Microbiological Profile of Surgical Site Infections in Orthopaedic Surgery at the University Teaching Hospital; Lusaka, Zambia

By

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A Dissertation Submitted to the University of Zambia in Partial Fulfilment of the Requirements of the Degree of Master of Medicine in Orthopaedics and Trauma Surgery.

The University of Zambia, Lusaka

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I now declare that this dissertation herein presented for the degree of Master of Medicine (Orthopaedic and Trauma Surgery) has not previously been submitted wholly or in part for any other degree.

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I, Dr Joel Kandila, now declare that this dissertation herein presented for the Master of Medicine Degree (Orthopaedic and Trauma Surgery) has not been previously submitted wholly or in part for any other degree at any other university for any other degree. Furthermore, I declare that all sources I have quoted have been indicated and acknowledged using complete references. It has been prepared as per the prescribed guidelines for the postgraduate studies dissertations of the University of Zambia.

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CERTIFICATE OF APPROVAL

This dissertation of Dr Joel Kandila is approved as fulfilling part of the requirements for an award of Master of Medicine (Orthopaedics and Trauma Surgery) degree by the University of Zambia, subject to the examiner's report.

Supervisor.....

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ABSTRACT

Background and purpose: Surgical site infection (SSI) is the infection to the surgical site occurring within a year of surgery (if an implant is used) or within 30 days if no implant is used. SSI is a known cause of poor outcomes, increased healthcare cost on patients, sometimes leading to significant disability and even death, following orthopaedic surgery the world over. The microbiological profile of SSI following orthopaedic surgery at University Teaching Hospital (UTH) in Lusaka, Zambia was unknown as, before this study, no such research had been conducted. The SSI following orthopaedic surgery at UTH was seen as a growing problem with the possibility of antimicrobial resistance. Hence, this study set out to investigate SSI following orthopaedic surgery in this setting, to determine the causative microorganisms, their prevalence and antimicrobial sensitivity patterns.

Methods: A cross-sectional study was conducted at UTH, Lusaka, Zambia from March 2019 to March 2020. A structured questionnaire was used to collect data and sampling was done using a systematic random sampling after getting informed consent. Using AMIES pus swabs, samples were collected and sent to the microbiology laboratory at UTH for microscopy, culture and sensitivity studies. All cultures were done on three primary media MacConky, chocolate and blood agar, and the antimicrobial sensitivity studies for the cultured microorganisms were done on Mueller Hinton agar. STATA statistical software version 13 was used for the analysis of results obtained to come up with a microbiological profile of SSI.

Results: A total of 119 (79 male and 40 female) participants were recruited. The mean age was 31.75 (SD, 17.07) of the participants; 66.4% of the participants were male. The HIV prevalence was 15.1%. Out of 119 participants, 100 had culture-positive results giving a prevalence of 84.0%. *S. aureus* was the most prevalent 35 (29.4%) causative microorganism, with MRSA comprising 54.3% of the *S. aureus*. Other prevalent organisms included *Pseudomonas aeruginosa* (*P. aeruginosa*) 17 (14.3%), *Klebsiella oxytoca* (*K. oxytoca*) 13 (10.9%), *Proteus mirabilis* (*P. mirabilis*) 13 (10.9%) and Coagulase-negative *staphylococci* (CNS) 7 (5.9%). Methicillin-resistance was 54.3% and 71.4% in *S. aureus* and CNS, respectively. Gentamicin sensitivity to *S. aureus* and CNS was 68.8% and 83.3%, respectively. *P. aeruginosa* exhibited relatively low resistance to most antibiotic classes. *K. oxytoca* and *E. coli* were resistant against most antimicrobial agents, including ciprofloxacin, co-trimoxazole, ampicillin/sulbactam, and third and fourth-generation cephalosporin. The percentages of the sensitive *P. aeruginosa* isolates against most antibiotics were relatively low in this study. There was no significant association between the various factors and SSI, each with a p-value greater than 0.05.

Conclusions: The prevalence of culture-positive SSI was 84.0%. The most prevalent SSI causative microorganisms included *S. aureus* (29.4%), *P. aeruginosa* (14.3%), *K. oxytoca* (10.9%), *P. mirabilis* (10.9%) and CNS (5.9%). More than half of *S. aureus* was MRSA while CNS had more than two-thirds being methicillin-resistant. Gentamicin is a promising treatment for both *S. aureus* and CNS SSI. Third and fourth-generation cephalosporin, penicillin and co-trimoxazole had low susceptibility against most isolates. The relatively higher resistance of *P. aeruginosa* isolates against most antibiotics is a concern for possible drug resistance in the near future. Further studies on the risk factors, prevalence and incidence of SSI following orthopaedic operations should be done.

Key Words: Surgical Site Infection, Microbiological Profile of SSI, Orthopaedic Surgery.

DEDICATION

I dedicated this work to my best friend, family, friends and colleagues.

ACKNOWLEDGEMENTS

I would like to thank Prof Mulla Yakubu, Dr Sitali Jonathan, Dr Kaonga Patrick (PhD), Nachombe N Kandila, my family, friends and colleagues for their patience and input. May the Lord God bless you all.

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LIST OF ABBREVIATIONS AND ACRONYMS

ASA: American Society of Anaesthesiologists

CDC: Centres for Disease Control and Prevention

CDC NNIS: Centres for Disease Control National Nosocomial Infections Surveillance

CNS: Coagulase-negative *staphylococcus*

E. coli: *Escherichia coli*

HIV: Human immunodeficiency virus

I: Intermediate sensitivity

K. oxytoca: *Klebsiella oxytoca*

MoH: Ministry of Health

MRSA: Methicillin-resistant *S. aureus*

n: Number

NA: Non-applicable

P. mirabilis: *Proteus mirabilis*

P. aeruginosa: *Pseudomonas aeruginosa*

PI*:* Principal investigator

R: Resistant

S: Sensitive

S. aureus: *Staphylococcus aureus*

Spp.: Specie(s)

SSI: Surgical site infection(s)

UTH: University Teaching Hospital(s)

DEFINITION OF TERMS

Antibiotic resistance: The ability of microorganisms to grow and multiply despite the effects of an antibiotic ("Antibiotic Resistance," n.d.).

HIV positive in this study means HIV infection regardless of the stage of disease (*CDC: HIV Surveillance Report.*, 2013).

Methicillin-resistant *S. aureus* (MRSA) in this study was defined as resistant to Cefoxitin screen, a surrogate for oxacillin ("Laboratory Testing | MRSA | CDC," 2019).

Organ/Space SSI in this study was defined as SSI involving a major joint that is the hip, shoulder, elbow and/or knee joints.

Surgical Site Infection in this study was defined as an infection of the surgical site or that of structures deep to the surgical site occurring within a year of surgery if an implant was used (left in situ) or within 30 days of operation if no implant was used (Kabirian et al., 2014, Owens and Stoessel, 2008).

CHAPTER ONE: INTRODUCTION

1.0 Background

Surgical Site Infection (SSI) is a known serious complication of surgical procedures (Baker et al., 2016). In this study, the microbiological profile was defined for microorganisms responsible for SSI, the prevalence rates of various organisms in SSI and the antimicrobial sensitivity pattern of various microorganisms was also determined.

SSI is a term that was first introduced in 1992 to replace the previous term, surgical wound infection (Owens and Stoessel, 2008). SSIs following orthopaedic operations are not uncommon (Olsen et al., 2008) SSIs are a significant problem, especially in developed countries; little data exists in the developing countries. Anecdotal evidence in Zambia suggests that SSI is a known problem in clinical practice. Unfortunately, no published literature was found in the Zambian setting on SSI.

SSIs are usually associated with poor outcomes. SSI can complicate orthopaedic operations, often ending with morbidity and at times, even mortality (Nel, 2014; Ovaska et al., 2013; Owens and Stoessel, 2008). SSI has been associated with a more extended hospital stay, including increased healthcare costs (Ovaska et al., 2013). The link to increased use of resources on the patient and the hospital as a result of SSI is visible despite improvement in infection prevention and control (Nel, 2014; Olsen et al., 2008; Owens and Stoessel, 2008). Different studies have identified *Staphylococcus aureus (S. aureus)* as the commonest causative microorganism of SSI (Al-Mulhim et al., 2014; Baker et al., 2016).

This study set out to determine the microbiological profile of SSIs following orthopaedic operations at the University Teaching Hospital (UTH), Lusaka.

The profile included the aetiological microorganisms that are responsible for SSIs and their antimicrobial sensitivity patterns. It also served to make recommendations on the antimicrobial treatment protocol for SSI at UTH. The information from this study should lead to a reduction in the cost of treatment of SSI at UTH. Furthermore, the results of this study will form the basis of any recommendations looking at the management of SSI at UTH. Beyond that, it is hoped that this study will provide the basis for further studies concerning SSI in Zambia.

1.2 Statement of the Problem

SSIs are a global problem in surgery, complicated with severe morbidity and sometimes mortality (Nel, 2014; Olsen et al., 2008). They are amongst the most prevalent nosocomial infections in surgical patients (Maksimović et al., 2008). In Zambia, UTH included, the profile of SSI is unknown though anecdotal evidence suggests that it is a significant problem. Therefore, in this setting, there is a clear need to determine the microbiological profile of SSI so as to base clinical practice on results from studies done in the local population.

1.3 Study Justification

SSIs pose a serious problem in orthopaedic surgical practice. SSI is a known cause of poor outcomes, increased healthcare cost on patients, sometimes leading to significant disability and even death, following orthopaedic surgery the world over.

Furthermore, the microbiological profile of these infections in Zambia is unknown. This scenario is because there are no local published studies on SSI following orthopaedic operations.

However, anecdotal evidence suggests that there is an increased frequency of SSI and antimicrobial resistance pattern.

This study addressed the above issues to better clinical practice and provided the basis for more research on SSI in this population. This study can lead to a reduced hospital stay, reduced cost to both the patient and the hospital, reduced morbidity and mortality.

1.4 Research Question

- What is the microbiological profile of SSI in orthopaedic surgery at UTH, Lusaka, Zambia?

1.5 OBJECTIVES

1.5.1 General Objectives:

To investigate the microbiological profile of SSI in orthopaedic surgery at UTH.

1.5.2 Specific Objectives:

i. To identify the microorganisms responsible for SSI.

ii. To establish the prevalence of various microorganisms in SSI.

iii. To the antimicrobial sensitivities of the various microorganisms responsible for SSI.

iv. To determine factors associated with SSI.

CHAPTER TWO: LITERATURE REVIEW

2.1 Definition of SSI

SSI can be defined as an infection of the surgical site or that of deep structures to the surgical site occurring within a year of surgery if an implant was used (left in situ) or within 30 days of operation if no implant was used (Kabirian et al., 2014; Owens and Stoessel, 2008). SSI is a known severe complication of surgical procedures (Baker et al., 2016).

2.2 Classification of SSI

SSI is classified into superficial incisional, deep incisional and organ/space SSI according to the Centres for Disease Control National Nosocomial Infections Surveillance (CDC NNIS) system (Owens and Stoessel, 2008). Superficial SSI is confined to the skin and subcutaneous tissues. Deep SSI involves the deep soft tissues such as fascia and the muscles while the organ/space SSI involves the more deep-seated organ or space to the surgical incision (Owens and Stoessel, 2008).

Deep SSI is when the following parameters are met: clinical signs (redness, swelling, drainage or dehiscence), positive bacterial culture from the wound and implant visible or palpable in the wound (Ovaska et al., 2013).

Joint or bone SSI is the infection involving the joint and bone (Ridgeway et al., 2005). This infection to the large joint is equivalent to organ space infection. The classification for this study was as adopted from the CDC work as per Table 2.1 (Horan et al., 1992).

Table 2.1; Classification of SSI

Criteria for defining SSI[1]
Incisional SSI *Superficial*: Infection involves the skin or subcutaneous tissue of the surgical incision and has at least one of: 1. Purulent drainage, with or without culture-positive results, from a superficial surgical incision. 2. Microorganisms isolated from an aseptically obtained culture from the superficial surgical incision. 3. The surgeon deliberately opens the surgical site with at least one of the following signs or symptoms, pain, localized swelling, erythema, or heat, and a superficial incision 4. Diagnosis of superficial SSI by the surgeon.
Deep: Infection involves deep soft tissues (i.e. fascial and muscle layers) of the surgical incision and at least one of: 1. Purulent drainage from a deep surgical incision, excluding organ/space. 2. A deep surgical incision that spontaneously dehisces or deliberately opened by the surgeon in a patient with one or more of the following; localized pain, fever (>38ºC), unless the surgical site has the culture-negative result. 3. An abscess or another evidence of infection is found on direct examination, during repeat surgery, or by histopathologic or radiological examination. 4. Diagnosis of a deep incisional SSI by the surgeon
Organ/space SSI:* Infection involves any large joint (e.g. organ spaces), which was opened or manipulated during operation and at least one of the following: 1. Purulent drainage from the site of a drain that is placed through the wound into the organ/space. 2. Organisms isolated from an aseptically obtained culture from the organ/space. 3. An abscess or another evidence of infection involving organ/space, which is found on examination (physical, histopathologic, or radiological) or during repeat surgery. 4. Diagnosis of an organ/space SSI by the surgeon.
[1] For all classifications, infection is defined as occurring within 30 days after the operation if no implant is placed or within one year if an implant is in place and the infection is related to the incision Adapted with permission from (Horan et al., 1992).
*Organ/Space SSI = Joint space SSI

2.3 Epidemiology of SSI

SSI is a well-known global health problem in surgery patients. It has an incidence ranging from 2%-5% globally (Bachoura et al., 2011; Baker et al., 2016; Nel, 2014).

A retrospective study done in Saudi Arabia found that the incidence of SSI was 2.55% which was lower than the worldwide incidence of 2.6% to 42.9% (Al-Mulhim et al., 2014). This finding in the above study was attributed to the younger population age due to trauma-related procedures as compared to the worldwide incidence, which had most of the population age above 55 years. The strengths of this study were five years of data used, whereas the limitations were the control over the data reviewed.

However, a prospective cohort study done in Serbia found a higher incidence of SSI (22.7%) in orthopaedic patients (Maksimović et al., 2008). Limitations in this study included the short six months duration with a relatively shorter period of 30 days of patient follow-up.

In a Brazilian study (Oliveira et al., 2016), the overall incidence was 6%, though higher in open (14.7%) than closed (4.2%) fractures. This study had the strength of having a large sample size analysed. However, it had a limitation regarding certain factors associated with SSI in that it was a retrospective study.

2.4 Microbiological Profile of SSI

Several studies done on SSI have shown that *Staphylococcus aureus (S. aureus)* is the most frequent cause (Al-Mulhim et al., 2014; Baker et al., 2016; Maksimović et al., 2008; Owens and Stoessel, 2008; Ridgeway et al., 2005). *S. aureus,* including Methicillin-Resistant *Staphylococcus aureus* (MRSA), is the most prevalent causative microorganism (Al-Mulhim et al., 2014; Baker et al., 2016; Gustilo and Anderson, 1976; Oliveira et al., 2016; Onche and Adedeji, 2004; Ridgeway et al., 2005; Tsukayama et al., 1996; Wang et al., 2018).

MRSA was the most prevalent type of *S. aureus* in orthopaedic patients in one prospective Serbian study (79.2% MRSA) (Maksimović et al., 2008) and an England study on SSI in hip arthroplasty (Ridgeway et al., 2005). MRSA and methicillin-susceptible *S. aureus* had an equal prevalence of *S. aureus* (34%) in another study (Baker et al., 2016). MRSA was found to be higher in open fractures than in closed fractures (Oliveira et al., 2016).

The 2016 study (Baker et al., 2016) had other isolates including *S. aureus* (34%), *Escherichia coli (E. coli), Enterococcus species (spp.)* (12), Coagulase-negative *staphylococci* (CNS) (9%), *Klebsiella spp.* (6%), *Streptococcus spp.* (6%), *Pseudomonas aeruginosa* (*P. aeruginosa)* (4%), *Enterobacter spp.* (4%). Similarly, in another study (Al-Mulhim et al., 2014) the common causative microorganisms isolated included *S. aureus* (29.11%), *Acinetobacter spp.* (21.5%), *Pseudomonas spp.* (18.9%), and *Enterococcus spp.* (17.7%).

Cephalosporin class was the most effective prophylaxis against both gram-positive inclusive of *S. aureus* and gram-negative isolates in patients with open fractures (Gustilo and Anderson, 1976). The gram-negative isolates sensitive to the cephalosporin class included *Proteus*, *Klebsiella* and *E. coli*.

Gram-positive microbes are the most prevalent isolates in both open and closed fractures (Oliveira et al., 2016).

Some studies isolated fungal causes of SSI (Baker et al., 2016; Oliveira et al., 2016).

2.5 Risk Factors of SSI

Sources of SSI could be attributed to both endogenous and exogenous flora (Owens and Stoessel, 2008).

Most of the causative microorganisms arise from the patient's endogenous flora as compared to the exogenous microorganisms resulting from the surgical team, operating theatre environment, contaminated wounds and instruments (Nel, 2014; Owens and Stoessel, 2008). Hence, the need to continuously improve the preventive measures by the team approach (Nel, 2014).

However, in a Texas study (Johnson et al., 2007) on war combat victims, *Acinetobacter, Enterobacter spp.*, and *Pseudomonas aeruginosa* were the most common SSI causative microorganism.

The increasing number of antibiotic-resistant microorganisms and immunosuppressed surgical patients are the likely causes of more usage of the broad-spectrum antibiotics seen in current practice (Owens and Stoessel, 2008). Anecdotal evidence suggests that this is a known problem, especially in Zambia as there are several orthopaedic patients with immunosuppression arising from Human Immunodeficiency Virus (HIV) and malnutrition.

There are several risk factors for SSI. Diabetes, smoking and prolonged operative time are well known independent risk factors for SSI (Nel, 2014; Ovaska et al., 2013). Trauma as an indication for orthopaedic operation, emergency operation and prolonged operation time are independent risk factors for SSI following orthopaedic surgery (Al-Mulhim et al., 2014). Smoking, diabetes, older age and colonisation with pathogens are well-known patient-related risk factors while prolonged operation time and poor surgical technique form part of the procedure-related risk factors (Owens and Stoessel, 2008). Lengthy operative time and higher American Society of Anaesthesiologists (ASA) score have been associated with increased risk (Ridgeway et al., 2005).

In a retrospective Brazilian study (Oliveira et al., 2016), open fractures were found to have a significantly higher incidence of SSI than closed fractures. This finding was attributed to a higher level of contamination seen in high energy injuries.

This finding in this retrospective Brazilian study was attributed to a higher level of contamination in open fractures. One of the strengths of this Brazilian study was the huge sample size.

There are more patient-related risk factors than procedure-related risk factors (Owens and Stoessel, 2008). However, immunosuppression due to AIDS and malnutrition are important risk factors for SSI, especially in the African population (Nel, 2014).

It took, on average, 7.4 days of symptoms before having the patient arrive at the military tertiary institution (Johnson et al., 2007).

2.6 Complications of SSI

SSI have been associated with a prolonged hospital admission period, hence the increased risk of nosocomial infections and antibiotic resistance (Nel, 2014; Owens and Stoessel, 2008). They can also lead to increased morbidity, such as cosmetically unacceptable scars and amputations (Nel, 2014). Mortality rates may be very high, especially in patients infected by highly virulent microorganisms such as MRSA (Owens and Stoessel, 2008).

In the USA, mortality in patients with SSI was estimated to be 3% in acute care hospitals (Baker et al., 2016b).

Orthopaedic SSI can increase the cost of healthcare by more than 300% and prolong the period of hospitalisation (Bachoura et al., 2011; Whitehouse et al., 2002). The prolonged hospital stay leads to unproductivity by the patient and families (Owens and Stoessel, 2008).

MRSA, a common cause of SSI, is associated with prolonged hospitalisation and increased healthcare costs (Baker et al., 2016; Ridgeway et al., 2005). SSI poses a considerable problem in terms of morbidity and mortality, leading to increased demands on healthcare resources, which are usually overburdened (Owens and Stoessel, 2008).

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Study Design

A cross-sectional study was done.

3.2 Study Setting

This study was conducted at UTH, a tertiary health institution with an orthopaedic surgery speciality, in Lusaka City, Lusaka Province, Zambia. This institution is a government hospital run by the Ministry of Health (MoH). UTH is the highest referral hospital in the country with multiple specialist services being provided. The study was conducted in the Surgery Department at the adult hospital of UTH.

3.3 Target Population

All patients (paediatrics and adults) that had developed SSI following orthopaedic operative management at UTH and met the eligibility criteria below were invited to join the study.

Study Population

The study population included all the participants that were part of this study.

3.4 Eligibility Criteria

Table 3.1; Eligibility Criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Informed consent	Documented pre-existing active systemic sepsis at the time of the operation
Post orthopaedic operation involving surgery on the bone or joint, within a one year period with an implant in situ or 30 days without implant	Documented pre-existing active local infection to the surgical site (clinical versus pus swabs)

3.5 Sample Size

A sample size calculation was done, using epi-info and the proportions formula for a cross-sectional study, as shown below:

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

Z= Standard normal variate

e= Absolute error

95% confidence interval

Using the prevalence of 17.7% (Al-Mulhim et al., 2014)

80% power

Therefore, the sample size (n) population was 102 participants. To cater for a 10% non-response rate rounded off as 11, brought the sample size population of 113 participants.

3.6 Sampling Procedures

A systematic random sampling method was used in this study. In four months it was expected that 400 possible participants would be seen.

In this study, the sample size calculated as outlined above was 113 and therefore, the calculated K^{th} value (400/113 = 3.54). Therefore, a sampling interval of 3 was used in this study. A blinded number picking picked the K^{th} value for the first participant and continued with a sampling interval of 3.

3.7 Data Collection

The participants were allowed to read the information sheet in order to understand the study. Informed consent was obtained from would-be participants once they had thoroughly read and understood the information sheet and consent form, and had all their questions answered. A structured questionnaire was used as a data collection tool to capture data from the study participants. The HIV determine rapid test (Abbott Oslo, California, USA) and SD BIOLINE HIV 1/2 3.0 (Abbott Oslo, California, USA) were used for each participant's HIV status. Using AMIES swabs (BD, California, USA) samples were collected from the participants with clinical SSI and sent to the microbiology laboratory. Gram staining and culture studies were done on the collected pus swabs. All cultures were done on three primary media MacConky, chocolate and blood agar (Oxoid, Basingstoke, UK). Incubation was done between 18 and 24 hours. Antimicrobial sensitivity studies were done on Mueller Hinton agar (Oxoid, Basingstoke, UK) for all microorganisms that were cultured.

The microbiology and antimicrobial sensitivity pattern were entered into Epi-data software and exported into STATA statistical software version 13 (STATA Corporation, Texas, USA) to complete the microbiological profile of SSI.

3.8 Variables of Interest

Table 3.2: Variables of interest

Dependent variables	Independent variables
Surgical site infection	Age
	Sex
	Causative micro-organism
	HIV status
	Duration of disease before the orthopaedic operation
	Emergency vs elective operation
	Open versus closed fracture at the time of operation
	Type of procedure, e.g. hip prosthesis, knee prosthesis, spinal fusion, open reduction of fractures, limb amputation, skin graft
	Trauma versus non-trauma
	Region of the body, e.g. lower limb, upper limb, spine

3.9 Data Analysis

The data analysis was done by the use of STATA statistical software version 13 (STATA Corporation, Texas, USA). The continuous variables of age and duration of disease before the operation were analysed by calculating the mean, median, range and standard deviation depending on the distribution of data. Shapiro Wilk test and graphical methods were used to determine whether the age and duration of disease were normally distributed. For the age with a normal distribution curve, mean and standard deviation were reported. For the duration of symptoms before the operation, which did not have a normal distribution curve, the median and an interquartile range were reported.

The categorical variables including sex, HIV status, emergency versus elective operation, open versus closed fracture, type of procedure, trauma versus non-trauma and region of the body, were analysed to determine their frequencies. Associations between paired categorical variables were analysed using contingency tables and the Chi-square test. In this study, to rule out confounders and to determine the predictors of SSI, multiple logistic regression analysis was done. All analysis was done at a 95% confidence interval, and the p-value was considered significant if less than 0.05.

3.10 Ethical Considerations

Ethical approval was sought from ERES CONVERGE IRB. Permission was also sought from UTH management to carry out the study in their facility. Informed consent was a requirement to participate in this study. The study purpose, benefits and risks of taking part in it were all explained to the would-be participants before obtaining their consent. The data collected was kept confidential and was only accessed by the researcher. Study participant's data were de-identified before entry into the database.

During the period of participation in this study, any information of clinical relevance obtained was shared with the attending surgeon. This information was only shared with the attending surgeon upon the verbal consent of the study participant. The results of the study will be published to enable informing the management of SSI.

CHAPTER FOUR: RESULTS

This chapter provides the findings of the study.

4.1 Demographic Characteristics of Study Participants

The mean age in years of the respondents was 31.75, with a standard deviation of 17.07. Approximately two-thirds (66.4%) of participants were male, and a third (33.6%) were female. The details are as shown in Table 4.1.

Table 4.1; Baseline demographic characteristic of study participants

Variable	
Age (years)*	31.75 (SD, 17.07)
	Proportion (%)
Sex	
Male	79 (66.4)
Female	40 (33.6)

*mean and standard deviation reported. SD= standard deviation.

Age was normally distributed on the Shapiro Wilk test with a p-value of 0.055. Similarly, the graphical methods gave a normal distribution curve for age. Details are shown in Table 4.2 and Figure 4.1.

Table 4.2; Shapiro Wilk test for age normality

Variable	**Obs**	**W**	**V**	**z**	**P-value**
Age	119	0.979	2.039	1.596	0.055

V= covariance matrix, W= W test, z= Standard normal distribution, Obs= number of participants

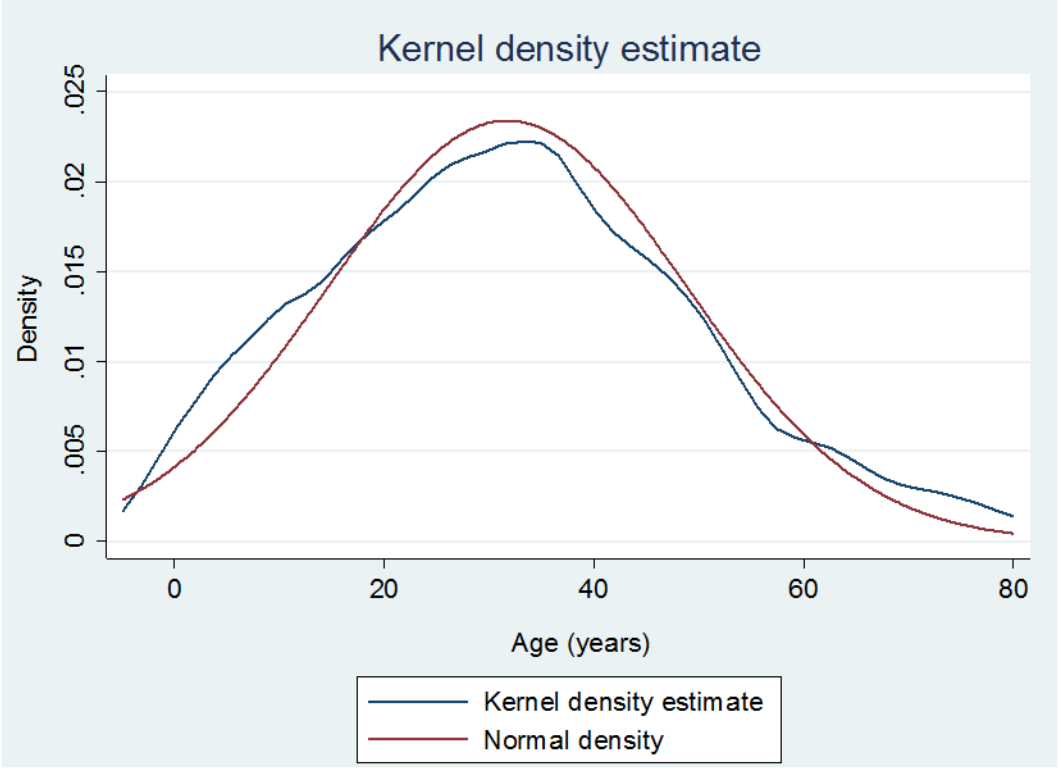

Figure 4.1; Graphical method test for age normality

4.2 HIV Status

In this study, 18 (15.1%) of the participants were HIV positive. Four (3.4%) study participants did not consent to an HIV test. The details are as shown in Table 4.3.

Table 4.3; HIV Status

Variable	Proportion (%)
HIV Status**	
Positive	18 (15.1)
Negative	97 (81.5)
Unknown	4 (3.4)

HIV= Human Immunodeficiency Virus. **The unknown HIV status was included.

4.3 The Clinical Characteristics of the Study Population

The period in days, for the duration of symptoms before surgery had a median of 9 days with an interquartile range (IQR, 1-60).

The duration of symptoms before surgery was not normally distributed on the Shapiro Wilk test with a p-value of less than 0.05. Similarly, the graphical methods gave a skewed distribution curve for the duration of symptoms before surgery. Details are shown in Table 4.4 and Figure 4.2.

Table 4.4; Shapiro Wilk test for duration of symptoms normality

Variable	Obs	W	V	z	P-value
Age	119	0.695	29.184	7.555	0.000

V= covariance matrix, W= W test, z= Standard normal distribution, Obs= number of participants

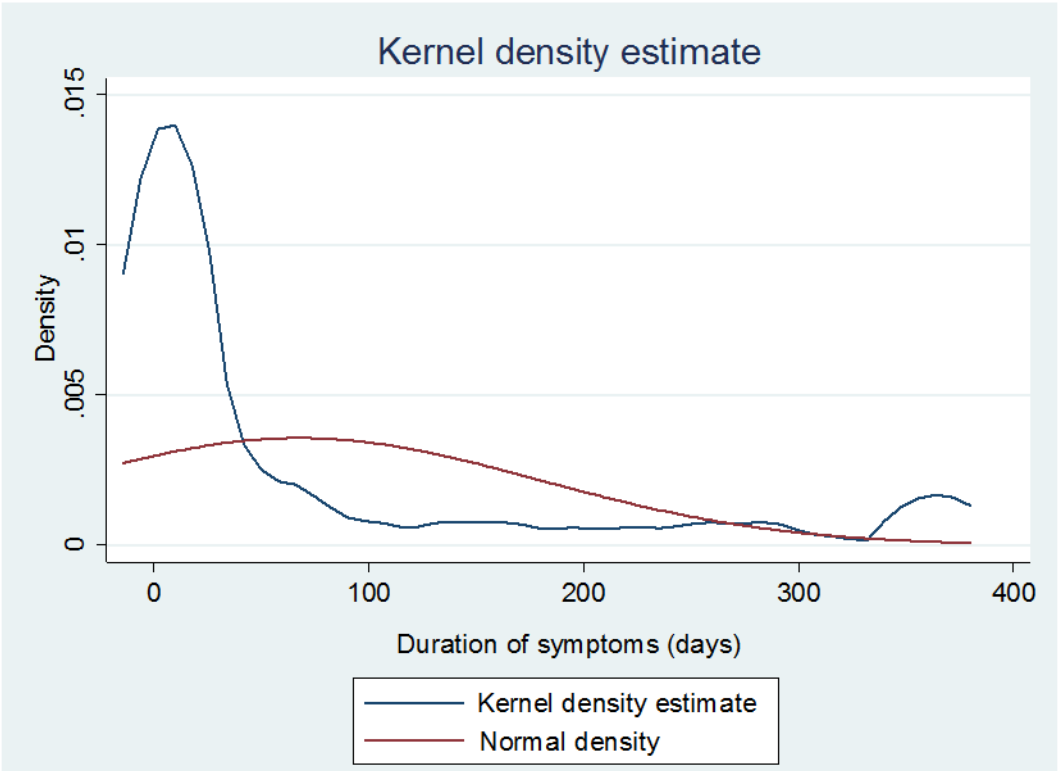

Figure 4.2; Graphical method test for the duration of symptoms normality

The majority 62 (52.1%) of the study participants had an elective indication for surgery. Most of the study participants, 60 (50.4%) had open fractures. The lower limb surgery 90 (75.6%) was the most prevalent region for the operation. Equally, most of the study participants 102 (85.7%) had trauma-related indications for the surgery.

The debridement and external fixation was the most frequent surgery 43 (36.1%) performed. Similarly, the majority of the study participants 67 (56.3%) had deep SSI classification while organ space SSI classification was the least 13 (10.9%). Details are as shown in Table 4.5.

Table 4.5; Clinical characteristics of study participants

Variable	
Duration of symptoms (days)*	9 (IQR, 1-60)
	Proportion (%)
Indication	
Emergence	57 (47.9)
Elective	62 (52.1)
Open vs Closed fracture	
Open	60 (50.4)
Closed	42 (35.3)
NA	17 (14.3)
Region of body	
Lower limb	90 (75.6)
Upper limb	17 (14.3)
Spine	11 (9.3)
Pelvis	1 (0.8)
Trauma vs non-trauma	
Trauma	102 (85.7)
Non-trauma	17 (14.3)
Procedure type	
Hip prosthesis	10 (8.4)
Knee prosthesis	1 (0.8)
Spine	11 (9.3)
Open reduction of fractures	40 (33.6)
Limb amputation	14 (11.8)
Other[y]	43 (36.1)
SSI	
Growth	100 (84.0)
No growth	19 (16.0)
Classification of SSI**	
Superficial	39 (32.8)
Deep	67 (56.3)
Organ space	13 (10.9)

*Median and interquartile range reported; **Organ/Space SSI = Joint space SSI, [y]debridement and external fixation of fractures. NA= Not applicable, SSI= surgical site infection(s), vs= versus

4.4 The association between demographic characteristics and SSI

There was a higher percentage of male with culture-positive SSI than among the female participants. However, the association between SSI and sex was not statistically significant (x^2=0.73, p=0. 393). There was an equal of culture-positive SSI in both the HIV-negative and the HIV-positive groups. When the association between HIV and SSI was determined, the association was not statistically significant (x^2 =0.77, p=0.0.675). The details are as shown in Table 4.6.

Table 4.6; Association between categorical demographic characteristics and SSI

Variable	**SSI**		**P-value**
	Growth (%)	No growth (%)	
Sex			
Male	68 (86.1)	11 (13.9)	0.393
Female	32 (80.0)	8 (20.0)	
HIV			
Positive	15 (83.3)	3 (16.7)	0.675
Negative	81 (83.5)	16 (16.5)	
Unknown status	4 (100.0)	0 (0.0)	

When age was compared between participants with and without culture-positive SSI, there was no statistically significant difference (p=0.500). There was no statistically significant difference, as shown in the Box and Whisker plot. Details are shown in Figure 4.3.

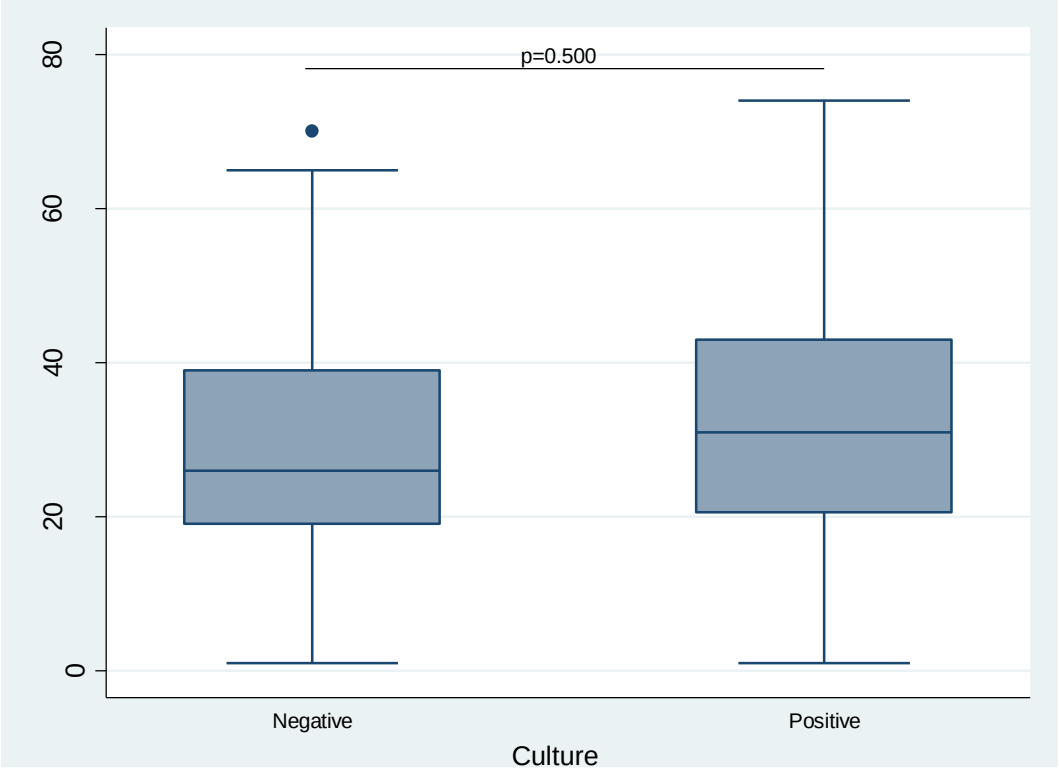

Figure 4.3; Comparison of age between study participants with and without SSI

4.5 The association between clinical characteristics and SSI

There was no statistically significant association between indication and SSI (x^2=0.00, p=0.960). Similarly, the association between open fractures versus closed fracture and SSI was not statistically significant (x^2=0.56, p=0.755). When the association between the region of surgery and SSI was determined, the association was not statistically significant (x^2=2.43, p=0.486). In a similar vein, the association between trauma versus non-trauma and SSI was not statistically significant (x^2=.026, p=0.609). Equally, there was no statistically significant association between the type of procedure performed and SSI (x^2=3.93, p=0.560). The association between SSI class and SSI was not statistically significant (x^2=4.19, p=0.123). Details are as shown in Table 4.7.

Table 4.7; Association between clinical categorical characteristics and SSI

Variable Category	**SSI**		**P-value**
	Growth (%)	No growth (%)	
Indication			
Emergency	48 (84.2)	9 (15.8)	0.960
Elective	52 (83.9)	10 (16.1)	
Open vs closed fracture			
Open	51 (85.0)	9 (15.0)	0.755
Closed	34 (80.9)	8 (19.1)	
NA	15 (88.2)	2 (11.8)	
Body region			
Lower limb	73 (81.1)	17 (18.9)	0.486
Upper limb	16 (94.1)	1 (5.9)	
Spine	10 (90.9)	1 (9.1)	
Pelvis	1 (100.00)	0 (0.00)	
Trauma vs non-trauma			
Trauma	85 (83.3)	17 (16.7)	0.609
Non-trauma	15 (88.2)	2 (11.8)	
Procedure type			
Hip arthroplasty	7 (70.0)	3 (30.0)	0.560
Knee arthroplasty	1 (100.00)	0 (0.00)	
Spine surgery	10 (90.9)	1 (9.1)	
ORIF	36 (90.0)	4 (10.0)	
Limb amputations	12 (85.7)	2 (14.3)	
Others*	34 (79.1)	9 (20.9)	
Classification			
Superficial	29 (74.4)	10 (25.6)	0.123
Deep	59 (88.1)	8 (11.9)	
Organ/space	12 (92.3)	1 (7.7)	

*Debridement and external fixation of fractures. ORIF= Open reduction and internal fixation of fractures, NA= Not applicable.

When the duration of symptoms before surgery was compared between participants with and without culture-positive SSI, there was no statistically significant difference (p=0.627). The median duration (in days) of symptoms was nine days and the interquartile range of 1 to 60 days. Mann-Whitney test was used to test for the difference, as shown in the Box and Whisker plot. Details are shown in Figure 4.4.

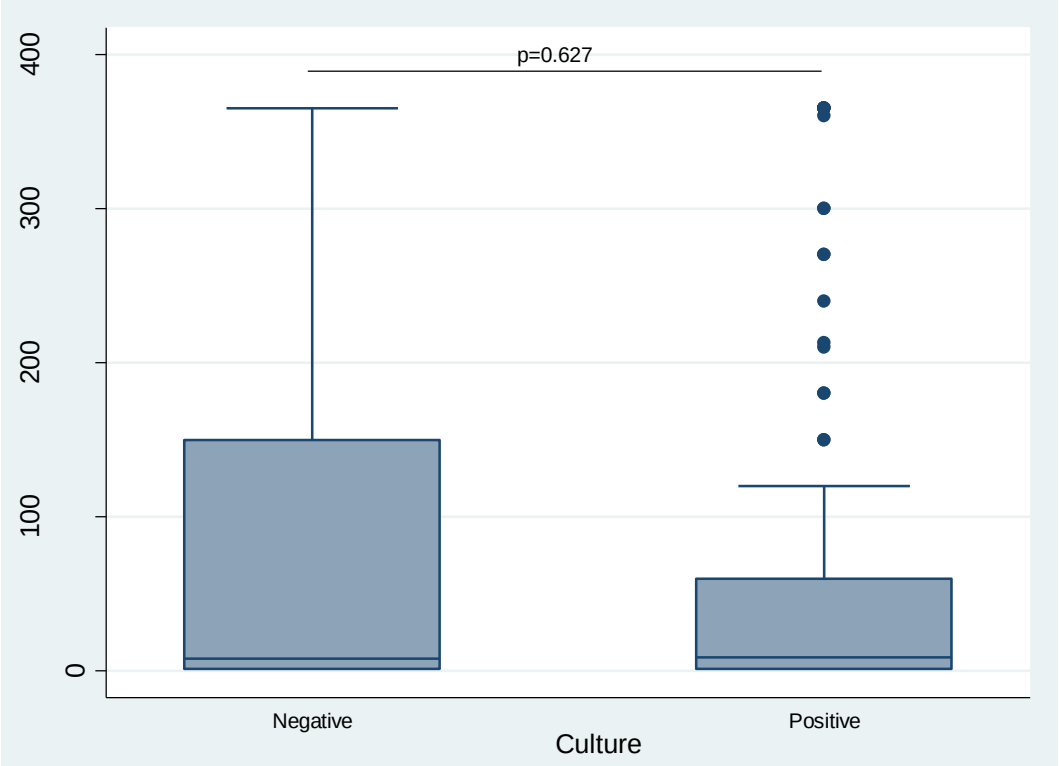

Figure 4.4; Comparison of duration of symptoms between participants with culture-positive SSI and those without

4.6 Logistic Regression Analysis

Multivariable logistic regression analysis was done on the clinical characteristic to rule out confounders and to determine the predictors for SSI. For the duration of symptoms, the results showed that for every one unit (day) increase it was associated with a 1% reduction in SSI. Study participants who had an elective indication for surgery were 57% less likely of having culture-positive SSI compared to those with an emergence indication. Those with closed fracture were 12% less likely of having culture-positive SSI than the participants with an open fracture. However, participants with no fracture-related indication had 1.55 times higher odds of SSI than those with open fractures. Orthopaedic operation in the upper limb showed 4.71 times higher odds of developing SSI than surgical procedures on the lower limb.

Meanwhile, Open reduction and internal fixation of fractures (ORIF) had 6.45 times higher odds for culture-positive SSI compared to those with hip arthroplasty surgery. Deep SSI had 2.86 times higher odds of developing SSI than superficial SSI.

Organ space SSI had 11.01 higher odds of developing SSI than the superficial SSI. Trauma versus non-trauma and spine procedure type was omitted from the multivariable logistic regression analysis because of collinearity. The details are as shown in Table 4.8.

Table 4.8; Multivariable Logistic regression analysis for SSI

Variable	**AOR**	**95% CI**	**P-value**
Duration of symptoms (days)	0.99	0.99-1.00	0.361
Indication			
Emergency	Ref		
Elective	0.43	0.09-2.1	0.304
Open vs closed fracture			
Open	Ref		
Closed	0.88	0.24-3.17	0.848
NA	1.55	0.14-17.8	0.721
Body region			
Lower limb	Ref		
Upper limb	4.71	0.51-43.38	0.171
Spine	4.87	0.30-77.95	0.391
Procedure type			
Hip arthroplasty	Ref		
ORIF	6.45	0.67-62.76	0.106
Limb amputations	2.49	0.15-39.60	0.517
Others*	2.09	0.30-77.95	0.567
Classification			
Superficial	Ref		
Deep	2.86	0.85-9.57	0.089
Organ/space	11.01	0.70-18.04	0.074

*Debridement and external fixation of fractures. ORIF= Open reduction and internal fixation of fractures, NA= Not applicable.

4.7 SSI Causative Microorganism

There was growth in most culture specimens 100 (84.0%), and no growth in 19 (16%) cases. The most cultured microorganism was *Staphylococcus aureus* 35 (29.4%) followed by *Pseudomonas aeruginosa* 17 (14.3%).

The other cultured microorganisms included *Proteus mirabilis* 13 (10.9%), *Klebsiella oxytoca* 13 (10.9%), Coagulase-negative *staphylococcus* (CNS) 7 (5.9%), *Enterobacter species* 5 (4.2%), *E. Coli* 5 (4.2%), *Citrobacter species* 4 (3.4%) and *Streptococcus species* 1 (0.8%). The details are as shown in Table 4.9.

Table 4.9; SSI causative microorganisms

Microorganism	**Proportion (%)**
Staphylococcus aureus	35 (29.4)
Coagulase-negative staphylococcus	7 (5.9)
Klebsiella oxytoca	13 (10.9)
Pseudomonas aeruginosa	17 (14.3)
Citrobacter species	4 (3.4)
Proteus mirabilis	13 (10.9)
Enterobacter species	5 (4.2)
Streptococcus species	1 (0.8)
Escherichia coli	5 (4.2)
Culture-negative	19 (16.0)

4.8 The Antimicrobial Sensitivity Pattern of SSI

Gram-positive microorganism comprised the majority (56%). The majority of *S. aureus* (19) were MRSA when tested with a Cefoxitin screen. Most of *S. aureus* isolates were sensitive against gentamicin (22), ciprofloxacin (19), clindamycin (20) and chloramphenicol (7) antimicrobial. Gentamicin resistant *S. aureus* comprised 30.3%. However, the majority of *S. aureus* isolated were resistant to co-trimoxazole, penicillin and erythromycin.

The Coagulase-negative *staphylococcus* (CNS) isolates were mostly resistant when tested against oxacillin (6) and co-trimoxazole (9). However, the majority of CNS isolates were sensitive to ciprofloxacin (3), clindamycin (5), tetracycline (4) and chloramphenicol (5).

P. aeruginosa was most sensitive to gentamicin (9), ciprofloxacin (10), Piperacillin/ Tazobactam (8) and cefepime (3). However, *P. aeruginosa* exhibited resistance against ceftazidime.

Klebsiella oxytoca was mostly resistance against all the antimicrobial tested. *Klebsiella oxytoca* exhibited resistance to the third (ceftriaxone, cefotaxime and ceftazidime) and fourth (cefepime) generation cephalosporin. Equally, *Escherichia coli* showed resistance against almost all the antimicrobial tested. Except for ciprofloxacin, *Proteus mirabilis* showed mostly resistance against gentamicin, co-trimoxazole, piperacillin/ tazobactam, cefepime, ceftriaxone and ceftazidime. On the other hand, *Citrobacter species* showed a varied antimicrobial sensitivity pattern against the different antimicrobial tested. Details are as shown in Table 4.10.

Table 4.10; Antimicrobial Sensitivity Pattern of SSI

	Gentamicin			**Cefoxitin***		**Ciprofloxacin**			**Co-trimoxazole**		
	S	***I***	***R***	***S***	***R***	***S***	***I***	***R***	***S***	***I***	***R***
S. aureus (35)	22	1	9	16	19	17	2	10	5	2	9
CNS (7)	5	1	0	2	5	3	2	2	0	0	5
Klebsiella oxytoca (13)	4	0	9			3	2	7	0	0	8
P. aeruginosa (17)	9	0	5			10	3	4			
Citrobacter species (4)	2	0	1			3	0	1	0	0	2
Proteus mirabilis (13)	5	0	6			5	2	4	2	1	5
Enterobacter species (5)	2	0	1			1	0	4	0	0	1
Streptococcus species (1)	1	1	1								
Escherichia coli (5)	1	1	1			1	1	3	0	0	3

*Cefoxitin= Oxacillin, CNS= Coagulase-negative *staphylococcus, P. aeruginosa= Pseudomonas aeruginosa*

S. aureus = staphylococcus aureus, S=sensitive, I=intermediate, R=resistant.

Table 4.10; Antimicrobial Sensitivity Pattern of SSI (continues)

	Penicillin		**Erythromycin**			**Clindamycin**			**Azithromycin**			**Tetracycline**		
	S	***R***	***S***	***I***	***R***	***S***	***I***	***R***	***S***	***I***	***R***	***S***	***I***	***R***
S. aureus (35)	2	32	13	8	14	20	1	5	3	2	4	6	1	3
CNS (7)	0	7	1	4	2	5	0	1	1	0	1	4	0	1

CNS= Coagulase-negative *staphylococcus, S. aureus=Staphylococcus aureus.* S=sensitive, I=intermediate, R=resistant.

Table 4.10; Antimicrobial Sensitivity Pattern of SSI (continues)

	Piperacillin/ Tazobactam			**Cefepime**			**Ceftriaxone**			**Cefotaxime**			**Ceftazidime**		
	S	***I***	***R***	***S***	***I***	***R***	***S***	***I***	***R***	***S***	***I***	***R***	***S***	***I***	***R***
Klebsiella oxytoca (13)	1	4	2	0	1	8	0	0	8	0	1	6	0	0	7
P. aeruginosa (17)	8	0	3	2	1	2							0	1	13
Citrobacter species (4)	1	1	1	3	0	1	3	0	1	1	0	1			
Proteus mirabilis (13)	3	1	7	2	1	8	2	2	5	0	0	6	1	1	8
Enterobacter species (5)	2	0	0	0	1	2	1	0	1	0	1	4	0	0	2
Streptococcus species (1)										1	0	0			
Escherichia coli (5)	0	1	1	0	1	3	0	0	2	0	0	1	1	0	4

P. aeruginosa= Pseudomonas aeruginosa. S=sensitive, I=intermediate, R=resistant.

Table 4.10; Antimicrobial Sensitivity Pattern of SSI (continues)

	Chloramphenicol			**Ampicillin/ Sulbactum**			**Imipenem**		
	S	***I***	***R***	***S***	***I***	***R***	***S***	***I***	***R***
S. aureus (35)	7	4	3						
CNS (7)	5	1	0						
Klebsiella oxytoca (13)	2	0	2	3	0	6	3	0	1
P. aeruginosa (17)							3	2	0
Citrobacter species (4)				2	0	0			
Proteus mirabilis (13)	1	2	5	2	1	7			
Enterobacter species (1)				0	0	3	0	0	1
Escherichia coli (5)	2	0	1	1	0	2			

CNS=Coagulase-negative *staphylococcus, P. aeruginosa=Pseudomonas aeruginosa, S. aureus=Staphylococcus aureus.* S=sensitive, I=intermediate, R=resistant.

CHAPTER FIVE: DISCUSSION

5.1 Demographic Characteristics and SSI

In this study, the mean age in years was 31.75, with a standard deviation of 17.07, with a normal distribution on graphical methods curve and Shapiro Wilk test. In keeping with this study, (Carragee et al., 1991) had a similar mean age of 34 years. However, Nigerian research (Onche and Adedeji, 2004) had a higher mean age of 42 years (SD±15).

Similarly, other studies (Al-Mulhim et al., 2014; Doshi et al., 2017) found a much higher mean age. In the above studies, they included only adult participants, unlike this study which included both adults and the paediatric population. This population was similar to another study (Classen et al., 1992).

Two-thirds of the participants in this study were males. This finding was in keeping with other studies, (Al-Mulhim et al., 2014; Doshi et al., 2017) majority of SSI participants being male, comprising about three-quarters. Sex distribution was in keeping with another study of two-thirds being male (Onche and Adedeji, 2004). The above was a Nigerian study with a probably similar setting to this study setting. There could be a possibility of more male orthopaedic patients given the male social and industrial exposure to the risk of orthopaedic conditions. This finding could also be explained by the Zambian scenario where more males were having surgical operations than females with the exclusion of caesarean section procedure (*DHS, Zambia,* 2018). However, another study (Carragee et al., 1991) had more female patients developing SSI following surgery.

There was a higher percentage of male with culture-positive SSI than female. There was no significant association between the demographic characteristics (age and sex) and SSI. Similarly, this finding was in keeping with another study (Classen et al., 1992).

5.2 HIV Status

About one-sixth (15.1%) of study participants were HIV positive. HIV prevalence is higher (15.1%) in urban areas (*DHS, Zambia*, 2018) like in the setting of this study. This finding (*DHS, Zambia*, 2018) could explain a similar percentage of HIV positive in this study. This finding was higher than 10% reported in an American review article (*CDC: HIV Surveillance Report.*, 2013; Grabowski et al., 2017). The difference could be due to a higher HIV prevalence in Zambia (*ZAMPHIA Report*, 2016) of 12.0% as was the case in this study. This group was considered potentially immunocompromised because of the underlying HIV (Nel, 2014; ZAMPHIA Report, 2016). There was no significant association between HIV and SSI in this study. This finding could be that the HIV positive participants might have been on treatment to counter the immunosuppression. Another possible explanation, maybe the number of HIV infected participants was too small to establish a significant association.

In this study, four (3.4%) did not have an HIV test done, which was a much lower per cent compared to the national picture of 15% and 25% among women and men with unknown HIV status, respectively (*DHS, Zambia*, 2018). Although the national figures are high, many of those do give consent as indicated in the report above.

5.3 Clinical Characteristics and SSI

The median duration (in days) of symptoms before surgery was nine days (IQR, 1-60). The odds of culture-positive SSI were reducing with each day of delay before surgery, though not statistically significant in this study. The possible explanation for the finding in this study is that orthopaedic patients with emergence indication were likely to have an operation done much earlier than the elective indications. A delay of symptoms beyond four days was associated with higher SSI cases (Carragee et al., 1991).

However, some of the referring hospitals are in a rural setup, which could further delay presentation to the facilities (Carragee et al., 1991).

Another factor could be that the waiting time could be prolonged due to possible overcrowding or overstay of patients versus available operating time (Tiwari et al., 2014).

More than three-quarters of the study participants in this study had a trauma-related indication for surgery. This observation is in keeping with the local scenario, in that most of the orthopaedic surgical procedures done at UTH are trauma-related. Similarly, (Al-Mulhim et al., 2014; Doshi et al., 2017) found that the majority of SSI were trauma-related. This finding could pose a risk for SSI due to preoperative compromised soft tissue state from trauma (Al-Mulhim et al., 2014; Bachoura et al., 2011). In this study, the association between trauma versus non-trauma and SSI was not statistically significant. This finding could be that the number of trauma-related cases was too small to find a significant association with SSI. Another reason could be those male participants being the majority, have a higher risk for occupational trauma-related injuries in Zambia as anecdotal data suggest.

More than half of the patients had an elective indication of surgery. However, other studies (Al-Mulhim et al., 2014) found that the majority of the participants with SSI had an emergency surgical procedure. The difference in findings could be due to differences in study design and sampling methods used. In the Serbian retrospective study (Al-Mulhim et al., 2014) all the records were included unlike in this cross-sectional study in which a systematic sampling method was employed. An elective indication for surgery had 0.43 fewer odds to have SSI compared to those with emergence indication in this study. This observation could be that in an elective setting, there was adequate patient preparation compared to an emergency setting. In an emergency theatre, there was little choice in separating the potentially contaminated cases from the clean surgical sites.

Most of the study participants had open fractures. However, there was no significant association between patients with and without open fractures and SSI.

Multivariable logistic regression analysis showed that closed fractures had fewer odds of SSI than open fractures. This finding was in keeping with other studies, (Doshi et al., 2017; Oliveira et al., 2016; Wang et al., 2018) open fractures had a significantly higher SSI incidence than closed fractures. This observation could be due to a higher degree of contamination in open fracture, mainly when associated with high energy injuries (Oliveira et al., 2016; Wang et al., 2018). However, in this study, the higher the odds for SSI in open fractures were not statistically significant.

Three-quarters of participants had an orthopaedic operation on the lower limb. In another study, (Hannigan et al., 2015) found that most of the trauma causing open fractures occurred in the lower limbs. However, the region of surgery had no statistically significant association with SSI. There is probably a need for a bigger sample to establish a significant association. The upper limb and orthopaedic spine surgeries had higher odds of developing SSI than the lower limb, but not statistically significant.

ORIF being the second most prevalent surgical procedure performed accounting for more than one-third. There was no significant association between procedure type and SSI. Arthroplasty had lower odds of SSI than the other procedure types. This observation could be due to the number of measures taken in avoiding devastating periprosthetic infection.

More than half had deep SSI classification while superficial SSI classification accounting for about one-third. However, (Onche and Adedeji, 2004) found that all case had superficial SSI. Similarly, (Wang et al., 2018) found that superficial SSI class was the commonest. Deep and organ/space (joint) classes had higher odds of SSI than the superficial type.

This difference with other studies could be that mostly those with more severe infection presented back to UTH, a tertiary institution.

5.4 SSI Causative Microorganism and Antimicrobial Sensitivity Pattern

This study, in keeping with other studies (Oliveira et al., 2016; Tsukayama et al., 1996) found that the majority of isolates were gram-positive. Cefoxitin screen was used as a surrogate for oxacillin in interpreting MRSA as per Clinical and Laboratory Standards Institute guidelines ("Laboratory Testing | MRSA | CDC," 2019).

The most prevalent causative microorganism was *S. aureus* 35 (29.4%) in this study, with MRSA comprising more than half of that 19 (54.3%). *S. aureus* is the most commonly isolated causative organism in several studies (Al-Mulhim et al., 2014; Gustilo and Anderson, 1976; Oliveira et al., 2016; Onche and Adedeji, 2004; Ridgeway et al., 2005; Tsukayama et al., 1996; Wang et al., 2018). In another African study, (Onche and Adedeji, 2004) *S. aureus* was the most prevalent (44%), and exhibited resistance to all the antimicrobial tested. In other studies, (Al-Mulhim et al., 2014; Oliveira et al., 2016) found that *S. aureus* inclusive of MRSA was the most causative microorganism for SSI. A British study (Ridgeway et al., 2005) on SSI *S. aureus* was isolated in more than half of SSI, MRSA comprising 59% of that. In American studies, (Classen et al., 1992; Gustilo and Anderson, 1976; Tsukayama et al., 1996) *S. aureus* was the most prevalent microorganism from the isolates. However, (Tsukayama et al., 1996) found that all the *S. aureus* isolates were sensitive to oxacillin while almost half of the CNS was methicillin-resistant.

The more than half of MRSA in *S. aureus* related majority SSI cases shows the critical implication on the prevention and management of SSI following orthopaedic operations. Methicillin resistance in this study was 54.3% *S. aureus* and 71.4% for CNS. This result was

a worryingly high prevalence of methicillin resistance, as it can cause severe morbidity and even high mortality in SSI. Resistance to methicillin was 72% against CNS and 20% against *S. aureus* in a Scottish study (Malhas et al., 2015).

In this study, the resistance of *S. aureus* and CNS to gentamicin was 31.3% and 16.7%, respectively. However, (Malhas et al., 2015) found higher resistance to gentamicin against CNS (40%) than *S. aureus* (4%). This finding could be attributed to the more prevalent CNS of 29.4% versus 5.9% isolated in this study. Similarly, another study (Onche and Adedeji, 2004) found a higher resistance of *S. aureus* against gentamicin. Gentamicin plays a vital role in the treatment of SSI with the use of gentamicin beads.

In keeping with the findings in this study, *S. aureus* was found to be mostly resistant to erythromycin (Onche and Adedeji, 2004). Similarly, *S. aureus* was resistant to another macrolide, azithromycin. However, *S. aureus* was most sensitive (76.9%) to clindamycin, a lincosamide antibiotic. Clindamycin is an effective antibiotic against most gram-positive bacteria. *S. aureus* was sensitive in more than half of isolates against ciprofloxacin, a fluoroquinolone. However, it was highly resistant in a Nigerian study (Onche and Adedeji, 2004).

P. aeruginosa (14.3%) was the second most prevalent causative microorganism. This result was in keeping other studies (Al-Mulhim et al., 2014) having (18.9%) and (Oliveira et al., 2016) 10% of *P. aeruginosa* isolates. *P. aeruginosa* is mostly a hospital-acquired infection. More than half of the *P. aeruginosa* isolates were sensitive to gentamicin (9/14), ciprofloxacin (10/17), Piperacillin/ Tazobactam (8/11) and cefepime (3/5). Similarly, another study (Onche and Adedeji, 2004) had *P. aeruginosa* isolates sensitive to gentamicin.

The other drug class *P. aeruginosa* was sensitive to for more than half (60%) of the tested isolates was carbapenems (imipenem), which was similar to (Oliveira et al., 2016) 57% sensitivity to imipenem. However, not all *P. aeruginosa* isolates were tested against carbapenems. The percentages of the sensitive isolates against most antibiotics were relatively low in this study, making concern for possible drug resistance in the near future.

Proteus mirabilis (10.9%) isolates, nearly half were resistant to gentamicin and ciprofloxacin. In keeping with this study, (Onche and Adedeji, 2004) *Proteus* was resistant in half of the isolates. In another study, *Proteus mirabilis* isolates accounted for only about one per cent of SSI (Al-Mulhim et al., 2014). In this study, *Proteus mirabilis* exhibited low rates of susceptibility towards most antimicrobial agents inclusive of the third (ceftriaxone, cefotaxime and ceftazidime) and fourth-generation (cefepime) cephalosporins. However, *Proteus* was found to be susceptible to cephalosporin in patients with open fractures.

Klebsiella oxytoca (10.9%) isolates had complete resistance against co-trimoxazole and, all the third and fourth-generation cephalosporin. This finding was contradictory to the findings (Gustilo and Anderson, 1976) in which *Klebsiella* was sensitive to the cephalosporin class of antimicrobials. Half of the strains in this study, tested against chloramphenicol were sensitive while three-quarters of those tested against imipenem were sensitive. However, not all the isolates were tested against these two promising drugs. Way more than half of these isolates were resistant to gentamicin, ciprofloxacin, piperacillin/tazobactam and ampicillin/sulbactam. Contrary to findings in this study of more than two-thirds *Klebsiella oxytoca* being resistant to gentamicin, another study (Onche and Adedeji, 2004) found that only a third of resistance to gentamicin.

Enterobacter species (4.2%) had two-thirds of isolates sensitive to gentamicin and sensitive to piperacillin/tazobactam (n=2).

In a similar finding of *E. coli* (4.2%), (Al-Mulhim et al., 2014) found approximately four per cent of isolates being responsible for the SSI. It exhibited resistance to the cephalosporin class (third and fourth-generation), ciprofloxacin and co-trimoxazole. However, another study found that *E. coli* was sensitive to cephalosporin.

In 16% (19/119), there was no growth in culture despite the multiple specimens collected per case. These cases had SSI clinically, as evidenced at the time of enrolment in the study. There was a possibility of self-medication which was not disclosed despite prompting question for that. Similarly, (Baker et al., 2016; Malhas et al., 2015) found that some cases had no growth in culture despite clinically having SSI. This observation of no growth in culture could be that another microorganism that could not grow on the culture medium used or the possibility of fungal cause (Baker et al., 2016; Malhas et al., 2015).

5.5 Strengths and Limitations

This study has both strengths and limitations. The strengths included the tertiary study site, which is the national referrals centre, meaning it represented the countrywide picture. The sampling method eliminated the possible bias during the recruiting of study participants.

The primary limitations included the unavailability of all the antibiotics for the entire period of study. Imipenem was not run for all the required samples as the antimicrobial was delivered late by the supplier, unlike other antimicrobials. This study, being a cross-sectional study, the postoperative antibiotic prophylaxis duration was not standardized. However, each procedure received preoperative antibiotic prophylaxis given within 60 minutes of an orthopaedic operative procedure (Classen et al., 1992).

Another limitation was that pus swabs were only collected on patients with clinical evidence of SSI. Hence this study picked on clinical cases, which meant possibly missing the subclinical cases.

5.6 Contribution to the Body of Knowledge

This study provided the prevalence of the causative microorganism and antimicrobial sensitivity pattern SSI following orthopaedic procedures, which was unexplored in Zambia. This study will guide the future development of prevention and treatment protocols. This study also provided the baseline for future studies on this subject.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

This study has shown the following after investigating SSI following orthopaedic operation:

The overall prevalence of culture-positive SSI was 84%. The various causative microorganism included *S. aureus, P. aeruginosa, Klebsiella oxytoca, Proteus mirabilis,* CNS, *Enterobacter species, E. coli, Citrobacter species*, and *Streptococcus species.*

The prevalence was determined, with *S. aureus* (29.4%) being the most prevalent and more than half of that being MRSA. The prevalence of other causative microorganism was *P. aeruginosa* (14.3%), Klebsiella *oxytoca* (10.9%), *Proteus mirabilis* (10.9%), CNS (5.9%), *Enterobacter species* (4.2%), *E. coli* (4.2%), *Citrobacter species* (3.4%), and *Streptococcus species* (0.8%).

More than half of *S. aureus* was MRSA while CNS had more than two-thirds being methicillin-resistant. Third and fourth-generation cephalosporin exhibited resistance to most isolates. The same pattern was shown for most strains tested against penicillin and co-trimoxazole. The percentages of the sensitive *P. aeruginosa* isolates against most antibiotics were relatively low in this study, making concern for possible drug resistance in the near future.

There was no significant association between SSI and each of the various variables.

6.2 RECOMMENDATIONS

The MRSA and CNS methicillin resistance screening should be made routine. The necessary antimicrobials should be made available for routine test in SSI cases.

There is a need to strengthen infection prevention measures. There is a need for strict appropriate antibiotic usage guidelines to prevent drug resistance. A more extensive multi-centre study is required to investigate the practices that might impact the SSI following orthopaedic operations. Further studies on the prevalence and incidence of SSI following orthopaedic operations should be done.

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APPENDICES

Appendix One: Participant Information Sheet

Participant Information Sheet

Title of Research: Microbiological Profile of Surgical Site Infection in Orthopaedic Surgery at the University Teaching Hospital; Lusaka.

Principal Investigator: Dr Joel Kandila

Introduction: You are being invited to be part of this study. This form explains the research study that you are being asked to join. Kindly review this form carefully and ask any questions about this research study if you would like information anymore or if there is anything that you do not understand before you decide whether or not you should agree to join. You are free to also ask questions at any time after joining the study, and at any time you can withdraw from this study if you so wish. We would like you to understand that you do not have to accept this invitation and that you should only agree to be part of this study if you want to.

Thank you for reading this.

Purpose of this Research Study: The purpose of this study is to help us learn more about the organisms that cause these infections happening following orthopaedic operations at UTH. In particular, we are looking to find out what microorganisms are responsible for these infections and what drugs are they respond to.

Who can join this study: All participants that have had an orthopaedic operation and develop infection to the site of their operation. The participants fitting the above description and are in the care of the University Teaching Hospital (UTH) are eligible.

You are being requested to join this study because you meet this description. A total of 102 participants will be taking part in this study.

Voluntary Participation: Your participation is entirely voluntary. You reserve the rights to withdraw from this research at any given time. Even if you do not join this research, or if you join and then, later on, decide you want to withdraw from this research, you will still receive the same quality of medical care available to you at this hospital.

You should ask the principal investigator [whose details are given below] any questions you may have about this research study. You may ask questions in the future if you do not understand something that is being done.

What Happens When You Join the Study: If you agree to join this study, we will ask you for your time to answer some questions. During this research, we will be looking through your medical records and then asking you several questions to try and see if you have an infection to the site of the operation.

If it is suspected that you have an infection, a swab will be collected from the site of infection and taken for analysis at the laboratories. We would then ask you further questions to help us understand more about the disease.

All these questions and pus swab sample will be done on the same day. Therefore No extra research study visits will be needed. The research team will share with you any findings that may help you while in this study.

Payment for Participating: You will NOT be paid for joining in this study.

Risks in taking part: There are NO perceived risks or disadvantages of taking part in this research study. If however, you should experience any discomfort or inconvenience as a result of taking part in this research study, you should make this known to the researcher immediately. In the unlikely event that you suffer any study-related injuries, you will get an appropriate referral for treatment to the relevant specialists at UTH.

Immediate Benefits of Participation: if during data collection some medical conditions that need to be addressed become apparent, you will get referred to the relevant specialists at UTH.

Confidentiality: Only the study investigators and the health care workers helping collect the data will be able to find out the results of the answers you give us to the questions. You will not be named in any reports about this research. All the data collected will only be used for this research. The data collected will be anonymized and stored as such.

Results of the study: The study team will do their best to inform you of the findings that potentially could improve your care. The results obtained in this study will be published in a medical journal. All participants will not be identifiable from the published results.

What happens if I want to stop taking part? As a participant in this study, you can withdraw at any time, without explanation. Results up to the period of your withdrawal from this study may be used if you are fine for this to be the case. Otherwise, you may request that they are destroyed, and no further use is made of them. Furthermore, you may at any time during the course of this study, refuse to answer any questions you deem personal or otherwise and it will not affect the care you receive or your continued participation in this study.

Contact Person: If you want to talk to someone about this study because you feel you have been mistreated or feel you have been hurt by taking part in the research, or you have any other questions about the study, you should contact the Principal investigator Dr Joel Kandila of the Department of Surgery at UTH on cell phone number 0965 153447 or e-mail: kandilajo@gmail.com, P.O. Box: P/Bag RW 1X, Lusaka and he will try to help you.

If however you are still unhappy or have a complaint which you feel you cannot come to him with, then you should contact the ERES CONVERGE IRB on telephone number: +260-955155633/4, e-mail: eresconverge@yahoo.com, 33 Joseph Mwilwa Road, Rhodes Park, Lusaka, Zambia.

Appendix Two: Consent Form

Title of Research: Microbiological Profile of Surgical Site Infections in Orthopaedic Surgery at the University Teaching Hospital; Lusaka.

Researcher: Dr Joel Kandila

	Tick in Box
1. I can confirm that I have read and understood the information sheet regarding this study. I have had an opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that the participation in this study is voluntary and that I am free to withdraw at any given time without giving any reason, without my rights being affected and that I can refuse to answer any questions I deem personal.	☐
3. I understand that I can at any time, ask for access to the information I provide, and I can also request the destruction of that information if I wish.	☐
4. I understand that I will be deidentified and not be identifiable in any report subsequently produced by the researcher.	☐
5. I accept that taking part in a study intervention is voluntary and confirm that any risks associated with this have been explained to me	☐
6. I agree to take part in the above study.	☐

Participant Name:……..Signature/ Right Thumbprint…….

Date…….

Witness:……Signature……..Date……

For Further Questions, Please Contact Dr Joel Kandila, UTH. Cell number: 0978153447 or Email: kandilajo@gmail.com

Appendix Three: Data Collection Sheet

Title: Microbiological Profile of Surgical Site Infections in Orthopaedic Surgery at the University Teaching Hospital; Lusaka.

Serial number: ……

Information	Coding category
Age	
Sex	1) Male 2) Female
HIV status	1) Reactive 2) Non-Reactive 3) Unknown
Duration of disease before the operation	
Emergency versus elective indication	1) Emergency 2) Elective
Open versus closed fracture	1) Open fracture 2) closed fracture 3) NA
Region of the body	1) Lower limb 2) Upper limb 3) Spine 4) Pelvis 5) Other
Trauma versus non-trauma:	1) Trauma 2) Non-trauma
Type procedure:	1) Hip prosthesis 2) Knee prosthesis 3) Spine 4) Open reduction of fractures 5) Limb amputation 6) Other
Classification of SSI	1) Superficial 2) Deep 3) Organ/space
Surgical site infection confirmed	1) Yes 2) No
Causative micro-organism(s)	
Sensitivity pattern	1) Sensitive 2) Intermediate 3) Resistant

BUDGET

Stationary…… K4, 000=00

Communication……...…… K3, 000=00

Ethics committee……..…….. K1, 000=00

Storage Drive……. K800=00

Supporting staff……..…….…..…. K10, 000=00

Data entry and Analysis……..... K7, 000=00

Consumables for laboratory cultures……..……. K30, 000=00

Publication to a peer-reviewed journal…… K4, 000=00

Dissemination meeting…… K1, 000=00

Contingency…….……... K3, 000=00

Total…….…….……. K63, 800=00

TIME TABLE

Task to be performed	Person responsible	2016	Jun 2017	Sep 2017	Jan 2018	Jan 2019	Feb 2019	Dec 2019	Dec 2019	Jan 2020	Mar 2020	Mar 2020
Department proposal presentation	PI											
Submit a proposal to the Assistant Dean (PG) office	PI											
Present to graduate forum	PI											
Submit the proposal to the ethics committee	PI											
Ethics review period	PI											
Ethics committee Approval	PI											
Enrol patients and collect data	PI											
Analyze data	PI											
Write a dissertation	PI											
Submit a final dissertation	PI											