RISK FACTORS AND ETIOLOGIES OF CLEAN AND CLEAN CONTAMINATED SURGICAL SITE INFECTIONS AT A TERTIARY CARE CENTER IN MALAYSIA

Wong Jun Leong[1], Habsah Hasan[2], Zaidi Zakaria[3], Mohamad Ziyadi Hj Ghazali[3], Siti Azrin Ab Hamid[4] and Siti Asma Hassan[2]

[1]Department of Pre-Clinical Sciences, Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, Bandar Sungai Long, Cheras, Kajang, Selangor; [2]Department of Medical Microbiology and Parasitology, [3]Department of Surgery, [4]Unit of Biostatistics and Research Methodology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Abstract. Surgical site infections (SSI) are among the most commonly encountered healthcare associated infections (HCAI). Identification of the risk factors and its causative agents may inform prevention and management strategies. The objective of this study was to determine risk factors and etiological agents of SSI and their sensitivities. We conducted a prospective cohort study at Hospital Universiti Sains Malaysia from June 2013 to July 2014. Seventy-two patients who underwent clean and clean-contaminated surgeries were included in the study. Each studied patient was followed for 30 days post-operation. Tissue samples or wound swab specimens were obtained and sent for culture and sensitivity testing. Among the patients who developed an infection during the 30 day follow-up period, patients with the highest rates of SSI were those who had undergone coronary artery bypass graft (CABG) surgery (50%, *n*=8) followed by thyroid surgery (15%, *n*=2), laparoscopic cholecystectomy (12%, *n*=2) and herniorrhaphy (4%, *n*=1). Risk factors significantly associated with a SSI on multiple logistic analysis were: having a history of diabetic mellitus (DM) (OR=6.97; 95%CI: 1.49-32.71) and having undergone CABG surgery (OR=5.54; 95%CI: 1.22-25.03). Antibiotic sensitive gram-negative bacilli were the most common organisms identified. Patients with DM and those undergoing CABG surgery were those at greatest risk for developing a SSI in the study population. Diabetic patients need to be monitored more carefully post-operatively for SSI and infection control procedures for patients undergoing CABG surgery need to be reviewed and upgraded.

Keywords: surgical site infections, clean surgery, clean contaminated surgery, risk factors

Correspondence: Dr Siti Asma' Hassan, Department of Medical Microbiology and Parasitology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.
Tel: +609 7676826; Fax: +609 767 6286
E-mail: sitiasmakb@usm.my

INTRODUCTION

A surgical site infection (SSI) is defined as an infection that occurs at the incision site, or an anatomical part that was either opened or manipulated during the procedure, that occurs within 30 days of the surgery, or within one year if the surgery involved implantation (Horan *et al*, 1992).

A SSI can negatively affect the patient's quality of life and is associated with morbidity and extended hospitalization. The duration of hospital stay for a SSI patient is longer than for other complications by 2-36 days, depending on the type of surgery (Broex *et al*, 2009; Jenks *et al*, 2014). Prolonged hospital stays require more resources, including diagnostic testing, antibiotics and reoperation fees. It also reduces availability of beds for other patients and human resources. As a consequences, a SSI can not only increase the financial burden to the patient but to society as well.

Many factors can affect the postoperative outcome of a patient, such as patient related factors [age, underlying disease, tobacco use, history of diabetes mellitus (DM) and obesity] and procedure related factors (method of skin preparation, selection of prophylactic antibiotics, duration of procedure and surgeon experience) (Arabshahi and Koohpayezade, 2006; Utsumi *et al*, 2010; Hafez *et al*, 2012). Some factors are modifiable and some are not. Patient nutritional status, cigarette smoking, immune status and colonization with microorganisms are modifiable risk factors, while age, and history of renal failure or cancer are non-modifiable risk factors. Identification of modifiable risk factors for SSI and correcting them can reduce the incidence of SSI.

Microorganisms responsible for SSI vary. SSI may be caused by contamination of the incision by instruments, health care workers, the environment or the patient's own body during surgery. Epidemiological studies have found the majority of SSI originate from the patient, such as endogenous flora and nasal colonization. *Staphylococcus aureus* is the leading causative agent of a SSI (NNIS, 2004; Magill *et al*, 2014). It is the cause of 50.9% of SSI (Weigelt *et al*, 2009). *Streptococcus* sp are the second most common group of pathogens causing SSI (3.5%), followed by *Enterococcus* sp (2.6%) and *Pseudomonas aeruginosa* (2.1%) (Weigelt *et al*, 2009).

Antibiotic prophylaxis is a commonly use method to prevent a SSI. It is not used for low risk procedures, such as clean surgeries, but is recommended for clean contaminated surgeries (Ministry of Health Malaysia, 2008). The choice of antibiotic used depends on the type of procedure and the type and sensitivity of the local causative bacteria. The purpose of this study was to determine risk factors for causative agents of SSI and their antibiotic sensitivities.

MATERIALS AND METHODS

We conducted a prospective cohort study from June 2013 to July 2014 on the surgical wards of the Hospital Universiti Sains Malaysia (USM) to determine the risk factors for SSI, organisms isolated and their sensitivities to antimicrobials. Hospital USM is a tertiary-care hospital located on the east coast of peninsular Malaysia. The hospital has three surgical wards comprised of 70 beds. We studied 72 patients aged >15 years who underwent clean [coronary artery bypass graft (CABG), herniorrhaphy repair and thyroid surgery] and clean-contaminated (laparoscopic cholecystectomy) surgeries. The number of participants was chosen based on those with risk factors and selected participants were chosen using the universal sampling method.

Data recorded for each participant included the presence of a SSI or not, the causative organism and its sensitivities to tested antibiotics, patient demographic data, history of underlying disease, body mass index, smoking status, history of DM, duration of the surgical procedure and prophylactic antibiotics used.

Patients were followed by phone for 30 days. If the participant developed any signs of SSI, the wound was examined. Infected wounds were cleaned using 4% Chlorhexidine solution and left to dry for 2 minutes before a tissue sample was obtained. If a tissue sample could not be obtained, a culture swab was obtained after the wound was cleaned with normal saline. Tissue samples and culture swab specimens were sent to the laboratory for culture and sensitivity testing. All samples were inoculated onto Columbia horse blood agar, Mac Conkey agar and Mannitol salt agar plates and incubated aerobically. An additional Columbia horse blood agar plate for culturing anaerobic bacteria was also conducted for tissue samples. All bacteria that grew on the plates was identified based on morphology and biochemical test results. Antimicrobial sensitivity testing was performed using the Kirby-Bauer or Vitek card methods. The infected wound was then managed by the medical officer on duty. Patients were then discharged from the study after completion of 30 days monitoring or upon treatment of the SSI.

Risk factors for the SSI were analyzed using simple logistic regression analysis and multiple logistic regression analysis. All statistical calculations were performed using the software Package for Statistical Analysis (SPSS), version 22 (IBM, Armonk, NY).

Written consent was obtained from each participant prior to inclusion in the study preoperatively. Ethical approval for this study was obtained from the Human Research Ethics Committee, Universiti Sains Malaysia on 26 March 2013. Reference: USMKK/PPP/JEPeM [261.3. (5)] (Appendices K).

RESULTS

Seventy-two participants were included in the study; 47 males (65.3%) with a male to female ratio of 1.8:1. The mean age of participants was 52 (range: 15-77; median: 53) years. The types of surgery included were CABG (*n*=16), herniorrhaphy (*n*=26), thyroid surgery (*n*=13) and laparoscopic cholecystectomy (*n*=17). The demographic data of the study participants is summarized in Table 1. The incidence of SSI among patients undergoing CABG surgery was 50% (*n*=8). Of these, three patients had both leg and sternal wound infections and 5 patients had leg wound infections only. Six patients had a history of DM. The incidence of SSI following thyroid surgery was 15% (*n*=2), following laparoscopic cholecystectomy was 12% (*n*=2) and following herniorrhaphy was 4% (*n*=1) (Fig 1). Antimicrobial prophylaxis among studied patients followed established guidelines. No antimicrobial prophylaxis was given prior to thyroid surgery. Antimicrobial prophylaxis was only given to high risk patients prior to herniorrhaphy. All patients undergoing CABG surgery were given antimicrobial prophylaxis due to the saphenous having an increased risk of having bacteria because of vein harvesting with bacteria being present at the harvest site. The list of antibiotics used for prophylaxis is given in Fig 2.

The factors significantly associated with SSI on simple and multiple logistic regression analysis is shown in Tables 2 and 3. On multiple logistic regression analysis, factors significantly

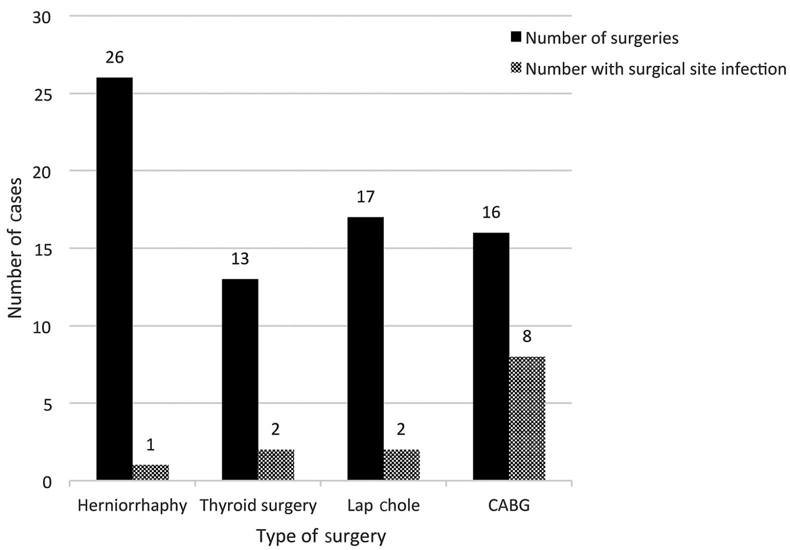

Fig 1–Number of infected cases by surgery type. Lap chole, laparoscopic cholecystectomy; CABG, coronary artery bypass graft.

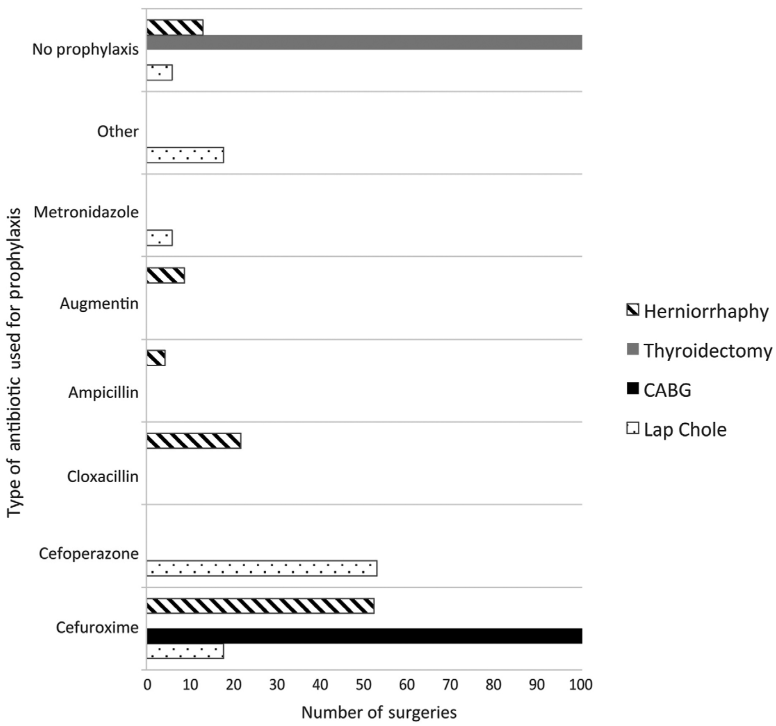

Fig 2–Antimicrobial prophylaxis by surgery type. Lap chole, laparoscopic cholecystectomy; CABG, coronary artery bypass graft.

associated with surgical site infection among study participants were: having a history of DM (OR=6.97; 95%CI: 1.49 - 32.71) and having undergone CABG surgery (OR=5.54; 95%CI: 1.22 - 25.03).

A total of 16 infected wounds were identified among 13 patients. Of these, 7 (44%) were identified during hospitalization and 9 (56%) were identified after discharge home. There was one deep wound SSI and one organ space SSI. The other 14 infected wounds were superficial SSI. Two CABG patients (15%, *n*=2) were readmitted due to seriously infected wounds.

Pathogens were isolated from seven of the 16 infected wounds (44%). Of the pathogen isolated, six (43%) were gram-positive cocci and eight (57%) were gram-negative bacilli. Microorganism isolated were methicillin-sensitive *Staphyloccoccus aureus* (MSSA), *Klebsiella pneumoniae* ssp *pneumoniae*, *Klebsiella pneumoniae* ssp *ozaenae*, *Citrobacter koseri*, *Streptococcus agalactiae*, *Pseudomonas aeruginosa*, *Staphylococcus haemolyticus*, *Staphylococcus epidermidis*, and *Esch-*

Table 1
Demographics of study participants (N=72).

Demographic details	*n* (%) Infected	*n* (%) Non-infected	Missing
Gender			0
Male	9 (19)	38 (81)	
Female	4 (16)	21 (84)	
Age group			0
≥ 50 years old	10 (23)	33 (77)	
< 50 years old	3 (10)	26 (90)	
Underlying diseases			0
Yes	12 (27)	33 (73)	
No	1 (4)	26 (96)	
Obesity[a]			13
Yes	4 (27)	11 (73)	
No	6 (14)	38 (86)	
Smoking			0
Yes	2 (17)	10 (83)	
No	11 (18)	49 (82)	
History of diabetes mellitus			3
Yes	8 (44)	10 (56)	
No	4 (8)	47 (92)	
Type of surgery			0
CABG	8 (50)	8 (50)	
Herniorrhaphy	1 (4)	25 (96)	
Thyroid surgery	2 (15)	11 (85)	
Lap. cholecystectomy	2 (12)	15 (88)	
CABG or none CABG surgery			0
CABG surgery	8 (50)	8 (50)	
None CABG surgery	5 (9)	51 (91)	
Duration of surgery in hours			1
>4	8 (38)	13 (62)	
< 4	4 (8)	46 (92)	
Prophylaxis antibiotics			0
Yes	10 (19)	42 (81)	
No	3 (15)	17 (85)	

[a]Body mass index ≥30.0. CABG, coronary artery bypass graft; Lap, laparoscopy.

erichia coli (Table 4). Of seven infected wounds, four (57.1%) were infected with polymicrobial microorganisms. All polymicrobial infected wounds occurred on the legs of patients who underwent CABG surgery. All gram-positive cocci isolated were sensitive to all tested antibiotics (clindamycin, fusidic acid, linezolid, rifampin, teicoplanin, and trimethoprim-sulfamethoxazole, cefoxitin, ciprofloxacin, erythromycin, and gentamicin). Of the Enterobacteriaceae isolates, there was one Extended Spectrum Beta-Lactamases (ESBL) producing strain of *Klebsiella pneumoniae* isolated. All Enterobacteriaceae isolated were sensitive to amikacin,

Table 2
Factors associated with a surgical site infection among study participants using simple logistic regression analysis.

Variable	Regression coefficient (b)	Crude odds ratio (95% CI)	Wald statistic	*p*-value
Gender				
Female	0	1		
Male	0.22	1.24 (0.34-4.53)	0.109	0.741
Age group in years				
< 50	0	1		
≥ 50	0.97	2.63 (0.66-10.53)	1.86	0.173
Underlying diseases	2.25	9.46 (1.15-77.50)	4.38	0.036
Obesity[a]	0.83	2.30 (0.55-9.64)	1.30	0.254
Smoking history	0.12	0.89 (0.17-4.65)	0.02	0.891
History of DM	2.24	9.40 (2.36-37.39)	10.12	0.001
CABG surgery				
Duration of surgery in hours	2.32	10.20 (2.66-39.08)	11.49	0.001
< 4	0	1		
≥ 4	1.96	7.08 (1.84-27.27)	8.08	0.004
Prophylactic antibiotics	0.30	1.35 (0.33-5.51)	0.17	0.677
Type of surgery				
Clean-contaminated	0	1		
Clean	0.63	1.88 (0.37-9.44)	0.58	0.446
Admission prior to surgery				
< 2 days before	0	1		
≥ 2 days before	2.54	12.67 (2.02-79.53)	7.33	0.007
Post operation stay				
< 3 days	0	1		
≥ 3 days	1.63	5.13 (1.39-18.84)	6.06	0.014
Total hospital stay in days				
< 7	0	1		
≥ 7	2.06	7.84 (2.12-29.0)	9.52	0.002

[a]BMI ≥30.0 classified as obesity. CI, confidence interval; CABG, coronary artery bypass graft.

imipenem, meropenem, piperacillin-tazobactam and 50% of the isolates were resistant to amoxicillin-clavulanate, cefepime, cefoperazone, cefotaxime, ceftazidime, netilmicin, ciprofloxacin, gentamicin, trimethoprim-sulfamethoxazole, ampicillin and cefuroxime. Of the *Pseudomonas aeruginosa* isolates, 100% were sensitive to all the antibiotics tested.

DISCUSSION

SSI are the most common healthcare associated infections (HCAI) (Dionigi *et al*, 2001). Compared to the US Centers for Disease Control and Prevention's National Healthcare Safety Network (CDC-NHSN) SSI report, our SSI rates were higher for CABG (50% *vs* 0.55%), thyroid

Table 3
Factors associated with surgical site infection among study participants on multiple logistic regression analysis.

Variable	Regression coefficient (b)	Adjusted odds ratio (95% CI)	Wald statistic	*p*-value
Diabetis mellitus				
No	0	1		
Yes	1.71	6.97 (1.49-32.71)	6.06	0.014
CABG surgery				
No	0	1		
Yes	1.94	5.54 (1.22-25.03)	4.94	0.026

CI, confidence interval; CABG, coronary artery bypass graft.

Table 4
Types and rates of bacterial culture from study participants with surgical site infection.

Microorganism	Isolates *n* (%)
Clean surgery	
Gram-positive	
Staphylococcus aureus	2 (14.2)
Staphylococcus epidermidis	1 (7.1)
Staphylococcus haemolyticus	1 (7.1)
Streptococcus agalactiae (Group B)	1 (7.1)
Gram-negative	
Escherichia coli	2 (14.2)
Citrobacter koseri	2 (14.2)
Klebsiella pneumoniae subsp *ozaenae*	1 (7.1)
Klebsiella pneumoniae subsp *pneumoniae*	1 (7.1)
Pseudomonas aeruginosa	2 (14.2)
Clean-contaminated surgery	
Gram-positive	
Staphylococcus aureus	1 (7.1)

surgery (15% *vs* 0.29%), cholecystectomy (12% *vs* 0.96%) and herniorrhaphy (3.8% *vs* 0.68%) (CDC, 2016). The SSI rate for thyroid surgery in our study was higher than a study from Vietnam, but the SSI rate for cholecystectomy was lower (12% *vs* 13.7%) in the same study (Viet Hung *et al*, 2016).

There are many possible reasons for the high SSI rates in our study that need to be investigated, such as the presence of risk factors, poor subject preparation prior to surgery, poor infection control practices, poor techniques, inexperienced surgeons and poor post-operative wound care. In this study we found patients who underwent cardiac surgery were 10.2 times more likely to develop a SSI than patients underwent general surgery. Our finding was also higher than a study from Egypt (Hafez *et al*, 2012), which reported a 1.84 times higher risk after CABG, but our patients had a 5.5 times higher risk. Most of the CABG surgery patients in our study were high risk for SSI: 75% had DM. Most infections in our study were first noticed at home, this could reflect poor wound care at home. Our study only has a small number of patients, which could result in overestimation of the SSI rate.

In our study, DM was a significant risk factor associated with SSI. Patients with DM had a 9.4 times greater risk of SSI than patients without DM. This result is higher than a study from Iran which reported a 4.9 times greater risk of SSI (Arabshahi and Koohpayezade, 2006). Diabetic patients have impaired monocyte and neutrophil function due to increased production of superoxide radicals increasing their risk for infection (Perner *et al*, 2002). In our study, DM patients who underwent CABG surgery had a significantly greater risk of developing SSI, similar to studies from Taiwan (Wu *et al*, 2006) and Brazil (Ledur *et al*, 2011).

CABG surgery is a major surgery that results in two large wounds: the sternal and leg wounds. The chest wound has a greater risk of becoming infected than the leg wound due to longer exposure to the air. However, in our study, SSI occurred two times more commonly in leg wounds than chest wounds. This is in contrast to studies from India and Germany that reported SSI occurred more commonly in chest wounds than leg wounds (Bhatia *et al*, 2003; Cristofolini *et al*, 2012).

The primary pathogen group isolated from infected wounds in our study patients was gram-negative bacteria. Isolated organisms were *Escherichia coli*, *Citrobacter koseri*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, similar to a study done at a tertiary care hospital in Mumbai, India and Gaziantep University Hospital, Turkey, which also found gram-negative bacteria was the primary pathogen group found among patients with SSI (Namıduru *et al*, 2013; Shah *et al*, 2015).

In conclusion, in our study participants with a history of DM or those undergoing CABG surgery were more likely to develop a SSI. Enterobacteriaceae was the most common group of bacteria isolated from SSI among our study participants. The isolates showed low rates of resistance. The currently recommended antibiotics for prophylaxis continue to be appropriate based on these results. The incidence of SSI among all our patients was unacceptably high. Further studies are needed to determine the best methods for preventing infections at the study institution.

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