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Review Article

Surgery Section

The Burden of Methicillin Resistant *Staphylococcus aureus* in Surgical Site Infections: A Review

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ABSTRACT

Despite increased pre and postoperative care including screening procedures, improvement in the operating room environment, and controlled prophylactic antibiotic therapy, the health burden of Surgical Site Infections (SSIs) in India is far more escalated than that in developed countries. SSIs ranging from superficial skin infection to life-threatening septicemia affect one third of the patient population undergoing surgery, thereby contributing to morbidity and mortality. One of the most dominant bacterial species that causes SSIs is *Staphylococcus aureus*, wherein Methicillin Resistant *S.aureus* (MRSA) alone contributes to a significant increase in both the cost and the length of hospitalisation along with an increased mortality rate among patients with SSIs. The rising resistance pattern among pathogens coupled with the concerns over the tolerance and safety of currently available agents against MRSA limits treatment options available for patients with SSIs. Levonadifloxacin and its oral prodrug alalevonadifloxacin are novel benzoquinolizine anti-MRSA agents which have recently been approved in India to tackle gram positive 'super-bugs'. Herein, the aim of this review article was to collate the possible factors contributing toward SSIs, its implications on health and economy, antibiotic resistance, possible preventive measures, and the need for new antimicrobial agents.

Keywords: Antibiotic resistance, Hospital acquired infection, Methicillin resistant *Staphylococcus aureus*, Surgical site infection

INTRODUCTION

With advancement in medicine and surgical technology, the life expectancy of humans has increased considerably; however, the risk of infections after surgery remains. Postoperative infections or SSIs can be defined as any infection that occurs within 30 days postoperative and usually at the site of the incision. They not only lead to increased morbidity and mortality rates, but are also associated with high economic burden due to increase in postoperative duration of hospitalisation and related costs to health care system [1]. Approximately 5% of patients who undergo surgery develop SSIs [2]. The incidence of SSIs has been reported to be 2.5-41.9%, with the incidence being significantly higher in developing countries than in developed countries [1]. SSIs causes one third of postoperative deaths and accounts for 8% of all deaths caused by nosocomial infections [3].

With the development of new drugs to treat infections and eradicate harmful pathogens, new and more dangerous strains of pathogens have evolved that are resistant to the current antibiotic regimen, such as Methicillin Resistant *Staphylococcus aureus* (MRSA). MRSA, known as the "Hospital Superbug", is a life-threatening nosocomial pathogen that is resistant to methicillin and other antibiotics due to multiple mutations that has made its treatment challenging [4]. In 2017, World Health Organisation (WHO) has listed MRSA as a 'high' priority pathogen, due to its increased prevalence of resistance, mortality rate and ever rising burden on community and health care settings [5]. Infections due to MRSA usually lead to increased treatment costs and hospital stay. A meta-analysis study has reported that approximately 19.1% of SSIs are caused by *S.aureus*, out of which >40% of SSIs are caused by MRSA [6].

In this review, authors have discussed the community and healthcare burden including risk factors and epidemiology of *S.aureus* including MRSA globally. In India, it is associated with resistant patterns, preventive strategies, impact of SSIs and also associated with economic burden, the need to develop new antibiotics and finally novel anti-MRSA agents for SSI treatment, which have recently been launched in India.

SOURCE OF LITERATURE

For this review, PubMed, Scopus including Medline and EMBASE, Database of Abstracts of Reviews of Effects (DARE), Cochrane Library, and Web of Science were searched for relevant literature. A total of 90 articles were studied, out of which 77 articles were published in the English language in the period from 1st January, 2008 to 31st August, 2020 were included. Thirteen articles for which full text was not available, were excluded. Furthermore, reference lists of all related studies were reviewed for any other related publication. The broad keywords used for the literature manual search were "India", "SSI," "postoperative infections," "*Staphylococcus aureus*," "gram positive bacteria," "MRSA," "methicillin resistance," "Hospital-Acquired Infection (HAI)," and "nosocomial infection."

Review of literature: Surgical Site Infections (SSIs) is a common menace for patients undergoing operative procedure which result in nearly 20% of unplanned readmissions [7]. Klevens RM et al., showed that in the United States (US), SSIs account for 11% of the total deaths in the Intensive Care Unit (ICU) [8]. The development of SSIs subsequently lead to patient distress, increased postoperative hospital stay, decreased quality of life, high expenditure for both the patient and the hospital, and compromised patient health outcome postoperatively [9].

According to Centre for Disease Control and Prevention (CDC) and European Centre for Disease Prevention and Control (ECDC), SSIs, which are one of the most frequent HAI, is defined as a postoperative infections occurring within 30 days of surgical procedure [10,11]. According to the CDC, SSIs or incisional site infections can be classified into the following three types based on how deep the surgical incision is made:

1. Superficial incisional SSI
2. Deep incisional SSI
3. Organ/space SSI

The common criteria for this classification is purulent drainage from the incisional site (either superficial, deep, or organ/space, deliberately

opened by the surgeon), identification of the causative organism by culture or non-culture microbiological tests, pain/tenderness at the incisional site (in case of organ/space SSI, there would be an abscess formation or any form of infection that can be determined by performing histopathological and physical examinations), and diagnosis by the surgeon or the attending physician [12].

CAUSES AND RISK FACTORS OF SSI

The main causative agents of SSIs are both gram negative and gram positive bacteria. Gram positive bacteria include *Staphylococci, Streptococci*, and *Enterococci* species and coagulase negative *staphylococci*, whereas gram negative bacteria include *Enterobacter, Klebsiella, Escherichia coli*, and *Pseudomonas* species. These bacteria possibly originate from two sources: endogenous, wherein the patient's own flora transfers to the incision site, and exogenous, wherein the bacteria arrive through any external mode of transport, even from operating room personnel [13]. These infections can arise because of multiple reasons, including environment, type of bacteria, virulence and number of contaminating bacteria, immunity and nutritional status of the patient [14].

Furthermore, a combination of various risk factors contributes to SSIs, some of which are patient related or procedure related. Patient related factors include advanced age, gender, diabetes mellitus, malnutrition and tobacco smoking. In addition to these factors, a recent study from West India identified preoperative anemia, preoperative hypoalbuminemia and perioperative blood transfusion to be significantly associated with SSIs [15]. Procedure related factors include the operative sites, duration of surgical procedure and patient preparation factors. According to a study by Marimuthu K et al., days from admission to the operation, re-interventions unrelated to infections, American Society of Anaesthesiology (ASA) score of >2, duration of surgery, and surgery under general anaesthesia are independent risk factors for *S.aureus* and MRSA SSI in patients undergoing surgery [16]. [Table/Fig-1] lists the risk factors associated with SSIs [17,18].

Patient related risk factors	Procedure related risk factors
• Age >45 years • Gender (male) • Obesity/High Body Mass Index (BMI) • Hypertension • Smoking • Diabetes • Wound type (dirty, clean, or clean-contaminated) • Low nutritional status • Serum albumin level (<3.5 g/dL) • Compromised immunity • Underlying disease	• Type of surgery • Complexity of surgical procedures • Prolonged surgical procedures • Increased preoperative stay • Inadequate preoperative sterilisation (instruments/equipment) • Inadequate preparation of skin • Poor surgical techniques • Preoperative shaving • Operating room ventilation • Surgical drains • Foreign material in the surgical site

[Table/Fig-1]: Risk factors associated with SSIs [17,18].
SSI: Surgical site infection

EPIDEMIOLOGY OF *S.AUREUS* INCLUDING MRSA IN SSIS

SSIs are a serious complication of any surgery, which leads to poor patient outcomes and increased hospital costs. [Table/Fig-2] shows the global data on the incidence of SSIs postoperatively based on the type of surgery and country [19-36].

Multiple studies has reported SSIs ranging from 4-38% across India [37-39]. In SSIs, *S.aureus* is the most dominant pathogen that plays crucial role in its aetiology. Among *S.aureus*, MRSA is associated with worse clinical outcomes and according to National Healthcare Safety Network (NHSN), it leads to 15% of total SSIs reported [40].

Marimuthu K et al., performed an extensive study in which data from a network of hospitals were analysed to elucidate the incidence, prevalence and risk factors of SSIs caused by MRSA. In their study, MRSA and Methicillin-Sensitive *S.aureus* (MSSA) infections

Author	Country	Type of surgery	Incidence of SSI postoperatively
Sun Y et al., [19]	China	Open reduction and internal fixation for ankle fracture	1.1%-40% (2.6%-24%, superficial SSI; 1.1%-6%, deep SSI)
Karakida K et al., [20]	Japan	Oral cancer surgery with microvascular-free flap reconstruction	36.5%-50%
Chang CC et al., [21]	Taiwan	Total hip or knee replacement	1.80%
Kalish JA et al., [22]	USA	Infrainguinal lower extremity bypass surgery	4.8% (0%-30%)
Olsen MA et al., [23]	USA	Mastectomy and breast reconstructive surgery	5.30%
Pull ter Gunne AF et al., [24]	USA	Adult spinal surgery	5.5% (3.5%, deep SSI)
Kiran RP et al., [25]	USA	Colorectal surgery	14%
Sugiura T et al., [26]	Japan	Pancreaticod-uodenectomy	62.74% (14.95%, superficial SSI; 47.75%, organ/space SSI)
Okabayashi T et al., [27]	Japan	Hepatic resection	14.50%
Watanabe A et al., [28]	Japan	Upper and lower gastrointestinal surgery	15.50%
Shirata C et al., [29]	Japan	Hepatectomy after hepatocellular carcinoma	11.03% (2.7%, superficial; 8.3%, organ/space SSI)
Dionigi G et al., [30]	Italy	Thyroidectomy	3.20%
van der Slegt J et al., [31]	Nethe-rlands	Vascular surgery	15.75% (9.4%, superficial SSI; 6.29%, deep SSI)
Olsen MA et al., [32]	USA	Low transverse caesarean	5%
Lemaignen A et al., [33]	France	Cardiac surgery	4.10%
Chiang HY et al., [34]	USA	Craniectomy	4.1% (0.47%, superficial SSI; 1.49%, deep SSI; 2.1% organ/space SSI)
Bhattacharya S et al., [35]	India	General surgery	15.51%
Pathak A et al., [36]	India	Obstetric and gynaecological surgeries	7.84% (5.62%, superficial SSI; 2.22%, deep SSI)

[Table/Fig-2]: Global incidence of SSI postoperatively based on the type of surgery [19-36].
SSI: Surgical site infection

contributed to 19.3% and 80.7%, of *S.aureus* SSIs [16]. Similarly, another study reported 28.5% MRSA prevalence among patients with SSIs. On univariate analysis, age, duration of surgery, duration of postoperative antibiotic treatment was significantly associated with MRSA SSIs [41]. In another extensive study by Baker AW et al., *S.aureus* (34%) was found to be the most common organism responsible for SSIs wherein both MRSA and MSSA were equally responsible (17%) for SSIs [42]. Further, a recent report by Akhi MT et al., showed high frequency of MRSA (83.3%) in SSIs [43].

In India, the prevalence of *S.aureus* ranges from 31.3-50.4% in SSIs. A recent Indian study from Kolkata showed that among *S.aureus* (35%) isolates in SSIs, MRSA prevalence was 25.4% with the majority being reported from the Surgery Department (12.5%) [35]. Similarly, Pal S et al., also demonstrated that among patients undergoing major surgeries, Staphylococcal species (64.8%) are the most common causative pathogen in developing SSIs. Among *S.aureus* (45.3%), MRSA prevalence was observed to be 28.1% [44]. Further, [Table/Fig-3] shows the type of surgery, incidence of SSI, and causative organisms of SSIs from studies conducted across India [18,45-48].

Author	Location	Type of surgery	Microorganisms involved	Incidence of SSI
Sharma MS et al., [45]	New Delhi	Neurosurgery	Staphylococci species	2.50%
Joyce SB and Lakshmidevi N [18]	Karnataka	Gastroenterological and gynaecological surgeries	*S.aureus*, MRSA, *P.aeruginosa*, *E.coli, Klebsiella* species	12%
Patel DA et al., [46]	Gujarat	Gastroenterological surgery and amputation	*S.aureus, Klebsiella* species	12.72%
Reddy BR et al., [47]	Andhra Pradesh	General and gastroenterological surgeries	*Enterococcus* species, MRSA, *Streptococci, E.coli, Klebsiella* species	3.63%
Patel SM et al., [48]	Gujarat	Gastroenterological, nephrological, and lower limb surgeries	*S.aureus, E.coli, Klebsiella* species, *P. aeruginosa*	16%

[Table/Fig-3]: Causative organisms and incidence of SSIs in India [18,45-48].
SSI: Surgical site infection; MRSA: Methicillin-resistant *Staphylococcus aureus*

ANTIBIOTIC RESISTANCE OF MRSA

Recent Indian Council of Medical Research- Antimicrobial Resistance Surveillance Network (ICMR-AMRSN) study showed that, as compared to ward/Out Patient Department (OPD), the ICU settings are associated with elevated MRSA rates along with increased resistance to antimicrobials [49].

For more than four decades, vancomycin remains the drug of choice to treat Multidrug Resistant (MDR) MRSA infections. However, increased usage of vancomycin has resulted in a steady decline of vancomycin susceptibility (Minimum Inhibitory Concentration (MIC) creep) as more resistant *S.aureus* strains called Vancomycin Intermediate *S.aureus* (VISA) and Vancomycin Resistant *S.aureus* (VRSA) have emerged. A recent study from Southern India showed that among the MRSA isolates, the heterogeneous VISA (hVISA) prevalence was as high as 12.4% [50]. Apart from vancomycin, linezolid and daptomycin are also used widely to treat MRSA infections. However, in 2011, the first case of linezolid resistant *Staphylococcus* spp. was found in India [51]. A recent study from Northern India reported that among *S.aureus* isolates, MRSA prevalence was as high as 51.2%. In the same study, 11.7% were VISA, 5.5% were teicoplanin resistant and 4.5% were linezolid resistant [52].

In 2017, Calina D et al., showed *S.aureus* (50.7%) to be the most prevalent pathogen isolated from SSIs. Moreover, strains isolated from the ICU showed higher resistance to antibiotics than those isolated from surgical wards [53]. A recent study from Northern India showed Methicillin resistant isolates (MRSA and Methicillin-Resistant Coagulase Negative Staphylococci (MR-CoNS)) to have higher antibiotic resistance rate than methicillin sensitive isolates including MSSA and MS-CoNS [44].

IMPACT AND ECONOMIC BURDEN OF SSIs

Development of SSIs is not only a clinical but also a financial burden on both patient and the health care settings. Reoperation, extended hospitalisation stay, laboratory tests and treatment leads to an increased financial burden on the patients with SSIs. Badia JM et al., analysed studies from six European countries and found that patients who developed SSIs have increased cost burden of surgery as opposed to uninfected patients [54]. Another review reported the length of hospitalisation to be more than twice as long for SSIs patients as compared to patients without any infection [55]. According to a study by Jenks PJ et al., the total hospital costs increase according to the length of hospital stay, type of room used, type of SSI, and the amount of antibiotics administered to treat SSIs [56]. Another study analysed 125,000 cases of SSIs which were estimated to cost USD 1.6 billion in added costs with 1 million additional hospital days [57]. Patients with SSIs are also vulnerable to secondary complications such as bacteremia [58] and deteriorating mental health. In 2017, Gelhorn HL et al., conducted interviews of patients who developed SSIs postoperatively, to study the burden and impact of such infections physically, emotionally and financially. The study revealed that the infections had impacted their daily activities and physical functioning that led to isolation, anxiety and depression among the patients recovering from SSIs [59].

In a clinical review on the epidemiology of SSIs and HAIs in India, Ramasubramanian V et al., reported that treatment cost increased with increasing intensity of infection in patients with SSI. Mild, moderate, and severe infections resulted in 3.8%, 14.7%, and 29.4% increase in treatment cost, respectively [17]. Tiwari P and Rohit M conducted a study in 2013 in a tertiary care hospital in Northern India and reported the average total cost for SSI to be INR 5,33,738±68,044 [60]. [Table/Fig-4] shows the different categories of costs incurred by patients, which include the cost for hospitalisation, consultation, investigation, and drugs, as the average cost in Indian Rupee (INR) and United States Dollar (USD) along with the standard error of the mean [56].

Component of cost	SSI in mean±SEM	
	INR	USD
Drugs' acquisition costs	1,65,400±49,234	3,007±895
Rent (ward/ICU)	1,06,003±39,723	1,927±722
Consultation fees	23,072±11,187	402±203
Investigations	51,413±6,655	935±121
Antimicrobial drugs	1,24,408±51,767	2,262±941
Total cost	5,33,738±68,044	9,704±1,237

[Table/Fig-4]: Total hospital treatment costs incurred by patients with SSIs [56].
USD 1=INR 55. SSI: Surgical site infection; ICU: Intensive care unit; SEM: Standard error of mean

According to a cost comparison study performed by Joyce SB and Lakshmidevi N, Indian patients with SSIs incurred a total expense of INR 29,000 (USD 527) on an average because of increased stay in ICU or wards, whereas the uninfected patients incurred a total expense of INR 16,000 (USD 290) on an average. The mortality rate was also higher among patients with SSIs (12.8%) compared with those not affected by SSIs (3.8%) [18].

In a multicentre matched outcomes study, Anderson DJ et al., found that SSI patients with MRSA infections had increased hospitalisation stay by six days, incurred an additional cost of USD 23,000 and were 2.6 time more likely to die within 90 days as compared to SSI patients infected with MSSA. This difference in cost (USD 40,000), hospital stay (16 more days) and death within 90 days (7 fold) was far higher for SSIs due to MRSA than uninfected controls [61]. In terms of the difference in economic burden between patients with SSIs due to MRSA or MSSA infection, Shorr AF et al., did not report any significant differences in inpatient hospital costs between the two, but their estimates were reportedly high at USD 70,028 and USD 71,186, respectively [62]. In contrast, Filice GA et al., estimated the mean cost of medical services to be higher in patients with SSIs due to MRSA than in patients with MSSA (USD 51,252 vs. USD 30,158) [63].

ISOLATION MEASURES AND PREVENTION STRATEGIES

With *S.aureus* being the most common pathogen in causing postoperative infections, prevention and management steps need to be taken by hospitals and health care centers to reduce the prevalence and growing incidence of *S.aureus* particularly MRSA. If required, hospitals must perform isolation procedures to avoid bacterial contamination to other patients in the same location. In 2017, CDC has set up standard protocols and guidelines for the prevention of SSIs, that need to be followed by all hospitals and health care centers to improve patient safety [64].

It has been shown that 26-37% of patients who are *S.aureus* carriers [65,66]; also have increased rates of SSIs [67]. Cadenazuluag J et al., have shown that patients with MRSA colonisation who are diabetic,

are undergoing surgery or dialysis are at a higher risk of developing MRSA infections as compared to patients who are non-carriers [68]. Kalmeijer MD et al., reported nasal carriage of *S.aureus* to be the only significant risk factor in developing SSIs [69]. Additionally, the incidence of SSIs increased from 12.5% among patients who are nasal carriers of *S.aureus* to 33% in patients with nasal carrier of MRSA [70]. Not only the patients, but the health care workers who are MRSA carriers, can also transmit this pathogen to the patients. van Vugt JL et al., have shown significantly increased *S.aureus* nasal carriage rate among surgeon and residents as compared to non-hospitalised patients [71].

Therefore, in 2018, Kavanagh KT et al., advocated that apart from the standard guidelines, two more additional strategies should be adopted to prevent the spread of MRSA and other MDR pathogens [72]. These include preoperative screening and decolonisation for *S.aureus* including MRSA in both patients and healthcare workers. A success rate of 90% is reported after MRSA decolonisation of the healthcare workers. Also, a preoperative decolonisation protocol has been shown to decrease SSIs among patients [65,73].

Apart from transmission of MRSA from carriers to patients, there is also a risk of MRSA transmission from donor to recipient(s) during transplantation surgeries. These are called donor derived infections and are defined as evidence of the same infection in the donor and the recipient(s) [74,75]. Wendt JM et al., described two cases of post-transplant MRSA infection in recipients whose common donor died of MRSA related complications [74]. Therefore, it is important to timely detect and determine the presence of infections transferred from the donor to the recipients and treat it with appropriate antibiotic prophylaxis.

Different surgical approaches and appropriate anaesthesia management can be adopted to reduce SSIs postoperatively. Chang CC et al., in their study performed total hip and knee replacements and reported that the incidence of SSI varied depending on the type of anaesthesia administered. They reported that the odds of SSIs for patients who underwent total hip and knee replacement under general anaesthesia were 2.21 times higher than those for patients who underwent surgery under spinal or epidural anaesthesia [21]. Apart from this, minimally invasive procedures have also been reported to decrease the incidence of postoperative infections. Kiran RP et al., reported that laparoscopic techniques significantly reduced SSIs after colorectal surgery. In their study, the incidence of SSIs was reported to be 9.5% using laparoscopic surgery as compared to 16.1% using open colorectal surgery [25]. This showed promising results in reducing SSIs as the risk of bacterial contamination reduces due to lesser human intervention.

CURRENTLY AVAILABLE ANTIBIOTICS TO TREAT MRSA SSIS AND ITS LIMITATION

In addition to the preoperative procedures such as MRSA screening, prophylactic antibiotics are also given to prevent SSIs. According to the WHO global guidelines, 39-51% of the SSI pathogens are resistant to standard prophylactic antibiotic regimen [76]. Therefore, the timing and the choice of prophylactic antibiotics also plays a major role.

Preoperative methods include screening of patients for MRSA with nasal swabbing to treat them in case they are tested positive for MRSA. Patients tested positive for MRSA preoperatively are at a high risk of developing SSI postoperatively. Tomov M et al., administered mupirocin to patients who were tested positive for MRSA. Intranasal swabbing of mupirocin is a relatively new method that is implemented for patients undergoing spinal surgery. Perioperative methods include antibiotic (first-generation cephalosporin for patients with MSSA and vancomycin for patients with MRSA or those who are allergic to β-lactam antibiotics) administration during surgery [77].

Currently, vancomycin or teicoplanin are being used as prophylactic agents for MRSA infections. However, these too come along with their limitations. Vancomycin and teicoplanin have shown variable tissue penetration and is a potential agent for nephrotoxicity if used in higher doses or for a longer duration [78]. Branch-Elliman W et al., reported that vancomycin usage in cardiac surgery patients was associated with significantly increased risk of acute kidney injury and that it is more harmful than beneficial for MRSA negative or MRSA unknown patients [79]. Other anti-MRSA drugs like linezolid and daptomycin have their own associated toxicity effect (linezolid cause myleosuppression and daptomycin is associated with myotoxicity) and drug interactions (linezolid with selective serotonin re-uptake inhibitors) which limits their therapeutic usage in SSI patients. Therefore, there is a need for a safe and efficacious option for tackling complicated MRSA infections.

Levonadifloxacin: A Novel Broad Spectrum anti-MRSA Agent

A recent new addition to the MRSA antibiotic armamentarium is levonadifloxacin and its oral prodrug, alalevonadifloxacin which have been granted approval in India in December, 2019. These novel broad spectrum antibiotics belonging to the benzoquinolizine subclass of fluoroquinolones have been approved for the treatment of Acute Bacterial Skin and Skin Structure Infection (ABSSSI) including diabetic foot infections and concurrent bacteremia in adults. With an established multi-spectrum antibacterial coverage ranging across MDR gram positive (MRSA and QRSA, hVISA and VRSA isolates), respiratory gram negative, anaerobes and atypical pathogens, levonadifloxacin promises favorable clinical outcome in severe infections. Additionally, levonadifloxacin has a dual mode of action where it targets both DNA gyrase (primary affinity) and Topoisomerase IV which equips levonadifloxacin to act against quinolone resistant *S.aureus* strains also [80]. Salient features such as narrow mutant selection window, ability to act in high bacterial load and not being a substrate of NorA efflux pumps conferred levonadifloxacin with low resistance potential in *S.aureus*. With an ability to act in acidic conditions, levonadifloxacin demonstrated potent bactericidal killing of MRSA in not only the phagocytic cells but also of biofilm embedded MRSA and QRSA strains which helps in combating difficult to treat MRSA infections [81]. Availability of both intravenous and oral formulation helps in easy switch over. In the phase 3 study, levonadifloxacin demonstrated excellent clinical activity and was safe and well tolerated in the treatment of ABSSSI caused by gram positive pathogens including MRSA [82]. The superior pharmacokinetic/pharmacodynamic profile of levonadifloxacin is expected to result in favourable clinical outcome in patients with MRSA SSIs.

CONCLUSION(S)

Surgical Site Infections (SSIs) are a major burden to not only the patients and their families but also to healthcare systems and society as a whole. They contribute to significant morbidity and mortality rates along with prolonged hospitalisation and associated costs. *S.aureus* is one of the most common pathogen causing SSIs. The rising incidence of MRSA has become a health concern and is associated with increased mortality rates, length of hospital stay and treatment costs when compared to MSSA. The toxicity profiles of the currently available anti-MRSA agents have limited the therapeutic options for the treatment of MDR MRSA infections. With MRSA being on the 'priority pathogen' list of the WHO, it is imperative to focus on the research and development activities directed towards the development of novel and effective antibiotics that can cater to these MDR gram positive superbugs. Recently, approved antibiotic, levonadifloxacin has the potential to provide an effective treatment option which can addresses the unmet need for a novel, efficacious and safe antibiotic agent, to combat MDR gram positive infections including SSIs caused by MRSA.

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