



A Systematic Review on Diabetes Mellitus and Other Risk Factors Associated with Surgical Site Infection

Dilshana Kp, Thara Baby, Amritha, Vineetha S, Tamilselvan T, Gopika Cs

Department Of Pharmacy Practice, Nehru College Of Pharmacy, Pampady, Thrissur, Kerala 680588 India.

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ABSTRACT

IMPORTANCE: SSIs can lead to major complications, including death, as well as significantly increase the cost of care. SSIs occur either during or up to 30 days after a surgical procedure, largely avoidable with proper infection control measures. This review focuses on diabetes mellitus and other risk factors associated with surgical site infection. **OBJECTIVE:** On completion of this article, the reader should be able to understand and summarize on diabetes mellitus and other risk factors associated with surgical site infection. **METHODS:** A vigorous, maximum sensitive and online search of the literature was performed in published articles in the last 24 years. The databases searched were MEDLINE (via PubMed) and Cochrane Library. **CONCLUSION:** Knowledge about Surgical site infection will help surgeon in diagnosis and treatment, early detection and intervention is a prerequisite in surgical patients. Although surgical wound infections cannot be completely eliminated, a reduction in infection rate to a minimum level could have significant benefits, by reducing burden to patients and their families. Intervention aimed at reducing Surgical site infection would provide cost savings and improve the efficiency of health care system. Our data suggest that all these risk factors could be regarded as potential indicators of SSI and that relevant preventive measures should be taken to reduce SSI and improve patient outcomes.

Keywords: surgical site infections, risk factors of surgical site infections, perioperative risk factors, diabetes mellitus on surgical site infections

INTRODUCTION

Surgical site infections are infections, which occurs after any surgical procedure along the surgical tract. In our population they are the common nosocomial infections. They occur at any level, accounting for 38% of all infections in post-surgical patients. Recent wide spread and indiscriminate use of antibiotics have made it difficult to prevent and control such infections. Increasing number of serious infections were due to long duration complicated surgeries, increase in older age group patients with chronic infections, usage of implants, immunosuppressants drug usage in organ transplant surgeries and newer diagnostic technique results in increased exposure to microorganisms.[1]

Multiple factors can affect the development of SSI, including patient-related factors (such as obesity, diabetes mellitus, age, gender, and smoking) and treatment-related factors (such as laparoscopic procedure, prophylactic antibiotics, and stoma creation). Unsatisfactorily, few risk factors are generally accepted and some findings on these factors in medical literature are often contradictory. [7]

Accordingly, many perioperative interventions are supported by very limited literature evidence. More importantly, many scholars have realized that the risk factors are different for the different types of SSI. The understanding of these risk factors might better prevent and treat SSI. Besides, SSI reduces the benefits of surgical treatment. Therefore, systematically assessing the common factors of the different types of SSI is a priority.[7]

The risk of developing an SSI is multifactorial. In observational studies, a wider breadth of risk factors and their impact on incidence of SSI can be observed based on routine clinical practice, and for a larger range of patients, as opposed to the narrow focus on particular risk factors that may be considered within clinical trials. However, investigators of observational studies cannot control the specific variables and level of detail available and it can be challenging to comprehensively adjust for all relevant confounding variables in the estimation of particular risk factors for SSI.[2]



METHODS

A vigorous, maximum sensitive and online search of the literature was performed. The search strategy was limited to published articles in the last 24 years (JUNE 2000–JUNE 2024) to include the most recent, up-to-date data that reflect the current clinical practice. The databases searched were MEDLINE (via PubMed) and Cochrane Library. The search terms used were, “surgical site infection”, “surgical wound infection”, “risk factors associated with surgical site infection”, and “diabetes mellitus associated with surgical site infection” combined with “AND” and “OR” operators as appropriate. The reference lists of the included studies were also searched manually to exhaustively retrieve additional relevant articles. The first stage of screening was performed based on the titles and abstracts. Eligible studies were screened based on the full text in the second stage.

DISCUSSION AND OBSERVATIONS

RISK FACTORS

The risk factors associated with the development of a surgical site infection (SSI) varies according to specific patient factors and clinical characteristics, in addition to the nature of the surgical procedure. Despite the considerable number of the clinical studies that have reported on these risk factors for SSIs following abdominal surgeries, it can be challenging to control the level of details available and to comprehensively adjust for all the variables in the estimation of particular risk factors. A comprehensive and detailed assessment of the multifactorial nature of these risk factors could help in improving the quality of surgical care.

Multiple risk factors have been identified which comes under four major determinants of surgical site infections namely

1. Bacterial factors
2. Local wound factors
3. Patient related factors
4. Peri-operative antimicrobial prophylaxis

A. Bacterial factors:

Depends upon the bacterial load and its virulence factors in the surgical site. The virulence factor contributing to pathogenicity by inhibiting phagocytosis are slime layer of coagulase negative Staphylococci and capsule of Klebsiella. Surface components such as endotoxins or lipopolysaccharides of gram negative bacteria and exotoxins of certain gram positive bacteria establish infections within 1-5 days.

Bacterial load (or) Inoculum is an inevitable factor in causing infections and the conditions associated with bacterial load are

- Length of the preoperative stay.
- Certain preoperative procedures such as shaving are associated with increased bacterial load and surgical site infections.
- Remote infections at the time of surgery, duration of procedure etc.

B. Local wound factors

- Invasiveness of an operation.
- Skill of the surgeon.
- Break in barrier defence mechanism (skin, mucosa of gastro intestinal tract).
- Adequate indications for use of sutures, drains and foreign bodies such as implants.

C. Patient related factors



Play a very important role in surgical site infections. They are;

- Age, immunosuppression, steroid, malignancy, smoking, diabetes, malnutrition etc. are the major factors causing surgical site infections.
- Maintaining normothermia.
- Improving oxygen tension and WBC function in surgical area.
- Control of glucose level in the perioperative period can prevent surgical site infections.

Demographic risk factors

Age greater than 65 years was a significant risk factor in the univariate model of one study ($p < 0.001$). [26] Two studies identified male sex as an independent risk factor for development of SSI in the multivariate model of two high- quality studies, [22, 24] with summary measures as follows: OR 2.6, 95% CI 1.02 to 6.6, $p < 0.001$, and OR 2.65, 95% CI 1.70 to 4.14, respectively. Overweight is additionally identified as a risk factor in the univariate model of one study (RR 2.1, 95% CI 1.11 to 3.98) [23] and in the multivariate model of other two studies that defined BMI of >25 as an independent risk factor, [25, 24] with summary measures of OR 7.6, 95% CI 2.1 to 27, $p = 0.002$ and $p = 0.007$, respectively.

D. Perioperative antimicrobial prophylaxis:

The interaction between the prophylactically administered antibiotics and the inoculated bacteria during surgery is one other most important determinant in development of surgical site infections. The principle of antibiotic prophylaxis is based on the belief that, antibiotics augment the natural host defence mechanisms, thereby removing the bacterial inoculum in the wound. So adequate antibiotic level should be maintained above minimum inhibitory concentration throughout the surgical procedure. Hence knowledge about pharmacokinetics of various antibiotics used in perioperative prophylaxis is important in preventing surgical site infections. Microorganisms causing surgical site infections were from external environment or from endogenous micro flora. Exogenous microorganisms include those from water, air of operating room, equipment used in surgery or from theatre staff. Study conducted by CDC have shown that the common pathogen causing infection at surgical site were E.Coli followed by Klebsiella pneumoniae, MRSA, MSSA, Acinobacter baumannii, Klebsiella aerogenes.

Escherichia coli remain the most common cause of surgical site infections in clean contaminated wound and in contaminated procedures. Some emerging infections are more common in recent years. Understanding the microbiology of surgical site infections is very important in treating the patients and taking prophylactic measures. The most important measure to decrease the bacterial load in surgical site include adapting aseptic precautions, following antiseptic methods and using antimicrobial prophylaxis. Antimicrobial prophylaxis used systemically acts as a powerful preventive measure in controlling surgical site infections. But indiscriminate use of antibiotics, has lead to the emergence of antibiotic resistant strains and increase the incidence of surgical site infections. [1]

Preoperative risk factors

Diabetes was identified as a risk factor in two studies, the first study through a univariate model (RR 1.68, 95% CI 0.76 to 3.71) [23] and the other one through a multivariate model ($p = 0.04$). [24] Two studies identified ASA classifications (3 and 4) as an independent risk factors, [24, 28] with measures of $p < 0.0001$ and OR 2.58, 95% CI 1.79 to 3.70, $p < 0.0001$, respectively, and another one study defined ASA classification (>2) as a risk factor in the univariate model (OR 6.37, $p < 0.001$). [29] Only one study identified previous chemotherapy as a risk factor using univariate model. [23] Hemoglobin level of <12 g/dL was identified as an independent risk factor in one study (OR 2.5, 95% CI 1.1 to 6.1, $p = 0.03$). [25]

Similarly, low albumin level was an independent risk factor in only one study ($p < 0.001$). [24] Preoperative hospital stay of >8 days was an independent risk factor in one multivariate model (OR 2.76, 95% CI 1.46 to 5.28, $p < 0.001$) [28]; additionally, two other studies [29, 26] defined preoperative hospital stay of ≥ 7 and >15 days as a risk factor in their univariate models (OR 6.62, $p < 0.001$ and $p < 0.018$), respectively. Smoking was an identified independent risk factor in one high quality study ($p < 0.0001$). [24]

Intraoperative and postoperative risk factors

Two studies identified intraoperative blood loss as an independent risk factor; the first study defined it as an estimated blood loss of >600 mL (OR 2.04, 95% CI 1.16 to 3.57 $p = 0.01$), [13] and the other study didn't give an estimation ($p = 0.0007$). [32]



intraoperative temperature nadir was an independent risk factor in only one study (OR 1.33, 95% CI 1.002 to 1.76); the same study reported the presence of perioperative infection as an independent risk factor (OR 2.46, 95% CI 1.00 to 6.04).[12] Only one study reported the number of people in the operative theater as a significant risk factor in the univariate model, the study demonstrated that people of >10 in the operative theater increase the risk of wound infection (OR 3.12, 95% CI 0.71 to 13.66). [23] Perioperative blood transfusion was found to be an independent risk factor in three studies.[13, 28, 12] Use of drains was identified as a risk factor in three studies.[27–29]. Additionally, healthcare institutions may be responsible for extrinsic risk factors such as poor ventilation or inadequate equipment sterilization. The adherence to infection control protocols, including preoperative antibiotic prophylaxis, can greatly influence SSI outcomes. Hospitals with strict adherence to these protocols generally report lower SSI rates. The quality of postoperative care, including wound care and monitoring for signs of infection, is vital. Early detection and treatment of SSIs can prevent more severe complications. Addressing these extrinsic risk factors can significantly improve the likelihood of a positive surgical outcome and decrease the incidence of surgical wound infections[3].

Abdominal Surgery

Alkaaki et al. conducted a prospective study to assess the incidence, bacteriology, and risk factors of surgical site infections in patients following abdominal surgery [14]. The study evaluated a total of 337 patients who underwent abdominal surgery over a one-year period. Of these, 55 patients developed SSIs, representing an overall incidence rate of 16.3%, of which 9% were deep. Among risk factors, the open surgical method, emergency surgery, and prolonged operation length were the most significant extrinsic risk factors, and the masculine gender was the most important non-modifiable intrinsic risk factor. *Escherichia coli* strains that produce an extended-spectrum beta-lactamase were the most often isolated bacteria, followed by *Enterococcus* spp. This result is in accordance with other research on colorectal surgery, which also identified *Escherichia coli* as a pathogen that was commonly involved.

Orthopedic Surgery

In a study conducted at the Hospital de la Santa Creu I Sant Pau in Barcelona, Benito et al. examined the incidence of surgical site infections (SSIs) following a total hip and knee arthroplasty [15]. They analyzed 2333 patients with knee/hip arthroplasties performed between 2004 and 2010. During the study period, the yearly incidence of SSIs did not change considerably (4.20%). In the same study, staphylococci were the most prevalent cause of monomicrobial infections (62.2%). A total of 28.6% of *S. aureus* isolates showed resistance to methicillin, while GNB and *Enterococcus* spp. were the most common pathogens isolated from polymicrobial infections. Another study on 503 patients found an infection rate of 39.60% in open reduction and internal fixation, 5.55% during total hip arthroplasty, and 9.40% in total knee arthroplasty. Most SSIs were detected after discharge from the hospital [16].

Cardiovascular and Cardiac Surgery

The incidences, risk factors, and microbiology of surgical site infections following cardiovascular surgery have been analyzed in three studies. Banjanovic et al. conducted a study on 2340 patients and observed that 37% of patients had two risk factors for deep sternal wound infection (25% were diabetic patients and 3% were overweight) [17]. In regard to etiology, *Enterococcus faecalis* was the most prevalent pathogen (27%), followed by *Klebsiella pneumoniae* (13%), *Proteus mirabilis* (9%), and *Serratia marcescens* (9%). In contrast, Morikane et al. observed that MRSA and CNS were the predominant pathogens responsible for surgical site infections [18].

Neurosurgery

Pereira et al. and Hamdeh et al. aimed to examine the prevalence, impact, and potential risk factors of surgical site infections in neurosurgery [19, 20]. The rate of SSIs was 4.85%, with a total of 26 infections. These infections were classified as 65.38% organ space infections, 30.77% deep infections, and 7.69% superficial infections. *Staphylococcus epidermidis* was the most frequently isolated microorganism, accounting for 23.08% and 34.8% of cases, respectively. Patients who received appropriate preoperative antibiotic prophylaxis had a significantly lower incidence of SSIs (4.43%) compared to those who received inappropriate or no antibiotic prophylaxis (11.23%). Additional risk factors are associated with SSIs, including meningiomas, longer operation times, craniotomies, and the use of dural substitutes. In another study conducted by Kolpa et al. SSIs accounted for 33% of all HAI incidences during the study period, with *S. aureus* being the most prevalent causative agent (35.9%), followed by CNS (28.9%). The most significant HAI incidence rates were observed in ventricular shunt implantation surgeries (77 cases, 18.6%) and craniotomies (235 cases, 8.0%) [21].



DIABETES MELLITUS

Previous studies have documented specific patient characteristics associated with increased risk for SSI, including diabetes mellitus. Trick et al. [11] demonstrated that a preoperative glucose level 200 in diabetic patients was an independent risk factor (OR 4.4, P = 0.01) for radial artery harvest site infections after coronary artery bypass graft surgery (CABG). Another study evaluated 15 risk factors for SSI, as defined by the CDC in 693 patients undergoing CABG; multivariate analysis revealed that diabetes was an independent predictor of SSI [10]. Karim et al. [9] studied 3000 surgical wounds for 10 days postoperatively and confirmed that diabetes mellitus was an independent risk factor for SSI in general surgical patients (P 0.005). Patients with diabetes in this current study were approximately 1.5 times more likely to develop SSI, demonstrating that in noncardiac surgical patients, diabetes mellitus was a significant independent risk factor for SSI.

CONCLUSION

Our data suggest that all these risk factors could be regarded as potential indicators of SSI and that relevant preventive measures should be taken to reduce SSI and improve patient outcomes. Identification of patients at risk for developing SSI is critical, because reduction of SSI can reduce the associated morbidity and mortality. Interdisciplinary cooperation between surgeons, anesthesiologists, infectious diseases specialists, operative theater and nursing staff is crucial for achieving the best possible outcomes in this high-risk group of patients. As patient safety is of utmost importance in the practice of surgery nowadays and as patients undergoing emergency surgery are more vulnerable and at higher risk of developing SSI, every surgical unit should audit their outcomes in order to pinpoint modifiable risk factors.

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