Prevalence, Resistance Profiles and Factors Associated with Skin and Soft-Tissue Infections at Jinja Regional Referral Hospital: A Retrospective Study

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Article

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Abstract: Skin and soft-tissue infections (SSTI) are common cases of hospital-acquired infections with aetiologic agents exhibiting antimicrobial resistance (AMR). We determined the prevalence, proportion of laboratory-investigated cases, AMR-profiles, and factors associated with SSTI and multi-drug resistance (MDR). This study was based on archived data of patients suspected of SSTI from 2019-2021 at Jinja Regional Referral Hospital. The analysis involved 268 randomly selected patient reports. Prevalence of SSTI was 66.4%. Laboratory-investigated cases were 14.11%. *Staphylococcus aureus* (n=51) was the most isolated organism. MDR pathogens explained 47% of infections. Methicillin-resistant *S. aureus* was up to 44%. In addition, 61% of Gram-negatives had the potential to produce extended-spectrum beta-lactamases, while 27% were non-susceptible to carbapenems. Ward of admission was significantly associated with infection (aPR=1.78, 95% CI: 1.003-3.18, p-value=0.04). Age category (19-35) was an independent predictor for MDR infections (aPR=2.30, 95%CI:1.02-5.23, p-value=0.04). The prevalence is relatively high with MDR pathogens responsible for almost half of the infections. Routine use of culture and sensitivity testing should be done for proper infection management. Gentamicin and ciprofloxacin can be considered for empirical management of emergency SSTI suspected of *S. aureus*. Recognizing SSTI under the Global Antimicrobial resistance Surveillance System would lead to improved preparedness and response to AMR.

Keywords: skin and soft-tissue infections; antimicrobial resistance; multidrug-resistance; hospital-acquired infections; global antimicrobial resistance surveillance system

1. Introduction

Antimicrobial resistance (AMR) is an emerging public health threat of concern globally (1, 2). It has been noted to be responsible for negative social, economic, and health consequences; higher healthcare costs; increased Disability Adjusted Life Years (DALYs); and decreased economic growth (3, 4). This burden is projected to increase in the near future if no proper attention is paid to managing it (3). Improper use of antimicrobials is one of the main factors contributing to the development of AMR (1, 5, 6). This has been reported in Uganda, which includes the prescription of

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antimicrobial agents for the wrong condition in lower health facilities (1, 5, 7). Using microbiology services such as culture and sensitivity (C&S) testing enables determination of the identity of the causative agents and the appropriate antimicrobial agents that can be used for proper management of individuals with infections, such as skin and soft-tissue infections (SSTI)(8, 9). However, this this is still far from the practice in this setting as most clinical management is still empirical. Laboratory surveillance is conducted in Uganda as part of the mechanisms to tackle AMR in line with the global action plan for AMR (10).

Skin and soft-tissue infections are some of the most commonly encountered cases of hospital-acquired infections (HAI) and are characterized by AMR mainly among post-operative patients in low and middle-income countries (LMICs) (11-13). These are a type of infection involving colonization and inflammation of the epidermis, dermis, and subcutaneous tissues (9, 14). *The colonizing agents such as bacteria are commonly from the hospital environment such as sinks, surgical beds, staff and wound dressings. These have been reported to be highly resistant to the commonly used antimicrobial agents (15-17).* Various factors have been reported to influence the occurrence of SSTI including the presence of comorbidities, 48-hour duration of surgical antimicrobial prophylaxis, contaminated and dirty wounds, sex, lack of prophylactic antibiotic treatment, postoperative length of stay, American Society of Anesthesiologists (ASA) score of ≥ 2, and the timing of prophylactic antibiotic, which is more beneficial 1-2 hours before surgery (13, 18, 19). Other independent factors include open surgery, emergency operations, male sex, long duration of surgery, intraoperative blood transfusion, age, smoking, and HIV (14, 20, 21).

Surgical site infections prevalence was between 1.5% and 3.64% in China (22, 23), 11.7% in Malaysia (19), 9.85% in parts of Europe (24), and ranged from 10.3% to 15.6% in sub-Saharan Africa (25). Microbial growth was 68.5% in Pakistan (6), 16.3% in Saudi Arabia (20), 62.1% in Sierra Leone (21), and 70.0% in Ethiopia(26). Positivity rates ranged from 81.93% to 92% in Uganda (27-29). Gram-negative organisms, such *as Pseudomonas aeruginosa, Acinetobacter species, Klebsiella species, Escherichia coli, Proteus species,* and other *coliforms* are the ones mostly responsible for wound infections (6, 21, 30). However, *Staphylococcus aureus* has been observed as the dominant wound pathogen elsewhere (2, 31-33). Mixed infections have also been reported, where the infection is due to more than one etiologic agent (12, 31, 34). A significant number of the isolated bacteria are multi-drug resistant (MDR) (21, 28, 34). The *Enterobacterales* were collectively resistant to ampicillin while the overall *S. aureus* resistance profile was oxacillin (23.9%), ciprofloxacin (18.9%), trimethoprim/sulfamethoxazole (55.7%) and clindamycin (8.8%) (2). Multi-drug resistant isolates were up to 22.6% in Poland(33) while MRSA levels have been reported up to 30.3% in Kuwait (34). The least resistance was observed against gentamicin (24%) and ciprofloxacin (27%) (26).

There is insufficient utilization of microbiology laboratory services during infection management in some health facilities in Uganda (5, 27), leaving room for non-targeted therapy. Further, the Global Antimicrobial Resistance and antimicrobial use Surveillance System (GLASS) (10, 35) does not currently consider SSTI despite their high cultural yields and associated AMR observed in the microbiology laboratory (26-28). This limits the availability of some essential information for an appropriate response towards the AMR epidemic. The actual status of SSTI is unknown at Jinja Regional Referral Hospital (RRH), with little knowledge about their influencers. This study therefore aimed to determine the prevalence of SSTI, proportion of SSTI that undergo laboratory investigation, common causative organisms and their antibiotic susceptibility profiles, and probable factors associated with SSTI and MDR infections. This information would enable formulation or/and review of guidelines for better management of SSTI and improve regional antimicrobial stewardship practices for containment of AMR.

2. Results

2.1. Demographic Characteristics

A total of 268 patient reports were included in the study. Of these, 55% (n = 148) belonged to males. The patients had a mean age of 31.5 years (SD = 20.8) and most of the patients (31%, n = 84)

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belonged to the age group of 19-35 years followed by 36-59 years (28%, n = 76). Nearly a third of the patients (n = 88) were admitted to the surgical unit. Moreover, two-thirds of the study patients were undergoing antibiotic treatment before any microbiology testing was done (**Table 1).**

Table 1. Demographic characteristics of the study population.

Variable		*n*	*(%)*
Year of Case	2019	44	16.4
	2020	120	44.8
	2021	104	38.8
Sex	Male	148	55.2
	Female	120	44.8
Age Category	≤12	48	17.9
	13-18	31	11.6
	19-35	84	31.3
	36-59	76	28.4
	≥60	29	10.8
Ward/Department	Accidents and emergency	16	6.0
	Gynecology	13	4.9
	Maternity	15	5.6
	Medical	15	5.6
	Surgical	88	33
	Outpatient Department	38	14.2
	Orthopedics	34	12.7
	Private wing	8	3.0
	Pediatrics	10	3.7
	Others	31	11.6
	Unknown	51	19
On antibiotics before testing	Yes	176	65.7
	No	92	34.3
Undergoing surgery	Yes	11	4.1
	No	98	36.6
	Unknown	159	59.3

2.2. Prevalence of Skin and Soft Tissue Infections

The prevalence of SSTI was 66.4% (n = 178, 95% CI = 60.7-72.1). Among the cases, 56.7% (n = 101) were males. The most affected age groups were those between 19 and 35 years (29.8%) followed by

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36-59(27.5%). Polymicrobial growth was observed in 7.2% (n=18) of the cases. Of these, *Candida species* 2% (*n*=5) were the major co-infection.

The pediatric ward had the highest prevalence of SSTI of up to 80% (8/10) while the accidents and emergency unit had the lowest, 43.7% (7/ 16) (Table 2).

Table 2. Prevalence of SSTI in the Respective Wards of Admission.

Ward/Department	*Total* no. of *Patients*	*Infection Frequency*	*Percentage*
Pediatrics	10	8	80
Medical	15	8	53
Accidents and emergency	16	7	43.7
Surgical	88	66	75
Outpatient	38	25	65.7
Maternity	15	8	53
Orthopedics	34	20	58.8
Private	8	6	75
Antenatal	13	7	53.8
Others	31	23	74.2

Approximately 3,720 cases were diagnosed and treated for SSTI during the study period. Only 14.1% (n = 526) of C&S tests were done among patients suspected of SSTI. In 2019, there were 8.1% (104/1278) cases that underwent laboratory testing for SSTI. Meanwhile, years 2020 and 2021 respectively had 21.1% (226/1072) and 14.3% (196/1370) cases diagnosed by the laboratory to guide management (Figure A3).

Only 2.1% (n = 11) of the patients' records were found to have C&S test results in patient files. The treatment records for outpatients were not readily available. Therefore, the representative percentage of de-escalation based on the C&S report could not be estimated.

2.3. Antimicrobial Resistance Patterns of Selected Bacteria Responsible for Skin and Soft-Tissue Infections

2.3.1. Major Bacteria Responsible for the Observed SSTI

The observed organism growth yielded 203 isolates. Approximately 44.4% (n = 119) of the infections were due to Gram-negative bacteria, 19.4% (n = 52) were Gram-positive cocci and 2.6% (n = 7) were yeasts. Most of the infections were due to *S. aureus* (19%, n = 51) followed by *E. coli* (10.4%, n = 28), *Coliforms* (10.4%, n = 28), *Klebsiella species* (6.7%, n = 18), *Citrobacter species* (6.3%, n = 17), and *Proteus species* 3.3%, n = 9). Non-*Enterobacterales* were mainly made up of *Pseudomonas species* (4.1%, n = 11) and *Acinetobacter species* (2.6%, n = 7). Nearly 3% (n = 7) of isolates from the SSTI were *Candida species*. Bacterial isolates also included *Coagulase Negative Staphylococci* (*CoNS*)(n=22).

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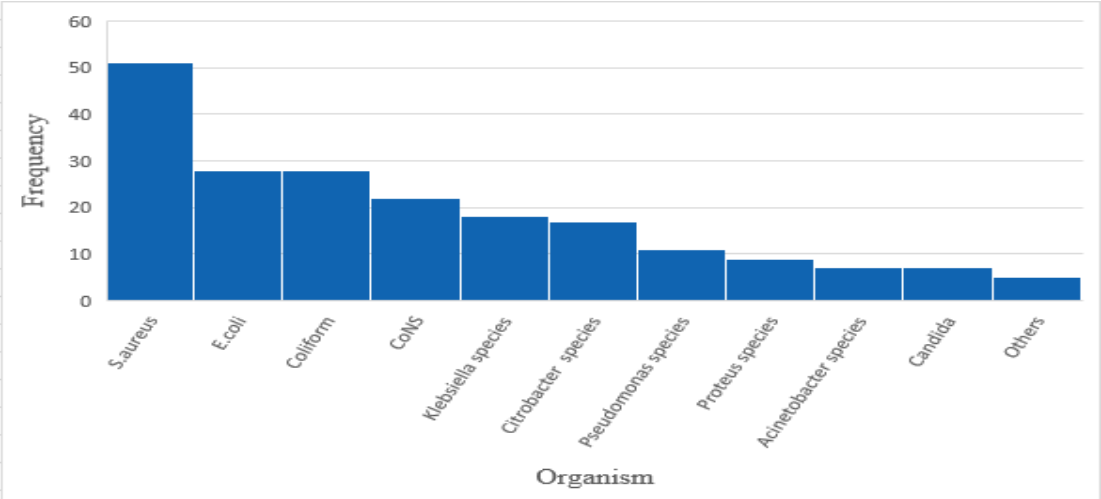

Figure 1. Frequency distribution of the isolated organisms responsible for the SSTI.

2.3.2. Percentage Resistance of the Bacteria to Common Antibiotics

Up to 47% (n = 79) of the infections were due to MDR pathogens. Among the Gram-negative bacteria, 61.3% (n = 73) were resistant to third-generation cephalosporins and hence possible ESBL producers while 27.7% (n = 33) were non-susceptible to carbapenems. All the tested isolates for *S. aureus* were resistant to penicillin G (n = 23) (Figure A2). Over 44.4% (n = 8, 95% C.I: 22.4-68.7) of the tested isolates were methicillin-resistant *Staphylococcus aureus* (MRSA; Table 3).

The highest percentage resistance among *enterobacterales* altogether was against ampicillin (97.1%, n=34). This group was least resistant to meropenem (0%) and imipenem (15.6%) (Table 4). Non-*enterobacterales* composed of *Pseudomonas* and *Acinetobacter* species together (n=18) had a percentage resistance of 55.6% (n = 7) for piperacillin, 50% (n = 1) for amikacin, 50% (n = 7) for ceftazidime, 36.4% (n = 5) for ciprofloxacin, 25% (n = 2) for gentamicin, and 22.2% (n = 2) for imipenem.

Table 3. Antimicrobial susceptibility profile for Staphylococcus aureus.

Antibiotic name	*Antibiotic class*	*Breakpoints*	*Number Tested*	*%R*	*%I*	*%S*	*%R, 95%C.I.*	*%S, 95%C.I.*
**Cefoxitin*	Cephems	S >= 22	18	44.4	0.0	55.6	22.4-68.7	31.3-77.6
Chloramphenicol	Phenicols	13 - 17	16	6.3	12.5	81.3	0.3-32.3	53.7-95.0
Ciprofloxacin	Quinolones	16 - 20	48	41.7	16.7	41.7	27.9-56.7	27.9-56.7
Clindamycin	Lincosamides	15 - 20	36	36.1	16.7	47.2	21.3-53.8	30.8-64.3
Erythromycin	Macrolides	14 - 22	37	70.3	21.6	8.1	52.8-83.6	2.1-23.0
Gentamicin	Aminoglycosides	13 - 14	35	28.6	8.6	62.9	15.2-46.5	44.9-78.0
Penicillin G	Penicillins	S >= 29	23	100.0	0.0	0.0	82.2-100	0.0-17.8
Tetracycline	Tetracyclines	15 - 18	9	22.2	44.4	33.3	3.9-59.8	9.0-69.1
Trimethoprim/Sulfamethoxazole	Folate pathway inhibitors	11 - 15	7	100.0	0.0	0.0	56.1-100	0.0-43.9

R-Resistant; S-Susceptible; I-Intermediate; C.I-Confidence Interval. *Note: Cefoxitin is the recommended surrogate test agent for determining the susceptibility of *S. aureus* to Oxacillin or Methicillin using the disk-diffusion method (36-38). *S. aureus* isolates that are resistant to Cefoxitin are regarded as Methicillin Resistant *S. aureus*(MRSA).

Table 4. Antimicrobial susceptibility profile for Enterobacterales.

Antibiotic name	*Antibiotic class*	*Breakpoints*	*Number Tested*	*%R*	*%I*	*%S*	*%R, 95%C.I.*	*%S,95%C.I.*
Amikacin	Aminoglycosides	15 - 16	19	15.8	26.3	57.9	4.2-40.5	34.0-78.9
Amoxicillin/Clavulanic acid	Beta-lactam+Inhibitors	14 - 17	7	71.4	0.0	28.6	30.3-94.9	5.1-69.7
Ampicillin	Penicillins	14 - 16	35	97.1	2.9	0.0	83.4-99.9	0.0-12.3

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Cefotaxime	Cephalosporin III	23 - 25	18	77.8	16.7	5.6	51.9-92.6	0.3-29.4
Ceftazidime	Cephalosporin III	18 - 20	38	73.7	10.5	15.8	56.6-86.0	6.6-31.9
Cefuroxime	Cephalosporin II	15 - 17	10	80.0	0.0	20.0	44.2-96.5	3.5-55.8
Chloramphenicol	Phenicols	13 - 17	78	46.2	10.3	43.6	34.9-57.8	32.6-55.3
Ciprofloxacin	Fluoroquinolone	22 - 25	83	51.8	9.6	38.6	40.6-62.8	28.3-49.9
Gentamicin	Aminoglycosides	13 - 14	71	33.8	12.7	53.5	23.3-46.1	41.4-65.3
Imipenem	Carbapenems	20 - 22	45	15.6	8.9	75.6	7.0-30.1	60.1-86.6
Meropenem	Carbapenems	20 - 22	5	0.0	0.0	100.0	0.0-53.7	46.3-100
Tetracycline	Tetracyclines	12 - 14	18	72.2	0.0	27.8	46.4-89.3	10.7-53.6
Trimethoprim/Sulfamethoxazole	Folate pathway inhibitors	11 - 15	21	90.5	4.8	4.8	68.2-98.3	0.2-25.9

R-Resistant; S-Susceptible; I-Intermediate; C.I-Confidence Interval.

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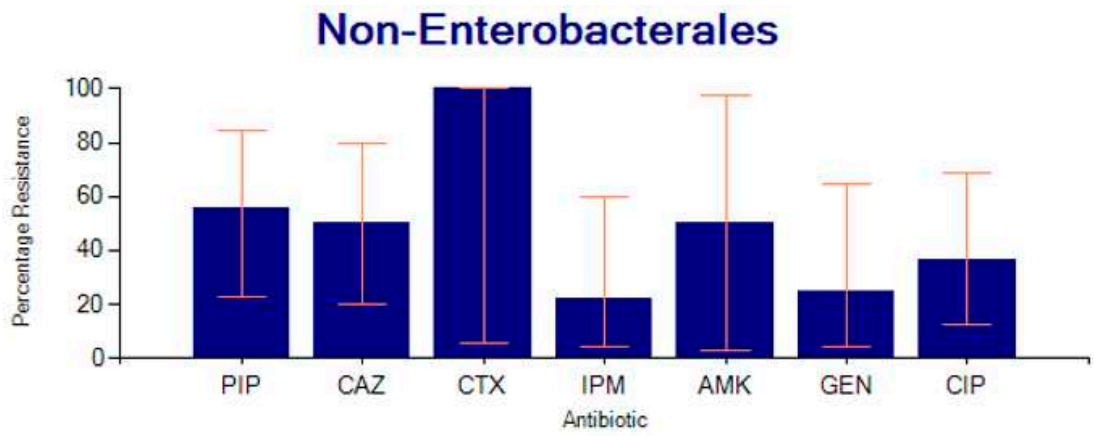

PIP-Piperacillin; CAZ-Ceftazidime; CTX-Cefotaxime; IPM-Imipenem; AMK-Amikacin; GEN-Gentamicin; CIP-Ciprofloxacin

Figure 2. Percentage resistance for Acinetobacter and Pseudomonas species together.

2.4. Factors Associated with SSTI

Patients in the surgical ward were significantly more likely to develop an SSTI compared to those in the A&E ward (aPR = 1.78, 95%, CI:1.003-3.18, p = 0.04). Age, gender, hospital admission hours, and status of antibiotic use before testing were not independently associated with risk for SSTI. (Table 5).

Table 5. Factors Associated with Skin and Soft Tissue Infections.

Variable	**Infection**		**Bivariate Analysis**	**Multivariate Analysis**
Ward, n (%)	**No** (n=90)	**Yes** (n=178)	**cPR**(95%CI),p-value	**aPR**(95%CI), p-value
A&E	9(10.0)	7(3.9)	1.00	1.00
Gynecology	6(6.7)	7(3.9)	1.23(0.58-2.61) 0.58	1.32 (0.61-2.88) 0.48
Maternity	7(7.8)	8(4.5)	1.22(0.59-2.53)0.59	1.30 (0.61-2.77) 0.48
Medical	7(7.8)	8(4.5)	1.22(0.59-2.53) 0.59	1.28 (0.61-2.70) 0.51
OPD	13(14.4)	25(14.0)	1.50(0.82-2.75) 0.18	1.60 (0.86-2.98) 0.13
Orthopedics	14(15.6)	20(11.2)	1.34(0.72-2.51) 0.35	1.43 (0.76-2.69) 0.26
Other	8(8.9)	23(12.9)	1.69 (0.94-3.07) 0.08	1.81 (0.98-3.35) 0.05
Private	2(2.2)	6(3.4)	1.71(0.86-3.40) 0.12	1.86 (0.91-3.77) 0.08
Pediatrics	2(2.2)	8(4.5)	1.83(0.97-3.46) 0.06	1.78 (0.92-3.46) 0.08
Surgical	22(24.4)	66(37.1)	1.71(0.97-3.03) 0.06	1.78 (1.00-3.18) **0.04**
Sex, n (%)				
Female	43(47.8)	77(43.3)	1.00	1.00
Male	47(52.2)	101(56.7)	1.06(0.89-1.26) 0.48	1.04 (0.86-1.24) 0.702
Age Group, n (%)				
12&below yrs.	14(15.6)	34(19.1)	1.00	1.00
13-18yrs	10(11.2)	21(11.8)	0.95(0.70-1.29) 0.77	0.97 (0.70-1.33) 0.841
19-59yrs	31(34.4)	53(29.8)	0.89(0.69-1.13) 0.35	0.90 (0.68-1.19) 0.479

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60+yrs	35(38.9)	70(39.3)	0.94(0.75-1.18) 0.60	0.92 (0.71-1.19) 0.534
Undergoing surgery, n (%)				
No	85(94.4)	172(96.6)	1.00	
Yes	5(5.6)	6(3.6)	0.81(0.47-1.40) 0.46	
Surgical type, n (%)				
Elective	2(2.2)	3(1.7)	1.00	1.00
Others	88 (97.7)	175 (98.3)	1.10 (0.54-2.28) 0.77	0.52 (0.20-1.30) 0.162
Hospital admission >48hrs, n (%)				
No	49(54.4)	100 (56.2)	1.00	1.00
Yes	41(45.6)	78(43.8)	0.97(0.82-1.16) 0.78	1.004 (0.79-1.27) 0.974
Year of case				
2019	13 (14.4)	31 (17.4)	1.00	1.00
2020	45 (50)	75 (42.1)	0.89 (0.70-1.12) 0.32	0.96 (0.73-1.27) 0.790
2021	32 (35.6)	72 (40.5)	0.98 (0.78-1.23) 0.88	1.05 (0.80-1.37) 0.732
Antibiotic use before testing				
No	31 (34.4)	61 (34.3)	1.00	1.00
Yes	59 (65.6)	117 (65.7)	1.002 (0.84-1.20) 0.97	1.04 (0.82-1.32) 0.721
Type of theatre				
Others	86 (95.6)	172 (96.6)	1.00	
Main theatre	4 (4.4)	6 (3.4)	1.11 (0.66-1.86) 0.68	

2.5. Factors Associated with MDR Pathogens Responsible for SSTI.

Age was the only factor significantly associated with MDR, where patients aged 19 to 59 years were over two times more likely to have MDR pathogens compared to those who were 12 years or younger (aPR = 2.30, 95%CI:1.02-5.23, p = 0.04) (Table 6).

Table 6. Factors associated with MDR pathogens among patients with Skin and Soft Tissue Infections.

Variable	**MDR**		**Bivariate Analysis**	**Multivariate Analysis**
Ward, n (%)	**No** (n=189)	**Yes** (n=79)	**cPR**(95%CI), p-value	**aPR**(95%CI), p-value
A&E	12(6.4)	4(5.1)	1.00	1.00
gynecology	8(4.2)	5(6.3)	1.54(0.51-4.60) 0.44	1.21 (0.39-3.74) 0.742
maternity	11(5.8)	4(5.1)	1.07(0.32-3.53)0.91	0.88 (0.25-3.09) 0.842
medical	12(6.4)	3(3.8)	0.80(0.21-3.00) 0.74	0.71 (0.19-2.67) 0.616
OPD	28(14.8)	10(12.7)	1.05(0.39-2.87)0.92	1.05 (0.39-2.80) 0.917
Orthopedics	25(13.2)	9(11.4)	1.06(0.38-2.93) 0.91	0.84 (0.29-2.41) 0.739
Other	22(11.6)	9(11.4)	1.16(0.42-3.20) 0.77	1.50 (0.54-4.15) 0.432

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Private	5(2.7)	3(3.8)	1.50(0.44-5.16) 0.52	1.49 (0.45-4.95) 0.512
Pediatrics	8(4.2)	2(2.5)	0.80(0.18-3.60) 0.77	1.49 (0.29-7.39) 0.627
Surgical	58(30.7)	30(38.0)	1.36 (0.56-3.35) 0.49	1.18 (0.47-2.94) 0.719
Sex, n (%)				
Female	88(46.6)	32(40.5)	1.00	1.00
Male	101(53.4)	47(59.5)	1.19(0.81-1.74) 0.36	1.25 (0.84-1.88) 0.276
Age, n (%)				
12&below yrs.	40(21.2)	8(10.1)	1.00	1.00
13-18yrs	22(11.6)	9(11.4)	1.74(0.75-4.03) 0.19	2.14 (0.79-5.73) 0.13
19-59yrs	54(28.6)	30(38.0)	2.14 (1.06-4.29) 0.03	2.30 (1.02-5.23) **0.04**
60+yrs	73(38.6)	32(40.5)	1.82(0.91-3.67) 0.09	1.96 (0.87-4.12) 0.10
Undergoing surgery, n (%)				
No	181(95.8)	76(96.2)	1.00	
Yes	8(4.2)	3(3.8)	0.92(0.34-2.46) 0.87	
Surgical type, n (%)				
Elective	2(1.1)	3(3.8)	3.69 (0.60-22.52) 0.15	
Others	187 (98.9)	76(96.2)	1.00	
Hospital admission >48hrs, n (%)				
No	112(59.3)	37(46.8)	1.00	1.00
Yes	77(40.8)	42(53.2)	1.42(0.98-2.05) 0.063	1.17 (0.71-1.94) 0.541
Year of case				
2019	36 (19)	8 (10.1)	1.00	1.00
2020	85 (45)	35 (44.3)	1.60 (0.81-3.19) 0.17	1.34 (0.61-3.03) 0.45
2021	68 (36)	36 (45.6)	1.90 (0.96-3.76) 0.06	1.63 (0.75-3.55) 0.21
Antibiotic use before testing				
No	72 (38.1)	20 (25.3)	1.00	1.00
Yes	117 (61.9)	59 (74.7)	1.54 (0.99-2.39) 0.05	1.28 (0.73-2.24) 0.38
Type of theatre				
Others	182 (96.3)	76 (96.2)	1.00	1.00
Main theatre	7 (3.7)	3 (3.8)	1.02 (0.39-2.68) 0.97	0.91 (0.34-2.46) 0.855

3. Discussion

This study provides the most recent epidemiology of SSTI and their resistance profiles in a Ugandan tertiary healthcare facility. The prevalence of SSTI was 66.4%, which was comparable to the prevalence reported in Pakistan (68.5%) (6), Sierra Leone (62.1%)(21) and Ethiopia (70%)(26). However, studies in the same settings including Mbarara RRH (81.93%, 92%) (27, 28) and Mulago National Referral Hospital (85%)(29) observed higher levels of infection. Much lower levels of skin

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infections, 1.5% (22), 3.1-4.4% (39), and 10.3-15.6% (25), have also been reported. These differences likely resulted from variations in the methods used to diagnose the infections. The clinical diagnostic approach based on physical examination was applied in some studies (22, 39) compared to the laboratory detection approach by C&S used in this research and the previous similar studies(27, 29).

Polymicrobial growth (7.2%) was observed where cases had more than one aetiologic agent isolated. This has been observed in other studies (12, 31, 34). In this study, *Candida* species were involved in more polymicrobial infections compared to the cases solely by a fungus, indicating that an SSTI by a fungal organism is more likely to occur with an existing bacterial agent. A higher proportion of mixed infections (21.4%) has previously been observed compared to only fungal infections (5.8%) (40). Also, there are significant interactions between bacteria and fungi to form biofilms reported to complicate healing, especially in chronic wound infections (41). This calls for further utilization of appropriate diagnostics to detect the fungal infections to limit unnecessary and prolonged use of antibiotics especially among patients with chronic deep tissue infections.

In this study, sex was not associated with SSTI or MDR as similarly observed in Benin (18) but contrary to other studies where sex was significantly associated with a higher risk for infection(19, 21). The age groups most affected by SSTI were those between 19 and 35 years followed by those between 36 and 59 years with SSTI in the 19-59 group being more likely to be due to MDR pathogens than those less than 12 years. This contrasts previous studies that reported a higher likelihood of infection among those above 35 years (24, 42). This might be because this age group is the most active in life, prone to injuries and risks that increase their probability of acquiring MDR infections. Age has previously not been associated with MDR infections elsewhere (43).

The proportion of patients tested in the microbiology laboratory for the management of SSTI was found to be 14.1%, which was slightly less than the 23% observed in California, USA (44). Treatment records for outpatients were not available while only 11 of the study patients' records were found to have culture and sensitivity result reports in inpatient files. These low numbers could be due to the non-electronic system used for patients' records and poor communication between attending clinicians and the laboratory. This increases chances for misdiagnosis and poor choice of antibiotics to manage cases.

Most of the isolated bacteria were Gram-negative (58.6%(119/203)) as similarly observed by other studies in which the Gram-negative accounted for most of the infections ranging from 72.9-91% (19, 21, 30). However, *S. aureus* was individually responsible for most of the infections observed in the current study. This is similar to studies conducted elsewhere (14, 31, 32). *S. aureus* was followed by *E. coli* then other bacteria such as *Coliforms*, *Klebsiella* species, *Citrobacter* species, and *Pseudomonas* species isolated. Similar organism rates have been reported in China, Ethiopia, and Rwanda (12, 22, 30).

This study observed that 47% of the infections were due to MDR pathogens, which are greater than the 22.6% prevalence observed in Poland (33). This difference could be due to the employment of better infection prevention measures compared to Ugandan settings. Other studies also reveal that a large number of the bacteria responsible for the SSTI are MDR (21, 28, 34).

Up to 61% of Gram-negative bacteria were resistant to third-generation cephalosporins hence the possible presence of ESBL producers which was similar to 59.2% in *Sierra Leone* (21). Meanwhile, 27% were non-susceptible to carbapenems which is higher than the 8.2% observed among the Enterobacterales (21). The study observed MRSA levels of 44% which is comparable to Ethiopia (49%) (26) but less than levels reported in Saudi Arabia(65.4%) (45). *The observation was greater than what is reported in previous studies from* Poland *(*23.6%) (33) and the average in Sub-Saharan Africa (23.9%) (2).

All the *S. aureus* isolates tested were resistant to penicillin G. However, gentamicin and ciprofloxacin had higher sensitivity compared to the other agents as similarly observed in Ethiopia (26). *Enterobacterales* on the other hand showed the highest resistance to ampicillin. A similar observation was reported earlier (2). The current study shows that the best agents for managing infections due to *Enterobacterales* currently include imipenem, gentamicin, and chloramphenicol. Isolates of *Acinetobacter* species and *Pseudomonas* species together (n=18) had a percentage resistance of 55.6%, 50%, 50%, 36.4%, 25%, and 22.2% against piperacillin, amikacin, ceftazidime, ciprofloxacin,

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gentamicin, and imipenem respectively. However, their number was less than the threshold necessary to generate reliable antibiograms. Therefore, recommendations about their empirical management cannot be appropriately made based on the available information. Previously, piperacillin+tazobactam has been recommended for use against Pseudomonas aeruginosa (6).

Patients in the surgical ward were 1.78 times more likely to develop an infection compared to those in the accidents and emergency ward. The outpatient department also had a lower prevalence of infection compared to the surgical ward. This could be due to the possession of open wounds from surgical repair that increase their liability to acquiring infections. Other studies have significantly associated infection with patients with a history of surgery and admission unit(12, 18).

Patients with prior antibiotic exposure before microbiology testing were not likely to have an SSTI due to MDR aetiologic agent compared to those who were unexposed. A similar outcome was observed earlier (34). The factors that had positive associations with MDR infections included type of ward, type of theatre, gender of the patient, and year of case. However, these were not statistically significant.

This study had some limitations, including being based at a single facility and missing data for some variables. Out-patients had no treatment files available and some inpatient files could not be located due to the manual hardcopy filing system. This limited the ability to obtain information such as surgical history, theatre involved, length of admission, and treatment records. These were recorded as unknown for some patients. Individual variables with insignificant data (Less than 30 observations) could not be concluded. The observed number of patients with culture and sensitivity results in their files could not be used to generate a representative proportion of de-escalation based on test results. Unknown data regarding some variables such as undergoing surgery, type of surgery, and the theatre could have affected their outcome as possible associated factors for SSTI and AMR. The private wing of the facility though on a small scale involves some specialized medical service units such as gynecology, and pediatrics, among others. However, no disaggregated data was readily available to individually analyze cases of their origin. Other conditions such as comorbidities, wound classes, surgical antimicrobial prophylaxis, and surgeons' experience were not assessed due to data shortage. There was no follow-up of patients to ascertain clinical outcomes post-treatment. This is encouraged for inclusion in future studies to provide a full picture and signify the relationship between practice, risk factors, and the final outcome for better management.

4. Materials and Methods

4.1. Study Design

This was a retrospective study based on the abstraction of socio-demographic and clinical charts of patients diagnosed with SSTI from January 2019 to December 2021. The data was accessed for analysis in June 2023. The study took place shortly after the establishment of microbiology services, majorly culture and sensitivity testing in 2018 and was made readily available for routine use in the region.

4.2. Study Setting

The study was carried out at Jinja RRH in the Eastern-central region of Uganda (Figure A1). The hospital is located in the center of Jinja city. Jinja is a focal point and refreshment area along the path from the Ugandan capital, Kampala towards the Kenyan border. This is a path that has encountered several traffic accidents in recent years, the majority of whose victims are managed at Jinja RRH(46-48). This facility serves the Eastern-central region of Uganda which involves a population of approximately 4.5 million people from within Jinja and the surrounding areas such as Iganga, Mayuge, Bugiri, Kamuli, Buikwe, Lugazi, Kayunga, and Mukono districts among others (49). The facility is equipped with a laboratory accredited by the South African National Accreditation System based on the requirements of ISO 15189 (50).

4.3. Laboratory Procedures

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Conventional microbiology methods for bacterial identification were employed and Antimicrobial Susceptibility Testing(AST) was carried out using the Kirby-Bauer disk-diffusion method following the Clinical and Laboratory Standards Institute (CLSI) guidelines (36-38). The laboratory observes quality control internally and by engagement in routine external quality assessments. Isolated organisms are periodically used for inter-laboratory comparison with the reference laboratory.

4.4. Study Population and Sampling

The investigated population included records of patients who were managed for SSTI with or without laboratory testing. Records for both inpatients and outpatients were considered. Laboratory records without updated results were not included. Only the first isolate of any patient was considered for analysis.

Out of 526 laboratory patient records, a total of 268 reports were selected by systematic random sampling for the study. The sample size was calculated using the formula ($n = p(1-p)z^2/d^2$) and had a power of 80% to estimate the prevalence and factors associated with SSTI at the 95% confidence level.

4.5. Data Collection

4.5.1. Extraction of Laboratory Generated Data

The data sample frame with the necessary variables for the study was extracted from the electronic African Laboratory Information System (ALIS) of Jinja RRH laboratory into an Excel sheet. This included demographic and clinical data of patients who underwent laboratory testing including age, sex, ward, hospitalization history before testing, isolated organism, and antimicrobial susceptibility testing (AST) results where applicable.

4.5.2. Review of Patients' Files

In addition to the existing laboratory-generated data, patients' files for the same study patients were sought and examined for more data necessary to investigate the associated factors. This was obtained using a predesigned data extraction tool transformed into the kobo-collect mobile application with kobo-toolbox open access software. The tool was piloted to confirm functionality and ability to obtain the required data before the actual study. This involved the entry of data for ten random patients admitted to the surgical ward into the electronic tool. This was saved on an online server and the aggregated data was downloadable in the form of a spreadsheet. Research assistants including a nurse, and records personnel were trained on the research tool in the same period and they became familiar with the data collection process. The collected data included admission periods, history of undergoing surgery, type of surgery, the theatre involved, and whether a patient was treated based on culture and sensitivity results from the laboratory.

4.5.3. Data Extraction from the District Health Information System

The overall number of patients diagnosed and treated for SSTI in the study period was obtained to aid the determination of the proportion of suspected SSTI that underwent microbiology testing for confirmation. This was done by examining standard Health Management Information System (HMIS 108 and HMIS 105:01) reports from the electronic DHIS2. The medical conditions considered for counting as part of SSTI included infections affecting the SSTI such as the middle ear, gangrenes, skin abscesses, and similar ones whether acute or chronic. These included the following as stated in the HMIS tools. Skin diseases (CD14), tetanus (CD15), otitis media (EN01), otitis externa (EN10), and burn injuries (OT04) from HMIS 105:01. Those in HMIS 108 included musculoskeletal and connective tissue diseases (LD04), cutaneous ulcers (LD09), osteomyelitis (CD11), tetanus (CD13), rheumatoid arthritis (RM01), septic arthritis (RM02), osteoarthritis (RM03), otitis media (EN01), injuries (IN01), diseases of the skin (LD03) and sepsis related to pregnancy (MC07). The total sum of diagnoses from

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the stated conditions was treated as the total number of patients with indication and treated for SSTI in the study period.

4.6. Data Analysis

The data collected was entered and cleaned in Microsoft Excel. Statistical analysis was performed using Stata 17. Categorical variables were summarized in the form of frequencies and percentages and presented by bar graphs and tables. Continuous variables were presented as means with standard deviation(SD). Prevalence of SSTI was calculated overall and relative to wards of admission. Microbiology service utilization to confirm and manage suspected SSTI was estimated using two proportions; 1) Percentage of suspected SSTI investigated by culture and sensitivity (C&S) was obtained as a proportion of C&S tests done to the total sum of SSTI diagnoses (∑C&S tests ÷ ∑SSTI Indications); 2) Percentage of patients managed based on microbiology (C&S) test results were calculated as the number of patients with de-escalation in treatment with antibiotics basing on C&S divided by the number of patients with positive C&S test (∑Patients with de-escalation ÷ ∑ Positive C&S tests). WHONET 2022 was used for antimicrobial susceptibility data analysis. Organisms with a minimum number of 30 isolates were considered individually to generate antimicrobial susceptibility profiles. Otherwise, organisms were grouped based on their microbiologic characteristics such as the order, Enterobacterales, and antibiograms generated for the group. Multi-drug resistance (MDR) was defined as an isolate resistant to at least three antibiotics of different clinical categories (51). Bivariate analysis was performed to test for associations between the presence of SSTI and MDR etiology independently with possible predictors. Factors with a P-value <0.2 were followed up with multivariate analysis by modified Poisson regression. Statistical significance was defined as a P-value of <0.05 at the 95% confidence level.

5. Conclusions

The prevalence of SSTI was high at Jinja RRH, with only a few cases of SSTI being tested for culture and sensitivity. The Gram-negative were the most responsible pathogens for the SSTI while the most isolated individual pathogen was *S. aureus*. Almost half of the infections were due to MDR pathogens including MRSA, possible ESBL-producers, and organisms that are non-susceptible to carbapenems. Recognizing SSTI under the GLASS would lead to enhanced surveillance, better preparedness, and response to AMR.

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Data Availability Statement: Dataset available on request from the authors.

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Appendix A

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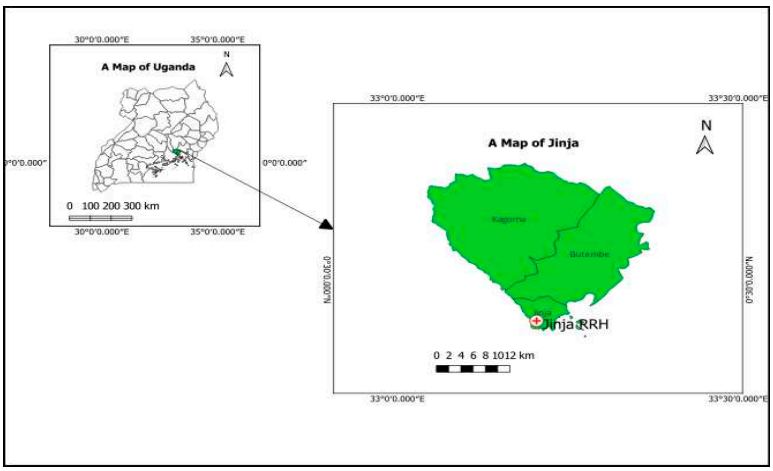
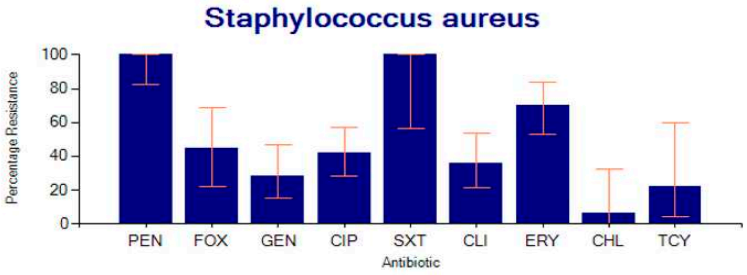


Figure A1. A map showing the location of the study site.



PEN-Penicillin G; FOX-Cefoxitin; GEN-Gentamicin; CIP-Ciprofloxacin; SXT-Co-trimoxazole; CLI-Clindamycin; ERY-Erythromycin; CHL-Chloramphenicol; TCY-Tetracycline

Figure A2. Percentage resistance for *S. aureus.*

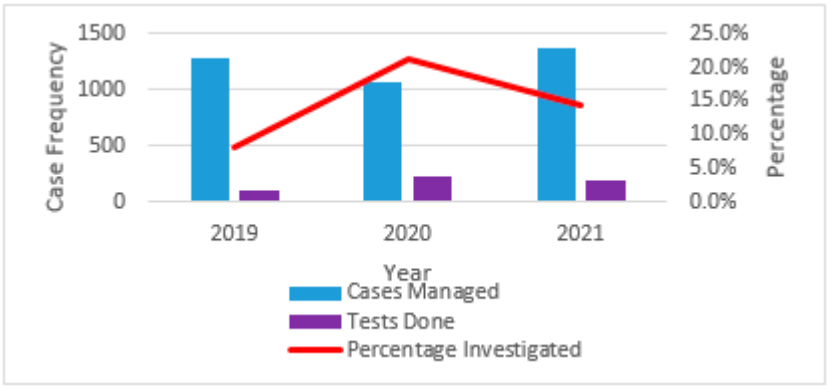


Figure A3. Proportion of cases that underwent laboratory investigation.

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