

Staphylococcus aureus: A predominant cause of surgical site infections in a rural healthcare setup of Uttarakhand

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ABSTRACT

Introduction: Surgical site infections (SSIs) represent the second most common type of healthcare-associated infections and remain a relatively common postoperative complication and the most common reason for readmission after surgery. SSIs have dire implications for the surgeon, patient, and institution which often require prolonged treatment, impose an economic burden and double the risk of patient mortality. *Staphylococcus aureus* is currently the most common cause of SSIs causing as many as 37% of cases of SSIs in community hospitals with methicillin-resistant *S. aureus* (MRSA) of particular concern. **Materials and Methods:** This cross-sectional study was conducted from January 2014 to December 2014 in a rural tertiary care hospital of Pauri Garhwal district of Uttarakhand state, India. Samples were collected using sterile cotton swabs from 269 patients clinically diagnosed with SSIs and were processed as per standard microbiological techniques. Antimicrobial susceptibility testing was done using a modified Kirby-Bauer disc diffusion method. **Results:** Out of 1294 patients, 269 (20.8%) were found to have SSIs and samples were collected from them. Out of a total of 269 samples, 258 (95.9%) yielded bacterial growth and 267 bacterial isolates were obtained. *S. aureus* (45.3%) was the commonest organism followed by *Escherichia coli* (13.9%), *Pseudomonas aeruginosa* (6.7%), and *Proteus* species (4.9%). Antimicrobial profile of *S. aureus* revealed maximum sensitivity to rifampicin, linezolid, teicoplanin, vancomycin, and amikacin whereas ampicillin, cefazolin, and gentamicin were found to be least sensitive. **Conclusion:** *S. aureus* played a predominant role in the etiology of SSIs in this hospital with MRSA being a major concern as the treatment options for such resistant strains are limited. Reduction in SSI rates can lead to both better clinical outcomes for patients and cost savings for hospitals. Adherence to strict infection control measures, maintenance of proper hand hygiene and optimal preoperative, intraoperative, and postoperative patient care can surely reduce the incidence of SSIs. A multifaceted approach involving the surgical team, microbiologist, and the infection control team is required to provide quality surgical services.

Keywords: Bundled intervention, infection control, methicillin resistance, multidrug resistance

Introduction

Surgical site infection (SSI) is among the most common problems for patients who undergo operative procedures and represents the second most common type of healthcare-associated infection (HAI).^[1,2] SSIs are the most common reason for readmission after surgery and account for nearly 20% of

unplanned readmissions.^[3] They are associated with increased morbidity, mortality, readmission, reoperation, limitation of the quality of life, loss of daily wages, prolonged hospital stays, and consequently increased health care costs, which may be considerably higher in drug-resistant organisms.^[4-6] The SSIs are usually caused by exogenous and/or endogenous microorganisms that enter the operative wound either during the surgery (primary infection) or after the surgery (secondary infection).^[7] Primary infections are usually more serious, appearing within 5 to 7 days of surgery.^[8] The majority of SSIs are uncomplicated involving only skin and subcutaneous tissue but sometimes can progress

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Received: 09-07-2019

Revised: 22-08-2019

Accepted: 16-10-2019

Published: 15-11-2019

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_521_19

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How to cite this article: Pal S, Sayana A, Joshi A, Juyal D. *Staphylococcus aureus*: A predominant cause of surgical site infections in a rural healthcare setup of Uttarakhand. J Family Med Prim Care 2019;8:3600-6.

to necrotizing infections. The usual presentation of infected surgical wounds can be characterized by pain, tenderness, warmth, erythema, swelling, and drainage.^[9,10] A number of patient-related factors (old age, nutritional status, pre-existing infection, comorbid illness) and procedure-related factors (poor surgical technique, prolonged duration of surgery, preoperative part preparation, inadequate sterilization of surgical instruments) can influence the risk of SSIs significantly.^[11-13] In addition to these risk factors, the virulence and the invasiveness of the organism involved, physiological state of the wound tissue, and the immunological integrity of the host are also the important factors that determine whether infection occurs or not.^[14]

Staphylococcus aureus is currently the most common cause of SSIs causing as many as 37% of cases of SSIs in community hospitals with MRSA of particular concern.^[15] *S. aureus* resides on skin surfaces and it is estimated that *S. aureus* colonizes the anterior nares in approximately 31% (range 6–56%) of the general population at any given time.^[16] Nasal carriage of *S. aureus* is epidemiologically linked to the development of *S. aureus* SSI notably in orthopedic surgery.^[17] Kaljimer *et al.*^[18] found that nasal carriage of *S. aureus* was the only independent risk factor for *S. aureus* SSI after orthopedic implant surgery. In general, patients who are carriers of *S. aureus* are two to nine times more likely to develop an SSI, and it has been shown that 85% of SSIs can be traced to endogenous colonization of the patients.^[19]

S. aureus can cause suppurative infections ranging from superficial skin lesions to deep-seated infections. The prevalence of SSI caused by *S. aureus* has been increasing over the past few decades, predominantly due to continuous upsurge in the drug-resistant isolates. According to the center for disease control and prevention (CDC), the proportion of SSIs due to *S. aureus* increased from 16.6% to 30.9% from 1992 to 2002 and the number of methicillin-resistant *S. aureus* (MRSA) isolates also raised from 9.2%–49.3%.^[20] Globally the prevalence of MRSA is progressively increasing with significant regional variation. Moreover, surveillance data have shown that in hospital settings methicillin-sensitive *S. aureus* (MSSA) tends to evolve into MRSA, an important cause of postoperative infection. More recently *S. aureus* has emerged as the single most common SSI pathogen and is associated with particularly severe patient outcomes.^[20]

Understanding the prevalence, antibiotic resistance patterns and information on accurate and reliable detection methods of *S. aureus* strains is necessary for appropriate antibiotic treatment and effective infection control. With the above background, the current study was undertaken to give an overview of the existing epidemiological data on the incidence of SSIs caused by *S. aureus* in our tertiary care center/Health care set up.

Materials and Methods

This cross-sectional study was conducted for a period of twelve months (January 2014 to Dec 2014) in a rural tertiary care hospital of Pauri Garhwal district of Uttarakhand state, India. Prior to

the sample collection, approval from the Institutional Ethical Committee was obtained (19.12.2013). The study population included 269 patients suffering from SSIs in the various surgical wards (orthopedics, general surgery, ophthalmology, obstetrics and gynecology, otorhinolaryngology) of our hospital. Patients of both sex, age >14 years, who had surgical wounds with pus discharge, with serous or seropurulent discharge and with signs of sepsis present concurrently (warmth, erythema, enduration, tenderness, pain, raised local temperature) were included. Patients who had suture abscesses; wounds with cellulitis and no drainage were excluded from the study. A detailed history regarding age, sex, type of illness, diagnosis, type and duration of surgery performed, antibiotic therapy and the associated co-morbid diseases was obtained from the patients.

Using sterile cotton swabs, two pus swabs/wound swabs were collected aseptically from each patient suspected of having SSI. Gram-stained preparations were made from one swab for provisional diagnosis. The other swab was inoculated on 5% sheep blood agar (BA) and Mac Conkey agar (MA) plates and incubated at 37°C for 48 hours before being reported as no growth. Growth on culture plates was identified by its colony characters and the battery of standard biochemical tests.^[21,22] Colonies that were suggestive of *S. aureus* were identified by gram's staining, catalase test, tube coagulase test, and mannitol fermentation test. Antimicrobial sensitivity testing (AST) was carried out by the modified Kirby Bauer disc diffusion method on Muller Hinton agar and results were interpreted in accordance with Clinical Laboratory Standards Institute guidelines.^[23] Methicillin resistance was detected by taking cefoxitin (30 µg) as a surrogate marker and was confirmed by using PBP2a latex agglutination test (Oxoid Ltd, Hampshire, UK). *Staphylococcus aureus* – ATCC25923, *Escherichia coli* - ATCC25922, and *Pseudomonas aeruginosa* - ATCC27853 were used as control strains for AST. All dehydrated media, reagents, and antibiotic discs were procured from Himedia Laboratories Pvt. Ltd., Mumbai, India.

Results

From January 2014 to December 2014, a total of 1294 patients underwent major surgeries in various departments of our hospital, out of which 269 patients (20.8%) were clinically diagnosed with SSIs. Out of total of 269 samples processed, 258 (95.9%) yielded aerobic bacterial growth and a total of 267 bacterial isolates were obtained. Monomicrobial growth was seen in 249 samples while nine samples showed polymicrobial growth. The mean age of the patients was 44.5 years (range 14 to 81 years). Males (79.6%) were more commonly affected than females (20.4%) with male: female ratio of 3.9:1.

Among the 267 bacterial isolates, *Staphylococcus* (173; 64.8%) was the most commonly isolated organism. Out of the total 173 Staphylococcal isolates 121 (69.9%) were *S. aureus* (87 MSSA; 34 MRSA) and 52 (30.1%) were coagulase-negative *Staphylococcus* (CONS): 38 MSCONS; 14 MRCONS. Other

predominant organisms that were isolated were *Escherichia*, *Pseudomonas*, *Klebsiella*, *Enterobacter*, *Proteus*, *Citrobacter*, and *Acinetobacter*. Table 1 depicts the characterization of various bacterial isolates obtained from patients with SSIs.

The antimicrobial profile of the Staphylococcal isolates is depicted in Table 2. Methicillin resistance was seen in 48/173 (27.7%) of Staphylococcal isolates among which 19.6% were MRSA and 8.1% were MRCONS. The high degree of resistance was seen for ampicillin and cefazolin.

Linezolid, ticoplanin, vancomycin, and amikacin were found to be the most sensitive antimicrobial agents. Methicillin-resistant isolates (MRSA and MRCONS) showed an overall higher degree of resistance in comparison to methicillin-sensitive isolates (MSSA and MSCONS).

Discussion

Although SSI is one of the preventable causes of nosocomial infections, it is an important contributor to HAIs worldwide.^[24] Despite the advances in surgical techniques and a better understanding of the pathogenesis of wound infection, management of SSIs remain a significant concern for surgeons and physicians in a healthcare facility. Moreover patients with SSIs are further exposed to the microbial flora circulating in a hospital set up which is always charged with pathogenic microorganisms. The unrestrained and rapidly spreading resistance to the available array of antimicrobials further potentiates the existing problem.^[25]

The rate of SSI is an important indicator of the quality of surgical procedures in a hospital. It may vary from hospital to hospital and has been reported to be 2.5% to 41.9%.^[26] In the present study, the overall rate of SSI was 20.8%, which was in concordance with the study conducted by Negi *et al.* (17.8%) and Bhattacharya *et al.* (15.51%).^[25,27]

Various studies from India have reported the rate of SSIs to vary from 6.1% to 39%.^[26,28-32] However, the rate of infection reported in various international studies is quite low in comparison to Indian studies, for instance, in the USA it is 2.8% and in European countries, it is reported to be 2–5%.^[33] The lack of attention towards infection control measures, inappropriate hand hygiene practices, and overcrowded hospitals can be the major contributory factors for higher infection rates in Indian hospitals.

It has been regularly noted that *S. aureus* continues to be the single most important bacterial species in the primary etiology of SSIs with a prevalence rate ranging from 4.6% to 54.4%.^[30] In the present study, *S.aureus* comprised of 45.3% of SSIs, a finding which was in tandem with the previous studies by Negi *et al.* (50.4%), Ranjan *et al.* (34%), Naik *et al.* (32.2%), and Krishna *et al.* (31.3%).^[25,34-36] Infections with *S. aureus* is most likely associated with endogenous source as it is a member of the skin and nasal flora, and also with contamination from the

Table 1: Characterization of various bacterial isolates obtained from patients with surgical site infections. (n=267)

Organism	Number of isolates (%)
<i>Staphylococcus species</i>	173 (64.8)
<i>S. aureus</i>	121 (69.9)
MSSA	87 (71.9)
MRSA	34 (28.1)
CONS	52 (30.1)
MSCONS	38 (73.1)
MRCONS	14 (26.9)
<i>Escherichia coli</i>	37 (13.9)
<i>Pseudomonas aeruginosa</i>	18 (6.7)
<i>Proteus species</i>	13 (4.9)
<i>P. mirabilis</i>	9 (69.2)
<i>P. vulgaris</i>	4 (30.8)
<i>Klebsiella species</i>	8 (3.0)
<i>K. pneumoniae</i>	5 (62.5)
<i>K. oxytoca</i>	3 (37.5)
<i>Enterobacter Species</i>	7 (2.6)
<i>E. aerogenes</i>	4 (57.1)
<i>E. cloacae</i>	3 (42.9)
<i>Citrobacter species</i>	7 (2.6)
<i>C. freundii</i>	5 (71.4)
<i>C. koseri</i>	2 (28.6)
<i>Acinetobacter species</i>	4 (1.5)
<i>A. baumannii</i>	3 (75.0)
<i>A. lowfii</i>	1 (25.0)

CONS: Coagulase negative staphylococcus; MSSA: Methicillin sensitive *S. aureus*; MRSA: Methicillin resistant *S. aureus*; MSCONS: Methicillin sensitive coagulase negative staphylococcus; MRCONS: Methicillin resistant coagulase negative staphylococcus

Table 2: Antibiogram of staphylococcal isolates obtained from patients with surgical site infections. (n=173)

Antibiotic	<i>S. aureus</i>		CONS	
	MSSA (n=87)	MRSA (n=34)	MSCONS (n=38)	MRCONS (n=14)
AMK	6.9	14.7	5.3	7.1
AMP	83.9	91.2	76.3	85.7
AMC	35.6	55.9	36.8	57.1
CFZ	79.3	82.3	65.8	71.4
CFX	0	100	0	100
CIP	32.2	44.1	34.2	42.9
CTR	21.8	26.5	13.2	21.4
GEN	44.8	47.1	42.1	42.9
LNZ	0	0	0	0
RIF	0	0	0	0
TEC	0	0	0	0
VAN	0	0	0	0

Sensitivity pattern shown in the table is the percentage of isolates resistant to the antibiotic. Intermediately sensitive isolates were considered as resistant. AMP: Ampicillin; AMC: Amoxicillin-clavulanate; AMK: Amikacin; CFZ: Cefazolin; CFX: Cefoxitin; CIP: Ciprofloxacin; CTR: Co-trimoxazole; GEN: Gentamicin; LNZ: Linezolid; RIF: Rifampicin; TEC: Teicoplanin; VAN: Vancomycin

environment, surgical instruments, or from hands of healthcare workers (HCW).^[37] Literature revealed that 80% of the healthy individuals across the world harbor *S. aureus* in their skin or anterior nares and integrity of the skin if breached during any surgery could commonly cause skin and soft tissue infections with this organism.^[38] All these factors have made up *S.aureus* as the most common organism causing SSIs.

S. aureus was the single predominant gram-positive bacterial isolate obtained in this study. Special interest in *S. aureus* SSI is mainly due to its predominant role in HAI and the emergence of MRSA strains. Methicillin resistance occurs due to the acquisition of *me cA* gene, which encodes a unique penicillin-binding protein, designated as PBP 2a. This reduces affinity for β -lactams and allows effective cell wall synthesis even in the presence of penicillins including antistaphylococcal penicillins, as well as, cephalosporins and carbapenems.^[39] Therefore, the choice of drugs becomes limited to combat MRSA strains. The prolonged hospital stay, arbitrary use of antibiotics, lack of awareness, over the counter dispensing of antibiotics, and so on are the potential predisposing factors for the emergence of MRSA strains.^[40] In our study, MRSA was seen in 12.7% of *S. aureus* isolates and the overall methicillin resistance among the Staphylococcal isolates (MRSA and MRCONS) was found to be 18%. This finding was in tandem with the previous studies by Negi *et al.* (15.7%), Aggarwal *et al.* (10%), and Naik *et al.* (9.6%),^[25,35,41] however, it was in contrast with the study conducted by Kaye *et al.* (58.2%), Eagye *et al.* (45%), and Kownhar *et al.* (21.7%), who reported a much higher rate of methicillin resistance in their studies.^[42-44] The variation in incidence of MRSA might depend on pre and postoperative antibiotic policy and surveillance programs prevailing in different setup.

Although SSIs can be reduced by appropriate use of surgical antimicrobial prophylaxis and in hospital practice 30–50% of antibiotics are prescribed for surgical prophylaxis but 30–90% of this prophylaxis is inappropriate.^[29] This inappropriate use increases selective negative pressure favoring the emergence of pathogenic drug-resistant bacteria which makes the choice of empirical antimicrobial agents more difficult and increases the risk of postoperative SSIs.

Antibiotic susceptibility results revealed that a high degree of resistance was seen for the majority of the bacterial isolates and the commonly used drugs were found to be more resistant. The development and spread of resistant bacterial strains have emerged as a global problem. The appearance of multidrug-resistant strains over the past decades has been regarded as an inevitable genetic response to the strong selective pressure imposed by antimicrobial chemotherapy which plays a crucial role in the evolution of antibiotic-resistant bacteria. All cases in our study received prophylactic antimicrobials prior to the surgery. Current recommendations for antimicrobial prophylaxis to prevent SSI advise that an antimicrobial agent be administered within 60 min prior to surgery and discontinued soon afterward.^[45] However, more than 50% of our patients received preoperative antimicrobials more than 6 h before surgery and almost all patients were treated with antimicrobials after surgery. Many of them were even treated until the day of discharge in an attempt to prevent infection while they were hospitalized. The most widely used combination was first-generation cephalosporin (cefazolin) and an aminoglycoside (gentamicin). However, the antimicrobial susceptibility results showed that the isolated *S. aureus* strains were mostly resistant to these agents. Invariably the maximum

resistance was observed for ampicillin by nearly all the isolates. The frequent empirical prescription of these antimicrobials as a treatment and prophylaxis in our hospital might have contributed for observed high degree of resistance. This situation raises serious concern and calls for immediate revision of antibiotic policy and antibiotic prescribing guidelines. The use of dual antimicrobial therapy (cephalosporin and aminoglycoside) and the unnecessarily extended duration of the prophylaxis remain the main concern in our set up. A prospective observational study may be undertaken in this regard to find out the effect of the prevalent pattern of surgical prophylaxis on the occurrence of SSI.

We found that all the staphylococcal isolates (irrespective of methicillin resistance) were sensitive to vancomycin, rifampicin, teicoplanin, and linezolid. Almost similar results were observed in studies from Uttarakhand, Gwalior, and Karnataka where vancomycin, teicoplanin, and linezolid showed 100% sensitivity to staphylococcal isolates.^[25,34,36] This finding could have a relevant clinical use in the antibiotic policy guidelines for hospitals. In this study, newer antibiotics like quinupristin, dalfopristin, and daptomycin were not tested, however, few reports from India have shown promising results with these antibiotics.^[46,47] As more and more resistance is developing, future work can be directed by performing *in-vitro* drug susceptibility testing with these newer antimicrobial agents, against MRSA.

Preventive measures

SSIs remain one of the most devastating complications for patients as well as surgeons, and the consequences can be detrimental both medically and financially. SSIs can prolong the hospital stays by a median of 2 weeks, nearly double re-hospitalization rates as well as increase health care costs by more than 300%.^[48,49] For the individual patient, the development of a serious SSI usually translates into months of parenteral antibiotics, additional surgical procedures, and extended inpatient and sub-acute care facility stays. The lengthy recovery can negate any benefit provided by the original operation and in a substantial portion, such infections can contribute to death.^[50,51] Prevention is therefore paramount and identifying potentially modifiable preoperative risk factor is of great interest. Despite all the recent focus on infection control, the incidence of SSIs seems to be on the rise worldwide.

SSIs which represent the second most common type of HAI is in most cases preventable when the patient and hospital staff members adhere to proper prevention practices such as the use of hand hygiene practices, minimizing operating room traffic, screening and decolonization of *S. aureus* carriers, and the appropriate timing and type of prophylactic antibiotic use.^[52]

In addition to the above, recently, there has been much focus on bundled interventions and investigators have demonstrated that the implementation of bundled interventions has greatly decreased the rate of specific SSIs.^[53,54] Bundled intervention

is comprised of three components: a) screening for *S. aureus* carriage; b) decolonization of carriers with intranasal mupirocin and chlorhexidine gluconate bathing; c) optimized perioperative antimicrobial prophylaxis (effective against gram-positive organisms, especially MRSA as well as Gram-negative organisms) An assessment of the effectiveness of this bundled intervention and the individual components of this bundle can greatly inform clinical practice.

Implementation of an evidence-based bundle of interventions to decrease SSIs could benefit both patients and hospitals. A bundled intervention that goes beyond measures advocated by the Surgical Care Improvement Project (SCIP) could potentially reduce rates of SSIs, specifically those associated with *S. aureus*.^[54,55] A meta-analysis found that a bundle approach was associated with lower rates of *S. aureus* SSIs among patients undergoing cardiac operations or hip or knee arthroplasties.^[53] Despite this evidence, surveys indicate that adoption of this bundled approach varies substantially; most clinicians do not screen patients for *S. aureus* carriage before operations and those who screen, often screen for MRSA alone. Similarly, clinicians that decolonize patients preoperatively usually decolonize only patients carrying MRSA despite the greater frequency of colonization by MSSA and the severity of MSSA infections.^[56,57]

Findings of our study can be helpful for primary care physicians to optimize the infection control measures in their set up, particularly in resource-constrained settings. Moreover periodic epidemiological surveillance will allow them to better understand the microbial etiology of SSIs and the predominant organisms responsible for such infections in a hospital, which will be further helpful in establishing improved antimicrobial prophylaxis guidelines in a given set up.

Conclusion

Our most common SSI isolate was *S. aureus* and the MRSA constituted 12.7% of the total SSI isolates. Due to the increased morbidity and mortality associated with these drug-resistant organisms, early detection and intervention are a prerequisite in surgical patients. Although completely eliminating SSIs seems to be a far cry, but the reduction in the infection rate to a minimal level could have significant benefits, not only by reducing patient morbidity and mortality but also by preventing the pharmacotherapeutic and pharmacoeconomic losses.

Infection control measures such as active surveillance of SSIs, the implementation of checklists, compliance observations, implementation of screening and decolonizing protocols for *S. aureus*, and maintaining proper hand hygiene are essential in order to prevent SSIs. It is high time for Indian hospital management to ensure a regular, close clinical liaison between the surgical team, the microbiologist and the infection control team to provide quality surgical services. We realize that data extrapolated from our study may not be representative of the whole Indian scenario and must be interpreted cautiously. However, the

findings of our study can be used as a template to optimize hospital antimicrobial policy and antimicrobial prescribing guidelines. The relevant and regular policy and protocol changes can definitely decrease the SSI rate in any healthcare facility. Given the considerable clinical and economic consequences of SSIs, the goal of a healthcare system should be “zero tolerance” to such infections and the associated adverse events. By all parameters, our war against the pathogenic organisms causing SSIs is far from winning. The question is – are we serious?

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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