

Original Research Article

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Bacterial Pathogens of Surgical Site Infections in Cancer Patients at a Tertiary Regional Cancer Centre, South India

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ABSTRACT

A retrospective microbiological study of surgical site infections (SSIs) from oncological departments of Surgery, Gynaecology, Head and Neck and Oral oncology was evaluated to estimate the percentage resistance pattern of gram negative and gram positive bacteria from cancer patients. Surgical site infections are the nodal sites and direct index factor for the assessment of health-care associated infections in a hospital with a potential high risk for cancer patients. A total of 1546 post operative infected wound discharges and post operative drains in-situ discharges from surgical oncology departments were analysed between 2012 to 2014 for bacterial infections. Bacterial isolation was done by conventional laboratory methods in the department of microbiology. Susceptibility and resistance pattern to isolated pathogens were done by the conventional Stokes' method of antibiotic testing and extended-spectrum beta-lactamases (ESBL) were estimated by conventional 3 disc synergy diffusion method. Anaerobic infections were not included in the study. One thousand five hundred and forty six post operative infected wound and discharges from drains in-situ were analysed which yielded polymicrobial and monomicrobial infections. Out of 1058 samples the predominant isolates was gram negative bacilli followed by gram positive cocci with 488 samples. The predominant pathogens were *E.coli* 632(59.73%); *Klebsiella* species 148 (13.98%); *Pseudomonas* species 110(10.39%); Non fermenting gram negative bacilli 86(8.12%); *Proteus* species and *Morganella morganii* 62(5.86%); *Citrobacter* species 20(1.89%) and *Enterococci* species 262(53.68%); *Staphylococcus aureus* 202(41.3%); *Methicillin Resistant Staphylococcus aureus* 14(2.86%); *Coagulase Negative Staphylococcus (CONS)* 8(1.6%); and β streptococci 2(.2%). Extended spectrum beta-lactamases production out of the total 1058 samples were *E.coli* 328 (31.00%); *Klebsiella* species 32(3.02%); Non fermenting gram negative bacilli 16(1.51%); *Proteus* species 12(1.13%); *Pseudomonas species* 6(0.56%) *Citrobacter* species 6(0.56%). Amongst the total gram negative bacilli (1058), SSI surgical oncology services had the maximum SSIs isolates 48.39%; followed by departments of gynaec oncology 20.79%; head and neck oncology 6.61%; oral oncology 1.70%. Among the gram positive cocci (488) surgical oncology department had the maximum isolates 40.98%; followed by gynaec oncology 31.14%; head and neck oncology 4.91%; oral oncology 1.63%. Polymicrobial infection isolates was 516(33.37%) and monomicrobial isolates was 386(24.96%). Bacterial surgical site infections is the complication of surgery. The spectrum of post operative oncological surgical site infections in a cancer hospital are a nidus for health-care associated infections and increased health care burden. Relevant oncological surgical risk factors and antibiotic therapy need be evaluated in high risk patients like cancer to avoid early mortality and morbidity. This is the first study on surgical site bacterial infections in cancer patients in our hospital, Kidwai Memorial Institute of Oncology, a regional cancer centre in South India.

Keywords

Cancer, Bacterial Surgical Site Infections, Solid tumors, Resistance, Gram Negative Bacilli, Gram positive Cocci.

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Introduction

Surgical-site infection (SSI) is defined as infections that occur within 30 days of a surgical procedure (or within 1 year, if an implant has been left in place) affecting either the incision or deep tissue at the operative site (Horan *et al.*, 1992; Mangram *et al.*, 1999).

The National Nosocomial Infection System (NNIS) of the US Centers for Disease Control and Prevention, modified the definition of surgical wound infection by introducing the concept of surgical site infection, divided into wound infection and organ/space infection. In an attempt to compare the prevalence of SSI between hospitals, the NNIS developed an SSI risk index based on the American Society of Anesthesiologists score, the degree of contamination of the wound, and duration of the operation (Horan *et al.*, 1992; Mangram *et al.*, 1999).

BSSI's are the point source for hospital infection and SSIs are associated with increase in hospital stay and thereby increase health care costs and morbidity/lethality (Paulo *et al.*, 2011), delay in rehabilitation, post operative adjuvant therapy which in turn may affect the overall prognosis (Jelena Sotirović *et al.*, 2015).

Patients with solid tumors frequently undergo various diagnostic and therapeutic surgical procedures and surgical site infections (SSIs) are more common in these patients in contrast to haematologic malignant patients (Sutton, 2014).

Procedure such as surgical interventions, tracheostomies, biopsies, bone marrow aspirations, endoscopy, and indwelling vascular and urinary catheters break the natural protective barrier between the

internal environment and/ external environment and allow entry of microorganisms and predispose to infection (Teresa, 2014). Presence of BSSI's in cancer with added presence of ESBLs give rise to multiply drug resistance which in turn reflect on the hospital health care system. SSI is a multifactorial condition and the risk factors involved in its onset are common for most surgeries like age, obesity and surgical time as from studies reported. Ashley *et al.*, in their study mention that the passage of bacteria through surgical drapes is a potential cause of wound infection which easily penetrate all woven re-usable fabrics within 30 min and recommend the use of non-woven disposable drapes or woven drapes with an impermeable operating tray in all surgical cases. SSI's vary with the source of primary solid tumors. Intra abdominal cancer patients require aggressive surgical intervention for proper diagnosis, staging, and cure and which in turn carry a high incidence of surgical site infections (Meuid *et al.*, 1988) and surgery for abdominal cancer is associated with a higher degree of morbidity and mortality than other standard procedures (Peter, 2003).

Rectal cancer operations are at a greater risk of SSI due to procedures as creation of ostomies, and total excision of the mesorectum with anastomoses close to the anal margin thereby lengthening surgical time and increase the likelihood of bacterial contamination (Tsuyoshi *et al.*, 2006; Law *et al.*, 2004).

Longer duration of hospital stay is the common factor for oncological SSIs as reported by studies.

Methicillin Resistant Staphylococci aureus (MRSA) another important drug resistant gram positive pathogens detrimental for SSIs need to be ruled out which may lead to

persistance of SSIs and nosocomial infection. SSI infections may present as monomicrobial or polymicrobial in high risk cancer patients.

Polymicrobial infections have precedence over monomicrobial infections and have doubled in frequency in recent years in cancer patients (Jeffrey *et al.*, 2003) and are predominantly tissue-based infections with associated greater morbidity and mortality than monomicrobial infections. Eighty percent of polymicrobial infections are gram-negative and 33% are caused exclusively by multiple species of gram-negative bacilli (Elting *et al.*, 1986). In the milieu of poly or monomicrobial infections presence of extended-spectrum beta-lactamases add to the delay in reducing SSIs within the first 72 hours due to tissue stress and related surgical risk factors. Presence of ESBL's may imply an additional therapeutic difficulties to treat cancer patients and be detected as a routine test to avoid multiply drug resistance and prevent avoidable surgical risk factors. Antibiotic pressure in high risk subjects may give rise to more ESBL,s and directly relate to health care associated infections.

Montes *et al.*, (2014) in their study of 173 SSI for ESBL's in cancer patients report that appropriate timing and duration of perioperative antimicrobial prophylaxis will lower the risk of ESBL's. Antibiotic prophylaxis guidelines and reduced exposure to cephalosporins may also potentially decrease the risk of ESBL and SSI's. The incidence of SSIs may be as high as 20%, depending on the surgical procedure, the surveillance criteria used, and the quality of data collection. In many SSIs, the responsible pathogens originate from the patient's endogenous flora (Owens *et al.*, 2008) and the causative pathogens related to the type of surgery; where the most

commonly isolated organisms are *S. aureus*, *coagulase-negative staphylococci*, *Enterococcus spp.* and *E. coli*.

The Centers for Disease Control and Prevention guidelines for the prevention of SSIs emphasise the importance of good patient preparation, aseptic practice, and attention to surgical technique; antimicrobial prophylaxis is also indicated in specific circumstances. Newer technologies as the microbial sealants, offer the ability to seal and immobilise skin flora for the duration of a surgical procedure; a strong case therefore exists for evaluating such technologies and implementing them into routine clinical practice as appropriate (Owens *et al.*, 2008).

Educating about hand hygiene, appropriate and timely use of antibiotics, careful insertion and monitoring of catheters, good asepsis and preventive measures during surgery can reduce the incidence of SSIs in oncology patients. Studies mention that half or more of SSIs are due to instrumentation and surgical intervention including pre, peri and post operatively. SSIs form a direct index to health-care associated infections and therefore a thorough evaluation of oncological surgical risk factors prior to onco surgeries may reduce health care burden in terms of period or length of hospital stay, cost and reduction in morbidity and mortality.

Subjects and Methods

A total of 1058 samples from cancer patients with surgical site infections which included post-operative site discharges and post-operative site drain discharges between 2012 and 2014 were received from oncological services of Surgery, Head and Neck, Oral, Gynaecology to the department of microbiology. Culture positive isolates were considered for analysis of bacterial infections and were identified by

conventional methods (Medical Microbiology, 1996). Culture negative samples, isolation of anaerobic infections, colonisers and contaminants were not included in our study. Patients with previous chemotherapy and/or radiotherapy were excluded in the study.

Antimicrobial Susceptibility Testing

The susceptibilities to antimicrobial agents were determined by Stokes' disc diffusion method using Amikacin (30mcg); Gentamicin (10mcg); Cefotaxime(30mcg); Ceftazidime (30mcg); Cefuroxime(30mcg); Ciprofloxacin (5mcg); Cefaperazone (75mcg); Imipenem(10mcg) Piperacillin/Tazobactam (100/10mcg); and simultaneous screening tests for ESBL's by CLSI disc diffusion method and phenotypic confirmation test by disc potentiation test with ceftazidime (30mcg) and cefotaxime (30mcg) and amoxicillin-clavulanic acid discs 30mcg(20/10mcg); (all commercially available discs, Hi-media, India) as recommended by the Clinical and Laboratory Standards Institute(CLSI) guidelines.

Screening for *Methicillin Resistant Staphylococcus aureus*(MRSA) was done by Stokes' disc diffusion method using ceftazidime(30µg) disc (commercially available discs, Hi-media, India). The antibiotic disc susceptibility testing is done based on the antibiotics advocated routinely to cancer patients in our hospital.

Results and Discussion

One thousand five hundred and fifty eight BSSI samples of cancer patients yielded predominantly polymicrobial, less monomicrobial infection and ESBL's.

E.coli 632(59.73%); *Klebsiella* species 148 (13.98%); *Pseudomonas* species 110 (10.39%); Non fermenting gram negative

bacilli 86(8.12%); *Proteus* species 62 (5.86%); *Citrobacter* species 20(1.89%) and out of the gram positive pathogens *Enterococci* species 262 (53.68%); *Staphylococcus aureus* 202(41.3%); *Methicillin Resistant Staphylococcus aureus* (MRSA) 14(2.86%); *Coagulase Negative Staphylococcus* (CONS) 8;(1.6%); and β streptococci 2(.2%) were predominant isolates from our study Table 1 and Table 2. CONS was considered as pathogen after repeat isolation from the BSSI. There were 4 vancomycin and 6 rifampicin resistant isolates of *S.aureus* however we did not have vancomycin resistant *Enterococci*. Our study correlates to the study of Jelena Sotirović *et al.*, (2015).

In their study by Diana Vilar-Compte *et al.*, bacteria most frequently isolated were *E. coli*, *Pseudomonas* sp *S.aureus*, and coagulase-negative *Staphylococcus*.

Extended-spectrum beta-lactamases (ESBL) production out of the total 1058 samples were *E.coli* 328(31.00%); *Klebsiella* species 32 (3.02%); Non fermenting gram negative bacilli 6 (1.51%); *Proteus* species 12 (1.13%); *Pseudomonas aeruginosa* 6 (0.56%) *Citrobacter* species 6(0.56%).

Overall ESBL was 37.80% (400/1058) with *Escherichia coli* (*E.coli*) being the highest ESBL producer.

Amongst the oncological services, the total gram negative bacilli was(1058), BSSI from surgical oncology department had the maximum isolates 48.39%; followed by departments of gynaec oncology 20.79%; head and neck oncology 6.61%; oral oncology 1.70%. Among the gram positive cocci (488) oncosurgery department had the maximum isolates 40.98%; followed by gynaec oncology 31.14%; head and neck oncology 4.91%; oral oncology 1.63%.

Polymicrobial infection isolates was 516(33.37%) and monomicrobial isolates was 386 (24.96%).

The maximum resistance of the gram negative bacilli was to cefataxime and to ceftazidime and gram positive cocci to erythromycin and gentamicin from our studies as in table 3 and table 4.

This is the first study on bacterial BSSIs in cancer patients reported from a referral regional cancer centre in South India. Our analyses shows a moderate BSSIs in cancer patients. Surgical site infection rate in non cancer patients in India vary from a low of 2.5% to a high of 41.9% over a period of decades (DianaVilar-Compte *et al.*, 2000). Cancer patients are classified as being at high risk for hospital acquired infections and becomes pertinent to identify risk factors for possible outbreaks in hospitalized cancer patients.

The microbiological pathogens of BSSIs in cancer patients from our study were predominantly from the alimentary tract very similar to the report of Nikolaos *et al.*, (2015) where the prominent pathogens in neutropenic hosts were from the alimentary tract.

Cancer or high risk patients are more susceptible than non cancer patients to hospital acquired infection due to underlying immunocompromised state, surgery, use of invasive technology (ie, catheters/drains in-situ) and environmental factors. Velasco Thuler *et al.*, (2005) found that the median infection rate was much higher in the oncology intensive care unit than in the non oncology intensive care unit. Ananya *et al.*, (1997) mention that the cardinal feature and independent risk factor in oncological surgeries is if the operative time duration longer than 2 hours. Data study from 611 patients done by Serra-Aracil X *et al.*,

(Anaya *et al.*, 2012) where 383 patients underwent surgery for colon cancer and 228 underwent surgery for rectal cancer, surgical site infection was observed in 89 (23.2%) colon cancer patients and in 63 (27.6%) rectal cancer patients. The prevalence of SSI in elective colon and rectal operations remains high despite the application of evidence-based preventive measures while in women undergoing surgery for gynecologic cancer are associated with longer mean hospital stay and higher rate of resurgery, sepsis, and wound dehiscence in a study by Mahdi *et al.*, (2011).

Risk factors for BSSIs are pre, peri and post surgery depending on the type of organ involved in cancer surgery. Common predictive risk factors are contaminated and infected operations, surgical duration greater than 280 minutes, male sex, prior radiotherapy, American Society of Anesthesiology class III to V, and antimicrobial prophylaxis not according to protocol. *E. coli*, *Klebsiella* species, non fermenting gram negative bacilli and *proteus* species were the main gram negative isolates and our study similar to Bodey *et al.*, who found *E. coli*, *Klebsiella* species, and *P. aeruginosa* accounting for the majority of microbiologically documented infections at most cancer centers. The presence of ESBL producing Enterobacteriaceae, carbapenem resistant *Enterobacteriaceae* and multidrug-resistant *A. baumannii* is now routinely encountered among cancer patients (Bodey *et al.*, 1966; Arnan *et al.*, 2011; Irfan *et al.*, 2008; Sood *et al.*, 2012). An increase of ESBL producing *E. coli* was observed throughout our study period 40% in 2008 to 77% in 2014 study similar to cancer patients by Maria Fernanda Golzarri *et al.*, (2009). Of the infections polymicrobial infection isolates was 516 (33.37%) and monomicrobial isolates was 386 (24.96%)

with the gram negative bacilli *E.coli* and *Enterococci* species as the main isolates respectively in contrast to the study by Kenneth Rolston *et al.*, (2015) on SSIs in cancer patients where 58% were monomicrobial and 42% were polymicrobial and 85% of the 215 monomicrobial infections were due to gram-positive organisms and 13% by gram negative bacilli. *S.aureus* was the predominant pathogen in monomicrobial infections (70%). Sixty (40%) of these *Staphylococcal*

isolates were *methicillin resistant* (MRSA). *P. aeruginosa* was the predominant gram negative pathogen (19 of 27, 70%).*E. coli*, *Klebsiella* and *Enterococci* species were the predominant gram negative bacilli and gram positive cocci pathogens isolated in polymicrobial infections while *E. coli* was the main isolate in monomicrobial infection (2010), a study on BSSIs had 60% monomicrobial and 40% polymicrobial infections.

Table.1
Main Bacteriological spectrum out of 1546 Surgical Site Infections

Sl. No.	Name	Total No.
1.	Gram Negative Bacilli	1058
2.	Gram Positive Cocci	488
3.	Polymicrobes	516
4.	Monomicrobes	386
5.	Extended-spectrum β-lactamases	400

Table.2 Spectrum Of Pathogens Causing Surgical Site Infections

Sl. No	Gram Negative Bacilli	<i>E.coli</i>	<i>Klebsiella</i> spp.	<i>Pseudomonas</i> spp.	NFGNB	<i>Proteus</i> spp	Citrobacter
1.		59.73%	13.98%	10.39%	8.12%	5.86%	1.89%
2.	ESβL	82%	8%	1.5%	4%	3%	1.5%
	Gram Positive Cocci	<i>Enterococci</i> Spp	<i>S.aureus</i>	MRSA	CONS	<i>B-Streptococci</i>	
3.		53.68%	41.30%	2.86%	1.6%	0.2%	

E.coli:*Escherichia coli*; NFGNB:Non Fermenting Gram Negative Bacilli; ESβL: Extended Spectrum beta-lactamases; *S.aureus*:*Staphylococcus aureus*; MRSA:*Methicillin Resistant Staphylococcus aureus*; CONS:*Coagulase Negative Staphylococcus*

Table.3 Resistance Pattern Of Gram Negative Bacilli
Total Number 1058

Pathogen	Amikacin	Cefataxime	Ceftazidime	Cefuroxime	Gentamicin	Ciprofloxacin	Cefaperazone	Imipenem
<i>E.coli</i>	104 (9.82%)	670 (63.32%)	428 (40.45%)	434 (41.02%)	114 (10.77%)	322 (30.43%)	44 (4.15%)	28 (2.64%)
<i>Klebsiella species</i>	38 (3.59%)	98 (9.26%)	82 (7.75%)	96 (9.07%)	52 (4.91%)	70 (6.61%)	18 (1.70%)	22 (2.07%)
NFGNB*	30 (2.83%)	36 (3.40%)	44 (4.15%)	56 (5.29%)	24 (2.26%)	40 (3.78%)	10 (0.94%)	18 (1.70%)
<i>Proteus species</i>	16 (1.51%)	12 (1.13%)	26 (2.45%)	26 (2.45%)	12 (1.13%)	10 (0.94%)	2 (0.18%)	2 (0.18%)
<i>Pseudomonas Species</i>	18 (1.70%)	18 (1.70%)	8 (0.75%)	4 (0.37%)	28 (2.64%)	20 (1.89%)	4 (0.37%)	6 (0.56%)
<i>Citrobacter species</i>	10 (0.94%)	16 (1.51%)	16 (1.51%)	18 (1.70%)	6 (0.56%)	6 (0.56%)	6 (0.56%)	-----
*NFGNB = Non Fermenting Gram Negative Bacilli								

Table.4 Resistance Pattern Of Gram Positive Cocci; Total Number 488							
Pathogen	Amkacin	Erythromicin	Gentamicin	Cephalexin	Netilmicin	Vancomycin	Rifampicin
<i>Enterococci</i> Species	40 (8.19%)	128 (26.2%)	114 (23.36%)	42 (8.60%)	-----	-----	-----
<i>Staphylococcus aureus</i>	12 (2.45%)	62 (12.70%)	68 (13.93%)	52 (10.65%)	2 (0.40%)	4 (0.81%)	6 (1.22%)
MRSA*	4 (0.81%)	4 (0.81%)	6 (1.22%)	10 (2.04%)	-----	-----	2 (0.40%)
CONS**	-----	4 (0.81%)	-----	4 (0.81%)	-----	-----	-----

*MRSA – Methicillin Resistant *Staphylococcus aureus*.

**CONS – Coagulase Negative *Staphylococcus*.

Methicillin Resistant Staphylococci aureus (MRSA) isolation in our study was low (0.20%) which co-relate to the study of Maria Fernanda Golzarri in a study of 1863 SSIs for over a period of 6 years. And to the contrary of study by Roy Chemaly who report increase in incidence of MRSA in their study of SSIs in cancer patients. Kenneth *et al.*, (2010) report a sixty (40%) isolation of MRSA from a study of 368 surgical site infections in cancer patients.

Study on surgical site bacterial infections at the national cancer institute in Mexico: A case-control study by Diana Vilar-Compte, found most frequently isolated pathogens were *E. coli* 38 (21.8%), *Pseudomonas* sp 22 (12.6%), *S. aureus* 16 (9.2%), and *coagulase-negative Staphylococci* 25 (13.6%) and infer that the surgical site infection rate in cancer hospital is slightly higher than the rates reported for general hospitals which is contrary to the BSSI's from our cancer hospital. Unhealing surgical site infections will be prone towards longer mean hospital stay, multiply drug resistance, probability of burst abdomen due to sepsis, and wound dehiscence. Surgical site infections protocol for patients with febrile and afebrile neutropenia may have to be implemented to reduce morbidity and mortality of the patients. Risk factors such as age, immunocompromised state, diabetes, duration of surgery, time of drain in – situ depending on the organ site may play a major role in BSSI's.

Diana Vilar-Compte, *et al.*, in their study found diabetes mellitus, obesity, and prolonged presence of a surgical drain as risk factors for SSI's. Whereas Jelena *et al.*, found age, sex, BMI, history of smoking and underlying diabetes were not associated with risk factors for their SSI's. H.Tominaga (2007) suggest that age, tumor site, operating time, amount of bleeding and SSI

risk index were all important SSIs risk factors in predicting colorectal cancer surgery.

Diana *et al.*, (2009) established concomitant preoperative chemoradiation, haematoma, age \geq 58 years, body mass index \geq 30.8 and duration of surgery \geq 160 minutes were found to be SSI-associated risk factors and emphasize the need to identify SSI-associated risk factors and improve quality of care to patients.

Our study involved all onco surgical services in our hospital and respective surgical risk factors were not done due to unavailability of many data. In our study we isolated *E.coli* and *Enterococci* as the predominant gram negative bacilli and gram positive cocci respectively as the main onco SSI bacterial pathogen.

In conclusion, despite suppressed immune status in cancer patients, infections and associated various risk factors, BSSIs is low in our hospital. To have a “no BSSI's” in a cancer hospital inadvertent overuse of higher antibiotics must be avoided to reduce multiply drug resistance, implementation of institutional antibiotic policy to oncosurgical patients, evaluation of inherent oncosurgical risk factors pre, peri and post operatively need to be defined and incorporated.

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