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Antimicrobial resistance patterns of WHO priority pathogens at general hospital in Southern Ethiopia during the COVID-19 pandemic, with particular reference to ESKAPE-group isolates of surgical site infections

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Abstract

Background Antimicrobial resistance represents a significant public health challenge, resulting in an estimated 4.95 million deaths annually. In response to the global escalation of antimicrobial resistance in prevalent hospitalacquired infections such as surgical site infections (SSIs), the World Health Organization (WHO) has identified critical and priority pathogens necessitating research and development. Nevertheless, there remains a paucity of data from numerous developing nations. Therefore this study was conducted to evaluate the prevalence of SSIs, examine the microbial profile, and identify factors associated with SSIs, with a particular emphasis on WHO-priority pathogens during the COVID-19 pandemic at a general hospital in southern Ethiopia.

Methods A cross-sectional study was conducted on 207 adult patients clinically suspected of SSIs from September 1, 2019, to November 2022. Demographic data, clinical characteristics, and surgery-related variables were collected using pre-tested, structured, interviewer-administered questionnaires and patient chart reviews. Wound samples (swabs and/or pus) were collected aseptically from each participant following standard microbiological procedures and processed for isolation and identification of pathogens by conventional culture and biochemical testing. Bacterial isolates subjected to antimicrobial susceptibility testing, including the detection of extended-spectrum beta-lactamase (ESBL) and methicillin-resistant *Staphylococcus aureus* (MRSA), by the standard Kirby-Bauer disk diffusion method in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. Data were analyzed by Statistical Packages for Social Science (SPSS) version 25, and bivariable and multivariable logistic regression was

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Results The overall prevalence of culture-confirmed SSIs among adult patients who underwent major surgery was 76.8% (95% CI: 71.0, 82.6). Among the 178 pathogens recovered, 58.5% were Gram-negative, 40.4% were Gram-positive, and 1.1% were *Candida* spp. The ESKAPE pathogens comprised 65.3% of the isolates, with *S. aureus* being the most common species, accounting for 43.5%, followed by *K. pneumoniae* (33.9%). Multidrug resistance (MDR) was observed in 84.37% of ESKAPE pathogens, with ESBL-producing and MRSA-producing isolates accounting for 88% and 76.5%, respectively. *A. baumannii* showed the highest MDR rate at 100%, followed by MRSA (90%) and *K. pneumoniae* (88.23%). Amikacin, meropenem, and piperacillin-tazobactam were effective against Gram-negatives, while linezolid, clindamycin, and gentamicin were most effective against Gram-positive bacteria. SSIs was significantly associated with emergency surgery (P < 0.001), prolonged surgery waiting time (P = 0.004), and clean-contaminated surgery (P = 0.008).

Conclusion The high prevalence of MDR-ESKAPE pathogens is concerning, highlighting the need for improved infection prevention practices and antimicrobial stewardship programs.

Keywords General surgery, Surgical site infections, Antimicrobial resistance, Nosocomial infections, WHO-priority pathogens, Developing country, Ethiopia

Introduction

Despite being preventable surgical site infections (SSIs) remain the second most common type of healthcareassociated infection(HAI), also referred to as "nosocomial" or "hospital-acquired infection" and substantially affecting the patient's health and healthcare system by increasing the length of hospital stay, the cost of treatment, and causing deaths [1, 2]. SSIs are frequent and severe complications or adverse events that occur within 30 days of the procedure and they can manifest as superficial infections involving skin and subcutaneous, deep infections affecting the facial and muscle layers, or organ/ space infections involving anybody other than the incision site [1, 3]. As with so many global health problems, low- and middle-income countries (LMICs), especially in sub-Saharan Africa, bear a significant burden of SSIs [4, 5]. Several factors related to surgical procedure, patient characteristics, and the environment have been identified to aggravate SSIs and the reported incidence of SSIs varies across countries, hospital settings, types of surgery, and patient characteristics [6, 7]. The global rise in the emergence and spread of antimicrobial resistance complicated the management of SSIs, resulting in the worst patient outcomes (poor prognosis, prolonged hospital stay, increased treatment cost, extended use of antimicrobial therapy, higher rate of undergoing repeated surgery, and high rate of mortality) [8]. However, as diagnosis of SSIs is often made clinically in the hospital setting many cases after discharge may go unrecognized and the impact due to antimicrobial resistance remains underestimated [6, 7].

Throughout historical publications, the microbiology of SSIs is summarized to include bacteria (Gram-negative and Gram-positive bacteria), and fungi [8]. To date, the overall understanding of microorganisms causing SSIs has evolved exhibiting variations in spectrum and shift from normal flora to highly antimicrobial-resistant pathogens. According to estimates antimicrobial resistance pathogens claim 1.3 million lives annually and contribute to nearly five million more deaths worldwide. With the changing epidemiologic of SSIs and rise in the incidence of antimicrobial resistance, the use of broadspectrum antimicrobial empirical therapy and antimicrobial prophylaxis use becomes a more difficult [9, 10]. Also, some concept terms have enhanced understanding of the source of infections and the danger associated with the emerging antimicrobial resistance pathogens, For example, the acronyms ESKAPE group members, namely, Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.), and they were first identified by the Infectious Diseases Society of America (IDSA) [11, 12]. These pathogens are notorious bacteria known to cause life-threatening infections, have a high tendency to acquire drug resistance, adapt to the healthcare setting environment, and erode and escape effective modern medicine, including the last resort antimicrobial agents and biocides [11, 13, 14]. If no action is taken and the problem of antimicrobial resistance remains unchecked the death toll due to antimicrobialresistant pathogens is forecasted to rise to 10 million by 2050" [15-17]. In response to concern over the growing threats of antimicrobial-resistant pathogens and to enhance the development of new effective interventions, the World Health Organization (WHO) has identified crucial and priority pathogens for research and development. Of which carbapenems-resistant A. baumanii, P. aeruginosa, third-generation cephalosporin-resistant K. pneumoniae, and Enterobacter spp were considered in the first line of priority pathogens as the "critical group".

In the second line of priority pathogens, Gram-positive bacteria namely Vancomycin-Resistant *E. faecium* and Methicillin-Resistant *Staphylococcus aureus* (MRSA) were listed [14, 18, 19].

Although the growing interest and support to monitor the emergence and spread of these pathogens in clinical settings and in the environmental samples, unfortunately, there have been gaps in establishing ongoing laboratory-based surveillance in LMICs [18]. Thus the true magnitude, the source, and the impact of infections due to WHO priority pathogens are poorly understood. The effectiveness of the recommended interventions to prevent and control SSIs such as the bundle of care and surgical antimicrobial prophylaxis in the face of increasing antimicrobial resistance has raised important knowledge gaps in clinical decision-making [7, 18, 20]. While patients' demography, clinical and surgical related factors as well as environmental factors correlate with clinical SSIs, these correlations have not yet been used to estimate the prevalence of antimicrobial resistance WHO priority pathogens in countries lacking surveillance [8, 21]. The Ethiopian government published a national strategy and action plan on the containment of antimicrobial resistance and since 2015 Ethiopia has pursued a national action plan for antimicrobial resistance in collaboration with WHO and other international stakeholders [22]. A report from numerous other previous studies in Ethiopia also highlighted the growing problem of antimicrobial resistance [23, 24]. However, to our best knowledge, no records were published based on WHO-priority pathogens. Therefore this study aimed to determine the prevalence, associated factors, and antimicrobial susceptibility pattern of ESKAPE group pathogens among patients who developed SSIs following major surgery at Arba Minch General Hospital, Southern Ethiopia.

Materials and methods

Study setting, design, and populations

This cross-sectional study was conducted during the acute phase of the COVID-19 pandemic (from September 01, 2019, to November 30, 2022) at Arba Minch General Hospital. Arba Minch General Hospital is one of the government-owned hospitals located in Arba Minch City, Gamo Zone, southern regional state of Ethiopia. The current capacity of the hospital is 300 beds.

A sample size for this study was calculated using the formula for a single population's proportion. Taking the proportions of culture-positive SSIs among adult patients from previous study (P=0.84) [25] and assuming a 95% confidence level, 5% margin of error a the total sample size was estimated to be 207.

Case definitions and eligibility criteria

SSIs were defined according to the Centers for Disease Control and Prevention (CDC) criteria [3] and cases were identified both during in-hospital routine visits and during readmission. Participants included in the study were further stratified into superficial, deep, and organ spaces. The criteria used to include participants were all sex, age \geq 18 years, underwent elective or emergency, admitted or readmitted to a surgical ward, symptomatic SSIs, and willingness to participate and provide written informed consent. However, patients with incomplete medical records, implanted medical devices, patients who received antibiotics two weeks before the study, and those who were seriously ill were excluded. Furthermore, all surgical procedures carried out by endoscopy or laparoscopy, or patients with dirty wounds, cellulitis, and stitch abbesses were excluded.

Data collection and laboratory procedures

The data used for analysis in this study were collected through methods including direct patient interviews, medical chart reviews, and microbiological analysis of a clinical sample. The interviewer-administered structure questionnaire was developed by reviewing similar previous studies [3, 21, 26], pretested, and used to collect patients' demography, clinical, and other potential risk factor data. Two wound samples (swabs or pus aspirates) were aseptically collected from each patient with clinical evidence of post-operative wound infections by trained nurses, the principal investigator, and an attending clinician and sent to the Medical Microbiology and Parasitology Teaching and Research Laboratory of the Medical Laboratory Science department at Arba-Minch University for processing. Wound swabs from each consented participant were collected using a sterile cotton-tipped swab by the Z-stroke or Levine's technique, or by swabbing by gently rolling the swabs over the surface of the wound approximately five times [27]. Specimens were collected before redressing and administration of antibiotic therapy and after aseptically cleaning the wound with sterile 0.9% saline. Moreover, pus samples collected with sterile disposable syringes were used to confirm the presence of wound etiologies and document the prevalence of infections. Once the specimens were obtained, they were immediately placed in a pre-labeled universal tube with Amies transport media, caped, and transported in a cold box with ice packs for microbiological processing with the minimum delay. However, in cases of unavoidable delay (more than 2 h), specimens were stored refrigerated. Upon receipt in the laboratory, all samples were checked and their details were entered into the registration logbook. Of the two swab samples, one was used for Gram stain, and the other was used for bacteriological culture. Gram staining was done on all the

swabs and pus as per the protocol developed for Gram staining, and the results were used as part of the sample quality assessment.

Culturing, isolation, and identification of bacteria

Microbial isolation and identification were performed using conventional culture methods following standard microbiological techniques. Each wound sample was inoculated on primary isolation media comprising Mannitol salt agar, MacConkey agar, and 5% Sheep blood agar (Oxoid, UK)) and plates of MacConkey agar and Mannitol salt agar were incubated aerobically at 35-37 °C for 24-48 h, whereas Blood agar and chocolate (If needed) agar was at 5–10% CO^2 in a candle jar for 24–48 h. Isolation of pure colonies was done through inspection of growth and colony characteristics, Gram staining, and sub-culturing of mixed colonies on appropriate media. Moreover, when yeast or fungi elements were observed on Gram-stained results from blood agar or direct smears of clinical wound samples, we cultured the sample or subculture the colony on sabouraud dextrose agar containing chloramphenicol and incubated it at 37°C for 24-48 h. Chocolate ager was only considered if Gramnegative bacteria were present on microscopic examination of the Gram-stained examination but no growth after 48 h of incubation. Microbial isolates were identified based on colony characteristics, swarming growth, hemolysis on blood agar, and change in color on mannitol salt agar used for preliminary identification. Biochemical tests such as catalase, coagulase (tube and slide), bile esculin test (6.5% salt-tolerant and 40% of bile), growth at wide temperature, indole, methyl red, Vogues-Voges-Proskaue (VP), citrate utilization (IMVIC), motility, triple sugar iron agar, urease test, oxidase test, arginine, and bacitracin susceptibility profile were used to final identification of isolates following standard microbiological procedure [28, 29]. Further characterization of the fungi was done by the germ tube test, staining, and morphological examination [29].

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed by the Kirby-Bauer disc diffusion method according to clinical laboratory standard institute guidelines CLSI-M100 [30]. Briefly, a bacterial suspension adjusted to the turbidity of 0.5 McFarland standard (approximately 1.5×10 8 CFU/ml) was used for lawn culture on Mueller-Hinton agar (Oxoid). Antibiotic discs were aseptically placed on inoculated plates within 10 to 15 min, and the plates were incubated at 37 °C for 16–18 h. However, Mueller Hinton agar supplemented with 5% sheep blood was used for antibiotic susceptibility testing of Beta-hemolytic streptococcal isolates, and plates were incubated at 37 °C in 5–10% CO² overnight. The zone of inhibition was

measured by a ruler to the nearest millimeter for each specific antimicrobial agent and results were interpreted according to CLSI [30]. In this study, bacterial isolates were tested against 27 antimicrobial agents in 14 classes of antimicrobial agents, namely Penicillin, Aminoglycosides, Carbapenems, Cephalosporin, Fluoroquinolones, Folate pathway inhibitors, Monobactam, Glycopeptides, Tetracycline, Macrolides, Lincosamide Oxazolidinone, Ansamycins, and Phenolic. Antimicrobial agents for Gram-positive isolates included Penicillin G (10 units), Ampicillin (10 µg), Erythromycin (15 µg), Clindamycin (2µg), Trimethoprim/sulfamethoxazole (1.25/23.75 µg), Linezolid (30 µg), Vancomycin (30 µg), Rifampin (5 µg), Chloramphenicol (30 µg), Ciprofloxacin (5 µg), Cefoxitin (30 µg), and Cefazolin (30 µg). For Gram-negative Ampicillin (10 µg), Pipiracillin (100 µg), Cefuroxime (30 µg), Ceftriaxone (30 µg), Cefotaxime (30 µg), Ceftazidime (30 µg), Cefepime (30 µg), Meropenem (10 µg), Amikacin (30 µg), Gentamicin (10 µg), Tobramycin (10 µg), Tetracycline (30 µg), Aztreonam (30 µg), Pipiracillintazobactam (100/10µg), Amoxicillin-clavulanic acid (20/10µg), Ampicillin-sulbactam (10/10µg). Finally, each specifically tested isolate was categorized as susceptible, intermediate, or resistant according to CLSI guidelines [30]. However, for statistical purposes, the antimicrobial susceptibility result was dichotomous, and intermediate resistant was considered resistant. Bacteria were defined as multidrug-resistant (MDR) if isolates were non-susceptible to at least one antimicrobial agent in three or more antimicrobial categories. However, extensively drug-resistant (XDR) was defined as non-susceptible to at least one agent in all but two or fewer categories [31].

Phenotypically methicillin-resistant Staphylococcus aureus (MRSA) was detected through the disc diffusion method on Mueller-Hinton agar using a cefoxitin (30 µg) disc. Zones of inhibition diameters ≤21 after overnight incubation of plates at 33-35 °C were considered MRSA strain. Vancomycin against E. feacium was subjected to an E-test for confirmation [30]. The presence of extended beta-lactamase enzyme (ESBL)-production among Enterobacteriaceae resistance to third-generation cephalosporin drugs (Ceftazidime 30 µg and Cefotaxime 30 µg disks) was done by the combination disk method (CDT) or double-disk synergy methods. Accordingly, a bacterial suspension equivalent to 0.5 McFarland standard was swabbed onto MHA, and the antibiotic disc of amoxicillin-clavulanic acid $(20/10 \ \mu g)$ was placed in the center of the plate, while the cephalosporin disk of ceftriaxone (30 μ g) and cefotaxime (30 μ g) disks were placed at a distance of 15 mm center-to-center each from the amoxicillin-clavulanic acid disk. The plate was then incubated at 37 °C for 24 h. The enhancement of the zone of inhibition of the cephalosporin disk towards amoxicillinclavulanic acid was inferred as a synergy, and the strain

was extrapolated as an ESBL producer [30]. Quality control strains from American type culture collection (ATCC) of *P. aeruginosa* (ATCC 27853), E. coli (ATCC 25922), ESBL-producing organisms *K. pneumoniae* (ATCC 700603), *S. aureus* (ATCC 25923), and MRSA strain *S. aureus* (ATCC 29213) were used. All the reference strains were procured from the Ethiopian Public Health Institute.

Data management and statistical analysis

Data cleaning and entry were done using Statistical Software for Social Science (SPSS) Statistics (IBM Corp., Armonk, NY, USA) version 25 for analysis. Descriptive statistics such as frequency and percentage were used to summarize the data, and a frequency table and figures were used to present the results. Continuous variables were presented as means ± standard deviation. The chi-square or Fisher's exact test was used to compare the association between two categorical variables. Bivariable and multivariable logistic regression analysis was performed to identify significant associations between dependent and independent variables. Variables with a *P-value* less than 0.25 in bivariate logistic regression were considered candidate variables and moved to the multivariable logistic regression model. The variables in the multivariable analyses were compared using the backward multiple logistic regression analysis method. Hosmer and Lemshow's goodness of fitness result indicated the final model properly reflected the data. We assessed multi-co-linearity between variables by computing the variance inflation factor. The results were reported as a crude and adjusted odds ratio with a 95% confidence interval, and a P-value of less than 0.05 was considered statistically significant.

Results

Characteristics of study participants

A total of 207 participants clinically diagnosed with SSIs were included in the study, with a response rate of 100%. The mean and standard deviation age of the study participants was 43.57 ± 13.8 SD, with the youngest and eldest being 18 years and 88 years, respectively. Male participants accounted for 56% (n = 116), and the male-to-female ratio was 1.27:1.

Prevalence of SSIs

Of the 207 patients included in the study, one hundred fifty-nine were culture-positive for aerobic microbial growth, and the overall prevalence of SSIs was (76.81%) [95% confidence interval: 71.0, 82.6]. The distribution of postoperative wound infections by the different age categories was the highest 35.2% (n = 56) among the age group of 31–30 years old. The prevalence of SSIs among

male and female participants was 90 (60.4%) and 63 (39.6%), respectively [Table 1].

Microbial profile of SSIs

A total of 178 isolates were recovered from 159 wound samples and a total of 10 genera. Out of these, 104 (58.5%) were Gram-negative bacilli, 72 (40.4%) were Gram-positive cocci, and 2 (1.1%) were Candida spp. Staphylococcus aureus was the leading bacterial isolate, accounting for 50 (28.4%), followed by Escherichia coli 39 (22.16%), and Klebsiella pneumoniae 34 (19.32%). However, Citrobacter fruendii, beta-hemolytic streptococci or Streptococcus pyogenes, and Candida spp. were the least frequently isolated, each 2 (1.14%), whereas the occurrence of Enterobacter spp. and Proteus mirabilis was rare; in each species, only four isolates (each 2.27%), A. baumannii, and Enterococcus faecium accounted for 3.37%(n=6). The prevalence of *P. aeruginosa* and Coagulase-negative Staphylococci (CoNS) were 15 (8.52%) and 14 (7.8%), respectively.

In this study, the overall prevalence of ESKAPE group pathogens was 115 (65.3%), and pathogens were isolated from 89 culture-positive wound samples. The most predominant species among the ESKAPE group pathogens was *S. aureus, which* accounted for 50 (43.5%), and the second most common isolate was *K. pneumoniae*, which accounted for 29.5%(n = 43). Among the ESKAPE group, *Enterobacter spp.* was the least frequently isolated species, accounting for 3.5% (n = 4)[Table 2].

Antimicrobial resistance patterns of bacterial isolates

In general, antimicrobial resistance was recorded in all classes of the tested antimicrobials except for Linezolid. Of which both Gram-negative and Gram-positive isolates showed comparable levels of the highest resistance towards penicillin and trimethoprim-sulfamethoxazole drugs. Among Gram-negative bacteria, irrespective of their different species, isolates demonstrated resistance ranging from 10.57 to 100%. Antimicrobial resistance was highest towards non-extended spectrum β-lactamase cephalosporin (first generation and second generation), reaching as high as 90%; Trimethoprim-Sulfamethoxazole 79 (88%); Aztreonams, one of the monobactam drugs, 77 (86.51%); and Penicillin (mean 86.5%). In addition, the observed level of resistance towards traditionally useful antimicrobials, including 3rd generation cephalosporin and fluoroquinolone, was less active, with the average resistance exceeding 85.0% and 81 (77.8%) [Supplementary Fig. 1: Frequency distributions of antimicrobial resistant bacteria isolates of Surgical wound infections at General hospital southern Ethiopia].

Table 1 Distribution of SSIs by demographic, clinical, and surgery-related characteristics of patients at major surgical unit of ArbaMinch General hospital, southern Ethiopia (n = 207)

Variables category	Total participants	SSIs (yes = 159)	
	No (%)	No (%)	
Age category in years			
Mean + SD	43.57±13.8		
18–30	39 (18.8)	24(15.1)	
31 – 30	75(36.2)	56(35.2)	
41–50	43(20.8)	36(22.6)	
51–60	20(9.7)	16(10.1)	
≥60	30(14.5)	27(17.0)	
Gender			
Male	116(56)	96 (60.4)	
Female	91 (44)	63(39.6)	
Highest level of education			
No formal education	45(21.7)	37(23.3)	
First cycle	68(32.9)	49(30.8)	
High school	50(24.2)	40(25.2)	
College/university	44(21.3)	33(20.8)	
Residence	· · ·		
Urban	79(38.2)	62(39)	
Rural	128(61.8)	97(61)	
Occupation	()		
Farmer	61(29.5)	47(29.6)	
Civil servant	44(21.3)	31(19.5)	
Student	18(8.7)	14(8.8)	
Daily labourer	9(4.3)	7(4.4)	
Housewife	54(26.1)	45(28.3)	
Merchant	21(10.1)	15(9.4)	
Smoking status	21(10.1)	15(9.4)	
Yes	47(22.7)	38(23.9)	
No			
	160(77.3)	121(76.1)	
Admission ward	150/762)	110(74.0)	
General surgery	158(76.3)	119(74.8)	
Gyn and obstetrics surgery	49(23.7)	40(24.2)	
Body mass index	100/00.0)	146(01.0)	
< 30 kg/m2	188(90.8)	146(91.8)	
> 30 kg/m2(obese)	19(9.2)	13(8.2)	
Type of operation			
Emergency	111(53.6)	85(53.5)	
Elective	96(46.4)	74(46. 6)	
Type of incision/surgical wound			
Clean	37(17.9)	17(45.94)	
Clean contaminated	80(38.6)	65(81.25)	
Contaminated	90(43.5)	77(85.55)	
Duration of Surgery (in min)			
< 60	132(63.8)	93(58.5)	
61–120	51(24.6)	44(27.7)	
>120	24(11.6)	22(13.8)	
History of antibiotic exposure in the past 3 months			
Yes	47(22.7)	41(25.8)	
No	160(77.3)	118(74.2)	
History of hospitalization			
Yes	78(37.7)	61(38.4)	
No	129(62.3)	98(61.6)	

Table 1 (continued)

Variables category	Total participants	SSIs (yes = 159)
	No (%)	No (%)
Presence of comorbid illness		
Yes	35 (16.9)	32(20.1)
No	172(83.1)	127(79.9)
Surgery waiting time		
<7 days	63(30.4)	41(25.8)
>7 days	144(69.6)	118(74.2)
Type of SSI		
Superficial	123(59.4)	95(59.1)
superficial and deep	65(31.4)	56(35.2)
organ/space	19(9.2)	9(5.7)

Table 2 Frequency distribution of microbial pathogens isolated from SSIs by category (ESKAPE group and non ESKAPE group) at general hospital, southern Ethiopia (*n* = 178)

Family /genus and species of isolates	Total isolates	ESKAPE group	Non ESKAPE
		(<i>n</i> = 115)	(n=65)
	No (%)	No (%)	No (%)
Gram negative isolates (n = 104)			
Enterobacteriaceae	83(46.62)	38(33.04)	45(69.23)
Escherichia coli	39(22.16)	-	39(60%)
Klebssiela pneumoniae	34(19.32)	34(29.6)	
Citrobacter freundii	2(1.14)	-	2(3)
Enterobacter spp	4(2.27)	4(3.5)	-
Proteus mirabilis.	4(2.27)	-	4(6.1)
Non fermenting	21(11.79)	21	0
Acinetobacter baumannii,	6(3.41)	6(5.2)	-
Pseudomonas aeruginosa	15(8.52)	15(13.4)	-
Gram positives isolates (n = 72)			
Staphylococcus aureus	50(28.40)	50(43.5)	0
CoNS	14(7.95)		14(21.5)
Enterococcus faecium	6(3.41)	6(5.2)	-
Strep. Pyogenes	2(1.14)	-	2(3)
Fungi	2(1.14)	-	
Candida spp	-	-	2(3)
Total	178(100)	115(65.3)	65(36.9)

Note. CoNS; Coagulase negative staphylococci,

ESKAPE; S. aureus, K. pneumoniae, Enterobacter spp, A. baumanii, P.aeruginosa,

Antimicrobial resistance patterns of Gram-negative isolates

Enterobacteriaceae family (both *K. pneumoniae* and *Enterobacter spp.*) showed the highest frequency of resistance to cephalosporin (Ceftazidime and Cefazolin, each 100%) and amoxicillin-clavulanic (100%) but isolates were highly susceptible to carbapenems. Regarding other antimicrobial agents, K. *pneumoniae* showed the lowest level of resistance (8,23.52%) against amikacin and piperacillin-tazobactam and the highest (100%) to tobramycin, third generation cephalosporin Cotrimoxazole, tetracycline, chloramphenicol, and piperacillin each 32 (94.1%). The non-fermenting Gram-negative isolates of *A. baumannii* and *P. aeruginosa* accounted

for 21 (18.26%) of ESKAPE group pathogens, and both species showed the highest level of resistance (80% and above) to ceftazidime and carbapenems (more than half to meropenem). The third predominant ESKAPE group pathogen, *P. aeruginosa* isolates, showed the highest percentage of resistance to ceftazidime 12 (80%), followed by fluoroquinolones 10 (66.6%), and carbapenems 8 (53.3%), but all isolates remain susceptible to amikacin and are fairly susceptible to piperacillin-tazobactam and gentamicin (80%). *A. baumannii* isolates showed resistance to all of the antimicrobial agents except amikacin, to which only one isolates were found resistant. Therefore, clinical effectiveness cannot be anticipated for commonly prescribed drugs such as Piperacillin, cefotaxime,

ceftriaxone, ceftazidime, cefepime, ampicillin-sulbactam, gentamicin, ciprofloxacin, and tetracycline against infections caused by *A. baumannii*. Moreover, the prevalence of ESBL-producing *Enterobacteriaceae* was estimated to be 49 (59.0%), and the distribution was highest among K. *pneumoniae* 26 (76.5%). The prevalence of multidrug resistance among the Gram-negative was 90 (86.53%). The percentage of MDR was highest among *A. baumannii* (100%), followed by *K. pneumoniae* (88.23%) and *P. aeruginosa* (80%) [Table 3].

Antimicrobial resistance patterns of Gram-positive isolates

For the most frequently isolated Gram-positive ESKAPE group pathogens, *S. aureus* was the most frequent, and 44 (88%) of isolates were phenotypically identified as MRSA strains, whereas six isolates were Methicillin-sensitive *Staphylococcus aureus (MSSA)* (12%). Both the MRSA and MSSA strains are invariably resistant to penicillin (100%) and co-trimoxazole (100% vs. 83.3%) and sensitive to linezolid, ceftaroline, and gentamicin. However, MRSA isolates demonstrated high levels of resistance to ciprofloxacin, chloramphenicol, and clindamycin as compared to MSSA. In this study, only six *E. faecium* were isolated

in this study and showed high levels of resistance to Penicillin G (100%), followed by rifampin and vancomycin (83.33%) by screening tests. The antimicrobial susceptibility pattern of *E. faecium* showed that erythromycin, was the most active agent, with resistance of 1 (16.66%), tetracycline 4 (66.6%), and ciprofloxacin 4 (66.6%). The prevalence of MDR among the Gram-positives was 55 (76.38%). The percentage of MDR was highest among MRSA (44%)[Table 4].

Multidrug resistance pattern and extensive drug-resistant (XDR)

The results showed that the overall prevalence of MDR was 145 (82.38%). Of which, the prevalence of MDR among ESKAPE group pathogens was 97 (84.34%), whereas it was 49 (75.38%) among non-ESKAPE pathogens. Of the MDR-ESKAPE pathogens, *S. aureus* and *K. pneumoniae* accounted for three-quarters of the total. Among ESKAPE group isolates, resistance to three, four, and five antibiotics in different classes of antibiotics was 42 (36.5%), 34 (29.6%), and 23 (20%), respectively. About 8 (6.9%) of the ESKAPE group isolates were considered XDR [Table 5].

Antimicrobial	ESKAPE group(n	ESKAPE group(n=59)					Non ESKAPE (n=45)		
agent	K. pneumoniae (n=34)	Enterobacter sp. (n=4)	P. aeruginosa (n=15)	A. baumanii (n=6)	C. freundii (n=2)	E. coli (n=39)	Proteus mirabilis (n=4)	Total (n = 104) No (%)	
	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)		
Ampicillin	IR	-	NA	NA	IR	39 (100)	4 (100) ^a	46(100)	
Pipiracillin	26(76.47)	3(75)	5(33.33)	6(100)	2(100)	30(76.92)	3(75)	75(72.11)	
AMC.	34 (100)	4(100) ^a	IR	IR	2(100) ^a	20(51.28)	1 (25)	61(73.44)	
PTZ	8 (23.52)	1(25)	3(20)	3(50)	0(0)	2 (5.88))	1 (25)	18(17.30)	
SAM	NA	4(100) ^a	NA	5(83.33)	2(100)	31(79.48)	4 (100)	62(69.66)	
Cefepime	15 (44.11)	NA	8 (53.33)	6 (100)	NA	24 (61.5)	NA	53(56.38)	
Ceftazidime	34 (100)	4(100)	12 (80)	5(83.33)	2(100)	31(79.48)	4 (100)	90(86.53)	
Ceftriaxone	27(79.41)	3(75)	IR	6 (100)	1(50)	31(79.48)	3(75)	71(79.77)	
Cefotaxime	32 (95)	3(75)	NA	6 (100)	2(100)	35 (90)	3(75)	81(90.01)	
Cefuroxime	32 (95)	4(100) ^a	NA	NA	IR	35 (90)	3 (75) ^a	71(85.54)	
Cefazolin	34(100)	IR ^a	NA	NA	IR	34(100)	4(100) ^a	72(93.5)	
Ciprofloxacin	31 (91.17)	2(50)	10(66.66)	5(83.33)	2(100)	28 (72)	3 (75)	81(77.88)	
Gentamicin	4 (11.76)	1(25))	3(20)	5(83.33)	2(100)	21 (54)	4 (100)	42(40.38)	
Amikacin	7 (20.48)	1(25)	0 (0)	1 (16.66)	1(50)	2 (5.88)	1 (24)	11(10.57)	
Tobramycin	34 (100)	3(75)	6 (40)	2 (33.3)	1(50)	21(54)	4 (100)	70(67.03)	
Meropenem	8 (23.52)	1(25)	8 (53.33)	3 (50)	0(0)	0 (0)	0 (0)	20(19.23)	
Tetracycline	27(79.41)	1(25)	IR	5(83.33)	1(50)	28 (72)	IR	62(67.39)	
Chloramphenicol	27(79.41)	3(75)	IR	IR	1(50)	21 (54)	2 (50)	54(60.67)	
Cotrimoxazole	32(94.11)	3(75)	NA	5(83.33)	1(50)	34 (88)	4 (100)	79(88.7)	
Aztreonams	27(79.41	3(75)	12 (80)	IR	2(100)	31(79.48)	2 (50)	77(86.51)	
ESBL	26(76.5)	1(33.3)	NA	NA	0	21(53,84)	1(25)	49(59.0)	
MDR	30(88.23)	2(50)	12(80)	6(100)	2	34(87.17)	4(100)	90(86.53)	

Table 3 Antimicrobial resistance patterns of Gram-negative bacteria isolated of SSIs at General hospital, southern Ethiopia (n = 104)

Note! AMC, Amoxicillin-clavulanic acid, PTZ; Piperacillin-tazobactam, SAM; ampicillin-sulbactam, IR; intrinsic resistance, NA; Not applicable, percentages are calculated from the number of participants in each column, ^asome species are intrinsically resistant to tested antimicrobial agents, ESBL; Extended spectrum beta lactamase

Antimicrobial agents	No (%) of resis	tance				
	ESKAPE group	(n = 56)		Non- ESKAPE (n = 16)		
	MSSA (n=6)	MRSA (n=44)	E. faecium. (n=6)	CoNs (n=14)	S. pyogenes (n=2)	
Penicillin G	6(100)	44(100)	6(100)	14(100)	0	72(100)
Cephoxitin	0(00)	44(100)	NT	8(54.14)	NT	52(81.25)
Ceftaroline	2(33.33)	9(20.45)	NA	5(35.71)	NS	16(25)
Tetracycline	2(33.33)	23(52.22)	4(66.66)	2(14.28)	2	33(44.59)
Ciprofloxacin	0(00)	28(63.63)	4(66.66)	1(7.14)	NA	34(47.22)
Gentamicin	1(16.66)	17(38.63)	IR	1(7.14)	NA	19(28.78)
Chloramphenicol	18(27.7)	22(50)	1(16.66)	5(35.71)	1	47(63.51)
Clindamycin	0(00)	9(20.45)	IR	4(28.57)	1	15(22.05)
Erythromycin	3(50)	32(72.72)	1(16.66)	7(50)	1	44(59.45)
Co-trimoxazole	5(83.33)	44(100)	IR	14(100)	NA	65(98.48)
Vancomycin	NA	NA	5(83.33)	NA	0(0)	5(62.5%)
Linezolid	0(00)	0(00)	0(0)	0(0)	0	0(0)
Rifampin	4(66.66)	37(80.43)	5(83.33)	10(71.42)	NA	56(77.77)
MDR	0(00)	44(90)	3(50)	8(57.1)	0(00)	55(76.38)

Table 4 Antimicrobial resistance patterns of Gram-positive bacterial isolates of SSIs at General hospital in General surgical ward, southern Ethiopia (n = 72)

Note: CoNS, coagulase-negative staphylococcus, MRSA methicillin-resistant Staphylococci aureus, MSSA, Methicillin susceptible Staphylococci aureus, NT; Not tested

Table 5 Multidrug resistant patterns of bacterial isolates of SSIs at General surgery Southern Ethiopia (n = 176)

Isolates	No (%) of N	1DR pattern				XDR
	R1	R2	R3	R4	≥ R5	No (%)
Gram-positive cocci	6(8.3)	11(15.8)	22(24.3)	23(30.5)	10(13.9)	0
S. aureus ($n = 50$)	3(6)	3(6)	17(26.2)	17(26.2)	9(18)	0
CoNS ($n = 14$)	2(1.4)	4(28.5)	4(28.5)	5(29.4)	1(7.1)	0
E. feacium(n=6)	1	2	1	1	0(0)	0
S.payogenes(n = 2)	0	2	0	0	0(0)	0
Gram negative isolates	3(2.9)	15(14.4)	44(42.3)	27(25.9)	19(18.3)	9(8.6)
E. coli (n = 39)	2(5.1)	3(7.7)	17(43.6)	12(30.6)	5(12.8)	0
K. pneumoniae (n = 34)	0	4(11.7.)	17(50)	8(23.5)	5(14.8)	4(11.7)
Proteus spp. $(n=4)$	0	1	2	1	1	2
C. freundii (n=2)	0	1	1	1	0	0
Enterobacter spp $(n=4)$	1	1	2	1	1	1
A. baumannii, (n=6)	0	2	1	3	5	3
P.aeruginosa (n = 15)	0	3(20)	4(26.66)	5(33.33)	3(20)	0
ESKAPE (n = 115)	3(3)	15(13)	42(36.5)	34(29.6)	23(20)	8(6.9)
Total (n = 176)	9(5.1)	26(14.8)	66(37.5)	50(28.4)	29(16.5)	9(5.1)

No: number of isolates, R1, resistance for single drugs, R3: resistant to three antibiotics, R4: resistant to four antibiotics, R5: resistant to five or more antibiotics, XDR, extensive drug resistant, ESKAPE; S. aureus, K. pneumoniae, Enterobacter spp, A. baumanii, P.aeruginosa

Factors associated with SSIs

The multivariable logistic regression analyses adjusted for potential confounders and covariates showed a significant association between SSIs and emergence surgery, prolonged duration of admission before surgery, and clean-contaminated surgery. Regarding the urgency of surgery, the odds of postoperative wound infections increased in emergency surgery by more than fourfold as compared to elective surgery (AOR = 4.3; 95% CI: 1.9, 9.5; P < 0.00). Moreover, prolonged hospital admission before surgery (a waiting time of seven or more days) was associated with an increased incidence of postoperative wound infections (AOR = 3; 95% CI: 1.4, 6.5; P = 0.004). It has been estimated that surgical patients have three-fold higher risk of developing SSIs if the patients underwent clean-contaminated surgery (AOR = 3.4, 95% CI: 1.4–8.7, P = 0.008). [Table 6].

Discussions

This observational cross-sectional study examined the prevalence of SSIs and provided an overview of the microbial profile, pathogens, and antimicrobial resistance profiles, with a focus on the emerging ESKAPE group pathogens at the major surgical unit of General Hospital, southern Ethiopia. To the best of our knowledge, this study was the first to provide insight into the

Table 6 Factors associated with SSIs ame	ong adult patients underwent r	najor surgery at General	l hospital southern Ethiopia ($n = 207$)

Categories	Total	SSI(n = 159)	Bivariate		Multivariable and	alyses
	No (%)	No (%)	COR(95%CI)	P-value	AOR(95%)CI	P-value
Type of surgery						
Emergence	111(53.6)	85(88.50)	2.16(1.2,3.95)	0.001	4.3(1.9,9.5)	0.001**
Elective	96(46.4)	74(66.70)	1		1	
Surgical Wound type						
Clean	37(17.9)	17(45.94)	1		1	
Clean-contaminate	80(38.6)	65(81.25)	5.09(2.2,12.0)	0.001*	3.4(1.4,8,7)	0.008**
contaminated	90(43.5)	77(85.55)	6.96(2.9,16.6)	0.001*	6.47(0.2, 9.6)	0.001
Surgery waiting time						
≤7 days	63(30.4)	41(65.10)	1	0.001*	1	
>7 days	144(69.6)	118(81.90)	2.43(2.4,8.8)		3.03(1.4,6.5)	0.004**

*Statistically significant at *p* < 0.05 in bivariable analysis, **Statistically significant at *p* < 0.05, AOR: Adjusted odds ratio, COR: Crude odds ratio,, CI: Confidence interval. 1, reference group

epidemiology of SSIs in the context of emerging "critical and high-priority pathogens" monitoring and efforts to control nosocomial infection and fight antimicrobial resistance.

These studies showed that SSIs among adults who underwent major surgery are caused by both ESKAPE group pathogens and non-ESKAPE group pathogens. ESKAPE group members represent three-quarters of the microorganisms isolated from SSIs. This finding highlights the importance of these pathogens as an infectious agent in SSIs. The finding concurs with other previous studies [14]. The finding has paramount clinical importance because treatment options for these group pathogens are limited, and it has been suggested to remain vigilant in monitoring ESKAPE group infections. Clinicians are encouraged to send wound samples for the detection and characterization of ESKAPE group pathogens in all patients presenting signs and symptoms of SSIs. This study's ESKAPE pathogen prevalence was higher than Tanzania's 43.28% [32] previous report's 47.5% [33] and 22.3% in Nepal [34] but was lower than the reported 97% [19]. This variation may stem from differences in nosocomial infection rates, surveillance methods, population selection criteria, and reporting platforms, as well as the challenge of maintaining harmonized systems and standardized case definitions. Nevertheless, was low rate of bacterial recovery from clinically suspected wound samples in this study could alternatively be due to the overlapping of the study period with the acute phase of the global COVID-19 pandemic and the enhanced infection prevention and control practices in the hospitals [21].

The result of our study showed the simultaneous detection of all six members of the ESKAPE pathogens, with the predominance of S. *aureus* 50 (43.5%), followed by *K. pneumoniae* 34 (29.56%), *P. aeruginosa* 15 (13%) while *Enterobacter spp*. as the least frequent isolates (two isolates). This finding was supported by other previous findings [34–36] and the concordance of findings suggested the predominant bacterial species causing SSIs can be predicted. However, in contrast to our findings, studies identified *P. aeruginosa* as the most frequent pathogens [19]. Given the variation in reporting the most common isolates among ESKAPE pathogens, relying on single data sets to draw overall conclusions and guide specific interventions may not be ideal. It is recommended to have a thorough understanding of the evolving epidemiology and microbiology of SSIs instead [10].

This study revealed an extremely worrying picture of MDR 97 (84.37%), MRSA 44 (88%), and ESBL producers 26 (76.5%). The finding was not novel, it was comparable with other studies [37-39] and all the isolates of ESKAPE pathogens fall under the World Health Organization (WHO) list of critical priority pathogens of interest for research and development of antimicrobials [40], which further highlighted the relevance of the findings. Our study highlighted alarming results of MRSA 44(88%), among S. aureus and MRSA stains were also considerably less susceptible to many other antimicrobial agents. The finding aligns with the national level report ranging from 76.7 to 100% [45]. Furthermore, our finding was in agreement with 88% reported in Bangladesh [41], 83.33% in Iran [42], and (83%) in Nepal [43], and 76.7% elsewhere [44]. The concordance of results across the study translates the unfolding practical challenge due to strain not only the more pathogenic or virulent strain but also having limited treatment options as methicillin resistance could make all the available β -lactam drugs, including penicillin, cephalosporin, and combination of β -lactam– β-lactamase inhibitors ineffective in treating MRSA-associated SSIs [30]. However, our finding was incomparably higher than the (0%) from Swiss [45], 15.7% from India [46], and 44.8% from Sierra Leone [47], and the report by Pradeep and Rao, et al. [48] and could be attributed to the absence of preoperative screening and decolonization of carrier among patients undergoing major surgery [12, 49]. However, the clinical effectiveness of MRSA isolates can be anticipated with Linezolid. The results of this

study correlate with 90% reported VRE and the known theory that the *Enterococcus spp* is intrinsically resistant to multiple antibiotics [50]. Interestingly *Enterococci spp* exhibited 100% sensitivity to Linezolid followed by a sensitivity of more than 80% to chloramphenicol and erythromycin (resistance of 16.66%), whereas *100%* resistance to penicillin (100%), 66.6% resistance to each of the drug Tetracycline, *R*ifampin, Ciprofloxacin, and the finding was accurate with the previous research finding.

In addition, the findings of this study confirmed the high rate of vancomycin-resistant E. faecium in the study setting. The results of this study are consistent with 90% of reported VRE, supporting the known theory that Enterococcus spp. is intrinsically resistant to multiple antibiotics [51]. Interestingly, E. faecium isolates exhibited 100% sensitivity to Linezolid, followed by sensitivity of more than 80% to chloramphenicol and erythromycin (resistance of 16.66%), 100% resistance to penicillin (100%), and 66.6% resistance to each of the drugs Tetracycline, Rifampin, and Ciprofloxacin. The finding was accurate with the previous research finding [52]. Phenotypic evaluation of the mechanism of drug resistance revealed ESBL production in 26 (76.5%) of K. pneumoniae isolates. The observation was in agreement with the conclusion of the recent systemic review [53]; suggesting ESBL production among Enterobacteriaceae is responsible for resistance to the extended beta-lactamase group of drugs. Therefore, limiting the inappropriate use of beta-lactamase drugs could have an impact on reducing the emergence and strain of the antimicrobial-resistant strain and helping to preserve the most potent drugs for future generations [39, 54]. A significant finding in this study was the high prevalence of MDR-97 (84.37%) of ESKAPE pathogens. The phenotypic evaluation showed a drug resistance mechanism of ESBL production among 26(76.5%) K. pneumoniae, isolates. The observation was in agreement with the conclusion of the recent systemic review [53] suggesting ESBL producing among Enterobacteriaceae is responsible for resistance to the extended beta-lactamase group of drugs. Therefore limiting the inappropriate use of the beta-lactam drugs could have an impact on reducing the emergence and strain of the antimicrobial-resistant strain and help to preserve the most potent drugs for future generations [39, 54].

The other important finding in this study was the high prevalence of MDR 97(84.37%) of ESKAPE pathogens. The prevalence of MDR has not changed since the previous report from Jimma [44] and it was in agreement with the report of 89.5% from Ghana [55], 90.8% in Benin [56], 78.3% in two studies from Uganda [37, 57] and Tanzania [38]. Convergent findings from similar studies highlight role of the selective pressure due to inappropriate antimicrobial use, including prolonged surgical antimicrobial prophylactic in post-operative continuation [58]. There was an intra-species difference in MDR level. Albeit *A. baumannii* accounted for a small portion of SSIs caused by ESKAPE member pathogens, the observation of MDR among all of the isolates makes these opportunistic pathogens a serious cause of concern. Another important finding to consider is that factors related to surgical procedures affect the risk of SSIs. In this study emergency surgery, prolonged surgical waiting time (prolonged admission before surgery), and clean-contaminated procedures were identified as high-risk procedures and the findings were similar to those of the report on systematic review and other independent studies [21, 26, 51].

The basic understanding of SSI magnitude and their microbiology, epidemiology, and antimicrobial resistance could be used to inform infection prevention and control practices, empirical therapy, and research in the field. The high prevalence of ESKAPE group pathogens that were resistant to the commonly prescribed drugs for surgical patient management and initial prophylaxis use highlights a potentially important area to improve in order to enhance patients' surgical outcomes, control the spread of antimicrobial resistant pathogens in the hospital and save the effectiveness of available empirical antimicrobial treatment. The observations that MDR-ESKAPE group pathogens account for over half of SSIs suggest a paradigm shift in the understanding of SSIs that questions several relevant practical issues such as the effectiveness of the antimicrobial protocol for empirical therapy and prophylaxis use, and surgical infection prevention practices. The infection prevention team could also increase compliance with the recommended guidelines to control infections inform research to develop robust infection prevention tools, and optimize the existing toolbox. This study confirmed that critical and high-priority pathogens are prevalent in the study setting, emphasizing efforts to mitigate this problem must consider planning and implementation of the most effective interventions that include strategies, and policies that reinforce and strengthen infection prevention practices, support surveillance and monitoring of antimicrobial resistance in developing nations like Ethiopia [10, 11]. Despite the fact that carbapenems are typically only used as last resort medications in African hospitals due to their high cost, the discovery of carbapenems (meropenem) resistance in roughly half of A. baumannii and P. aeruginosa isolates was a startling and unexpected finding because it emphasizes the presence of critical pathogens, serious infections, and emerging ESKAPE pathogens. The results were consistent with a previous evaluation of research conducted in Sub-Saharan Africa by Njeru, J. (2021) and were utilized to support additional study and cooperative initiatives aimed at preventing diseases and limiting their spread [59].

The high prevalence of MDR-ESKAPE pathogens in SSIs would help explain the source of infections and be used to advise global and national programs to provide funds in support of developmental research and surveillance.

The detections of ESBL producing, and MRSA strains among among bacterial pathogens isolated from SSIs were used to understand the mechanism of drug resistance and predict the clinical outcome of patients infected with these pathogens. This highlights the importance of planning and implementing screening and decolonizing of patients before surgery, advancing the current laboratory to support microbiology diagnosis of postoperative wound infections, and establishing an antimonial stewardship program. Consequently, improving the local situation will support the global communities in addressing the rising problem of antimicrobial resistance threats. Furthermore, awareness of independent risk factors documented in this study may assist in identifying and advancing patients about the high risk and implementing strict infection preventive measures pre-, during, and post-surgery. Taking all together this report lays out the important of multifaceted science-based solutions that, if taken together through a one health framework, will prevent, detect and address the emerging problem of antimicrobial resistance by collaboration across human, animal and environmental health sectors, to achieve sustainable and long-lasting results [60].

Limitations

Some limitations need to be considered when interpreting the results of this study, first methodological limitations as the study addressed only aerobic bacteria and fungi. Furthermore, this study was a single-center study and some isolates were very few in number to calculate the percentage of antimicrobial resistance. Analysis of associated factors in this study may not be explicit observation, thus some important significant factors might have been missed. The antimicrobial sensitivity patterns to last-line agents like vancomycin, tigecycline, and colistin against the Gram-negatives, were not considered due to limitations of resources. Future studies are expected to address these limitations by characterizing antimicrobial resistance with advanced methods, thoroughly detailing the molecular epidemiology of the antimicrobial-resistant strains. Future studies are also consider evaluating the effectiveness of the ongoing infection prevention and control practice, and the treatment outcomes of ESKAPE group pathogens.

Conclusions

Antimicrobial-resistant ESKAPE and non-ESKAPE pathogens contribute to surgical site infections (SSIs) in the major surgical unit of the general hospital. The

finding highlights the importance of attention and further actions in improving infection prevention practices, and diagnostic and antimicrobial stewardship programs to monitor and control the emergence and spread of the antimicrobial resistance threat.

Abbreviations

SSIs	Surgical site infections
MHA	Mueller Hinton agar
AMP	Amoxicillin-clavulanic acid
PTZ	Piperacillin-tazobactam
SAM	ampicillin-sulbactam
IR	intrinsic resistance
CoNS	coagulase-negative staphylococcus
MRSA	Methicillin-resistant Staphylococcus aureus
MSSA	Methicillin susceptible Staphylococcus aureus
CLSI	Clinical and Laboratory Standard Institutes
ESKAPE	Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae,
	Acinetobacter baumannii, Pseudomonas aeruginosa, and
	Enterobacter species
MDR	Multidrug-resistant
SPSS	Statistical Packages for Social Science
ESBL	Extended-Spectrum Beta-Lactamase

Supplementary Information

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Supplementary Material 1

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Author contributions

SM, AA, DT, BB Conceptualization, SM, AA, DT, BB, KK, MA, AM methodology, SM, KK, MA, AM; software, AM, SM.; AA, DT, BB, AM validations, SM, MA; formal analysis, SM, IA, DT, BB, KK, MA investigation KT, AA, DT, BB, AM; resources KT, AH, SM, KK, BB; data curation, BB, SM, AM, KK; IA writing—original draft preparation, IA, SM, AM, MA, KK; writing—review and editing, AH, IA, DT, KK, MA, SM; visualization, MA, BB, AA; supervision, SM; project management. All authors have read and agreed to the final version of the manuscript.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted under the International Ethical Guidelines for Health-Related Research involving Humans issued by ethical principles in the Declaration of Helsinki. Ethical clearance was obtained from the Institutional Review Board (IRB/152/12) of the College of Medicine and Health Sciences, Arba Minch University. Written informed consent was also obtained from each study participant before the study. The positive findings in the culture and the antimicrobial susceptibility test were kept confidential and were also communicated to attending physicians for patient management.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

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