



# **Effectiveness of Ceftriaxone in the treatment of Post-Surgical Infections: Alone and in combination with Ascorbic acid**

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## **ABSTRACT**

Post surgical infections (PSI) are among the most common hospital acquired infections comprising 14-16 percent of inpatient infections. PSI is a dangerous condition, a heavy burden on the patient and social health system. PSI risk factors are diabetes, malnutrition, smoking and obesity. The aim of the study was to observe the effectiveness of ceftriaxone in the treatment of post surgical infections alone and in combination with antioxidant Ascorbic acid. A retrospective study was conducted on surgically operated patients in the region of Lahore and Sialkot, 100 patients were included in study through random sampling technique. Results showed that some patients were taking prophylactic treatment with ceftriaxone and with any other antibiotics, due to lack of sterility factor, inappropriate ventilation and poor patient compliance leads to post surgical infections. Private sector utilized preventive strategy to maintain the sterile conditions in operating room while in public sector preventive strategy not applied. Mostly post surgical infections occur in patients within 7 days of surgery. Staphylococcus aureus was the microorganism most commonly cultured from PSI. The treatment given to patients for PSI include ceftriaxone in combination with NSAIDS, antioxidants and other antibiotics. In patients treating with ceftriaxone in combination with Ascorbic acid, the healing of infection was so rapid as compared to other combinations of ceftriaxone. It was also studied that the cost of treatment also reduced with the use of combination (Ceftriaxone+ Ascorbic acid).

**Key words:** Post surgical infections (PSI), antioxidant, ceftriaxone, Ascorbic acid, Staphylococcus aureus

## **INTRODUCTION**

A Post surgical infection (PSI) is an infection that occurs after surgery in the part of the body where the surgery took place. Most patients who have surgery do not develop an infection. However, infections develop in about 1 to 3 out of every 100 patients who have surgery. PSI are most common type of nosocomial infections in surgical patients accounting for 38% of all such infections. These infections occur up to 30 days after surgery. Some procedures monitored up to 90 days for PSI [1]. PSI increases

hospital length of stay 7-10 days and increase cost. Some of the common symptoms of a surgical site infection are redness and pain around the area where patient had surgery, drainage of cloudy fluid from surgical wound and fever. Three types of surgical site infections include superficial incisional which occur in the area of skin where surgical procedures have been done, deep incisional occur either beneath incision site or at muscle tissue and organ or space surgical site infections can be present in body organ or space between body organs These infections are frequent cause of morbidity and mortality [2] [3]. Etiology of surgical site infection include bacterial factors, local factors, systemic factors. In surgical site infections sepsis may be caused by bacteria either gram positive or gram negative, fungal, viral and other infection but 50% of sepsis cases are due to gram negative bacteria. Most common clinical isolates of surgical site infections include *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *E.coli*, *klebsiella* species, *Proteus* species. Sources of infecting pathogen are endogenous (patient's own flora, seeding from pre-existing sites of infection) and exogenous (hospital environment, medical personnel) [4] [5] [6]. *Staphylococcus aureus* is the microorganism most commonly cultured from PSI. When a viscous, such as the large bowel, is opened, tissues are likely to be contaminated by a whole range of organisms. For example, after colorectal surgery enterobacteriaceae and anaerobes are encountered and may act in synergy to cause PSI [7].

Pathogenesis of PSI include non-specific and specific infections. Non-specific infection include bacteria proliferation leucocyte infiltration, inflammatory media and cytokines release, congestion, exudation , accumulation of serum, blood cells, necrotic tissues, redness, swelling, hot and soreness, and dysfunction. While specific infection include tuberculosis, tetanus, gas gangrene and fungal infections [8]. Factors responsible for PSI are bacterial factors, local factors and systemic factors. Bacterial factors include adherence of bacteria, toxins (exotoxin, endotoxin) and numbers of bacteria upto  $10^5$ . If a surgical site is contaminated with  $>10^5$  microorganisms per gram of tissue, the risk of PSI is markedly increased. Local factors include injury of skin or mucosa, duct obstruction, blood supply, skin or mucosal diseases .Systemic factors include severe disease, hormonal imbalance, malnutrition and AIDS. The development of PSI depends on contamination of the wound site at the end of a surgical procedure and specifically relates to the pathogenicity and inoculum of microorganisms present, balanced against the host's immune response [9]. Other factors include age of patient, gender ,period of surgical procedure, duration of hospital stay, sterility of instruments used during surgery and in addition to this application of aseptic technique before, during and after surgical procedure and contaminated environment of surgical wards and type of antibiotic that have been given to patient for prophylaxis. The term risk factor has a particular meaning in epidemiology and in the context of PSI pathophysiology and prevention, strictly refers to a variable that has a significant, independent association with the development of PSI after a specific operation [10].

Risk factors associated with surgical site infection include diabetes, obesity and prolong presence of surgical drain at the infection site. Proper surgical technique is most important factor in prevention of surgical site infections. PSI prevention measure can be defined as an action or set of actions intentionally taken to reduce the risk of PSI. Many such techniques are directed at reducing opportunities for microbial contamination of the patient's tissues or sterile surgical instruments; others are adjunctive, such as using antimicrobial prophylaxis or avoiding unnecessary traumatic tissue dissection [8]. PSI is a major complication, with the better understanding of risk factor and epidemiology, effective preventive strategies can utilize to reduce the surgical site infections. Surgical site infection is among the leading nosocomial causes of complications and increased medical expense [11].

Factors that trigger the risk of PSI include diabetes. A significant relationship exist between increasing levels of HgA1c and PSI rates. Also increased glucose levels ( $>200$  mg/dL) in the immediate postoperative period ( $<48$  hours) were associated with increased PSI risk [12]. Another factor that delays primary wound healing and may increase the risk of PSI is nicotine. For some types of operations, severe protein-calorie malnutrition is crudely associated with postoperative nosocomial infections, impaired wound healing dynamics, or death. Prolonged preoperative hospital stay is frequently suggested as a patient characteristic associated with increased PSI risk [13].

Optimum application of PSI prevention measures requires that a variety of patient and operation characteristics be carefully considered. Patient characteristics possibly associated with an increased risk of a PSI include coincident remote site infections or colonization, diabetes, cigarette smoking, systemic steroid use, obesity, extremes of age, poor nutritional status and perioperative transfusion of certain blood products. Operative characteristics include preoperative antiseptic showering, patient skin preparation in the operating room, preoperative hair removal, antimicrobial prophylaxis. Intraoperative characteristics include (operating room environment, surgical attire and drapes (surgical attire refers to scrub suits, caps/hoods, shoe covers, masks, gloves, and gowns) [14].

Penicillins, cephalosporins, gentamicin, ceftazidime, metronidazole, vancomycin are commonly used antibiotics for prophylaxis. First generation cephalosporins are sufficient for prophylaxis for majority of surgical procedures to reduce infections. The most commonly prescribed antibiotics were combination of ceftriaxone and metronidazole [15]. Intra abdominal infections can be treated by different types of antibiotics depending upon types of pathogens causing intra abdominal infections. Ceftriaxone is proved more effective to prevent deep wound infections. Ceftriaxone based prophylaxis is useful for preventing surgical site infections and urinary tract infection considering its effectiveness and safety profiles [16]. Ceftriaxone is semisynthetic cephalosporin with long half life having effectiveness against gram positive, gram negative, aerobic and anaerobic bacteria and prescribed in complicated and uncomplicated infections. Administration of ceftriaxone six hours after infection produce rapid bacteriolysis [17]. Ceftriaxone proved more effective than ciprofloxacin for short term prophylaxis due to greater antibiotic sensitivity for microbes. A single dose of ceftriaxone before surgery is effective in preventing major pelvic infections and urinary tract infections [18]. Clinical efficacy and safety of ceftriaxone when administered twice daily was evaluated in treatment of serious infections, bacteremia, pneumonia. Cure rate of ceftriaxone was achieved in infections due to organism resistant to ampicillin, ceftazidime, cefamandole, carbenicillin and gentamycin [19]. Resistance to ceftriaxone developed during therapy with several *Enterobacter* and *Pseudomonas* species isolates. Ceftriaxone appears to be a useful agent for treatment of serious gram-negative infections in seriously ill patients [20].

Ascorbic acid is an antioxidant which markedly reduce the growth of *E.coli*, *Pseudomonas aeruginosa* and *Staphylococcus*. Ascorbic acid at lower concentration and within shortest exposure of time is proved bactericidal against *Staphylococcus aureus*, *E.coli* and *P.aeruginosa* [21]. Ascorbic acid increases wound healing, immune system activation, collagen formation due to its oxidative property. Nutritional deficiencies decreases wound healing after surgeries. Efficacy of ceftriaxone may be enhanced by prescribing it along with Ascorbic acid [22].

This study aims to observe the effectiveness of ceftriaxone alone and in combination with antioxidant Ascorbic acid in the treatment of post surgical infections.

## **MATERIALS AND METHODS**

### **Study design**

Retrospective study (an observational and questionnaire based study) was conducted during June -2015 to August-2015 in various hospitals of Lahore.

### **Inclusion and exclusion criteria**

Surgically operated patients, both male and female were included in the study. While patients having infection before surgical procedure were excluded from the study.

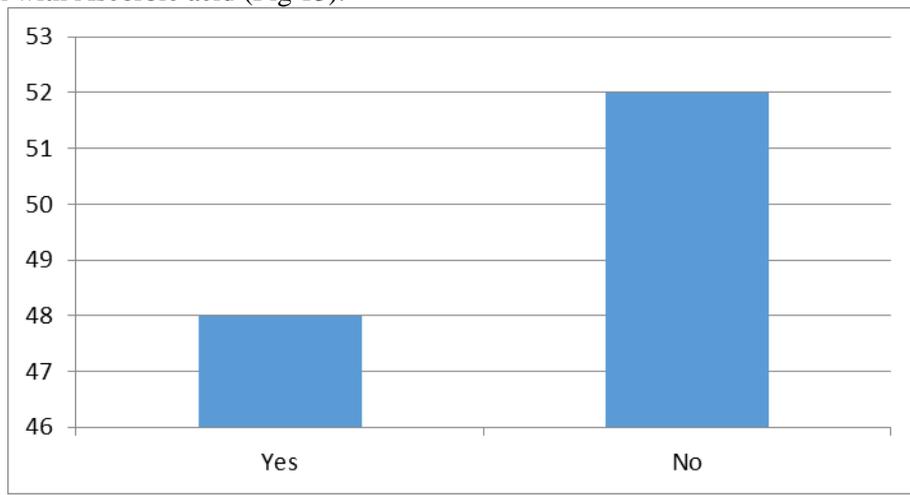
### **Data collection and analysis**

Data was collected from 100 patients, using random sampling technique. A data collection form was developed to obtain patient's demographic data, patient complaints regarding management of disease and observational data. Collected data was analyzed & presented in the form of graphs.

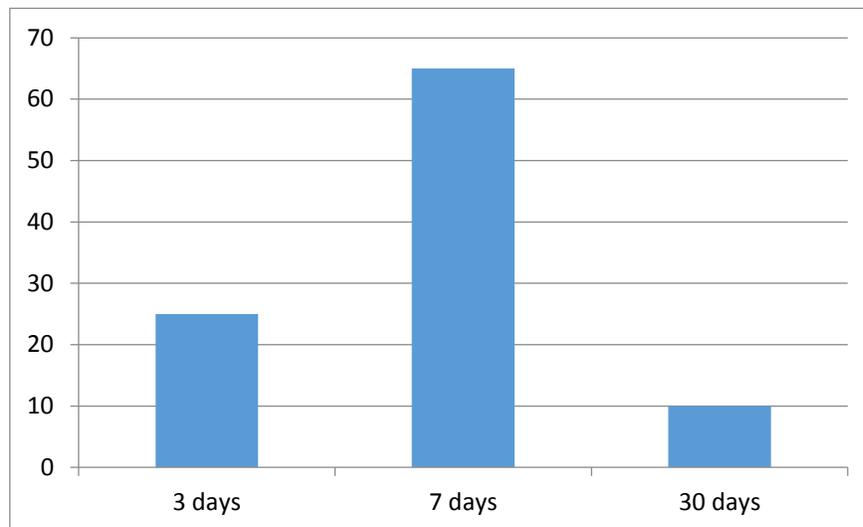
## **RESULTS**

Results showed that 48% of patients were familiar with the term of PSI, while 52% not (Fig 1). PSI appeared in 25% of the patients within 3 days, 65% of the patients within 7 days and in 10% patients

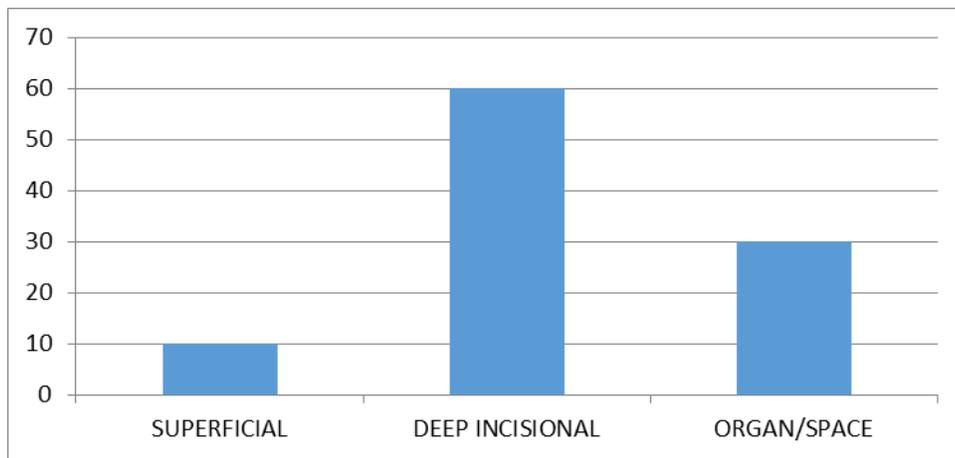
within 30 days (Fig 2). Among the types of PSI, 10% of the patients had superficial, 60% deep incisional and 30% organ/space infection (Fig 3). Results further showed that 50% of the patients had malnutrition, 30% diabetes and 20% obesity (Fig 4) ,40% patients were smokers while 60% non-smokers (Fig 5). 55% of the patients used prophylactic treatment while 45% patients not (Fig 6). Results showed that 25% patient used prophylactically ceftriaxone while 75% patients were found to use other antibiotics (Fig 7). Among pathogens causing PSI, it was found that 25% were E.coli, 25% Pseudomonas aeruginosa, 45% Staph .aureus and only 5% Klebsiella species (Fig 8). Among 40% cases preventive strategy was utilized to reduce PSI while in 60% cases no prevention was used (Fig 9). In 65% cases ceftriaxone was used alone while in 35% cases it was used in combination (Fig 10). In 40% cases ceftriaxone was used with Ascorbic acid while in 60% cases it was used with other combinations (Fig 11). As far as dose of Ascorbic acid is concerned, among 45% cases Ascorbic acid was used in 500mg dose while in 55% cases it was used in 1000mg dose (Fig 12). Results further showed that when Ceftriaxone was used alone/in combination with other antibiotic, the cost was high as compared to the cost of Ceftriaxone in combination with Ascorbic acid (Fig 13).



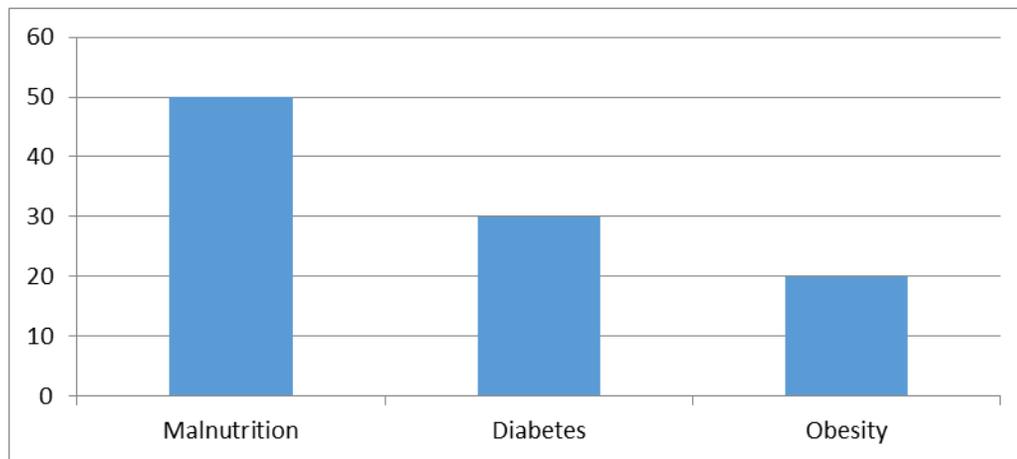
**Fig 1: Patients familiar with the term PSI.**



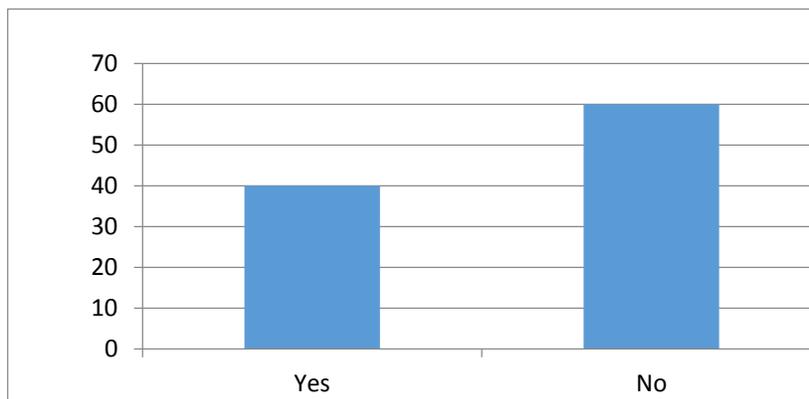
**Fig 2: Appearance of PSI in patients**



**Fig 3: Types of PSI.**



**Fig 4: Patients suffering from other problems.**



**Fig 5: Patients who were smokers**

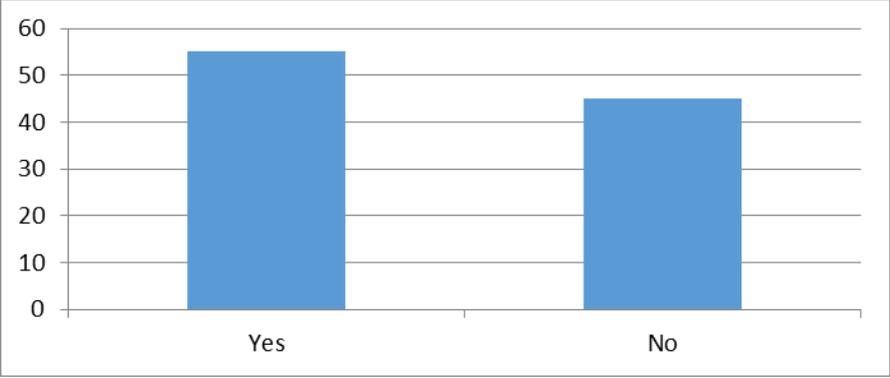


Fig 6: Patients using prophylactic treatment

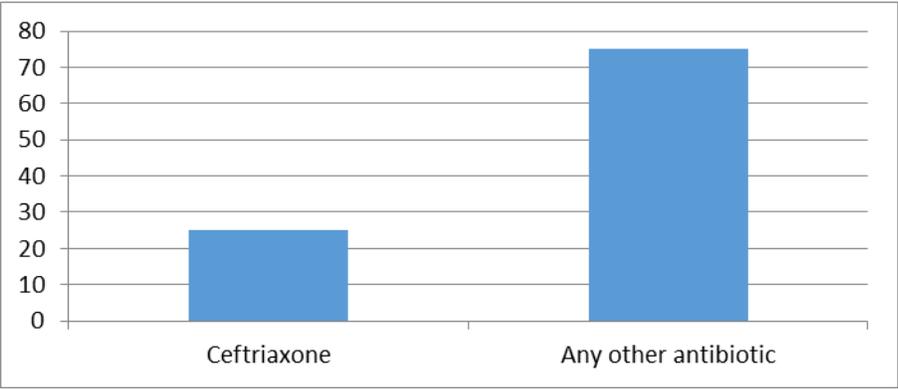


Fig 7: Prophylactic use of ceftriaxone and other antibiotics among patients.

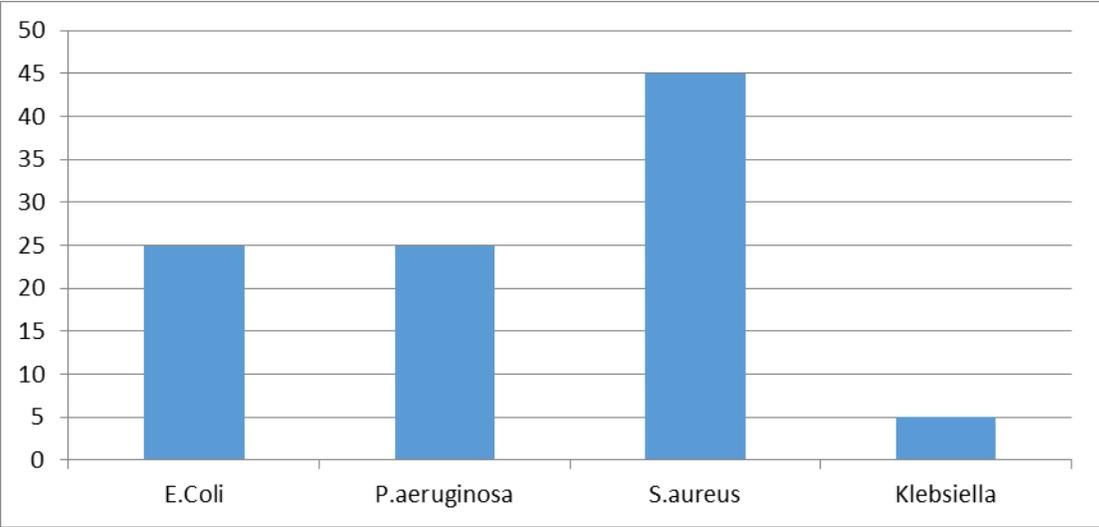
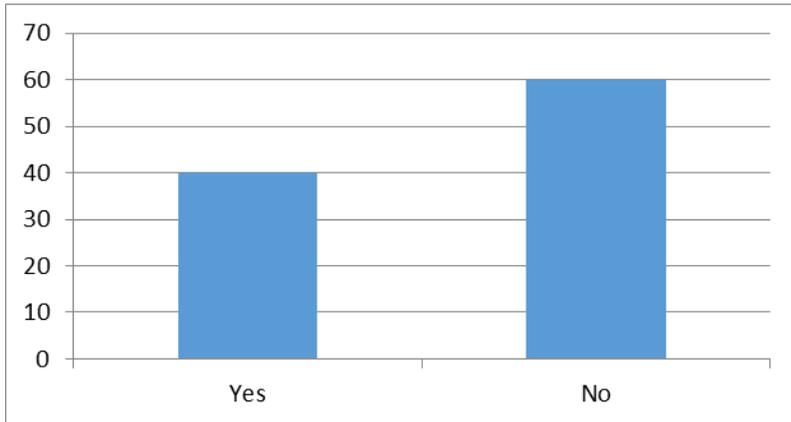
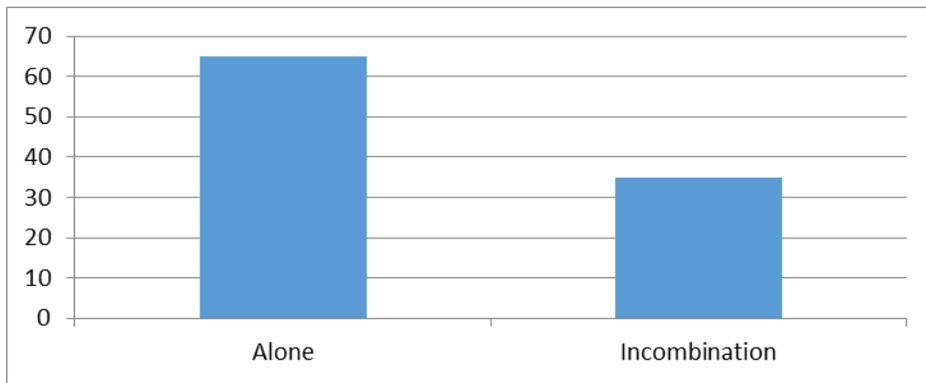


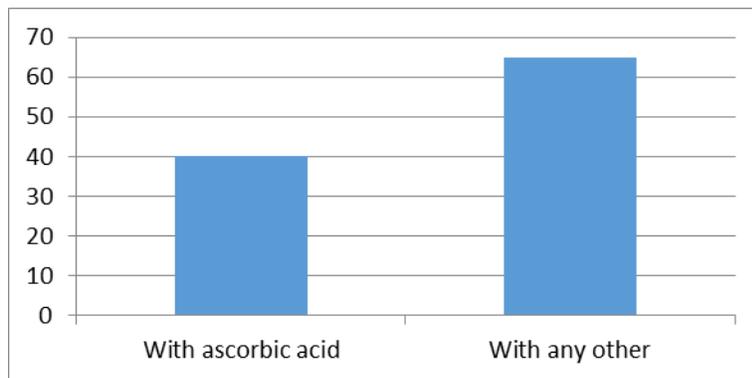
Fig 8: Pathogen causing PSI.



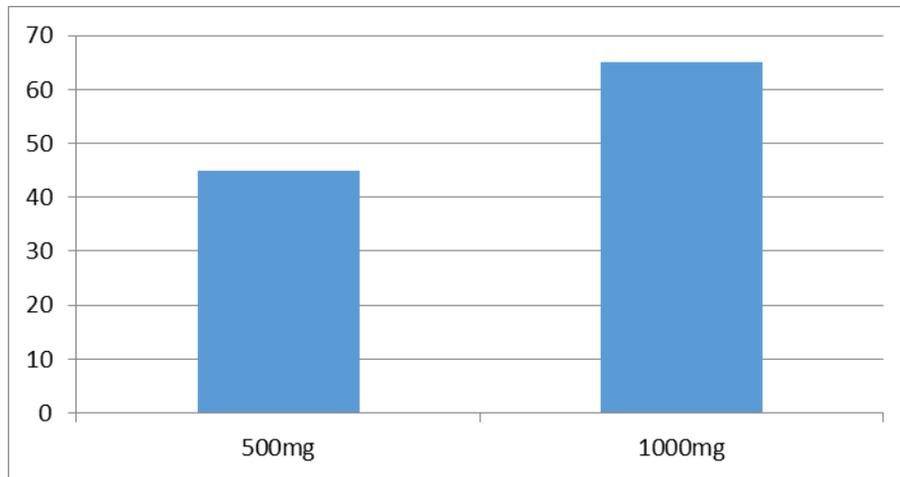
**Fig 9: Preventive strategy utilized to reduce PSI.**



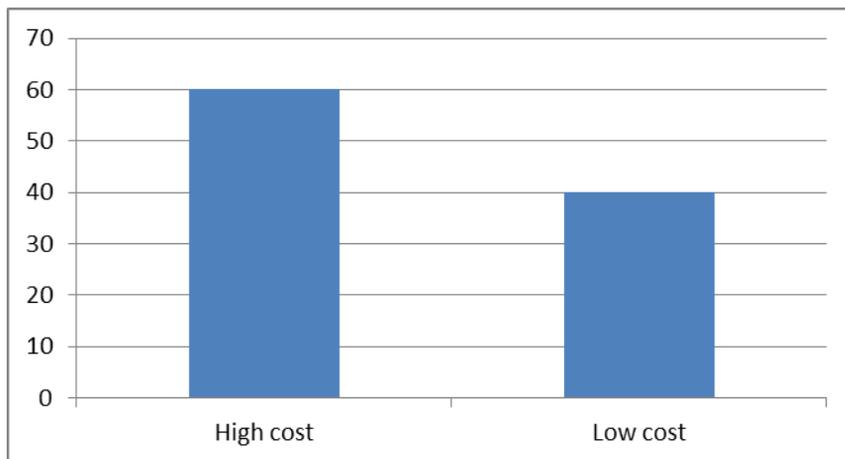
**Fig 10: Use of ceftriaxone alone and in combination.**



**Fig 11: Ceftriaxone used with Ascorbic acid and other combination.**



**Fig 12: Dose of Ascorbic acid used in**



**Fig 13: Cost of treatment**

## DISCUSSION

Infections that occur in the wound created by an invasive surgical procedure are generally referred to as PSI. Open injuries have a potential for serious bacterial wound infections, including gas gangrene and tetanus, and these in turn may lead to long term disabilities, chronic wound or bone infection, and death. A surgery is one of the most stressful procedures a patient could undergo, therefore a high risk of infections associated with surgical procedures. The use of prophylactic antimicrobial drugs before and after surgical procedures becomes imperative to reduce infection possibility [23]. Post surgical infections, also called surgical site infections are very common and have been frequently reported by several health care units worldwide. Patients undergoing surgery may develop surgical site infections within three months of surgery. PSI are responsible for 77% of deaths in surgically operated patients [24].

Poor wound healing and development of infection in incisional wound continue to be among most common complications of open surgery. Various bacteria contaminate the surgical wound and is treated by antibiotic loop suture for abdominal wall closure can decrease number of wound infection. The oxidative killing is most important defense against surgical pathogen. Thus increase in concentration of inspired oxygen preoperatively decrease incidence of wound infection [25]. Ascorbic acid is a popular antioxidant therefore its immune stimulant, anti-inflammatory, antiviral and antibacterial roles are well known so the

future studies will take into consideration for the research of new combinations of antioxidant natural substances and drugs. Deficiency of Ascorbic acid hinder wound healing. Ascorbic acid should be included in differential diagnosis of non specific bleeding in surgical patients. Prolonged hospitalization, severe illness and poor diet create Ascorbic acid deficiency with significant clinical consequence [26]. Wound healing complications is a clinical problem with a considerable burden. Oral nutritional supplements and enteral formulas providing arginine, glutamine and micro nutrients such as ascorbic acid and zinc improve healing of ulcer. Large doses of Ascorbic acid daily 1000 mg for three days before surgery and keeping high level maintained are utmost important to wound healing [27].

Orange juice intake can reduce patient discomfort in colonoscopy resulting in improved acceptability. Postoperative increase oxidative stress was overcome with consumption of antioxidant. Ascorbic acid decreases postoperative oxidative stress, systemic inflammation and lower fluid requirements after thermal injury therefore it has been adopted in many burn centers as an adjunct resuscitation [28]. Ceftriaxone plus administration of antioxidant provide better protection by decreasing oxidative stress limiting stay in hospital and improving survival. The effect of Ascorbic acid in Complex Regional Pain Syndrome (CRPS) in patient with distal radius fracture studied in America, and it was recommended that Ascorbic acid administration is of relatively low cost in useful in prevention of CRPS [29].

During the survey of hospitals, 100 patients both male and female of post surgical infection were visited. Out of 100 patients 40 were in private sector and 60 were found in public sector. In most patients PSI appeared within 30 days of surgery. Mostly patients had superficial infections. Patients of diabetes, cigarette smoking and obesity shown to have significant PSI prediction. The extent of PSI was doubled for obese patients and delay of wound healing. Infection rate increased with cigarette smoking, which increases the postoperative infection rate 5 folds. These observations are in line with previous studies [8]. Entry of E.coli in hollow viscera also responsible of these infections, although the pathogen isolated varies according to the surgical site. Abdominal surgical site infections are among the most common complications of inpatient admissions in hospital and have serious consequences for outcomes and costs.

Aseptic surgical techniques are claimed to decrease the infection rate, though not to zero. In the majority of PSI cases, the pathogen source is the native flora of the patient's skin, mucous membranes or hollow viscera, hospital environment, contaminated food, other patients, infected surgical instruments and dressings. However, the administration of prophylactic antibiotics before surgery, decreases the incidence of PSI. The causative agent or pathogen for PSI was found to be *Staphylococcus aureus*, this observation is in line with previous studies [7]. Some other species may also caused infections in surgically operated patients. It was observed that the first step in the treatment of PSI was preventive measure that was taken before surgery that was maintenance of the sterility factor, as mentioned in previous studies [4] [5] [6]. The contaminated bandages and disinfectant solutions were responsible for PSI.

To overcome the risk of PSI ceftriaxone prophylactically administered [16]. Ascorbic acid in high doses was found efficacious in improving endothelial function, reducing heart attack risk thus preventing and fighting the infections. Injections of mega doses of Ascorbic acid were successfully used in treating polio, diphtheria, herpes zoster, herpes simplex, chicken pox, influenza, measles and mumps. Ascorbic acid requirement increased in surgically operated patients. The potential advantage of supplementation to increase the plasma and tissue level of Ascorbic acid thereby reduced the oxidative stress.

## CONCLUSION

Post surgical infections have been estimated to occur in upto 15% of surgical patients and approximately 30% of patients whose surgical procedure was classed as contaminated or "dirty". Such infections lengthen bed stay which in turn increases cost of treatment morbidity and the possible long term consequences of a surgical procedure. *Staphylococcus aureus* is the causative agent in 15 to 20% of these infections. PSI is treated with ceftriaxone alone and in various combinations i.e antibiotic, NSAIDS, antioxidants and multivitamins. The most effective combination used in treating PSI was found to be ceftriaxone + Ascorbic acid. Strong antioxidant property of Ascorbic acid reduces the oxidative stress of the infection so healing of infection was so rapid that it decreases the hospital stay of the patient and

reduces the patient-treatment cost and also overcome the risk factors of PSI. Moreover, a higher level of sterility and prophylaxis will surely improve outcomes of surgery.

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