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

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Abstract: Orthopaedic surgeries contribute to the 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 incidence and risk factors for SSIs, and antibiotic prescription and susceptibility patterns of infecting bacteria among the operated orthopaedic 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 guidelines. The American Society for Anesthesiologists classification system was used to predict patients' operative risk. Univariable and multivariable backward stepwise logistic regression 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 SSIs 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 hospitalisation (OR 2.15; 95%CI 1.25–3.69), prescription of antibiotics during hospitalisation 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 orthopaedic SSIs. Also, preoperative shower significantly increased the risk of SSIs (OR 4.73; 95%CI 2.72–8.22), which is unforeseen so far.

Keywords: surgical site infections; SSI; incidence; risk factors; orthopaedic; 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 the 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 an administration of systemic antibiotics shortly before a surgery, i.e., perioperative antibiotic prophylaxis (PAP) [3]. *Staphylococcus aureus* is the most common cause of orthopaedic implant-associated infections, which can be difficult to treat due to high levels of antibiotic resistance [4]. Some risk factors for orthopaedic 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]. Also, 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, the common pathogens causing SSIs and their antibiotic susceptibility, and to analyse antibiotic use among the operated orthopaedic 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, antibiotic prescriptions. In total, 1205 operated orthopaedic patients were included in the analysis. Patients were characterized based on the SSI occurrence and antibiotic use. SSI occurrence was defined by the Centre for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) definition with 30- or 90-day SSI surveillance period, which is determined by the NHSN operative procedure category and the tissue level of 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 (CLSI) guidelines [11,12]. Prescribed antibiotics were classified according to the WHO Anatomical Therapeutic Chemical (ATC) classification system [13].

Data were analysed 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 (≥0.5) were excluded from multivariable analysis. Independent variables included in Model 1 were: male sex, ASA II and III scores, previous hospitalisation, 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, 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%) operated patients developed SSI 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 five strains of *S. aureus* were resistant to cefoxitin (methicillin-resistant *S. aureus*, MRSA). However, gram-negative organisms showed more than 50% susceptibility to 3rd generation cephalosporins.

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 beta-lactamase inhibitor together with intravenous amikacin. Table 2 presents the results of 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 hospitalisation 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, following risk factors were found to be significantly associated with SSIs: male sex (OR 2.64; 95% CI 1.32–5.30), previous hospitalisation (OR 2.15; 95% CI 1.25–3.69), antibiotic treatment during hospitalisation before PAP (OR 4.19; 95% CI 2.51–7.00), postoperative LOS >15 days (OR 3.30; 95% CI 1.83–5.95), preoperative shower (OR 4.73; 95% CI 2.72–8.22).

Table 1. Antibiotic susceptibility patterns of the bacterial isolates in orthopaedic 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

Susceptibility to colistin in GNB organisms was 100%, one *Klebsiella* isolate was ESBL producer.

4. Discussion

SSI incidence of 7.6% over three years is in the range of overall SSI incidences reported in the EU countries (0.5–10.1%) [14]. However, a study from Madhya Pradesh reported a lower SSI rate (2.1%) in orthopaedic ward compared to our study [15]. In general, studies show that orthopaedic 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 orthopaedic 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 orthopaedic SSIs, responsible for 54% and 29% culture-positive samples, respectively. However, in a study from China, *Coagulase-negative Staphylococcus* (CoNS) was the predominant SSIs causing pathogen (42.8%) in orthopaedic 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].

Table 2. Univariable and multivariable analyses of risk factors associated with orthopaedic 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 hospitalisation		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						

In orthopaedic 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 orthopaedic procedures is cefazolin [16,20]. In our study, the most used PAP was 3rd generation cephalosporin (ceftriaxone or cefoperazone in combination with beta-lactamase inhibitor) with intravenous amikacin. Different choices of PAP might be explained with different prevalent bacteria, susceptibility patterns and operating theatre conditions in 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.

Postoperative LOS longer than 15 days and previous hospitalisation 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 orthopaedic SSIs by a cohort study from Jordan [17]. Previous hospitalisation might also be associated with increased LOS [22]. In our study, 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 orthopaedic 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 orthopaedic surgery patients (14 days) [24].

Antibiotic treatment during 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 infection (e.g., pus, swelling or abscess) [25]. Prolonged antibiotic treatment contributes to the development of antibiotic resistance [26], which has most likely contributed to the development of SSIs [27].

Preoperative shower is found to significantly increase the risk of orthopaedic SSIs. The literature on the benefit of antiseptic preoperative shower is controversial. Some studies list preoperative shower as a protective factor that reduces the incidence of SSIs, which is explained by the reduction of 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 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 the case of late implant infection. However, the postoperative follow-up was only done in 27% of patients, so there is a chance of underestimation of SSI rate. Data analysis was done five years after data collection, which might have influenced the accuracy of 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 reported SSI incidences for orthopaedic surgeries in high- and middle-income countries. The most common SSI-causative pathogen was *S. aureus* and the most prescribed PAP was 3rd generation cephalosporin with intravenous amikacin. Factors that significantly increased the risk of orthopaedic SSIs were male sex, previous hospitalisation, antibiotic treatment during hospital stay before PAP and postoperative LOS >15 days. 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. Identification of the SSI incidences and risk factors in orthopaedic surgery wards supports overall measures to prevent and mitigate SSIs in hospitals.

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