THE ROLE OF ANTIMICROBIAL PROPHYLAXIS IN CLEAN OPERATIVE PROCEDURES AT MUHIMBILI NATIONAL HOSPITAL

By
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A dissertation submitted in partial fulfillment of the requirements for the award of the degree of Master of Medicine (General Surgery) of the University of Dar-es-Salaam.

University of Dar es Salaam
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CERTIFICATION

The undersigned certify that he has read and hereby recommend for acceptance by the University of Dar-es-salaam a dissertation entitled: *The Role of Antimicrobial Prophylaxis in Clean Operative Procedures at Muhimbili National Hospital,* in partial fulfillment of the requirement for the award of the degree of Master of Medicine (General Surgery).

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I, Dr Steven Nicholas Kaali, declare that this dissertation is my own original work and that has not been presented and will not be presented to any other University for a similar or any other degree award.

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Dedication

To My Wife and our three Children

ABSTRACT

OBJECTIVES:

To determine the role of antimicrobial prophylaxis in clean category of surgical operations at Muhimbili National Hospital, and the rate of postoperative wound infection, the duration of postoperative stay, and the need for postoperative antibiotics.

METHODS

Patients who were scheduled for and underwent clean elective operations from January 2002 to November 2002 were randomized into two groups and followed for 30 days. One group, the study group, was given Ceftriaxone (Powercef®) at the induction of anaesthesia. The other group, the control group, was not given the antibiotic. Their demographic data were obtained, wounds examined and those who were found to have infected wounds, had pus swabs obtained for culture and sensitivity. Bacteriological pattern and the sensitivity pattern of the isolates were studied.

RESULTS

During the study period, 246 patients who underwent clean operations were registered into the study. The study consisted of 156 males and 90 females. The overall wound infection rate was (4.9%). The wound infection rate in the study group was 3.2% (4/123) and that in the control group was 6.5% (8/123), p value = 0.2. The mean duration of postoperative hospital stay was 2.6 days in the study group and 3.2 days in the control group, p value = 0.15. The mean postoperative non-routine hospital visits for wound related problems was 0.06 days in the study group and 0.43 days in the control group, p value = 0.07. The rate of use of postoperative antibiotics was 4.9% (6/123) in the study group and 22.2% (27/123) in the control group, p value = 0.000085. Staphylococcus aureus was the most commonly isolated organism accounting for 52.2% of the isolates. There was no emergence of resistance to ceftriaxone after its use as a prophylactic agent in the study.

CONCLUSION

There are no obvious benefits of use of antimicrobial prophylaxis in clean surgical operations. Though emergence of resistance was not

observed in this study, repeated injudicious use can certainly lead to this. It was concluded that antibiotic prophylaxis should not be used in clean operations.

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LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
CDC	Center for Disease Control
CMV	Cytomegalovirus
CNS	Central nervous system
ESBL	Extended spectrum beta-lactamase
HIV	Human immunodeficiency virus
ITP	Idiopathic thrombocytopaenic purpura
LMB	Lean body mass
MUCHS	Muhimbili University College of Health Sciences
SSI	Surgical site infection
UK	United Kingdom

1. CHAPTER ONE

1.1 INTRODUCTION

Postoperative wound infection is the most common nosocomial infection in patients undergoing surgery. [1,2] It is an important cause of illness resulting in a prolongation of hospital stay, an increase in the cost of medical care and an inconvenience to patients and their families. [1,2,3]

Antibiotics have been used for prophylaxis in surgical patients with the hope of reducing the rate of postoperative wound infection. [1,2,4,5,6] Clinical surgery has witnessed a remarkable reduction in postoperative wound infection over the past 25 years, mainly because of empiric but rational use of antibiotics as prophylactic agents. [7] After gaining widespread use as therapy for infection, antibiotics were subsequently overused. By 1960, most surgeons agreed that the routine use of antibiotics in clean operations was not only unnecessary, but also undesirable. [7] The use of prophylactic antibiotics implies that a microorganism is attacked by an antimicrobial agent at the time of its lodgement in a surgical wound or body cavity before colonization takes place, certainly before suppuration or invasive infection begins. The aim

is to prevent the development of clinical surgical infection rather than to treat the process after it is already established. [3]

The prophylactic use of antibiotics for clean operative procedures has remained controversial. [1,7] It has been postulated that clean surgery does not justify the use of prophylactic antibiotics, but whenever a foreign body, even a braided suture, and certainly a prosthesis, is left within the wound, the risk of infection is increased. This is particularly desirable following prosthetic orthopedic or vascular surgery, where infection can be disastrous. As early as 1957, experimental evidence showed that foreign materials increased the risk of infection. Specifically the number of pathogens accepted as causing a wound infection (10^6 / g of tissue) was found to be logarithmically reduced when a silk suture was present. [7]

It is generally agreed that prophylaxis in clean surgery be reserved for such procedures in which the occurrence of an infection is a life threatening event. [1,7,8,9] Prophylactic antibiotics remain the single most important factor in reducing post-surgical infection however. In clean surgery, which does not include insertion of prosthesis, use of prophylactic antibiotic is difficult to justify when the infection rate is less than 2%. [7] It is therefore generally accepted for use in such

procedures as insertion of a prosthetic device and coronary artery bypass surgery. [1,4,7,9]

The administration of prophylactic antibiotics for most other clean operations has been considered inappropriate, as the risk of clinically important infection was perceived to be too low to justify the use of antibiotics. [1]

1.2 OBJECTIVE

A recent study done at Muhimbili National Hospital revealed a high and unacceptable rate of postoperative wound infection in clean surgical procedures, 10.1%. [10] As an interventional study, it is the aim of this study to determine the role of antimicrobial prophylaxis in clean category of surgical procedures in terms of reduction in wound infection rate, reduction in duration of postoperative stay and use of postoperative antibiotics and reduction in non-routine postoperative hospital visits for wound related problems. Some studies have shown benefits in use of prophylaxis in such terms in clean surgery. [11]

2. CHAPTER TWO

2.1 LITERATURE REVIEW

2.1.1 HISTORICAL BACKGROUND

In the 1600s wound infection was so common that redness, warmth and purulence were thought to be desirable features of wound healing. Despite the documented efficacy of hand washing in reducing puerperal sepsis in the mid 1800s, which was introduced by Semmelweis and popularized by Holmes, the widespread practice of hand washing was not established until the early 20th century. [12, 13,14]

The practical source of belief in "laudable pus" is likely based on the fact that only living patients produced pus. Major surgery was almost invariably followed by infection; typified by erysipelas, rapidly progressive soft tissue infection (streptococcal or mixed synergistic infections) and tetanus. [15] The associated mortality was high. The introduction of carbolic acid spray (used on the entire operating room, patient and surgeon) by Lister in 1867 led to a dramatic reduction in infection rates to less than 10 per cent. [1,13] Nevertheless, the "antiseptic

principle" was not widely accepted. Lister's results however, fostered a context more accepting of Pasteur's theory of putrefaction: "purulence was caused by microorganisms".

After the adoption of hand washing and the use of sterile gloves, gowns and supplies (i.e. after introduction of autoclaves), infection rate from clean procedures approached modern rates. [1,13] However, infection rates for procedures of the gastrointestinal tract remained high as a result of endogenous origin of the bacteria.

Following the introduction of antibiotics, early clinical trials in the 1950s reported rather no benefit or a higher infection rate with antibiotic prophylaxis. [16,17,18] Moreover, the emergence of resistant strains was attributed in part to such use of antibiotics. Although a small number of researchers supported the use of prophylactic antibiotics for dirty or contaminated cases most did not recommend their use in cleaner cases.

Fortunately studies by Burke in the early 1960s revealed the critical flaw in previous investigations and clinical failures. Burke administered a single dose of penicillin systemically at various times before and after the inoculation of penicillin sensitive staphylococcus aureus in the

dermis of guinea pigs. Administration of antibiotics either shortly before or after the inoculation of organisms resulted in lesions histologically identical to lesions induced by intra-dermal inoculation with killed organisms. Delaying the administration of antibiotics by as little as three hours resulted in lesions identical to those animals not receiving antibiotics. [19]

The critical dependence of prophylactic efficacy on timing of administration was soundly established and subsequently shown to depend on the presence of peak antibiotic levels in the tissue at a time when the local concentration of microorganism would otherwise be high. Subsequent investigation has focused on the delineation of specific procedures, prophylactic regimes and optimization of efficacy.

2.1.2 CLASSIFICATION OF SURGICAL PROCEDURES

Establishing a "prophylaxis indicated" status for a given procedure requires consideration of likelihood of infection without antibiotics and morbidity and cost of an infectious complication. A taxonomy that classifies a procedure according to the level of microbial contamination routinely associated with that procedure and likelihood of infection has been established. [3,6,20,21,22] The incidence of infection ranges widely

across classes being less than 2 per cent for clean procedures (e.g. breast biopsy) to over 40 per cent for dirty procedures (e.g. colon perforation with diffuse faecal contamination). It is generally agreed that antibiotic prophylaxis is warranted in all procedures in the categories of clean contaminated, contaminated and dirty. Endogenous organisms cause infections following these operations and all such cases justify prophylactic antibiotics. It should be emphasized here that dirty wounds require both prophylactic and therapeutic regimes. [7]

2.1.2.1 CLEAN SURGICAL PROCEDURES

These are elective surgeries, which are non-emergency, non-traumatic and primarily closed. No acute inflammation is encountered and there is no break in aseptic technique. The respiratory, gastrointestinal, biliary and genito-urinary tracts are not opened. The risk of postoperative wound infection is < 2 %. [1,3,7]

Sepsis in clean wounds is a reflection of surgical and nursing standards. Contamination during surgery is usually minimal and limited to the patient's own skin flora. However, exogenous infection of clean wounds can occur following contamination as a result of sloppy nursing or postoperative wound care. [7]

Clean surgeries account for 75 % of all operations. If antibiotics were used for all clean operations a great number of persons would be exposed unnecessarily to the risk of adverse drug effects including development of drug resistance. Therefore routine use of prophylactic antibiotics cannot be recommended in clean operations. [3] Sound clinical judgement, however, accepts their use in a limited number of situations:[3]

- Involving insertion of implants.
- In known carriers of pathogenic microorganisms.
- In patients with preexisting distant infection from operative site.
- In operations on patients with history of rheumatic valve disease or previously infected valves.
- In patients with known or suspected tuberculosis.
- In clean procedures with extensive tissue dissection or result in diminished tissue blood supply.
- In immunocompromised patients.

In our environment, however, with regard to the prevailing theatre conditions these operations are hardly clean, as there is always a break in technique. They can therefore virtually be classified as clean

contaminated rather than clean operations. [10] This may warrant the use of prophylactic antibiotics. [7]

2.1.2.2 CLEAN CONTAMINATED PROCEDURES

These are urgent or emergency cases that are otherwise clean; elective opening of respiratory, gastrointestinal, biliary or genito-urinary tract with minimal spillage (e.g. appendicectomy) mostly encountering uninfected urine or bile; Minor technique break. The risk of postoperative wound infection is < 10%. [1,3,7]

2.1.2.3 CONTAMINATED PROCEDURES

Non purulent inflammation; gross spillage from gastro-intestinal tract; entry into biliary or genito-urinary tract in the presence of infected bile or urine; major break in technique; penetrating trauma < 4 hours old; chronic open wounds to be grafted or covered. The risk of postoperative wound infection is ~ 20 %. [1,3,7]

2.1.2.4 DIRTY PROCEDURES

These are operative procedures in which purulent inflammation (e.g. abscess), or preoperative perforation of respiratory, gastro-intestinal, biliary or genitourinary tract is encountered. Penetrating trauma > 4 hours old. The risk of postoperative wound infection is ~ 40 %. [1,3,7]

2.1.3 PRINCIPLES OF ANTIMICROBIAL PROPHYLAXIS

The generally accepted principles of antimicrobial prophylaxis in surgery involve five considerations: [23]

1. Using antimicrobials for surgical procedures in which prophylactic antimicrobials have been found to be beneficial. [1] This is the essence of classification of surgical procedures according to the risk of contamination and subsequent infection. Clean operations have the lowest risk of contamination and subsequent postoperative wound infection being < 2%. However it is argued that only the strictest surveillance and audit measures can ensure maintenance of such a level. [7]

2. Timing the antimicrobial administration such that the agent is present in the potentially contaminated tissue before the bacteria enter the site (i.e. at the time of surgical incision) and persisting in tissues throughout the period of potential contamination. [23,24,25] Antimicrobials vary in their distribution pharmacokinetics. Some must be administered prior to the patient going to the operating room. Others can be given after the intravenous line is placed in the operating room. It is generally accepted that the initial dose should be given parenterally immediately before operation. Delay of the initial dose until after the operation or administration of the antibiotic too long before the procedure is associated with an increased rate of wound infection. [26,27,28] A problem is encountered when antibiotics with a short serum half-life are used or the operative procedure is prolonged or both. In these situations a second dose should be administered during the operation to maintain effective levels of the drug in the tissues. [1]

3. Limiting the duration of antimicrobial prophylaxis. Studies document that postoperative antimicrobial administration is not necessary for many surgeries. Single dose before operation for most surgical procedures is adequate. [29] In many studies comparing single dose and multidose regimes there was no

difference in rates of postoperative wound infection between study and control groups. [30,31,32] Some researchers have suggested that prolonged prophylactic use of antibiotics is appropriate when drains or catheters remain in situ for several days after the operation. The antibiotic would presumably protect the wound from secondary infection that originated in the foreign body and reached the wound by a haematogenous route. [33]

4. Planning the route of antimicrobial administration. Intravenous administration is the optimal method to ensure adequate levels in tissues during most operative procedures. [33] Oral administrations of antimicrobials are recommended for colorectal operations to decontaminate the gut as part of chemical bowel preparation. [34]

5. Selecting an antimicrobial active against the most common surgical wound pathogens. Cephalosporins are antimicrobials with a broad spectrum of activity against many invading pathogens. The study done at Muhimbili National Hospital revealed that the most common organisms infecting wounds after clean surgery were Staphylococcus aureus (36.1%); Klebsiella spp (31.2%); and Escherichia coli (14.8%). Other organisms were less frequently isolated and included Pseudomonas spp (6.6%);

Proteus spp (4.9%); Beta haemolytic Streptococci (3.2%); Streptococcus spp (1.6%) and unidentified coliforms (1.6%). [18] These organisms were all susceptible to Ceftriaxone which is a third generation cephalosporin coming under the trade name Powercef which is a relatively affordable product from India compared to Rocephin which is a trade name of the same drug product from UK.

2.1.4 ABOUT CEFTRIAXONE

2.1.4.1 MECHANISM OF ACTION AND PHARMACOKINETICS

Ceftriaxone is a third generation cephalosporin. It is bactericidal in action. Its action results from inhibition of mucopeptide synthesis in the bacterial cell wall. It can be administered intramuscularly or intravenously. A peak plasma concentration of 38μg/ml is obtained 2 hours after intramuscular injection of 500mg. Following intravenous infusion of 1g over a 30 minutes period, a plasma concentration of approximately 150μg/ml is achieved. 83-96% of the circulating drug is protein bound. [35]

Following intramuscular or intravenous administration, Ceftriaxone is widely distributed into body tissues and fluids including gallbladder, lung, bone, bile, prostate, adenoma tissue, uterine tissue, atrial appendage, sputum, tears and pleural, peritoneal, synovial, ascitic and blister fluids. [35]

Ceftriaxone is not metabolized in the body. 40-65% is excreted unchanged in urine and the remainder in the bile and ultimately in feces as metabolically inactive compound. The elimination half-life is between 6-9 hours in healthy volunteers and is prolonged only slightly in severe renal impairment, and dose adjustments are unnecessary provided total daily dose does not exceed 2g. The effect of hepatic dysfunction on Ceftriaxone elimination is also minimal. However accumulation occurs in dose with combined renal and hepatic impairment and dose adjustments are needed. [35]

2.1.4.2 ANTIMICROBIAL ACTIVITY

Ceftriaxone exhibits high degree of stability in the presence of β-lactamase, both penicillinases and cephalosporinase, of gram negative and gram-positive bacteria. It is usually active against the following microorganisms in vitro. [35]

Gram-negative aerobes

Acinetobacter, calcoaceticus, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae (including Ampicillin-resistant strains), Haemophilus parainfluenzae, Klebsiella oxytoca, Klebsiella pneumoniae. Morganella morganii, Neisseria gonorrhoeae (including penicillinase and non penicillinase producing strains), Neisseria meningitides, Proteus mirabilis, Proteus vulgaris, Serratia marcescens. Some strains of Pseudomonas aeruginosa are sensitive to Ceftriaxone. [35]

Gram-positive aerobes

Staphylococcus aureus (including penicillinase producing strains), Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes, Viridans group of Streptococci.

Anaerobes

Bacteroides fragilis, Clostridium spp., Peptostreptococcus spp.

2.1.4.3 INDICATIONS

Ceftriaxone is indicated for the treatment of a wide variety of infections caused by sensitive gram-positive, gram-negative and anaerobic organisms: [35]

- Lower respiratory tract infections
- Skin and skin structure infections
- Urinary tract infections
- Uncomplicated gonorrhoea
- Pelvic inflammatory disease
- Bacterial septicaemia
- Bone and joint infections
- Meningitis
- Surgical prophylaxis
- Intraabdominal infections

2.1.4.4 CONTRAINDICATIONS, PRECAUTIONS AND WARNINGS

- Ceftriaxone is contraindicated in patients with known allergy to cephalosporin class of antibiotics.

- Pseudomembranous colitis has been reported as with nearly all other antibacterial agents
- Prolonged use may result in over-growth of non-susceptible bacteriae. [35]

2.1.4.5 SIDE EFFECTS

Ceftriaxone is usually well tolerated. Some of the side effects are local reactions including pain, induration and tenderness at injection site. Rash, pruritus and fever have been reported. Eosinophilia, thrombocytosis, leukopaenia, anaemia, haemolytic anaemia, neutropaenia, lymphopaenia, thrombocytopaenia and prolongation of prothrombin time are seen. Nausea, vomiting, diarrhoea increased serum concentrations of AST and ALT have been reported. [35]

2.1.4.6 DOSAGE AND ADMINISTRATION

The usual dose for treatment of most infections is 1-2g/day in one or two divided doses depending on the type of infection. Total daily dose should not exceed 4g/day. For preoperative prophylaxis in adults 1g should be given intramuscularly or intravenously half to two hours prior to surgery. [35]

In children, those older than 12 years of age receive the adult dose. The usual dose of Ceftriaxone in neonates and children 12 years of age and younger for the treatment of skin and skin structure infections and serious infection other than CNS infection (e.g. meningitis) caused by susceptible organisms is 50-75mg/kg (not to exceed 2g) daily in two equally divided doses or a single daily dose. [35]

For treatment of meningitis the recommended daily dose is 100mg/kg (not to exceed 4g) once daily or two equally divided dosages every 12 hours, the duration of therapy is 7-14 days.

Therapy should be continued for at least two days after the signs and symptoms of infection have subsided. The usual duration is 4-14 days.[35]

2.1.5 FACTORS CONTRIBUTING TO WOUND INFECTION

To effectively prevent wound infection knowledge of the factors contributing to wound infection is important. These factors can be classified into four namely bacterial factors; local wound factors; systemic factors and environmental factors. [21]

2.1.5.1 BACTERIAL FACTORS

The deposition and growth of bacteria within wounds is a prerequisite for the development of infection, this is the only factor that can be influenced by antibiotic administration. [6] The kind and numbers of bacteria contribute significantly to the establishment of overt infection or the lack of it. The virulence of the deposited bacteria and the toxins it produces are important bacterial factors for wound infection. For clean surgical procedures the normal skin flora becomes important and the risk increases with contamination and patient's vulnerability. [21,36] The common skin flora are Streptococcus epidermidis, Staphylococcus aureus and Streptococcus pyogens. Estimates of the number of bacteria found on the skin vary from study to study and according to the method of assessment used. Bacteria range from 1,400,000 to 11,000 colony-forming units per square centimeter. [36] The highest figure comes from the scalp, followed in declining rank order by the axilla, back, abdomen, thigh, breast and forearm. [36] The perineum is also a good source of organisms causing postoperative wound infection for operations done at the site, organisms like Escherichia coli and enterococci may have their origin there. Klebsiellae may colonize the skin and they are regarded as normal flora in the colon and the intestines. [5] Studies have shown that bacterial contamination with more than 10^5 organisms frequently causes

infection, whereas contamination with less than 10^5 organisms usually does not. The normal defense mechanisms are therefore of great importance in preventing infection at its inception but wound infection is inevitable if the bacterial inoculum is sufficiently large. [21]

2.1.5.2 LOCAL WOUND FACTORS

In everyday practice, inhibition of local defense mechanisms for clearing bacteria is perhaps the most important cause of wound infection. Anything that interferes with the ability of phagocytic cells to contact directly and kill bacteria potentiates wound infection. The use of foreign bodies including sutures and drains, lack of accurate approximation of tissues, strangulation of tissues with sutures that are too tight, and the presence of any dead tissue, haematomas or seromas all increase the risk of infection. [3,6,36] Fortunately most of these factors can be minimized by good surgical technique. [7,21]

2.1.5.3 PATIENT FACTORS

Wound infections are very common in the very young and the very old, perhaps because of immature or senescent resistance mechanisms. [3,21] Patient's age influences the rate of infection of clean wounds with

patients more than 66 years old being six times more likely to develop infection than are patients 1-14 years old. [3] Reduced blood flow to the surgical incision by hypovolaemic shock, use of vasopressors locally or systemically, or vascular occlusive disease also predispose to wound infection. Local decrease in tissue oxygen tension by decreased blood flow or by systemic hypoxemia is also a risk factor. [5,21] Conditions that reduce vascular reactivity as in uremia, old age, use of high doses of corticosteroids cancer and trauma lead to increased susceptibility to infection. [7,21,25] Diabetes mellitus and immunossupression such as in AIDS also carry a high risk of infection. [5] The presence of more than three other diagnoses in the individual present the highest risk. [5]

2.1.5.4 ENVIRONMENTAL FACTORS

Engineering and architectural advances have helped limit airborne contamination in modern operating rooms to very low levels. These have not been followed by substantial reduction in wound infection rates because the two greatest sources of significant microbial contamination of operative wounds are exogenous contact from breaks in technique by the operating team and endogenous contamination from the patient's skin and various bacteria contaminating tracts. Of the two, endogenous contamination causes a greater number of infections in all types of

wounds except in those classified as clean. The use of ultraviolet light for decontamination of operating room and laminar flow ventilation systems may be helpful in certain situations, such as insertion of prostheses for orthopedic reconstruction. [21]

Perhaps as important are limiting traffic in and out of the operating room, and limiting activity and talking within the operating room. With increasing numbers of people at the operating table, there is increased opportunity for breaks in sterile technique and increased dispersion of airborne bacteria. In addition to air handling, sterilization techniques must be strictly monitored. [21]

Preoperative preparation of the patient

Many patients who are in hospital for prolonged periods of time or who have substantial illness have increased numbers of resident microorganisms on the skin especially in the groin and intertriginous areas. [22,36] These and perhaps all patients, whenever possible, should take a preoperative shower the night before operation using an antibacterial soap such as chlorhexidine or povidone-iodine. [3,21,36] Chlorhexidine seems to be the preferred material for reducing residual bacteria for a prolonged period. Whenever possible, all cutaneous infection should be controlled or cleared before the time of an elective

operation. Presence of a distant site infection at the time of an elective clean operation doubles the postoperative infection rate. [21]

Hair removal

When the operative area is shaved the night before the procedure, the injury of shaving itself promotes bacterial growth. This practice increases the infection rate about 100% compared with removing hair by clippers at the time of the procedure or not removing it at all. [13] Therefore the patient should not be shaved before an operation. Extensive removal of hair is not needed, and electric clippers should perform any that is done with disposable heads in the operating room at the time of the procedure. [3,21,36]

Preoperative hospital stay

Studies have shown that prolonged preoperative hospital stay is associated with a high risk of postoperative wound infection. One day preoperative hospitalization is associated with a rate of infection of 1.2%; a one-week stay with a rate of 2.1% and a more than two weeks stay with a rate of 3.4%. [3] It is likely that the patient's skin becomes colonized with bacteria to which he/she is not resistant. [5]

Skin preparation

The skin is an important source of organisms contaminating surgical wounds. [9] Two methods can be recommended to prevent skin organisms from entering the wound. First, the time honored technique is to scrub the entire operative area of the patient for 5 to 7 minutes with a germicidal detergent solution and then paint the region with an antimicrobial solution of either tincture of iodine, povidone-iodine, or chlorhexidine. Second, an alternative way to isolate the skin from the wound is to use an antimicrobial incise drape applied to the entire operative area, with the incision made through the plastic. Before the incise drape is applied, the skin should be scrubbed for 1 minute with a 70% solution of alcohol or a solution of 2% iodine in 90% alcohol to kill surface bacteria. When the incise drape is used, the skin should not be scrubbed with detergent solution because it interferes with the ability of the incise drape to adhere to the skin; effectiveness is lost when the drape lifts from the skin at the incision site. Thus, the technique of drape application, including cleaning of surface fat and debris from the skin and application only to a dry surface, becomes important for its success. [21]

The operating room team and discipline

Contamination occurs easily from the operating room team, and this is as an aggregate, one of the most important sources of organisms causing infection in clean cases. [21,37] The operating team should wear clean scrub suits, caps that do not shed lint and completely cover the hair, and masks that effectively filter the exhaled air. Before each operation, the hands and forearms should be cleansed and scrubbed thoroughly with an antimicrobial soap for at least 5 minutes for the first case or after any dirty case and for 3 minutes for subsequent cases. It has been shown that there is no difference in infection rate between 5-10 minutes surgical scrub. Most surgeons scrub 3-5 minutes for the first case and 2-3 minutes for subsequent cases. There is no observed increase in infection rates of the clean wounds. [3] The most popular antimicrobial scrubs are chlorhexidine and povidone-iodine. Careful gowning and gloving technique should be used, and special attention should be paid to avoiding contamination when the patient is draped. It is perhaps during the gowning/gloving procedures and draping of the patient that most breaks in technique occur in the modern operating rooms. Another frequent source of contamination is the use of sterile light handles, which become contaminated by the headgear of the operating team. [21]

As many as 90% of an operative team puncture or tear their gloves at some time during a long operation. These must be changed immediately to prevent bacterial contamination of the wound. Even though the numbers of organisms present after a surgical scrub are low, they increase with the length of operation, and the numbers of organisms inside gloves at puncture sites increase remarkably when blood has gained entrance. The safest glove practice is to wear two pairs of gloves with one pair a half size larger than usual under the standard size. This practice has become popular to reduce the risk of getting the patient's blood onto the surgeon's hands, but it is equally effective in keeping the surgeon's bacteria out of the patient's wound. Two pairs of regular gloves are substantially more effective than a single pair of reinforced (orthopaedic) gloves. [14] Gowns worn by the operating room team may also be an important source of contamination, and the contact areas (i.e. sleeves and front of the gown) should be impervious to bacteria and fluids whether the gowns are disposable or reused. [21] The duration of operation is another important risk factor for postoperative wound infection. There is a direct relationship between the length of time of operation and the postoperative infection rate. [3] Operations lasting more than 2 hours carry a high risk of infection.[5] Infection rate roughly doubles with every hour. [3] The possible explanations are: the dosage of bacterial contamination increases with time; wound cells are damaged

by drying and exposure to air and retractors; increased amount of sutures and electro-coagulation may reduce local resistance of the wound; longer procedures are more likely to be associated with blood loss and shock leading to decreased general resistance of the patient. [3]

2.1.6 DEFINITION OF WOUND INFECTION

Wound infection was once defined as a clear collection of pus that empties itself spontaneously or after incision. [38,39] This clinical definition is not necessarily supported by positive cultures. The reason is that a negative culture does not rule out wound infection because a false negative culture may occur as a result of a culture technique inadequacy, presence of fastidious organisms or in a patient who has received antimicrobial therapy. On the other hand positive cultures do not necessarily mean infection as many wounds, infected or not, are colonized by bacteria. Therefore from this argument a wound is infected if it suits a clinical definition. The Center for Disease Control (CDC) considers a wound to be infected if the patient has at least one of the following: [40]

a. Purulent drainage from the superficial incision;

b. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision;

c. At least one of the following signs or symptoms of infection:

- Pain or tenderness
- Localized swelling
- Redness or heat and

Surgeons deliberately open superficial incision, unless the incision is culture negative;

d. Diagnosis by the surgeon or attending physician;

e. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms:

- Fever 38° C or
- Localized pain or tenderness, unless incision is culture negative;

f. An abscess or other evidence of infection involving the deep incision is found on direct examination, during re-operation or by histopathologic or radiologic examination. [40]

The infection can also be defined using a time scale. It is early if it presents within 30 days of operation; intermediate if between one and three months and late if presenting more than three months after surgery. [40]

Wound infection in this context would therefore mean the invasion and multiplication of microorganisms in or on a surgical wound producing cellular injury that results into purulent drainage and an organism identified by culture is present. [40]

2.1.7 WOUND HEALING

Surgeons depend on wound repair, and understanding of the mechanisms that control wound healing is fundamental to the practice of surgery. Tissue loss or damage causes either regeneration or repair by scar tissue, or a combination of both. The amount of tissue injury and degree of contamination influences the speed and quality of healing. Tissue injury may follow surgery or accidental trauma, burns or cold exposure, or contact with chemical agents or foreign bodies. A superficial skin injury may remove only the epithelial cell layer, leaving the epithelial-dermal basement membrane intact. Healing then occurs rapidly by simple re-epithelialization with no scar. Small, clean, closed wounds heal quickly with little scar formation, whereas large, open, dirty wounds heal slowly with significant scarring. [41]

2.1.7.1 TYPES OF WOUND HEALING

Wound healing is customarily divided into repair by first, second, or third intention. [41,42,43]

Healing by first intention

Occurs in closed wounds in which the edges are approximated, such as clean skin incisions closed with sutures. The incision defect re-epithelializes rapidly, and matrix deposition seals the defect. Since there is minimal tissue destruction, healing is accompanied with little scar formation. [41,42,43]

Healing by second intention

This occurs when the wound edges are not apposed, such as an open punch skin biopsy wound, a deep burn, and an infected wound left open to granulate. Granulation tissue fills the wound, and wound contracts and re-epithelializes. Tissue destruction is significant and healing is associated with formation of large scars. [41,42,43]

Healing by third intention

Occurs when an open wound is secondarily closed several days after injury. Such a wound is initially left open because of gross

contamination. A classic example is wound management after removal of a ruptured appendix. [41,42,43]

2.1.7.2 PHYSIOLOGY OF WOUND HEALING

Wound healing involves a complex interaction between epidermal and dermal cells, the extracellular matrix, controlled angiogenesis, and plasma derived proteins all coordinated by an array of cytokines and growth factors. This dynamic process is classically, but somewhat artificially, divided into three overlapping phases inflammation, proliferation, and remodeling. Thrombus formation, which requires interaction between endothelial cells, platelets, and coagulation factors, achieves haemostasis after tissue injury. Trapped cells within the clot, predominantly platelets, trigger an inflammatory response by the release of vasodilators and chemoattractants and activation of the complement cascade. [42,43,44]

Inflammation

In the early phase of inflammation neutrophils predominate, removing bacteria and other foreign material from the wound by releasing enzymes and by phagocytosis. Later in the inflammatory phase neutrophils reduce in number and are replaced by macrophages.

Interest has focused on the role of macrophages in coordinating the transition from inflammation to proliferation through the release of soluble mediators, which include platelet derived growth factor, tumour necrosis factor, transforming growth factor, and insulin growth factor-1.[42,43,44]

Proliferation

Fibroblasts are the key cells involved in the production of the extracellular matrix. In addition to producing collagen, they produce tenascin, fibronectin, and proteoglycans such as hyaluronic acid. Production of extracellular matrix is seen clinically as formation of granulation tissue. The combination of new tissue and contraction of surrounding tissues is essential for the healing of ulcers. While new matrix is synthesized, existing matrix in and around the wound margin is degraded by several enzyme systems such as matrix metalloproteinases and plasminogen activators. Research interest has centered on the role of the metalloproteinases, a family of over 14 enzymes with proteolytic activity. The effect of these enzymes is regulated by tissue inhibitors, which are believed to be important in healing by preventing excessive matrix degradation. While some keratinocytes at the wound edge proliferate, others undergo a marked transformation to enable them to phagocytose debris and migrate across

the wound bed. Keratinocyte migration coupled with wound contraction results in re-epithelialisation and wound closure. [42,43,44]

Remodeling

Once closure of the wound has been achieved, remodeling of the resulting scar takes place over months or years, with a reduction of both cell content and blood flow in the scar tissue. Collagen is degraded and deposited in an equilibrium-producing fashion. Collagen deposition in normal wound healing reaches a peak by the third week after wound is created. Wound contraction is an ongoing process due to myofibroblasts and occurs to a greater extent with secondary healing than primary healing. Maximum tensile strength is achieved by the 12th week and the ultimate resulting scar has only four fifths or 80% of the tensile strength of the original skin that it has replaced. [42,43,44]

2.1.7.3 WOUND STRENGTH

The wound healing only gains 20 - 25% of its maximum strength by the third week after injury. [45] Wound strength is influenced by the rate of collagen deposition as well as remodeling, alignment and formation of larger collagen bundles and intermolecular cross-links. [43, 45]

Wound strength varies with different types of tissues. [43] Highly vascular areas such as head and neck attain strength faster than poorly vascular tissues such as bone.

2.1.7.4 FACTORS IMPEDING HEALING

There are local and systemic factors. [46]

2.1.7.4.1 LOCAL FACTORS IMPEDING HEALING

Inadequate nutrients

No aspect of healing can proceed if there is inadequate energy to perform the metabolic reactions such as protein synthesis. In turn, protein synthesis cannot occur if there is insufficient protein substrate available to produce new tissue. [46]

Tissue hypoxia

Because all phases of healing are oxygen dependent, a local decrease in wound tissue oxygen tension is the major impediment to proper healing. The most common causes of tissue hypoxia are:

- A decrease in systemic blood volume and O_2 delivery,
- A decrease in O_2 saturation of hemoglobin,

- Eschar on the wound surface, and
- Surface exudates or infection consuming local oxygen. [46]

Quirinia and Viidik in an experimental study on biomechanical testing of ischaemic wounds found that a decrease in blood flow results in a significant decrease in all biomedical parameters and caused significant delay in the healing of the test wound. [47]

It has been demonstrated that supplementary postoperative oxygen improves wound healing. [48,49] Quirinia et al [48] while determining the effect of hyperbaric oxygen on ischaemic wounds and normal incisional wounds found that hyperbaric oxygen on day 0 to 3 significantly improved healing on ischaemic wounds by 41- 57%. No effect on healing on day 4 to 9 or on healing of normal incisional wounds was found.

Grief et al [49] randomized 500 patients who were to undergo colorectal resection to receive 30% or 80% inspired oxygen during operation and for two hours afterwards. Results revealed that wound infection rate was 11.2% in the group that received 30% oxygen versus 5.2% for the group that received 80% Oxygen. This difference was statistically significant ($p = 0.01$).

Wu and Mustoe [50] in an experimental study to determine the influence of ischaemia on incisional wound healing found that; Healing was impaired through day 28 (3.21 versus 1.90 newtons, $p \leq 0.001$). Transforming growth factor beta (1 microgram) and Kaposi's fibroblast growth factor (20 microgram) increased breaking strengths under both normal ($p < 0.05$) and ischaemic conditions ($p < 0.05$). Platelet-derived growth factor-BB (10 micrograms) was effective only under normal condition (2.67 versus 2.15 newtons, $P < 0.02$). Basic fibroblast growth factor (20 micrograms) was ineffective in both ischaemic and normal wound healing.

Local infection

There is a distinction made between surface wound colonization and wound infection. Colonization itself should not impede healing unless exudate buildup occurs. Infection by microbial tissue invasion destroys new tissue growth and accentuates inflammation. The infection is controlled with local wound antibiotics and, if systemic symptoms are present, with systemic antibiotics. Of concern is that many local antibiotics retard healing. [46]

Rico *et al* [51] examined the effect of sepsis on the inflammatory and proliferative phases of wound healing and found that infected wounds

exhibited delayed re-epithelialization, 76.3% versus 97.3% at day 5 ($p < 0.05$) and collagen synthesis was reduced by 55.3%. Therefore, to have strong wounds necessary precautions should be taken to prevent wound infection like use of aseptic technique, good surgical technique and judicious use of perioperative antibiotics.

Wound exudates

The presence of surface inflammation and/or infection will result in buildup of exudates, which are mainly dead and dying white blood cells and their contents, all of which are toxic to new tissue growth. The increased release of proteinases on the wound retards the formation of new proteins, especially collagen. In addition, the excess surface of white blood cells can consume immense amounts of oxygen, depriving new tissue cells of O_2, which in turn retards healing. Treatment is focused on preventing and removing exudates. [46]

Foreign body

Postlethwait *et al* [52] studied the tissue reaction to sutures in 666 patients from one day to 23 days after operation and found that, non-absorbable sutures are encapsulated by a rim of connective tissue, with histocytes, giant cells and lymphocytes found near the suture. This is most marked with silk and cotton, less with Dacron and least with nylon

and wire. In a later study Postlewait [53] found that tissue reaction around nylon and Dacron was minimal compared to Teflon coated Dacron. Van Rijssel *et al* [54] assessed tissue reaction histologically using 2/0 and 4/0 coated polyglycolic acid and coated polyglactin sutures and two different knots. Results revealed that an increase in suture size resulted in a more than 4 – 6 fold increase in knot volume and more than 2- 3 fold increase in the tissue reaction. It was concluded that, use of thick-gauge suture material adds much more to the total amount of foreign body and tissue reaction in the wound and impairs wound healing. Shanklin and Smalley [55] in 1999 studied the effect of implantation of silicone mammary devices and found that silicone causes significant delay in wound healing due to prolonged inflammatory reaction.

Wound trauma

This component covers everything from the use of toxic antibiotics or cleansing solutions, which injure tissue, to mechanical trauma caused by dressing changes. [46]

Wound tension

Skin sutures should be just tight enough to unite the wound edges, and as suture tension increases, blood supply from the dermal plexus will be increasingly compromised. [56]

Stone *et al* [57] in an experimental study on biochemical effects of tight suture closure of fascial incision found that in the loosely approximated group there was a proper alignment of the wound edges and greater proliferative activity. Tensile strength was greater in loosely approximated than in the tightly closed group, $p < 0.001$. Johnsson and Hogstrom [58] studied the influence of the site and tension of sutures on early breaking strength in intestinal anastomoses in 161 experimental animals. Anastomoses were done using polypropylene 7/0 placed at 3mm from the cut edges. The results showed that breaking strength decreased proportionally the tighter the sutures were tied, and the differences were significantly greater when the sutures were placed closer to the cut edge. It was concluded that tight sutures promote proteolytic tissue degradation by reducing the local availability of circulating proteinase inhibitors.

Johnsson *et al* [59] studied the influence of small bowel anastomoses made with interrupted (loose) or continuous (tight) sutures on breaking strength. Results revealed that all anastomoses had similar strength immediately after surgery but, after 72 hours, breaking strength was decreased by 50-55% ($p < 0.001$) in tightly (continuous) sutured anastomoses and by 10- 15% ($p > 0.05$) if sutures were made loose (interrupted).

Wound desiccation

A dry wound surface impairs epithelial migration, decreases local wound defenses, and can lead to further surface necrosis. A thin moisture layer is needed to optimize the wound surface environment. [46]

2.1.7.4.2 SYSTEMIC FACTORS IMPEDING HEALING

Inadequate wound blood volume and oxygen delivery

The most important components of wound blood flow are adequate blood volume and cardiac output. These components are needed to deliver adequate amounts of oxygen. Neutrophils require oxygen for bacterial killing, fibroblasts require oxygen for collagen deposition and matrix deposition, and epithelial cells require oxygen for proliferation and wound contraction. Acute or chronically injured patients are commonly dehydrated and/or hypovolemic, and adequate hydration is critical to maintain wound oxygenation. [46]

Loss of body protein

Protein is found in muscle, but protein also makes up collagen and all the elements involved in healing, including growth factors. More than half the weight loss occurring with illness or injury is muscle, with the breakdown of other critical proteins, including those involved with

immune defenses. The wound requires protein to heal and, in the malnourished patient, the amino acids must come from muscle and other stores. The body can deal with the increased demand until there is a loss of more than 15% of LBM. Beyond this point, there is competition for nutrients -- protein replacement vs wound healing -- with the net result being a decrease in wound healing rate. It is therefore critical that a patient who has lost significant weight regains the muscle component as quickly as possible. [46]

Optimum nutrition and resistance exercise is essential to increase anabolism. The addition of an anabolic agent will markedly accelerate restoration of lost weight. Maintaining body weight and protein (muscle mass) is an essential aspect of the wound healing management plan. [46]

Inadequate nutrition

The wound consumes large amounts of energy (calories), amino acids (protein), and key macro- and micronutrients. Because the wound is often present with other injuries or illness, the amount of nutrition needed exceeds normal levels by as much as 50%. [46]

Systemic infection

A systemic infection is a drain on all the metabolic processes and will adversely affect local wound healing. Distant infection decreases all of the wound-healing processes, which depend on anabolic or protein synthesis. Blood flow is often shunted away from the wound to the core or visceral organs. And increased generalized collagenolytic activity decreases the collagen already deposited in the wound. [46]

Uncontrolled stress response

The stress response to injury or illness increases catecholamine release and peripheral vasoconstriction. Any process that increases the release of catecholamines will further decrease wound blood flow. This includes pain and anxiety, reinforcing the need for adequate pain and anxiety management. [46]

Smoking

Hoogendoorn *et al* [60] reported that the pathophysiological effects of smoking include arteriolar vasoconstriction, cellular hypoxia, demineralization of bone, and delayed re-vascularisation. All these lead to delayed wound healing.

Jaundice

Armstrong *et al* [61] studied the effect of jaundice on wound healing on 373 patients who underwent surgery for obstructive jaundice versus 760 unicteric patients who underwent cholecystectomy. Results revealed reduced wound healing was manifested by a higher frequency of wound dehiscence (5.0% versus 3.2%) and incisional hernia (10.3% versus 1.8%) in jaundiced patients.

In this study, the causes of reduced wound healing were associated with;

- Initial low haematocrit (< 30 %)
- Initial low plasma albumin (< 30gm/L)
- History of pancreatitis, malignant obstructing lesion
- Postoperative wound and/or abdominal sepsis.

Raised plasma bilirubin was not significantly associated with poor wound healing.

It was concluded that reduced wound healing in jaundiced patients is associated with poor nutritional status, expressed as low haematocrit and low plasma albumin and malignancy and not raised bilirubin per se.

Age

Quirinia and Viidik [62] in an experimental study on the effect of age on ischaemic wound healing revealed that normal incisional wounds healed equally well in both groups but, the ischaemic wounds in the older animal were found to be impaired by 40 to 65% and decreased healing by 67% after 10 days and 64% after 10 to 20 days. It was concluded that impaired wound healing in old age is based on concomitant diseases in old patients, contributing to varying degrees of ischaemia in traumatized tissues. Norman et al [63] studied 238 patients who underwent clean surgery and found that the rate of wound infection was higher in elderly patients compared to patients below 60 years old (25% versus 6%, $p = 0.011$).

Temperature

Beilin *et al* [64] randomized 60 patients who were planned for elective abdominal surgery into two groups, hypothermic group (those with routine care whereby a core body temperature is lowered by anaesthesia by 1°C) and normothermic group (those maintained by forced–air warming). Blood sample analysis revealed that in hypothermic group, mitogenic responses (induction of proliferation, and natural killer cells activity) were suppressed, production of Interleukin-1 β significantly lower after 24 hours of surgery. Melling *et al* [65] assessed whether

warming patients for clean surgery would have the same effect by randomization of 421 patients into standard (not warmed) and warmed (local and systemic). Results show that the wound infection rates were 14% in non warmed versus 5% in warmed patients. This difference was statistically significant (p = 0.007). Rabkin and Hunt [66] in 1987 studied the effect of local hyperthermia on subcutaneous tissue oxygen tension ($PsqO_2$) and perfusion in contaminated wounds and found that local hyperthermia ameliorated infections. Flores-Maldonado *et al* [67] in 2001, studied the effect of mild perioperative hypothermia on 290 surgical patients and found that the rate of wound infection in hypothermic group was 11.5% versus 2% in normothermic group. This difference was statistically significant (p = 0.004).

Diabetes mellitus

Galeano *et al* [68] studied experimental animals and found that diabetic animals had delayed wound healing, low collagen content, low breaking strength and increased myeloperoxidase activity when compared to healthy animals.

Vitamins

Ramesh *et al* [69] in 1993, studied the action of cholecalciferol on dermal wound healing and found that vitamin D increases wound breaking

strength and promotes epithelialisation. Galeano *et al* [68] in an experimental study on the effect of systemic administration of Raxofelast (vitamin E-like antioxidant) on wound healing found that vitamin E significantly improved wound healing in diabetic animals through stimulation of angiogenesis, re-epithelialization, synthesis and maturation of extra-cellular matrix . It was also found that vitamin E increases wound breaking strength and collagen content of the wound.

Vaxman *et al* [70] studied the effect of vitamins B5 and C on the healing process of colonic anastomoses and found that vitamin B5 and C decreased the number of burst anastomoses, $p = 0.03$ and $p < 0.01$ respectively. Both vitamins restored zinc level to normal and increased iron, copper, manganese levels, all involved in collagen synthesis. Smith *et al* [71] and Raju and Kulkarni [72], did similar studies and found that vitamin A reversed depressant effects of steroids and increased wound strength to a greater extent than controls. The difference was statistically significant ($p < 0.01$).

Drugs- corticosteroids, antineoplastic agents

Jung *et al* [73] assessed the effects of the corticosteroids, prednisolone and budesonide on different aspects of intestinal epithelial wound healing in vitro and found that corticosteroids caused a significant dose dependent

inhibition of intestinal epithelial cell migration and proliferation. Cohen *et al* [74] studied the influence of antineoplastic agents on wound healing in experimental animals and found that;

- Vincristine and methotrexate decreased wound strength at 3 days and not day 7 or 21.
- Actinomycin D interfered with early phases of wound healing and had less effect on later phases.
- Bleomycin had no effect on wound strength at days 3 or 21 but prevented an increase in wound strength from day 3 to 7.
- *1,3-bis-1-nitrosurea* decreased wound strength at all points after operation.
- 5-Flourouracil had no significant effect at any time.

Malignancy

Mc Phee *et al* [75] determined the influence of risk factors for wound breakdown and infection in 75 patients who underwent surgery for spinal metastases. The results showed that wound breakdown and infection occurred in 15 of 75 (20%) wounds. Wound infection was significantly associated with preoperative protein deficiency ($p < 0.01$) or perioperative corticosteroid administration ($p < 0.10$)

Irradiation

Vegesna *et al* [76] investigated the impact of postoperative irradiation on wound strength in experimental animals and found that irradiation on the same day as wounding or to 2-day old wounds reduced wound tensile strength. However, postoperative irradiation delivered at 7, 9, 14 days transiently enhanced wound tensile strength. Kunisada *et al* [77] analyzed wound complications in 43 patients with soft tissue sarcoma who were treated with combined pre-operative radiotherapy and surgery. Results revealed that 84% of patients developed acute skin toxicity following radiotherapy and 27% developed flap necrosis.

HIV

Ferguson [78] assessed the role of the general surgeon in the care of patients with AIDS and AIDS-related complications who underwent major abdominal operations. The results showed that the indications for operation were;

- Gastrointestinal perforation of ileum and colon by CMV
- AIDS related immune thrombocytopenia leading to splenectomy for ITP

- Gastrointestinal complications of opportunistic infections and neoplasms such as tuberculosis, Kaposis sarcoma, lymphoma leading to bowel obstruction.
- Retroperitoneal lymphadenopathy
- Cryptosporidium cholecystitis

Emparan et al [79] determined the influence of low CD4 lymphocytes count in 24 patients with HIV undergoing abdominal surgery after receiving selective antibiotic prophylaxis depending on the surgical procedure performed. Results revealed a high overall wound infection rate accounting for 58.3%. Among those patients who developed wound infection, mean CD4 count was 221 versus 386 of uninfected group. Wound infection rate for clean wounds was 50%, clean-contaminated wound was 62.5% and contaminated wound was 62.5%.

Davis *et al* [80] reviewed the incidence of wound complications following laparotomy for HIV positive patients and compared with non-HIV patients. The results showed a significantly greater incidence of wound complication ($p = 0.0003$) and wound breakdown ($p = 0.012$) in the HIV group than on the non-HIV control group. Morandi *et al* [81] studied the healing time after haemorrhoidectomy in 48 patients with HIV infection

and AIDS. The results showed the healing rate in HIV-positive patients to be 66% after 14 weeks and 100% after 32 weeks; compared to 0% and 50% for patients with AIDS. All controls were healed after 14 weeks. This difference was statistically significant ($p < 0.01$). It was concluded that indications for haemorrhoidectomy in patients with AIDS need to be considered extremely carefully because of high incidence of delayed wound healing.

2.1.8 CLINICAL FEATURES

Postoperative wound infection is an infection in the tissues of the incision and operative area. It can occur from one day to many years after an operation, but the clinical features of such an infection commonly occurs between the fifth and tenth day after surgery. [5] Clinical manifestations tend to vary depending on the depth of the infection, the source of contamination, the causative microorganisms and the immune status of the host. The contamination, which occurs during operation, tends to cause infections, which are deep seated. These are seen at the first dressing. [82] Such early presentation of wound infection, within 24-72 hours is due to virulent microorganisms such as Clostridium spp, Streptococcus spp. and Staphylococcus. [83]

Infections acquired in the ward are seen after the first dressing or 3 to 4 days postoperatively. They are usually superficial. Other patients in the ward may have the same or similar type of infections. [82]

Overall most wound infections are apparent within the first week following operation. Less than 5% become apparent more than four weeks after surgery and many involve implants. [84]

2.1.9 DIAGNOSIS OF WOUND INFECTION

The diagnosis of postoperative wound infection is based mainly on clinical criteria. [85,86,87] Bacteriological results, both microscopic and culture are merely supportive. False negative results of culture may occur and difficulties may be encountered in the interpretation of some cultures leading to a false positive diagnosis.

Clinically the wound is infected if the patient develops fever postoperatively, the skin adjacent to the wound is erythermatous, tender, oedematous and there is extension of the margin around the wound. The infection is therefore present as cellulitis. [86,87] This is classified as non-purulent wound infection. When there is pus discharge

from the superficial subfascial or visceral locations it is referred to as purulent wound infection. [88]

Despite the importance of the clinical criteria in defining wound infection, the diagnosis still remains non-specific. Clinically the aetiology can hardly be deduced. With the help of the laboratory a particular organism can be isolated. Also assessment of the response to treatment can be made.

For bacteriological diagnosis a sample of exudates or pus should be taken via aseptic technique and examined for organisms and their sensitivity to antibiotics. The examination here involves microscopy, culture and bacteriological tests that are used in the identification of microorganisms. [89,90]

3. CHAPTER THREE

3.1 STATEMENT OF THE PROBLEM

A recent study done at Muhimbili National Hospital showed that the incidence of postoperative wound infection after clean operations is 10.1 per cent. [10] This rate is considered alarmingly high [3,7,10] and calls for intervention to lower it and to improve on patients care at our hospital. The postoperative wound infection rate in clean surgical procedures is supposed to be < 2% and, acceptably, not to exceed 5%. [7,10]

Clean procedures usually carry a small risk of infection when given proper environment, expertise and technique. In our environment something is amiss leading to an unacceptable incidence of postoperative infection. The theatre layout in terms of clean and dirty traffic is conducive for higher chances of contamination, [10] also there is a free communication of the operating theatre and the external environment, the swinging doors in our theatre cause turbulence of air in theatre, which also increases the risk of infection. There is lack of air exchange and laminar airflow facilities in our theatre. Shortage of trained nursing personnel also adds to the risk of break in aseptic

technique and subsequently infection. Overcrowding in theatre due to an overwhelming number of medical students is a definite problem in our environment. There is lack of antiseptic for surgical scrub. There is shortage of theatre boots and theatre clothes, which has necessitated theatre staff to carry their clothes home for keeping and care. It is not easy to ensure the same standard of cleanliness of these clothes, which are carried out of the theatre environment and into it thus providing a communication between the theatre and the external dirty environment. Boots and shoes are likewise not standard and every member buys a pair of boots or shoes according to his/her preference and convenience and these are also taken home thus providing a communication between the clean theatre environment and the dirty external environment. All these factors lead to a high risk of postoperative wound infection.

This has lead to the practice of many surgeons prescribing antimicrobial agents in clean surgeries empirically with prophylactic or therapeutic intentions. The current practice entails use of antibiotics on an empirical basis perioperatively or postoperatively in both the oral and intravenous routes. Oral antibiotics are given postoperatively and usually a course of 5 days is administered. Usually cloxacillin, ampicillin, ampiclox, amoxicillin and erythromycin are prescribed. Intravenous antibiotics are given peri-operatively and usually a course

of 2-3 doses of ceftriaxone is prescribed. Initiation of the intravenous antibiotic course is variable usually started in theatre at induction of anesthesia but many times started in the ward several hours before operation or started several hours postoperatively.

A recent study in Boston by Platt R et al [11] has prompted re-evaluation of the concept of anti-microbial prophylaxis in clean surgery. It comprised 1218 patients undergoing herniorrhaphy or surgery involving the breast. Patients who received prophylaxis had 48% less infection rate than those who did not, $p = 0.01$. It showed comparable reduction in the need for postoperative antibiotic therapy and the number of non-routine visits to physicians for wound related problems in the group that received prophylaxis. This suggests that prophylactic use of antibiotics may reduce peri-operative illness and lower costs in clean surgery. [1,11]

The aim of this study was to investigate the use of perioperative antibiotics in clean operations in our environment in terms of reducing the rate of postoperative wound infection. It is the aim of this study also to investigate the benefits of using anti-microbial prophylaxis in clean surgical operations and to lay a basis for further studies in the process of setting standard guidelines for its use at Muhimbili National Hospital and our country at large.

3.2 RATIONALE OF THE STUDY

The wound infection rate for clean surgical procedures in our hospital is unacceptably high. [10] This requires intervention to lower it to acceptable levels. In the previous study at Muhimbili National Hospital, Wayi found a wound infection rate of 10.1% in clean category of surgical operations.[10] This rate of wound infection is unacceptable in this category of surgical procedures in which it is normally < 2% under strict surveillance but it should not exceed 5% however under any conditions.[7] All these factors are unlikely to change in the near future for economical reasons and it poses a burden to the administration with limited amount of funds. Other means of reducing the rate of postoperative wound infection need to be sought.

Prophylactic antibiotics remain the single most important factor in reducing post-surgical infection. [7] However, its use in clean category of surgical procedures is controversial. Currently there is no standard policy for use of prophylactic antibiotics in our hospital although heads of firms have their own. This study will be used as the basis for further extensive studies in the process to set up policies and guidelines for use of prophylactic antibiotics for clean surgical procedures.

Furthermore, a study done in Boston [11] by Platt R et al, showed that use of prophylactic antibiotics in clean surgical procedures has the benefit of lowering the overall infection rate by 48%, p = 0.01. There was also a comparable reduction in the need for postoperative antibiotic therapy and the number of non-routine visits to physicians for wound related problems. This suggests that prophylactic use of antibiotics in clean surgery may reduce perioperative illness and lower the costs of medical care. It is the purpose of this study to validate this in our set up. Prophylactic antibiotics have also been shown to reduce the rate of postoperative wound infection in ultra clean surgeries like operations involving the central nervous system, the cardiovascular system and orthopaedic surgery. [7]

3.3 STUDY OBJECTIVES

3.3.1 BROAD OBJECTIVE

To determine the role of antimicrobial prophylaxis in clean surgical procedures at Muhimbili National Hospital

3.3.2 SPECIFIC OBJECTIVES

1. To determine the rates of wound infection among the study and the control groups.
2. To determine the mean duration of postoperative hospital stay among the study and the control groups.
3. To determine the rate of postoperative non-routine hospital visits for wound related problems among the study and the control groups.
4. To determine the need and the indication for postoperative antibiotic therapy among the study and the control groups.
5. To determine the bacteriological pattern and antimicrobial sensitivity among postoperatively infected wounds.
6. To determine the rate of emergence of resistance to Ceftriaxone among the study group.
7. To determine the incidence of side effects of Ceftriaxone among the study group.

3.4 PATIENTS AND METHODS

3.4.1 TYPE OF STUDY

A prospective interventional study was conducted at Muhimbili National Hospital between January 2002 and November 2002. Patients who were scheduled and underwent elective clean surgical procedures were randomized into two groups. One group received prophylactic antibiotic at the induction of anaesthesia and the other group did not. Factors studied include the prevalence of postoperative wound infection, need for postoperative use of antibiotic in relation to occurrence of postoperative wound infection, length of postoperative hospital stay. Comparison of the findings was made between the two groups. Bacteriological pattern of the infecting organisms and their sensitivity was determined. Emergence of resistant organisms to ceftriaxone was also studied.

3.4.2 STUDY AREA

The study was done at the Muhimbili National Hospital. This is located in Upanga area in the city of Dar es salaam Ilala district and is a University teaching Hospital. Patients admitted to general surgical

wards formed the study population. The general surgical wards serve both children and adult patients who require surgical care. The wards are identified by numbers. Ward 2 and 21 serve as female surgical wards while 11, 13 and 14 serve as male surgical wards. Ward 12 is for male and female pediatric surgical patients. Ward 15 is for grade one female surgical patients and ward 16 is for grade one male surgical patients.

3.4.3 STUDY POPULATION

Patients eligible for study were all those planned for and actually underwent elective surgery during the study period. This included all age groups male and female patients except neonates and other patients with risk for postoperative wound infection. Known diabetic patients, jaundiced patients, patients with AIDS, and patients with advanced malignancy were excluded from the study.

3.4.4 THE PROPHYLACTIC ANTIBIOTIC

Ceftriaxone under the trade name of Powercef manufactured by Wockhardt Limited Company in India and distributed by the Salama Pharmaceuticals Company in Tanzania was used as a prophylactic

antibiotic. It was administered intravenously at the time of induction of anaesthesia. The dosage for adults was 1 gm and for paediatric cases it was 50mg /kg body weight not to exceed 2g. The dosage was repeated if surgery was prolonged beyond 3 hours and if large quantities of fluids were infused intraoperatively. Tolerance to the drug was assessed during the operation and within 24 hours postoperatively. Patients were observed for development of rash, fever, nausea, vomiting and pruritus intraoperatively and within 24 hours postoperatively after administration of ceftriaxone.

3.4.5 SAMPLE SIZE

The sample size was calculated using the formula:

$$N = \frac{ZPq(Z_\alpha + Z_\beta)^2}{(P_1-P_2)^2}$$

Where N= minimum required sample size

Z_α = level of significance (alpha risk)

Z_β = study power

P = expected prevalence of infection among the controls

q = 1-P

Using the above formula, the calculated sample size was 122 for the study group and 122 for the control group making a total of a minimum of 244 patients. A convenience method of sampling was used in which patients were recruited into the study as they came for surgical services. The study and the control groups were matched in terms of age, sex, preoperative diagnosis, and the duration of preoperative hospital stay. The author did the sampling and randomization.

3.4.6 DATA COLLECTION

Data collection was done using an English written questionnaire, which was prepared by the author and used partly by the nurses and by the author. Special forms for investigations were designed and used in the reporting of wound infection culture results. The author and the laboratory technicians used these forms. The information obtained from these forms was transferred to the questionnaire from which the final data analysis was made. Each questionnaire consisted of open ended and closed ended questions. The information was obtained from anaesthetic charts and the patient's file as well as by interviewing the patient. The author examined wounds to reach the diagnosis whether infected or not infected.

3.4.7 FOLLOW UP OF PATIENTS

Patients were reviewed on days 1, 3, 7 14 and 30 postoperatively. Patients who were discharged before the planned days of review were appointed to a special clinic where they were reviewed. Those patients who presented with evidence of wound infection had a pus swab taken under aseptic technique for bacteriological evaluation. Once taken, the specimen were kept in a sterile Stuart's transport medium and then sent to the microbiology laboratory for analysis within one hour after collection. In the laboratory the pus swab was inoculated on two blood agars and one McConkey agar plate. One of the blood agar was incubated anaerobically and the remaining two inoculates were incubated aerobically, all at temperatures between 35^0 and 37^0 C. These were incubated for 24 hours and 48 hours for aerobic and anaerobic cultures respectively.

3.4.8 DEFINITION OF WOUND INFECTION

The clinical definition of wound infection was adopted in this study. The wound was considered infected when there was frank discharge of pus from the incision. The wound was also considered infected if there was

cellulitis, pain, tenderness, induration and fever. Culture results were merely supportive.

3.4.9 DATA ANALYSIS

The author analyzed data manually and using the EPI6 computer program to determine if the difference observed between the two groups was statistically significant. Chi Square was used when comparing the proportions of the two groups.

3.4.10 ETHICAL ISSUES

The Research Ethical Committee of MUCHS granted ethical clearance to carry out the study. An informed consent was obtained from the patients before being enrolled into the study. Patients were explained the steps of the whole exercise and what was expected from them. No special risks were associated with being enrolled into the study as ceftriaxone is an antibiotic that is being used daily and is proved to be safe, well tolerated and efficacious. Patients were informed that it was of no consequence to reject to be enrolled and that if they chose so they could have continued receiving the routine surgical care unbiased. All patients randomized into the group that was receiving the antibiotic

were given the antibiotic free of charge at the time of induction of anaesthesia. Laboratory costs were included in the budget and patients were not burdened with this. Confidentiality was assured and no names appeared in the final analysis and report.

3.4.11 NULL HYPOTHESIS

This states that there is no difference in the rate of postoperative wound infection in clean category of surgical procedures between those who receive perioperative antibiotic prophylaxis and those who do not.

3.5 RESULTS

3.5.1 STUDY POPULATION

During the study period between January 2002 and November 2002 a total of 246 patients who underwent clean surgical procedures on an elective basis were enrolled into the study. These patients were admitted in the general surgical wards, which include a paediatric surgical ward.

Age And Sex Distribution

The patients' mean age was 37.8 years with a standard deviation of 25.9. The maximum age was 84 years and the minimum age was 2 months. The peak age was 41-60 years, which accounted for 27.6% of the study population. This was however closely followed by the ages > 60 and ≤ 10 which accounted for 24.4% and 22.8% of the study population respectively. There were a total of 156 males (63.4%) and a total of 90 (36.6%) females in the study population. The male to female ratio was then calculated to be 1.7:1. Table 1 summarizes these results.

Table 1. Age and sex distribution.

Age group (years)	Sex		Total (%)
	M	F	
≤10	44	12	56 (22.8%)
11-20	15	8	23 (9.3%)
21-40	13	26	39 (15.8%)
41-60	30	38	68 (27.6%)
>60	54	6	60 (24.4%)
Total	156 (63.4%)	90 (36.6%)	246 (100%)

Chi Square = 49.98 p = 0.0

3.5.2 CHARACTERISTICS OF THE STUDY POPULATION

Follow ups were conducted on days 1, 3, 7, 14 and 30 postoperatively. Patients were requested to come to special clinics for inspection of

wounds or removal of sutures. The follow up attendance declined with increasing number of visits. It was 100% for the first visit and declined to 52.4% for the last (fifth) visit. There was no significant difference in distribution of the patients according to ward of admission and prophylaxis status, p = 0.2. Figure 1 illustrates this.

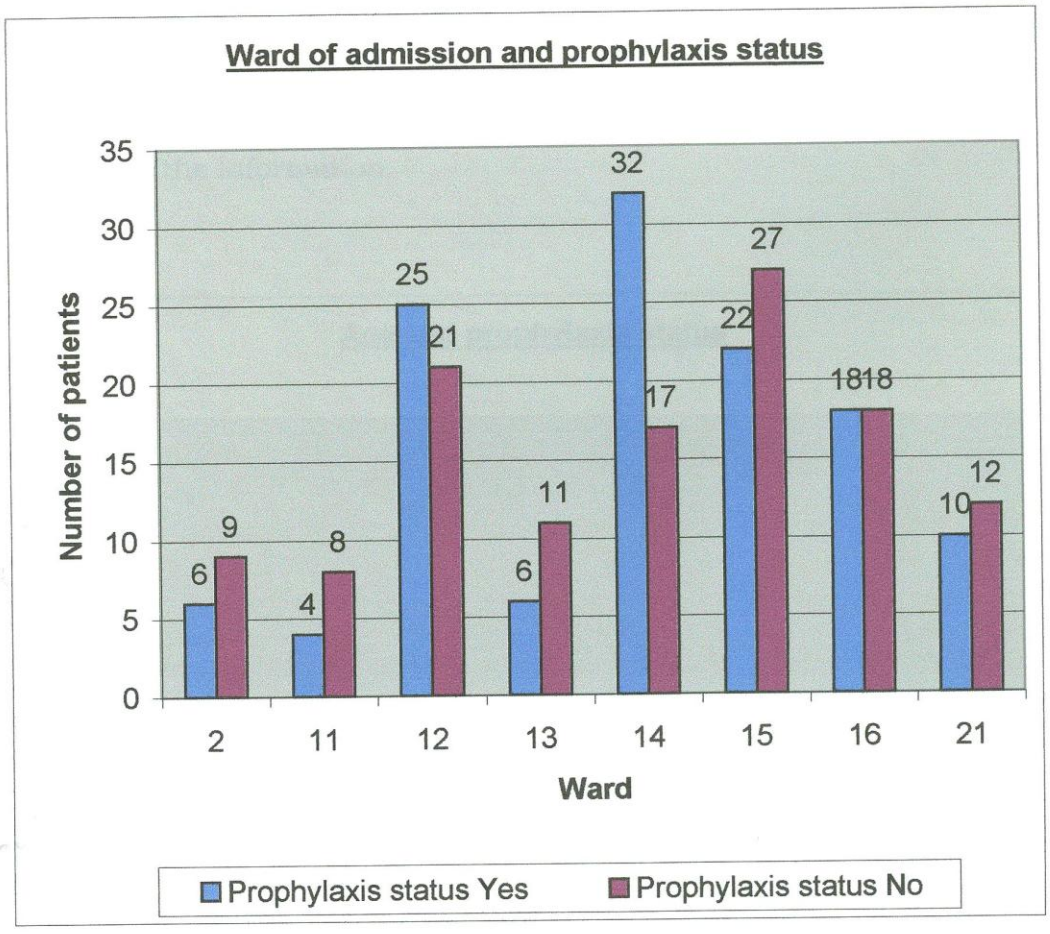


Figure 1. Distribution of the study population according to ward of admission and prophylaxis status.

Age And Prophylaxis Status

There was no significant difference in the distribution of patients according to age and prophylaxis status, p = 0.5. The study population comprised 27.6% patients aged 41-60 years and 24.4% aged > 60 years. The age group ≤ 10 contributed 22.8% of the study population. Patients aged 11-20 and 21-40 contributed 9.3% and 15.8% of the study population respectively. For each age group patients were randomized into the study and the control groups roughly half to each. Figure 2 illustrates the information.

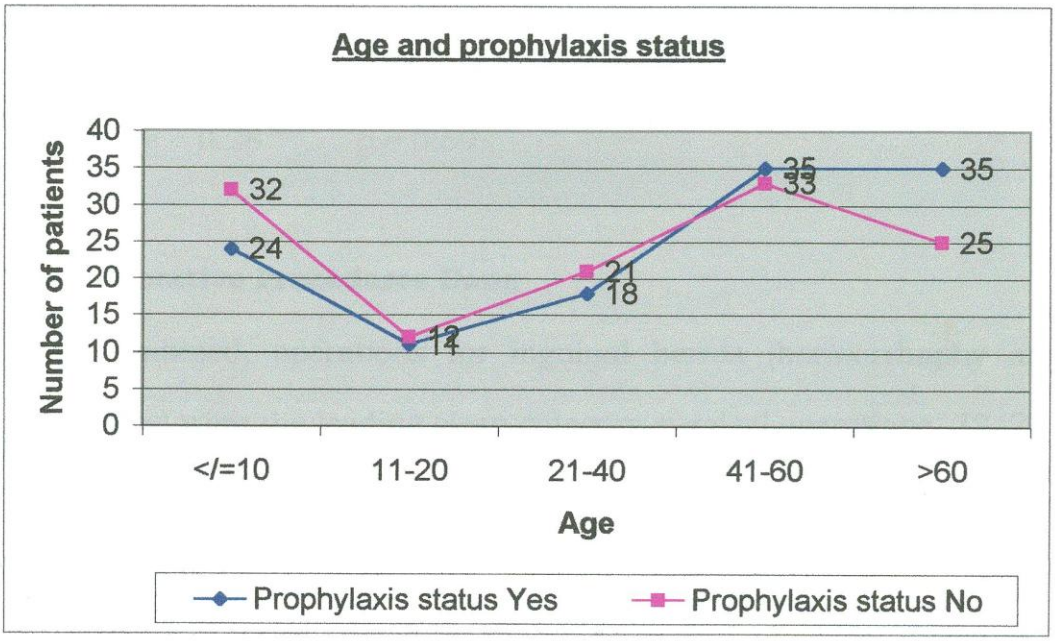


Figure 2. Distribution according to age and prophylaxis status

Sex And Prophylaxis Status

Sixty five percent of the study group consisted of male patients while the remaining 35% was formed of females. On the other hand 61.4% of the control group was formed of males and the remaining 38.6 % consisted of females. There was no significant difference in sex distribution between the study and the control groups. Table 2 summarizes this information.

Table 2. Sex and prophylaxis status.

Sex	Prophylaxis status		Total
	Yes	No	
Male	80 (65.0%)	76 (61.8%)	156 (63.4%)
Female	43 (35.0%)	47 (38.2%)	90 (36.6%)
Total	123 (100%)	123 (100%)	246 (100%)

Chi Square = 0.28 p = 0.59

Clean Operative Procedures Done

When combined, operations for inguinal hernia (herniorrhaphy and herniotomy) were the leading clean category surgical operations, 72/246 (29.3%). Subcapsular orchiectomy was the second common clean operative procedure done during the study period comprising 42 (17.1%) operations. "Others" comprised a category of rare operations contributing one operation each, it included, excision of keloid, orchiectomy, repair of epigastric hernia, scrotoplasty, excision of

lymphangioma, exploration of left kidney, excision of thyroglossal cyst and excision of sebaceous cyst. They accounted for 3.2 % of all the operations. Figure 3 illustrates these data.

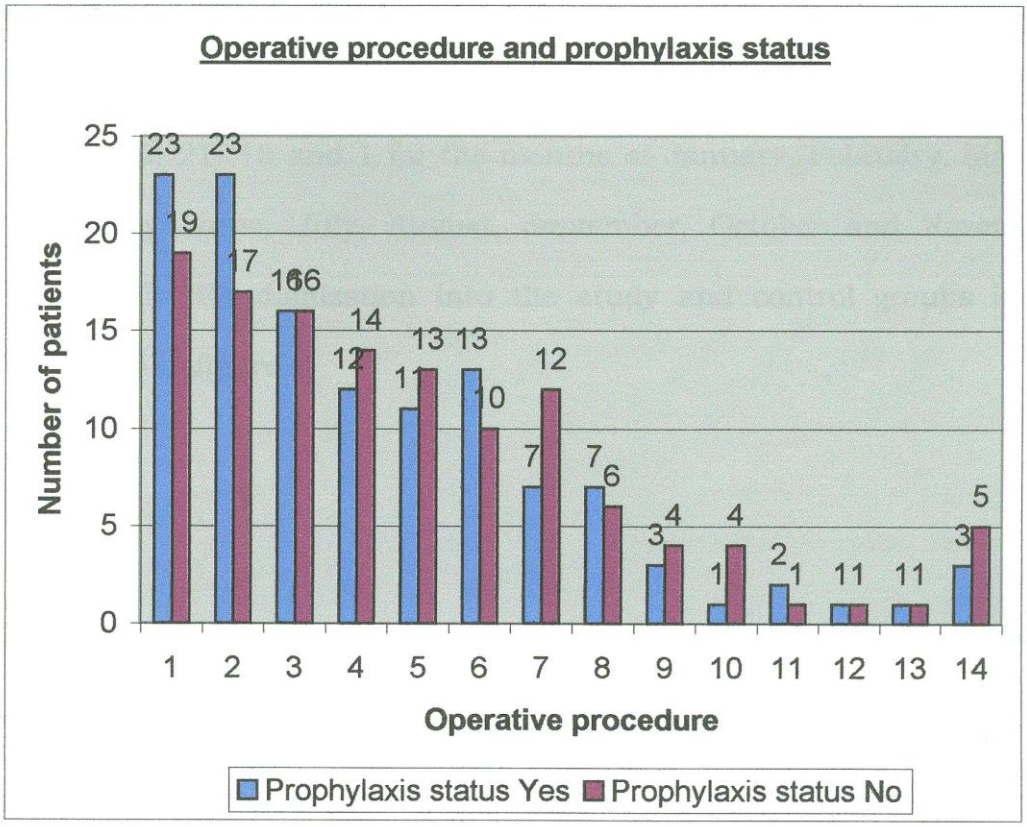


Figure 3. Distribution of patients according to type of clean operative procedure and prophylaxis status.

Key for the X-axis

1 = subcapsular orchiectomy; 2 = herniorrhaphy; 3 = herniotomy; 4 =hydrocelectomy; = 5 = mastectomy; 6 = thyroidectomy; 7 = umbilical hernia repair; 8 = breast lumpectomy; 9 = microdochotomy; 10 = Lipoma excision; 11 = orchidopexy; 12 = incisional hernia repair; 13 = thyroid cyst excision; 14 = others.

Month Of Operation And Prophylaxis Status

The monthly enrollment into the study and subsequent clean operations done are as illustrated in figure 3. Convenience sampling method was used and patients were subsequently randomized into the prophylaxis and no prophylaxis groups. Enrollment was done from January to November, the numbers of patients enrolled were: 29, 36, 20, 21, 27, 22, 32, 22, 21, 15 and 1 for the months of January, February, March, April, May, June, July, August, September, October and November respectively. Randomization into the study and control groups is as illustrated in figure 4.

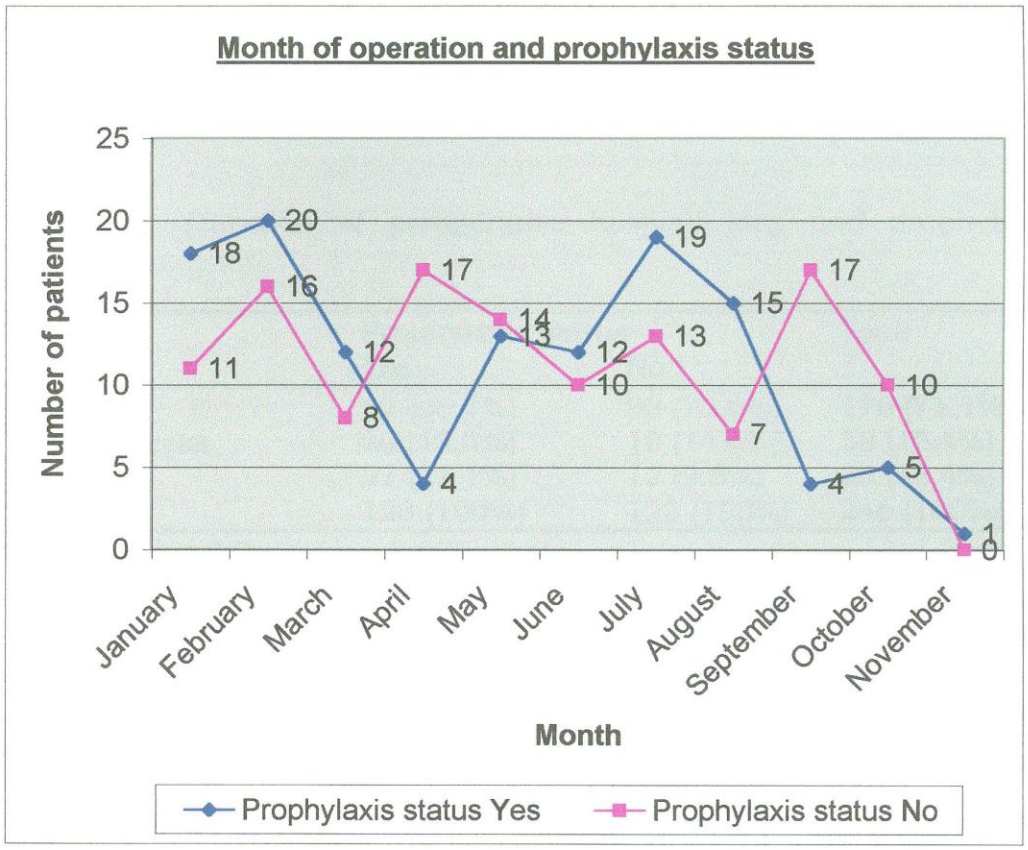


Figure 4. Distribution of patients according to month of operation and prophylaxis status.

Preoperative Hospital Stay

The majority of patients, 175 (71.1%) stayed not more than 24 hours preoperatively. There were 38 (15.4%) patients who stayed between 2 days and two weeks. The others, 33 (13.4%), stayed longer than two weeks. There was an approximate equal distribution of the study

population as regards preoperative hospital stay and prophylaxis status. Table 3 summarizes the information.

Table 3. Duration of preoperative hospital stay and prophylaxis status.

Duration	Prophylaxis status		Total
	Yes	No	
≤1 day	82 (66.7%)	93 (75.6%)	175 (71.1%)
Up to 2 weeks	20 (16.3%)	18 (14.6%)	38 (15.4%)
>2 weeks	21 (17.1%)	12 (9.8%)	33 (13.4%)
Total	123 (100%)	123 (100%)	246 (100%)
Chi Square = 3.2	p = 0.2		

Duration Of Operation

The maximum duration of operation was 2 hours (120 minutes). Operations commonly reaching this duration were mastectomies. The minimum duration of operation was 10 minutes; this was for excision of a lipoma. Most (211) operations were done within one-hour duration. This accounted for 85.8% of all the clean operations. The rest of the operations (35) were done between one hour and two hours duration and not exceeding two hours. This accounted for 14.2% of the clean operations in the study. There was an even distribution of patients according to duration of operation and prophylaxis status. Table 4 summarizes the data.

Table 4. Duration of operation and prophylaxis status

Duration (min)	Prophylaxis status		Total
	Yes	No	
≤60	106 (86.2%)	105 (85.4%)	211 (85.8%)
61-120	17 (13.8%)	18 (14.6%)	35 (14.2%)
Total	123 (100%)	123 (100%)	246 (100%)
Yates corrected Chi Square = 0.0		p = 1.0	

3.5.3 WOUND INFECTION

Overall Wound Infection Rate

Wound infection was observed in 12 patients who underwent clean surgical procedures during the study period. This gave a 4.9% overall postoperative clean wound infection rate during the study period. Table 5 summarizes this data.

Wound Infection And Prophylaxis Status

In the group that was receiving prophylactic antibiotic, 4 patients had postoperative wound infection. This was equivalent to a wound infection rate of 3.2% in this group. On the other hand, 8 patients had postoperative wound infection in the group that was not receiving the prophylaxis (the control group). This was equivalent to a wound infection rate of 6.5% in this group. All wound infections were culture

positive. However these results were found not to be statistically significant. Table 5 summarizes the data.

Table 5. Wound infection and prophylaxis status.

Wound infection	Prophylaxis status		Total
	Yes	No	
Yes	4 (3.2%)	8 (6.5%)	12 (4.9%)
No	119 (96.7%)	115 (93.5%)	234 (95.1%)
Total	123 (100%)	123 (100%)	246 (100%)
Chi Square = 1.40	p = 0.2		

Wound Infection And Age

When analyzed for age, wound infection rate was highest in the age group > 60 years which is an upper extreme of age. It involved 7/60 patients making an 11.7% wound infection rate in this age group. In this age group 2 of the 7 infected patients received antibiotic prophylaxis. The next affected age group was 41-60 years; it involved 4/68 patients who made an infection rate of 5.9 in this age group. In this age group 2 of the 4 infected patients had received prophylaxis. The least affected age group was the lower extreme of age,≤ 10 years, which involved 1/56 patient making an infection rate of 1.8% in this age group. This patient did not receive antibiotic prophylaxis. No wound infection was observed in the middle range of ages 11-20 years and 21-

40 years. These results were statistically significant. See table 6 for summary.

Table 6. Wound infection and age.

Age group (years)	Wound infection status		Total
	Yes	No	
≤10	1 (1.8%)	55 (98.2%)	56 (100.0%)
11-200	(0%)	23 (100.0%)	23 (100.0%)
21-400	(0%)	39 (100.0%)	39 (100.0%)
41-60	4 (5.9%)	64 (94.1)	68 (100.0%)
>60	7 (11.7%)	53 (88.3%)	60 (100.0%)
Total	12 (4.9%)	234 (95.1%)	246 (100.0%)
Chi Square = 10.44	d f = 4	p = 0.03	

Wound Infection With Prophylaxis Status And Age

Wound infection was observed with increasing age in both the study and the control groups. When prophylaxis was used no wound infection was observed in the ages≤ 40 years in contrast to a rather similar picture but with a 3.1% (1/32) wound infection rate in the≤ 10 years in the control group. There was numerically less wound infection when prophylaxis was used for the age groups 41-60 and > 60. The infection rates were 5.7% (2/35) for each age group when prophylaxis was used, and 6.1% (2/33) and 20% (5/25) for each age group respectively in the control group. The Chi Square could not be calculated due to some cells containing zero numbers. Table 7 details the findings.

Table 7. Wound infection, prophylaxis status and age.

Age	Rate of wound infection	
	With prophylaxis	Without prophylaxis
≤10	0/24	1/32 (3.1%)
11-20	0/11	0/12
21-40	0/18	0/21
41-60	2/35 (5.7%)	2/33 (6.1%)
>60	2/35 (5.7%)	5/25 (20%)

Chi Square could not be calculated, zero number in some cells

Wound Infection And Sex

Wound infection was higher among males than female patients, 9/156 (5.8%) and 3/90 (3.3%) respectively. These findings were not statistically significant, p = 0.58. Table 8 shows the results in detail.

Table 8. Wound infection and sex.

Sex	Wound infection status		Total
	Yes	No	
M	9 (5.8%)	147	156 (100%)
F	3 (3.3%)	87	90 (100%)
Total	12	234	246

Yates Corrected Chi Square = 0.30 p = 0.58

Wound Infection With Prophylaxis Status And Sex

The rates of postoperative wound infection were approximately halved in both sexes when the prophylactic antibiotic was used. They were found

to be 3.8% (3/80) in males in the study group compared to 7.9% (6/76) in the control group, and 2.3% (1/43) in females in the study group compared to 4.2% (2/47) in the control group. These results were not statistically significant, p = 0.48. Table 9 summarizes the results.

Table 9. Wound infection, prophylaxis status and sex.

Sex	Rate of wound infection	
	With prophylaxis	Without prophylaxis
M	3/80 (3.8%)	6/76 (7.9%)
F	1/43 (2.3%)	2/47 (4.2%)
Yates Corrected Chi Square = 0.50		p = 0.48

Wound Infection And Type Of Operation Done

Mastectomy had the highest rate of wound infection among the clean operative procedures during the study, 3/24 (12.5%). One of the eight patients in the group of "other" operations (repair of epigastric hernia) had wound infection giving a 12.5% infection rate in this group of clean operations. Hydrocelectomy, Herniorrhaphy and subcapsular orchiectomy had similar rates of wound infections, 2/26 (7.7%), 3/40 (7.5%) and 3/42 (7.1%) respectively. The Chi Square could not be calculated due to some cells containing zero number. Figure 5 summarizes this account.

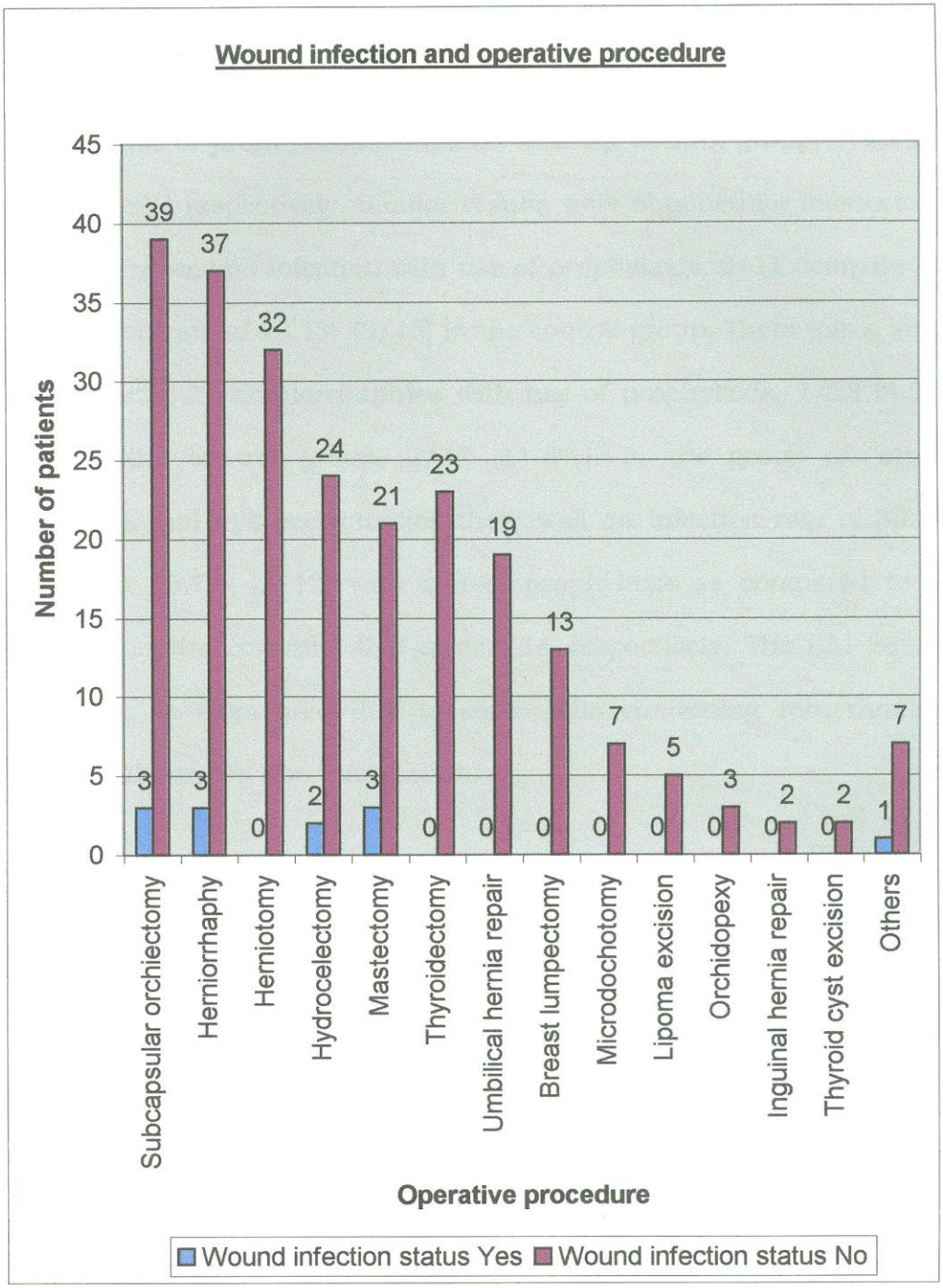


Figure 5. Wound infection and type of operation done.

Wound Infection With Prophylaxis Status And Type Of Operation

There was elimination of wound infection in subcapsular orhiectomy with the use of prophylaxis compared with the control group, 0/23 and 3/19 (15.8%) respectively. Similar results were obtained for mastectomy where there was no infection with use of prophylaxis, 0/11 compared to an infection rate of 23.1% (3/13) in the control group. There was a lower infection rate in herniorrhaphies with use of prophylaxis, 1/23 (4.3%) than in the control group, 2/17 (11.8%). In the group of "other" operations and hydrocelectomies there was an infection rate of 33.3% (1/3) and 16.7% (2/12) with use of prophylaxis as compared to no infection in the controls, 0/5 and 0/14 respectively. The Chi Square could not be calculated due to some cells containing zero number. Figure 6 illustrates this information.

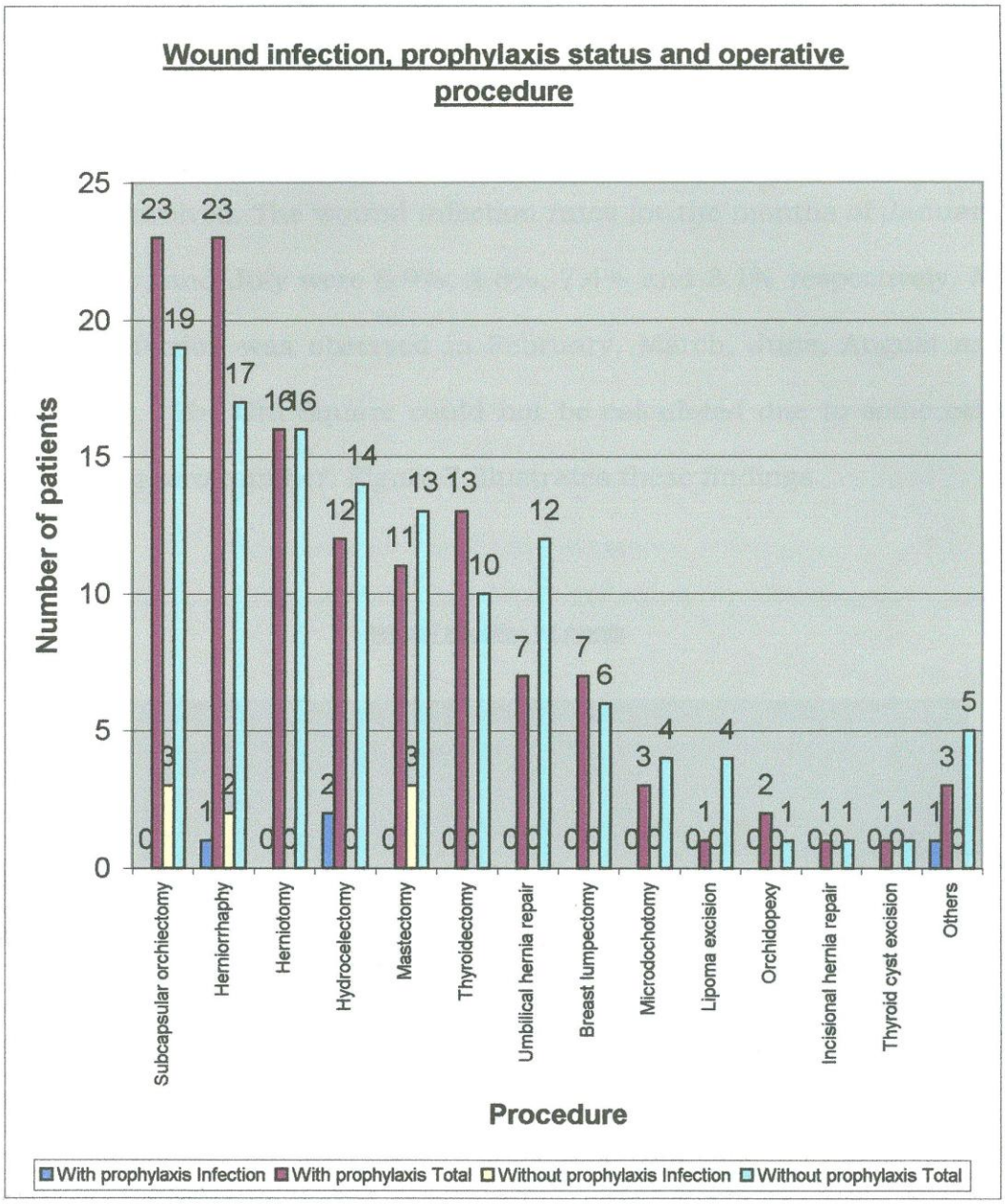


Figure 6. Wound infection according to prophylaxis status and type of operative procedure.

Wound Infection By Month

Wound infection peaked in the month of October when 4/15 patients were involved (26.7%). September was the next with 2/21 (9.5%) patients involved. The wound infection rates for the months of January, April, May, and July were 6.9%, 4.8%, 7.4% and 3.1% respectively. No wound infection was observed in February, March, June, August and November. The Chi Square could not be calculated due to some cells containing zero number. Figure 7 illustrates these findings.

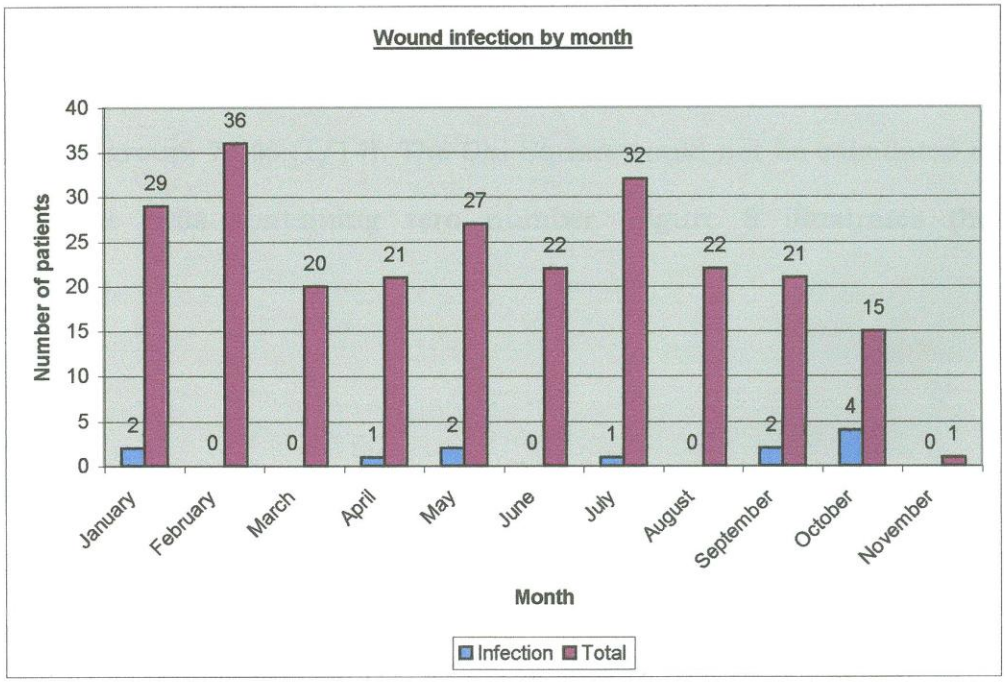


Figure 7. Wound infection and month of operation.

Wound Infection With Prophylaxis Status And Month Of Operation

A lower rate of wound infection, 20% (1/5), was found in October with use of prophylaxis than in the control group in the same month, 30% (3/10). There was no wound infection in the month of September with use of prophylaxis, 0/4, as compared to an infection rate of 11.8% (2/17) in the same month for the control group. In January, wound infection rate was lower in the study group (5.6%) compared to the control group, 9.1%. There was no wound infection in the month of April, 0/4, for the study group while there was a 5.9% (1/17) wound infection rate in the same month for the control group. In May there was a higher infection rate in the study group, 7.7% (1/13) than in the control group, 7.1% (1/14). The Chi Square could not be calculated due to some cells containing zero number. Figure 8 illustrates these findings.

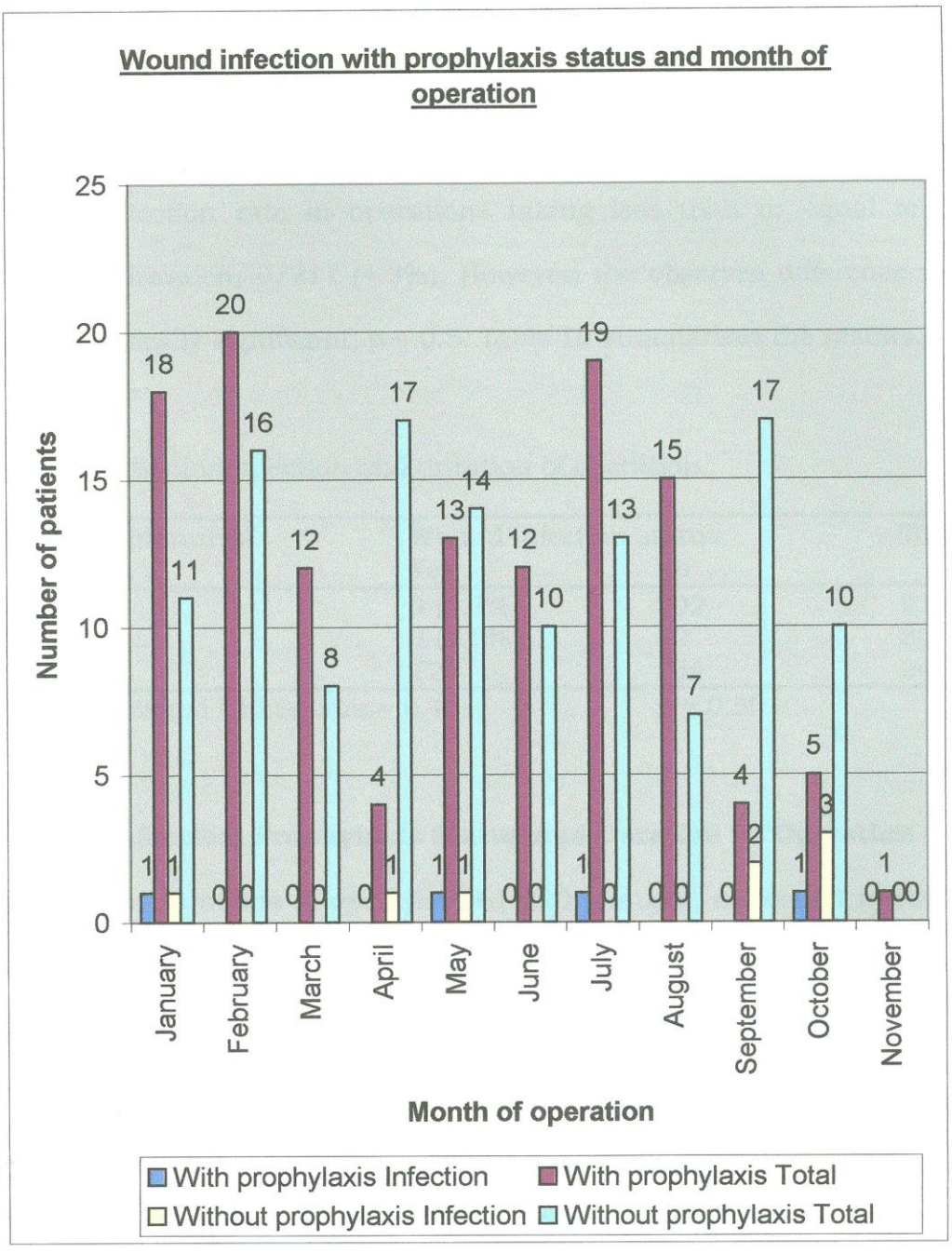


Figure 8. Wound infection with prophylaxis status and month of operation.

Wound Infection and Duration of Operation

The wound infection rate doubled for operations taking longer than an hour and not going beyond two hours duration, 3/35 (8.6%), compared to the infection rate in operations taking less than or equal to 60 minutes duration, 9/211 (4.3%). However, the observed difference was not statistically significant, p = 0.5. Table 10 summarizes the results.

Table 10. Wound infection and duration of operation.

Duration (minutes)	Wound infection status		Total
	Yes	No	
≤60	9 (4.3%)	202	211
61-120	3 (8.6%)	32	35
Total	12	234	246
Yates Corrected Chi Square = 0.45		p = 0.50	

Wound Infection, Prophylaxis Status And Duration Of Operation

For longer durations of operation, 61-120 minutes, no wound infection was found, (0/17), when prophylactic antibiotics were given compared to an infection rate of 16.7% (3/18) when no prophylactic antibiotics were used. It was also found that a lower rate, 3.8% (4/106), of wound infection was associated with use of prophylaxis for operations lasting up to 60 minutes than that found in the control group for the same duration of operation, 4.8% (5/105). These findings were not statistically significant, p = 0.25. Table 11 summarizes these findings.

Table 11. Wound infection, prophylaxis status and duration of operation.

Duration (minutes)	Rate of wound infection	
	With prophylaxis	Without prophylaxis
≤60	4/106 (3.8%)	5/105 (4.8%)
61-120	0/17	5/18 (16.7%)

Yates' corrected Chi Square = 1.31 p = 0.25

Wound Infection And Preoperative Hospital Stay

Wound infection rate increased with increasing duration of preoperative hospital stay. It was highest, 12.1%, for patients who stayed longer than two weeks in hospital preoperatively and lowest, 3.2%, for patients who stayed 24 hours or less. For patients who stayed preoperatively between one day and two weeks the postoperative wound infection rate was 5.3%. These findings were not statistically significant, p = 0.1. See table 12 for details.

Table 12. Wound infection and preoperative hospital stay.

Preoperative stay	Wound infection		Total
	Yes	No	
Up to 24 hours	6(3.4%)	169	175(100%)
>24hours-2weeks	2(5.3%)	36	38(100%)
>2weeks	4(12.1%)	29	33(100%)

Chi Square = 4.54 p = 0.1

Wound Infection, Prophylaxis Status And Preoperative Hospital Stay

When analyzed against prophylaxis status, wound infection was observed solely in patients who stayed not more than 24 hours preoperatively, 4/82 (4.9%), for the study group. In the control group postoperative wound infection rate increased with increasing duration of preoperative hospital stay, being 2.1% (2/93) for the duration of stay up to 24 hours, 11.1% (2/18) for the duration of stay between one day up to two weeks and 33.3% (4/12) for those who stayed longer than two weeks in this group. The Chi Square could not be calculated due to some cells containing zero number. Table 13 details the findings.

Table 13. Wound infection, prophylaxis status and preoperative hospital stay.

Preoperative stay	Rate of wound infection	
	With prophylaxis	Without prophylaxis
≤1 day	4/82 (4.9%)	2/93 (2.1%)
Up to 2 weeks	0/20	2/18 (11.1%)
>2 weeks	0/21	4/12 (33.3%)

Chi Square could not be calculated, zero number in some cells.

Wound Infection And Postoperative Hospital Stay

Higher rates of wound infection were associated with an increasing duration of postoperative hospital stay. A postoperative wound infection

rate of 33.3% (2/6) was found in patients who stayed longer than two weeks in hospital postoperatively. This is opposed to only 3.3% of patients who stayed up to only three days. Patients who stayed between 4 and 7 days postoperatively had a wound infection rate of 7.1% (1/14), and those who stayed between 8 and 14 days had a postoperative wound infection rate of 12.5% (2/16). These results were statistically significant. Table 14 shows the results in detail.

Table 14. Wound infection and postoperative hospital stay.

Postoperative stay (days)	Wound infection status		Total
	Yes	No	
Up to 3 days	7 (3.3%)	203 (96.7%)	210
4-7	1 (7.1%)	13 (92.9%)	14
8-14	2 (12.5%)	14 (87.5%)	16
>14	2 (33.3%)	4 (66.7%)	6
Total	12	234	246

Chi square = 13.63 Degree of freedom = 3 p value = 0.003

3.5.4 MEAN DURATION OF POSTOPERATIVE HOSPITAL STAY

The mean duration of postoperative hospital stay was found to be 2.6 days for the group of patients who were receiving the prophylactic antibiotic and 3.2 days for the group that was not receiving the prophylactic antibiotic. These findings were not statistically significant, p value = 0.15. Table 15 summarizes this information.

Table 15. Mean postoperative hospital stay and prophylaxis status.

Prophylaxis status	Mean postoperative stay (days)
Yes	2.6 (SD = 2.8)
No	3.2 (SD = 3.6)

P = 0.15

3.5.5 POSTOPERATIVE NON-ROUTINE HOSPITAL VISITS

The mean postoperative non-routine hospital visits for wound related problems was 0.06 days for the group that was receiving the prophylactic antibiotic and 0.43 days for the group that was not receiving the prophylaxis. These results were not statistically significant. Table 16 summarizes the results.

Table 16. Mean postoperative non-routine hospital visits and prophylaxis status.

Prophylaxis Status	Mean postoperative visits (days)
Yes	0.06 (SD = 0.52)
No	0.43 (SD = 2.22)

P = 0.07

3.5.6 NEED FOR POSTOPERATIVE ANTIBIOTICS

With regard to the postoperative use of antibiotics 6/123 patients in the group that was receiving the prophylactic antibiotic received

postoperative antibiotics. This is equivalent to a rate of 4.9%. On the other hand 27/123 patients in the control group received postoperative antibiotic (22%). The observed difference was statistically significant, p = 0.000085. Table 17 summarizes this data.

Table 17. Use of postoperative antibiotics and prophylaxis status.

Antibiotic use	Prophylaxis status		Total
	Yes	No	
Yes	6 (4.9%)	27 (22%)	33 (13.4%)
No	117 (95.1%)	96 (78%)	213 (86.6%)
Total	123 (100.0%)	123 (100%)	246 (100.0%)
Chi square = 15.43		p = 0.000085	

3.5.7 BACTERIOLOGICAL PATTERN OF ISOLATES

Staphylococcus aureus was the most frequent isolate accounting for 52.2% of the isolates. Klebsiella spp. was ranking second in the frequency of isolation accounting for 34.8% of the isolates. Escherichia coli accounted for 13% of the isolates. A mixed type of infection with two infecting organisms was a common finding. Table 18 summarizes the results.

Table 18. Bacteriological pattern of the isolates.

Organism	Frequency	Percent
Staphylococcus aureus	12	52.2%
Klebsiella spp.	8	34.8%
Escherichia coli	3	13.0%
Total	23	100%

Bacteriological Pattern And Site Of Operation

When analyzed for the sites of operation, the bacteriology of wound infection showed that Escherichia coli were isolated solely from the perineum. Other isolates were more or less evenly distributed to the sites of infection namely the groin, the perineum and the chest. Table 19 shows the results in detail.

Table 19. Bacteriological pattern and site of operation.

Organism	Site Of Operation			Total
	Groin	Perineum	Chest	
Staphylococcus aureus	3 (25.0%)	5 (41.7%)	4 (33.3%)	12 (100%)
Klebsiella spp.	3 (37.5%)	2 (25.0%)	3 (37.5%)	8 (100%)
Escherichia coli	0	3 (100%)	0	3 (100%)
Total	6 (26.1%)	10 (43.5%)	7 (30.4%)	23 (100%)

3.5.8 ANTIMICROBIAL SENSITIVITY PATTERN

There was 100% susceptibility of the isolated Staphylococcus aureus to ceftriaxone (12/12). Similar results were obtained with cloxacillin (10/10). The sensitivity of Staphylococcus to ciprofloxacin was also 100% in this study (9/9). 100% of these organisms were resistant to penicillin G (5/5). Sensitivity to tetracycline was found to be 63.6% (7/11) and that to ampicillin was 54.5% (6/11). Table 20 summarizes this information.

Table 20. Antimicrobial Sensitivity Pattern.

Organism	Ceftriaxone N (%)	Ciprofloxacin N (%)	Cloxacillin N (%)	Gentamicin N (%)	Chloramphenicol N (%)	Augmentin N (%)	Ampicillin N(%)	Tetracycline N (%)
Staphylococcus aureus	12/12 (100)	9/9 (100)	10/10 (100)	2/2 (100)	1 (100)	2/2 (100)	6/11 (54.5)	9/11 (81.1)
Klebsiella spp.	8/8 (100)	7/7 (100)	0/2 (0)	6/6 (100)	4/4 (100)	2/3 (66.7)	2/6 (33.3)	1/5 (20)
Escherichia coli	3/3 (100)	3/3 (100)		2/3 (66.7)	½ (50)	2/2 (100)	1/3 (33.3)	0/2 (0)

3.5.9 EMERGENCE OF RESISTANCE TO CEFTRIAXONE

From the ongoing account of the antimicrobial sensitivity pattern it is clear that there was no development of resistance to ceftriaxone encountered in the study.

3.5.10 SIDE EFFECTS OF CEFTRIAXONE

Seven patients experienced nausea in the group that was receiving the prophylaxis. One patient had fever postoperatively but was found to have clinical malaria. Two patients vomited intraoperatively. Table 21 summarizes this information.

Table 21. Side Effects 0f Ceftriaxone.

Side effects	Frequency	Percentage	Cumulative Percentage
Fever	1	0.8	0.8
Nausea	7	5.7	6.5
Vomiting	2	1.6	8.1
No side effects	113	91.9	100

3.6 DISCUSSION

In the present study the overall prevalence of wound infection is 4.9%. This rate is far lower than the rate found three years ago by Wayi [10] when it was 10.1%. This rate is encouraging and it is within the acceptable limits of the expected rates of postoperative wound infection of clean surgical procedures, which is 1-5%. [91,92,93] Ideally the rate is supposed to be < 2%. [7] However this is possible only under strict surveillance programs. Other studies have reported different rates of

infection. In Mexico a lower rate of wound infection was reported in 1999. [94] The rate was found to be 1.3%. In the same study the rates of wound infection following clean-contaminated and contaminated operations were found to be low at 1.9% in each category. In another study done in Nigeria in 1992, the rate of wound infection in clean surgical procedures was found to be 2%. [95] Shija in 1973 reported a 6.6% rate of wound infection in Dar es Salaam. [96]

Other studies still, have reported higher rates of wound infection, in India for example a rate of wound infection in clean surgeries of 12% was reported in 1998. [97]

The number of patients with wound infection in the group that was receiving the antimicrobial prophylaxis was found to be 4/123 (3.2%) and that in the group that was not receiving the prophylaxis 8/123(6.5%). This apparently lower rate of wound infection in the study group compared with the control group was found not to be statistically significant, $p = 0.2$. These results are not consistent with the study in Boston which showed statistically significant decrease in overall wound infection rate with the use of prophylactic antibiotics. With a closer look at these results one will see that the rate of postoperative wound infection for the control group is still high beyond the acceptable limits

(of 1-5%) while that for the study group is within the acceptable limits. These results can still be due to a mere chance, as the statistical tests show no significance.

Wound infection when distributed according to age shows increase in rate with advancing age of the patient. This finding agrees with other findings by Wayi [10] and the rest of the world. In a recent study done at Muhimbili National Hospital, Wayi found an increasing rate of wound infection with increasing age. Cruse et al in a 10 year prospective study of 62,939 wounds found that age was a factor influencing the rate of infection of clean wounds with patients more than 66 years old being six times more likely to develop infection than are patients 1-14 years old. [3] Generally wound infection is common at the extremes of age. [91, 98] This study shows similar results marked by absence of wound infection in the middle age groups. In this study wound infection was observed in higher age groups, 2/35 (5.7%) in each age groups: 41-60 and > 60 years for the study group, a similar trend was also observed with the control group with wound infection rates of 6.1% (2/33) and 20% (5/25) for age groups 41-60 and > 60 respectively. The differences were however not statistically significant. The difference in infection rates observed in different age groups with use and non-use of prophylaxis was also not statistically significant. For example, for the age group > 60

the wound infection rate was 20% for the control group and 5.7% for the study group, these differences were found not to be statistically significant.

Wound infection rates in males and females were 5.8% (9/156) and 3.3% (3/90) respectively. Though numerically higher in males, the observed difference in rates of postoperative wound infection was not statistically significant. This is in keeping with the findings 3 years ago by Wayi [10] who found no significant difference in the rates of wound infection between sexes. In the literature, sex has not been cited as a predisposing factor to wound infection. Use of prophylaxis halved the infection rates in both sexes. The difference was, however, found not to be statistically significant, $p = 0.5$.

Wound infection was also found to be increasing numerically with the duration of preoperative hospital stay. It was highest in patients who stayed longer than two weeks and lowest in patients who stayed for up to 24 hours only. Although not statistically significant, $p = 0.1$, the trend is in keeping with the findings by Cruse [3] et al who found that the longer the patient stays in hospital before an operation the more susceptible he or she becomes to wound infection. Similar results were obtained by Wayi [10] three years ago who found statistically significant increase in

wound infection rates with increasing duration of preoperative hospital stay. It is likely that the patient's skin becomes colonized with bacteria to which he or she is not resistant. [5] In the clinical practice at Muhimbili patients who stay long in hospital preoperatively are those who are referred from upcountry and their surgical problems not sorted out early. Others are patients with suspected malignancies who undergo confirmatory investigations prior to surgery. Both these patients can be further delayed by lack of funds for the required investigations and a large back-load at the pathology department leading to a delay in providing histological diagnosis. Shortage of theatre time is another confounding factor prolonging preoperative hospital stay. In the study the observed effect of use of prophylaxis was a reduction in the rates of wound infection with preoperative stay. However, the difference was not statistically significant.

The mean duration of postoperative hospital stay was found to be shorter for the group that was receiving the prophylactic antibiotic. However these results were not statistically significant, $p = 0.2$. This difference can be reflected on the effect of the prophylaxis to reduce the rate of wound infection as it was also shown in the study that postoperative hospital stay was longer for patients with wound infection, $p = 0.003$. This prolongation of hospital stay for wound infection is not a

new phenomenon and has been reported by several studies. Haley and colleagues found that surgical nosocomial infections resulted in an average of 1.3 to 26.3 extra days of hospitalization and an extra cost of hospitalization of 670 to 2400 dollars. [2]

The mean postoperative non-routine visits to physician for wound related problems was lower in the group that was receiving the prophylactic antibiotic. However the difference was not statistically significant, $p = 0.2$. These findings do not match those reported in Boston by Platt R and colleagues in 1990. [11] They reported significant reduction in the number of postoperative visits to physician for wound related problems with the use of prophylactic antibiotics in clean surgery. This reduced the cost of postoperative care of the patients.

The need for postoperative antibiotics was low in the group that was receiving the prophylaxis. This is a reflection of low rate of wound infection in this group compared to the control group. It also is a reflection of lack of confidence on the part of the surgeon not to give antibiotics postoperatively when no prophylaxis was given. Majority of the postoperative antibiotics were prescribed empirically. These findings match those in Boston where less need for postoperative antibiotics was observed among those getting the prophylactic antibiotic. This also has

a direct bearing on the reduction of the cost of postoperative care, as antibiotics are costly. It also reduces the inconvenience of having to take a five days course of antibiotics postoperatively with therapeutic intentions. Other indications for postoperative antibiotics included urinary tract infection and respiratory tract infections, which are both common causes of postoperative fever.

The bacteriological pattern of the isolates was not a surprising outcome as it compares with other studies. In the present study there was predominance of Staphylococcus aureus. In India in 1998 Murthy found staphylococcus aureus accounted for 32% of isolates and Pseudomonas spp were 21%. [97] In England, Staphylococcus aureus comprised 29% of the isolates. [22] Staphylococcus aureus has been documented as the major cause of surgical site infections (SSIs). It accounted for almost 40% of the pathogens identified as causing infections in the survey from the English hospitals [37] and was responsible for 35% of the microbiologically documented infections in the Dutch study. [37] In clean surgical procedures, the impact of Staphylococcus aureus is even greater. Staphylococcus aureus has been the leading cause of SSIs since the 1950s, whereas in the beginning of the 19th century, in the pre-sulphonamide era, Streptococci were predominant. The natural and main niche for Staphylococcus aureus is the human nose, but other

skin sites also can be colonized. Many patients and hospital staff members carry these microorganisms. The prevalence of carriage in both groups is 30% to 35%. As such Staphylococcus aureus can be an exogenous or endogenous cause of SSIs. However evidence has accumulated that the majority of Staphylococcus aureus strains recovered from wound infections are endogenous. [37]

Klebsiella spp ranked second in the frequency of isolation, accounting for 34.8% of the isolates. These results are similar to other studies in this region by Wayi [10] and Shija [96] who found Klebsiella ranking second in each of their studies. It supports the speculation by Wayi that probably the pathogenicity of this microorganism in this hospital is high.

Worldwide, it has been reported that the role of Klebsiella in nosocomial infection is increasing. Klebsiellae are ubiquitous in nature. In humans, they may colonize the skin, pharynx, or gastrointestinal tract. They may also colonize sterile wounds and urine. Carriage rates vary with different studies. Klebsiellae may be regarded as normal flora in many parts of the colon and intestinal tract and in the biliary tract. Oropharyngeal carriage has been associated with endotracheal intubation, impaired host defenses, and antimicrobial use. Extensive use of broad-spectrum

antibiotics in hospitalized patients has led to both increased carriage of klebsiellae and, subsequently, the development of multidrug-resistant strains that produce extended-spectrum beta-lactamase (ESBL). In United states klebsiellae account for approximately 8% of all hospital-acquired infections. Common sites include the urinary tract, lower respiratory tract, biliary tract, and surgical wound sites. [5]

Escherichia coli formed 13% of the isolates; these are not uncommon organisms to be isolated from wound infection though one may wonder as to their source in clean wounds. When analyzed for the type of operation done, p value = 0.2, it was found that of the three patients in whom Escherichia coli were isolated, two underwent bilateral subcapsular orchidectomy for prostatic cancer and one underwent hydrocelectomy. These surgical sites are in close proximity to the perineum, which can be the source of infection if dressings are improperly applied or changed. Also infection could set in following contamination at the time of operation with poor aseptic technique due to poor skin preparation, or during application of sterile drapes with break in technique and during the final dressing of the wound in theatre.

The sensitivity pattern of the isolates did not differ much from Wayi's results three years ago. All Staphylococcus aureus strains isolated were susceptible to ceftriaxone. This implies that there was no development of resistance to ceftriaxone after its prophylactic use. Sensitivity to tetracycline remained more or less the same that is 81.1% compared to 85.7% found by Wayi three years ago. Resistance to penicillins is still high as shown by a sensitivity of staphylococci to ampicillin of only 54.5% and to penicillin G 0%. It is encouraging that the sensitivity of Staphylococci to cloxacillin in this study was 100%. Cloxacillin is a fairly affordable drug and in cases of single bacterial infection with staphylococci it can be used with great hope of success. It is unfortunate that Wayi did not report this in the previous study so no comparison can be made. Ciprofloxacin is an alternative drug to ceftriaxone in this study to which all isolated organisms were sensitive.

As said earlier no resistance to ceftriaxone was observed, all isolated organisms were found to be sensitive. Therefore there was no emergence of resistance to ceftriaxone in this study when used for prophylaxis. This is probably because ceftriaxone is relatively a new drug in our area and also relatively expensive so it is difficult for endogenous organisms to become resistant with a single shot use of the antibiotic. [7]

Side effects to ceftriaxone were minimum. It was tolerated well by more than ninety percent of the study group. Observation of fever in one patient who was also found to have malaria may only be a coincidental finding. Nausea and vomiting can also be triggered by other stimuli during the operative procedure like anaesthetics, pain and other visual or olfactory stimuli.

3.7 CONCLUSION

From the results and discussion above prophylactic use of antibiotic in clean surgical procedures did not demonstrate significant reduction in rate of postoperative wound infection though there was a numerical reduction of 3.3%. This confirms that the use of prophylactic antibiotics in surgical procedures is not a substitute for proper aseptic and surgical techniques. As regards postoperative use of antibiotics antimicrobial prophylaxis significantly reduced the need for use of postoperative antibiotics. However most antibiotics in the control group were prescribed on an empirical basis. The predominant isolate was Staphylococcus aureus which is in keeping with the results elsewhere and the results from a study by Wayi. Ceftriaxone in this study was well tolerated with few side effects and there was no emergence of resistant strains with its use.

3.8 RECOMMENDATIONS

1. Prophylactic antibiotics are an integral part in the prevention of postoperative wound infection. However in the case of clean wounds its role is yet to be defined, more extensive studies need to be done to validate the benefits. From this study the use of prophylactic antibiotics in clean category of operative procedures cannot be justified except for the defined groups with medical conditions placing them at a high risk of postoperative wound infection. Committees on prudent use of antibiotics should be formed or activated to check injudicious use of antibiotics and prevent development of antimicrobial resistance.

2. Preoperative hospital stay if prolonged is one factor that is related to the acquisition of hospital organisms including multiresistant isolates. In this study patients stayed long preoperatively for one reason or another and this was associated with a high prevalence of wound infection. It is time to look into the factors that lead to prolongation of preoperative hospital stay and avoid them. Care of the patients referred from upcountry should be improved. Observation should be made that they are treated and discharged early.

3. Strictly abiding to theatre technique is one important factor in controlling postoperative wound infection. This is an indispensable aspect of surgery. In this study it is possible that through the awareness of the high rate of wound infection observed from a study by Wayi, surgeons and the theatre staff were more strict in abiding to the technique which led to the reduction in wound infection rate even among the controls. It is therefore emphasized here that abiding to the technique is the first line in the prevention of postoperative wound infection. For this reason there is a need for continuing education to theatre staff and young surgeons and their assistants on theatre and surgical techniques. Surveillance on the implementation of the techniques is also important.

4. An effective and a well functioning infection control unit is an essential and integral part of the running of any health care service and reflect a well-governed hospital. Wayi suggested the formation of one such unit and I further emphasize its importance here. It is only this unit that will integrate the outcomes of various studies done around the subject of wound infection and use them for improvement of patient's care and prevention of wound infection. The unit must be interdisciplinary and

interdepartmental. It should affect all personnel from the medical director and chief executive to the domestic and ancillary staff. A policy of continuous re-education and watchfulness should improve infection control in the health care setting.

3.9 LIMITATIONS

1. Fund allocated for the study was a limiting factor in that it did not suffice to make available all the materials intended for the study and to hire personnel to facilitate the carrying out of the study. At times materials were acquired late resulting in for example inconsistence of choice and use of sensitivity discs. It also interfered to some extent with the randomization procedure when drugs were not available. It also limited the size of the population that could be sampled.

2. Drop out from follow up was also a limiting factor in this study.

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