Determination of Bacterial Isolate Profiles, their Antimicrobial Susceptibility Patterns and Trends of Antibiotic Use In Patients with Open Fractures

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This is to certify that this thesis is the original work of the author. This research was carried out at Kenyatta National Hospital's Orthopedic Department.

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Signed……..

Date…….

DEDICATION

I dedicate this work to my loving Wife and Children,
And to all my Teachers and Colleagues in this great field
Of Orthopedics Surgery

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The Almighty God who gives life, strength, knowledge and wisdom, and on whose purpose this research work will impact quality health provision.

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LIST OF ABBREVIATIONS

SSI	Surgical Site Infections
KNH	Kenyatta National Hospital
HVAC	Heating/ Ventilation and Air Conditioning
PMNL	Polymorphonuclear Leucocytes
ACS TQIP	American College of Surgeons' Trauma Quality Improvement Program
BOAST	British Orthopedic Association Standards for Trauma
EPMG	East Practice Management Guidelines
RCT	Randomized Controlled Trial
MIC	Minimum Inhibitory Concentration
CDC	Centers for Disease Control
NINSS	Nosocomial Infection National Surveillance Scheme
SPSS	Statistical Package for Social Sciences
ORIF	Open Reduction and Internal Fixation
AO/ASIF	Association for the study of Internal Fixation
MCS	Microscopy Culture and Sensitivity
RTA	Road Traffic Accidents
MRSA	Methicillin Resistant Staphylococcal aureus.

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ABSTRACT

Background: Open fractures are a high burden both locally and globally. Their commonest complication is wound infection, which often escalates to sepsis, osteomyelitis, amputation and even death. The morbidity and mortality from these infections is particularly high in developing countries. The use of prophylactic antibiotics is one of the most effective strategies to prevent infection. The selection of antibiotics for both prophylactic and empiric therapy must be guided by the institution's microbial profile and susceptibility patterns of possible infecting organisms.

Study objective: To determine the microbial profile and susceptibility patterns of bacterial isolates from infected open fractures.

Design: Descriptive Cross-Sectional Study.

Setting: Orthopedic wards at Kenyatta National Hospital.

Patient and methods: Patients presenting to the hospital with open appendicular skeleton fractures whose wounds developed infection were recruited into the study. Their baseline characteristics as well as details relating to the fracture patterns were recorded. The wounds were assessed for infection after the 3rd and 8th day following initial debridement. Swab specimens were collected for Microscopy Culture and Sensitivity. The profile of cultured isolates were recorded as well as their antimicrobial susceptibility patterns. The prescribed antibiotics and their duration was also recorded. Data was analyzed in IBM SPSS version 22. Means, median and proportions were used to analyze the descriptive.

Results: There were 45 (73%) gram negative and 17 (27%) gram positive bacterial isolates. The most pre-dominant bacterial isolate was *Pseudomonas aeruginosa* at 21 (34%). There were 17 (27%) *Staph. aureus* isolates, 12 (20%) *E.Coli*, 10 (16%) *Proteus mirabilis* and 2(3%) *Klebsiella pneumoniae* isolates. Among the Gram positive isolates, there was high resistance against Benzyl penicillin (100%), Amoxicillin Clavulanate (82%), Erythromycin (80%), Cefuroxime (75%), Ceftriaxone 60% and Clindamycin (50%). There were 4 Methicillin Resistant staph. aureus isolates. There was 100% sensitivity to Meropenem, Amikacin, Vancomycin, Piperacillin and Linezolid. Among the Gram Negative isolates, there was high resistance to Clindamyci (100%), Erythromycin (100%), Amoxicillin Clavulanate (94%), Ampicillin (80%), Cefuroxime (68%), Rifampicin (65%) and Ceftriaxone (54%). There was 100% sensitivity to Meropenem, Amikacin and Piperacillin. More than 80% of the isolates showed resistance to more than 3 commonly used drugs. The most commonly prescribed prophylactic antibiotics were intravenous Ceftriaxone and Cefuroxime, either singly or in combination with Metronindazole, for a duration of 4-5 (58%) days and 2-3 days (39%).

Conclusion: There was a higher proportion of gram negative (73%) than gram positive (27%) bacterial isolates, with high antimicrobial resistance to the commonly used prophylactic antibiotics. The duration of antimicrobial prophylaxis is longer than the recommend for open fractures.

INTRODUCTION

Surgical Site Infection (SSI) is one of the commonest complications of open fractures. Infected open fracture wounds have historically been dreaded because of the debilitating effect to the patient. These infections when not well managed escalates to sepsis, chronic osteomyelitis, amputations and even death. Up to the beginning of the 20th century, open wounds were often treated by prophylactic amputation to avoid the sequelae of infection, sepsis, and death (1).

Globally, the estimated incidence of long bone fractures is 11.5 per 100,000 people per year, occurs more in men than women, and has a bimodal age distribution, with the tibia being the most commonly affected bone (2 - 4). The incidence of these open fractures is particularly higher in lower socioeconomic settings due to unsafe modes of transport; particularly the use of motorcycles for public transport. This is true for our setting (5, 6).

Open fractures are known to carry a very high risk for infection, with most studies reporting infection rates between 10 - 50% (6, - 10). Local studies have revealed higher rates than those observed globally (8, 10, 11). Three studies have been conducted at KNH; Mogire J. in 1995 found an infection rate of 85% in all open tibia fractures. Asif A in 2011 reported an SSI rate of 50% in all open fractures while Ondari S. in 2016 found a 28% infection rate in Gustilo II fractures. (80, 8, 10). The socioeconomic burden of treating these infections is very high. One study showed a 300% increase in healthcare costs (12). Total hospital length of stay was prolonged by a median of 2 weeks, and patients had substantial physical limitation and reduced quality of life. In another study, deep infections of open tibia fractures had 6.5 times higher cost of treatment (13).

Many guidelines have been developed with the aim of reducing these infections (14-16). The cardinal principles include antibiotic prophylaxis, debridement/irrigation, fracture stabilization and soft tissue coverage. Early administration of antibiotics and urgent surgical debridement are the most critical strategies in infection prevention (17, 18). Determining the profile of microbial isolates from infected wounds and their sensitivity/resistance patterns is crucial in developing antibiotic protocols for both prophylaxis and empirical therapy.

The target population shall include patients aged between 18 and 75 years at Kenyatta National Hospital (KNH) with infected open fractures. The purpose of the study is to determine the microbial isolates from infected open fractures and their resistance patterns. The results of this study shall guide the surgeons in selecting the most appropriate antibiotics for empiric antibiotic therapy based on; the commonest microbial isolates, and the antibiotics with the widest spectrum to which most isolates are sensitive.

2.1 LITERATURE REVIEW

Surgical Site Infections in open fractures

Open fractures result from high energy injury mechanisms. They occur most commonly in the tibia. The incidence of these open fractures is particularly high in lower socioeconomic settings due to unsafe modes of transport; particularly the use of motorcycles for public transport on roads that lack designated cyclists' paths. A study by Waithiru Peris in 2015 at KNH showed that tibia/fibula fractures accounted for 36.9% of all appendicular fractures, and most resulted from motorcycle accidents. Another study by Gachathi in Eldoret, found 65% of tibia shaft fractures result from motorcycle accidents and 40.9% of them are open (5,6).

The leg is precariously exposed as it dangles on the sides as the cyclist meanders through traffic. The leg can get caught or hit between vehicles, injured when motorcycle rams into other vehicles or get crushed under the weight of motorcycle should it fall. The subcutaneous position of the tibia and the high energy mechanism of injury explains the high rate of open fractures in this bone. Its precarious blood supply is a risk factor to the development of infection as well as delayed fracture healing**.** Open fractures often result from high energy injuries that cause significant soft tissue damage, periosteal stripping, fracture comminution, and wound contamination. This allows bacteria to easily gain access to the site of injury through the breached skin barrier.

Sources of airborne microorganisms in a built environment

Acute SSIs mostly arise from wound contamination caused by a small inoculum during the peri-operative period (19). Wounds that are not closed during debridement retains the potential to be infected from dressings and airborne microorganisms. The commonest sources of airborne microorganisms in a built environment in a hospital set-up include humans, plumbing systems, Heating/ Ventilation and Air Conditioning (HVAC) systems, mold, dust resuspension, and the outdoor environment. Humans shed bacterial organisms in the rate of $3.7 * 10^{7}$ genome copies per person-hour (19). Charlson et al. found high relative abundances of *Staphylococcaceae spp., Corynebacteriaceae spp., Streptococcaceae spp., Propionibacteriaceae spp., Prevotellaceae spp., Veillonellaceae spp., Fusobacteriaceae spp.,* and *Neisseriaceae spp*. in human nasopharynx and oropharynx, many of which have been identified in indoor air (20).

The bacteria may attach to dead bone or implant surfaces and establish a biofilm with which they protect themselves against both host immune defense mechanisms and antibiotics. This biofilm formation makes the treatment of these infections very challenging (21). Patients with high energy trauma develop immune system dysfunction with decreased Polymorphonuclear Leucocyte (PMNL) chemotaxis, decreased superoxide production and decreased rate of microbial elimination (22). All these factors contribute to higher infection rates with high mortality and morbidity bearing enormous socioeconomic impacts.

INFECTION PREVENTION

The cardinal principles in preventing post traumatic infection in open wounds include; Antibiotic prophylaxis, Debridement/irrigation, Fracture stabilization and Soft tissue coverage. Of all these, early administration of prophylactic antibiotics and urgent surgical debridement are the most critical strategies in infection prevention (17, 18).

Prophylactic antibiotics

Timing, choice and duration:

Several studies have provided information to guide surgeons on the best time to start the antibiotics, the best choice of drugs and the optimal duration of administration. Most guidelines recommend early initiation of intravenous prophylactic antibiotics.

The East Practice Management Workgroup Guideline advocates starting antibiotics 'as soon as possible' (14). The American College of Surgeons' Trauma Quality Improvement Programme (ACS TQIP) guidelines and the British Orthopedic Association Standards for Trauma (BOAST) guidelines advocate for the administration of antibiotics within 1 hour of presentation (21, 22). This is based on a key study by Lack et al who found that a delay in initiation of antibiotics after 66 minutes had a 3-fold increased risk of infection in Gustilo III open fracture wounds (23).

The choice of antibiotic is informed by the pattern of infecting organisms and their resistance characteristics. These may vary from one institution to another and from time to time. Most studies have shown that *Staphylococcus aureus* is the commonest bacteria isolated in infected open fracture wounds (8, 10, 24, 25).

A study by Shanker et al showed that microbial isolates cultured from samples taken before debridement differed significantly from those taken from the same wounds after debridement. Another study by Sitati et al carried out at KNH Kenya showed similar results. In their study, 52% of all open fractures following debridement had a positive culture result with an equal distribution of gram positive and negative organisms. The study also recorded high resistance to tetracycline, erythromycin and Amoxicillin clavulanic acid. These two studies demonstrated that the infecting organisms are not necessarily the initial contaminants, thus pre-debridement cultures have little or no role in guiding the choice of prophylactic antibiotics (25, 26).

First generation Cephalosporins are mainly active against the gram positive cocci like staphylococci. The drug of choice in surgical prophylaxis is Cefazolin. Second generation Cephalosporins are also active against organisms under the spectrum of first generation cephalosporin but they also cover gram negative bacteria like *Klebsiella spp*. Other guidelines and recommendations exists

In general:
Gustilo I & II - 1st generation Cephalosporin, eg Cefazolin.
Gustilo III - 1st generation Cephalosporin with an aminoglycoside, eg. Gentamycin.
Farmyard injuries - add Benzyl penicillin or Metronidazole (15).

Farm injuries are treated as a special entity because they involve a high inoculum of organisms. These organisms are mainly anaerobic and produce toxins which penetrate tissues. Debridement and lavage is usually inadequate in reducing the inoculum. Metronidazole or Benzyl penicillin are recommended to cover for Clostridium and other anaerobes (21).

Current guidelines recommend a short duration of prophylactic antibiotics as prolonged durations have not shown added benefits and could be associated with drug resistance and higher overall cost. Dunkel et al, carried out a retrospective case control study, comparing the infection rates when the antibiotics were given for one day, two - three days, four - five days and above five days. The infection rates were not significantly different. (27).

Ondari et al conducted a Randomized Controlled Study (RCT) at KNH in year 2015. He compared 24 hours versus 5 days of antibiotics. His study showed no difference in rates of infection. A recent meta-analysis by Messner et al in 2017 involved 6,692 fractures (1970-2017) had similar results and validated current guidelines (8, 28).

Both the East Practice Management Guidelines (EPMG) and British Orthopedic Association & British Orthopedics Association Standards for Trauma (BOAST) guidelines recommend antibiotics to be discontinued at 24 hours after wound closure in type I and II fractures. For type III fractures, antibiotic should be continued for 72 hours subsequent to the injury or not >24 hours after wound closure (14, 16).

WOUND ASSESSMENT

Wound classification

A reliable open fracture wound classification system must allow easy communication that infers morphology, guides treatment and predicts prognosis. In open fractures, the most commonly accepted classification is that of the Gustilo and Anderson. It was developed in 1976 based on a retrospective and prospective study of 1025 patients (42). This system is based on the amount of energy causing the fracture, extent of soft-tissue damage and degree of wound contamination. The classification was later refined by Gustilo by subdividing grade III wounds into A, B and C (30). This allowed more accurate prognostication for these severe injuries.

The reliability of this system has been investigated for reproducibility (31, 32). In one of the studies, 245 orthopedic surgeons interpreted color videos of patients' examinations and radiographs then classified the injuries. The overall agreement rate was 60% (31). This finding notwithstanding, the Gustilo system is still recommended as useful in predicting both infection

rates and bone union. The final assessment should be done intraoperatively when a detailed inspection is possible.

Table I Gustilo classification of open fractures (adapted from Rockwood and Green's Fractures in adults, 8th edition (2015) P-353 (33)

Type	Wound	Level of Contamination	Soft Tissue Injury	Bone Injury
I	<1 cm long	Clean	Minimal	Simple, minimal comminution
II	>1 cm long	Moderate	Moderate; some muscle damage	Moderate comminution
III A	Usually >10 cm	High	Severe with crushing	Usually communited; soft tissue cover-age of bone possible
III B	Usually >10 cm	High	Very severe loss of cover	Bone cover poor; usually requires soft tissue reconstructive surgery
III C	Usually >10 cm	High	Very severe loss of cover and vascular injury requiring repair	Bone cover poor; usually requires soft tissue reconstructive surgery

Infection scoring systems

This study will involve collecting pus swabs and necrotic tissues from infected open fractures for microscopy, culture and sensitivity testing. All wounds with purulent discharge shall be classified as infected. Where doubts exist as to whether the infection is present or not (e.g. Tissue separation without visible exudates), a clinical scoring criteria will be used to determine wound infection.

Researchers have found it challenging to get a standard definition criteria for determining surgical site infection, as many are vague and non-objective. The most commonly used definitions include:

- The Centers for Disease Control & Prevention (CDC)
- ASEPSIS Wound Scoring System (33)
- Nosocomial Infection National Surveillance Scheme (NINSS)
- Southampton scoring system.

The ASEPSIS system is a validated tool for both clinical and research purposes. It has been reviewed by several studies and found to be reliable, objective and repeatable, and therefore recommended as a clinical criteria for wound definition (34-37).

The ASEPSIS scoring system will be used for this study. It has been successfully used before in a study conducted in the same hospital – KNH in 2015 by Ondari et al (8) on open tibia fractures.

A Additional Treatment: (Antibiotics, Drainage of Pus, Debridement)
S Serous Discharge
E Erythema
P Purulent exudate
S Separation of deep tissues
I Isolation of bacteria
S Stay in hospital over 14 days

Table II. Points scale used to calculate total ASEPSIS score

Criterion	Points
Additional treatment	
Antibiotics	10
Drainage of pus under local anaesthetic	5
Debridement of wound under general anaesthetic	10
Serous discharge	0 to 5
Erythema	0 to 5
Purulent exudate	0 to10
Separation of deep tissues	0 to 10
Isolation of bacteria	10
Stay in hospital over 14 days	5

Table III. Points scale for ASEPSIS daily wound inspection

	Proportion of wound affected (%)					
	0	> 0 to 19	20 to 39	40 to 59	60 to 79	80 to 100
Serous exudate	*0*	*1*	*2*	*3*	*4*	*5*
Erythema	*0*	*1*	*2*	*3*	*4*	*5*
Purulent exudates	*0*	*2*	*4*	*6*	*8*	*10*
Separation of deep tissues	*0*	*2*	*4*	*6*	*8*	*10*

Table IV. Breakdown of ASEPSIS scores

Score	Meaning
0 to10	No infection Normal healing
11 to 20	Disturbance of healing
21 to 30	Minor infection
31 to 40	Moderate infection
≥ 41	Severe infection

MICROBIAL PROFILE AND SUSCEPTIBILITY PATTERNS IN INFECTED OPEN FRACTURES

About 70% of all open fractures get contaminated at the time of injury mainly by organisms from the patient's skin and the surrounding environment (29). Further contamination occur in the course of management at the hospital. Studies have been done to determine if organisms isolated from wounds before debridement are similar to those causing infections after debridement. Few studies found that these isolates were similar (38, 39). Others found that the isolates are not similar and that infections were mainly caused by nosocomial microorganisms. (40, 41, 25, 26).
The profile of microbial isolates from infected open wounds vary from one health institution to another and from time to time. Overall, the commonest isolate is *Staph. aureus* (8, 10, 24, 25).
A study at a private fracture-clinic in Al- Diwaniya city, Iraq by Al-Saadi et al found that the most frequent bacterial isolate was *Staph. aureus* (23.52%) followed by *Acinetobacter spp* (19.32%), *E.coli* (14.28%), Pseudomonas spp (11.76%), *Enterobacter spp* (9.24%) and *Klebsiella spp* (6.72%) (42).

A study by Ashwin et al in India found the isolation rate from Gustilo III fracture wounds to be 26.9%. *Staph. aureus* was the commonest isolate followed by *Acinetobacter, Pseudomonas, Klebsiella, E-coli, Enterococcus, Streptococcus* and *Enterobacter*. In regard to antibacterial sensitivity, the study found that majority of these organisms were sensitive to Gentamicin, amikacin, doxycycline, ciprofloxacin, vancomycin, piperacillin + tazobactum and cefoperazone + sulbactum (24)

A study in Nigeria by Ako-Nai et al reported a 53.2% rate of Gram-negative bacteria isolates with E. coli being most predominant (12.8%). Among the Gram Positive isolates, *Staph. aureus* was the most predominant (15.3%), followed by *Staph. epidermidis* (13.3%). The study also found that superficial and deep wounds had similar bacterial species. Antimicrobial resistance was high for penicillins (amoxicillin and cloxacillin), at 68.6% and 58.3% respectively. The resistance for superficial and deep wound isolates was 58.2% and 31.9%, respectively (43).

In a study by Yishak Abraham at the largest tertiary level hospital in Ethiopia, *Staph aureus* was the most dominant bacteria at 14.8% followed by *Acinetobacter spp* at 11.4%. 51.2% of the wounds had monomicrobial growth while 48.8% had polymicrobial isolates. Gram-positive and negative bacteria were 34.0 and 66.0%, respectively. The gram-positive bacterial isolates had low resistance levels (<60%) to all antibiotics tested except for ampicillin and amoxicillin to which they had intermediate resistance levels (60 -80%). (52.7%) of Gram positive isolates showed multiple drug resistance (resistance to three or more drugs). The gram negative bacteria exhibited low resistance levels (<60%) to most antibiotics tested and intermediate resistance (60-80%) to ampicillin and amoxicillin. 51% of the gram negative bacterial isolates had multiple drug resistance (MDR) (44).

A study by Nobert et al at a hospital in Mwanza, Tanzania found an infection rate of 6.3%. There were 9 infected wounds with 15 bacterial isolates. 5 patients had single bacteria growth, 2 patients had two bacteria while the other 2 patients had three isolates each. The most common bacteria was *Pseudomonas aeruginosa* (40.0 %), followed by *Escherichia coli* (20.0 %), *Klebsiella pneumoniae* (20.0 %), *Proteus mirabilis*, *Pantoea agglomerans* and *Staph. aureus*. Gram negative bacteria showed high resistance to ampicillin (100 %) - (8/8), trimethoprim sulphamethoxazole (87.3 %) and ceftriaxone (62.5 %). They showed low resistance to gentamicin (14.3 %, ciprofloxacin (14.3), cefepime and meropenem (9.1 %). *Staphy. aureus* isolates showed sensitivity to all antibiotics tested apart from trimethoprim sulphamethoxazole (45)

At the Kenyatta National Hospital, a study done in 2006 by Joshua Ondari found an infection rate of 28% in Gustilo II open fracture wounds. Out of 16 infected wounds, 15 showed culture growth: with 13 having one isolate, 1 with two organisms and the other 1 with three organisms. The total number of bacterial isolates was 18. The commonest isolate was *Staph. aureus* (50%), followed by *pseudomonas aeruginosa* 22%, *proteus mirabilis* 11%, and *Acinetobacter baumanii, Providencia stuartii, Morganella morgagni* each at 6%. With regard to resistance patterns, there was high resistance to Gentamycin and Cefuroxime and low resistance to fluoroquinolones. The highest resistance was to Cephalosporins including 4th generation. There was 100% resistance to Ceftriaxone (8).

Another more recent study at KNH was done in 2016 by Sitati et al. The focus of this study was to determine if pre-debridement bacterial isolates (contaminants) were different from the post-debridement isolates in infected wounds. They found an infection rate of 58.9%. - 59 wounds. There were 24 positive cultures (growths): 15 samples had multiple organisms while 9 had single isolates. 11 types of organisms were isolated in total. The most predominant gram positive isolate was *Staph. aureus* (25%), while for gram negative isolates *Pseudomonas spp*. (20.8%) and *Klebsiella spp*. (10.4%) were predominant. With regard to comparison between pre and post debridement isolates, only in 5.7% of the pre-debridement cultures was there similar isolates in post-debridement cultures (26).

SUMMARY

There is a high incidence of open fractures of the appendicular skeleton with a high rate of infections at our setting. The sequelae of these infections are devastating and include sepsis, osteomyelitis, amputations and even death. The cardinal strategies in infection prevention include early initiation of appropriate prophylactic antibiotics, timely debridement, early soft tissue closure and fracture stabilization.

The Gustilo classification of open fractures has stood the test of time and despite some inter-observer variations, it is still the most preferred for both treatment planning and prognostication.

The ASEPSIS scoring criteria for wound infection is a validated tool for determining wound infection. It has been found to be reliable, objective and repeatable and highly recommended for both clinical application and research.

The choice of antibiotics for both prophylactic and empiric therapy depends on the bacterial profile and susceptibility patterns in the health institution.

Most of the studies on microbial profiles in open wounds showed *Staphylococcal aureus* as the most predominant isolate among gram positive bacteria while *Pseudomonas aeruginosa* was predominant among the gram positive bacteria, but Staph. Aureus was the most predominant isolate overall. Studies done previously at KNH showed that bacterial isolates were highly resistant to ceftriaxone, tetracycline, erythromycin and amoxicillin clavulanate.

2.2 STUDY QUESTION AND HYPOTHESIS

2.2.1 Study Question

What is the profile and resistance patterns of bacterial isolates from infected open fracture wounds at Kenyatta National Hospital?

2.2.2 Hypothesis

The microbial isolates from infected open fractures has high resistance to the commonly used antibiotics.

2.3 STUDY PROBLEM

There is a high incidence of open bone fractures in our setting, accelerated further by an upsurge in the use of motorcycles for public transport. The rate of early infection is high despite following existing protocols, which often results to delays in definitive fixation with implants. This causes significant increase in healthcare cost, hospital length of stay, and poor patient outcomes. The clinical sequelae of these infections is devastating and may include sepsis, acute/chronic osteomyelitis, amputations or even death.

2.4 STUDY JUSTIFICATION

One of the critical strategies in preventing these infections is early initiation of appropriately selected prophylactic antibiotics. Once wound infection has been detected, it is crucial to start empiric therapy awaiting the microscopy, culture and sensitivity results. A clear knowledge of the profile of pre-dominant causative microbial agents and their sensitivity patterns will aid the surgeon in initiating appropriate antibiotics. The purpose of this study therefore was to provide information on the bacterial profile and their antimicrobial sensitivity patterns. This will inform the development of prophylactic antibiotic protocols at the orthopedic department and also enhance antimicrobial resistance surveillance in the hospital.

2.5 OBJECTIVES

2.5.1 Broad Objective:

To determine the microbial profile and susceptibility patterns of bacterial isolates from infected open fractures.

2.5.2 Specific objectives:

1. To determine the profile of bacterial isolates from infected open fractures.
2. To determine the sensitivity and resistance patterns of bacterial isolates from infected open fractures.
3. To determine the trends of antibiotic use in patients presenting with open fractures at KNH.

3.0 MATERIALS AND METHODS

3.1 STUDY SETTING

The study was conducted at the Kenyatta National Hospital Orthopedic. KNH is the largest Teaching and referral hospital in Kenya with over 1800 bed capacity. It is situated along Hospital road, Upper Hill area in Nairobi about 5km from the city center and receives the highest number of trauma patients in the country.

3.2. STUDY DESIGN: Descriptive Cross-sectional Study

3.3 STUDY POPULATION

All patients aged between18 and 75 years with open fractures showing clinical signs of infection, in the KNH Orthopedics wards.

3.4 SAMPLE SIZE: The Fisher's formula was used (50).

$$n_0 = \frac{Z^2 (1-\infty/2) \times P (1-P)}{d^2}$$

Whereby;

n_0 = Sample size to be determined

$Z^2 (1-\infty/2)$ = The standard error of the mean corresponding to a 95% confidence interval, whose corresponding value from the T-table is 1.96.

P = The expected prevalence of the event to occur. Value of P will be put at 0.59 from Sitati's study in 2016 which found the infection rate to be 58.9%. (26) This is best average estimate for the infection rate.

d = is the target margin of error which will be 5 %(0.05).

$$n_0 = \frac{1.96^2 \times 0.59 (0.41)}{0.05^2}$$

$n_0 = 372$

However, given the small population, the finite population correction factor was aqpplied:

$$n = \frac{n_0 \times N}{n_0 + (N-1)}$$

Where n = the sample from the finite population

N = Total population

72 – Estimated number of patients with infected open appendicular fractures treated over a similar 3 months period.

$\mathbf{n_0}$ retains the earlier definition

$$\mathbf{n = \frac{372 \times 72}{372 + 72 - 1}}$$

$$\mathbf{n = 60}$$

Add 10% attrition rate = **+6**

= 66 subjects

3.5 INCLUSION CRITERIA

- All patients with infected open fractures of the appendicular skeleton aged between 18 and 70 years.

3.6 EXCLUSION CRITERIA

- Patients on chemotherapy or long term corticosteroids
- Patient with known DM, HIV/AIDS, Chronic Renal Failure

The above categories were excluded because these conditions are known to affect the host's immunity and could skew the findings on microbial isolates as well as susceptibility patterns.

3.7 SAMPLING PROCEDURE

Patients presenting to the hospital with open appendicular skeleton fractures whose wounds developed infection were recruited into the study. Recruitment was done by the principal investigator and the two research assistants using an informed consent form. The first participant was randomly selected. All subsequent eligible patients were recruited until the sample size was achieved.

3.8 DEFINITION OF INFECTION

The wounds were assessed for infection at day 3 following initial debridement. For purposes of this study, the presence of pus indicated wound infection. For the wounds with any of these signs; tissue planes separation, serous discharge or surrounding erythema without obvious pus discharge, the ASEPSIS score was used to determine infection -scores of 21 and above (48). Non infected wounds were assessed again 5 days later. Pus swabs were taken from all the infected wounds using the Levine Method.

Superficial infection meant involvement of only skin and subcutaneous tissue with no fluctuation in deep tissue nor deep tissue dehiscence beyond the fascia. Deep infection meant involvement of deep tissues, fluctuation or purulent discharge from deep tissues layers below the

fascia (51). Patients with deep infections who were scheduled for debridement in theatre had infected tissue biopsy taken for MCS to increase the chances of a positive culture growth.

3.9 SAMPLE COLLECTION AND CULTURE PROTOCOL

- Swab specimens were collected from wounds deemed clinically infected.
- Wound was first cleaned with normal saline.
- Antiseptic solutions were avoided prior to taking the specimen
- Purulent fluid, necrotic debris or drainage over hard eschars were avoided.
- Wound were cleansed by removing excess debris from wound base by flushing with normal saline
- Excess saline from the wound bed was gently blotted with a dry sterile gauze.
- Soiled gloves were removed and clean ones worn.
- The sterile culture collection tube was opened and swab removed.
- If the wound was dry, the tip of the swab was moistened with sterile normal saline.
- Levine technique was used to obtain the specimen - tip of swab rotated over a 1 cm^2 area at the base of the wound for 5 seconds (37)
- Sufficient pressure was applied to cause tissue fluid to be expressed. This was the desired tissue fluid for culture.
- The swab was then placed in the culture transport tube avoiding contamination.
- The Culture collection/transport kit was then labelled with study number, age, specimen source, date and time of culture.
- Specimens were submitted to the Microbiology Laboratory within one hour of collection for MCS.
- The specimens were cultured within one hour after delivery to the laboratory. Sheep or chocolate blood was used for culture, incubated at 35 to 38 degrees Celsius for 18 hours followed by further 18 hours of sensitivity testing if growth was obtained.

3.10 DATA COLLECTION

Information filled in the standard data collection sheet was as follows:

- Baseline characteristics/demographics – study number. Age, Gender
- Injury mechanism.
- Time of Admission, time of I initial debridement.
- Size of wound.
- Site of wound.
- Fracture pattern by AO classification.
- Gustilo Grade.
- Fracture stabilization method used.
- Number of days since initial debridement.
- Presence of pus / ASEPSIS score
- Culture results: Isolates, Sensitivity patterns
- Antibiotic(s) prescribed by the attending surgeon and their duration.

3.11 DATA MANAGEMENT AND ANALYSIS

Data was verified and cleaned continuously for accurate data entry. The final data was entered into SPSS version 22. Demographic data and other baseline characteristics were analyzed descriptively as frequencies, means, modes and medians where applicable Results were presented in tables, graphs and pie charts.

3.12 QUALITY CONTROL

The 2 research assistants were trained on the use of ASEPSIS scoring tool and on specimen collection procedure.

Swab specimen collection was aimed at tissue fluid and exfoliations from the wound bed and not merely pus fluid to increase the culture yield.

Data was cleaned daily for accuracy before entry to avoid errors.

Data analysis was done with the help of a statistician.

3.13 ETHICAL CONSIDERATIONS

Since this is a research involving human subjects, the WHO International ethical guidelines for biomedical research was followed and adhered to. Specific reference was made to the World Medical Association Declaration of Helsinki (as last amended 2013).

Ethical approval was sought from the Orthopedics Department, University of Nairobi, as well as the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee.

The purpose of the study was explained to the participants in detail to obtain a written informed consent prior to enrolling the subjects.Participation in the study was totally voluntary. It was emphasized that the participants could decline to participate or withdraw at any point during the study without any consequence to them or their treatment.

Strict confidentiality was observed throughout the study. Codes were assigned to avoid use of personal identifiers.

The findings of this study shall be disseminated through the Orthopedics Department as well as the University of Nairobi Library.

3.14 STUDY LIMITATIONS

Possible lower culture yields of swab specimen compared to deep tissue specimens.

Possible lower culture yields in patients already taking antibiotics.

Only aerobic cultures were done

3.15 DE-LIMITATIONS

There was strict use of the Levine method of swab specimen collection to increase the yield

Proper training of the research assistants was done

Deep tissues were taken for MCS for all the patients who underwent debridement for deep infections.

4.0 RESULTS

4.1 BASELINE CHARACTERISTICS

Between 7th October 2019 and 3rd January 2020, a total of 66 subjects with infected open fracture wounds were recruited into the study.

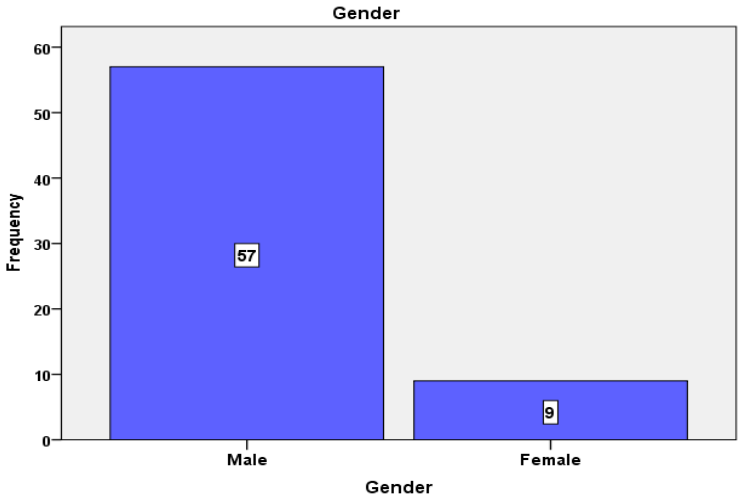

Figure 1. Gender Distribution.

There were 57 (86%) male and 9 (14%) female subjects. The male to female ratio was 6.3:1
The minimum age was 19 years while the maximum age was 59, with a range of 40 years. The median age was 36 and the mean age was 36.38 years.

Causes of Injury

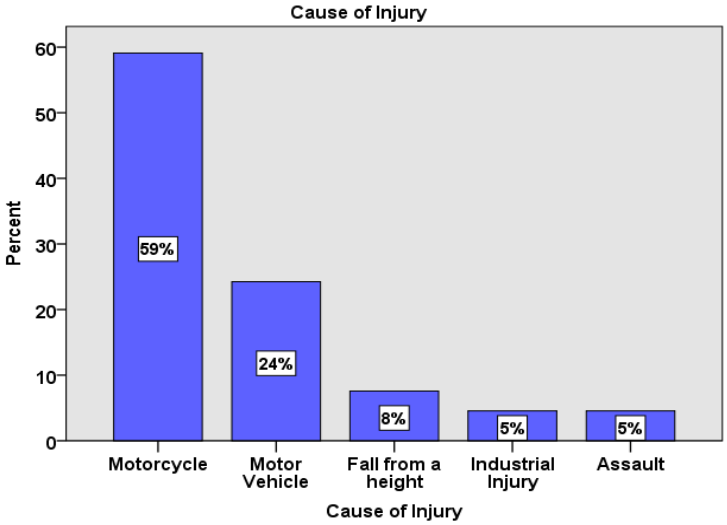

Figure 2: Causes of Injury

Motorcycle accidents were the highest causes of injury at 59% followed by motor vehicles- 24%, fall from height- 8%, industrial injury- 8% and assault.

Site of open fracture

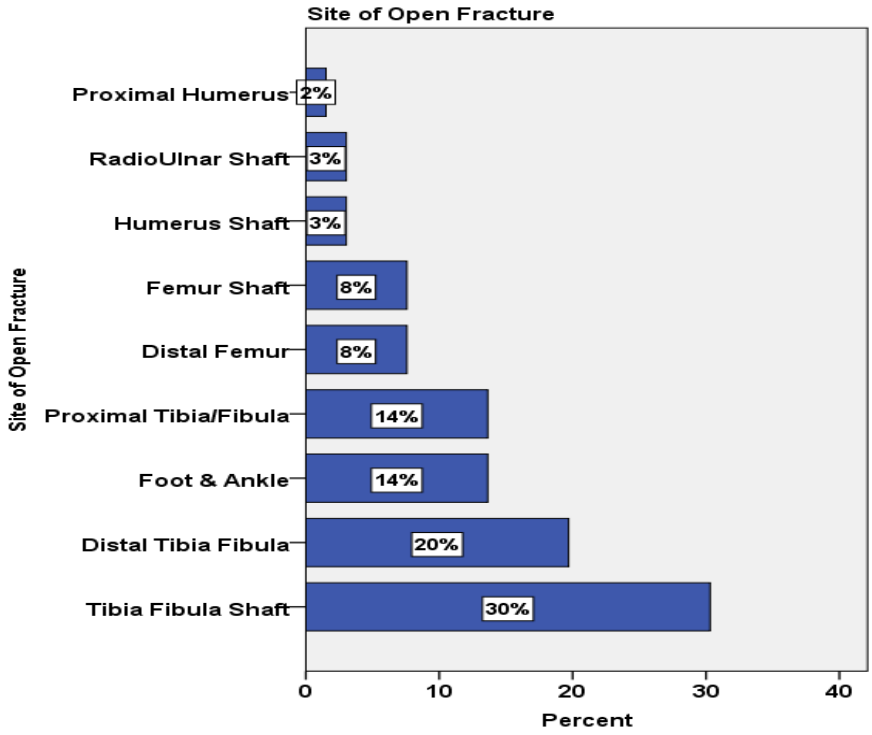

Figure 3: Sites of open fracture

Most injuries were of the tibia-fibula shaft at 30% followed by distal tibia-fibula at 14%. Foot/ankle and proximal tibia-fibular open fractures had a similar occurrence rate of 14%. Other sites included distal femur and femur shaft both at 8%. Humerus shaft, Radio/ulnar shaft and proximal humerus open fractures were the least frequent at 3%, 3% and 2% respectfully.

Gustilo Classification

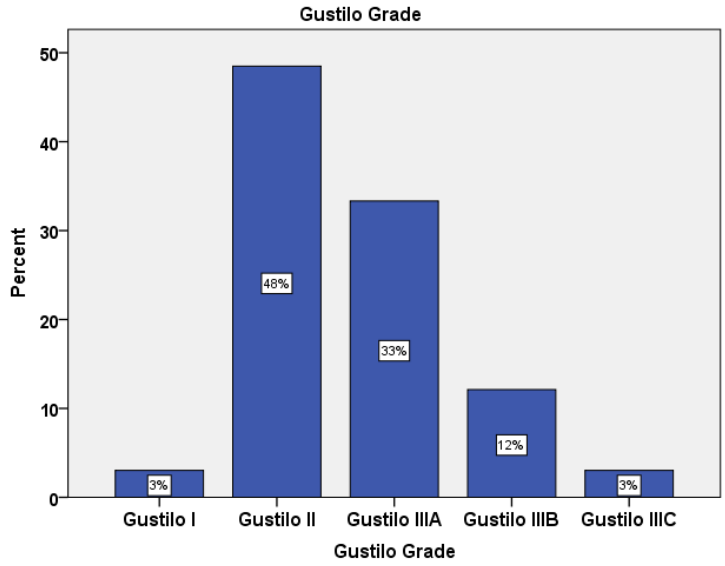

Figure 4:Gustilo Classification of the open fracture wounds

The most prevalent Gustilo class of open fractures was Gustilo II - 32 (48%), followed by Gustilo IIIA - 22 (33%), Gustilo IIIB - 8 (12%) and Gustilo I and IIIC - 2 (3%) each.

Time to Initial Debridement

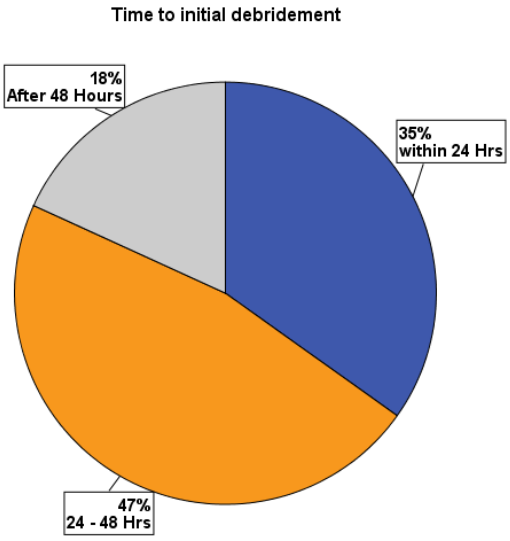

Figure 5: Time to Initial debridement

Time to debridement was between 24-48 hours for most subjects (47%). Those who had debridement within 24 hours were 35% while 18% had debridement done after 48 hours.

Method of Fracture Stabilization

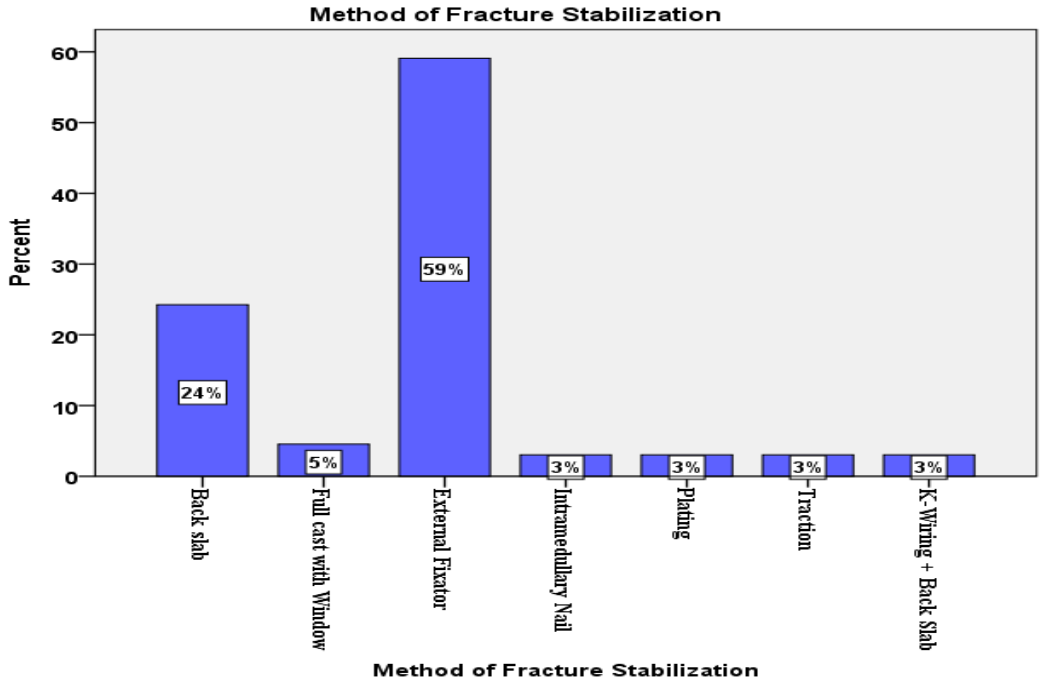

Figure 6: Method of initial fracture stabilization following debridement

Most fractures were initially stabilized with External fixators – 39 (59%). Backslab was used in 16 (24%), Full cast with a window was used in 3(5%). Other methods included IM nailing - 2(3%), Plating -2(3%), Skeletal Traction -2(3%) and K-wiring + Backslab 2(3%).

Presence of pus, ASEPSIS Score, Depth of infection

There was presence of pus in 55(83%) wounds. 11(17%) Wounds did not have pus discharge but had an ASEPSIS score above 21 thus clinically considered infected. There were 43 (66%) superficial and 22 (34%) deep infections.

4.2 BACTERIAL PROFILE

Culture Growth

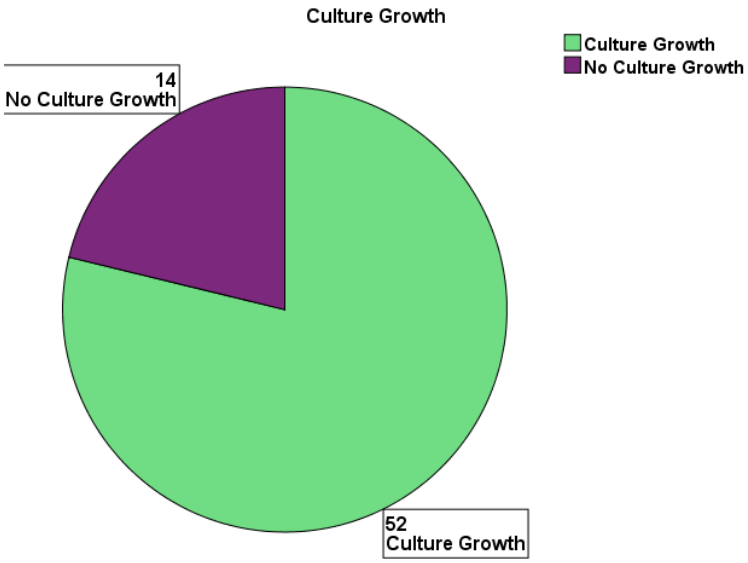

Figure 7: R*ate of culture growth*

Out of 66 samples taken to the lab, there was a positive culture in 52(79%) and No Culture growth in 14(21%) of the samples.

Out of the 52 samples with a positive culture growth, 42(81%) had a single bacterial isolate while 10(19%) had 2 isolates each, making a total of **62 Isolates** that were studied.

Bacterial Isolates

There were 45 (73%) gram negative and 17 (27%) gram positive bacterial isolates. Gram positive bacteria comprised of *Staphylococcus aureus* while Gram negative organisms included *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus Mirabilis* and *Klebsiella pneumoniae*.

The most pre-dominant bacterial isolate was *Pseudomonas aeruginosa* at 21(34%). There were 17 (27%) *Staph. aureus* isolates, 12(20%) *E.Coli*, 10(16%) *Proteus mirabilis* and 2(3%) *Klebsiella pneumoniae* isolates.

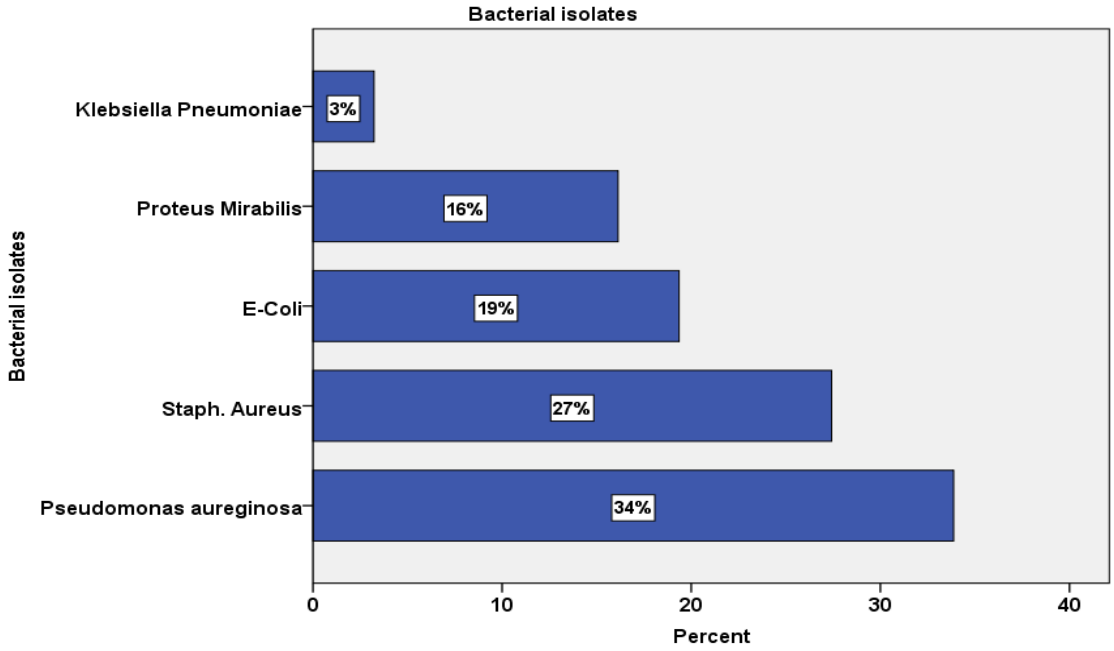

Figure 8: Bacterial isolates

Antibacterial Susceptibility

There was high resistance against commonly used antibiotics. Among gram positive bacteria, the highest resistance was against Benzyl penicillin (100%), Amoxicillin Clavulanate (82%), Erythromycin (80%), Cefuroxime (75%), Ceftriaxone 60% and Clindamycin (50%). 4 Staph. aureus isolates were resistant to Oxacillin, which denotes Methicillin Resistant Staph. aureus (MRSA), but they were all sensitive to vancomycin. There was 100% sensitivity to Meropenem, Amikacin, Vancomycin, Piperacillin and Linezolid.

Among the Gram Negative isolates, there was high resistance to Clindamycin (100%), Erythromycin (100%), Amoxicillin Clavulanate (94%), Ampicillin (80%), Cefuroxime (68%) and Rifampicin (65%). Ceftriaxone resistance was in 54%. There was 100% sensitivity to Meropenem, Amikacin and Piperacillin. More than 80% of the isolates showed resistance to more than 3 commonly used drugs.

Table 6: Antibacterial susceptibility patterns

ANTIBIOTIC	No. of Isolates Tested	RESISTANCE					
		OVERALL	***Staph. aureus***	***Pseudomonas. Spp***	***Proteus. Spp***	***E.Coli***	***Klebsiela. Spp***
Amixicillin /Clavulanate	46	**85%**	82%	100%	60%	100%	100%
Cefuroxime	35	**86%**	75%	91%	100%	78%	0%
Ceftriaxone	37	**55%**	60%	64%	40%	57%	0%
Ceftazidime	38	**53%**	67%	29%	69%	67%	-
Cefotaxime	12	**58%**	75%	-	50%	100%	0%
Cefazolin	14	**100%**	-	-	-	-	-
Clindamycin	41	**85%**	50%	100%	100%	100%	100%
Ciprofloxacin	42	**12%**	13%	21%	0%	11%	0%
Oxacillin	4	**100%**	100%	-	-	-	-
Vancomycin	14	**0%**	0	-	-	-	-
Gentamycin	44	**34%**	29%	27%	71%	33%	0%
Levofloxacin	10	**80%**	80%	-	-	-	-
Meropenem	21	**0%**	0%	0%	0%	50%	-
Amikacin	25	**0%**	0%	0%	0%	0%	-
Ampicillin	10	**80%**	-	-	67%	100%	-
Piperacillin/ Tazobactam	24	**0%**	0%	0%	0%	0%	0%
Rifampicin	39	**51%**	0%	88%	60%	45%	45%
Linezolid	8	**0%**	0%	-	-	-	-
Benzyl Penicillin	8	**100%**	100%	-	-	-	-
Erythromycin	14	**86%**	80%	-	-	100%	100%

Prophylactic antibiotics

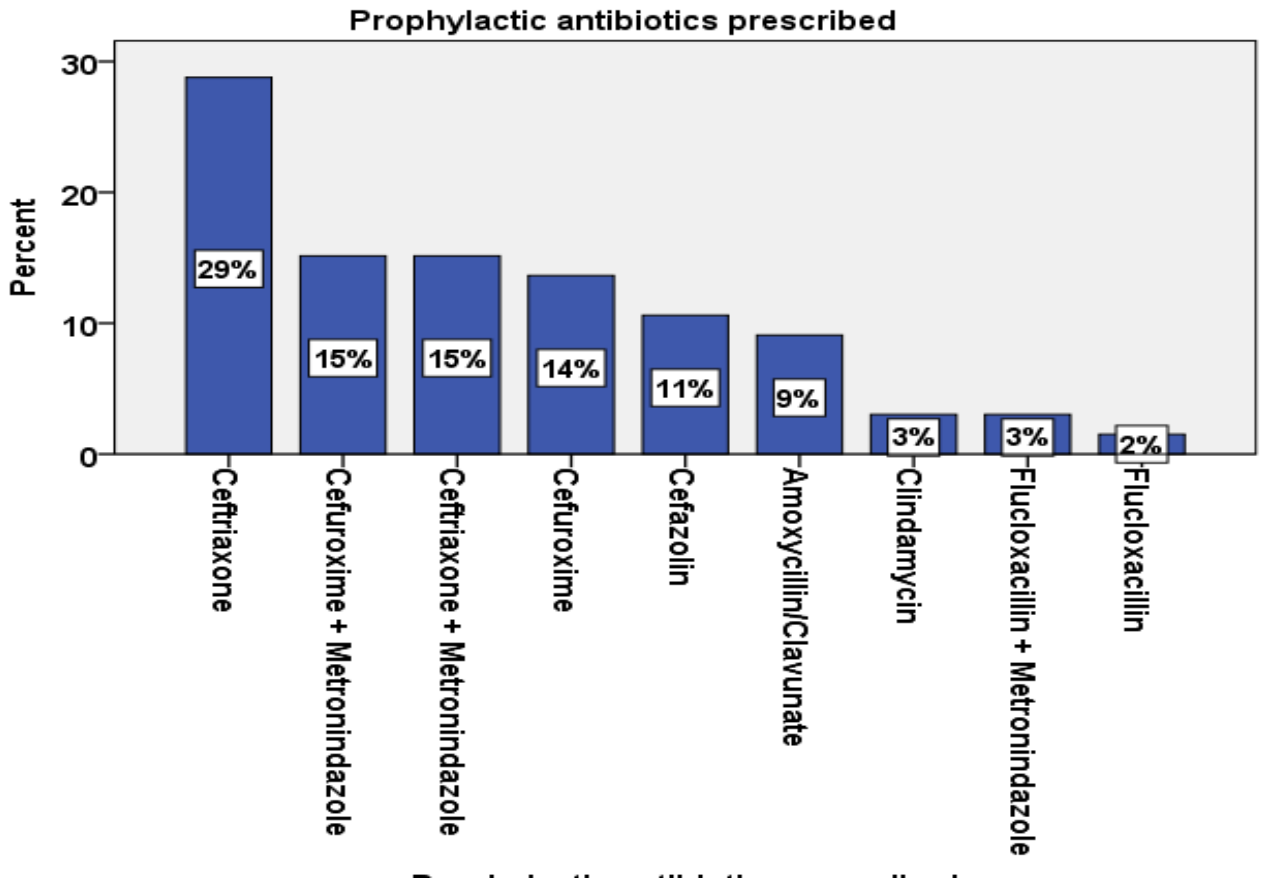

Figure 9: Prescribed prophylactic antibiotics

The surgeons' most preferred prophylactic antibiotics were Ceftriaxone – (29%), followed by Cefuroxime + Metronindazole (15%), Ceftriaxone + Metronindazole (15%), Cefuroxime (14%), Cefazolin (11%), and Amoxycillin/Clavulanate (9%). Others were Clindamycin (3%), Flucloxacillin + Metronindazole (3%) and Flucloxacillin (2%).

Duration of Prophylactic antibiotics

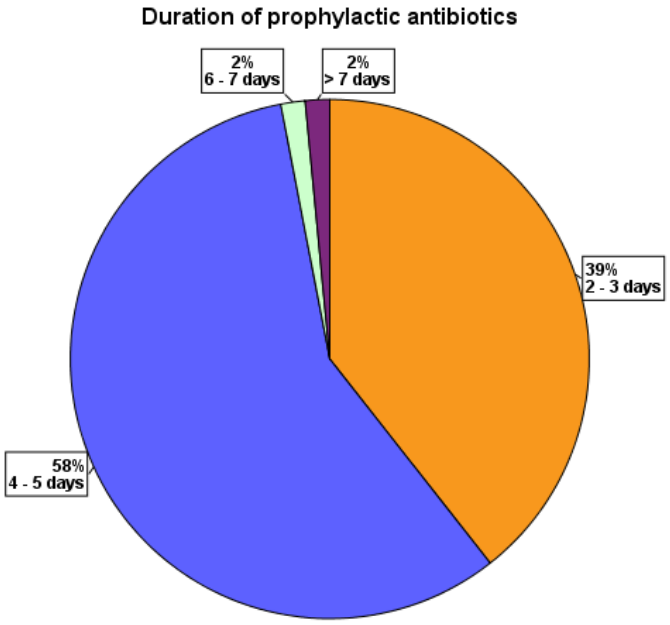

Figure 10: Duration of prophylactic antibiotics

Most of the patients (58%) were put on prophylactic antibiotics for a period of 4 -5 days. 39% of patients had prophylactic antibiotics for 2 – 3 days while others received antibiotics for 6 – 7 days (2%) and another group for more than 7 days (2%).

5.0 DISCUSSION

This prospective cross-sectional study was conducted at Kenyatta National Hospital Orthopedics department over the period of October 2019 to January 2020. 66 patients were recruited into the study. Each of them had a single open fracture wound with clinical signs of infection; the presence of pus discharge or an ASEPSIS score higher than 21 points. None of the patients was lost to follow-up nor withdrew from the study.

The baseline characteristics with regard to gender and age were similar or close to what was observed in other local studies (5, 6, 8). The male to female ratio was 6.3:1, and the median age was 36.38 years. The youthful male preponderance is consistent with the normal gender roles in the society where the males are mostly the bread winners thus more likely to be involved in risky activities in the transport sector and other industries.

Most of the injuries (59%) resulted from motorcycle accidents followed by motor vehicle accidents at 24%. Similar findings were noted in the study by Waithiru Peris at KNH where 83% of all appendicular skeleton fractures were caused by Road Traffic Accidents (RTA)s. In the study by Gachathi Wanjama in Eldoret, 67% of all injuries resulted from RTAs, among which 65% were from motorcycle accidents while 33% resulted from motor vehicle accidents (5, 6).

The commonest sites of open fracture were the Tibia/fibula shaft followed by the Tibial plafond and Foot/ankle at 30%, 20% and 14% respectively. Most fractures were of Gustilo grade II (48%) followed by Gustilo IIIA (33%). This is different from the study by Gachathi where majority of the open fractures were in Gustilo class IIIA (42%) followed by class II and IIIB at 21% each. There were only 2 patients with infected Gustilo I fractures. This is in keeping with the known minimal infection rate in this category with most studies recording less than 1% infection rate in this class (18, 29).

35% of the patients had their initial wound debridement done within 24 hours as recommended by current literature. Many studies have shown no increase in infection rate when debridement is not done within the historical 6 hours (18, 47 - 48). The current consensus is to debride wounds within 24 hours on a semi-emergency theatre list, mostly at day time when optimum operating room equipment and personnel is accessible, except for wounds with vascular injury, gross contamination or compartment syndrome (15 – 16)).

47% and 18% of our patients had debridement done between 24 – 48 hours and after 48 hours respectively. The main reasons given for the delays were; lack of blood and blood products, patients being too sick for operations and needing to be stabilized by specialists in other departments and lack of theatre space.

The commonest form of fracture stabilization was external fixation (59%) followed by the use of back slab (24%). Back slab was used for length stable fractures with small or closable wounds while external fixators were mainly used for unstable fractures and for large wounds, mainly Gustilo III. Skeletal traction was used for few patients, mainly those with open femur fractures whose wounds were small and easily accessible for dressing. Schandelmaier et al found Intramedullary Nail and External fixators to be the better options in infection prevention in open

tibia fractures, with IMN being superior (39). In our setting, the delays experienced with initial debridement explain why only 6% of patients were treated definitively with IMN and plating, a treatment whose key pre requisite is early debridement and absence of gross contamination.

There was a 79% (n = 52) culture growth rate out of the 66 pus swab specimen. 81% (n = 42) had single bacterial isolates while 21% (n = 10) had 2 isolates each, thus the total number of isolates were 62. The high culture growth rate achieved (79 %) is attributed to the use of the Levine technique for pus swab specimen collection. In a study comparing 3 different methods, Levine technique had the highest accuracy with a sensitivity of 90%. The mean concordance between swab specimens obtained using Levine's technique and tissue specimens was 78% (49).

The overall proportion of gram negative bacterial isolates (73%) was higher than that of gram positive isolates (27%). The most pre-dominant bacterial isolate was *Pseudomonas aeruginosa* (34%), followed by *Staph. aureus* (27%), *E.Coli* (20%*), Proteus mirabilis* (16%) and *Klebsiella pneumoniae* (3%). This was similar to other studies by Al – Saadi et al in Iraq, Ako Nai et al in Nigeria, Yishak et al in Ethiopia and Nobert et al in Tanzania. These studies found an overall higher proportion of gram negative bacteria. Among the gram positive bacteria, all these studies found *Staph. aureus* to be the most predominant (42 – 45). Local studies at KNH by Ondari et al and Sitati et al showed a higher overall proportion of Gram positive than Gram negative isolates, with *Staph. aureus* being the most predominant (8, 26).

There was high resistance against commonly used antibiotics. Overall, there was high resistance against Benzyl penicillin (100%), Cefuroxime (86%), Erythromycin (86%), Amoxycillin Clavulanate (85%) and Clindamycin (85%). 4 isolates had Oxacillin resistance which was classified as MRSA and treated with Vancomycin to which they were sensitive. More than 80% of the isolates had resistance to at least 3 commonly used antibiotics. The high resistance to penicillins was also found in other similar studies (43 - 45). Locally, the susceptibility patterns were very similar to previous studies done at KNH. The study by Ondari J et al at found high resistance to Gentamycin and Cephalosporins including 4th generation. There was 100% resistance to Ceftriaxone. The study by Sitati et al found high resistance to Amoxicillin clavulanate, Tetracycline and Fluoroquinolones, with high sensitivity to Vancomycin, Meropenem, Linezolid and Cefuroxime (8, 26).

The most commonly prescribed antibiotics were Intravenous Ceftriaxone and Cefuroxime, either singly or in combination with Metronindazole. This finding was similar to a study at Mulago hospital by Kigela et al where Ceftriazone was the most prescribed prophylactic antibiotic (52). In our study, the resistance to ceftriaxone was 60% among gram positive isolates and 54% among Gram negative bacteria. Cefuroxime resistance was in 75% of the gram positive isolates and in 68% of the gram negative category. Such a resistance pattern in Cephalosporins as well as in the penicillin group quite often limits the surgeon’s choices in selecting appropriate prophylactic antibiotics. This is compounded further by the fact that most of the drugs with high sensitivity are reserved for serious overt infections directed by culture results. Institutional or national surgical prophylactic-antibiotics protocols developed to curb injudicious use of antibiotics are critical to dealing with the high rates of anti-microbial resistance in open fractures

in our setting. One such protocol was in the process of development at KNH during the period of this study.

Majority (58%) of the patients were put on prophylactic antibiotics for 4 – 5 days while 39% had their antibiotics prescribed for 2 – 3 days. The study at Mulago Hospital in Kampala reported longer durations of prophylaxis, which varied from 1 to 13 days with an average of 7.3 days (52). Both the 'EAST Practice Management Guidelines Work Group' and the 'American College of Surgeons Trauma Quality Improvement Program (ACS TQIP)' guidelines advocate for cessation of prophylactic antibiotics at 24 hours following wound closure for Gustilo I and II, and 72 hours following closure of Gustilo III wounds (14, 15). The local study by Ondari et al showed no decrease in infection rate in the 5 days group compared to the 24 hours group. They concluded that additional antibiotics increases hospital costs, puts the patient in unnecessary risks of possible adverse reactions and may contribute to drug resistance (8). Perhaps the reasons for the long duration of prophylaxis at our setting includes the absence of an institutional guideline and limited choice of appropriate drugs due to resistance. Delayed debridement may also be a factor whereby the antibiotic regimen is given as preemptive therapy.

5.1 CONCLUSION

The is a higher proportion of gram negative (73%) than gram positive (27%) bacterial isolates in infected open fracture wounds in our setting. The most common isolates are *Pseudomonas aeruginosa*, followed by *Staph. aureus, Escherichia Coli*, *Proteus mirabilis* and *Klebsilella pneumoniae*.

There is high antimicrobial resistance to commonly used antibiotics, mainly the Penicillins and Cephalosporins. The study also identified 4 cases of MRSA infection.

The most commonly prescribed prophylactic antibiotics are intravenous Ceftriaxone and Cefuroxime with or without the addition of Metronindazole, and high rates of resistance against them was noted. The drugs are mostly prescribed for 4 – 5 days (58%) or for 2 -3 days (39%) which is longer than the recommended 24 hours for Gustilo I and II and 72 hours for Gustilo III.

5.2 RECOMMENDATIONS

Implementation of the institutional protocol for surgical antibiotic prophylaxis that will be constantly updated based on trends of bacterial isolate profiles and their susceptibility patterns, both of which are dynamic parameters that may vary from time to time.

Enhancement of the hospital's Infectious Disease Control strategies to reduce surgical site infection rates, and to conduct focused surveillance for antimicrobial resistance aimed at prevention and detection of resistant bacterial strains, especially MRSA.

The government to put in place policies aimed at curtailing injudicious acquisition and use of antibiotics in the country.

APPENDIX A

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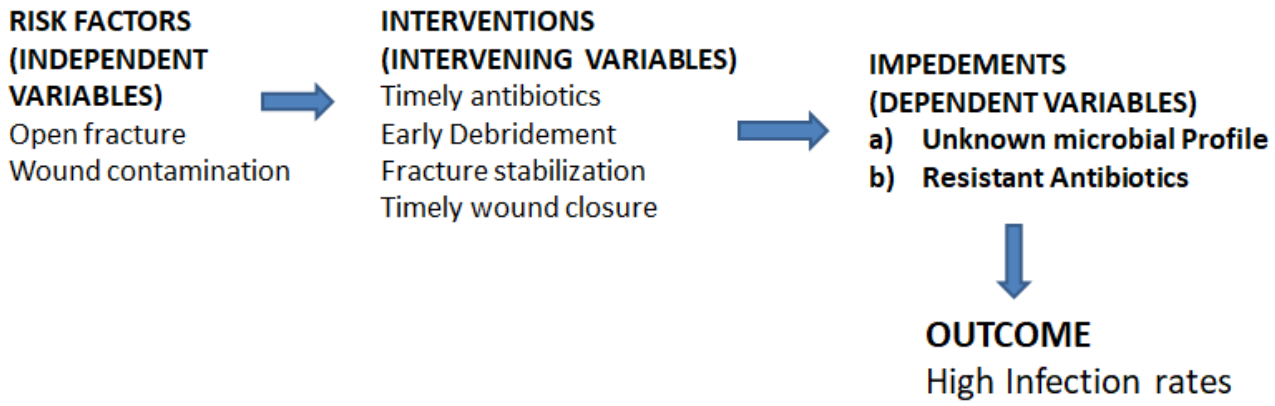
APPENDIX B: CONCEPTUAL FRAMEWORK



APPENDIX C:

CONSENT FORMS

ENGLISH

TITLE

Determination of Bacterial Isolate Profiles, Their Antimicrobial Susceptibility Patterns And The Trends Of Antibiotic Use In Patients With Open Fractures

INVESTIGATOR
Dr. Joseph T. Macharia

SUPERVISORS
Dr. Edward Gakuya
Dr. Fred Sitati

Introduction
An open fracture is one that has a wound through the skin communicating with the fracture site. Infections in open fractures are very common due exposure of the fractured bone to the environment. One of the ways to prevent and treat these infections is by using antibiotics. It is very important to know which bacteria are commonly found in these wounds and which antibiotics the bacteria are sensitive to. This will help the doctor in selecting the most appropriate antibiotics.

Study Purpose
This study aims to determine the types of bacteria that are found in infected open fracture wounds and their sensitivity or resistance to antibiotics.

Procedure
If you agree to participate in this study, your wound will be assessed for signs of infection. If found to be infected, a pus swab will be taken from the wound to the laboratory for microscopy, culture and sensitivity testing.

Benefits of participation
The results of the tests I take may also be used by your doctor in your management. Your Participation in this research will help to get information that other doctors can use to design treatment strategies for this type of infections.

Risks
There are no risks to you for participating in this study

Voluntariness and Right of Withdrawal
Please note that your participation is voluntary and you have a right to decline or withdraw your consent to participate at any time. This will not affect your management in any way.

Confidentiality
The information obtained from you will be treated with confidentiality and will be handled only by me and my assistants. Only your study number will be used. Your identity will not be revealed in any publication.

CONSENT CERTIFICATE

I certify that the study has been fully explained to me and I am willing to participate in the study.
Participant's Signature (or thumbprint)……
Date……

I confirm that I have clearly explained to the participant the nature of the study and the contents of this consent form in detail and the participant has decided to
Participate voluntarily without any coercion or undue pressure.

Investigator's Signature……. Date ……

For Any Enquiries, please contact:

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5.3 FOMU YA IDHINI

FOMU YA IDHINI YA MSHIRIKA KWENYE UTAFIT

KICHWA

UTAFITI JUU YA BAKTERIA ZINAZOLETA MAAMBUKIZI KATIKA VIDONDA KWENYE MIFUPA ILIYOVUNJIKA

MTAFITI
Dkt. Joseph T. Macharia

WASIMAMIZI
Dr. Edward Gakuya
Dr. Fred Sitati

UTANGULIZI
Mfupa uliovunjika na kupasua ngozi hutengeneza kidonda ambacho huwa na hatari ya kupata maambukizi ya bakteria. Hii ni kutokana na mfupa kufunuliwa nje kuliko na bakteria.

Njia mojawapo ya kuzuia maambukizi haya ni kutumia antibiotiki . Ni muhimu sana kujua ni bakteria zipi ambazo hupatikana zaidi katika vidonda hivi, na pia ni antibiotiki gani huweza kuua zile bakteria. Ufahamu huu husaidia madaktari kuchagua antibiotiki zilizo mwafaka

Umuhimu wa utafiti
Utafiti huu unalenga kutambua ni bakteria zipi ambazo zinapatikana katika vidonda hivi na ni antibiotiki zipi zinaweza kuziua.

Utaratibu
Ukikubali kuhusika katika utafiti huu, utakaguliwa kwenye kidonda chako kubainisha iwapo una maambukizi ama usaha. Ukipatikana kuwa na maambukizi, sampuli ya usaha itachukuliwa na kupelekwa kwenye maabara ili kufanyiwa kipimo
.
Manufaa ya kushiriki
Matokeo ya kipimo cha usaha yanaweza kutumika katika matibabu yako. Kuhusika kwako hakutakugharimu malipo yoyote.

Madhara
Hakuna madhara yoyote ambayo yanaweza kukupata kutokana na kuhusika katika utafiti huu.

Kujitolea na Kujiondoa kwa hiari
Ni muhimu kuelewa ya kwamba kushiriki ni kwa kujitolea. Sio lazima kushiriki katika huu utafiti, na pia waweza kubadili nia yako wakati wowote kuhusu kuendelea kushiriki, bila kuathiri huduma zako za afya.
Usiri
Habari utakayotoa au itakayopatikana kukuhusu itakuwa siri wakati wote na itatumika kwa huu utafiti pekee yake. Tutatumia nambari maalum kukutambua na wala sio jina lako.
Asante sana kwa ushirikiano wako.

AZIMIO
Nimekubali kwamba nimeelezwa kikamilifu kuhusu utafiti huu na nakubali 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 yoyote kuhusu utafiti huu, wasiliana na:
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And Research Committee
College of Health Sciences
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APPENDIX D:

DATA COLLECTION SHEET

PATIENT DATA

1. Study number ……

2. Age in years ……

3. Sex: M F

4. Date of injury …….

5. Date of admission ……

6. Date and time of initial debridement Date …… Time……..…….

7. Hours or days after initial debridement……..

FRACTURE/WOUND DATA:

1. Cause of injury

a. Pedestrian ……

b. Automobile …….

c. Motorcycle……...

d. Bicycle ……

e. Fall from height

f. Industrial injury……

g. Assault ……

f. Fallen on by weight……..

g. Farm injury ……..

i. Sport injury ……..

2. Site of the open fracture

……

3. Size of Wound……by……..cm

4. Fracture pattern: a) Simple. Transverse……..b. Oblique……..…c. Spiral……..

b) Wedge …….. c) Segmental …….

d). Comminuted……..

AO Classification of fracture …….

5. Gustilo grade ……

6. Method of fracture stabilization

a. Long back-slab ……

b. Long full cast with a window……

c. External fixation……

d. Intramedullary nailing……

e. Plating……

ASSESSMENT FOR INFECTION

Pus present? Yes …… No ……

If no Pus, ASEPSIS SCORE? ……..

If no Infection, Assessment after 5 days:

Pus present after 5 days: Yes ……..No ……..

If no Pus, ASEPSIS SCORE ……

Repeat debridement and infected tissue biopsy done for infected wound? ……..…..……

Infection Present? YES……NO ……... If yes: Deep …… Superficial ……

CULTURE RESULTS:

1. Growth

a. Yes…… If yes, list organism(s) ...…….……..……..……..…….……..….

…….

……..

b. No……

2. Sensitivity pattern…… …… …… ……...…

……..

3. Resistance pattern …… ……..

……..

List of prescribed antibiotics ……

……...

Duration of Prophylactic antibiotics ……

APPENDIX E: ETHICAL APPROVAL

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Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

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Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/331

9th September, 2019

Dr. Joseph T. Macharia
Reg. No.H58/81043/2015
Dept.of Orthopaedic Surgery
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Macharia

RESEARCH PROPOSAL: DETERMINATION OF BACTERIAL ISOLATE PROFILES, THEIR ANTIMICROBIAL SUSCEPTIBILITY PATTERNS AND THE TRENDS OF ANTIBIOTIC USE IN PATIENTS WITH OPEN FRACTURES (P708/08/2019)

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 9th September 2019 – 8th September 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. Edward Gakuya, Dept. of Orthopaedic Surgery,UoN
Dr. Fred Sitati, Dept.of Orthopaedic Surgery,UoN

APPENDIX F :

ORIGINALITY REPORT:

Determination of Bacterial Isolate Profiles, their Antimicrobial Susceptibility Patterns and The Trends Of Antibiotic Use in Patients With Open Fractures

ORIGINALITY REPORT

6%	2%	4%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Njee Nobert, Nyambura Moremi, Jeremiah Seni, Ramesh M. Dass, Isdori H. Ngayomela, Stephen E. Mshana, Japhet M. Gilyoma. "The effect of early versus delayed surgical debridement on the outcome of open long bone fractures at Bugando Medical Centre, Mwanza, Tanzania", Journal of Trauma Management & Outcomes, 2016 Publication	1%
2	Aaron J. Prussin, Linsey C. Marr. "Sources of airborne microorganisms in the built environment", Microbiome, 2015 Publication	1%
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