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Systematic Review

Analyzing the Prevalence and Patterns of Antibiotic-Resistant Pathogens Causing Surgical Site Infections

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ABSTRACT

Surgical Site Infections (SSIs) remain a critical healthcare challenge, contributing to increased morbidity, mortality, and healthcare costs. SSIs represent the third most common nosocomial infection globally with an incidence of 19-20%, while their prevalence in Pakistan was significantly higher, ranging up to 33.6%. The emergence of Multidrug-Resistant (MDR) organisms has worsened this issue. Objective: To determine the prevalence of antibioticresistant pathogens responsible for SSIs and analyze their antibiotic susceptibility patterns over the past decade. Methods: A systematic review was conducted adhering to PRISMA guidelines. Studies published between 2006 and 2023 were included. Data on the prevalence of antibiotic-resistant organisms associated with SSIs were extracted and analyzed through several databases (PubMed, Google Scholar, Sci-hub and Science Direct) using Boolean logic "AND" and "OR", and Medical Subject Headings (MeSH Terms) and keywords. A total of 70 articles were retrieved from which 16 articles were considered eligible after applying detailed inclusion/exclusion criteria and removing the duplicates and irrelevant articles. Results: The study identified Staphylococcus aureus, coagulase-negative staphylococci, Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli, and Acinetobacter spp. as predominant MDR pathogens. A significant increase in the prevalence of antibiotic-resistant strains was observed over the study period. Gram-negative bacteria exhibited a higher resistance rate (66.8%) compared to Gram-positive organisms (51.1%). **Conclusions:** The increasing prevalence of antibiotic-resistant pathogens underscores the urgent need for comprehensive infection prevention and control measures to address the burden of SSIs. Targeted interventions, antimicrobial stewardship, and continued surveillance were essential to combat this growing challenge.

INTRODUCTION

Surgical Site Infections (SSIs) remain a significant challenge in surgical care, complicating the management of patients with surgical Site Infections (SSIs) by contributing to increased morbidity, mortality, and healthcare costs. They are characterized by inflammation of the surgical wound occurring within 30 days of surgery. These infections arise from microbial contamination of surgical wounds, often involving the patient's endogenous flora, such as Staphylococcus aureus and Escherichia coli, and can be exacerbated by the emergence of antibioticresistant pathogens [1, 2]. These infections are classified clinically based on the degree of contamination encountered during the operative procedure. Clean wounds are those without inflammation, while cleancontaminated wounds carry a minimal risk of infection. Contaminated wounds exhibit inflammation without purulent discharge but may involve contact with the gastrointestinal tract. Finally, dirty wounds are exposed to faecal matter, debris, or foreign bodies [3]. SSI prolong hospital stays, increases patient suffering, and imposes a substantial financial burden on healthcare systems. Globally, SSIs rank as the third most common nosocomial

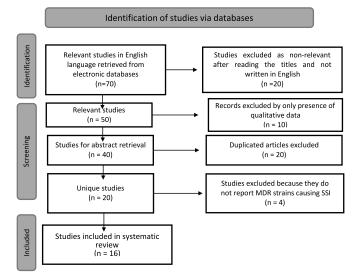
infection, with incidence rates varying from 19% to 20% based on patient demographics and surgical procedures [2]. Within Pakistan, the prevalence of SSIs is notably higher, ranging from 9.3% to 33.6% according to available literature [4]. Multiple factors contribute to the heightened risk of SSIs, including patient-related vulnerabilities such as immunosuppression and pre-existing infections. Surgical risk factors involve prolonged procedures, accidental contamination, inadequate sterilization, and improper instrument handling. Additionally, physiological conditions like multi-trauma, postoperative hyperglycemia, and hypoxia increase SSI susceptibility [5]. Other independent determinants of SSI risk include pathogen virulence, preoperative hospitalization, operative duration, surgical complexity, and the presence of wound debris, which collectively elevate the likelihood of severe infections caused by multidrug-resistant organisms [6]. The emergence of Multidrug-Resistant (MDR) organisms has further complicated the treatment of SSIs. Antimicrobial resistance was recognized as a global health threat at the 68th meeting of the United Nations General Assembly. The prevalence of such resistant bacteria associated with Surgical Site Infections (SSIs) has escalated dramatically in recent decades. These pathogens, including Staphylococcus aureus (methicillinresistant), Enterococcus spp., Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli, exhibit resistance to multiple antibiotic classes, necessitating a comprehensive understanding of their prevalence and antibiotic susceptibility patterns [7-9]. Predominant MDR pathogens isolated from hospital-acquired SSIs include Gram-positive bacteria such as Staphylococcus aureus (methicillin-resistant) and Enterococcus spp., as well as Gram-negative bacteria like Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli, which exhibit resistance to a broad spectrum of antibiotics, including tetracycline, cephalosporins, ampicillin, penicillin, and methicillin [10, 11]. The increasing prevalence of Surgical Site Infections (SSIs) coupled with the challenge of antibiotic resistance underscores an urgent need for comprehensive research. A comprehensive analysis of the evolving landscape of antibiotic-resistant pathogens responsible for these infections remains limited. This systematic review aims to address this critical gap by providing a comprehensive overview of the predominant antibiotic-resistant pathogens associated with SSIs and their historical trends. Understanding the dynamics of these pathogens is essential for developing effective prevention and control strategies, optimizing antibiotic use and ultimately improving patient outcomes. By identifying the prevalence and antibiotic susceptibility patterns of these organisms, this study contributes to the growing body of knowledge in this field and informs evidence-based practices in surgical care.

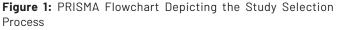
Therefore, based on this rationale, this systematic review

was conducted to identify the predominant antibioticresistant pathogens responsible for SSIs and assess their prevalence rates over the past decade. By understanding the evolving landscape of these pathogens, surgeons can implement targeted infection prevention and control measures to improve patient outcomes and optimize antibiotic use.

METHODS

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed to perform this systematic review. The data for the last eighteen years (2006-2023) was collected using several databases (PubMed, Google Scholar, Sci-hub and Science Direct) using Boolean logic "AND" and "OR", Medical Subject Headings (MeSH Terms) and keywords. Different terminologies were used to explore the literature "Surgical site infections", "Antibiotic-resistant strains", and "Postoperative wound infections". A total of 70 articles were retrieved from the included databases. Out of all these articles 16 articles were considered eligible after applying inclusion/exclusion criteria and deleting the duplicates and irrelevant articles (Figure 1).





All the required data were extracted from the eligible studies. Table 1 represented the epidemiological characteristics of studies included in the analysis of SSI. **Table 1:** Basic Attributes of the Studies Incorporated in this Review

S.No.	No of Isolates	Positive	Negative	Sample Source Post-Operative	Study type	References
1	147	95	NR	Pus Swab	Cross-Sectional	Palikhey et al., 2023 [1]
2	147	147	NR	Wound Swabs	Cross-Sectional	Manyahi <i>et al.,</i> 2014[2]
3	250	156	94	Wound Swabs	Prospective	Bhatt et al., 2014 [3]
4	107	104	NR	Wound Swabs	Hospital-Based	Dessie et al., 2016 [4]
5	177	177	NR	Wound Swabs	Cross-Sectional	Guta et al., 2014 [5]
6	380	234	NR	Wound Swabs	Cross-Sectional	Hailu et al ., 2016[6]
7	41	41	NR	Wound Swabs	Cohort Study	Abayneh et al., 2022 [7]
8	168	168	NR	Wound Swabs	Cross-Sectional	Asres et al., 2017[8]
9	102	91	NR	Wound Swabs	Descriptive Cross-Sectional	Narula et al., 2020 [9]
10	699	695	4	Wound Swabs	Cross-Sectional	Nobel et al., 2022 [10]
11	150	145	NR	Wound Swabs	Cross-Sectional	Mama and Sewunet 2014 [11]
12	116	116	NR	Wound Secretion	Survey Study	Garoy et al., 2021[12]
13	128	123	NR	Wound Swabs	Prospective	Mengesha et al., 2014 [13]
14	53	42	11	Wound Swabs	Cohort Study	Misha et al., 2021[14]
15	158	158	NR	Wound Swabs	Hospital-Based	Mwambete and Rugemalila 2015 [15]

NR=not reported

RESULTS

The following Factors Were Identified to Be Involved in Surgical Site Infection Showed in figure 2.

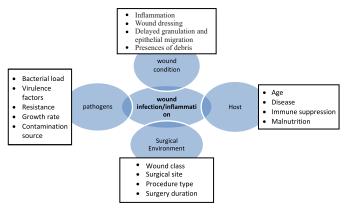


Figure 2: Factors Involved In Surgical Site Infection Evolution

To determine the antibiotic susceptibility profiles of bacteria associated with Surgical Site Infections (SSIs), numerous studies have employed the Kirby-Bauer disk diffusion method. A broad spectrum of antibiotics was tested, including tetracycline, cefoxitin, ciprofloxacin, gentamicin, penicillin and erythromycin for both Grampositive and Gram-negative organisms. Additionally, ampicillin, ceftriaxone, and cefotaxime were utilized specifically for Gram-negative bacteria [12]. The frequency and percentage of isolated Gram-positive and Gramnegative resistant strains associated with SSIs were presented in tables 2. The percentage of antibioticresistant bacterial isolates was calculated using the following formula: Gram-positive bacteria represent a significant etiology of Surgical Site Infections (SSIs), with emerging antibiotic resistance posing a substantial clinical challenge. Staphylococcus aureus (S. aureus) and Coagulase-Negative Staphylococci (CoNS) have consistently emerged as predominant pathogens within this category. Studies have demonstrated a variable prevalence of S. aureus as a causative agent of SSIs. While Manyahi J et al., reported a frequency of 21.3% in 2014, subsequent investigations have revealed a wider range. Guta M et al., observed a prevalence of 25.5% in 2014, whereas Hailu D et al., and Abayneh M et al., reported slightly lower rates of 20.5% and 19.5%, respectively [2, 5, 6, 13-15]. Notably, Palikhey A et al., identified the highest reported prevalence of S. aureus at 37.8% in 2023[1,7]. The World Health Organization (WHO) has further emphasized the significance of S. aureus as a leading cause of SSIs, with a global estimate of up to 30.4% incidence. CoNS have also been linked as a common pathogen in SSIs. Although generally considered less virulent than S. aureus, the development of antibiotic resistance has mitigated this distinction. Reported prevalence rates of CoNS in SSIs have ranged from 5.49% to 13.5% in various studies consistently lower than those observed for S. aureus[13, 15, 16-19].

S.aureus N (%)	CoNS N (%)	Enterococcus spp N (%)	Streptococcus spp N (%)	Total Number of Isolates	MDR / Total Isolates N (%)
11(7.05%)	1(0.64%)	1(0.64%)	0	156	102(65.3%)
274 (21%)	36(2.84%)	49(3.87%)	4(0.31%)	1266	850(67.1%)
9(1.29%)	70(10.0%)	NR	NR	695	578 (83.1%)
36(37.8%)	5(5.26%)	NR	NR	147	95(64.63%)
8(5.44%)	8	4(2.7%)	NR	147	75 (51%)
20(17.2%)	NR	NR	NR	116	55.1(64%)
48(20.5%)	3(1.2%)	NR	NR	234	127(54.3%)
31(21.3%)	17(11.7%)	NR	NR	145	123 (8.4%)
NR	NR	NR	NR	123	102(82.9%)
14 (15.3%)	5(5.49%)	1(1.0%)	NR	91	73 (80.2%)
25(14.8%)	16(9.5%)	1(0.5%)	NR	168	110 (65.5%)
16(10.1%)	NR	NR	NR	158	87 (55.5%)
45(25.4%)	24(13.5%)	NR	9(5.0%)	177	164(92%)
8(19.5%)	2(4.8%)	NR	NR	41	41 (100%)
5(9.4%)	1(1.88%)	NR	3(5.6%)	53	42(79.2%)
18(17.3%)	4(3.8%)	NR	NR	104	77 (74.0%)

MDR: Multi-drug-resistant; NR: Not reported; Spp: Species

The recorded percentage of *enterococcus spp* (0.64%, 2.7%, and 3.87%) and streptococcus spp (5.0%, 0, and 0.31%) were very low or was not reported in most of the studies carried out(figure 3).

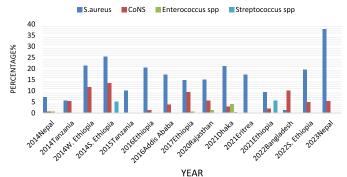


Figure 3: Isolation Frequency of Resistant Gram-Positive Strains from Post-Operative Wound Infections Gram-Negative Bacterial Strains: a Growing Threat in Surgical Site Infections

Gram-Negative Bacteria (GNB) pose a significant challenge in the prevention and management of Surgical Site **Table 3:** Frequency of Gram-Negative Antibiotic-Resistant Strain Infections (SSIs). While Gram-positive organisms have traditionally been the primary focus of SSI research, the increasing prevalence of antibiotic-resistant GNB has underscored their critical role in postoperative morbidity [17]. Pseudomonas aeruginosa, Escherichia coli, and Klebsiella pneumoniae have emerged as the most prevalent GNB implicated in SSIs. Data from multiple studies reveal variability in the prevalence of these pathogens over time. Pseudomonas aeruginosa exhibited a wide range of reported prevalence, from 10.25% to 57.6% between 2014 and 2022[6, 19-21]. Escherichia coli demonstrated a higher prevalence, with Mama M et al., reporting a peak of 29.2%. Klebsiella pneumoniae prevalence ranged from 8.42% to 12.9% during the same period [1, 6, 11, 13, 15, 22]. Proteus mirabilis, although less frequently isolated, exhibited increasing trends, with reported percentages ranging from 0.64% to 14.6% [6, 13, 15] (Table 3). These data underscore the dynamic nature of the GNB landscape in the hospital setting. Effective prevention and control strategies should account for the evolving epidemiology of these pathogens to optimize patient outcomes.

Frequency and Percentage of Isolated Gram-Negative Antibiotic Strains							
Citrobacter N (%)	Acinetobacter spp N(%)	P.aeruginosa N (%)	E.coli N (%)	Klebseilla N (%)	Enterobacter spp N (%)	Proteus mirabillus N (%)	A.batumanni N (%)
NR	36(23%)	16(10.25%)	12(7.6%)	16(10.25%)	8(5.1%)	1(0.64%)	NR
23(1.8%)	51(4.0%)	145(11.4%)	115 (9.0%)	65(5.1%)	39(3.0%)	44 (3.47%)	NR
NR	NR	401(57.6%)	NR	54(7.7%)	NR	44(6.3%)	NR
NR	15(15.79%)	11(11.58%)	20 (21.05%)	8(8.42%)	NR	NR	NR
NR	NR	1(0.68%)	13 (8.84%)	14 (9.5%)	NR	12 (8.1%)	15(10.2%)
15(12.9%)	2(1.7%)	8(6.8%)	10 (8.6%)	10(8.6%)	5(4.3%)	8(6.8%)	NR
3(1.2%)	NR	15(6.4%)	26(11.1%)	12 (5.1%)	2(0.8.5%)	18(7.6%)	NR
NR	NR	11(7.5%)	29(20%)	13 (8.9%)	NR	22(15.1%)	NR
NR	NR	NR	NR	NR	NR	NR	NR

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NR	NR	15(16.4%)	11(12.0%)	21(23.0%)	NR	6(6.5%)	NR
0	7(4.1%)	2(1.1%)	21(12.5%)	14 (8.3%)	4(2.3%)	0	NR
NR	NR	16(10.1%)	6(3.79%)	6(3.79%)	16 (10.1%)	15(9.4%)	NR
4(2.2%)	NR	16 (2.2%)	NR	23(12.9%)	3(1.69%)	12 (6.77%)	NR
3 (7.31%)	NR	5(12.1%)	12(29.2%)	4(9.7%)	NR	6(14.6%)	NR
4(7.5%)	NR	8(15.0%)	9(16.9%)	5(9.4%)	NR	6(11.3%)	NR
2(1.9%)	22(21.1%)	4(3.8%)	20(19.2%)	6(5.7%)	0	1(0.96%)	NR

NR: Not reported; Spp: Species

Graphical representation of recorded data demonstrates that K. pneumonia, Acinetobacter spp, P. aeruginosa and E.coli along, with proteus mirabillus were the most commonly observed resistant strains in cases of postoperative wound infections (figure 4). The isolation rates of Enterobacter spp and Citrobacter were low and not reported in a few studies. In another study carried out by Ali KM et al., the reported percentages of P. aeruginosa, Enterobacter spp and Citrobacter were 14.58% 6.25% and 2.08% [23].

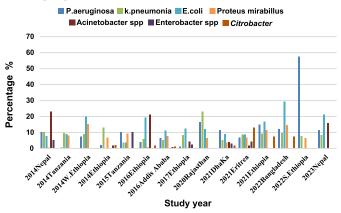


Figure 4: Isolation Frequency of Resistant Gram-Negative Strains from Postoperative Wound Infections

Prevalence of Antibiotic-Resistant Strains: Surgical Site Infections(SSIs)pose a significant challenge in the present healthcare system, ranking as a leading cause of healthcare-associated infections. A global multicenter study spanning 66 countries, comprising both developed and developing nations, reported a concerning overall SSI prevalence of 12.3% [24]. A meta-analysis of diverse geographical regions revealed a substantial increase in antibiotic-resistant strains associated with SSIs. While studies conducted in 2014 documented a prevalence ranging from 51% to 92% [2, 6, 13, 22], subsequent investigations in 2020 and 2022 reported even higher rates, with peaks of 80.2%, 83.1%, and an alarming 100% in certain regions [15, 19, 21] (table 3). Mukagendaneza MJ et al., highlighted the substantial contribution of GNB to SSIs, constituting over 25% of cases [25]. This finding underscores the need for heightened surveillance and targeted interventions to address this emerging threat. This increasing trend of antibiotic resistance underscores the critical need for effective prevention and management strategies to mitigate the harmful effects of SSIs[25].

Table 4: Prevalence of Gram-Positive and Gram-Negative

 Resistant Strains of Post-Surgical Wounds

Prevalence	Country	References		
64.4	Nepal	Palikhey et al., 2023[1]		
51	Tanzania	Manyahi et al., 2014 [2]		
65.3	Nepal Bhatt et al., 2014[3]			
74	Addis Ababa Dessie et al., 2016			
92	Southern Ethiopia	Guta et al., 2014 [5]		
54.3	Ethiopia	Hailu et al., 2016[6]		
100	Southwest Ethiopia	Abayneh et al., 2022 [7]		
65.5	Ethiopia	Asres et al., 2017[8]		
80.2	Rajasthan	Narula et al., 2020 [9]		
83.1	Bangladesh	Nobel et al., 2022 [10]		
84	West Ethiopia	Mama et al., 2014 [11]		
67.1	Dhaka	Garoy et al., 2021[12]		
82.9	Ethiopia	Mengesha et al., 2014 [13]		
79.2	Ethiopia	Misha et al., 2021[14]		
55.5	Tanzania	Mwambete and Rugemalila et al., 2015 [15]		

The predominant antibiotic-resistant strains identified as causative agents of surgical site infections in the present study were *Staphylococcus aureus* (16.2%) and coagulase-negative staphylococci (CoNS) among Gram-positive bacteria, while *Pseudomonas aeruginosa* (11.5%), *Klebsiella pneumoniae* (9.09%), *Escherichia coli* (13.8%), and *Acinetobacter spp.* (11.6%) were the most prevalent Gram-negative isolates(figure 5).

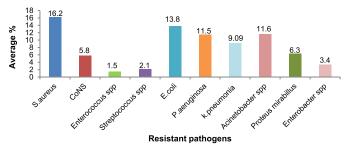
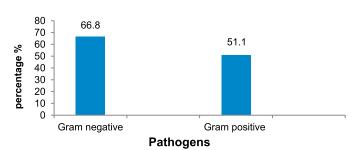
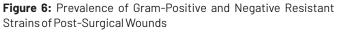


Figure 5: Frequency of Bacterial Strains Isolated from Surgical Site Infection

Overall prevalence of Gram-Positive and Negative resistant strains of Post-Surgical wounds is shown in figure 6





DISCUSSION

The current study underscores the worsening burden of antibiotic-resistant pathogens contributing to Surgical Site Infections (SSIs). Our findings align with the global trend of increasing SSI rates, particularly those caused by multidrug-resistant organisms. The predominance of Staphylococcus aureus, coagulase-negative staphylococci, Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli, and Acinetobacter spp. as causative agents highlights the urgent need for comprehensive infection prevention and control measures. The complex relationship between patient-related factors, surgical procedures, and the emergence of resistant strains necessitates a multidisciplinary approach to address this critical challenge. Effective strategies must include antimicrobial stewardship, adherence to surgical best practices, and robust surveillance systems to monitor the evolving landscape of SSI pathogens. The predominant antibiotic-resistant strains identified as causative agents of surgical site infections in the present study were Staphylococcus aureus (16.2%) and coagulase-negative staphylococci (CoNS) among Gram-positive bacteria, while Pseudomonas aeruginosa (11.5%), Klebsiella pneumoniae (9.09%), Escherichia coli (13.8%), and Acinetobacter spp. (11.6%) were the most prevalent Gram-negative isolates. These findings align with previous research conducted by Mshana et al., and Mulu A et al [2, 26]. The elevated prvalence of S. aureus can be attributed to its status as a common skin commensal, facilitating its colonization of surgical wounds. Other potential sources include the hospital environment and contaminated surgical instruments. Our results were consistent with those reported by Shahane V et al., and Kakati B et al., in different geographic regions [27, 28]. In a study by Ali A et al., S. aureus (66.7%) and CoNS (19.05%) were the predominant Gram-positive pathogens, while E. coli (33.3%) and K. pneumoniae (25%) were the most frequent Gram-negative isolates, demonstrating a similar pattern of antibiotic resistance [24]. The predominant etiological agent of Surgical Site Infections (SSIs) has been the subject of extensive investigation. Multiple studies have consistently identified Gram-negative bacteria as the primary causes. Staphylococcus aureus (31%), Escherichia coli (20.7%), and Klebsiella pneumoniae (8.9%) were frequently associated in these studies. A geographic expansion of this analysis revealed similar trends. Singh PP et al., reported a predominance of Gram-negative organisms (56.25%) over Gram-positive bacteria (43.75%) in postoperative wound infections [29, 30]. Our systematic review supports these findings, demonstrating a higher prevalence of Gramnegative(66.8%) compared to Gram-positive(51.1%) strains associated with SSIs . These results align with the observations of Raza MS et al., and Biadglegne F et al., who also documented a higher incidence of resistant Gramnegative pathogens [31-36]. Maoulainine FM et al., and Alkaaki A et al., reported Escherichia coli as the most prevalent organism in their respective cohort studies [37, 38]. The prevalent nature, antimicrobial resistance, and potential faecal contamination during surgery have contributed to the emergence of Klebsiella pneumoniae as a significant pathogen, as highlighted by Hope D et al., Worku S et al., Kalayu AA et al., and Bitew Kifilie A et al., further emphasized the association between specific bacterial isolates and SSIs [39-42]. Dessie W et al., highlighted the dominance of Gram-negative organisms in postoperative wound infections, underscoring the evolving landscape of Surgical Site Infection (SSI) pathogens [4, 12]. To effectively combat this challenge, identifying the precise origins of resistant pathogens was necessary for the effective selection of antimicrobial therapy and the prevention of antimicrobial resistance. Antimicrobial resistance poses a significant threat to global health and modern surgical practices. Characterizing the spectrum of resistant pathogens associated with SSIs was crucial for healthcare providers to develop and implement tailored antibiotic stewardship strategies. This systematic review offers valuable insights into the prevalence of drugresistant organisms in postoperative wounds, enabling surgeons to make informed treatment decisions, reinforcing targeted infection control measures, and stimulating research into novel antimicrobial agents and alternative therapeutic approaches. Ultimately, these efforts contribute to improved patient outcomes and the preservation of effective antimicrobial therapies. This systematic review provides a comprehensive overview of the prevalence of antibiotic-resistant strains associated with Surgical Site Infections (SSIs). By systematically reviewing a range of studies, this has contributed to the growing body of knowledge on this critical issue. The inclusion of both Gram-positive and Gram-negative bacteria expands the scope of this study and enhances its clinical relevance. The discussion effectively highlights the implications of the study's findings for clinical practice and future research, emphasizing the need for targeted infection prevention and control strategies. The present study is subject to certain limitations. The heterogeneity of study designs, patient populations, and geographical settings may have influenced the overall findings. Additionally, the published literature might have excluded studies with negative or inconclusive results. Furthermore, the absence of data on greater patient comorbidities limits the ability to draw definitive conclusions about the impact of these factors on SSI rates and antibiotic resistance. While the study provides valuable insights into the prevalence of antibiotic-resistant pathogens, further research was needed to develop a deeper understanding of the underlying mechanisms of resistance and to develop novel strategies for optimal surgical care.

CONCLUSIONS

The emergence of antibiotic-resistant pathogens has significantly complicated the management of Surgical Site Infections (SSIs), necessitating a comprehensive understanding of their prevalence and antibiotic resistance patterns. This systematic review underscores the increasing burden of antibiotic-resistant organisms associated with SSIs, particularly Gram-negative bacteria. The predominance of Staphylococcus aureus, coagulasenegative staphylococci, Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli, and Acinetobacter spp. highlights the urgent need for targeted infection prevention and control measures. To effectively combat this challenge, multidisciplinary collaboration, antimicrobial stewardship, and robust surveillance systems were imperative. By implementing evidencebased strategies, surgeons can mitigate the impact of antibiotic resistance and improve post-operative patient outcomes. Further research was needed to explore the underlying mechanisms of resistance and to develop innovative interventions for the surgical management of SSI caused by multidrug-resistant pathogens.

Authors Contribution

Conceptualization: SM Methodology: ZA, HA, AS Formal analysis: KR Writing, review and editing: AS, SA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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