.g. clindamycin, trimethoprim-sulfamethoxazole, and tetracycline), and also tends to be more aggressive (13)

In another study to determine nasal carriage of MRSA and its antibiotic susceptibility pattern in adult hospitalized patients and medical staff in some hospitals in Cameroon the prevalence of nasal carriage of MRSA in medical staff was 41.3% and 32% for in-patients. The carriage rates of MRSA at the regional hospital, Limbe, Yaoundé University Teaching Hospital and Laquintinie Hospital, Douala were 38%, 37.1% and 32.1% respectively. Those who carried MRSA were 34.2% and 35% for males and females respectively. It was noted that most MRSA strains were highly sensitive to vancomycin and teicoplanin in patients; while in medical personnel, most strains were sensitive to clindamycin. In the medical staff, the highest rate of resistance was recorded with penicillin G, trimethoprim/sulfamethoxazole and amoxicillin/clavulanic acid; while in the in-patients the highest rate of resistance was with gentamicin and erythromycin.

According to a review that looked at staphylococcus isolates from Denmark and UK between 1957 and 1960 (14), all early MRSA strains isolated resembled a large group of the early MSSA blood isolates in phenotypic and genetic properties, including phage group, antibiotype (resistance to penicillin, streptomycin, and tetracycline), pulsed-field gel electrophoresis pattern, and *spaA* type and multilocus sequence type. This strongly suggested that the early MSSA examined here represented the progeny of a strain that served as one of the first *S. aureus* recipients of the methicillin-resistance determinant in Europe.

Vancomycin intermediate *S.aureus*/vancomycin resistant *S.aureus*

Vancomycin used to be an effective antistaphylococcal agent. Not any more, according to the current in vitro and clinical data. The concentration required to inhibit the growth of *S.aureus* is progressively increasing. Current evidence provides little hope that increasing the dose or using it in combination with another antistaphylococcal agent will improve its efficacy. These strategies, however, require further randomized clinical trials to either reject or validate them (15).

Vancomycin-intermediate *S. aureus* (VISA) refers to *S.aureus* that might still respond to large doses of vancomycin. It is also termed glycopeptide-intermediate staphylococcus aureus (GISA), implying resistance to all glycopeptide antibiotics. Vancomycin-resistant *S. aureus* (VRSA) on the other hand refers to strains of *S.aureus* that have become resistant to vancomycin. These are extremely rare, though people with the following conditions are more likely to get VISA/VRSA: Underlying medical conditions (such as diabetes or renal disease), previous infections with methicillin-resistant *S. aureus* (MRSA), recent hospitalizations, use of catheters (e.g. IV lines), recent use of vancomycin or other antibiotics. Detection of VISA

is difficult in the laboratory, and special inquiries about susceptibility testing methods may be needed (28).

Reduced vancomycin susceptibility can occur in *S. aureus* irrespective of background methicillin susceptibility and that development of intermediate vancomycin susceptibility in MSSA may result in increased tolerance to several classes of anti-staphylococcal agents (16). The historical U.S. VRSA case count and geographical information found 13 cases isolated in different states (Centre for Disease Control and Infection). The sources included plantar ulcers, toe wound, urine from a nephrostomy tube, and vaginal swab. Their underlying medical conditions included diabetes, obesity, vascular disease, multiple sclerosis, and hypertension and end stage renal disease.

1.2 Epidemiology of MRSA

The frequency of MRSA infections continues to grow in both hospital and community-associated settings, as a consequence, ironically, of advances in patient care and of its ability to adapt to a changing environment (17).

MRSA first appeared in 1960 (Jevons MP et al., 1963), and since then MRSA associated infections have become widespread in hospitals and intensive care units (ICUs) (19). American National Nosocomial Infection Surveillance (NNIS) System data demonstrated a steady increase in the incidence of nosocomial infections caused by methicillin-resistant *S. aureus* (MRSA) among ICU patients over time. MRSA today accounts for >60% of *S. aureus* isolates in US hospital ICUs (20).

Infection due to *S. aureus* also imposes a high and increasing burden on health care resources (21), as well as increasing morbidity and mortality. MRSA infections kill ~19,000 hospitalized American patients annually; this is similar to the number of deaths due to AIDS, tuberculosis, and viral hepatitis combined (9).

Two well-conducted meta-analyses showed that mortality due to MRSA infection was greater than that due to methicillin-susceptible *S. aureus* (MSSA) infection from the 1980s to 2000 and from 1990 to 2000 (22)

A study was conducted on HCWs at Dessie Referral Hospital, North East Ethiopia to determine nasal carriage rate of MRSA (23). Of the 118 HCWs, 34 (28.8%) carried *S. aureus* of which 15(44.1%) were methicillin resistant. Therefore, 12.7% of all HCWs were identified as MRSA carriers. The carriage of MRSA was particularly high among nurses (21.2%). The highest number of MRSA isolates were from the surgical wards (57.1%)

In a study to characterize MRSA from skin and soft tissue infections in patients in Nairobi, Kenya, it was found that SCCmec 11MRSA and a Panton-Valentine Leukocidin(PVL) strain of MRSA are significant pathogens in patients with skin and soft tissue infections presenting to hospitals in Kenya, and that MRSA cases are prevalent at public health care facilities (24). Of the 60 boil cultures, 39 (65%) grew *S. aureus*, out of which 34 (87.2%) were MRSA. Of the 60 abscess cultures, 14 (23.3%) grew *S. aureus*, of which 10 (71.4%) were MRSA. Of 34 cellulitis cultures, 18 (52.9%) grew *S. aureus*, of which 16 (88.8%) were MRSA. Of 25 ulcer cultures, 11 (44%) grew *S. aureus*, of which nine (81.8%) were MRSA. 69 of 82 *S. aureus* (84.1%) were MRSA, with 52 (75.4%) possessing SCCmec II type and 14 (20.3%) being positive for the PVL gene. It was noted that most MRSA were isolated at public health care facilities serving a poorer section of Nairobi's population, such as those living in informal settlements in urban areas (24).

A cross-sectional study was conducted between July and December 2010 to determine the prevalence of nasal carriage of MRSA among HCWs at the AKUH in Nairobi (25). Nasal swabs were taken from 246 randomly selected HCWs. MRSA was identified using both phenotypic and genotypic methods. The prevalence of MRSA carriage was 0% [95% CI: 0–1.5%] whereas that of MSSA was 18.3% (95% CI: 14.0–23.6%).

The table below summarizes the findings on Carriage of MRSA among HCWs in some studies done in India, Saudi Arabia and a few countries in Africa:

Table 1: Carriage of MRSA among HCWs in some studies across the world

AUTHOR	YEAR	COUNTRY	STUDY DESIGN	PREVALENCE (%)	N
Agumas et al	2013	Ethiopia	Cross sectional	12.7	118
Ahmad S et al	2010	Saudi Arabia	Cross Sectional	8	352
Revathi et al	2010	Kenya	Cross Sectional	0	246
Kumar P et al	2011	India	Cross Sectional	21.4	84
Ahmed MO et al	2012	Libya	Cross sectional	19	569
Gonsu et al	2013	Cameroon	Cross sectional	34.6	295

1.3 Mechanism of antibiotic resistance

Resistance of staphylococcus to penicillin is mediated by a beta-lactamase, penicillinase production: This enzyme cleaves the B-lactam ring of the penicillin molecule, making the antibiotic ineffective. Penicillinase-resistant β -lactam antibiotics, such as methicillin, oxacillin, nafcillin, flucloxacillin, cloxacillin, and dicloxacillin, are able to resist degradation by staphylococcal penicillinase.

Oxacillin resistance (presence of the *mecA* gene responsible for oxacillin resistance) is a specific predictor of resistance to all β -lactam antibiotics including carbapenems (7). Vancomycin is one of the last therapeutic options available for MRSA infections. Therefore, the prevention of staphylococcal infections and reduction of the spread and emergence of MRSA are essential. *S. aureus* (MSSA as well as MRSA) ranks as the second most common cause of hospital-acquired (nosocomial) bloodstream infections. Methicillin resistance is due to the presence of *mecA* genes coding for penicillin binding protein (PBP2A) with a low affinity for β -lactam antibiotics (27).

S. aureus adapts rapidly to the selective pressure of antibiotics, and this has resulted in the emergence and spread of MRSA. *mecA* gene is situated on a mobile genetic element, the Staphylococcal Cassette Chromosome *mec* (SCC*mec*) (29). To date, five SCC*mec* types (I-V) have been identified, and several types of these SCC*mec* types have been described. All SCC*mec* elements carry genes for resistance to beta-lactam antibiotics, as well as genes for the regulation of expression of *mecA*. Additionally, SCC*mec* types II and III carry non beta-lactam antibiotic resistance genes on integrated plasmids and a transposon. Pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST), *spa* typing and SCC*mec* typing have both been used to investigate the epidemiology of MRSA. Several clones have emerged and disseminated worldwide.

In contrast to the multidrug resistance usually seen in HA-MRSA strains, antibiotic resistance in CA-MRSA strains is often limited to β -lactams. The small size of SCC*mec* type IV may preclude its carriage of additional genetic material, in contrast to the characteristic presence of additional genetic material in SCC*mec* type II and SCC*mec* type III (30). This does not, however, preclude chromosomally encoded resistance or the presence of resistance plasmids in strains carrying any of the *mec* types. For instance, some CA-MRSA strains isolated in Western Australia contain a 41.4-kb plasmid encoding resistance to tetracycline and trimethoprim, as well as resistance to mupirocin and cadmium (31). Fluoroquinolone resistance is frequent in CA-MRSA carrying SCC*mec* type IV isolated from homeless youth

in San Francisco (32). Nonetheless, in contrast to HA-MRSA strains, most CA-MRSA isolates remain susceptible to tetracyclines, clindamycin, and trimethoprim-sulfamethoxazole (TMP-SMZ) (33).

Resistance of staphylococcal strains to aminoglycoside antibiotics is now a reality. Mechanisms have evolved to inhibit the aminoglycosides' action, which occurs via protonated amine and/or hydroxyl interactions with the ribosomal RNA of the bacterial 30S ribosomal subunit (34). Currently, there are three main mechanisms of aminoglycoside resistance which are widely accepted: aminoglycoside modifying enzymes, ribosomal mutations, and active efflux of the drug out of the bacteria.

Aminoglycoside-modifying enzymes inactivate the aminoglycoside by covalently attaching either a phosphate, acetyl moiety or nucleotide to either the amine or the alcohol key functional group (or both groups) of the antibiotic. This decreases its ribosomal binding affinity by changing the charge or sterically hindering the antibiotic. Aminoglycoside adenyltransferase 4' IA (*ANT(4')IA*) is the best-characterized aminoglycoside-modifying enzyme in *S.aureus*. It is able to attach an adenylyl moiety to the 4' hydroxyl group of many aminoglycosides, including kanamycin and gentamicin.

The *VanA* gene acquisition mediates the glycopeptide resistance. It originates from the *enterococci* and codes for an enzyme that produces an alternative peptidoglycan to which vancomycin will not bind.

1.4 Risk factors for MRSA

A search of the literature was conducted from January, 1980, to March, 2006, to determine the likelihood of MRSA colonisation and infection in HCWs and to assess their role in MRSA transmission (35). In 127 investigations, the average MRSA carriage rate among 33,318 screened HCW was 4.6%; 5.1% had clinical infections. Risk factors included comorbidities: cutaneous lesions or conditions (e.g., dermatitis, eczema, psoriasis, pemphigus), Sinusitis, rhinitis (chronic, allergic, infectious), chronic otitis externa, earlobe dermatitis, recent urinary tract infection, Cystic fibrosis, other endogenous factors: recent antibiotic use, work-related factors: Work experience (e.g., student HCW, longer duration of service) (36), area of service (e.g., medicine, surgery, renal unit, burns unit, long-term care facilities, decreasing risk from ward to ICU to operating theatre, employment in areas of high patient MRSA prevalence (e.g., patients from high-prevalence countries), Close contact with patients (e.g., dressing changes, wound contact)(37), poor attention to infection control (e.g. poor hand hygiene)(38), high work load(39)

1.5 Determinants of nasal carriage of *S.aureus* / MRSA

Longitudinal studies distinguish at least three kinds of staphylococcus nasal carriage: persistent (20%), intermittent (30%) and non-carriers (50%) (3). Nasal carriage of *S.aureus* may result in infection by this organism. There are several postulated theories on the role of host and bacterial factors in carriage. Some of the likely explanations include variability in host adhesions, immune responses or secretion of antimicrobial molecules. There is also the observation that persistent carriers often carry a single strain whereas intermittent carriers can be colonized with unrelated strain over time, indicating that bacterial factors could also play a role (40).

There are four factors that are important to nasal carriage of *S. aureus*. These include direct nasal contact, adherence to certain nasal receptors, ability to overcome host defences, and finally ability to propagate in the nostrils (3).

The main vector for transmitting *S. aureus* from surfaces to the nasal niche are hands—e.g., nose picking(41). Nasal and hand carriage of *S. aureus* are strongly correlated.

Air borne transmission is another less common mechanism of transmission of *S. aureus* to the nose. It however plays a significant role of dispersal into several other reservoirs from where, via the hands, they can reach the nose. Nasal carriers of *S. aureus* with conditions such as rhinitis will disperse a higher load of *S. aureus* into the environment and may be the source of outbreaks of *S.aureus* infections (42).

Nasal secretions play a critical role in the host's innate defence. These secretions contain lactoferrin, lysozyme, immunoglobulin A and G and antibacterial peptides. Carriers of *S. aureus* may have dysregulation of these components in their nasal secretions (43).

Bacterial interference seems to be a major determinant of the nasal carrier state of *S. aureus*. Occupation of an ecological niche with bacteria seems to prevent occupation by other bacterial strains (44). Cross-inhibition of the expression of various virulence factors by the accessory gene regulator (*agr*) and staphylococcal accessory regulator (*sar*) may be one mechanism by which one strain excludes others from colonising sites including the anterior nares (45). Keratinised epithelial cells are important in the binding *S. aureus*. This was demonstrated by Bibel DJ and his colleagues in 1983.

A meta-analysis showed a clear association between exposure to antibiotics and MRSA isolation. The risk of acquiring MRSA was increased 1-8 times (95% CI) in patients who had taken antibiotics earlier. The relative risk for single classes of antibiotics was 3 for quinolones, 2.9 for glycopeptides, 2.2 for cephalosporins and 1.9 for other *B*-lactams (46)

1.6 Public health burden of MRSA in Africa

Methicillin-resistant *S.aureus* is a global public health problem, that carries with it considerable morbidity and mortality. Infections caused by MRSA are associated with longer hospital stay, prolonged antibiotic administration, and greater costs than infections caused by MSSA (47).

Every year, about 500,000 patients in American hospitals contract a staphylococcal infection (5) and in New York hospitals it was discovered that attributable mortality rate for MRSA is greater than for MSSA (48)

One study sought to assess the prevalence of methicillin-resistance among *S. aureus* isolates in Africa. It included articles published in 2005 or later reporting for the prevalence of MRSA among *S. aureus* clinical isolates. The prevalence of MRSA in most African countries, including Algeria, Ethiopia, Nigeria, Egypt, Ivory Coast and South Africa was less than 50%, although it appears to have gone higher since 2000 in many African countries, except for South Africa.

The prevalence of MRSA in Africa during the last 10 years appears to have increased compared with that before 2000. Tunisia has had the greatest increase in prevalence after 2005 from 12-18% in the earlier years to 41-46% after 2005(49).

1.7 Infection control strategies

Transferring of a known MRSA infected or colonized patient must be notified to the receiving health facility. An increase in the incidence of nosocomial MRSA infection was associated with an increased frequency of transfer of colonized patients from nursing homes and other hospitals (50).

Hand washing, gloving, linen handling and environmental cleaning are some of the preventive measures of infection control for MRSA. Hand washing is the single most important factor in preventing MRSA spread and any skin-to skin contact with a patient must be followed with hand washing. It must also be done between care of different anatomical sites on same patients, before eating and drinking, and before leaving work.

For any contact with a wound, sore, invasive site, or mucous membrane of a patient gloves should be worn. This must happen for all patients regardless of their MRSA status. Use of gowns is also advised in situations where there is possibility of extensive soiling.

MRSA colonized or infected patient should not be put in a room with a patient who is at high risk of contracting MRSA infection e.g. patients with indwelling catheters etc. In a case-control study conducted at a medical intensive care unit (ICU) of a French university hospital

with a 4 % prevalence of MRSA carriage at ICU admission it was discovered that selective screening and isolation of carriers on ICU admission are beneficial in reducing transmission of MRSA compared with no isolation (51).

1.8 Treatment of MRSA

MRSA nasal colonization eradication among HCWs and patients has been a successful control measure though with variability (52). Eradicating MRSA nasal carriage from epidemiologically-implicated healthcare workers has been used on a number of occasions to control outbreaks. Efforts to eradicate MRSA colonization among affected patients has proven difficult. Over 40 different decolonization regimens have been tried in the last 60 years. Of all these, only topical intranasal application of mupirocin ointment has proven to be the most effective. However, intranasal application of mupirocin has limited effectiveness though in eradicating colonization in patients who carry the organism at multiple body sites. In addition, because decolonization of patients has almost always been used concurrently with other control measures, its efficacy has been hard to determine. MRSA is transmitted primarily on the hands of HCWs, therefore, greater emphasis should be given to improving hand hygiene practices among them.

Results of a study to determine the control of spread of MRSA in burns units in Kenya show that nosocomial infections in burns units are due to MRSA (53). 90% of patients admitted in burns units get colonized or infected with MRSA. The strain prolongs the duration of patients in hospitals. The burns degenerate to second and third degree burns, thereby necessitating skin grafting. The environment was found to be contaminated with this strain with some members of staff acquiring chronic infections of the throat. Minocycline was found to be efficacious in treating the infected members of staff. Cleaning this environment with Sodium dichloroisocyanurate (precepts)/Sodium hypochlorite (JIK) reduced the mechanical transmission of bacteria in the units drastically. There was significant reduction in the patient length of hospital stay. This showed that MRSA which is spread in government and private hospitals can cheaply be controlled by the proper use of disinfectants, antiseptics, and use of effective antibiotics when necessary.

In a study conducted in Cameroon most MRSA strains identified were very sensitive to vancomycin and teicoplanin in patients; while in medical staff, most strains were sensitive to clindamycin. The highest rate of resistance in medical staff was recorded with penicillin G, trimethoprim/sulfamethoxazole and amoxicillin/clavulanic acid; while in hospitalized patients, gentamicin and erythromycin had the highest rate of resistance (26).

Antibiotics available for the treatment of MRSA Infection

a) Vancomycin

Vancomycin therapy has been associated with less clinical response and longer duration of MSSA bacteremia when compared with beta-lactam antibiotics. In patients who have endocarditis it has been associated with more frequent complications (32). Failure of vancomycin therapy may be observed in the treatment of patients with bacteremia due to strains of MRSA that have MICs of vancomycin well within the range considered susceptible (54). The appearance of vancomycin-intermediate *S. aureus* and vancomycin-resistant *S. aureus* is a great challenge (55).

b) Linezolid.

Linezolid and vancomycin produced the same results in hospitalized patients with MRSA infections at various anatomic sites in a randomized, open-label trial [56], as well as in the treatment of skin and skin-structure infections due to gram-positive organisms. Linezolid was superior to vancomycin in the treatment of hospital-acquired pneumonia due to MRSA according to a retrospective subset analysis of 2 prospective randomized clinical trials [57]. Linezolid is an effective agent whose use has been limited by its cost.

c) Tetracyclines.

Minocycline was found to have bactericidal activity similar to that of vancomycin against a single strain of MRSA in an animal model of endocarditis [58]. Of 14 patients with MRSA infection who were treated with doxycycline or minocycline, either alone or in combination with rifampin, 3 (21%) experienced treatment failure (59).

d) Quinupristin/dalfopristin.

This drug combination is bactericidal against *S. aureus*, although in the presence of constitutive expression of macrolide-lincosamide-streptogramin resistance, it is only bacteriostatic [60]. Patients with nosocomial MRSA pneumonia who received quinupristin/dalfopristin had a clinical response rate of 19.4%, compared with 40% in vancomycin recipients according to a randomized trial [61].

e) Fluoroquinolones.

Fluoroquinolone use is linked to an increased risk of nosocomial acquisition of MRSA (but not of MSSA) [62]. The fluoroquinolones with C8 substitutions, eg gatifloxacin and moxifloxacin, appear to be more potent against *S. aureus* than are older drugs of this class, and they may be less likely to select resistant mutants, an effect that may be enhanced by adding rifampin [63].

f) TMP-SMZ.

A randomized trial of treatment of *S. aureus* infections, 47% of which were due to MRSA, found that therapy with TMP-SMZ was inferior to treatment with vancomycin [64]. An extensive literature review, however, concluded that TMP-SMZ “may be effective therapy for infections due to low bacterial burdens of susceptible strains of *S. aureus*” (65).

g) Clindamycin.

Invasive CA-MRSA infections in children have responded effectively to clindamycin [66].

h) Rifampin.

Rifampin will select resistant mutants from among both MSSA and MRSA strains, but using rifampin together with a second active drug may curtail this [67].

Systemic antibiotic therapy choice

For some infections that require parenteral therapy and are due to MRSA strains that are multi drug resistant, the treatment choices may be restricted to vancomycin, daptomycin, linezolid, and quinupristin/dalfopristin therapy. The potential superiority of linezolid therapy over vancomycin therapy in treating nosocomial infection pneumonia due to MRSA has been noted (57). Daptomycin can't be used in the treatment of pneumonia (76). The bacteriostatic activity of linezolid may prove to limit its effectiveness in circumstances in which bactericidal activity is required (56).

1.9 Management of nasal carriage of MRSA

In a study by Hill RL et al in 1988, 40 patients and 32 HCWs who were stable methicillin-resistant *S. aureus* nasal carriers received 2% mupirocin to the anterior nares over a five day period. Within 48 hours of treatment nasal carriage was eliminated in 100% of the stable

nasal MRSA carriers. It was also noted that immediately after the course of treatment the number of patients with MRSA in wounds reduced from 16 to 7.

A systematic review in 2009 by Heidi S.M et al found that short term (4-7 days) topical nasal application of mupirocin is the most effective treatment modality for eradication of MRSA, with a success rate of 90% one week after treatment and 60% after a longer period of follow up (14-365 days) (68)

1.10 STUDY JUSTIFICATION

MRSA is associated with high levels of morbidity and mortality, hence the need for screening and treating the bacteria. No accurate and systematic studies on carriage of *S.aureus*/MRSA have been undertaken at KNH. Findings of the study will inform health policy makers on strategies to be employed to reduce colonization and transmission of MRSA.

2.0 RESEARCH QUESTION

What is the burden of colonization with *S.aureus*/MRSA in HCWs at KNH?

2.1 OBJECTIVES

2.1.1 Broad objective

1. To determine the prevalence of MRSA colonization among HCWs at KNH.

2.1.2 Specific objectives

1. To determine the nasal and hand carriage of MRSA among HCWs at KNH
2. To determine the antibiotic susceptibility profile of the isolates.
3. To determine MRSA carriage rate among HCWs at KNH.

2.3.3 Secondary objective

1. Identify the risk factors associated with MRSA colonization. These were : use of gloves while handling patients, hand cleaning habits, length of work at the different units, co-morbidities such as cutaneous lesions, sinusitis, rhinitis, recent urinary tract infection, area of service : renal unit, burns unit, medicine or ICU.

3.0 METHODOLOGY

3.1 Study design

This was a cross sectional study.

3.2 Study site

The study was conducted at Kenyatta National hospital, which is the largest referral hospital in the Republic of Kenya. The facility is divided into several units comprising of Acute and Emergency, surgical, laboratories, obstetric and gynaecological, medical and paediatric, oncology, Radiology, Physiotherapy, Burns, ICU and renal units. It has 50 wards, 22-outpatient clinics, 24 theatre's (16 specialised), over 30,000 daily public traffic.

The ICU, burns unit, renal unit and one medical ward were studied. The ICU, burns and renal units are associated with the highest burden of staphylococcal infections, particularly MRSA. One medical ward, among the six medical wards in Kenyatta, was included as a low risk area. It represented all the medical wards as they all share similar characteristics of the staffing levels as well as the kind of patients they handle. This inclusion was important in drawing comparisons between low and high risk areas.

3.3 Study Population

The study population consisted of HCWs in the renal ward, burns unit, the ICU and one medical ward (Ward 8B).

3.4 Case Selection

3.4.1 Case definition

HCW attending to patients at the Kenyatta National Hospital's critical care, Burns and Renal units and a medical ward, found to harbour *S.aureus*, that is resistant to Methicillin

3.4.2 Definition of MRSA

MRSA was defined as an isolate of *S.aureus* screened for oxacillin-resistance by 24 hour incubation on oxacillin screen agar, resulting in a colony inhibition zone under 11mm.

3.5 Inclusion/Exclusion criteria

3.5.1 Inclusion Criteria

1. All HCWs attending to patients in ICU, Renal ward, Burns unit
And one medical ward
2. HCWs who gave informed recent written consent

3.5.2 Exclusion Criteria

1. Recent use of antibiotics by health care workers (within 1 week of collection of the swabs).
2. Presence of nasal pathology/deformity in the HCWs

3.6 Sample size calculation

Daniel, 1999

$$n = \frac{Z^2 \times P(1-P)}{d^2}$$

– Sample size

Z – 1.96 (95% confidence interval)

P – Estimated prevalence of MRSA= 12.7 % (from a similar study at Dessie Referral Hospital, Ethiopia)

d – Margin of error (precision error) = ±5%

Substituting into the formula,

n = 170

3.7 Sampling frame and sampling procedure

Stratified sampling procedure was used to select patients into the study as shown in table 2. The four units of interest that include the burns, renal, the critical care and medical ward units formed strata for sampling. Probability proportional to size (PPS) was used to select patients in each stratum. Sampling frame was created from the list of HCWs working in the unit as shown in the table below. In each stratum, HCWs were recruited consecutively into the study based on their availability.

Table 2: Sampling Frame

Unit	Number of healthcare workers		
	Total	Ratio	Sample
Renal	62	1.5	54
ICU	63	1.5	55
Burns	35	1	31
Medical ward 8b	35	1	31
Total	195	5	170

3.8 Recruitment and consenting procedure

The ward in charge was informed about the nature and intent of the study. HCWs in the units were then provided with the study details/information. Those who agreed to the study signed an informed written consent after which they were enrolled into the study. The study participants were consented by the principal investigator and the research assistant. During data collection, the names and other personal identifiers were not used in the data collection tools but study numbers were assigned. The principal investigator maintained a log book separate from the data collection tools which contained personal identifiers as well as the study numbers for the participants. This log book was useful in counter-checking to avoid re-sampling of study participants in the units.

3.9 Data collection

3.9.1 Clinical methods

A study proforma which included demographic data, training on infection control practices, length at work station, hand washing habit, presence of co-morbidities, and use of gloves on patients, were used.

3.9.2 Laboratory Methods

3.9.2.1 Specimen collection and processing

The principal investigator and a trained research assistant explained in detail what nasal and hand swabs are and how to collect them. Swabs were obtained using sterile cotton swabs previously moistened with 2-3 drops of normal saline.

Nasal swabs were obtained by rolling at the entrance of both sides of the nose, using same swab for both nostrils while hand swabs were taken from the palm and web spaces within at least 30 minutes of washing hands. The bottles were labeled with unique numbers, date and time. Swabs obtained were sent to the lab in a cold chain within 2 hours and were processed within 24hours.

3.9.3.2 Isolation and Identification of *S.aureus*

Nasal and hand swabs were streaked in Blood agar after primary enrichment on nutrient broth for 24hrs at 37°C. Verification of *S.aureus* was by characteristic phenotypical growth on Blood agar plate, gram stain, and positive catalase reaction and coagulase reaction. Suspected colonies were incubated on Mannitol Salt Agar (MSA) plates. Isolates were verified by Analytical Profile Index (API).

3.9.3.3 Antibiotic Susceptibility testing

Suspected colonies were purified for Antibiotics susceptibility testing .This was done using the standardized Kirby-Bauer disc diffusion method (recommended by CLSI). A filter paper disk impregnated with antibiotics was placed on Mueller-Hinton agar (MHA).

3.9.3.4 Detection of MRSA

Identified isolates of *S.aureus* were screened for oxacillin-resistance by 24 hr incubation on Oxacilin Screen Agar. Colonies with an inhibition zone of under 11mm were read as “methicillin” resistant

3.10 Definition of study variables

Independent study variables

Co-morbidities

Co-morbidities referred to co-existing medical conditions affecting the skin, the ear, nose and throat, such as rhinosinusitis, chronic otitis media, eczema,

Department

Department referred to the station of work. They were the critical care unit, the medical ward, the renal unit and the burns unit.

Designation

Study participants were the different cadres of HCWs working at the four study areas of KNH

Working Hours

Working hours were classified as either day shift, night shift or both

Length of Service

Since the different units have different cadres of HCWs who work in those units for periods not longer than one month, the length of service at the units were captured and truncated as follows: Days 0-7,8-15,16-23,>24

Hand Hygiene habits

Study participants were classified as using or not using gloves after handling patients, washing hands with water only or with both soap and water after attending to patients.

3.11 QUALITY ASSURANCE

The principal investigator had been trained by the supervisors on questionnaire administration.

He, together with the research assistant was trained on sample labelling, collection, storage and transportation. All laboratory personnel had training on Good Laboratory Practice and Good Clinical Practice. Standard operating procedures of UON/KNH were adhered to, especially those pertaining to labelling of specimen containers, specimen collection, transportation, analysis and posting of results. All reagents were prepared in accordance with standard operating procedures (SOPs) used at UON/KNH. Equipment operation will be done according to manufacturer's instructions.

3.12 ETHICAL CONSIDERATIONS

1. The study was conducted after approval by the Department of Clinical Medicine and Therapeutics, University of Nairobi, and Kenyatta National Hospital Scientific Committee.
2. The participants were recruited on a voluntary basis and could withdraw at any time.
3. The cotton wool swab to be used in obtaining the samples was moistened with sterile distilled water to reduce discomfort/annoyance.
4. Results were conveyed to the participants and anyone found to harbor *S. aureus*/MRSA was referred to a physician for decolonization and/or treatment.
5. Written informed consent was obtained from each individual participant prior to enrolment in the study.
6. Data sheets contained only HCW's study information and numbers were provided in each sheet
7. MRSA carriage or infection was considered an occupational hazard, thereby abating negative career consequences.

3.13 DATA MANAGEMENT AND ANALYSIS

Data collected in questionnaires were entered and managed in Microsoft Access database. Data analysis was conducted using SPSS 21.0. The study population characteristics were summarized using descriptive statistics where age was presented in ranges while gender, marital status and level of training were presented as proportions. Prevalence of MRSA in HCWs was calculated and presented as a proportion with 95% confidence interval. Also, the MRSA carrier rate and antibiotic susceptibility was presented as proportions with 95% CI.

The risk factors of MRSA colonization were established through associations between prevalence and other selected factors. Associations with categorical data were done using Chi square/ Fisher's exact test and comparison of means was performed using Student's t test. All the statistical tests were performed at 5% level of significance.

4.0 STUDY RESULTS

4.1 Recruitment of Health care workers

One hundred and ninety HCW were selected by stratified sampling procedure. As shown in the flow chart below two were excluded because of nasal pathologies, a further one due to prior antibiotic use, seven declined to consent .One hundred and eighty HCW were studied.

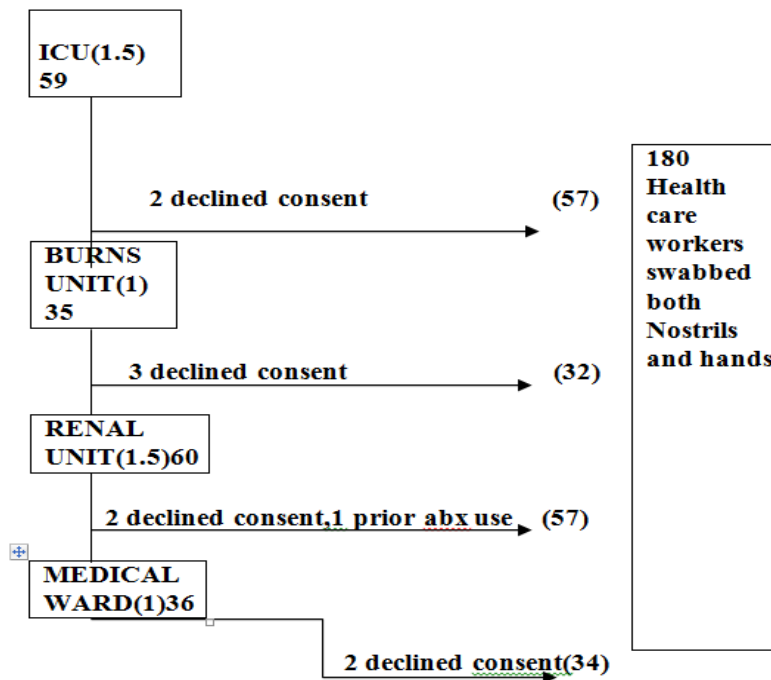


Figure 1: Recruitment of health care workers flow Chart

4.2 Socio demographic characteristics of the HCWs

Out of the 180 HCWs who were screened for MRSA, 115(63.9%) were females and 65 (36.1%) were males as depicted in table 3. Their age ranged between 20 and 59 years, with most (40.0%) being in the 30-39 age group. Ninety eight (54.4%) were nurses, 11(6.1%) were medical specialists, 30(16.7%) were registrars, 3(1.7%) were medical officer interns, 4(2.2%) were clinical officers and 34(18.9%) were physiotherapists, nutritionists or porters (others).

Table 3. Socio-demographic characteristics of the HCWs recruited (n=180).

Variable	Frequency (%)
Unit	
ICU	57 (31.7)
Burns unit	32 (17.8)
Renal unit	57 (31.7)
Medical ward	34 (18.9)
Age	
20-29	40 (22.2)
30-39	72 (40.0)
40-49	48 (26.7)
50-59	20 (11.1)
Gender	
Male	65 (36.1)
Female	115 (63.9)
Cadre of HCWs	
Doctors	44(24.4)
Clinical officer	4 (2.2)
Nurse	98 (54.4)
Other	34 (18.9)
Level of training	
Masters	19 (10.6)
Bachelors	67 (37.2)
Diploma	77 (42.8)
Certificate	11 (6.1)
Other	6 (3.3)

4.3 Rate of Isolation of *S.aureus* and MRSA

The number of HCWs who carried *S.aureus* in the nostrils were 45(25%), while 27(15%) carried it in the hands. Those who carried it in both the hand and the nose were 10(13.9%). Therefore, the overall carrier rate for *S.aureus* was 34.4%(62/180) .The overall MRSA positivity rate was 34(18.9%) with 17(9.4%) and 20(11.1%) nasal and hand carriage rates respectively, while 3(1.6%) had both nasal and hand carriage as shown in table 4. Of these 12(18.5%) were males and 22(19.1%) were females.

Table 4: Prevalence of *S.aureus* and MRSA

Variable	Overall		Nose		Hand	
	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
<i>S. aureus</i>						
Present	62 (34.4)	27.2, 41.7	45 (25.0)	18.9, 31.7	27 (15.0)	9.4, 20.5
Absent	118 (65.6)		135 (75.0)		153 (85.0)	
MRSA						
Present	34 (18.9)	13.3, 24.4	17 (9.4)	5.6, 13.9	20 (11.1)	6.7, 16.1
Absent	146 (81.1)		163 (80.6)		160 (88.9)	

4.4 Antibiotic susceptibility of the *S.aureus* isolated

The antibiotic susceptibility of the *S.aureus* isolated was determined using various antibiotics as shown in table 5 below. Linezolid had the highest sensitivity at 98.4% while penicillin had the lowest at 19.4%. The overall oxacillin (methicillin) resistance was 18.9%. The proportion of MRSA isolates from the nose and the hands were 9.4% and 11.1% respectively. Vancomycin showed unexpected resistance of 53.2%. As shown in table 8 the renal unit recorded the highest rate of vancomycin resistance at 81.8%, followed by Burns unit at 57.1%. The medical ward recorded the least resistance at 41.2% of all isolates.

Table 5: Antibiotic susceptibility tests for *S.aureus*

Variable	Overall (n=62) n (%)	Nose (n=45) n (%)	Hand (n=27) n (%)
Sulfamethoxazole			
Sensitive	33 (53.2)	28 (62.2)	11 (40.7)
Resistant	29 (46.8)	17 (37.8)	16 (59.3)
Gentamycin			
Sensitive	60 (96.8)	45 (100.0)	25 (92.6)
Resistant	2 (3.2)	0	2 (7.4)
Linezolid			
Sensitive	61 (98.4)	45 (100.0)	26 (96.3)
Resistant	1 (1.6)	0	1 (3.7)
Ciprofloxacin			
Sensitive	48 (77.4)	36 (80.0)	20 (74.1)
Resistant	14 (22.6)	9 (20.0)	7 (25.9)
Erythromycin			
Sensitive	30 (48.4)	27 (60.0)	12 (44.4)
Resistant	32 (51.6)	18 (40.0)	15 (55.6)
Tetracycline			
Sensitive	40 (64.5)	34 (75.6)	14 (51.9)
Resistant	22 (35.5)	11 (24.4)	13 (48.1)
Vancomycin			
Sensitive	29 (46.8)	18 (40.0)	17 (63.0)
Resistant	33 (53.2)	27 (60.0)	10 (37.0)
Ampicillin			
Sensitive	21 (33.9)	16 (35.6)	10 (37.0)
Resistant	41 (66.1)	29 (64.4)	17 (63.0)
Penicillin			
Sensitive	12 (19.4)	7 (15.6)	9 (33.3)
Resistant	50 (66.1)	38 (84.4)	18 (66.7)
Oxacillin			
Sensitive	146(81.1)	163(80.6)	160(88.9)
Resistant	34(18.9)	17(9.4)	20(11.1)

Table 6: The rate of vancomycin resistance across the different departments

Variable	Vancomycin		P value
	Resistant n (%)	Sensitive n (%)	
Unit			
ICU	9 (45.0)	11 (55.0)	0.166
Burns unit	8 (57.1)	6 (42.9)	
Renal unit	9 (81.8)	2 (18.2)	
Medical ward	7 (41.2)	10 (58.8)	

4.5 Distribution of MRSA Isolates among the different cadre of HCWs

The highest carrier rate was among the doctors at 27.9% while the lowest was among the nurses at 16.3%. The clinical officers recorded 0 % carriage. The other category had 17.6% as depicted in table 7 below.

Table 7. Distribution of MRSA isolates among the different cadre of HCW

Cadre of HCW	MRSA present	P value
Doctors	12(27.9)	0.555
Clinical officer	0 (0.0)	
Nurse	16 (16.3)	
Other	6 (17.6)	

4.6 Risk factors associated with MRSA carriage during the study period

Several risk factors associated with MRSA carriage were assessed as shown in table 8, but none achieved statistical significance except working at the different units($p=0.044$). The medical ward had the highest carriage rate of 29.4%, while the renal ward had the lowest, 8.8%. HCWs in the age group 30-39 years had the highest carrier rate of 22.2%, followed by age group 50-59 years 20%. The lowest carrier rate was in the age group 40-49 years at 14.6%.

Female HCWs had a slightly more carriage, at 19.1% compared to their male counterparts at 18.5%.

HCWs with low (water only), moderate (soap and water) and high (sanitizer) sterilization score had carrier rate of 20%, 18.6% and 17.6% respectively. But these were statistically insignificant.

Table 8: Risk factors associated with MRSA carriage during the study period

Variable	MRSA		P value
	Present n (%)	Absent n (%)	
Unit			
ICU	10 (17.5)	47 (82.5)	0.044
Burns unit	9 (28.1)	23 (71.9)	
Renal unit	5 (8.8)	52 (91.2)	
Medical ward	10 (29.4)	24 (70.6)	
Cadre of HCW			
Medical specialist	3 (27.3)	8 (72.7)	0.555
Registrar	8 (26.7)	22 (73.3)	
Medical officer intern	1 (33.3)	2 (66.7)	
Clinical officer	0 (0.0)	4 (100.0)	
Nurse	16 (16.3)	82 (83.7)	
Other	6 (17.6)	28 (82.4)	
Age			
20-29	7 (17.5)	33 (82.5)	0.773
30-39	16 (22.2)	56 (77.8)	
40-49	7 (14.6)	41 (85.4)	
50-59	4 (20.0)	16 (80.0)	
Gender			
Male	12 (18.5)	53 (81.5)	0.912
Female	22 (19.1)	93 (80.9)	
Level of training			
Masters	4 (21.1)	15 (78.9)	0.184
Bachelors	13 (19.4)	54 (80.6)	
Diploma	11 (14.3)	66 (85.7)	
Certificate	5 (45.5)	6 (54.5)	
Other	1 (16.7)	5 (83.3)	
Using gloves while handling a patient			
Yes	32 (18.3)	143 (81.7)	0.239
No	2 (40.0)	3 (60.0)	
Wearing a different pair of gloves while handling a different patient			
Yes	34 (19.7)	139 (80.3)	0.350
No	0 (0.0)	7 (100.0)	
Hands sterilization score			
High*	6 (17.6)	28 (82.4)	0.957
Moderate*	16 (18.6)	70 (81.4)	
Low*	12 (20.0)	48 (80.0)	

**High sterilization score (always using sanitizers);* Moderate (always using water/soap or plus sanitizers sometimes) *Low (always using water only or water/soap sometimes or sanitizers sometimes)*

4.7 Training in prevention and control of infectious diseases

4.7.1 Number of HCWs trained in prevention and control of infectious diseases

A total of one hundred and fourteen HCWs(63.3%) responded that they had received training in prevention and control of infectious diseases, while sixty six responded that they had not received any kind of training as shown in figure 2.

Figure 2: Number of HCWs trained in prevention and control of infectious diseases



4.7.2 Training on Infectious Disease control across the different departments

The burns unit represented the unit with the highest level of training on infectious disease control among its staff 24(75%).This was followed by the renal unit at 38(66.7%).The ICU had 37(64.9%),while the medical ward had the lowest at 15(44.1%) as shown in table 9.

Table 9: Training on Infectious Disease Control across the various Departments

Variable	Number of HCWs trained in infectious disease control	P value
Unit		
ICU	37(64.9%)	0.055
Burns Unit	24(75.0%)	
Renal Unit	38(66.7%)	
Medical Ward	15(44.1%)	

5.0 DISCUSSION

In this study of HCWs at a tertiary referral hospital, there was a high prevalence of nasal carriage of MRSA more so in the medical ward workers. Most of the cultured isolates were sensitive to common antibiotics. Training in infectious disease control was generally low.

5.1 The overall *S.aureus* and MRSA carriage rate

The overall carriage rate for *S.aureus* was 34.4% while for MRSA was 18.9%. This was in agreement with the internationally reported range of MRSA carriage (5.8 to 17.8%) among HCWs in the hospital setting (69). This carriage rate compares with the study at Abidjan Teaching Hospital, where the carriage rate was 17.8 % (70). A study at the Dessie Referral Hospital in Ethiopia found an MRSA carriage rate of 12.7% among HCWs (23). These were isolated from the nostrils. This was slightly less compared to our findings. These two studies were done on HCWs in both high and low risk areas, while our study was mostly based on high risk workers hence the high rate. A similar study at a private hospital, the AKUH in Nairobi, Kenya found carriage of 0 % (25). The difference could be attributable to several factors. AKUH's infrastructure is better developed due to better funding, thus minimizing the chances of hand contamination, HCWs are supplied with alcohol-based sanitizers for hand cleaning after handling patients and also, the number of patients per HCW is considerably less compared to the one at KNH. This implies less workload and better hygienic practices.

5.2 Antibiotic susceptibility pattern for *S.aureus*

The highest sensitivity was with linezolid (98.4%) while the lowest was with penicillin at 19.4%. Vancomycin showed high resistance of 53.2%. In the Cameroonian study (26) the highest rate of resistance in medical workers was recorded with penicillin G, trimetoprim/sulfamethoxazole and amoxicillin/clavulanic acid, while most strains were sensitive to clindamycin. The high resistance to vancomycin in our study could be due to the liberal use of the antibiotic before determination of sensitivity patterns from sites of infection. A similar study at Shamazi hospital in Iran showed there was full susceptibility of *S.aureus* to linezolid and vancomycin, while significant resistance to ciprofloxacin(66%) and gentamycin(69%) were found(72). By 2010 in the US there had only been 8 reported cases of VRSA(71). Disturbingly, we seem to be losing the efficacy of vancomycin at an alarming rate.

5.2.1 Vancomycin Resistance

The overall resistance of staphylococcus to vancomycin was 53.2 % with the Renal Unit recording the highest rate of resistance at 81.8%. The overall resistance to vancomycin was much higher than in a Japanese study that found the highest resistance at 20% among the eight university hospitals studied (75). This difference could be explained by the fact that the use of vancomycin for empirical treatment of infections in our setting is probably higher. For example, in the renal unit, routine use of vancomycin to cover for catheter site sepsis among patients on haemodialysis is high. This is usually done without antibiotic susceptibility testing.

5.3 Distribution of MRSA isolates among the different cadre of HCW

The overall MRSA carriage rate among the doctors (medical specialists, registrars and medical officer Interns) was 27.9% compared to 21.2% among the nurses. There was 0% carriage among the clinical officers. These findings are different from the Dessie Study (23) where the MRSA carriage was higher among the nurses (21.2%) compared to 12.5% among the doctors. Higher carriage rates among the doctors and nurses of 65.2% and 64.2% respectively were found in a Nigerian study (35). The explanation for the higher carriage among the doctors in our study could be due to a general observation that doctors handle patients during the ward round without washing of hands in between patients.

5.4 Risk Factors Associated With MRSA Carriage

Our study found out that female HCWs were more likely to get MRSA than their male counterparts. We found a carrier rate of 19.1 % and 18.5 % respectively. This predilection was similar to a study carried out in Cameroonian Hospitals (26) that found higher carrier rates, though, of 35% in females and 34.2 % in males. The findings were, however, not statistically significant.

The highest MRSA carriage was in the medical ward, 10(29.4%) followed closely by the Burns unit 9(28.1%) while the lowest was in the Renal unit at 5(8.8%). The ICU had a carriage rate of 10(17.5%). This is possibly attributed to infrastructural differences among the various units. The ICU and renal units have more sinks available for hand washing, have sanitizers strategically placed and are more readily available compared to the medical ward

which has only one central sink for the HCWs, and has no sanitizers readily available. This finding was statistically significant ($p < 0.044$)

HCWs between 30-39 years old had the highest carrier rate of 22.2% , while the lowest was in those between 40-49(14.6%).This was followed closely by those between 50-59(20%).This would probably be explained by the assumption that those playing administrative roles and therefore having less patient contact are likely to be older HCWs. In a similar study at Dessie Referral Hospital, Ethiopia (23), the highest carrier rate was among those aged between 20-29 years old.

HCWs who reported not using gloves while handling patients had higher carrier rate (40%) compared with those that used gloves (18.3%).

HCWs with the highest sterilization score (using a sanitizer) had the least carrier rate of MRSA 6(17.6%).The lowest hand sterilization score had the highest rate of MRSA carriage 12(20%). This implies that using sanitizer (alcohol based hand rub) is more impactful in reducing carriage of MRSA among HCWs. A campaign at a teaching hospital in Switzerland to assess the effectiveness of improving the overall compliance of hand hygiene during routine patient care produced a sustained improvement in compliance with hand hygiene, coinciding with a reduction of nosocomial infections and MRSA transmission. The promotion of bedside, antiseptic hand rubs largely contributed to the increase in compliance (74).

The percentage of HCWs who reported to have received training on infectious diseases control were spread across the various departments as follows: ICU 64.9%, Burns Unit 75.0%, Renal Unit 66.7%,and Medical ward 44.1%.The carriage of MRSA in these departments were 17.5%.28.1%,8.8%,29.4% respectively. The medical ward reported the least number of trained personnel and also represented the ward with the highest carriage of MRSA among HCWs .The renal ward had the second highest number of trained personnel, and represented the department with the least carriage of MRSA. This underscores the importance of training on prevention of infectious diseases on reducing the spread of nosocomial infections. The high carriage rate of MRSA (28.1%) in the burns unit despite having the highest percentage of trained personnel (75%) may be explained by the fact that the patients in this unit have large surface area of denuded skin and, therefore, the risk of contamination is quite high as they can produce a large inoculum of organisms that can be easily transmitted. A study on environmental cleaning intervention in an academic institution

in the US indicated that providing education for environmental services staff, increasing the volume of disinfectant applied to environmental surfaces reduced the frequency of MRSA and VRE (Vancomycin resistant enterococcus) contamination(73). In a Slovenian study (University clinic of respiratory and allergic disease), it was found that with a comprehensive infection control programme (education), it was possible to reduce nosocomial transmission of MRSA in a highly endemic setting. In this period (1999-2002), the proportion of MRSA cases acquired in the institution decreased from 50.0% to 6.1 % ($p < 0.01$) (74)

6.0 CONCLUSION AND RECOMMENDATION

6.1 Conclusions

The prevalence rate of MRSA among health care workers at KNH was high at 18.9%. The medical ward was found to be a high risk area for carriage of MRSA (29.4%). Vancomycin resistance among the isolates was also found to be unexpectedly high (53.2%). Sensitivity to linezolid was high at 98.4%. Lack of training in infection control and prevention was associated with transmission of MRSA with the medical ward having the highest MRSA carriage and the lowest number of trained HCWs (44.1%).

Health care workers who had used alcohol based sanitizers were found to have the least carriage of MRSA (17.6%).

Well powered studies, however, may need to be done in order to link the above findings and conclusions.

6.2 Recommendations

1. There is need for regular screening of HCWs for MRSA and treatment of the same
2. Periodic training of HCWs on control and prevention of infectious diseases needs to be enhanced in order to reduce the nosocomial spread of MRSA.
3. Alcohol-based hand sanitizers should be used more frequently by improving accessibility and providing periodic hand hygiene training sessions to HCWs. In our study, this seemed to play a role in decreasing the risk of MRSA acquisition among them.
4. Because of the high resistance of staphylococcus to vancomycin it is recommended that its use for empiric treatment should be controlled. There was high vancomycin resistance in the renal unit which empirically treats catheter site sepsis with vancomycin.
5. There was an unusually high carriage of MRSA among HCWs in the medical wards. However, the small number of the HCWs calls for a more comprehensive study in the medical wards to determine the actual magnitude of MRSA carriage
6. The antibiogram results from this study indicate that there is need for regular monitoring and review of antibiotics in order to ensure appropriate and rational use.

9.3 STUDY LIMITATIONS

Since HCWs work in several other health institutions the findings may not be totally representative of KNH.

The study was only conducted in three high risk areas and one low risk area, therefore, it lacks generalizability.

REFERENCES

1. Mary Anne Luzar, Gerald A. Coles, Bernadette Faller, et al. *Staphylococcus aureus* nasal carriage and infection in patients on continuous ambulatory peritoneal Dialysis. *N Engl J med* 1990;322:505-509 February 22 1990.
2. Christof Von Eiff, Karsten Becker, Konstanze Machka, et al. Nasal carriage as a source of *staphylococcus aureus* Bacteremia. *N Engl J Med* 2001;344:11-16 January 4, 2001.
3. Heiman FL Wertheim, Damian C Melles, Margreet C Vos, et al. The role of nasal carriage in *Staphylococcus aureus* infections. *The Lancet Infectious Diseases*, Volume 5, Issue 12, December 2005, Pages 751–762.
4. Kluytmans J, van Belkum A, Verbrugh H (July 1997). "Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks". *Clin. Microbiol. Rev.* 10 (3): 505–20
5. Bowersox ,John(27 May 1999), "Experimental staph vaccine Broadly protective in Animal studies". NIH. Archived from the original on May 2007. Available from: http://web.archive.org/web/20070505/05/0641/http://www3.niaid.nih.gov/news/news_releases/1999/staph.htm
6. Barber M. Methicillin-resistant staphylococci. *J Clin Pathol* 1961;14:385-393.
7. H.F. Chambers. The changing Epidemiology of *Staphylococcus aureus*. *Emerging infectious Diseases* 2001 Mar-Apr;7(2):178-182
8. Barrett FF, McGehee RF Jr., Finland M. Methicillin-resistant *Staphylococcus aureus* at Boston City Hospital: bacteriologic and epidemiologic observations. *N Engl J Med* 1968;279:441-448.
9. Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. *JAMA* 2007;298:1763-1771.
10. Rehm SJ. *Staphylococcus aureus*: the new adventures of a legendary pathogen. *Cleveland Clin J Med* 2008;75:177-180. 183–186, 190–192.
11. Herold BC, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. *JAMA* 1998;279:593-598.
12. McDougal LK, Stewart CD, Killgore GE, et al. Pulsed-field gel electrophoresis typing of oxacillin-resistant *Staphylococcus aureus* isolates from the United States: establishing a national database. *J Clin Microbiol* 2003;41:5113-5120.
13. Boyle-Vavra S, Daum RS. Community-acquired methicillin-resistant *Staphylococcus aureus*: the role of Pantone-Valentine leukocidin. *Lab Invest* 2007;87:3-9

14. M. Inês Crisóstomo, Henrik Westh, Alexander Tomasz, et al. The evolution of methicillin resistance in *Staphylococcus aureus*: Similarity of genetic backgrounds in historically early methicillin-susceptible and -resistant isolates and contemporary epidemic clones. PNAS, volume 98, issue 17, Aug 2001
15. Stan Deresinski. Counterpoint: Vancomycin and *Staphylococcus aureus*—An Antibiotic Enters Obsolescence. Clin Infect Dis. (2007) 44 (12): 1543-1548.
16. Satish K. Pillai, Christine Wennersten, Lata Venkataraman, et al. Development of Reduced Vancomycin Susceptibility in Methicillin-Susceptible *Staphylococcus aureus*. Clin Infect Dis. (2009) 49 (8): 1169-1174
17. Fowler VG Jr, Miro JM, Hoen B, et al. *Staphylococcus aureus* endocarditis: a consequence of medical progress. JAMA 2005;293:3012-21.
18. Jevons MP, Coe AW, Parker MT. Methicillin resistance in staphylococci. Lancet 1963;1:904-7.
19. Diekema DJ, Boots Miller BJ, Vaughn TE, et al. Antimicrobial resistance trends and outbreak frequency in United States hospitals. Clin Infect Dis 2004;38:78-85.
20. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004;32:470-85.
21. Chu VH, Crosslin DR, Friedman JY, et al. *Staphylococcus aureus* bacteremia in patients with prosthetic devices: costs and outcomes. Am J Med 2005;118:1416.
22. Cosgrove SE, Sakoulas G, Perencevich EN, et al. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. Clin Infect Dis 2003;36:53-9.
23. Agumas Shibabaw, Tamrat Abebe, Adane M. Nasal carriage rate of methicillin resistant *Staphylococcus aureus* among Dessie Referral Hospital Health Care Workers; Dessie, Northeast Ethiopia. Antimicrobial Resistance and Infection Control 2013,2:25
24. Edward K. Maina, Ciira Kiiyukia, C. Njeri Wamae, et al. Characterization of methicillin-resistant *Staphylococcus aureus* from skin and soft tissue infections in patients in Nairobi, Kenya. International Journal of Infectious Diseases, Volume 17, Issue 2, February 2013, Pages e115–e119
25. Omuse G, Kariuki S, Revathi G: Unexpected absence of methicillin-resistant *staphylococcus aureus* nasal carriage by healthcare workers in a tertiary hospital in Kenya. J Hosp Infect 2012, 80(1):71-73.

26. Gonsu K. H, Kouemo S. L, Toukam M, et al. Nasal carriage of methicillin resistant *Staphylococcus aureus* and its antibiotic susceptibility pattern in adult hospitalized patients and medical staff in some hospitals in Cameroon. *Journal of Microbiology and Antimicrobials* Vol. 5(3), pp. 29-33, March 2013
27. Hsu L Y, Koh T H, Tan T Y, et al. Emergence of community-associated methicillin-resistant *staphylococcus aureus* in Singapore: a further six cases. *Singapore Med J* 2006;47(1):20
28. Robert A. Weinstein and Scott K. Fridkin. Vancomycin-Intermediate and -Resistant *Staphylococcus aureus*: What the Infectious Disease Specialist Needs to Know. *Clin Infect Dis.* (2001) 32 (1): 108-115
29. R.H. Deurenberg, C. Vink, S. Kalenic, et al. The molecular evolution of methicillin-resistant *Staphylococcus aureus*. *Clinical Microbiology and Infection* Volume 13, Issue 3, pages 222–235, March 2007
30. Hiramatsu K. Elucidation of the mechanism of antibiotic resistance acquisition of methicillin-resistant *Staphylococcus aureus* (MRSA) and determination of its whole genome nucleotide sequence. *JMAJ* 2004;47:153-9
31. Pearman JW, Grubb WB. Emerging strains of multiresistant methicillin-resistant *Staphylococcus aureus* threaten success of screening policy. *APUA Newsletter* 1993;11:1-8.
32. Lodise TP, McKinnon PS, Levine DP, et al. Program and abstracts of the 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy. Alexandria, VA: Infectious Diseases Society of America; 2002. Predictors of mortality and impact of initial therapy on outcomes in intravenous drug users (IVDU) with *Staphylococcus aureus* (SA) infective endocarditis (IE) [abstract L-765].
33. S Deresinski. Methicillin-resistant *staphylococcus aureus*. *Evolutionary, Epidemiologic, and Therapeutic Odyssey.* *Clin Infect Dis.* (2005)40(4):562-573
34. Carter AP, Clemons WM, Brodersen DE, Morgan-Warren RJ, Wimberly BT, Ramakrishnan V (September 2000). "Functional insights from the structure of the 30S ribosomal subunit and its interactions with antibiotics". *Nature* 407(6802):340-8.
35. Werner c albrich, Dr. stephan Harbath. Health-care workers: source, vector, or victim of MRSA? *The Lancet infectious Diseases*, Volume 8, Issue 5, May 2008, Pages 289–301
36. Berthelot P, Grattard F, Fascia P, et al. Implication of a healthcare worker with chronic skin disease in the transmission of an epidemic strain of methicillin-resistant *Staphylococcus aureus* in a pediatric intensive care unit. *Infect Control Hosp Epidemiol* 2003; 24: 299-300

37. Maury Ellis Mulligan, Katherine A. Murray-Leisure, Bruce S Ribner, et al. Methicillin-resistant *Staphylococcus aureus*: A consensus review of the microbiology, pathogenesis, and epidemiology with implications for prevention and management. *The American Journal of Medicine* Volume 94, Issue 3, pages 313-328, March 1993
38. Faibis F, Laporte C, Fiacre A, et al. An outbreak of methicillin-resistant *Staphylococcus aureus* surgical-site infections initiated by a healthcare worker with chronic sinusitis. *Infect Control Hosp Epidemiol* 2005; 26: 213-215.
39. Price EH, Brain A, Dickson JA. An outbreak of infection with a gentamicin and methicillin-resistant *Staphylococcus aureus* in a neonatal unit. *J Hosp Infect* 1980; 1: 221-228.
40. Sharin J, Peacock, Ishani de Silva, Franklin D. Lowy. What Determines nasal carriage of *Staphylococcus aureus*? *Trends in Microbiology* 1 December 2001, Vol.9(12):605-610
41. Heiman F. L. Wertheim, Menno van Kleef, et al (2006). Nose Picking and Nasal Carriage of *Staphylococcus aureus*. *Infection Control*, 27, pp 863-867.
42. Sherertz RJ, Bassetti S, Bassetti-Wyss B. "Cloud" health-care workers. *Emerg Infect Dis* 2001; 7: 241-244.
43. Kaliner MA. Human nasal respiratory secretions and host defense. *Am Rev Respir Dis* 1991; 144: S52-S56.
44. Bibel DJ, Aly R, Bayles C, et al. Competitive adherence as a mechanism of bacterial interference. *Can J Microbiol* 1983; 29: 700-703.
45. Lina G, Boutite F, Tristan A, et al. Bacterial competition for human nasal cavity colonization: role of staphylococcal agr alleles. *Appl Environ Microbiol* 2003; 69: 18-23.
46. Evelina Tacconelli, Giulia De Angelis, Maria A. Cataldo, et al. Does antibiotic exposure increase the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) isolation? A systematic review and meta-analysis. *Journal of antimicrobial chemotherapy* (2008) 61(1):26-38
47. Kumar P, Shukla I, Varshney S: Nasal screening of healthcare workers for nasal carriage of coagulase positive MRSA and prevalence of nasal colonization with *Staphylococcus aureus*. *Biology and Medicine* 2011, 3(2):182-186.
48. R. J. Rubin, C. A. Harrington, A. Poon, et al. The economic impact of *Staphylococcus aureus* infection in New York City hospitals. *Emerg Infect Dis*. 1999 Jan-Feb; 5(1): 9-17.
49. Kesah C, Ben Redjeb S, Odugbemi TO, et al. (2003) Prevalence of methicillin-resistant *Staphylococcus aureus* in eight African hospitals and Malta. *Clin Microbiol Infect* 9: 153-156.

50. Jernigan JA, Clemence MA, Stott GA, et al. Control of methicillin-resistant *Staphylococcus aureus* at a university hospital: one decade later. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* [1995;16(12):686-696]
51. Carine Chaix, Isabelle Durand-Zaleski, Corinne Albert, et al. Control of Endemic Methicillin-Resistant *Staphylococcus aureus*, A cost-Benefit Analysis in an intensive Care Unit. *JAMA*. 1999;282(18):1745-1751
52. J.M Boyce. MRSA patients: proven methods to treat colonization and infection. *Journal of Hospital Infection*, Volume 48, Supplement A, August 2001, Pages S9–S14
53. Muthotho JN, Waiyaki PG, Mbalu M, et al. Control of spread of Methicillin Resistant *Staphylococcus aureus* (MRSA) in Burns Units. *Afr J Health Sci*. 1995 Feb;2(1):232-235.
54. Sakoulas G, Moise-Broder PA, Schentag J, et al. Relationship of MIC and bactericidal activity to efficacy of vancomycin for treatment of methicillin-resistant *S.aureus* bacteremia. *J clin microbial* 2004;42:2398-402
55. MMWR Morb Mortal Wkly Rep. 2002 Jul 5;51(26):567-7
56. Stevens DL, Herr D, Lampiris H, et al. Linezolid versus vancomycin for the treatment of methicillin resistant *S.aureus* infections. *Clin Infect Dis* 2002;34:1481-90
57. Kollef MH, Rello J, Cammarata SK, et al. Clinical cure and survival in gram-positive ventilator-associated pneumonia: retrospective analysis of two double-blind studies comparing linezolid with vancomycin. *Intensive Care Med* 2004;30:343-6.
58. Nicolau DP, Freeman CD, Nightingale CH, et al. Minocycline versus vancomycin for the treatment of experimental endocarditis caused by oxacillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother* 1994;38:1515-8
59. de Gorgolas M, Aviles P, Verdejo C, et al. Treatment of experimental endocarditis due to methicillin-susceptible or methicillin-resistant *Staphylococcus aureus* with trimethoprim-sulfamethoxazole and antibiotics that inhibit cell wall synthesis. *Antimicrob Agents Chemother* 1995; 39:953-7.
60. Livermore DM. Antibiotic resistance in Staphylococci. *Int J Antimicrob Agents* 2000;16(suppl 1):3-10
61. J.-Y. Fagon, H. Patrick, D.W. HAAS, et al. Treatment of Gram-positive Nosocomial Pneumonia; Prospective Randomized comparison of Quinupristin/Dalfopristin versus vancomycin. *American Journal of Respiratory and critical care medicine* vol.161:issue.3:pages 753-762 (volume publication date: March 2000).

62. Weber SG, Gold HS, Horper DC, et al. Fluoroquinolones and the risk of methicillin-resistant *S. Aureus* in hospitalized patients. *Emerg Infect Dis* 2003; 9:1415-22
63. Shopsin B, Zhao X, Kreiswirth BN, et al. Are the new quinolones appropriate treatment for community acquired –MRSA? *Int J Antimicrob Agents* 2004; 24:32-4
64. Markowitz N, Quinn EL, Saravolatz LD. Trimethoprim-sulfamethoxazole compared with vancomycin for the treatment of *Staphylococcus aureus* infection. *Ann Intern Med* 1992; 117:390-98.
65. Adra M, Lawrence KR. Trimethoprim/sulfamethoxazole for treatment of severe *S. aureus* infections. *Ann Pharmacother* 2004; 38:338-41
66. Frank A L; Marcinak, John F, et al. Clindamycin treatment of methicillin-resistant *Staphylococcus aureus* infection in children. *Pediatric Infectious Disease Journal*: June 2002-volume 21-issue 6-pp 530-534
67. Schmitz FJ, Krey A, Sadurski R, et al. Resistance to tetracycline and distribution of tetracycline resistance genes in European *S. aureus* isolates. *J Antimicrob Chemother* 2001; 47:239-46
68. Heidi S. M, Ammerlaan, Jan A. J. W. Kluytmans, et al. Eradication of Methicillin-Resistant *Staphylococcus aureus* Carriage: A Systematic Review. *Clinical Infectious Diseases*, volume 48, issue 7, pp.922-930.
69. Shakya B, Shrestha S, Mitra T. Nasal carriage rate of methicillin resistant *Staphylococcus aureus* at the National Medical College Teaching Hospital, Birgunj, Nepal. *Nepal Med Coll J* 2010; 12(1): 26-29.)
70. Akoua Koffi C, Dje K, Toure R: Nasal Carriage of methicillin resistant *Staphylococcus aureus* among health care personnel in Abidjan (Cote d'ivoire). *Dakar med* 2004, 49:70-74
71. Gould IM (December 2010). "VRSA-doomsday superbug or damp squib?". *Lancet Infect Dis* 10 (12): 816–8
72. Mehdrdad Askarian, Alihosein Zeinalzadeh, Azi Japoni, et al. Prevalence of nasal carriage of methicillin-resistant *Staphylococcus aureus* and its antibiotic susceptibility pattern in healthcare workers at Namazi Hospital, Shiraz, Iran. *International Journal of Infectious Diseases*, Volume 13, Issue 5, September 2009, pages e241-e247.
73. Eric R. Goodman, Richard Piatt, Richard Bass et al. Impact of an Environmental Cleaning intervention on the presence of Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant Enterococci on Surfaces in Intensive Care Unit Rooms. *Infection Control and Hospital Epidemiology*/Volume 29/Issue 07/July 2008, pp 593-599.

74. Didier Pittet, Stephane Hugonnet, Stephan Harbarth et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *The Lancet*, Volume 356, Issue 9238, 14 October 2000, pages 1307-1312.
75. Keiichi Hiramatsu, Nanoe Aritaka, Hideaki Hanaki et al. Dissemination in Japanese Hospitals of strains of *Staphylococcus aureus* heterogeneously resistant to vancomycin. *The Lancet*, vol 350, No. 9092 p1670-1673, 6 December 1997.
76. Loreto Vidaur, Gonzalo Sirgo, Alejandro H Rodriguez, et al. Clinical Approach to the patient with suspected Ventilator-Associated Pneumonia. *Respiratory Care* July 1.2005 Vol.50 no.7 p965-974

APPENDICES

APPENDIX I: STUDY TIME FRAME

Activities	Aug 2014	Sep 2014	Oct 2014	Nov 2014	Dec 2014	Jan 2015	Feb 2015	Mar 2015	Apr 2015
Proposal Presentation									
Ethics Approval									
Data collection									
Data Analysis									
Results presentation									

APPENDIX II: STUDY BUDGET

ITEM	COST
PRINTING/STATIONARY	15,000
STATISTICIAN	20,000
RESEARCH ASSISTANT STIPEND	15,000
KNH/UON ERC PROCESSING FEE	2,000
REAGENTS/LABORATORY	50,000
TOTAL ESTIMATES	102,000

APPENDIX III: CONSENT EXPLANATION

My name is Dr. Alex Wagucu Mogere of the University of Nairobi pursuing a master's degree in Internal Medicine.

I am conducting a study broadly aimed at determining the carriage rate of methicillin resistant *Staphylococcus aureus* among health care workers at Kenyatta National hospital's ICU, Renal and Burns units. Specifically I aim to determine the nasal and hand carriage rate of MRSA among Health Care Workers at Kenyatta National Hospital and to determine the antibiotic susceptibility profile of the isolates. This will be conducted through performing nasal and hand swabs of the participating health care worker.

Methicillin resistant *Staphylococcus aureus* is a worldwide problem in clinical medicine as it's involved in serious and fatal infections. Healthcare workers are stable nasal carriers and can be a source of infections. These infections can affect both the patients they take care of and themselves.

The information obtained from this research will lead to better ways of reducing or preventing nosocomial transmission of infections, especially related to methicillin resistant *staphylococcus aureus*.

It will be carried out in strict confidence and you will not be required to give your name. You will also be free to answer all questions but should there be any questions that you feel you are not comfortable with, you will be under no obligation to answer. The process of obtaining the samples is safe. There may just be associated discomfort while obtaining the nasal swabs.

The results of the study may not benefit you directly but they might benefit the future management of nosocomial infections. However, the results will be conveyed to you and if found to harbour *Staphylococcus aureus/MRSA* you will be referred to a physician for decolonization and/or treatment. You will not be asked to shoulder any cost of the study. The study will also enhance infection, prevention and control practices within the hospital and facilitate training of health care workers in this aspect. You can withdraw from this study without individual or career consequences.

In case of any problem or questions, you may either contact me, Dr. Alex Mogere, the principle investigator of this study on mobile no. 0721294134 or University Of Nairobi, Department of Internal Medicine Box 19676,Nairobi,Kenya,or Prof K.M.Bhatt and Prof E.Amayo, Department of Internal Medicine UON,Ms Winnie Mutai ,Department of microbiology at UON or Prof. M.L.Chindia, the Secretary to the Kenyatta National Hospital/University of Nairobi-ethics & Research committee (KNH/UON-ERC) P.O Box 20723-00202.

APPENDIX IV: CONSENT FORM

....., after reading the consent explanation form and having been explained to by Dr. Alex Mogere (The Principal Investigator) and/or a trained research assistant do voluntarily agree to take part in this research study on **“The carriage of methicillin resistant *Staphylococcus aureus* among health care workers at Kenyatta National Hospital”**. I am aware results of the study may not benefit me directly but they might benefit the future management of nosocomial infections.

I have also been informed that the process of obtaining the samples is safe. There may just be associated discomfort while obtaining the nasal swabs.

I am aware that the cost of the research shall be met by the researcher.

I am also aware I can withdraw from this study without jeopardizing my career.

Signed.....

Witness.....

Dated.....

APPENDIX V: STUDY QUESTIONNAIRE

Questionnaire for the research on the Carriage of Methicillin resistant *Staphylococcus aureus* among Health care workers at KNHs ICU, Renal and Burns units

Instructions:

1. The purpose of this questionnaire is to obtain information for study purposes only. The Information obtained will go a long way in minimizing nosocomial spread of infections.
2. Your responses will be held in total confidence.
3. The questionnaire has 3 sections. Complete all the sections.
4. Put the filled questionnaire in the given envelope and seal it. Hand it over to the researcher or the research assistant.

UNIT

ICU	
BURNS UNIT	
RENAL UNIT	
MED WARD	

Study Number -----

Date.....

A.SOCIAL DEMOGRAPHIC DATA

1. CATEGORY OF STAFF

CONSULTANT	
REGISTRAR	
GENERAL PRACTITIONER	
CLINICAL OFFICER	
NURSE	
OTHER	

2. AGE IN YEARS

20-29	
30-39	
40-49	
50-59	
>60	

3. GENDER

Male	
Female	

4. MARITAL STATUS

Single	
Married	
Separated	
Divorced	
Widowed	

5. TRAINING BACKGROUND OF RESPONDENT

Masters	
Bachelors	
Diploma	
Certificate	
Other	

B. TRAINING ON INFECTION CONTROL PRACTICES

1. Have you undergone any training programme on control of infectious diseases?

Yes	
No	

2. Indicate in the table below the up-date courses on infection control program that you have attended, if any

Title /course	Date (year/month)	Duration(days)

C. RISK FACTORS

1. How long have you worked at the unit (days)

0-7	
8-15	
16-23	
>24	

2. Do you use gloves while handling a patient?

Yes	
No	

3. Do you wear a different pair of gloves while handling a different patient?

Yes	
No	

4. I clean my hands after handling a patient

	With water only	With water and soap	With Sanitizer
Always			
Sometimes			
Rarely			

5.Co-morbidities

	Yes	No
Skin lesion		
Sinusitis, rhinitis		
Chronic otitis externa		
Recent uti		

6. Working hours/Shift

Day	
Night	
Both day and night	

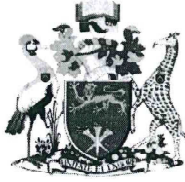
LABORATORY RESULTS

REF NO:		
DESIGNATION:		
TEST	POSITIVE	NEGATIVE
1.COAGULASE TEST		
2.CATALASE TEST		
3.OXACILLIN RESISTANCE		

ANTIBIOTIC SUSCEPTIBILITY

ANTIBIOTIC	SENSITIVE	RESISTANT
SULFAMETHOXAZOLE/TRIMETHOPRIM		
GENTAMYCIN		
LINEZOLID		
CIPROFLOXACIN		
ERYTHROMYCIN		
TETRACYCLINE		
VANCOMYCIN		
AMPICILLIN		
PENICILLIN		

APPENDIX VI: KNH/UON-ERC LETTER OF APPROVAL



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14th January 2015

Dr. Alex W Mogere
Dept of Clinical Medicine & Therapeutics
School Of Medicine
University Of Nairobi

Dear Dr. Mogere



RESEARCH PROPOSAL: CARRIAGE RATE OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS AMONG KENYATTA NATIONAL REFERRAL HOSPITAL HEALTH CARE WORKERS (P617/10/2014)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 14th January 2015 to 13th January 2016.


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 severe 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) 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*).
- f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
- 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 www.erc.uonbi.ac.ke

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Yours sincerely



PROF. M. L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director CS, KNH
The Assistant Director, Health Information, KNH
The Chairperson, KNH/UON-ERC
The Dean, School of Medicine, UoN
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