

# Low-Level Antibiotic Resistance among *Staphylococcus aureus* and Gram-Negative Pathogens from Infected Skin and Soft Tissues in Rural Kenya

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## Abstract

**Introduction:** Bacterial skin and soft tissue infections (SSTIs) are a cause of frequent inpatient and outpatient care visits whose causative agents are associated with a high antimicrobial resistance burden. For insights on antimicrobial susceptibilities in a rural setting, we examined specimens from suspected SSTIs from two public health facilities in Kenya. We additionally assessed antibiotic use, appropriateness of empiric therapy and risk factors for SSTI. **Methodology:** Between 2021 and 2023, 265 patients at Kisii and Nyamira County Referral hospitals were enrolled. Wound swabs/aspirates were collected and processed following standard microbiological procedures. Identification and antimicrobial susceptibility were performed using the VITEK 2 Compact platform. Demographic, clinical, and microbiological data were analyzed with R Statistical software. **Results:** *S. aureus* was isolated in 16.2% (43/265) of patients with a methicillin resistance (MRSA) proportion of 14% (6/43). While 13/15 drugs elicited susceptibilities ranging from 84% - 100%, penicillin (16%) and trimethoprim-sulfamethoxazole [TMP-SXT] (23%) yielded the lowest susceptibilities. *Escherichia coli* (n = 33), *Klebsiella pneumoniae* (n = 8), *Pseudomonas aeruginosa* (n = 8), and *Citrobacter species* (n = 4) were the most commonly isolated gram-negative species. Gram-negative strains showed high susceptibilities to most of the tested drugs (71% - 100%) with the exception of ampicillin (18%), TMP-SXT (33%), and first and second generation cephalosporins. **Conclusions:** The low MRSA prevalence and generally

high antibiotic susceptibilities for *S. aureus* and gram-negative bacteria present opportunities for antibiotic stewardship in the study setting. Diminished susceptibilities against penicillin/ampicillin and TMP-SXT accord with prevailing local data and add a layer of evidence for their cautious empiric use.

## Keywords

*S. aureus*, MRSA, Gram-Negative Bacteria, Antimicrobial Resistance, SSTIs, Kenya

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## 1. Background

Skin and soft tissue infections (SSTIs) are a common occurrence among inpatient and outpatient populations. It has previously been estimated that SSTIs have an incidence of 47.9 cases/1000 person years in the USA, more than twice that of urinary tract infections and over 10 times that of pneumonia [1]. Bacterial SSTIs have become increasingly frequent over the last two decades [2] and consequently, they represent a common indication for antimicrobial prescription globally. The bacterial etiology of SSTIs is diverse and infections may present in varying degrees of severity [3] ranging from impetigo (epidermis), erysipelas (dermis), cellulitis (subcutaneous fat layer) and necrotizing fasciitis & myositis (muscle fascia) [4]. Common bacterial species implicated in SSTIs include *Staphylococcus aureus*, *Beta-hemolytic streptococci*, *Enterococci*, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Aeromonas hydrophila*, *Vibrio* species alongside a range anaerobic bacteria [3].

Besides, their clinical burden, common SSTI bacterial pathogens have been implicated in high antimicrobial resistance (AMR) leading to costly consequences such as prolonged therapy, high treatment costs and relatively poor clinical outcomes [5]. A recent examination of 471 million health records globally estimated AMR to account for at least 4.95 million and 1.27 million deaths by association and direct attribution respectively [5]. The report identified *S. aureus* (methicillin resistance), *Acinetobacter baumannii* & *Pseudomonas aeruginosa* (extended spectrum beta lactam and carbapenem resistance), *Enterobacteriaceae* (extended spectrum beta lactam and carbapenem resistance), *Streptococcus pneumoniae*, and *Enterococci* (vancomycin resistance) as highly problematic [5]. On account of their clinical significance and AMR burden, the WHO has identified these bacteria as priority pathogens for the surveillance and development of new therapies [6].

Regionally, Sub-Saharan Africa bears the brunt of AMR even though a lack of robust AMR data is a recognized bottleneck. Currently, there is sporadic collection and reporting of antimicrobial use and resistance data from developing countries which constitute up to 60% of the global population [6]. Such a skew in AMR data may lead to misleading estimates of the global AMR burden. To improve such estimates and inform mitigative interventions, increased and sys-

tematic surveillance for AMR especially among WHO priority pathogens is warranted.

In Kenya, drug-resistant bacterial infections have been commonly encountered among SSTIs. In one study, surgical site infections (SSIs) occurred in 7% of patients at a private tertiary health facility with *S. aureus* constituting 30% of all bacterial isolates [7]. According to Omuse and colleagues, over 79% of *S. aureus* strains examined originated from SSTIs [8]. Langat and colleagues identified *S. aureus* as constituting 47.6% of all bacterial isolates from SSTIs with 45% of such strains possessing the MRSA phenotype in one of Kenya's largest national referral hospitals. The same study identified pan-drug resistance in *Acinetobacter baumannii* [9].

Whereas previous Kenyan studies have served to shed light on the epidemiology of SSTIs and associated antimicrobial susceptibility patterns, two gaps remain unaddressed: First, data on antimicrobial use to contextualize susceptibility patterns and empiric prescription practices have rarely been reported and second, studies have largely represented either large tertiary facilities or urban settings thus ignoring lower-tier health facilities and rural settings where at least 71.5% of the population resides.

In this study, we report the findings from microbiological examinations of specimens from suspected SSTIs from rural health facilities in Kenya. Additionally, we examine empiric antibiotic use and explore potential risk factors for SSTI infection in the study population.

## 2. Methods

### 2.1. Study Design and Setting

A prospective, cross-sectional study was conducted in two rural public hospitals in Kenya: Kisii Teaching & Referral Hospital (KTRH) and Nyamira County Referral Hospital (NCRH). KTRH is located in Kisii County in southwestern Kenya with a population of 1,266,860. KTRH is the county's largest and only referral facility with a bed capacity of 650 and a range of specialized services such as radiology, oncology, and dialysis among others. Nyamira County is located in southwestern Kenya and has a population of 605,576. NCRH, the county's largest health facility, is a medium-level health facility offering both inpatient and outpatient services with a bed capacity of approximately 150. Both KTRH and NCRH have diagnostic laboratories with microbiology, clinical chemistry, hematology, and histology sections/benches. There are no dedicated clinical microbiologists in both facilities. The counties were selected based on limited previous AMR data and the fact that they currently do not form part of Kenya's national AMR surveillance network despite serving a population of nearly two million people.

### 2.2. Ethical Approvals

This study was approved by the Aga Khan University, Nairobi's Institutional

Scientific and Ethics Review Committee (ISERC) [Ref: 2020/IERC-131 (v4)]. Further, the study was granted a research permit by the National Commission for Science, Technology and Innovation (NACOSTI) [Ref: NACOSTI/P/22/20660]. Permission to conduct research was granted by the administration of individual health facilities. Permission to publish was granted by Aga Khan University, Nairobi's Research Office.

### 2.3. Patient Recruitment and Specimen Collection

A total of 265 participants were recruited between November 2021 and March 2023. Patients showing symptoms of an active SSTI such as erythema, edema, pain and tenderness were recruited into the study by signing an informed consent form. Specimens (wound swabs or pus aspirates) were aseptically collected by study personnel from SSTI sites and preserved in Amies transport media (Deltalab, Barcelona, Spain). Specimens were promptly transported to Aga Khan University Hospital, Nairobi for microbiological processing. A questionnaire collecting clinical and demographic information such as age, sex, residence, admission status, underlying conditions and antibiotic therapy was administered to the study participants after consenting. Where such information was not provided by the patient, patient chart reviews were conducted.

### 2.4. Microbiological Procedures

Samples were streaked on blood agar base (Oxoid, Cheshire, England) with 5% sheep blood and McConkey Agar (Oxoid, Cheshire, England) and incubated at 37°C for 24 hours. A further 24 hours of incubation was allowed for plates showing no growth after the first day of incubation. *S. aureus* was identified by gram stain, beta hemolysis, catalase enzyme and presence of clumping factor, protein A and staphylococcal capsule (Pastorex™ Staph Plus Latex Agglutination, Biorad, USA). Identity of *S. aureus* was confirmed with VITEK® 2 Compact GP ID card (Biomérieux, Marcy-l'Étoile, France). Gram-negative bacteria were identified by presence/absence of lactose fermentation on McConkey agar, gram stain, oxidase test and VITEK® 2 Compact GN ID card (Biomérieux, Marcy-l'Étoile, France). Antimicrobial susceptibility testing (AST) was based on the VITEK 2 Compact GP (P580) and GN AST (GN83) cards following the guidelines of the manufacturer. Guidelines of the 31<sup>st</sup> Edition of the Clinical Laboratory Standards Institute (CLSI) were used for interpretation of AST results [10]. All bacterial strains were preserved in brain heart infusion broth with 15% glycerol at -80°C.

### 2.5. Data Analysis

Data analysis was performed using R Package Version 4.3.0. Categorical demographic, clinical, and microbiological data were summarized as proportions, whereas numerical data were expressed using appropriate measures of central tendency. AST data in “susceptible”, “intermediate” or “resistant” categories was expressed as proportions representing percentage susceptibility. To test for possible associations between individual demographic/clinical variables and the

risk of infection with either *S. aureus* or *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, *Citrobacter* species, *S. marcescens* and *M. morgani* (n = 99), t-test (numerical variables) and chi-squared (categorical variables) tests of association were performed. A p-value threshold for significance of 0.05 was used. Selected variables were fitted into a multivariable logistic regression model based on a Bayesian model.

### 3. Results

#### 3.1. Clinical and Demographic Summary of the Study Population

The participant population of 265 patients from two facilities (KTRH, n = 221 and NCRH, n = 44) had mean and median ages of 39 and 37 years respectively, with a standard deviation of 20 and an inter-quartile range (IQR) of 26 - 55 years. There were 130 males (49%) and 135 females (51%) representing a male:female ratio of 0.96. Inpatients dominated the studied population (75.8%, 201/265) compared to outpatients (24.2%, 64/265). Patients were drawn from 8 hospital locations with the surgical ward constituting 65.7% (174/265). About 85% (224/265) of the patients reported a lack of underlying conditions whereas the remaining 15% (41/265) had comorbidities ranging from diabetes (n = 21), hypertension (n = 6), malignancy (n = 3) to diabetes & hypertension (n = 2). Conditions for 9 patients were not specified. Transfer from other facilities (n = 9), hospital admission in the previous 6 months (n = 8), and residence in long-term care facility (n = 1) occurred infrequently in the studied population. **Table 1** summarizes the demographic and clinical characteristics of the patient population.

At the time of consenting, 66% (175/265) of the patients were not on any antibiotic therapy whereas the remaining 34% (90/265) were. Ten different antibiotics amounting to 99 prescriptions were administered for patients in this study whereby flucloxacillin, ceftriaxone and cefuroxime constituted 80% (79/99). Eighty patients were on a single antibiotic therapy while 8 [flucloxacillin/metronidazole, n = 5; ceftriaxone/metronidazole, n = 3] were on dual therapy. One patient was on a flucloxacillin/ceftriaxone/metronidazole regimen. For one patient, the type of antibiotic treatment was not specified. A majority of patients on antibiotic therapy (87%, 78/90) were inpatients. The mean duration for antibiotic therapy (as at the time of consenting) was 5.0 days with a median of 3.5 days, standard deviation of 4.2 days and IQR of 3 - 5 days. **Figure 1** summarizes drug use in the studied population.

#### 3.2. Species Diversity from Skin and Soft Tissue Infections

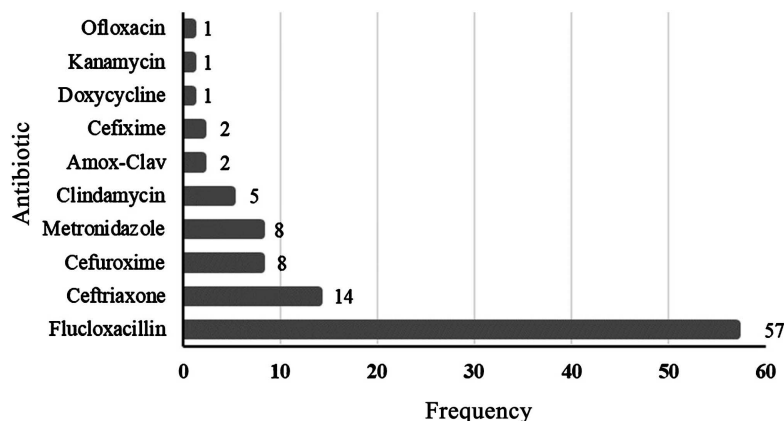
Of the 265 specimens processed, 112 showed no growth while 31 had polymicrobial growth and were considered contaminants where a cardinal microorganism such as *S. aureus* was absent and where the patient had no underlying conditions. A total of 102 specimens showed monomicrobial growth while 20 specimens yielded two microbial species. Overall, *S. aureus* was the most common

species isolated at a rate of 16.2% (43/265) representing 36.4% (43/118) of all bacterial pathogens isolated (**Figure 2**). Other gram-positive bacteria identified were 11 and 4 beta- and alpha-hemolytic streptococci respectively. Among gram-negative bacteria, *E. coli* (n = 33) was the most common species followed by *K. pneumoniae* (n = 8), *P. aeruginosa* (n = 8), *Citrobacter* species (n = 4) and *S. marcescens* (n = 3).

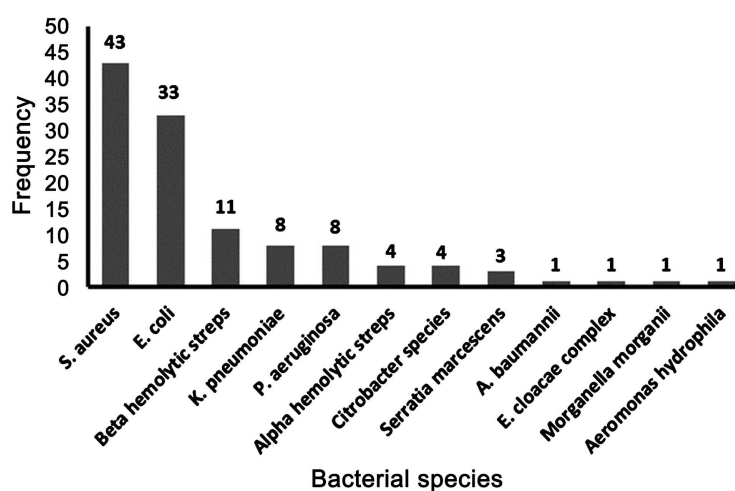
**Table 1.** Demographic and clinical summary of the study population.

Variable	Indicator	Value
Age	Mean [SD]	39 [20] yrs
	Median [IQR]	37 [26 - 55] yrs
	Range	1 month - 90 yrs
Sex	Male	49% (130/265)
	Female	51% (135/265)
	Male: Female ratio	0.96
Admission status	Inpatient	75.8% (201/265)
	Outpatient	24.2% (64/265)
Patient location	Surgical ward	65.7% (174/265)
	Outpatient	24.2% (64/265)
	General ward	5.3% (14/265)
	Pediatric	2.6% (7/265)
	Orthopedic	0.8% (2/265)
	Obs. Gyn.	0.8% (2/265)
	Maternity	0.4% (1/265)
	Newborn Unit	0.4% (1/265)
Underlying conditions	None	84.5% (224/265)
	Diabetes	7.9% (21/265)
	Hypertension	2.3% (6/265)
	Malignancy	1.1% (3/265)
	Diabetes/Hypertension	0.8% (2/265)
	Other conditions	3.4% (9/265)
Antibiotic use	No	66% (175/265)
	Yes	34% (90/265)
Period of antibiotic use	Mean [SD]	5.0 [4.2] days
	Median [IQR]	3.5 [3 - 5] days
	Range	1 - 21 days

SD: Standard deviation, IQR: Interquartile range.



**Figure 1.** A summary of the different drugs prescribed in the study. Amox-clav: Amoxicillin-Clavulanic acid.



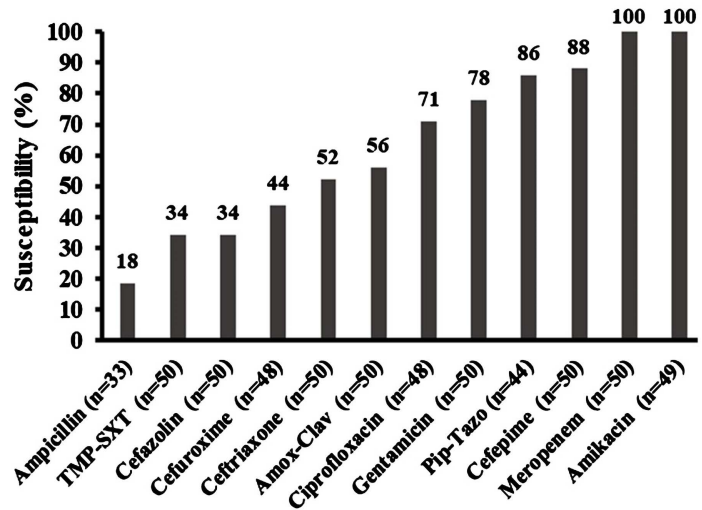
**Figure 2.** A summary of bacterial species distribution from infected skin and soft tissues.

### 3.3. Antimicrobial Susceptibility Patterns of *Staphylococcus aureus*

The MRSA proportion in this collection was 14% (6/43). Regarding other antibiotics, the isolates showed the lowest susceptibilities to penicillin (16%) and TMP-SXT (23%). The collection of 43 isolates showed susceptibilities of between 84% and 100% for the remaining 11 antibiotics as shown in **Table 2**.

### 3.4. Antimicrobial Susceptibility Patterns of Dominant Gram-Negative Bacteria

Antimicrobial susceptibility testing was performed for 50 members of *Enterobacteriaceae* [*E. coli* (n = 33), *K. pneumoniae* (n = 8), *S. marcescens* (n = 3), *Citrobacter species* (n = 4), *E. cloacae* (n = 1), and *M. morganii* (n = 1)]. Generally, the isolates showed lower susceptibilities to ampicillin, TMP-SXT and early generation cephalosporins. In contrast, there were higher susceptibilities to ciprofloxacin, gentamicin, cefepime, meropenem and amikacin (71% - 100%). **Figure 3** summarizes the observed patterns.



**Figure 3.** Antibiotic susceptibility patterns of dominant *Enterobacteriaceae* isolates from infected skin and soft tissues. TMP-SXT: Trimethoprim-sulfamethoxazole; Pip-Tazo: Piperacillin-Tazobactam.

**Table 2.** Antimicrobial susceptibility patterns of the 43 *S. aureus* isolates.

Antibiotic	Susceptible isolates	Susceptibility (%)
Penicillin	7	16.2
TMP-SXT*	10	23.2
Tetracycline	36	83.7
Erythromycin	36	83.7
Cefoxitin	37	86
Oxacillin	37	86
Clindamycin	40	93
Levofloxacin	40	93
Gentamicin	41	95.3
Rifampicin	43	100
Fusidic acid	43	100
Linezolid	43	100
Tigecycline	43	100
Vancomycin	43	100
Teicoplanin	43	100

\*TMP-SXT: Trimethoprim-sulfamethoxazole.

AST was performed for *P. aeruginosa* (n = 8) and *A. baumannii* (n = 1). Generally, the isolates of *P. aeruginosa* were susceptible to the drugs tested whereas in contrast, the single strain of *A. baumannii* was resistant to all the drugs tested as shown in **Table 3**.



**Table 3.** Antimicrobial susceptibility profiles of *P. aeruginosa* and *A. baumannii*.

Participant ID	Species	TMP-SXT	Ampicillin-Sulbactam	Pip-Tazo	Ceftriaxone	Ceftazidime	Cefepime	Meropenem	Gentamicin	Amikacin	Ciprofloxacin
KTRH/052	<i>P. aeruginosa</i>	-	-	S	-	S	S	S	S	S	S
KTRH/055	<i>P. aeruginosa</i>	-	-	S	-	S	S	S	S	S	S
KTRH/117	<i>P. aeruginosa</i>	-	-	S	-	S	S	S	S	S	S
KTRH/185	<i>P. aeruginosa</i>	-	-	S	-	S	S	S	S	S	S
KTRH/204	<i>P. aeruginosa</i>	-	-	S	-	S	S	S	S	S	S
NCRH/010	<i>P. aeruginosa</i>	-	-	S	-	S	S	S	S	S	S
NCRH/026	<i>P. aeruginosa</i>	-	-	SDD	-	S	S	S	S	S	S
NCR H/033	<i>P. aeruginosa</i>	-	-	R	-	S	S	S	S	S	S
KTRH/189	<i>A. baumannii</i>	R	R	R	R	R	R	R	R	-	R

SDD: Susceptible dose dependent, TMP-SXT: Trimethoprim-sulfamethoxazole, Pip-Tazo: Piperacillin-Tazobactam, KTRH: Kisii Teaching & Referral Hospital, NCRH: Nyamira County Referral Hospital.

### 3.5. Assessment of Empiric Therapy Appropriateness

A sub-assessment of the 90 patients on antibiotic therapy was performed to gain insights on the appropriateness of empiric therapies. Specimens from 53 patients showed either no growth or polymicrobial growth without any target organism. Cultures from 11 patients grew organisms for which AST was not performed (e.g., beta hemolytic streptococci) leaving 26 patients for whom antibiotic prescription, organism identity and AST information were available for comparison. Of these 26, 7 patients were on treatments for which the resultant organism was susceptible, 3 were on treatments for which the organism showed resistance and the remaining 16 were on treatments for which AST is not routinely reported for the resultant organism, for example clindamycin for *K. pneumoniae*. For the 6 MRSA reported in this study, one patient was on ceftriaxone treatment whereas the remaining 5 had not been on antibiotic treatment at the time of enrollment. **Table 4** summarizes these comparisons.

Chi-squared and t-tests of association between individual variables and infection with *S. aureus* or selected gram-negative bacteria did not attain statistical significance. A multivariable logistic regression analysis involving seven independent variables that have been previously identified as risk factors for SSTI infection did not yield any statistically significant findings as summarized in **Table 5**.

**Table 4.** Comparisons between empiric prescription, organism identity and drug susceptibility for 26 patients with complete records.

Culture result	Empiric antibiotic	Susceptibility
<i>S. aureus</i>	Flucloxacillin IV	Susceptible
<i>S. aureus</i>	Flucloxacillin IV	Susceptible
<i>S. aureus</i>	Flucloxacillin IV	Susceptible
<i>S. aureus</i>	Flucloxacillin IV	Susceptible
<i>S. aureus</i>	Flucloxacillin IV	Susceptible
<i>S. aureus</i>	Flucloxacillin IV	Susceptible
<i>K. pneumoniae</i>	Cefuroxime	Susceptible
<i>M. morgani</i>	Kanamycin	Resistant
<i>E. coli</i>	Cefuroxime Tabs	Resistant
<i>E. coli</i>	Ceftriaxone IV	Resistant
<i>K. pneumoniae</i>	Clindamycin	*
<i>Citrobacter freundii</i>	Flucloxacillin	*
<i>K. pneumoniae</i>	Flucloxacillin/Flagyl	*
<i>E. coli</i>	Flucloxacillin IV	*
<i>Serratia marcescens</i>	Clindamycin	*
<i>E. coli</i>	Clindamycin	*
<i>E. coli</i>	Flucloxacillin IV/Flagyl	*
<i>E. coli</i>	Flucloxacillin IV	*
<i>E. coli</i>	Flucloxacillin IV	*
<i>P. aeruginosa</i>	Flucloxacillin IV	*
<i>S. aureus</i>	Ceftriaxone IV	*
<i>Citrobacter freundii</i>	Flucloxacillin IV	*
<i>A. baumannii complex</i>	Flucloxacillin IV	*
<i>E. coli</i>	Flucloxacillin IV	*
<i>S. aureus</i>	Ceftriaxone IV	*
<i>P. aeruginosa</i>	Flucloxacillin IV	*

\*AST for the drug the patient was treated with is not routinely reported for that organism.

**Table 5.** Logistic regression model for risk of infection with dominant bacteria and seven clinical/demographic variables.

Variable	Indicator	Uninfected (n = 166)	Infected* (n = 99)	P value	Adj. Odds Ratio (95% CI)
Age	Mean [SD]	39.7 (20.2)	38.1 (19.9)	0.521	0.994 (0.556 - 1.006)

## Continued

Sex	Female	82 (49.4%)	53 (53.5%)	0.6	Ref
	Male	84 (50.6%)	46 (46.5%)		0.867 (0.552 - 1.331)
Transfer from other facilities	No	160 (96.4%)	96 (97.0%)	1.0	Ref
	Yes	6 (3.6%)	3 (3.0%)		0.976 (0.245 - 3.232)
Admission in the last months	No	161 (97.0%)	96 (97.0%)	1.0	Ref
	Yes	5 (3.0%)	3 (3.0%)		2.810 (0.256 - 52.417)
Underlying conditions	No	140 (84.3%)	84 (84.8%)	1.0	Ref
	Yes	26 (15.7%)	15 (15.2%)		1.647 (0.782 - 3.463)
Admission status	Inpatient	124 (74.7%)	77 (77.8%)	0.676	Ref
	Outpatient	42 (25.3%)	22 (22.2%)		0.747 (0.447 - 1.229)
Antibiotic use	No	102 (61.4%)	72 (72.7%)	0.0823	Ref
	Yes	64 (38.6%)	27 (27.3%)		0.459 (0.262 - 0.781)

CI: 95% Confidence Interval Ref: Reference indicator, SD: Standard deviation, \*The number of patients infected with either *S. aureus* or *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, *Citrobacter species*, *S. marcescens* and *M. morgani*.

## 4. Discussion

### 4.1. Antimicrobial Susceptibility Patterns

In this study, *S. aureus* was identified at a rate of 16.2% among the 265 specimens examined. In previous Kenyan studies, isolation rates have varied from as low as 2% in blood [11]; 18.3% among healthcare workers (HCWs) [12] to 32.6% in the pediatric ICU [13]. Generally, *S. aureus* is more common among SSTIs with even higher isolation rates of 65.4% among surgical and outpatient populations in Egypt [14] and 45.3% in Indonesia [15] being reported.

We observed an MRSA rate of 14% among *S. aureus* isolates in this study setting. In different settings and at different times, other Kenyan studies have reported variable MRSA rates including zero among HCWs [12], 3.7% in two private facilities in Nairobi [8], 7% among inpatient carriage specimens [16] and 27.8% at Kenyatta National Referral Hospital [17]. The latest Kenya national AMR surveillance report covering 22 surveillance sites estimated an MRSA rate of 32% among *S. aureus* isolates. This figure is more than twice that observed in our study (14%). Continued systematic surveillance will help refine the national MRSA prevalence figure that will serve as a reference.

Consistent with previous findings, penicillin (84%) and TMP-SXT (77%) eli-

cited the highest resistance in the collection of strains tested [8]. Schaumburg and colleagues reported a dichotomy in resistance levels to penicillin, TMP-SXT and tetracycline between urban (>89%) and rural settings (<35%) in different parts of Africa [18]. However, our data from a rural setting contradicts this assertion. Outside of Africa, TMP-SXT has elicited high susceptibilities ranging from 98% in Taiwan region [19] to 100% in Korea [20]. The widespread TMP-SXT resistance in Africa has been attributed to its use prophylactically among HIV/AIDS patients for malaria and pneumocystis infections [21].

Besides penicillin and TMP-SXT, the collection of study isolates showed low resistance levels to all other tested drugs (<16%). Varying resistance against tetracycline (21% - 35%), erythromycin (11% - 51.6%), clindamycin (2% - 28%), gentamicin (1% - 38%) and ciprofloxacin (7% - 36%) have been observed in Kenya before [13], perhaps a result of study setting, design and methodological variations. Mirroring our findings, other studies showed high susceptibilities against last line agents such as vancomycin, teicoplanin, daptomycin, linezolid and tigecycline [13]. These observations serve to highlight the utility of these agents and strengthen the evidence for their reservation as last resort agents.

Whereas Gram-positive bacteria like *S. aureus* and  $\beta$ -hemolytic Streptococci are the common causes of SSTIs, Gram-negative bacteria are also implicated especially in complicated SSTIs occurring in people with comorbidities [22]. We identified *E. coli* as the most common gram-negative species among SSTIs. A study of patients in surgical and outpatient settings in Egypt identified *P. aeruginosa* as the most common species followed by *K. pneumoniae* and *E. coli* [14]. A South African study identified *P. aeruginosa*, *Acinetobacter* and *K. pneumoniae* in order of decreasing frequency [4]. Fourth generation cephalosporins and carbapenems showed excellent activity against members of *Enterobacteriaceae* and the extended spectrum beta lactamase (ESBL) phenotype was low in the examined collection. Furthermore, *P. aeruginosa* showed remarkable susceptibility against first and second line anti-pseudomonal treatments, an observation noted in the latest national AMR surveillance report. The single *A. baumannii* strain however showed resistance to almost all the drugs tested and serves to highlight the existential threat of AMR and the need for vigilance.

#### 4.2. Empiric Antimicrobial Therapy for Suspected SSTIs

All patients on antimicrobial therapy in this study were being treated empirically with beta lactams accounting for about 80% of all prescriptions. Langat and colleagues identified flucloxacillin and metronidazole as the most frequently prescribed drugs for SSTIs at a major referral facility in Kenya [9]. In Europe, up to 98% of SSTI patients were treated empirically, mainly with beta lactams [23]. It is encouraging that both gram-positive and gram-negative isolates identified in this study were generally susceptible to first line drugs and that second line drugs such as cefepime, carbapenems, amikacin and vancomycin were not prescribed. Penicillin/ampicillin and TMP-SXT were equally not prescribed in this

study, perhaps a practice in keeping with their limited efficacy in *in vitro* testing.

Inasmuch as SSTIs are not routinely diagnosed by culture and hence are treated empirically, regular monitoring of the changing susceptibilities to different drugs is warranted as a way of maintaining and refining antibiotic stewardship. Further, definitive culture and AST may be required in circumstances such as when an atypical etiology is suspected [24] or when empiric therapy fails as was observed in some instances (Table 4). Indeed, bacterial identification and AST have proved useful in the tailoring of empiric treatment for full recovery [23].

In this study, none of the evaluated variables showed any association with the risk of infection with either *S. aureus* or selected gram-negative pathogens. An assessment of risk factors for SSTIs among American patients with SSTI diagnosis identified age, income, diabetes and race as significant factors whereby being younger than 5 years, having a lower income, a diabetes diagnosis and belonging to ethnicities other than Asian elevated one's risk of SSTIs [25]. Elsewhere, liver and kidney disease, advanced age, critical illnesses and vascular insufficiency have been significantly associated with higher risks of SSTIs [24]. The lack of association in our study could be explained by the fact that the study was not sufficiently powered to explore all the risk factors and/or inherent differences in the design and settings of other comparable studies.

## 5. Conclusion

Despite the limitations of sample size, restricted spatial coverage and a focus on SSTIs only, our findings have served to demonstrate low MRSA prevalence and generally high susceptibilities to a majority of tested drugs both for *S. aureus* and dominant gram-negative pathogens in a rural Kenyan setting. High susceptibilities to last-line agents coupled with their limited empiric prescription bodes well for antimicrobial stewardship. Diminished susceptibilities against penicillin/ampicillin and TMP-SXT accord with prevailing local data and add a layer of evidence for their cautious empiric use.

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## Conflicts of Interest

The authors declare that they have no competing interests.

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## Availability of Data and Materials

The datasets used during the current study are available from the corresponding author on reasonable request.

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