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Surgical Site Infection

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Abstract Surgical Site Infections (SSIs) are a serious public health concern. The SSI is a common postoperative complication that can occur anywhere in the body, including the site of the incision, the surgically operated organs or tissues, or other locations where surgical instruments were placed. Along with other pathogens obtained in the community or hospital, opportunistic endogenous bacteria can cause Surgical Site Infections (SSIs) by contaminating surgical wounds or implanted medical devices. A substantial cost on patients, healthcare providers and the healthcare system overall is linked to SSIs, which impacts 0.5% to 3% of surgical patients. When compared to patients without SSIs, SSIs may result in longer hospital stays. The rates of SSI remain surprisingly high, even though many laws and standards have been put in place to avoid these infections ; this puts the healthcare system at risk for morbidity and mortality. This review presents brief information about the incidence, microbiology, preventive strategies and management of these infections.

Key Words SSI, Wound infection, Surgical site infections, Post-operative Infections, Antimicrobial Resistance

INTRODUCTION

Surgical site infection (SSI) is that infection that appears at the site of the incision or close by up to 30 days (or for up to a year following implant surgery) following surgery [1]. In 1992, the US Centers for Disease Control and Prevention (CDC) coined the term "SSI" [2].

SSIs can be divided into three classes in accordance with the definitions provided by the CDC and National Healthcare Safety Network (NHSN) [1]:

- Superficial incisional: Affects subcutaneous tissues and skin
- Deep incisional: Impacts deeper tissues, such as fascia and muscle
- Organ and/or space infections that affect any part of the body other than the operative site

Incidence

One of the most prevalent healthcare-associated infections (HAIs) is SSI. It accounts for 29% of admitted patients and 38% of patients in surgical wards, making it the second cause of HAI [3]. The CDC reports that the annual rate of surgical procedures is relatively high. Approximately 0.5% to 3% of surgical patients will get an infection at or near the site of the incision [1].

SSIs are one of the largest financial strains on the healthcare system . Individuals with SSIs are more likely to experience surgical complications, longer stays in the ICU, disfiguring scars and hospital readmission. Patients with SSIs stay in the hospital for an additional 7 to 11 days [4,5].

SSI remains a significant cause of death and extended hospital stays even with advancements in infection control measures, such as better Operating Room (OR) ventilation, sterilization procedures, surgical methods and the availability of antibiotic prophylaxis. More specifically, SSIs account for 75% of SSI-related deaths and have a 3% mortality rate [6].

The operation type, the patient's condition, the surveillance criteria applied and the type of data gathered all have an impact on the incidence of SSIs. Several reports declared that for an elective clean operation the risk of SSI is about 1-3% [7].

The incidence of SSIs is higher in developing countries than in developed ones because of a lack of infection control procedures, inadequate sanitation and limited resources. In developed countries, the incidence varied from 1.2 to 5.2%. The decreased incidence may be due to recent developments in medical procedures, such as the introduction of less invasive surgeries with smaller incision sizes and quicker mobilization, improved security of patients' immune systems and a reduction in the use of central venous catheters for

parenteral nutrition. But in the USA and Europe, SSI continues to be one of the most common forms of HAIs [8].

There is extensive data on the prevalence of SSI in low middle-income countries (LMIC) and developing nations . The overall incidences of SSI in Africa were 20% while in South-East Asia and LMIC were 7.8%, 6.1% respectively . According to WHO reports, the rate of SSIs in LMICs was 11% on average (range: 1.2% to 23.6%) which was 3-5 times than developed countries and it was the most common HAI in LMICs [8].

There are no comprehensive statistics on the prevalence of SSIs in the Eastern Mediterranean Region (EMR). SSIs had a combined overall frequency of 7.9%. The rate is double that of the world. According to several studies, the prevalence of SSIs in Egypt varied between 18% and 30% [9].

Microbiology

The microbial contamination of the surgical site at the operation time, which may be obtained internally through the patient's skin flora or via an opening viscus, is what leads to the development of SSI. Moreover, it can be obtained externally via the surgical equipment, the OR environment, or the flora of medical professionals [10].

Between 70 and 95 percent of cases are caused by the patient's internal flora [11]. Among these are microorganisms that thrive on the skin or within the organ that has been operated on (e.g., gut bacteria in gastrointestinal surgery) [12].

After surgery, pathogens may occasionally infiltrate a wound before the skin has had a chance to close. Less commonly, germs from an unrelated source adhering to a prosthesis, implant, or other device left at the surgical site during surgery can cause SSI (primarily through hematogenous dissemination). Exogenous contamination risk is typically exacerbated by prolonged operating times [3].

Staphylococcus aureus, Coagulase negative *Staphylococci*, *Enterococcus* spp., *Escherichia coli*, *Acinetobacter* species, *Corynebacterium* spp. (diphtheroids), *Pseudomonas aeruginosa*, *Serratia marcescens* and anaerobic bacteria like *Bacillus fragilis*, *Peptoniphilus* spp. and *Prevotella* spp. are common organisms isolated from patients with SSI [13].

About 30% of all SSIs are caused by *S. aureus*, which is found on the skin or anterior nares of about 80% of healthy individuals. About half of the cases are caused by strains of Methicillin-resistant *S. aureus* (MRSA) [4,14]. Methicillin-sensitive *S. aureus* (MSSA) infections were more common from 2013 to 2018 compared to MRSA infections, even though MRSA was previously more likely to cause SSIs [15].

The microbiological profiles of SSI are influenced by the kind and location of surgical procedures. Infections caused by *S. aureus* are more commonly associated with patients undergoing cardiac, neurosurgery, breast and orthopedic surgeries, as well as those receiving grafts, implants, or prostheses, whereas Gram-negative bacilli infections are more commonly associated with patients undergoing appendectomy, urologic, colorectal, gynecologic and obstetric procedures. Through the entry of hollow viscera, surgery exposes the surrounding tissue to Gram-negative bacterial infections and, on occasion, anaerobes [15].

Both monomicrobial and polymicrobial SSIs are possible. Mixed aerobic and anaerobic microorganisms often cause polymicrobial illnesses in the oropharyngeal, perineum, axilla and GIT regions. *Candida* species of yeasts have the potential to cause polymicrobial SSIs [3].

Pathophysiology

The presence of foreign material, the extent of bacterial contamination of the wound, the use of antibiotic prophylaxis and the host's capacity to manage the inevitable bacterial contamination of the incision are some of the factors that affect the acquisition of an SSI. They are frequently caused by microbes that are introduced into the surgical site during the procedure [16].

Occurrence of SSI Depends on 4 Factors

Bacterial load or inoculum

The female genital tract (10^6-10^7 bacteria/ml) and the gut (10^3-10^{12} bacteria/gm), which are heavily populated with bacteria, are surgical sites that are more likely to experience SSIs. This is because a large inoculum of bacteria can contaminate the wound site during surgery. When microbial concentration exceeds 10^4 microbes per gram of tissue, there is usually a significant risk of an infected wound [17].

Bacterial virulence

Infection is more likely to occur when bacteria are more virulent. The virulence factors of bacteria include the type of endotoxins, lipopolysaccharide composition, or exotoxins present in their cell walls respectively. Only a small amount of *S. aureus*, *Clostridium perfringens* and *St. pyogenes* is needed to cause severe necrotizing infections at the surgical site. Anaerobic bacteria (*Bacteroides fragilis*) and colonic Gram-negative (*E. coli*) bacteria work in concert to produce greater virulence than when both species are present at the same time in critical inoculum counts at the surgery site [3].

The pathogenicity factor of bacterial contaminants is the best strategy to interpret the antibiotic resistance. Patients who are admitted to chronic care facilities, have recently consumed antibiotics to treat other infections, have recently been hospitalized for other reasons, or have had a lengthy preoperative hospital stay will have more virulent microbes colonizing them than any other patient undergoing surgery. Therefore, one might anticipate that their chances of having SSI will be higher [3].

Microenvironment around surgical site

Even with a decreased bacterial load, the presence of necrotic tissue, foreign objects, or hematoma at the incision site enhances the risk of infection. After the wound is closed, the

dead area in the surgical incision acts as a dependent basin to collect serosanguinous fluid. Afterwards, this drainage basin has bacterial pollutants in a moist environment that are challenging for the host's immune system or inflammatory response to successfully fight [18].

Host defenses

The host tissue's reaction is essential. An acquired disruption of the host's immune and inflammatory response is likely to result from a variety of factors. These acquired factors may include chronic disorders such as diabetes mellitus and chronic organ illnesses. Additionally, other acute conditions like hyperglycemia, hypothermia, hypoalbuminemia, hypoxemia, or acute anemia are associated with an increased risk of SSI. Complement activation will continue if secondary infection or wound contamination persists and new pathways with a steady flow of chemotactic factors may appear. This will increase the number of polymorphs that enter the wound. Monocytes contribute to a proinflammatory response by secreting a variety of powerful cytokines. They generate serotonin, which causes vasodilation and vascular permeability to increase. Increased arterial permeability and intense vasodilation produce the typical clinical manifestations of inflammation, including redness, swelling and pain [3].

Clinical features

SSIs' median time to diagnosis varies according to the procedure. It often manifests 2-7 days following the procedure, while they can manifest later with any prosthetic device or implant. *S. aureus* infections are generally identified 14 days, 24 days and 28 days, respectively, following plastic surgery, general orthopedic surgery and orthopedic procedures where a prosthetic device was implanted [15]. Physical examination of the surgical site may demonstrate local erythema, discomfort, wound dehiscence and oedema. About two-thirds of all SSIs have purulent discharge. Purulent discharge at the incision site or signs of an abscess affecting the surgical bed are indicators that SSI is present [3].

Symptoms of a deep-seated infection typically have a widespread constitutional nature. In fewer instances, patients may potentially get end-organ failure and severe sepsis. Deep infections frequently lack obvious superficial symptoms, making a diagnosis a guess. Pus may be seen coming from a drain during an organ or space SSI. Collection of such purulent discharge and decomposing tissue that is encircled by inflammation and epithelium form abscess [3].

Many variables, including the surgical site, the host and the interval between the operation and presentation, affect whether there are any symptoms or not [6] (Figure 1).

Risk factors

Numerous intrinsic patient- and extrinsic procedure-related risk factors are known to impact the onset and course of SSI.

The procedure-related risk factors

According to the CDC's definition, surgical wounds are often classified into four types based on how clean or infected they are [19]:

- **Class I:** Clean wound; infection risk <2%; e.g., laparotomies, breast resections and vascular procedures
- **Class II:** Clean/contaminated wound; infection risk <10%; e.g., laryngectomy, small bowel resection and elective cholecystectomy
- **Class III:** Polluted wound: 20% chance of infection, e.g., appendiceal phlegmon or gangrenous cholecystitis

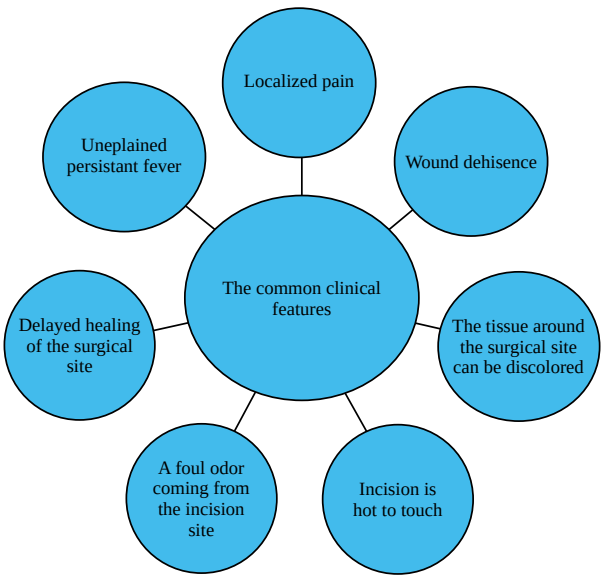

Figure 1: The common clinical features of SSI

- **Class IV:** Unclean or infected wounds with an infection risk >40%; e.g., testicular abscess and infected traumatic wounds

Procedure-related risk factors includes wound microbial infection, the type of surgical intervention, the surgical site and the level of pre- and postoperative care [3].

The length of the operation, the complexity of the surgical procedures, the length of pre-operative hospital stays and the kind of surgery (emergency or elective) are all associated with SSIs. According to European surveillance research (2010-2011), the largest cumulative incidence of SSI in patients is associated with colon surgery (9.5%), followed by coronary artery bypass graft (3.5%) and caesarean delivery (2.9%) [20]. The clinical state of the patient and the level of wound contamination are additional procedure-related risk factors [21].

Patient-related Risk Factors

Age, sex, lifestyle, body mass index, smoking, comorbidities, low serum albumin concentration, diabetes, pre-existing infections, antibiotic use and surgical history are among the patient-related risk factors for SSI [22].

Age

As the skin ages, its basement membrane and dermis shrink, its supply of blood vessels and nerves is depleted and its immunity is weakened, all of which reduce the skin's capacity to repair [23].

Foreign Bodies

Exogenous bacteria can hide from the host's defenses by growing on the surface of foreign items like medical implants, which also serve as a reservoir for them [3].

The surface provided by sutures is favorable for adhesion, biofilm formation and bacterial colonization. It is well known that multifilament sutures have a higher density of bacterial cells than monofilament sutures, even though the interstices on suture knots provide a sizable surface area for bacterial development and colonization. According to a study comparing absorbable and non-absorbable sutures used in dento-alveolar surgery, biofilms were more likely to form non-absorbable sutures [24] (Table 1).

Nutrition

In surgery, malnutrition is a common problem that affects both the patient's health and the outcome of the operation. It causes poor tissue repair, granulation tissue to form in surgical wounds, changes in body composition and a decrease in collagen synthesis [15].

Innate immunity is weakened by hypoalbuminemia, which also causes macrophage death and decreases macrophage activation. Additionally, low albumin promotes tissue oedema and speeds up interstitial fluid seepage into the surgery site [25].

Table 1: Risk factors for SSIs

Patient related	Operation related
Age	Airborne contamination
Malnutrition	Blood transfusion
Obesity	Anticoagulation
Immunosuppressive medication & condition	Decreased tissue oxygenation
Diabetes	Foreign materials
Tobacco use	Preoperative hypothermia
Preoperative infections	Perioperative hyperglycemia
Prior skin and soft tissue infections	Surgical technique
Prior radiation therapy	Duration of the operation
	Subsequent wound care
	Wound contamination

Malnutrition was found to be a significant risk factor for SSIs . On the other hand, obesity (BMI >30) has a variety of effects on the healing of wounds. The SSI rate was 4.66% for those with a BMI of 20 to 25, 7.06% for those with a BMI of 30 to 40 and 10.58% for those with a BMI of 40 or above [16].

High metabolic demands are required for tissue healing and a lack of oxygen slows down the entire process. High oxygen is needed by immune cells to produce antimicrobial reactive oxygen species. Achieving an adequate antibiotic concentration for perioperative prophylaxis is more challenging in obese patients. Higher dosages of medication are needed to reach the same serum levels as in non-obese people due to the larger distribution volume. All those factors have an adverse effect on the postoperative wound healing process for obese patients [26].

Immunosuppressive Therapy

It has been demonstrated that immunosuppressive drugs lower inflammation, impede wound healing and raise the risk of infection. However, discontinuing immunosuppression could make the underlying illness worse [27].

SHEA (Society for Healthcare Epidemiology of America) guidelines advise discontinuing immunosuppressive medication before surgery, if possible [28].

Blood Transfusion

The American College of Surgeons (ACS) defines a substantial blood loss as a loss of 30-40% of the Total Blood Volume (TBV). Perioperative blood loss results in a significant loss of proteins, coagulation factors and antibodies in addition to circulatory failure. Contrarily, blood donation in humans triggers two distinct immunological reactions, namely immunosuppression and immunization. It most likely happens when humoral immunity rises and cell-mediated immunity declines. It was determined that receiving blood transfusions increased the frequency of Th2 cells in comparison to Th1 cells, lowered their cytotoxic activity and altered the ratio of CD4+ to CD8+ cells [12].

Ssis Prevention

Infection prevention strategies emphasize bacterial load reduction, host optimization, the operational environment and

patient-specific modifiable risk factors. Up to 60% less SSI can be obtained by following evidence-based recommendations [16].

Preoperative Phase

Surgical Site Shaving

Safety razor use has been shown to cause epithelial microinjuries, which raises the risk of infection. If hair removal is necessary, it is best to use a clipper or an electric razor with a single-use tip in the preoperative holding area rather than in the operating room (4.4% with razors vs. 2.5% with clippers) [29].

Antibiotic Prophylaxis

Antibiotic prophylaxis is recommended for both clean/contaminated wounds and clean wounds with foreign items implanted. Instead of a prophylactic dosage for dirty and contaminated wounds, the patient should receive an entire course of antibiotics [12].

The NNIS (National Nosocomial Infections Surveillance) scale is commonly used for determining the requirement for perioperative antibiotics. It has three attributes. The first feature is the grading of wounds based on their risk of infection. The patient is then evaluated using the American Association of Anesthesiologists' (ASA) score. The length of the surgery is the third feature.

The patient should receive antibiotic prophylaxis when necessary. Although a single dose is optimal, more doses can be required based on the procedure's duration, the drug's half-life, or significant blood loss . The antibiotic should typically be effective against anaerobes, Gram-negative bacteria and MRSA. The most used antibiotic for prophylaxis is cefazolin, which is effective against all pathogens besides anaerobes [5,30].

In order to prevent SSIs, dual antibiotic prophylaxis (oral+intravenous) works better. Combination therapy has a 4.14-6.87% risk of SSI compared to intravenous (12.76%) or oral (7.95%) routes alone; the differences are statistically significant [31].

Antimicrobial prophylaxis prior to surgery does not lead to drug resistance in microorganisms. To maximize the concentration of antibiotic in tissues, the antibiotic should ideally be administered during the induction of anesthesia, 30 to 60 minutes before the skin incision. The administration time should be extended to 60-120 minutes when vancomycin or fluoroquinolones have been selected as antibiotic prophylaxis [32].

Long-term use of antibiotics is increasingly associated with patient assault such as acute renal injury, even though the ideal period of prophylactic antibiotics is unknown. According to CDC recommendations, prophylactic antibiotics should be stopped when the surgical site has sealed [6].

Decolonization

Decolonization is one technique used to lower the risk of SSIs. Patients are given an intranasal antibacterial, a topical antiseptic, or both to temporarily remove or minimize *S. aureus* colonization prior to surgery (0.8% with decolonization versus 2% without). This procedure can be done by using an anti-staphylococcal skin antiseptic (e.g., chlorhexidine gluconate solution or wipes), as well as receiving an intranasal treatment with an anti-staphylococcal agent (such as povidone iodine or mupirocin ointment) for 5 days [5,15].

The decolonization plan should be finished as soon as the surgery is performed. According to numerous studies, nasal decontamination was linked to a lower incidence of SSIs brought on by Gram-positive bacteria than when decolonization was not performed [33].

However, in other trials with a more varied spectrum of surgeries, the incidence of SSI with decolonization remained unchanged. Hence, decolonization frequently concentrates on orthopedic, cardiothoracic, or high-risk operations including spine and brain surgeries [34].

All patients having high-risk surgical operations undergo decolonization at several hospitals. Contrarily, widespread usage of anti-staphylococcal drugs like mupirocin may eventually lead to a rise in the number of infections caused by resistant *S aureus* [35].

The WHO's Surgical Safety Checklist

It is a 19-item list designed to increase best practice commitment and improve surgical outcomes in under-resourced settings. This safety check list was created by WHO to encourage best practices to be applied more consistently. Both SSI and non-SSI items were included in this 19-item checklist. According to multicenter research, the infection rate was 6.2% prior to the checklist's implementation and 3.4% after it was put into place. Further multi- and single-center prospective investigations have backed up these findings [16] (Figure 2).

Intraoperative Phase

Operating Room Architecture

Every surgical hospital's OR serves as its beating center. The purpose of OR is to uphold the most hygienic and sanitary standards. Limiting the pathogen contamination over all surfaces is the basis of an effective microbiological regime. Zones for increasing sterility should be present in a well-constructed OR. To reduce hospital pathogen contamination of the OR environment, workers should move through cleaning zones. Distinguishment between "clean" and "dirty" portions is the core principle of OR organization. According to the one direction rule, "clean" and "dirty" pathways cannot intersect [12].

According to the surgery type, The OR's air conditioning system should provide enough fresh air and the proper exchange volume, often 15 to 30 times the room volume. Additionally, laminar air flow should be established to divide the operational field from the clean zone [12].

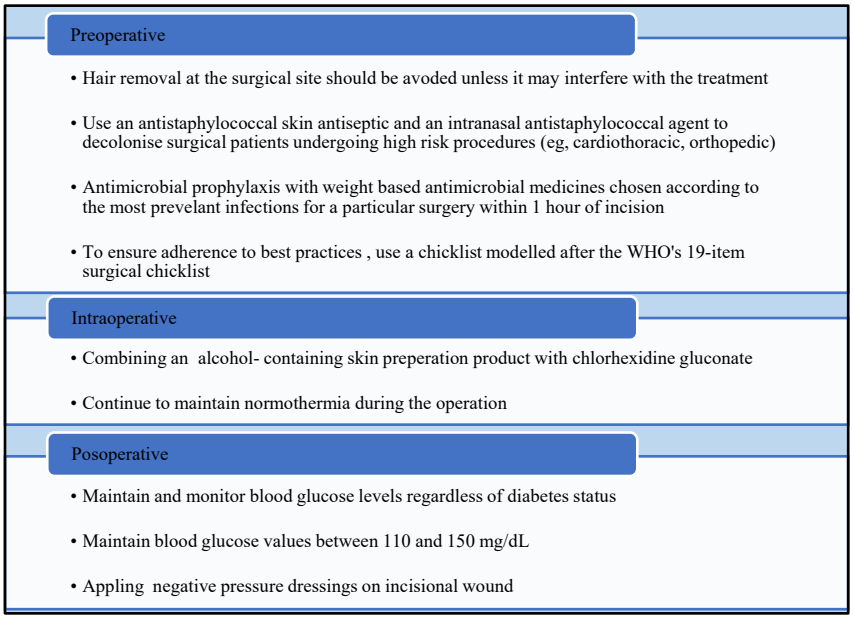

Figure 2: SSI preventive strategies

Surgical Field Asepsis

The objective of surgical field asepsis is to lessen the quantity of possible pathogens that are already present on the skin and to restrict their ability to proliferate both during and after surgery. Although topical alcohol has a strong bactericidal effect, its effectiveness is short-lived. Many guidelines advise using a product that comprises alcohol and another antiseptic agent when doing surgical site antisepsis. Alcohol solutions of chlorhexidine and gluconate povidone iodine are the two most often utilized preoperative skin decontamination [36].

Alcohol causes bacterial cell lysis and desaturates proteins. It works well against enterococci resistant to vancomycin, methicillin-resistant *S. aureus* and Mycobacterium tuberculosis [37].

The bacterial cell wall's phosphorus-containing proteins adsorb chlorhexidine. In bacteriostatic concentrations, it enters the cell and destroys the membrane, allowing cytoplasmic leakage. In bactericidal quantities, it enters the bacterial cell, where it forms an irreversible bond with the ATP and nucleic acids. Chlorhexidine can also neutralize some viruses and exhibits fungistatic and fungicidal characteristics. Because chlorhexidine has a greater affinity for Gram-positive cell walls, Gram-positive bacteria have lower minimal inhibitory concentrations than Gram-negative bacteria. The bactericidal range of chlorhexidine can be expanded by mixing it with isopropyl alcohol, povidone iodine, or ethanol [38].

Povidone iodine has 1% free iodine in its solution. Iodine molecules enter cells through the cell wall, where they oxygenate cysteine and iodinate unsaturated fatty acids and amino acids, reducing protein synthesis and damaging the cell wall. Gram-positive and Gram-negative bacteria, certain spore-forming bacteria, Mycobacteria, viruses and fungus can all be killed by iodine [39].

Chlorhexidine and povidone iodine have similar antibacterial spectra, according to research, but chlorhexidine has a longer-lasting effect because it forms a covalent interaction with the proteins in the skin and mucous membranes. It is commonly used to preserve vascular catheters because, unlike povidone iodine, it isn't affected by blood or other bodily fluids . For the prevention of SSIs, chlorhexidine gluconate plus alcohol is superior to povidone iodine plus alcohol [40] (Figure 3, Table 2).

Hand Disinfection

Medical staff members' hands may harbor bacteria that cause HAIs. Gram-negative bacilli and *S. aureus* make up most of the bacteria in the superficial skin bacterial flora. Chlorhexidine solution reduces the number of microorganisms, which ensure surgical sterility. The logarithmic decline in the number of microbes is used to gauge the efficacy of disinfection [41].

The US Food and Drug Agency (FDA) defines effective disinfectants as those that reduce the bacterial count by one logarithmic unit (logarithmic unit) in one minute and by two logarithmic units (logarithmic units) over five minutes. Products with chlorhexidine and alcohol are regarded as the most effective since they combine alcohol's quick start with chlorhexidine's long-lasting effects [40].

Maintaining Patients' Homeostasis

The ECDC 2017 Guidelines stated that both diabetic and non-diabetic patients should have perioperative glucose levels below 200 mg/dL. All surgical patients, not just diabetics,

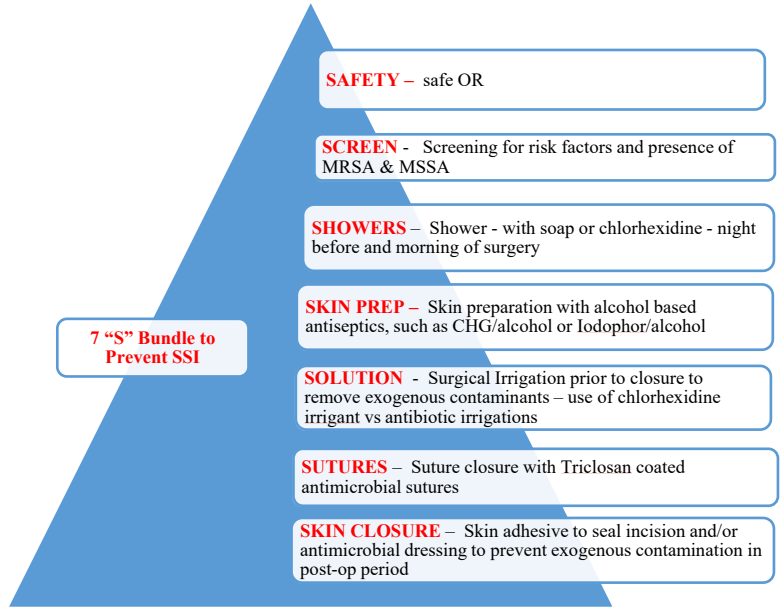

Figure 3: 7 "S" Bundles to prevent SSIs

must have their blood sugar levels monitored. For 48 hours following surgery, hyperglycemia >180 mg/dL is linked to an increased risk of complications, including SSIs [42].

The body's temperature should be kept within normal range . A temperature drop of 1.6°C results in poor peripheral circulation, substantial intraoperative blood loss and coagulation issues. SSIs can also be facilitated by hypothermia (4.7% with active warming vs. 13% without). Keeping the body temperature above 36°C is the aim of normothermia. It may keep going with a combination of warmed intravenous fluids, cutaneous warming and forced heated air [5,43].

Patients with normal respiratory function who receive general or endotracheal anesthesia during surgery and immediately after extubation should receive increased forced inspiratory oxygen (FiO2) . Throughout the surgical operation, blood oxygen saturation (SpO2) was 95%. Perioperative normothermia and sufficient volume exchange should be offered to maximize oxygen supply [28].

Postoperative Phase

Control Hyperglycemia

Postoperative hyperglycemia was linked to an increased risk of SSIs in patients with and without diabetes, even though no random clinical trials have investigated the efficacy of intensive glucose control in reducing preoperative average glucose (haemoglobin A1c) prior to surgery in comparison to standard care [44].

For the prevention of SSI, all significant guidelines recommended avoiding postoperative hyperglycemia. In a meta-analysis comparing the use of tight glycemic control (150 mg/dL) with conventional control (>150 mg/dL), tight control was associated to lower rates of SSIs for the following reasons: 9.4% versus 16% [45].

Wound Hygiene

After surgery, wound hygiene is essential . The gold standard is to use "non-touch" procedures to avoid dealing with wounds and bandages with bare hands. The wound should be rinsed with sterile saline [46].

Negative Pressure Wound Therapy

Incisional negative pressure wound therapy is the practice of using a system for dressing a wound that continuously or sporadically applies a lower pressure than atmospheric. It enhances the healing of primary wounds by decreasing fluid accumulation in the wounds, promoting angiogenesis to increase blood flow to the wound and accelerating the formation of granulomatous tissue [16].

It was found that using incisional negative pressure wound care for primary wound closure was associated with lower rates of surgical site infections (SSIs) compared to using conventional bandages (9.7% vs. 15%) [47].

SSI Surveillance

The aim of various surveillance techniques is to reduce SSIs. After 24 to 48 hours following surgery, a doctor, nurse, or infection control specialist will monitor the surgical site every day as part of the direct technique. Although it is the gold standard for studies, its resource usage requirements and practical impracticality make it hardly employed in actual life [28].

Table 2: Some of CDC approved strategies for prevention of SSI

Evidence	Recommended strategies	Category
Parenteral Antimicrobial Prophylaxis	It should be administered only when indicated	IA
	It should be timed (30-60 min of incision)	IB
	In clean and clean-contaminated procedures, No additional prophylactic antimicrobial agent postoperatively ,even in the presence of a drain	IA
Removal of hair	No hair removal unless it will interfere with the operation	II
Non-parenteral Antimicrobial Prophylaxis	No antimicrobial agents (i.e., ointments, solutions, or powders) to the surgical incision	IB
	Use of triclosan-coated sutures	II
Glycemic Control	Implement intraoperative and perioperative glycemic control less than 200 mg/dL in patients with and without diabetes	IA
Smoking	Encourage smoking cessation within 30 days of procedure	I
Normothermia	Maintain perioperative normothermia	IA
Oxygenation	administer increased FIO2 during surgery and after extubating in the immediate postoperative period for surgical procedures involving mechanical ventilation	IA
Decolonization using anti-staphylococcal agent	Use anti staphylococcal agent in the preoperative setting for high-risk procedures	II
Antiseptic wound lavage	Dilute povidone-iodine lavage of the surgical wound	II
Hand antiseptic for surgical team	Preoperative hand/Forearm antisepsis prior to every procedure	I
Antiseptic Prophylaxis	Perform intraoperative skin preparation with antiseptic unless it is contraindicated	IA
	Advise patients to shower or bathe with soap (antimicrobial or nonantimicrobial) or an antiseptic agent on at least the night before the operative day	IB
	Consider intraoperative irrigation of deep or subcutaneous tissues with aqueous iodophor solution for the prevention of SSI	II
Use impervious plastic wound retractors	Facilitate retraction of an incision without the need of mechanical retractor (For GIT and biliary tract surgery)	I
Operation time	Minimize as much as possible	I
WHO Checklist	Improve adherence with best practice	I
Blood Transfusion	Do not withhold transfusion of necessary blood products from surgical patients	IB
OR ventilation	Maintain positive pressure ventilation	I
Perform surveillance for SSI	Identify high risk, high volume operative procedure. Identify , collect , store analyze data needed for surveillance	IB
Sterilization of surgical instruments	Sterilize all surgical instruments	I
Use automated data for surveillance	Increase the efficiency of surveillance	II
Observe and review practice in the post-anesthesia care unit, ICU, surgical wards	Provide feedback and review infection control measures with staff	II

Category IA: A strong recommendation supported by high to moderate quality evidence
Category IB: A strong recommendation supported by low-quality evidence
Category IC: A strong recommendation required by state or federal regulation
Category II: A weak recommendation supported by any quality evidence

The indirect approach of SSI surveillance combines the following: (i) Examination of microbiological reports and patient health records, (ii) Surveys of doctors and/or patients, (iii) Screening for readmission and/or a return to the OR, (vi) As well as other data, including prescribed antimicrobials, diagnoses and procedures. Infection control

specialists can easily conduct the indirect way because it takes less time. When compared to the gold standard direct surveillance, it is more dependable. Hospital datasets can be used to increase SSI surveillance. These techniques lessen the infection control specialist work while increasing the sensitivity of indirect surveillance for SSI identification [28].

It has been shown that post-discharge surveillance that has low sensitivity and specificity is based on data from patient and surgeon questionnaires. Whatever the approach, the implementation of post-discharge surveillance techniques frequently results in an increase in the overall institutional SSI rate by making reporting more comprehensive [28].

Antimicrobial resistance and SSIs

Antibiotic-resistant bacteria have started to appear in healthcare institutions all around the world because of improper antibiotic use. WHO cautioned that if the issue is not under control, antibiotic-resistant bacteria could pose serious hazards to human health [48].

Antibiotic resistance characteristics are acquired by bacteria through intrinsic, acquired and adaptive mechanisms. The term "intrinsic antibiotic resistance" describes the inherent characteristics of bacteria that result in resistance to any antibiotic class. For instance, Gram-positive bacteria are considerably more sensitive to β-lactam antibiotics than Gram-negative bacteria. Gram-negative bacteria have a lipopolysaccharide cell wall, which serves as a physical barrier to keep hydrophilic β-lactam drugs out and confers inherent antibiotic resistance [49].

Conversely, acquired antibiotic resistance occurs when bacteria become resistant to antibiotics that were once-effective due to changes in cellular physiology, the adoption of foreign genes encoding antibiotic resistance through horizontal gene transfer, or mutations in the drug targets [50].

Adaptive antibiotic resistance occurs when bacteria develop resistance to antibiotics in a temporary, reversible manner because of metabolic changes, changes in gene/protein expression profiles and changes in environmental stress in the presence of antibiotics [49].

First-generation cephalosporins and anti-staphylococcal penicillins are common antimicrobial treatments for MSSA SSI, while vancomycin is the standard antibiotic used for MRSA SSI [50].

While vancomycin-containing antibiotic prophylaxis has reduced SSI rates, vancomycin alone has been associated with a higher risk of MSSA in individuals who test negative for MRSA. Thus, routine vancomycin antibiotic prophylaxis therapy in MRSA-negative patients is not advised. The proportion of SSIs caused by MRSA has increased from 9.2% to 63.5% since the superbug's introduction, depending on postoperative antibiotic policies and surveillance programs at various healthcare settings. There aren't many medication options available to treat MRSA infections [51].

Multidrug-resistant (MDR) strains of *P. aeruginosa* and *E. coli* are frequently involved in SSI cases. Cefuroxime-resistant bacteria were detected in 68.6% of orthopedic-related SSIs at a major teaching hospital in China. The most prevalent multi-drug-resistant HAI among ICU patients in South-East Asia were found to include MRSA, vancomycin-resistant enterococci (VRE), extended-spectrum-lactamase (ESBL)-producing organisms, MDR *A. baumannii*, MDR *P. aeruginosa* and MDR *Klebsiella pneumoniae*.

SSIs caused by MDR bacteria often result in prolonged hospital stays, increased mortality and readmission rates, higher costs and more difficult treatment. Patients and the healthcare system are stated to be seriously at risk due to high rates of SSIs caused by MDR bacteria [52].

Antimicrobial sutures

Antimicrobial-coated sutures are recommended by numerous organizations as a prophylactic step against SSI. The WHO and CDC guidelines on minimizing the risk of SSI recommend the use of triclosan-coated sutures regardless of the kind of surgery [8,36].

Triclosan-coated sutures were shown to be more successful than non-antimicrobial sutures at preventing SSI in several clinical studies and meta-analyses. Antiseptic-impregnated sutures are not recommended for routine use as a preventative measure against SSI by the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) guidelines since it is unclear how they may impact the emergence of antiseptic medication resistance [10].

The first antimicrobial suture approved by the FDA for clinical use is braided polyglactin 910 coated with triclosan (Vicryl Plus). Moreover, a variety of sutures made of chlorhexidine have been commercially available for veterinary use. The goal of every healthcare professional is to have a zero SSI rate. The perfect surgical suture should not cause harm to the host, not trigger inflammation and simultaneously reduce the rate of SSIs. The most effective wound care results using antimicrobial sutures would come from a combination of aseptic technique and adherence to infection control procedures in healthcare settings [4].

Biofilm-associated Infections

According to the National Institutes of Health (NIH), biofilm-forming bacteria are thought to be responsible for about 80% of SSIs, including persistent wound infections [17].

The multilayered structure known as a biofilm is composed of microbial populations embedded in extracellular polymeric matrixes comprising extracellular DNA, proteins, lipids, metals, enzymes and polysaccharides [53].

Comparing the microbial communities in the biofilm to their planktonic counterparts, the biofilm’s microbial populations exhibit increased resistance to antimicrobial therapy (up to 1000-fold). Numerous mechanisms have been implicated in the increased antibiotic resistance of bacteria

submerged in biofilms. Selecting the best antimicrobial therapy for MDR bacteria can be challenging by several factors, including (i) Ineffective infiltration of antimicrobials via the biofilm matrix, (ii) Modified physiological reactions of microorganisms to the diverse environment of the biofilm, (iii) The apperance of persister or dormant cells and (iv) The existence of polymicrobial communities in a biofilm (i.e., co-infection of bacteria and fungi). Also, because diverse bacterial species can coexist in proximity in biofilms, this may make it easier for plasmid exchange or the spread of genes expressing drug resistance to spread throughout the microbial populations [54].

Even with systemic antibiotics, biofilms on implanted medical devices (such catheters, implants and surgical sutures) are difficult to be removed . Surgical intervention is necessary to manage infected tissues and implanted medical devices [17].

S. aureus is known to be a significant contributor to biofilm-associated infections in medical devices and exhibits a strong potential to colonize new surfaces [24].

Quorum sensing and numerous genetic variables influence the production of biofilms, a process involving bacterial adhesion, accumulation, maturation and dispersion. The density of a biofilm depends on the kind of bacteria, the nutrients that are available and the charges on the cell surface. Due to the widespread development of antibiotic resistance in clinical settings, there are few options for treating *S. aureus* biofilm-associated illnesses [17].

Inhibiting *S. aureus* virulence may be a promising treatment for *S. aureus* biofilm-associated infections since it is anticipated to have a lower selective pressure for antibiotic resistance [24].

Biofilm-associated SSIs are very challenging to treat with standard antibiotics because the MDR bacteria, which are typically structured as polymicrobial communities, have multiple tolerance mechanisms [17].

Management

The management of SSI typically involves a combination of medical and surgical interventions. The extent of the infection and the patient's general health will determine the strategy used.

- Evaluation is required to determine the risk variables that affect the healing of surgical wounds before, during and after surgery
- Dead space should be minimized to the greatest extent practicable. Moreover, delicate tissue handling and sparing use of electrocautery should lessen wound damage
- After surgery, the patients should shower and wash their body with soap 48 hours later
- According to published guidelines, more proof is still required to show that topical and local antibiotic therapy, such as antibiotic irrigations, antimicrobial-impregnated dressings and wound sealants, may decrease the incidence of SSI
- The bacteria in antiseptic-impregnated dressings exhibits a bacteriostatic action when the antiseptic agent is released into the wound. Because microorganisms stick to the dressing materials and are then physically removed from the wound when the dressing is changed, certain dressings utilize passive antimicrobial ways
- Hyperbaric oxygen therapy (HBOT) may be helpful for open surgical wounds

It is crucial to note that the treatment of SSI should be customized for each patient based on the specific infection circumstances. Therefore, to maximize the management of SSI, a multidisciplinary strategy comprising surgeons, infectious disease specialists and other medical professionals is frequently required.

Treatment

Treatment modality in SSIs varies depending on whereas infection is tissue based, or device based. In tissue-based infection, the infected region must be opened and the pus drained [12].

Deep incisional SSIs frequently necessitate surgical debridement, full drainage and frequently adjuvant antibiotic treatment, but superficial SSIs are usually simpler to treat and just require simple opening and partial drainage. Intracavitary SSIs usually necessitate surgery [17].

A gentle vacuum pump may help wound healing by drawing fluid and infection out of it and encourages the formation of new tissue. After these treatments, irrigation-ideally with an antiseptic-and parenteral antibiotics are administered [55].

When device-related infections occur, parenteral antibiotics are usually given after the implanted device or material is removed to ensure that the biofilm is eliminated. This two-stage surgical treatment, which has a 93-100% success rate, involves removing the contaminated device, devitalizing the affected tissue and filling the incision with an antibiotic-impregnated material [17].

The 2014 IDSA guidelines suggest that if there is a minor inflammatory infiltrate (less than 5 cm around the incision) and no signs of a generalized infection-which are characterized by a fever >38.5°C and a heart rate >110/min-the use of antibiotics is not recommended. However, it is recommended to start antibiotics when the inflammation is greater than 5 cm and there are signs of generalized inflammation [56].

Gram staining of wound smears and local epidemiological factors should be taken into consideration while choosing the first-line treatment. If a patient with SSI has a severe clinical illness, needs antibiotic therapy, has suspected drug-resistant organisms, or has an allergy to first-line medication, microbiological testing may be necessary.

It is possible to treat a suspected staphylococcal infection with cefazolin, cefuroxime, or cloxacillin. Glycopeptides or linezolid are appropriate treatments for MRSA infections. When Gram-negative infection is suspected, fluoroquinolones

or second- or third-generation cephalosporins are the first-line antibiotic that can be used [56].

Biofilm-mediated infections are commonly treated with a combination medication consisting of rifampin and glycopeptide. Cephalosporins, carbapenems, amoxicillin, tigecycline, linezolid, daptomycin and sulfamethoxazole trimethoprim are other options for the combined treatment. Based on susceptibility testing, new anti-infectives such avibactam and dalbavancin should be used when appropriate substitutes are not available [17].

An infected wound should be treated with a variety of antimicrobial regimen. Commonly used antiseptics have concentrations that are even 100 times greater than their minimal inhibitory concentrations, which allows them to kill pathogens long after they become less sensitive to them [57].

Negative pressure therapy should be taken into consideration for difficult deep wounds that are not healing. By encouraging angiogenesis, negative pressure promotes blood supply to the site and speeds up the development of granulomatous tissue. Debridement and the start of targeted antibacterial therapy are necessary beforehand.

CONCLUSION

It might be difficult to identify and subsequently treat SSI. Careful patient management and all necessary measures are essential to prevention. Therefore, the health care system may be able to prevent SSIs, decrease mortality rates and save money if hospital administrators provide basic support, surgical teams have the necessary knowledge and skills, resources are available, patients receive excellent care throughout their hospital stay and patients are monitored after they are discharged.

Thus, collaboration between clinicians and microbiologists is essential for the prompt detection and management of such illnesses. Every tertiary healthcare facility should adopt a unified policy to provide the essential direction in this situation.

Only six general measures have been shown to be effective in randomized studies, even though several strategies are advocated by international organizations to reduce SSI. Interventions associated with reduced infection rates include avoiding the use of razors for hair removal, decolonization with intranasal anti-staphylococcal agents, using alcohol-based skin preparation and chlorhexidine gluconate, maintaining normothermia, perioperative glycemic control and negative pressure wound therapy. Guidelines recommend the appropriate choice, timing and dosage of preoperative parenteral antibiotic prophylaxis.

Recommendations

One of the key measures of the healthcare system's ability to control HAIs is its level of care. To effectively reduce the rate of SSIs, strict adherence to infection control methods is advised.

According to CDC recommendations, several actions must be taken to ensure a considerable reduction in SSIs: (1) Making sure that the patient has no indications of ongoing infections is crucial; (2) The technique and infection control measures are explained to the patient; (3) Decolonizing *S. aureus* prior to surgery; (4) Encouraging patients and healthcare staff to practice good hygiene; (5) Using the right antiseptics for disinfection; (6) Hair removal at the preoperative surgical site is suitable for the procedure's location and type and (7) Patient's preoperative surgical site is free from infection.

Additionally, patients undergoing heart surgery should have postoperative morning blood glucose levels under control (200 mg per dL or less) and patients undergoing colorectal surgery should be normothermic (36°C or greater) during the first 15 minutes after leaving the operating room. Improving the patients' nutritional health and early mobilization of their natural defense mechanisms are two further factors that significantly affect the rate of recovery.

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