Assessment of Antibiotics Use as surgical Prophylaxis and Post-Operative Treatment at Saint Paul's Hospital Millennium Medical College; Cross-sectional Study

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This is to certify that the thesis prepared by Kerebih Alamrew, entitled: "*Assessment of Antibiotics Use as surgical Prophylaxis and Post-Operative Treatment at Saint Paul's Hospital Millennium Medical College"*, submitted in partial fulfillment of the requirements for the degree of Masters of Pharmacy in Pharmacy Practice (M. Pharm), complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Abstract

Assessment of Antibiotics Use as surgical Prophylaxis and Post-Operative Treatment at Saint Paul's Hospital Millennium Medical College (SPHMMC).

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Surgical site infectionsare the most common types hospital acquired infections. Use of antibiotic, when sound and in the appropriate principle of prophylaxis can result in reduced postoperative infections and mortality. The main objective this work was to assess antibiotics use for prophylaxis and post-operative Treatment of surgical patients in surgical wards of SPHMMC. prospective cross-sectional study was conducted by reviewing records of 413 patients who admitted at the surgery wards of SPHMMC between June 10 and September 10, 2016. Descriptive statistics and binary logistic regression were used for statistical analysis. Of the 413 patients studied,231(55.9%) weremales withmean age of patients 38.1±15.1years (range 13 to 82 years). Most surgical patients 187(54.8%) were given Ceftriaxone as prophylaxis and treatment. Among those who received antimicrobial prophylaxis the time of administration was not recorded in 22 (9%) of the patient.Selection was the most deviated parameter from surgical antibiotic prophylaxis 205(91.5%) followed by duration 99(44.2%), and indication 22(5.3%).Surgical site infection rate was 11.1%. Type of admission (p=0.003) and status surgical antibiotic prophylaxis of use(p=0.045) at $p< 0.05$ (95% confidence interval) were the risk factors associated with surgical site infection. among patients undergoing surgical procedure at the hospital during the study period. In conclusion the study indicates that ceftriaxone was the most used antibiotics. Use of broader spectrum antibiotics for extended period was common.Areas of non-concordance to the guideline require further investigation.

Key words: surgical site infection, Surgery, Antibiotic use, appropriateness, Saint Paul's Millennium Medical College, Ethiopia.

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List of Abbreviations

ASHP	American Society of Hospital Pharmacists
CDC	US Centers for Disease Control and Prevention
E. coli	Escherichia coli
ICU	Intensive care unit
NNIS	National Nosocomial Infection Surveillance
PO	per os
SAP	Surgical antibiotic prophylaxis
SIGN	Scottish Intercollegiate Guidelines Network
SPHMMC	Saint Paul's Hospital Millennium Medical College
SSIs	Surgical Site Infections
WHO	World health organization

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1. INTRODUCTION

1.1. Background

Despite the advances in the operative techniques and a better understanding on the pathogenesis of the surgical wound infections, post-operative wound infections continue to be a major challenge for surgical society (Akalin, 2002). Aseptic techniques alone do not avoid surgical site infectious (SSIs). To overcome this problem antibiotics treatment begun prior to contamination is required which is an important adjunct to control bacterial growth and significantly lower the incidence of SSIs (Tan *et al*.,2006). It is now estimated that as many as 60% of SSIs are preventable, mostly related to the use of recommended evidence-based practices such as the timing, selection, and duration of preoperative prophylactic antibiotics (Meeks *et al.*, 2011).

Infection is defined an invasion of tissue by pathogenic microorganisms. Through their history, hospitals have coexisted with nosocomial infection(NI) which has been defined as the infection that was not presented neither was incubated at moment of patient admission at the hospital. surgical site infections (SSIs) are the most common types of NI (Gottrup *et al.*,2005).

A surgical site infection (SSI) is an infection that develops within 30 days after an operation or within one year if an implant was placed and the infection appears to be related to the surgery. Post-operative infections are the most common health care associated infection in surgical patients (patel *et al.*,2012). SSI is the second most common hospital associated infections accounting 14-16% of all hospitalized patients and 38% among that of surgical patients (Cannon *et al.*,2012). In developing countries, especially in sub-Saharan Africa this figure is twice or three times higher than developed countries (Mengesha *et al.*, 2014).

SSIs remain among the main causes of post-operative morbidity, prolonging hospitalization and increasing the cost of medical treatment in surgical units. It is found that patients who develop SSI are up to 60% more likely to spend time in the intensive care unit, five times more likely to be readmitted to hospital and twice as likely to die as compared to patients without an SSI (Perencevich *et al.*,2003).

Antibiotics have two uses in surgery, to treat established infections and to prevent postoperative infection (Mohammad e*t al*., 2014). Nearly 30-50% of antimicrobials used in hospitals are prescribed for surgical prophylaxis and 30–90% of this prophylaxis is inappropriate. Antimicrobials are often used in wrong timing, for too long and with too broad spectrum of antimicrobial activity (Munckhof, 2008).

Excessive or improper use of antibiotics has brought about growing antibacterial resistance in microorganisms, treatment failures, increasingly frequent side effects, a rise in morbidity and mortality, and a climb in the cost of treatment (Yavuz*et al.*,2015). Surgical antibiotic prophylaxis (SAP) is administration of short course of antimicrobial agent prior to surgery to prevent SSI. Patients undergoing procedures associated with high infection rates, those involving implantation of prosthetic material, and those in which the consequences of infection are serious should receive perioperative antibiotics (Antibiotic prophylaxis for surgery, 2004).

SAP is not a method of tissue sterilization, but a precisely timed measure to decrease the microbial load of intraoperative contamination to a level that does not overwhelm the host immune defense. It also does not refer SSIs following postoperative contamination (WHO, 2008).

Treatment, rather than prophylaxis, is indicated for procedures associated with obvious preexisting infection (i.e. abscess, pus, or necrotic tissue). Cephalosporin (such as cefazolin) are appropriate first line agents for most surgical procedures, targeting the most likely organisms while avoiding broad-spectrum antimicrobial therapy that may lead to the development of antimicrobial resistance. The duration of prophylaxis should not exceed 24hours (Antibiotic prophylaxis for surgery,2004).

In spite of extensive knowledge about the effectiveness of antibiotic prophylaxis, its administration is often inappropriate. The proper use of antibiotic prophylaxis in surgical procedures requires the consideration of several factors. Effectiveness depends on the correct application of the following items: appropriate antibiotic choice, timing of the initial administration, the number of dosages administered during surgery, and post-operative drug use. Incorrect execution of any of these factors can influence the rate at which infections at the surgical site occur. Therefore, it is very important to be aware of what is being done in surgical prophylaxis in order to establish improvement strategies (Steinberg *et al.*, 2009).

That's why drug therapy should be scrutinized at international, national, regional and institutional level and efforts are required to evolve a consensus protocol and policy for the same. In Saint Paul's Hospital MillenniumMedical College(SPHMMC), due to lack Information about the appropriateness of regimens for SAP to standard guidelines and guideline for antimicrobial prophylaxis in surgery, there is a need to generate baseline data on the pattern of use of prophylactic antimicrobials and rate of surgical site infection.

Therefore, the aim of this study was designed toasses antibiotic use pattern and toevaluate appropriateness of SAPanddetermine the rateofsurgical site infectioninsurgically operated patient's cases at SPHMMC, Addis Ababa, Ethiopia.

1.2. Statement of the Problem

Even though,there aremany improvements in surgical techniques and methods that are designed to reduce post-surgical infections and availability of prophylactic antibiotics, the prevalence of morbidity and mortality related to surgical infections still remains to be the major hospital acquired infection throughout the world (Awad, 2012). SSI is a worldwide problem that has far reaching implications on patient morbidity and mortality as well as significant financial implications. As approximately 30% of patients undergoing surgery will develop post-operative surgical site infections. Worldwide it has an incidence of between 2- 20% (Waqar *et al.,* 2010).

In the United States of America approximately one million patients develop SSI each year, increasing duration and cost of hospital stay. SSI in United States of America has been reported to be 2.6 %, while a report from an African country Tanzania shows this figure to be 19.4 % (Arias *et al.,* 2008).

In Ethiopia studies made on the practice SAP and SSI is scare but existing studies show that inappropriate SAP and high incidence of SSI. For example, the prevalence of post-operative surgical site infection was reported as 44.1% of the patients with nosocomial infection from Mekelle, Ethiopia which is markedly higher (Tesfahunegn *et al.,* 2009). Similar study in Jimma at gynecology and obstetrics wards showed that 35% patients developed post-operative surgical wound infections (Amare *et al.,* 2011).

Increasing health-care costs have led hospitals to review procedures to adjust their budgets in world wide. At the same time, concerns about antimicrobial resistance have pressured infection control specialists to decrease antimicrobial usage. Multidisciplinary development of evidence-based prophylaxis guidelines incorporating local microbiology and resistance patterns can improve antimicrobial use (Parviz, *et al.,* 2013).

An estimated 40-60% of SSI is preventable with use of prophylactic antibiotics (Geroulanos *et al.,* 2001). Appropriately administered antibiotic prophylaxis before surgery plays an important role in reducing the incidence of postoperative infections, duration of stay in hospital, cost of treatment, mortality, and helps the patient go back to the normal life more quickly (Waqar *et al.,* 2010). However, previous reports indicated that timing of administration, selection of the antibiotic, and duration of prophylaxis was inappropriate in the great majorities of cases. Most commonly, the antibiotic is either given at the wrong time or continued for too long (Kasteren *et al.,* 2013). Unnecessary use of antibiotics and prolonged antibiotic prophylaxis (more than 48 hours) are significantly associated with increased risk of antimicrobial resistant microorganisms (Mohammad *et al.,*2014). Once antimicrobial resistance develops, it can have a significant impact on the patients' morbidity and mortality, thereby increasing the health care costs (Talbo, 2010).

On the other hand, use of antimicrobials in the treatment of surgical patients mirrors the larger problems associated with use of antibiotics for hospitalized patients. The important difference is that prophylaxis, rather than treatment of infection is more common (John and biruk, 2001).

Since errors in the antimicrobial prophylaxis for surgical patients remain one of the most frequent types of medication errors due to the unavailability of adequate information and absence of facility based standard treatment guidelines for surgical antimicrobial prophylaxis in the hospital. Therefore, there should be baseline data on the pattern of the use of prophylactic antimicrobials before recommending any desired modifications (Rehanet *et al.*, 2010).

But still there is no study at SPHMMC on the rational of prophylactic and post-operative treatment antimicrobial use in surgery. Therefore, this study was used to find the pattern antibiotics usage in surgery, rationality of SAPby evaluating time of the first dose, antibiotic selection, the intraoperative redosing and the total duration after surgery, in order to detect any inappropriateness, so that corrective measures could be suggested. This study was also address the development of surgical site infection.

1.3. Literature Review

1.3.1. Use of Antibiotics in Surgery

Antibiotics are one of the pillars of modern medical care and play a major role both in the prophylaxis and treatment of infectious diseases. The issues of their availability, selection, and proper use are of critical importance to the global community (Seikh, 2012). However, antibiotic misuse is greater in the developing countries through their purchase (without prescription) in local pharmacies and drug stores, and through inappropriate prescribing habits and an over-zealous desire to treat every infection (Ibeawuchi & Mbata, 2002).

It is important to recognize the difference between therapeutic, prophylactic and empiric therapy. Therapeutic antimicrobial therapy prescribed to clear infection by an organism or to clear an organism that is colonizing a patient but is not causing infection. Prophylactic antibiotic should cover the most likely contaminating organisms and be present in the tissues when the initial incision is made and must be given 30-60 minutes before incision (Zeenat, 2012). Empiric therapy is the continued use of antibiotics after the operative procedure based upon the intraoperative findings (SIGN, 2008).

Prophylactic use of antibiotics in surgery was introduced first in 1957 by Miles and in 1961 by Burke. It is currently an essential component of the standard of care in virtually all surgical procedures and has resulted in reduced post-operative infections (Yogesh *et al.*, 2013). But its use should be limited to specific, well-accepted indications to avoid excess cost, toxicity, and antimicrobial resistance. The intent of prophylactic antimicrobials is to decrease the number of microorganisms to a level that the host defense mechanisms can effectively eradicate (Chavda *et al.*, 2014). Ideally, an antimicrobial agent for surgical prophylaxis should prevent SSI, SSI-related morbidity and mortality, reduce the duration and cost of health care, produce no adverse effects, and have no adverse consequences for the microbial flora of the patient. To achieve these goals, an antimicrobial agent should be given in an appropriate dosage and at a time that ensures adequate serum and tissue concentrations during the period of potential contamination, safe, and administered for the shortest effective period to minimize adverse effects, the development of resistance, and costs ((SIGN, 2008).

Hospital-based prospective study conducted on surgical patients has been admitted in Gondar College of Medical Sciences Hospital Ethiopia for whom major surgical procedures were done. The case notes of 236 admitted surgical patients were surveyed prospectively during a three-month period. Out of 236 admitted surgical patients, 167(70.8%) were prescribed antibiotics whereas the remaining 69(29.2%) received no antibiotics. Antibiotics were prescribed for prophylaxis in 75 patients and for treatment in 92 patients (Abula &Kedir, 2004).

Cross-sectional study was conducted at referral Medical-Educational Centers from northwest of Iran in a 24 months' period since Feb 2009 to Feb 2011. A total number of 409 antibiotics were prescribed. The most frequently prescribed classes of antibiotics were Cefazolin (90%), Vancomycin (1.8%), Ceftriaxone (8.5%), Metronidazole (4.5%), Erythromycin (1%) and gentamicin (18.5%). Six different combinations of antimicrobial drugs were used. The use of antimicrobials in all the cases was empirical based on operating surgeon's clinical experience

(Parviz *et al.*,2013). Other prospective, observational study was performed on patients undergoing surgery, in a tertiary care teaching hospital in India from June 2011 to June 2012, Most common antimicrobial prescribed postoperatively was Ceftriaxone in 208 (68.20%) patients and Amikacin in 184 (60.33%) patients. Most of the patients 113 (37.05%) received Ceftriaxone and Amikacin combination (Vimesh *et al.,* 2013).

A descriptive retrospective study was done amongst the patients admitted in the surgical postoperative ward of UP RIMS & R, Saifai, and Etawah in India during the months between January 2015 to March 2015, on total 251 patients were included. The most frequently prescribed classes of antibiotics were cephalosporin (35%) followed by Aminoglycosides (24%) and penicillin (14%) but least number of antibiotic was amongst Nitroimidazoles group (5%) (Chaudhary *et al.,* 2015).258 patients' medical records of general surgical cases are randomly selected and retrospectively reviewed over an 8-month period in a tertiary care teaching hospital of India between May 2011 and January 2012. Oral antimicrobials were prescribed on discharge, to 247(95.7%) patients. Cefixime was mainly prescribed, followed by metronidazole, levofloxacin, cefpodoxime and amoxicillin. In addition, topical antimicrobials were also prescribed in 134(52%) patients. Fusidic acid was most commonly used in 93(36%) cases, followed by povidone iodine alone in 41(16%) cases and as a combination with topical metronidazole in 21(8%) cases (Salman *et al.,* 2008).

In Lady Harding, Medical College and Smt.S. K. Hospital, New Delhi, prospective observational study was conducted. That shows prophylactic antimicrobials were indicated in 67% of all cases but were administered to 86 % patients, being inappropriate in 19% (Rehan *et al.,*2010). Other Survey was conducted between July 2012 and January 2013 in 21 surgical wards Turin, Italy,the study found an unjustified continuation of antimicrobial prophylaxis in 17.1 % of the 257 cases, an unjustified re-start of antimicrobial therapy in 9.7 % and a re-dosing omission in 7.8 % (Marco *et al.,* 2015). A study carried out using cohort design method on 605 patients the Marilia Medical School Hospital in Brazil, shows that, antibiotics were prescribed for 55.4% of the patients and combinations were used in 43%. Prophylaxis was indicated in 73.7% of the surgeries. It was not administered in 1.1% of the surgeries for which it was indicated, and it was given unnecessarily in 48 surgeries (Laura & Lucieni, 2004). Similar descriptive study was done on 8586 patients who received prophylactic antibiotics before surgery from April 2011 to March 2012, in Iran at Razi Hospital. Of the total 8586 patients who took antibiotics for preventive purposes, 4815 (56%) required antimicrobial prophylaxis, and 3771 (44%) patients did not. Of the 4815 patients who received prophylaxis, 86.9% received it appropriately, 13.1% received it inappropriately; 8.2% received inappropriate dosage, and 9.5% received antibiotic longer than 24 hours. Totally, approximately 45% of antibiotics were prescribed without indication and were unnecessary. Approximately 13% (8.2% to 13%) of the indicated antibiotic prophylaxis was inappropriate at least in antibiotic regimen, dose, or duration of antibiotic administration (Seyed *et al.,* 2014).

prospective cohort study was performed to collect baseline data concerning surgical site infections (SSIs) and antimicrobial prophylaxis in a remote sub-Saharan district hospital in District Hospital in Ifakara, southern Tanzania. It demonstrated that 88% of the patients received

prophylaxis after incision, and only 5% within the 30-min period before incision. The antibiotics given most frequently were chloramphenicol (60%), aminopenicillins (23%) and benzyl penicillin (15%) (Falagas *et al.,* 2006). Similar study was performed in patients undergoing abdominal aortic aneurysm repair, hip replacement and largebowel resection in 44 hospitals in New York State, Silver and colleagues at 2001 demonstrated that 14% did not receive antimicrobial prophylaxis, and only 63% of those who received antimicrobials had them administered in the 2 hours before incision (Dale *et al.,* 2005).

Study carried out in thirteen Dutch hospitals Between January 2000 and January 2001 on 1763 surgical procedures. Antibiotic choice, duration, dose, dosing interval and timing of the first dose were concordant with the hospital guideline in 92%, 82%, 89%, 43% and 50%, respectively. Overall adherence to all aspects of the guideline, however, was achieved in only 28%. The most important barriers to local guideline adherence were lack of awareness due to ineffective distribution of the most recent version of the guidelines, lack of agreement by surgeons with the local hospital guidelines, and environmental factors, such as organizational constraints in the surgical suite and in the ward (Kasterenet *et al.,* 2003).

1.3.2. Development of Surgical Site Infection (SSI)

SSI Follow interference with the skin barrier and are associated with the intensity of bacterial contamination of the wound at surgery or later in wards during wound care. The magnitude of SSI varies considerably in different parts of the world (Naras *et al.,*2012).

The Centers for Disease Control and Prevention (CDC) term for infections associated with surgical procedures was changed from surgical wound. The criteria used to define surgical site infections have been standardized and described three different anatomic levels of infection: superficial incisional surgical site infection, deep incisional surgical site infection and organ/space surgical site infection (Doherty &Way, 2006).

The bacteria may be transferred by contact from surgeons or nurses' hands, the bacterial could be airborne during surgery, and or the patient may come in contact with bacteria after surgery (About Surgical Care Improvement Project Information, 2008).

SSI is considered when there is at least one of the following: redness, edema, tenderness, gaping, abscess or purulent discharge, occurrence of fever (> 38°C), or positive culture of fluid or tissue from the surgical site within 30 days of the operation (Ai, 2014).

Most surgical wound infections are limited to the skin but can spread occasionally to deeper tissues. Infections are more likely to occur after surgery on parts of the body that harbor lots of germs. It may affect closed wounds or wounds left open to heal; superficial or deep tissues; and in severe cases, the internal organs. A surgical wound infection can develop at any time from two to three days after surgery until the wound has healed (usually two to three weeks after the operation). Very occasionally, an infection can occur several months after an operation (Zeenat, 2012).

Surgical procedures can be broadly categorized as either elective which is planned or emergency that which is unplanned.

Elective surgery aims to be performed when the patient is in optimal health but before the surgery affects the quality and threatens their life: e.g. an inguinal hernia can become life threatening if the bowel becomes obstructed. Clinicians decide if a planned procedure is 'urgent' or can be arranged at a time convenient for the surgeon and patient. Emergency surgery may be as a result of trauma or an accident, gastrointestinal obstruction, or from perforated viscera. The injury may be immediately life threatening, and therefore the procedure will be carried out within 1–2 hours from admission (Phillips, 2004& Smith, 2000).

The likelihood of infection varies by type of surgical incision site and the physical status of the patient. The wound classification system designed by the CDC classifies the increased risk and extent of bacterial contamination during the surgical procedure (Seyed *et al.,* 2014). A wound infection is described as minor if there is discharge without cellulitis or deep tissue destruction, and major if the discharge of pus is associated with tissue breakdown. CDC provides guidelines and tools to the healthcare community to stop surgical site infections and resources to help the public understanding these infections and take measures to safeguard their own health when possible (CDC, 2012).

According to the degree of contamination wounds may be classified as clean, potentially contaminated, contaminated, and dirty. The incidence of infection, morbidity and mortality increases from clean to dirty. The accurate identification of risk factors is essential to develop strategies to prevent these potentially devastating infections (Suzanne, 2007).

Prophylaxis is uniformly recommended for all clean-contaminated and contaminated and procedures. It is considered optional for most clean procedures, although it may be indicated for certain patients and clean procedures that fulfill specific risk criteria (CDC, 2012).

A retrospective chart review study done at Monmouth Medical Center, New Jersey, USA from January 2003 to December 2007 identified 312 surgical patients with SSI, with incidence of 0.56% SSIs per year among all surgical services. The most common procedures among all surgical services was general surgery (Kassavin *et al.,* 2011).Similar observational prospective study had been conducted at Surgical Units I and II of the Rajiv Gandhi Institute of Medical Sciences (RIMS), a Government Medical College cum Teaching Hospital in a rural setup in Srikakulam, Andhra Pradesh. The Incidence of surgical site infections (SSI) in this Study was 9.81%; 17 (5.94%) cases in the clean surgical group, 9(9.28%) cases in the clean-contaminated group, 6(22.22%) cases in the contaminated group and 10(55.56%) cases in the dirty group developed infections (Egide, 2007). But there are only a few reports from the developing world SSI especially from Africa. In Khartoum Teaching Hospital crosses sectional study was carried on the patients who were admitted from March 1st to 31st October 2010. Out of the total patients included in the study 10.9% had wound infection. The rate of post-operative wound infection was 8.9% and 15.4% for clean and clean-contaminated procedures respectively. The signs of wound infections were detected during hospital stay for 8.5% patients. Wound infection was recognized during the post-discharge period for 91.5% patients and 59.3% of them wound infection was confirmed by the surgical units that performed the procedures when they returned back to the hospital and 22 (40.7%) reported the signs of infection through telephone contacts (Abubaker *et al.,* 2013).

Another investigation was carried by using prospective observational method on total of 162 patients who presented to the Medicine surgical inpatient ward in Basaweshwara Medical College and Research Centre, Chitrad in India Hospital during the period from February 2014 to April 2014. Among them, Surgical Site Infection (SSIs) was found in 37 (22.8%) patients and patients without SSIs are 125 (77.2%). The patients with age group 25-60 years were 104 (64.2%) in which SSIs are more (23). According to the study male patients underwent more surgeries 107 (66%)) in which 21 (56.8%) are with SSIs. The rate of SSI is high with the patients who have not received any prophylactic antibiotics 22 (59.5%) (Dinesh *et al.,* 2015)

In Ethiopia, although a high incidence of wound infection is suspected, the magnitude of the problem is not known. But a previous study (Taye *et al.,* 2005), Showed that surgical infection to be the commonest nosocomial infection around clean 8%, clean-contaminated14.8%, contaminated 22%, and dirty 44.1%. There has been a report from North West Ethiopia of high wound infection rate; 38.7% among 129 SSI with clean infection rate of 22.2% (Kotisso, 1998).

In a retrospective observational study done in Raja Rajesh Wari medical college hospital, Pakistan General Surgery & Obstetrics and Gynecology department, tertiary care center reported that the overall surgical wound infection rate for 1000 abdominal surgeries was 13.7%. Infection rate is 3.9% in clean wounds where as it was 56.7% in dirty wounds. Thus, there was clear correlation between the wound infection rate and the contamination of the wound. The infection rate was more with emergency surgery [87/345(25.2%)] when compared to elective surgery [50/655(7.6%)] which was statistically significant (P<0.001). The surgical wound infection rate increased as the administration of prophylaxis longer than two hours prior to surgery or post-operatively was confirmed to be associated with a higher SSI rate (Satyanarayana *et al.,* 2011).

In another a prospective cohort study of prediction of SSI which wasdone in San- Vicente, DePaul Hospital, trauma center in Medellin, Colombia inpatients who underwent an exploratory laparotomy for trauma. In the studyperiod, 614 exploratory laparotomies were performed.Of these, 85(13.8%) patientsexperienced deep incisional and organ infection SSIs. Sex, age, the mechanism of injury, the time between trauma and surgery not associated with the development of SSIs (all p>0.05) (Carlos *et al.*,2011).

Orthopedic unit of the Jakarta Hospital Indonesia, cross sectional study was conducted in the, between Januarys to December 2012 with sample size of 163. The antibiotic was administered within 30 min before the skin incision in only 91 (55.8%) of the 163 patients. Total of 8 (4.9%) patients developed SSI who received antibiotic prophylaxis. The appropriateness of prescribing antibiotic prophylaxis in regard to the choice of antibiotics this study with respect to the timing of antibiotics administration, it shows that 91 (55.8%) in 163 patients received prophylactic antibiotics appropriately, and the SSI rate was 4.9% (Maksum *et al.,* 2014).

A cohort study was carried out at the Marilia Medical School Hospital Brazil 2004 and showed those who received appropriate prophylactic antibiotics had a lower rate of SSI than those who received inappropriate antibiotics [RR=0.49/95%; CI=0.25-0.90]. Patients who received prophylactic antibiotics correctly in the post-operative period had a lower risk of SSI than those who did not (RR=0.21/95%; CI=0.70-0.63) (Sae &Chongsomchai, 2006).

A study which was done at Imam Khomeini hospital Iran showed that the incidence SSI is 17.4% and the majority of the infected wounds were dirty. The increased operation time, increased bed stays, electivity of the operation, type of incision, the administration of prophylactic antibiotic, type of operation, background disease, and the increased time lapse between shaving and operation all significantly associated with SSI ($p<0.001$) (Ra*zavic et al.*,2005). In another prospective descriptive study in Jimma University, Obstetric ward showed that the overall SSIrate was 11.4%. Of those who had surgical site infections, 64.8% had clean-contaminated wound and 35.2% had contaminated /dirty wounds. Wound class at time of surgery has a statistically significant association with Surgical Site infections ($p <0.001$) (Demisew &Fitsum, 2011).

2. OBJECTIVE

2.1. General Objective

Assessment of Antibiotics Use as surgical Prophylaxis and Post-Operative Treatment at Saint Paul's Hospital Millennium Medical College among surgically operated patients from 10 Juneto September 10, 2016.

2.2. Specific Objectives

- To assess the pattern of antibiotic usage in surgical patients
- To evaluate prophylactic antibiotics practices in surgical patients according to clinical practice guideline for antimicrobial prophylaxis in surgery, 2013(commonly adopted guidelines by the department).
- To document the timing of prophylactic antibiotics in surgical patients
- To determine duration of prophylactic antibiotics, post operatively among surgical patients.
- To determine the rate of SSIdevelopment in post-operative patients during hospital stay.

3. METHODS

3.1. Study Setting and Period

This study was conducted at the surgery wards of SPHMMC located in Addis Ababa, capital city of Ethiopia and Africa Union.SPHMMC is one of the biggest tertiary referral government hospitals.The hospital was a total of about 654 beds. Through its different ambulatory clinics and wads, it provides ambulatory and in-hospital care for patients coming from different corners of the country. Large number of patients have been seen each year at both outpatient and inpatient level. For instance, 287,875 patients were seen in 2016. Physicians and other professionals have a well-established role in the hospital with the ultimate patient care but full-time pharmacists in some wards resumed providing service since September 2013.

In Surgery department there were 15 surgeons, 45 nurses and various group of surgery residents. It provides surgery service for 12654 patients per year. The study is conducted in adult surgery wards, from 10 June to September 10, 2016 for 3 consecutive months.

3.2. Study Design

Hospital-based prospective cross-sectional study was employed to conduct the study. Quantitative methods were used by simple random sampling technique in the data collection. Data were collected from the patient chart by reviewing the patient's medical record of surgical patients. Data abstraction format was developed to collect information on the practice of SAP, postoperative treatment, and development of SSI in patient that had surgery in the study period.

3.3. Source and Study Population

All patients who were admitted for surgical procedure at SPHMMC surgical wards during study period. On the other hand, the study populations were surgical patients who had been admitted to the adult general, orthopedic, Gyn&obs, urology and neurology surgerywards at SPHMMC during the study period.

3.4. Inclusion Criteria and Exclusion Criteria

Inclusion Criteria: Adult patient that had been admitted and undergoing urologic surgery, neurologic surgery, gynecological and obstetrics surgery, general surgery and orthopedic surgery.

Exclusion Criteria: -Those patients below 13 years of age, lost to be followed less than 24 hours after surgery, Patients who were operated in another hospital and later referred to SMPHMMC, and death cases within three days' post-surgery. (The median day without SSI in African countries was reported to be 7, ranging from 3-63 days (Kathryn et al., 2014).

3.5. Sample Size Determination

The sample size is calculated by using single proportionformula (lwanga &lemeshow,1991). Assuming that expected level of patient receive antibiotic for prophylaxis and post-operative treatment to be 50%. So, sample size will determine by using 50% % proportion (since there is

no local data) with marginal error 5% and the confidence interval of 95 %(**Z=1.96).** hence the sample size was calculated to be **384.**

$$n=\frac{Z^2P(1-p)}{E^2}$$

n= required sample size
P= level of antimicrobial administration
E= margin of the error

$$n=\frac{1.96^2\times0.5\times0.5}{0.05^2} = 384.16 =\sim 384$$

With the assumption of 10% incomplete records, the number of patient to be part participated in the study has to be **422**. This number was distributed in to following surgery departments: - general surgery, urology, gynecology &obstetrics, orthopedics and neurologic surgery units based on study period patients load.

3.6. Study Variables

Dependent Variables

- appropriateness of Surgical antimicrobial prophylaxis/treatment.
- Surgical site infection development.

Independent Variables

- Sociodemographic characteristics of patient
- Duration of postoperative prophylaxis
- Class of wound
- Timing of antibiotic prophylaxis
- Selection antibiotics
- Type of patient admission.

3.7. Data Collection and Management

3.7.1. Data Collectors

Data was collected by clinical pharmacists. Four clinical pharmacists from SPHMMC have been recruited, oriented and trained about how to collect data using data abstraction format for one day. The completeness of the data collected was checked by the principal investigator in order to maintain consistency and the same procedure followed for data collection.

3.7.2. Data Collection

Data was collected using a structured data collection format which contains of the age, sex, types of surgery, development of SSIs, class of SSI, surgical ward in which the patient was admitted, prophylactic and post-operative treatment antimicrobial agent prescribed, rout and time of antimicrobial administration, intraoperative redosing and base of antimicrobial prescription for post-operative treatment.

3.7.3. Data Quality Assurance

To maximize quality of the data, training of the data collectors on how to fill the data collection instruments and extract the necessary information was conducted. Besides, the investigator did adequate supervision and monitoring.The data collectionformat was pretested on 21 patients (5% of the sample size)outside of the study period. In each ward, the principal investigator was the supervisor leading the team of data collectors and fully responsible for the whole quality of data.

3.7.4 Data Analysis

The collected data was checked and cleaned for any deficit prior to data entry. Errors in data entry were also checked for accuracy using double data entry technique. Epi info 7 was used for data entry. The data was then exported to SPSS for windows version 20.0 for additional and advanced data analysis. Descriptive analyses are used to describe patients' demographic data, types of surgery, development of SSIs, class of SSI, surgical ward in which the patient was admitted, prophylactic and post-operative treatment antimicrobial agent prescribed, rout and time of antimicrobial administration, intraoperative redosing, duration of operation, and base of antimicrobial prescription for post-operative treatment. Rate of SSI was calculated. Bivariate analyses were carried out toexamine the relationship between the outcome variable and predictors; variables with value $p<0.2$ was retained for subsequent multivariate analyses using multiple logistic egressions. $P<0.05$ was considered as statistical significant.

3.8. Ethical Consideration

Ethical approval for the protocol was obtained from the Ethical review board of School of Pharmacy, College of Health Sciences andSPHMMC research review board before data collection. Concerned bodies at all levels, including the hospital clinical director and department heads had been communicated and approval was granted.Privacy and Confidentiality was guaranteed by storing data in a safe place, by excluding identifiers (Patients' files were coded and name was not recorded) and only the researcher or data collector had access to the data.

3.9. Operational Definitions.

Surgical site infection (SSI): Infections in the area of operational wound within 30 days of operation, confirmed by clinical examination were regarded as SSI.Clinically, accompanied by erythema, induration and local tenderness or presence of purulent discharge at the wound site.

Wound: is defined by the Centers for Disease Control (CDC) as an interruption or break in the continuity of the external surface of the body or the surface of an internal organ caused by surgical or other forms of injury or trauma.

clean wound: An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow non-penetrating (blunt) trauma should be included in this category if they meet the criteria.

Clean contaminated wound: an operative wound in which the respiratory, alimentary, genital or urinary tracts are entered under controlled condition and without contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in sterility technique is encountered.

Contaminated wound: Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g. open cardiac massage) gross spillage from the gastrointestinal tract and incision in which acute nun purulent inflammation is encountered are included in this category.

Dirty or infected wound: Old traumatic wounds with retained devitalized tissue and those that involved existing clinical infection or perforated viscera. This definition suggests that the organisms causing post-operative infection were present in the operating field before the operation.

Prophylactic antibiotics: Refers to a very brief course of antimicrobial agent initiated just before an operation begins with an attempt to sterilize the tissue, but a critically timed adjunct used to reduce the microbial burden on of intra-operative contamination to a level that cannot overwhelm host defense.

Adult patient

In this study adults' patients are those patients above the age of 13 years.

4. RESULTS

4.1 General Description and Demographical Data

During the study period 524 elective and emergency operation were done andonly 413 of the patients were full the criteria. The elimination criteria were incompleteness of the patient's charts. operations were viewed on practices of antibiotics usageand on development of SSI prospectively.

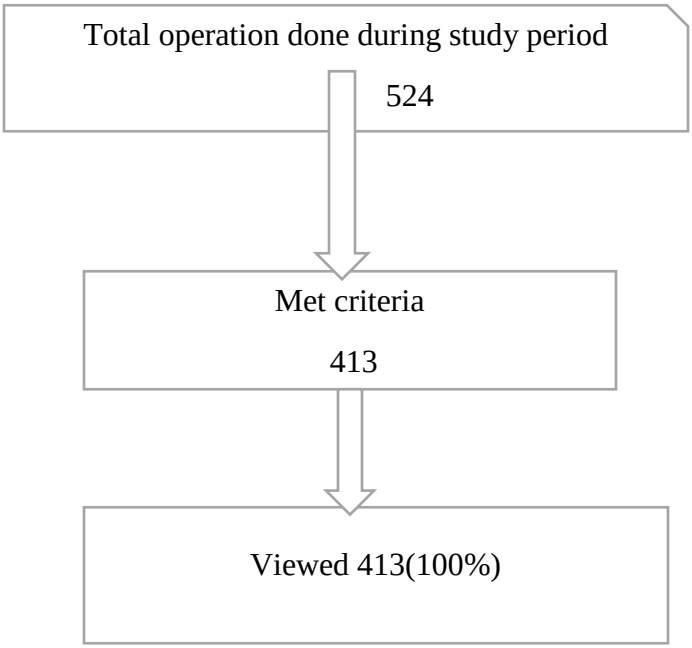

Figure 1: Flow chart of study population sampling

Age of study population ranges from 13 years to 82 years with mean and standard deviation of 38.1±15.1. Male were the majority with a ratio of (55.9:44.1). Among all type operation done, there were 231(55.9%) for male patients and 182(44.1%) for female patients. Proportionally more patients were between twenty and thirty-nine years old at 241(58. 4%).Of the total 413 surgical operations, 281(68%) of the surgical operations were elective surgeries whereas therest were emergency operations.

The duration of operation, 175 (42.4%) were less one hour, 154 (37.3%) between one and two hours, 52(12.6%) between two and three hours, 25(6.1%) between three and four hours and 7 (1.7%) were greater than four hours.

Out of admitted surgical patients, for 341(82.6%) antibiotics were prescribed whereas the remaining 72(17.4%) didn't receive antibiotics. Most of them, 303 (73.4%), were with no any comorbidity. Surgical Site Infection (SSIs) were found in 46 (11.1%) patients and patients without SSIs were 367(88.9%) **(Table 1).**

Table 1: Demographic characteristics of patients and surgical informationSPHMMC, from 10 June to September 10, 2016

		N=413	Percent
Sex	Male	231	55.9
	Female	182	44.1
Age	<20	13	3.1
	20-39	241	58.4
	40-59	106	25.7
	≥60	53	12.8
Comorbid illness	Yes	110	26.6
	No	303	73.4
Types of admission	Elective	281	68
	Emergency	132	32
Duration of surgery (hour)	<1	175	42.4
	1-2	154	37.3
	>2- 3	52	12.6
	>3-4	25	6.1
	>4	7	1.7
Antibiotics status	Yes	341	82.6
	No	72	17.4
Surgical site infection	Yes	46	11.1
	No	367	88.9

4.2. Surgical Clinics

Majority of patients,152 (36.8%) were from general surgery ward while 76 (18.4%), 64 (15.5 %) 92(22.3%) and 29(7%) participants were respectively from urology, gynecology/obstetrics, orthopedics and neurology wards. The Least common procedure was neurologic surgery **(figure 2).**

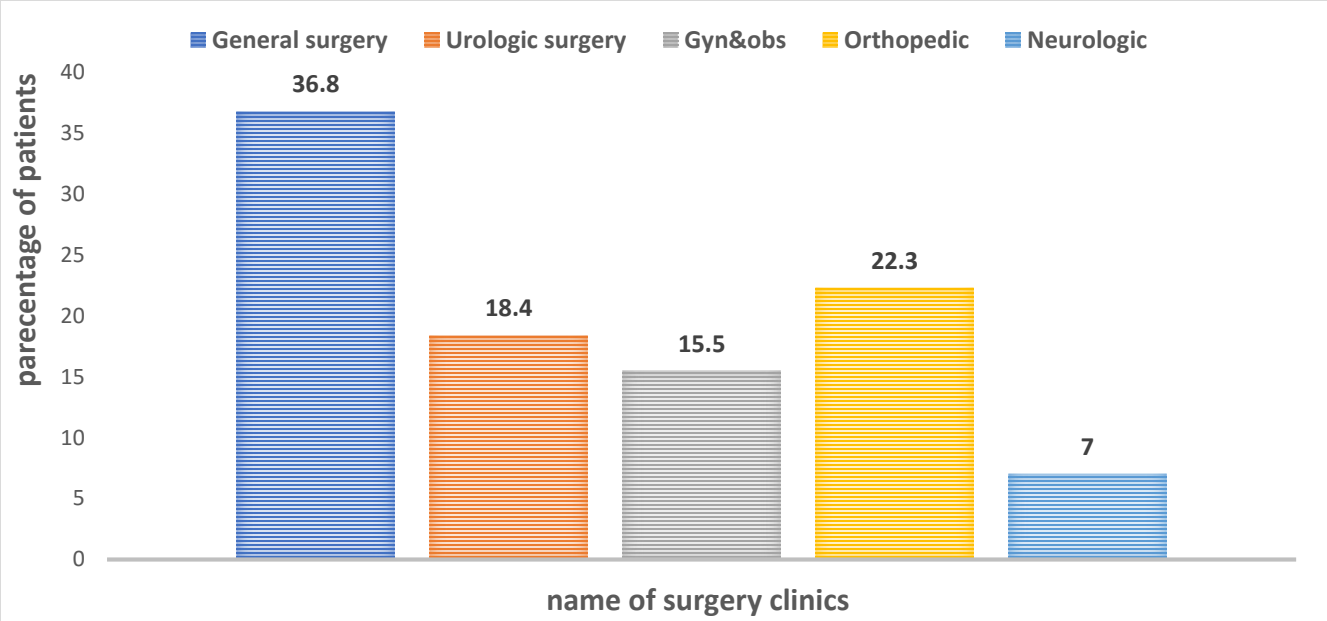

Figure 2: Distribution of patients according to surgery clinics SPHMMC, from 10 June to September10, 2016

4.3 Wound Classification

From the total of 413 patients, the distribution of wound classifications was found to be:95(23%) patients with clean, 172(41.6%) with clean-contaminated, 63(15.3%)with contaminated and 83(20.1%) with dirt wounds **(figure 3).**

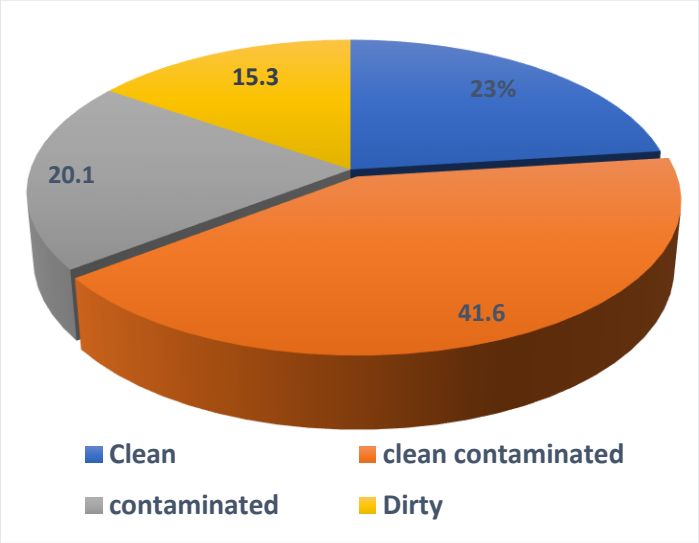

Figure 3: Surgical procedures classification according to wound class SPHMMC, from 10 June to September 10, 2016

4.4 Antibiotic Usage in Surgery

4.4.1. Reasons for Prescribing Antibiotics

Among the total patients antibiotics were prescribed, 246(72%) were prescribed for prophylaxis and 95(28%) for treatment. From the total 95(28%) patients antibiotics were prescribed for treatment, the basis for their prescription was empirical in all (**Table2).**

Table 2: Distribution of study subjects according to purpose of prescribing Antibiotics at SPHMMC, 2016

	Type of prescription	n=341	Percent
Reason forprescribing antibiotics	Prophylaxis	246	72
	Treatment	95	28
Basis of treatment prescription	Empirical	95	100
	Targeted	-	-

4.4.2. Surgical Antibiotic Prophylaxis Usage Pattern

Of the selected participants (n=413), 341 (82.6 %) received antibiotics. The most commonly used antibiotics was ceftriaxone,174(70.7%) and 13(13.7%) for prophylaxis and treatment respectively as single agent.

Ceftriaxone was also the most commonly prescribed drug for prophylaxis and treatment in combination with other antibiotics. The most frequent combination was ceftriaxone with metronidazole, vancomycin and ampicillin.

In totalofpatients antibiotics were prescribed, majority of 196(57.4%) patients were on single antibiotics, followed by 142(41.6%) on two antibiotics and 3(1%) on three antibiotics.

The most preferred route of administration for surgical antibiotic prophylaxis and treatment were parenteral route220(89.4%)and69(72.7%) thanboth IV & PO 18(7.3%)and10(10.5%) followed bythe oral routein 8(3.3%) and 16(16.8%) patients respectively (**Table 3).**

Table 3:Distribution of study subjects according to antibiotics prescribed for prophylaxis, treatment, route of administrationand types of drug combination in SPHMMC, 2016.

Name of Antibiotic(s) used (n=341)		Prophylaxis		Treatment	
		n=246	Percent	n=95	Percent
Ceftriaxone		174	70.7	13	13.7
Ceftriaxone + Metronidazole		22	9.0	47	49.5
Ceftriaxone + ampicillin		24	9.8	-	-
Vancomycin+ ceftriaxone		-	-	14	14.7
Cloxacillin		2	0.8	6	6.3
Ciprofloxacillin		16	6.5	10	10.5
Amoxicillin		4	1.6	-	-
Gentamycin+ Ceftriaxone		4	1.6	5	5.3
Number of Antibiotic(s) used (n=341)	One	174	70.7	22	23.1
	Two	72	29.3	70	73.7
	Three	-	-	3	3.2
Rout of administration(n=341)	IV	220	89.4	69	72.7
	PO	8	3.3	16	16.8
	IV+PO	18	7.3	10	10.5

4.4.3 Timing of the first Prophylactic Antibiotic Administration.

Out of 246 of patient who were given prophylactic antibiotics, the majority 124 (50.4%) received prophylactic antibiotic less than 30 minutes before surgery. The patient where preoperative antibiotics was given, time administration of 22(9%) patient notdocumented (**Figure 4**).

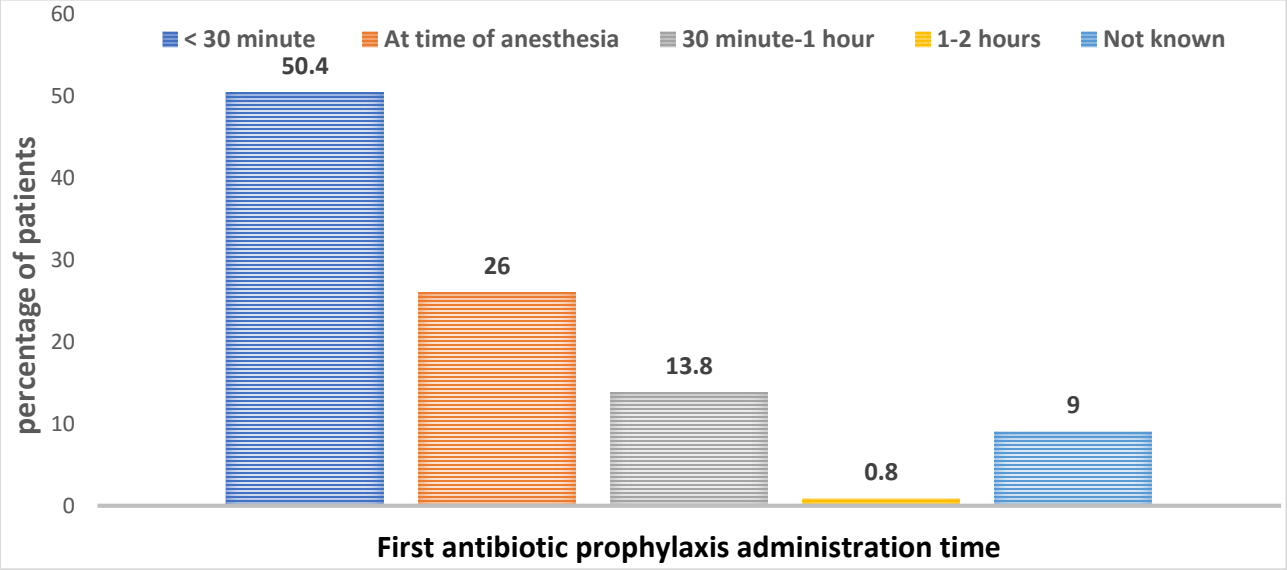

Figure 4: Distribution of timing of prophylactic antibiotic given to the study population SPHMMC, from 10 June to September 10, 2016

4.4.4 Duration of Surgical Prophylaxis

Among 246 patients that received surgical prophylaxis the duration of administration was more than 72 hours in 22(8.9%) of cases and while 93(37.8%), 28(11.4%),47(19.1%) and 56(22.8%) patients were taken the prophylaxis for 24 hours, single dose, 48 hours and 72 hours respectively. Re-dosing was not considered for any operations **(figure 5**).

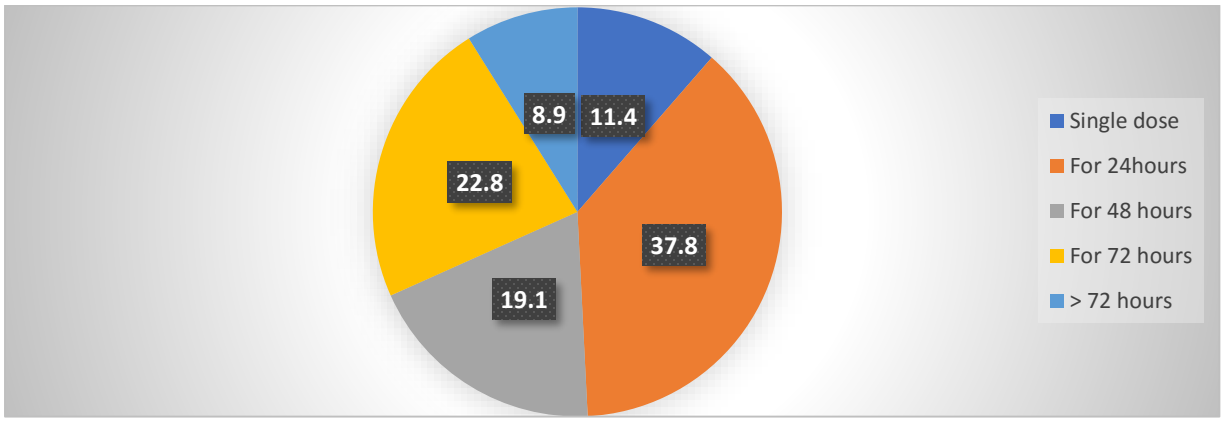

Figure 5: Distribution of duration of prophylactic antibiotic given to the study population SPHMMC, 2016

4.4.5 Evaluation of Surgical Antibiotic Prophylaxis

Of the patients (n=246) to whom SAP were given, 224(54.2%) had indication and 22(5.3%) had no indication to use.Of the patients (n=224) to whom SAP were indicated and administered; 205(91.5%) of them have been selected inappropriately.

Of the patients (n=224) to whom SAP were indicated and administered; 224 (100%) of their administered doses were accurate.Of patients (n=224) to whom SAP were indicated and administered, 224(100%) were given rightroute of administration.The majority of patients 125 (55.8%) received prophylaxis for extended duration.The most common reasons for inappropriate prophylactic antibiotics use wereinappropriate choice of antibiotic 205 (91.5%), inappropriate duration 125 (55.8%) andusing without indication 22(5.3%) **(Table 4.)**

Table 4: Appropriateness of antibiotic prophylaxis according to clinical guideline for antimicrobial prophylaxis, 2013 in surgical patients at SPHMMC, from 10 June to September10, 2016

Parameters	Categories	frequency	Percent
Use of antibiotics	Indicated and administered	224	54.2
	Not indicated and not administered	167	40.5
	Not indicated but administered	22	5.3
Choice of Antibiotic	Appropriate	19	8.5
	Inappropriate	205	91.5
Appropriateness of Dosage	Accurate	224	100
	Inaccurate	0	0
Duration of Prophylaxis	Correct	99	44.2
	Incorrect	125	55.8
Route of Administration	Right rout of administration	224	100
	Incorrect rout of administration	0	0

4.6 Development of SSI

Total 413 patients belonging to various age group were include in the study, out of which 46(11.1%) patients were identified with SSIs. Rate of SSI was found more in people belong to age group above 60, 8(15.1%) followed by 40-59, 15(14.2%), 20-39,21(8.7%) and less than20 ,2(7.7%).Male patients underwent more surgeries in the study of count 231(55.9%), in which 33 (14.3%) were with SSI and 198 (85.7%) without SSIs. 182 (44.1%) was females in which 13(7.1%) patients were with SSIs and 169 (92.9%) patients without SSI. Infection rate were more in males when compare to females in the study.

Among the SSIs case, 25(8.9%) were from elective admission whereas 21 (15.9%) were from emergency admission. From the total 46(11.1) patients who developed SSI, the rate of SSI was 5(5.3%), 13(7.6%), 10(15.9%) and 18(21.7% in clean, clean- contaminated, contaminated and dirty wound respectively.

A total 413 patients, 246(59.6%) patients received prophylactic antibiotics and 167(40.4%) patients have not received prophylactic antibiotics. The rate of SSI was with the patients who have not received any prophylactic antibiotics 6(3.6%). The duration of operation ranges from less than one hour to greater than four hours. The SSI rate in patients with duration of operation less than 1 hour was 18 (10.3%), 1-2 hrs. is 18(11.7%), greater than 2-3hours is 5(9.6%) and greater than 3-4 hours is 5(20%)(**Table 5).**

4.6.1. Factors Associated with SSI.

There were seven variables in binary logistic regression which had p value of≤0.2; and became candidate for multiple logistic regression; age, sex, comorbid illness, status of antimicrobial prophylaxis use, types of admission, duration of surgery and class of wound.But only patients having an emergency surgery, not using prophylactic, and class wound was significantly associated for the development of SSI (**Table 5).**

Emergency surgical cases were 2.6 times more likely to develop SSI than the elective surgical cases (AOR= 2.647; 95%CI= 1.406, 4.983). Patients who do not received antibiotic prophylaxis are 2.6 times more likely to develop SSI compared to those who received preoperative antibiotic prophylaxis AOR=2.572; 95%CI= 1.02, 6.485).

Table 5: Associationof selected parameters with SSI in patients who underwent surgery in surgical wards of SPHMMC from 10 June to September 10, 2016.

Variables		**SSI**		**No SSI**		**AOR (95% CI)**	**P value**
		N	**Percent**	**N**	**Percent**		
Age	≤20	1	7.7	12	92.3	1	
	20-39	21	8.7	220	91.3	.360(.086-.787)	0.067
	40-59	15	14.2	91	85.8	1.234(.389-3.306)	0.918
	≥60	8	15.1	45	84.9	.881(.249-2.451)	0.771
Sex	Male	33	14.3	198	85.7	.596(.252-.979)	.053
	Female	13	7.1	169	92.9	1	
Comorbid illness	Yes	7	6.4	103	93.6	.489(.211-1.131)	.094
	No	39	12.9	264	87.1	1	
Prophylactic antibiotics	Received	40	16.3	206	83.7	1	
	Not received	6	3.6	161	96.4	2.572(1.02-6.485)	0.045
Duration of surgery	<1	18	10.3	157	89.7	1	
	1-2	18	11.7	136	88.3	1.221(.606-2.462)	.577
	>2-3	5	9.6	47	90.4	.989(.346-2.823)	.983
	>3-4	5	20	20	80	1.859(.569 6.076	.305
	>4	-	-	7	100		.999
Type of admission	Elective	25	8.9	256	91.1	1	
	Emergency	21	15.9	111	84.1	2.647(1.406-4.983)	.003
Class of wound	Clean	5	5.3	90	94.7	1	
	Clean contaminated	13	7.6	159	92.4	.118(.033-.416)	.001
	Contaminated	10	15.9	53	84.1	.293(.136-.633)	.002
	Dirty	18	21.7	65	78.3	.694(.295-1.632)	.403

SSI: surgical site infections; AOR: adjusted odds ratio; p-value: the value obtained using multivariate logistic regression.

5. DISCUSSION

5.1 Evaluation of Prophylactic Use of Antibiotics in Surgery

Although the principles of antimicrobial prophylaxis for surgical procedures have been well defined for many years. Inappropriate and excessive use of for surgical prophylaxis is worldwide problem. One of aim a study was to evaluate the appropriateness of antibiotics use in surgical prophylaxis. The result of this study suggests that compliance with all principle of antibiotics prophylaxis was very low (8.5%) in our study. This reflects that there are wide discrepancies between the guideline on surgical antibiotics prophylaxis and current clinical practice. The study in Brazilian, considering all the aspects of antibiotic prophylaxis for surgical procedures, only 5.1% of the patients were treated correctly which similar with this study (Laura & Lucieni, 2004).

The audit results show that third generation cephalosporin were routinely used for prophylaxis. This group of agents is not used for surgical prophylaxis for many reasons: they are active against bacteria rarely encountered in elective surgery, their wide spread use is associated with the emergence of bacterial resistance, they are less active against staphylococcus, and they are generally expensive (Abubaker *et al.*,2012). International guidelines advocate the use of narrow spectrum antibiotics for surgical prophylaxis. Cefazolin is generally viewed as first choice for many procedures. However, for distal intestinal tract operations, third generation cephalosporins with anaerobic coverage are recommended (Bratzler *et al.*,2013). However, Cefazolin was not available for use in our hospital during the study.

We assessed different criteria (choice of antibiotics, timing, duration, dosage and route of administration) of the appropriateness of prophylaxis in the 224(71.3%) patients in which prophylaxis was justified and provided. For our study, we have adopted American society of health-system pharmacist (ASHP) guideline as reference. Because this guideline is provided for practitioners with a standardized approach to the rational, safe, and effective use of antimicrobial agents for the prevention of surgical site infections (SSIs) based on currently available clinical evidence and emerging issue (Geroulanos *et al.,* 2001).

The total cases receiving antibiotic prophylaxis were 246(72%) while only 224(71.3%) patients prophylaxis was justified and in 22(6.5%) patients prophylaxis was not necessary according to guidelines. it is very important that the true role of prophylaxis, when it is indicated, and the consequences of bacterial resistance when it is used inappropriately, be made known to and understood by the physician. the reason behind for unjustified use may be lack of agreement on the guideline which surgery require prophylaxis and which doesn't. Similar result was observed study from brazil were only 3% was unjustified (Laura G & Lucieni D ,2004).

The present study demonstrates that ceftriaxone was excessively and inappropriately used for antibiotic in SPHMMC. 70.7% of the participants were given ceftriaxone only as surgical prophylaxis despite the fact that ASHP recommends its use to be limited as single agent for high risk biliary tract procedures and combined with metronidazole for colorectal surgery. As per the general principle of SAP, it is recommended to use antibiotic with narrowest antibacterial spectrum that is effective against the likely pathogens that would contaminate the wound. Ceftriaxone is broad spectrum antibiotic therefore it should be used only for the treatment of established infections (sepsis, meningitis, pneumonia, pyelonephritis etc.). Furthermore, ceftriaxone is costlier and less effective than cefazolin does in S. aureus (Bratzler *et al.*,2013). Overuse ceftriaxone could be a potential threat in our setting and should lead to heightened vigilance in the selection of antibiotics for surgical prophylaxis and treatment.

Prophylaxis with broad spectrum antibiotics is not recommended because it leads to unnecessary increase in hospital costs and emergence resistant bacteria without increasing of effectiveness.

Fluoroquinolones or fourth or third generation cephalosporines should not be prescribed. ASHP suggests prophylaxis with cefazolin 1gm intravenous single dose or maximum of 3 doses 8 hourly for 24 hours postoperatively appropriate first line agents for most surgical procedures, targeting the most likely organism (Bratzler *et al.*,2013). But in our study, Of the patients 224(71.3%) to whom SAP were indicated and administered, 91.5% of them have been selected inappropriately. This corroborates the study from Iran (92.5%) (Vessal et al., 2011) but higher than studies from Sudan (64.4%) (Elbur et*al.*,2013) and Netherland (8%) (Kasteren *et al.*,2003). In the present study, the main reasons for noncompliance with SAP selection was the use of agents having a broader spectrum than recommended. This may due to false belief that broad antibiotics are more effective in preventing SSIs.

The hospital's supply of available antibiotics has been previously reported to have an important effect on the selection of SAP (Thomas *et al.,* 2008). The most commonly used drugs for SAP were not available SPHMMC at the time of this study; the unavailable drugs include cefazolin, cefuroxime, ampicillin-salbuctam and neomycin. This is in line with study from Jordan which found that 68.1% of inappropriate drug selection for SAP was contributed by drug unavailability (Alazzam *et al.*,2012). The high rate of inappropriate choice of prophylactic antibiotic may also be due to the unavailability of a unit-based clinical pharmacist to assist physicians in correct choice of medications according to guidelines.

One of the common failures to compliance to SAP guidelines is prolonging the duration of SAP beyond the recommended time. regards to the duration of antibiotic prophylaxis, a prophylactic antibiotic administered within 24 hours following the end of the surgery is considered appropriate except in cardiothoracic surgery up to 72 hours. Very similar to most of the previous studies, which was noted in our study was the prolonged duration of the antibiotic prophylaxis. In this study, out of 224 patients who receive antibiotics prophylaxis according to justification Only 99(44.2%) patients received the antibiotics for 24 hours after the end of surgery.125(55.8%) of the cases had prophylactic antibiotics administered more than 24 hours postoperatively. This inappropriate practice is higher compared to Dutch hospitals (18%) (Kasteren *et al.*,2003) and Iran (43%) Vessal *et al.*,2012). However, lower than to that of in Qatar (59.3%) (Abdel-Aziz *et al.*,2013) and Sudan (97%) (Elbur *et al.,* 2013). The reason for longer courses of antibiotics might falsely believe to be a good preventive measure against SSIs. Excessive duration of antibiotic use during the postoperative period might also be a consequence of the surgeon's conception of the necessity of providing extra protection due to risks from serum lines, tubes or catheters, or because of the impossibility of distinguishing infection from contamination and inflammation from another site.

A systematic review of single versus multiple dose antimicrobial prophylaxis for major surgery studies in between 1974 - 1999 have shown that a single dose of antibiotic is just as effective as multiple doses and there are no differences on the prevention of SSI risk (McDonald *et al.*,1998). Moreover, prolonged use of SAP has been associated with emergence of resistant bacterial strains, increased incidence of antibiotic associated diarrhea as well as increased costs (Herbart *et al.*,200).

Timing of the first dose of antibiotic therapy is important, as it aims to achieve adequate serum and tissue drug level for a period exceeding the duration of the operation to target the organisms likely to be encountered during the operation. Various studies suggested the optimal timing of administration was within one hour and close to the time of incision (at anesthesia induction) (Geroulanos *et al*.,2001). During the study, we found that 158(90.2%) of the prophylactic antibiotics were administered within one hour prior to the surgical incision, which were concordant with the guideline. Of this, around 124(50.4) % of the antibiotics were given within 30 minutes preoperatively. Regarding to this parameter, the adherence status was better than compared to a Dutch hospital (51%) (Kasteren *et al.*,2003), and hospitals in the United states (55.7%) (Bratzler *et al.*,2004).

The relatively high rate of correct timing of antibiotic administration. But, appropriate timing was lower in the study performed in Jordan (99.1%) (Al-Momany *et al.*, 2009).

Additionally, it was also noted that the timing of prophylactic antibiotic administration in our setting was poorly documented. 22 (9%) patient charts were not recorded. One reason for this may be that documentation of prophylactic antibiotic administration is performed by anesthesiologists on induction forms, whereas the time of surgical incision is documented by surgeons. The other reason for Poor documentation could be due to work overload on attending nurses and lack of awareness to record SAP administration time.

Another reason for wrong choices and duration of prophylactic antibiotics might be due to lack of written unit-based guidelines for prophylactic antibiotics in surgery patients. Although ASHP recommendations were used as rational and evidencedbasedinternational guidelines, ASHP recommendations may not in fact be practical in our patients and setting or for the situation in the SPHMMC. This is because different countries and institutions may have different microbial flora, resistance patterns, antibiotic availability, rate of post-operative surgical site infection and operation room sterility.

So, to increase the quality of prophylaxis in surgery effort are need to be put to facilitating logistics and development of guidelines includes type of surgery, the optimal time of antibiotic administration, choice of antibiotics and an alternative, address intra-operative redosing and duration of use. it should be also based on hospital-specific bacterial epidemiology patterns, the best evidence derived from the literature. The support and collaboration of hospital administrators and medical staff of such guidelines is essential for their development, implementation and maintenance

5.2 Pattern of Antibiotic Usage in Surgery

The present study was carried out during10June,2016 – September10, 2016 in inpatient departments of surgery, SPHMMC multi-specialty hospital. This study attempts to assess the general pattern how antibiotics were used in surgical wards, to evaluate the surgical prophylaxis appropriateness and to determine the rate of surgical site infection.

The use of antibiotics in surgical patients both for the prophylaxis and treatment of infections is a justifiable practice that, however, requires a regular review of the chosen regimen on the grounds of rational, safe, and effective usage of antibiotics for the prevention and treatment of surgical site infections (SSIs) based on currently available clinical evidence and emerging issues (Abulaand Kedir, 2004).

The data was collected from 413 patients matching inclusion criteria that underwent surgery and were in their postoperative period till they were discharged, in the surgical ward of our hospital. In our study the predominance of male patientswas 56% which was comparable with the study done by (Ali *et al.*,2010) in which 58.85% of patients were male. Age group of the patients ranges from 13 to 85 with mean age of patients 38.1 years mean age of patients is similar study by (Mallol *et al.*,2012).

In our study majority of patients were of the age group of 20-39 years which supported to a study done by (Sapna *et al.*, 2012) who stated that majority of cases in their study were between the age group of 20-40 years. The reason behind it can be concluded that it was the productive

age group that was actively involved in socioeconomic activities, and this might be making them vulnerable to diseases, which may need surgical interventions. In contradiction to this (Bhansali *et al.,* 2013) reported 57.08% of patients from 40-60 age group. This my duet to variation of inclusion criteria.

In this study, most common surgery was general surgery and accounted for a total of36.8%patients. Similar result showed from study in India (Rehan *et al.,*2010). This finding was higher than findings of (Chaudhary*et al.,*2015) who stated 31.07 % of surgery of were general surgery of all surgeries. The other common procedure done wassurgery of orthopedic surgery accounting (22.3 %) of total patientswhich was higher than the findings of (Bhansali *et al.,*2013) which accounted for 17.92%. this my due tothe increment of accidents.

This study revealed that antibiotics were used for about 341(82.6%) of the patients who undergo different types of operation. all patients taking antibiotics on empirical basis of prescription. This figure is greater than to the 70% and 51.4% seen in Gondar and Greek hospitals, as described by (Gikas *et al.,*2012) and (Abula and Kedir, 2004) respectively.

From a total of 341(82.6%) surgical cases that has been receiving antibiotics, 95(28%) were for treatment and 246(72%) prophylactic purpose which was similar finding found by other authors, 34 (20.2%) were for treatment purpose and 134 (79.8%) prophylactic purpose (Huduma,2016).

In the present research, antibiotic prophylaxis was used in 72% of cases, which was less than observed by other authors, who found rates ranging from 81.4% to 97.5% (Napolitano *etal.,*2013). However, other articles showed results inferior to the aforementioned frequencies, with a variation for the use of the antibiotic prophylaxis in the range of 58% to 73% (Gul *et al.,*2005)

The present study showed thatsingle drug therapies were prescribed more followed by two drug therapy and tripe drug therapy. The prevalenceof use of two or more antibiotics during the study period was in 142 (41.6%) of the cases. But it was less than data in audits of surgical antimicrobial use showed that the majority of the admitted patients (53.6%) received two or more antimicrobials in different combinations for their treatments (Bhansali *et al.,*2013) and study conducted in India have shown that the use of two antimicrobials agents was most common 48(31.17%) followed by three or more than three antimicrobial agents 36(23.38%). Monotherapy for antibiotic prophylaxis or treatment of infection is considered as an ideal situation from the point of view of rational use and the prescriber must be objective. Antibiotics, which were used for the prophylactic and treatment regimens in this study, were the same and combinations of antibiotics are also common practice. Although the, simultaneous use of two or more antibiotics has a certain rationale, routine combination of antibiotics may increase the risk of toxicity, increased cost and emergence and spread of drug-resistant microorganisms (Donald *et al.,*2001).

Taking the basis of prescription of antibiotics, the number and type of antibiotics prescribed, the duration of administration, and non-periodic assessment of the sensitivity pattern of the likely pathogens in the study setting into consideration, antibiotics might have been overused particularly for the prophylactic regimens.

Ceftriaxone was the most frequently prescribed antibiotic in our hospital as single or in combination with other antibiotics, the reason might be easy availability of the drug in the hospital pharmacy.Combination of ceftriaxone and metronidazole was the most used prophylactic antibiotics because these are the antibiotics which are available widely covering most bacteria, ceftriaxone covering mostly gram positive and metronidazole covering mostly gram negative.ceftriaxone was usually combined with metronidazole, ampicillin and vancomycin for prophylaxis and treatment. InIndia study, Ceftriaxone was most frequently prescribed (Sapna et al.,2012) whichwas concordant with our study, while in a study done in Nepal, combination of ampicillin and floxacillin was the most commonly used antibiotic regimen (Bishnu *et al.*,2008). In a Brazilian study, the most commonly used antibiotics for prophylaxis were first generation cephalosporins (Laura *et al.*,2008). This difference may be due to difference in the availability of drugs.

The intravenous route was the most preferred method (84.8%) used to administer of the cases. route of administration is essential as certain drugs may not be as effective if given via other routes.

5.3 Incidence Rate of SSI

The rate of SSI varies greatly worldwide and from hospital to hospital. The rate of SSI varies from 2.5% to 41.9% as per different studies (zeenat, 2012).In this study, out of the 413 surgical site patients, 46(11.1%) developed surgical site infection. This is lower than with the findings of (Taye, 2005) and in study done in Nigeria (Michalopoulos *et al.*, 2003) which were 14.8% and 17.5% respectively. The variation in the incidence of SSI in this study in contrast with other studies could be, due to antimicrobial agent choice, susceptibility pattern of pathogens, operation theatre setup and difference in study design and time.

However, it was above the SSIs in some places. The incidence in America was reported as 5% (Cheadle, 2006) and 4.65% in England (Hospital Infection Society and Tissue Viability Nurses Association, 2007). The reason for this is uncertain but the impact of a high prevalence of inappropriate antibiotic use for prophylaxis, current infection control policies or a combination of these factors requires further considerations or might be due to inclusion of contaminated and dirty wound in these studies while only clean and clean-contaminated woundwere included in those study.The higher SSIs rate in present study compared to developed countries might be also due modern instruments, rooms and adequate trained manpower in developed countries.

In this study, age was not associate with SSIs. Even though the rates of SSI increase with the increase in age. The findings of this study weredifferent from findings of Taye (2005) and Seyd *et al.*, 2005.This is in contrary to the fact that increasing age is correlated with greater likelihood of certain chronic conditions, malnutrition and fall in the body immunological efficiency, causing more extensive surgical site infection (Patel *et al.*,2012). In the present study surgical site infection was not correlated with sex. Although there were a significant proportion of males (14.3%) developed SSI compared to females (7.1%) which was similar tostudies showed no significant difference in SSIs rate between males and females in India where males were 62.68%

and females were 37.32% (Anusha *et al.,* 2010) and Pune, there was a preponderance of male patients developing SSI (7.4%) over female patients with SSI (5.1%) (Varsha *et al.,* 2012).

Infection rate was more in emergency operations (15.9%) than in elective operations (8.9%). In analysis of the association of potential risk factors for individuals with wound infection revealed that patients who were operated as emergency surgical cases were 2.6 times more likely to develop SSI than the elective surgical cases (AOR= 2.647; 95%CI= 1.406, 4.983).Studies have shown that the emergency operations are prone to develop wound infection because of the environmental factors and the already infected cases (Anant *et al.*,2014).

The rate of SSI according to the US National Nosocomial Infection Surveillance (NNIS) system hospitals were reported to be: clean 2.1%, clean-contaminated 3.3%, contaminated 6.4% and dirty 7.1% (Culver *et al.*,2012) which was comparatively lower than the study result which are, clean 5.3%, clean-contaminated 7.6%, contaminated 15.9% and dirty 21.7%.%. The above findings from different studies and settings show wound class as a common risk factor associated with SSI which is similar to the findings of this study.As it is clearly stated in many literatures, the infection rate increases with classes of wounds, the highest rate being in dirty or infected woundsby Shojae (2005).

Patients who had not given prophylaxis antibiotic were 2.6 times more likely to develop SSI than patients who were took preoperative prophylaxis antibiotic (AOR= 2.572, 95%CI 1.02, 6.485). Studies conducted in Uganda and Pakistan (Carlos *et al.,* 2011) have proven the use of prophylactic antibiotics to prevent SSIs when administered with appropriate antibiotics, dosage and timing.

6. Limitation

Some limitations of this study have been identified. The study was a cross-sectional type and thus it did not investigate cause and effect relationship. In addition, the study was conduct in only the general, orthopedic, urology, obstetrics and gynecology and neurology ward so that it is not generalizable to the other disciplines.Apart from this, the data retrieval was based on the written information in medical records, which might be confounded by personnel negligence in documentation and thus not truly reflect the real practice, especially regarding the timing of antibiotic prophylaxis.

Another limitation was etiological agents responsible for surgical site infections were not considered due non-availability and the relation between surgery types and incidence of SSI could not bestablished as the study considered broad category of surgery.

7. Conclusion

Antibiotics are a key component for the treatment and prevention the of SSIs but the inappropriate use causes increased cost, stay prolongation and even infections due to resistance. This study indicated that majority of 341(82.6%) patients who underwent surgical procedures the received antibiotics. Ceftriaxone was mostly used drug. The current prophylactic antibiotics practices at SPHMMC showed gap between international standards and local prescribing practices and need for interventions to improve this situation. Appropriateness pertaining to the choice and duration of antibiotic usage in surgical prophylaxis were low SAP guidelines was largely due to the use agents having broader spectrum than the recommended as well as extending the duration of SAP beyond the recommended. The overall incidence rate of SSIs was 11.1% after emergency and elective surgeries in SPHMMC which was lower compared with report from some developing. but it was higher than studies done in developed countries. Provision of prophylactic antibiotics, class wound and admission type of patient were significantly associated with development of SSI.

8. Recommendation

From the study findings, it is recommended tothe need evidence-based guide-line for the practice of SAP in the surgery unitetaking resistance pattern and common micro-organism responsible for SSI in consideration and limit the use of ceftriaxone in surgical prophylaxis.

SPHMMC should establish continuous surveillance to monitor antimicrobial susceptibility pattern of the common isolates found in SSI.

This study suggests the need to avail most of the recommended SAP antibiotics, specifically cefazolin. It might also be important to perform continued surveillance of SAP practice and continuous educational programs all surgical wards.

It can also be recommended that hospital infection control system as well as wound surveillance program has to be established to reduce the surgical wound infection rate to acceptable standard.

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10. ANNEXES

Annex 1: Data Abstraction Format

1. Name of ward _____ bed no _____

2. Date of surgery _____

3. Age _____

4. Sex: male f[ ]le [ ]

5. Types of admission

a. Emergency Yes No [ ] [ ]

1. Diagnosis _____
2. Types of operation _____
3. Comorbid disease _____
4. Class of wound _____

b. Elective Yes No [ ] [ ]

1. Diagnosis _____
2. Types of operation _____
3. Comorbid disease _____
4. Class of wound _____

6.Duration of surgery _____

7. Is surgical antimicrobial given yes [ ] No [ ]

8. If yes question 7 fill out the following

Name antibiotics	Dose	Rout of administration		
		IV	PO	IM

9.What is the time of first antimicrobial prophylaxis administration?

a) At time of induction of anesthesia
b) ≤ 30 mints before the start of surgery
c) 30-1hour before start of surgery
d) 1-2 before start of surgery
e) > 2 hours before start of surgery
f) Not known

10. Is there antibiotics re -dosing during surgery? Yes ☐ No ☐

11. If yes question 11

Name of antibiotics	Dose	Time of administration (hr /min/sec)

12. Is antibiotics given after the end of the surgery? Yes ☐ No ☐

If yes 12 pleas answer question number 13, 14, 15 and 16

13. For what purpose antibiotics was given?

Treatment prophy ☐ ☐

14. Detail of antibiotics given

Name of antibiotics	Does	Frequency

15.Duration of surgical antibiotic prophylaxis

a) Less than 24 hours
b) For 24 hours
c) For 48 hours
d) For 72 hours
e) For greater than 72 hours

16. The bases of treatment prescription

a) Definitive
b) Empirical

17. commonly used surgical prophylactic agent available during study period

A) ----------c) ----------e) ----------

B) ----------d)----------f) ----------

18. Did the patient develop surgical site infection at time of discharge?

Yes ☐ No ☐

Annex 2: surgical antibiotics prophylaxis guideline

Timing of administration

The prophylactic agent administered in a dose which provides an effective tissue concertation prior to intra -operative bacterial contamination.

**the first dose does should always be given before the skin incision is performed ideally within 30 min and certainly within 2hours before the time of incision.*

Dose of administration

Only sing does prophylactic does sufficient for the procedures lasting lesser than 3hours.For procedures lasting greater than three hours, require an additional effective dose.

**which should be give given at interval of one to two times of half-lives of the drug*.

Duration administration

Antibiotics prophylaxis after wound closer is unnecessary. Prolonged use prophylactic antimicrobial associated with emergence of resistant bacterial strain.

**Guideline recommend that prophylaxis should end within 24 after the end of surgery except cardiology surgery where it should be 72 hours.*

Rout of administration

Intravenous administration of antibiotics prophylaxis immediately before or after induction of an aesthesia is most reliable method of effective serum concentration at time of surgery.

Choice of antibiotics for surgical prophylaxis.

1) Antibiotics should cover all most likely contaminating organisms.

**generally, first generation cephalosporin like (cefazolin) is best option for the majority of procedures(in these cases species of staphylococcusMaye be common cause.*

2) For procedures of alimentary tract,Genito urinary tract and hepatobiliary system coverage should beadditionallyinfluenced by site specificflora such as gram negative and anaerobic microorganisms.

**in such case cefotetan or cefoxitin is suitable*.

3) Metronidazole and aminoglycosidesmay be used for coverage of anaerobes and gram-negative organisms respectively.

4) Ciprofloxaciilin also effective for gram negative organisms.

5) Generallybroad-spectrum antibiotics should be avoided.

Annex 2: - surgical antibiotics prophylaxis guideline

Procedure-specific surgical prophylaxis recommendations.

	Indication	Drug choice	
1	Appendectomy –perforated	Cefazolin 1-2 gm IV+ Metronidazole 0.5gm **or** Cefotetan or cefoxitin 1-2mg IV 3-5 days.	Gentamycin 80mg &clindamycin 600mg
2	Appendicectomy-non-perforated	Cefazolin 1-2 gm IV+ Metronidazole 0.5gm or Cefotetan or cefoxitin 1-2mg IV up to 3 does or 24 hours	Gentamycin 80mg IV&clindamycin 600mg IV
3	Colorectal surgery	Cefazolin 1-2 gm IV+ Metronidazole 0.5gm or Cefotetan or cefoxitin 1-2mg IV +- Gentamycin 80mg	Neomycin 1 gm+erythromycin 1gm po
4	Abdominal gastroduodenal surgery	If high risk: - Cefazolin 1 gm IV or Ceftriaxone 1g+ Metronidazole 500mg	Gentamycin 80mgIV &clindamycin 600mg IV
5	Biliary tract surgery – a) if high risk cholecystectomy, jaundice, biliary obstruction	Cefazolin 2g Iv cefoxitin2g IV or ceftriaxone1g or metronidazole0.5g IV	Gentamycin 80mg &clindamycin 600mg
	b) laparoscopiccholecystectomy	No prophylaxis	
6	Laparoscopic or non-laparoscopic a) hernia repair with mesh	Cefazolin 1-2g Iv or ceftriaxone 2g IV	
	b) hernia repair without mesh	None	
7		Cefazolin 1-2g Iv cefoxitin2g IV or ceftriaxone 1-2g	
8	Non-cardiac vascular surgery • Low extremity amputation • Aortic resection • Prosthesis • Groin incision	Cefazolin 1-2gm or Cefuroxime 1.5gm	Vancomycin 500mg+-gentamycin or clindamycin
9	Cardio thoracic surgery	Cefazolin 1mg or cefuroxime 1.5g	Vancomycin IV + Gentamycin IV
10	Head and neck surgery clean contained	Cefazolin 1-2gm IV +-metronidazole 500mg IV or Amoxa+clavulunate1-2gmiv	Clindamycin600mg IV Gentamycin 80mg
11	Gynecology surgery • C-section • Hysterectomy	Cefazolin 1-2gm or Cefuroxime 1.5gm or Cefoxitin1-2g IV or	Clindamycin +gentamycin
12	Neuro surgery	Cefazolin 1-2gm or or ceftriaxone 1-2g	Clindamycin
13	Urologic surgery	Ciprofloxacillin 500mg po stat Cefazolin 1gm	Gentamycin
14	Orthopedic surgery	Cefazolin 1gm IV	Clindamycin+ aminoglycoside

Patient will be given alternative agent whenever they state they state prior allergy.