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Antibiotic Use, Incidence and Risk Factors for Orthopedic Surgical Site Infections in a Teaching Hospital in Madhya Pradesh, India †

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Abstract: Orthopedic surgeries contribute to overall surgical site infection (SSI) events worldwide. In India, SSI rates vary considerably depending on geographical location (1.6–38%); however, there is a lack of a national SSI surveillance system.. This study aims to identify the SSI incidence, risk factors, antibiotic prescription and susceptibility patterns among operated orthopedic patients in a teaching hospital in India. Data for 1205 patients were collected from 2013 to 2016. SSIs were identified based on the Centre for Disease Control and Prevention's guidelines. The American Society for Anesthesiologists classification system was used to predict patients' operative risk. Univariable and multivariable backward stepwise logistic regressions were performed to identify risk factors for SSIs. Overall, 7.6% patients developed SSIs over three years. Out of 68 samples sent for culture and susceptibility testing, 22% were culture positive. The most common SSI-causing microorganism was *Staphylococcus aureus* (7%), whose strains were resistant to penicillin (100%), erythromycin (80%), cotrimoxazole (80%), amikacin (60%) and cefoxitin (60%). Amikacin was the most prescribed antibiotic (36%). Male sex (OR 2.64; 95%CI 1.32–5.30), previous hospitalization (OR 2.15; 95%CI 1.25–3.69), prescription of antibiotics during hospitalization before perioperative antibiotic prophylaxis (OR 4.19; 95%CI 2.51–7.00) and postoperative length of stay >15 days (OR 3.30; 95%CI 1.83–5.95) were identified as significant risk factors for orthopedic SSIs. Additionally, a preoperative shower significantly increased the risk of SSIs (OR 4.73; 95% CI 2.72–8.22), which is unconfirmed in the literature so far.

Keywords: surgical site infections; SSI; incidence; risk factors; orthopedic; antibiotic susceptibility patterns; teaching hospital; India

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1. Introduction

Surgical site infections (SSIs) are the most frequent healthcare-associated infections (HAIs). Orthopedic surgeries contribute to SSI events in hospitals worldwide and remain a challenge for patients and surgeons [1,2]. One of the recommended measures for the prevention of SSIs is the administration of systemic antibiotics shortly before a surgery, i.e., perioperative antibiotic prophylaxis (PAP) [3]. *Staphylococcus aureus* is the most common cause of orthopedic implant-associated infections, which can be difficult to treat due to high levels of antibiotic resistance [4]. Some risk factors for orthopedic SSIs are well known, e.g., male sex and age, while others remain to be confirmed [5]. In India, there are considerable variations in SSI rates depending on geographical location, ranging from 1.6% to 38% [6–8].

Additionally, there is a lack of a national surveillance system and guidelines on antibiotic use for common infections. This study aims to assess the incidence and risk factors for SSIs as well as the common pathogens causing SSIs and their antibiotic susceptibilities, and to analyze antibiotic use among the operated orthopedic patients in a private teaching hospital in Ujjain, India.

2. Methods

Data were collected from 2013 to 2016 by trained hospital personnel using locally developed paper forms. The following information was collected: patients' demographic characteristics, potential risk factors for SSIs, patient history, clinical diagnoses, type of performed procedures, surgery outcomes, confirmation that samples were sent for culture and antibiotic susceptibility testing and antibiotic prescriptions. In total, 1205 operated orthopedic patients were included in the analysis. Patients were characterized based on SSI occurrence and antibiotic use. SSI occurrence was defined by the Centre for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN) definition indicating a 30- or 90-day SSI surveillance period, which is determined by the NHSN operative procedure category and the tissue level of the SSI event [9]. SSI surveillance period was one year for patients with implants [10]. The American Society for Anesthesiologists (ASA) classification system was used to assess the patients' physiological status to predict the operative risk. Standard methods were followed to process the samples sent for culture and susceptibility tests [11]. The inoculated blood agar and McConkey agar plates were incubated at 37 °C for 18–24 h. Microorganisms were identified by using standard laboratory techniques and the Clinical and Laboratory Standard Institute's (CLSI) guidelines [11,12]. Prescribed antibiotics were classified according to the WHO Anatomical Therapeutic Chemical (ATC) classification system [13].

Data were analyzed using Stata 15.1 (Stata Corp., College Station, TX, USA). Univariable logistic regression was performed to identify risk factors for SSIs. Statistically significant risk factors (p-value < 0.05) were included in multivariable backward stepwise logistic regression analysis. Pearson's correlation coefficients were calculated for statistically significant risk factors from univariable analysis, and the coefficients which showed high correlation ($\geq$0.5) were excluded from multivariable analysis. Independent variables included in Model 1 were: male sex, ASA II and III scores, previous hospitalization, antibiotic(s) prescribed 14 days before hospital admission, perioperative antibiotic prophylaxis (PAP), antibiotic treatment during hospital stay before PAP, duration of postoperative antibiotic treatment >14 days, postoperative length of stay (LOS) >15 days, preoperative shower, compound fracture, drain and implant. Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) were calculated to compare the models and choose the best model.

3. Results

Overall, 91/1205 (7.6%) of the operated patients developed SSIs over three years. Table 1 shows that 68 pus/wound samples were sent for culture and susceptibility testing, out of which 15 were culture positive. The most common microorganism that caused SSIs was *S. aureus* (5/68, 7%) followed by gram-negative organisms: *Klebsiella* spp. (4/68, 6%), *Pseudomonas* spp. (4/68, 6%) and *Escherichia coli* (2/68, 3%). All strains of *S. aureus* were resistant to penicillin. High resistance was also seen against erythromycin (80%), cotrimoxazole (80%) and amikacin (60%). Three of the five strains of *S. aureus* were resistant to cefoxitin (methicillin-resistant *S. aureus*, MRSA). However, gram-negative organisms showed more than a 50% susceptibility to third generation cephalosporins.

Table 1. Antibiotic susceptibility patterns of the bacterial isolates in orthopedic surgical site infections in a teaching hospital, Ujjain, Central India.

Antibiotics Tested	Gram-Positive Organisms	Gram-Negative Organisms			
	S. aureus (N = 5)	*Pseudomonas* (N = 4)	*Klebsiella* (N = 4)	*E. coli* (N = 2)	Total
Penicillin	5	-	-	-	-
Erythromycin	4	-	-	-	-
Ciprofloxacin	3	3	1	1	5/10
Cefoxitin	3	-	1	1	2/6
Tetracycline	2	-	3	1	4/6
Cotrimoxazole	4	-	2	2	4/6
Vancomycin	-	-	-	-	-
Linezolid	-	-	-	-	-
Clindamycin	-	-	-	-	-
Amikacin	3	3	1	0	4/10
Gentamycin	3	3	1	1	5/10
Ampicillin	-	-	3	1	4/6
Amoxiclav	-	-	2	1	3/6
Piperacillin Tazobactam	-	3	1	0	4/10
Cefuroxime	-	-	2	1	4/6
Cefepime	-	3	2	1	6/10
Cefotaxime	-	-	2	1	3/6
Ceftriaxone	-	-	2	1	3/6
Ceftazidime	-	3	2	1	6/10
Meropenem	-	1	0	0	1/10
Aztreonam	-	3	0	1	4/10

The susceptibility to colistin in GNB organisms was 100%; one *Klebsiella* isolate was an ESBL producer.

The most prescribed antibiotic was amikacin (J01GB06, 37%) followed by a combination of ceftriaxone with a beta-lactamase inhibitor (J01DD63, 24%) and cefoperazone with a beta-lactamase inhibitor (J01DD62, 13%). Additionally, the most prescribed PAP was ceftriaxone or cefoperazone in combination with a beta-lactamase inhibitor together with intravenous amikacin. Table 2 presents the results of the univariable logistic regression analysis, which indicate that the following factors were significantly associated with the risk of developing SSIs: male sex (OR 3.42, 95% CI 1.79–6.49), ASA II score (OR 2.63, 95% CI 1.57–4.43), previous hospitalization (OR 4.14, 95% CI 2.57–6.66), history of antibiotic(s) 14 days before admission (OR 4.71, 95% CI 2.59–8.58), PAP (OR 0.34, 95% CI 0.21–0.53), antibiotic(s) prescribed during hospitalization before PAP (OR 3.75, 95% CI 2.42–5.80), duration of postoperative antibiotic treatment >14 days (OR 4.23, 95% CI 2.32–7.69), postoperative LOS >15 days (OR 5.99, 95% CI 2.59–13.87), preoperative shower (OR 3.94, 95% CI 2.49–6.24), compound fracture (OR 4.87, 95% CI 2.21–10.76), the presence of drain (OR 3.21, 95% CI 1.43–7.20) and implant (OR 4.07, 95% CI 2.64–6.29). Based on these risk factors, three multivariable models were built, out of which Model 3 showed the best combination of AIC and BIC (Table 2). According to Model 3, the following risk factors were found to be significantly associated with SSIs: male sex (OR 2.64; 95% CI 1.32–5.30), previous hospitalization (OR 2.15; 95% CI 1.25–3.69), antibiotic treatment during hospitalization before PAP (OR 4.19; 95% CI 2.51–7.00), postoperative LOS >15 days (OR 3.30; 95% CI 1.83–5.95) and preoperative shower (OR 4.73; 95% CI 2.72–8.22).

Table 2. Univariable and multivariable analyses of risk factors associated with orthopedic surgical site infections.

Risk Factor		Univariable Analysis			Multivariable Analysis								
					Model 1			Model 2			Model 3		
					AIC = 454, BIC = 523			AIC = 482, BIC = 512			AIC = 447, BIC = 487		
		OR	95% CI	*p*–Value	OR	95% CI	*p*–Value	OR	95% CI	*p*–Value	OR	95% CI	*p*–Value
Sex	Female	1											
	Male	3.42	1.79–6.49	0.000	2.57	1.25–5.29	0.010	2.93	1.48–5.77	0.002	2.64	1.32–5.30	0.006
Age, years	≤18	1.00											
	19–60	1.45	0.84–2.48	0.182									
	>60	1.05	0.46–2.39	0.911									
ASA score	ASA I	1											
	ASA II	2.63	1.57–4.43	0.000	1.30	0.67–2.49	0.437						
	ASA III	2.45	0.99–6.01	0.051	2.08	0.76–5.72	0.156						
Previous hospitalization		4.14	2.57–6.66	0.000	1.65	0.85–3.19	0.139				2.15	1.25–3.69	0.006
Antibiotic prescribed 14 days before hospital admission		4.71	2.59–8.58	0.000	1.45	0.61–3.42	0.400						
PAP		0.34	0.21–0.53	0.000	1.11	0.52–2.34	0.789						
Antibiotic treatment during hospital stay before PAP		3.75	2.42–5.80	0.000	3.93	2.33–6.63	0.000	3.92	2.40–6.43	0.000	4.19	2.51–7.00	0.000
Duration of preoperative antibiotic, days	1–7	1											
	8–14	1.2	0.51–2.85	0.674									
	>14	1.48	0.55–3.96	0.438									
Postoperative antibiotic		0.75	0.42–1.31	0.311									
Duration of postoperative antibiotic, days	1–7	1											
	8–14	1.71	0.90–3.23	0.100									
	>14	4.23	2.32–7.69	0.000	1.05	1.00–1.09	0.043	1.05	1.01–1.09	0.028	1.04	1.00–1.09	0.051
Preoperative LOS, days	1–3	1											
	4–7	1.00	0.57–1.76	0.999									
	8–15	0.68	0.35–1.30	0.243									
	>15	1.39	0.62–3.12	0.419									
Postoperative LOS, days	1–3	1											
	4–7	1.07	0.38–2.99	0.900									
	8–15	2.10	0.90–4.88	0.086									
	>15	5.99	2.59–13.87	0.000	3.03	1.65–5.58	0.000	2.95	1.67–5.20	0.000	3.30	1.83–5.95	0.000
Preoperative shower		3.94	2.49–6.24	0.000	4.14	1.99–8.56	0.000	5.49	3.29–9.16	0.000	4.73	2.72–8.22	0.000
Hair removal	Not done	1.00											
	Previous night	0.65	0.36–1.19	0.161									
	Same day	0.56	0.15–2.03	0.375									
	Shaving	0.59	0.33–1.08	0.087									
Type of fracture	Closed	1											
	Compound	4.87	2.21–10.76	0.000	1.97	0.73–5.35	0.182						
Nature of surgery	Elective	1											
	Emergency	1.72	0.39–7.66	0.476									
Duration of surgery, min	≤60	1.00											
	61–120	0.60	0.35–1.03	0.064									
	>120	0.64	0.34–1.23	0.180									
Blood transfusion		0.88	0.54–1.43	0.601									
Oxygen support		0.75	0.29–1.93	0.547									
Drain		3.21	1.43–7.20	0.005	1.83	0.74–4.50	0.189				1.73	0.71–4.22	0.231
Implants		4.07	2.64–6.29	0.000	1.34	0.71–2.50	0.366						

4. Discussion

The SSI incidence of 7.6% over three years is in the range of overall SSI incidences reported in EU countries (0.5–10.1%) [14]. However, a study from Madhya Pradesh reported a lower SSI rate (2.1%) in orthopedic wards compared to that of our study [15]. In general, studies show that orthopedic procedures have somewhat lower SSI rates in both high- and middle-income countries, as reported by studies in New Zealand (1.3%), China (2.18%) and Jordan (2.8%) [1,16,17]. A systematic review from 57 hospitals across the world reported an orthopedic SSI rate of 2.7% [18]. The difference in the incidence rates can partially be attributed to higher standards of care in high- and some middle-income countries and stricter policies for delivering care.

S. aureus was the most common pathogen causing SSIs, responsible for 33% of the culture-positive samples. Likewise, studies from New Zealand [16] and India [15] reported *S. aureus* to be the main causative organism of orthopedic SSIs, responsible for 54% and 29% culture-positive samples, respectively. However, in a study from China, *Coagulase-negative Staphylococcus* (CoNS) was the predominant SSI-causing pathogen (42.8%) in orthopedic surgery, followed by *S. aureus* (11.4%) [1]. Moreover, in our study, 60% of *S. aureus* samples were methicillin-resistant (MRSA). More than 50% of *S. aureus* HAIs in Europe and the US are caused by MRSA, which is becoming increasingly challenging to treat due to antibiotic resistance [18].In orthopedic surgery, PAP is considered to be one of the most effective measures to reduce the risk of SSIs [19]. In the western literature, the most widely recommended PAP for orthopedic procedures is cefazolin [16,20]. In our study, the most used PAP was third generation cephalosporin (ceftriaxone or cefoperazone in combination with a beta-lactamase inhibitor) with intravenous amikacin. The different choices of PAP might be explained by the different prevalent bacteria, susceptibility patterns and operating theatre conditions in an Indian setting [19]. However, given that 20% and 47% of our culture-positive bacterial isolates were resistant to ceftriaxone and amikacin, respectively, appropriate modifications to the usual choice of PAP are suggested to prevent SSIs more efficiently.

A postoperative LOS longer than 15 days and previous hospitalization significantly increase the risk of SSIs. Previous surgery was confirmed as a risk factor by previous research [1], especially in the case of spinal surgery [21]. Postoperative LOS was also identified as a risk factor for orthopedic SSIs by a cohort study from Jordan [17]. Previous hospitalization might also be associated with an increased LOS [22]. In our study, the median LOS was significantly higher in SSI patients (13 days) compared to non-SSI patients (8 days). A Swedish study showed that 42% of all adverse events in orthopedic surgery prolong the LOS for an average of 6.1 days [23]. One study from India showed that the maximum median LOS was in surgical oncology patients (31.5 days) followed by orthopedic surgery patients (14 days) [24].

Antibiotic treatment during a hospital stay before PAP is significantly associated with the risk of developing SSIs. The patients who needed prolonged preoperative and postoperative antibiotic treatment are mostly the patients with implants or osteomyelitis who had come to the hospital with signs of delayed or late infections (e.g., pus, swelling or abscesses) [25]. Prolonged antibiotic treatment contributes to the development of antibiotic resistance [26], which has most likely contributed to the development of SSIs [27].

A preoperative shower is found to significantly increase the risk of orthopedic SSIs. The literature on the benefit of an antiseptic preoperative shower is controversial. Some studies list the preoperative shower as a protective factor that reduces the incidence of SSIs, which is explained by the reduction in the microbial colonization of skin [28,29]. On the other hand, certain studies found no clinically relevant benefit of preoperative chlorhexidine showers [29,30]. Contrary to these findings, the results of our study suggest that the preoperative shower is a significant risk factor for SSIs. This might be due to the fact that in our study hospital, patients are only advised to take a shower or bath before surgery, hence we do not know if patients had actually taken a shower and with what (water, soap, chlorhexidine, etc.). Furthermore, the microbiological quality of water that people use for washing in the Ujjain district has been questioned earlier; therefore, a similar study is proposed to check the water quality in the setting [31].

This study had a long follow-up time, which allowed enough time to identify SSI cases, even in cases of late implant infection. However, the postoperative follow-up was only conducted in 27% of patients, so there is a chance that the SSI rate has been underestimated. Data analysis was conducted five years after data collection, which might have influenced the accuracy of the follow-up of some details. A relatively small sample size might have affected the multivariable analysis of potential confounders and risk factors for SSIs.

5. Conclusions

The SSI incidence rate of 7.6% over three years in this study is relatively low compared to reported incidence range for India, yet higher than the reported SSI incidences for orthopedic surgeries in high- and middle-income countries. The most common SSI-causing pathogen was *S. aureus* and the most prescribed PAP was third generation cephalosporin with intravenous amikacin. Factors that significantly increased the risk of orthopedic SSIs were the male sex, previous hospitalization, antibiotic treatment during hospital stay before PAP and a postoperative LOS >15 days. A preoperative shower was also found to be a significant risk factor for SSIs, which is undocumented in the literature so far, to the best of our knowledge. Further studies are needed to confirm this finding and explore the possible reasons behind it. The identification of SSI incidences and risk factors in orthopedic surgery wards supports overall measures to prevent and mitigate SSIs in hospitals.

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Institutional Review Board Statement: The study was approved by the Ethics committee of Ruxmaniben Deepchand Gardi Medical College, Ujjain, with approval letter number 311/2013.

Informed Consent Statement: There was no need for informed consent. Trained nurses recorded data using patient files. There was no direct interaction with patients, nor interference with the treatment procedure. Patient data were analyzed anonymously at a group level.

Data Availability Statement: As per the policy of the institute, the metadata of any research are not shared with the general public. This is to protect the patients' confidentiality and hospital and hospital staff safety concerning the medical, ethical and legal issues. However, the data can be made available to the researchers who meet the criteria to access the confidential data via the Chairman of the Ethics Committee, R.D. Gardi Medical College, Agar Road, Ujjain, Madhya Pradesh, India, 456006 (email: iecrdgmc@yahoo.in), by giving all details of the article. A request can be made by quoting the ethical approval number: 311/2013.

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