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ORIGINAL RESEARCH

Antimicrobial Resistance Surveillance of Skin and Soft Tissue Infections: Hospital-Wide Bacterial Species and Antibiograms to Inform Management at a Zonal Tertiary Hospital in Mwanza, Tanzania

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Purpose: The National Action Plan on antimicrobial resistance (NAP-AMR) in Tanzania is focused on blood stream infections and urinary tract infections despite skin and soft tissue infections (SSTIs) being common. This study assessed the proportion of laboratory-confirmed SSTIs, identify bacterial species involved, analyze AMR phenotypes, and investigate the risk factors associated with multidrug-resistant (MDR) SSTIs.

Patients and Methods: Analytical cross-sectional study was conducted between January and June 2023, involving 614 patients with SSTIs. Patients' information was collected using standard AMR surveillance tools, and either pus swabs or pus aspirate or necrotic tissues were collected and analyzed using standard microbiological procedures, WHONET and STATA software programs.

Results: The median age (interquartile range) of patients was 34 (14–54) years with males accounting for 54.4%. Laboratory-confirmed SSTIs was 72.5% (445/614), yielding 586 bacterial isolates. The most frequent SSTIs types were surgical site infections (30.0%), chronic wounds (27.9%), and traumatic wounds (19.7%). The commonest pathogens were *Staphylococcus aureus* (17.1%), *Escherichia coli* (17.1%), and *K. pneumoniae* (16.0%). The AMR phenotypes identified were methicillin resistant *Staphylococcus aureus*, 29.0%; Extended-spectrum beta lactamase producing Gram-negative bacteria, 47.3%; and carbapenem resistant Gram-negative bacteria, 12.9%. The overall MDR SSTIs was 40.9% (251/614) and was significantly higher among inpatients compared to outpatients [OR (95% CI); p-value: 1.86 (1.33–2.59); p-value<0.001].

Conclusion: Approximately three-quarter of patients have laboratory-confirmed SSTIs caused predominantly by MDR pathogens. Revisiting SSTIs treatment guidelines at BMC and inclusion of SSTIs in the on-going AMR surveillance in Tanzania are recommended.

Plain Language Summary:

- Tanzania National Action Plan on combating resistant bugs is exclusively focused on urinary tract infections and blood stream infections despite enormous impact conferred by skin and soft tissue infections.
- Bugs which are resistant to commonly used antibiotics were found more among patients admitted in the hospital in contrast to those attending outpatient clinics.
- This study highlights a pressing need to develop treatment guidelines based on generated local research-evidence to foster favorable patients' outcomes.

Keywords: skin and soft tissue infections, antimicrobial resistance, surveillance, Tanzania

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Introduction

Skin and soft tissue infections (SSTIs) arise as a result of inflammatory reactions triggered by microbial pathogens, leading to structural damage of skin and/or underlying soft tissues.[1–3] Anatomically, these infections are classified into superficial, deep-seated, and organ SSTIs.[4] They are also categorized as primary SSTIs when microbes invade intact healthy skin, or secondary SSTIs when microbial pathogens infect previously compromised skin due to underlying medical conditions or traumatic injuries; and a recent classification was proposed on necrotizing and non-necrotizing SSTIs based on the pathological features at the implicated site(s).[1,5] The growing burden of antimicrobial resistance (AMR) in SSTIs causing pathogens is challenging the antimicrobial therapeutic options available in low-and-middle-income countries (LMICs), including Tanzania, leading to longer hospital stays, extra costs, morbidity, and mortality.[6–8] Previous studies have shown varying occurrence of AMR pathogens causing SSTIs, ranging from 0.4% to 21.6% in the USA and 20% to 70.4% in developing countries. The differences were largely attributed to varying infectious prevention and control practices (IPC), existing diagnostic infrastructures, and available antimicrobial therapeutic options and expertise.[6,8–10]

Studies conducted in Mwanza, Tanzania, between 2011 and 2014 showed varying proportions of SSTIs from 10.9%, 26%, to 67% in women post-caesarian sections, patients undergoing abdominal surgeries, and patients with chronic lower limb ulcers, respectively.[11–13] The most common AMR phenotypes documented among pathogens causing SSTIs are Methicillin-resistant *Staphylococcus aureus* (MRSA) (18.8%–44%), Extended spectrum beta lactamase (ESBL) producing Gram-negative bacteria (35%–70.8%) and low percentage of carbapenem-resistant Gram-negative bacteria (CarbR), 0.0%–4.0%, with the exception of *Acinetobacter* spp. in Dar es Salaam, Tanzania, which showed remarkably high resistance to Carbapenem of 40%.[8,12,13]. Of note, patients with multi-drug resistant SSTIs post-caesarian sections were associated with prolonged hospital stay and deaths are most often associated with adverse Patients with traumatic open wounds post-road traffic accidents or post-surgeries, animal or insect bites, and those with underlying conditions like HIV/AIDS and diabetes mellitus are at increased high risk of SSTIs and adverse management outcomes.[14–17]

The majority of studies on SSTIs in Tanzania and many other LMICs are research-based with limited number of patients (and bacterial isolates) to provide credible extrapolation of findings to inform evidence-based clinical practices and changes in the management guidelines, underscoring a need for strengthening country- and regional-specific surveillance programs.[6,18,19] In Tanzania, the implementation of the first National Action Plan of AMR (NAP-AMR, 2017 to 2022) and the second plan (2023 to 2028) are exclusively focused on blood stream infections and urinary tract infections despite significant impact of SSTIs.[8,12,13,20,21] This study hypothesized that the NAP-AMR implementation in Tanzania would decipher increase in the proportions of the three key AMR phenotypes (MRSA, ESBL and CarbR) compared with research-based historical controls in the same hospital. The pre-existing technical challenges related to processing of samples from non-sterile sites (ie pus from SSTIs) which limited universal roll-out of SSTIs in the ongoing Tanzania AMR surveillance was also addressed at BMC tertiary hospital with potential to be replicated in other AMR sentinel sites country-wide. Therefore, to fill these critical research gaps, this study has generated AMR surveillance data on the patterns of bacteria species causing SSTIs, antibiograms, and associated factors for multidrug resistant (MDR) SSTIs. Additionally, this study provided evidence-based data to support SSTIs inclusion in the Tanzania NAP-AMR surveillance to ensure holistic patients management.

Patients, Materials and Methods

Study Design, Settings and Duration

This study was conducted from 1st January to 31st June 2023 at Bugando Medical Centre (BMC), a tertiary hospital in the north-western part of Tanzania with approximately 1000 bed-capacity (https://bmc.go.tz/public/). This is a teaching hospital for the Catholic University of Health and Allied Sciences (CUHAS), https://www.bugando.ac.tz/index.php. Surgical departments attend an average of 1160 patients per month in the clinics, approximately 300 surgical patients are admitted and 260 undergo surgeries monthly. It was conducted in two phases. Firstly, a retrospective extraction of SSTIs patients' demographic, clinical and laboratory data from existing hospital and laboratory systems (eHMIS/DISA) from January to April 2023. Secondly, a cross-sectional analytical study was conducted from May and June 2023 involving

patients with SSTIs whose pus samples (or pus aspirate or necrotic tissues) were submitted to the BMC Clinical Microbiology Laboratory for culture and antimicrobial susceptibility testing (AST). The aim was to complete a total of six months' timeframe for SSTIs AMR surveillance. The study included all patients with SSTIs (irrespective of age, sex, units or departments) whose samples were received at BMC Clinical Microbiology Laboratory for culture and AST. A total of 614 patients were enrolled based on the Kish-Leslie formula using a previous proportion of laboratory confirmed SSTIs of 26.0% in the same hospital. This was calculated from the two arms ie a minimum of 296 patients in the retrospective component and 296 patients in the prospective component.[12]

Participant Enrollment and Laboratory Procedures

Patients with SSTIs who fulfilled the inclusion criteria were serially enrolled at the BMC Clinical Microbiology Laboratory (one sample per patient). Data were collected/extracted from the laboratory request forms and patient electronic files in the hospital and laboratory electronic systems (eHMIS/DISA) using a well-structured data collection tool which included sociodemographic and clinical information from patients like age (years), gender, residence, referral status, inpatients/outpatients, payment modality, SSTI category, SSTI site, fever, and the department where the patient was attending.

The BMC Central Pathology Laboratory is ISO 15189 accredited, and Clinical Microbiology Laboratory is one of its core departments/units.[22] The Clinical Microbiology Laboratory has been participating as one of the nine sentinel sites for AMR surveillance in Tanzania since 2019, and therefore, operates in conformity with the global standards.[20] Patients' particulars were serially entered into the system for each sample received. Then, primary Gram stain of pus sample was performed based on the average observations from 10 fields to characterize and quantify polymorphonuclear cells (PMNCs) and microorganisms. The presence of moderate (2–10 PMNCs and microorganisms) per oil 100× immersion field; and many cells (>10 PMNCs and microorganisms) per oil 100× immersion field were considered positive, and therefore, subjected to culture. Each sample fulfilling these criteria was cultured in aerobic condition into blood agar (Oxoid, UK), and MacConkey agar (Oxoid, UK).[23,24] After growth, biochemical identification tests were systematically carried out for Gram positive bacteria based on hemolysis on blood agar, catalase, coagulase/Staphlex/DNase, bile esculin, optochin, and bacitracin tests. Gram negative bacteria identification tests were lactose fermentation on MacConkey agar (Oxoid, UK), oxidase, triple sugar iron agar (TSI), sulphur indole and motility agar (SIM), urease and citrate tests (Oxoid, UK).[24] Antimicrobial susceptibility test was performed on Muller Hinton agar (Oxoid, UK) using the conventional disc diffusion method as previously described by the Clinical Laboratory Standard Institute (CLSI) for the respective antibiotic disks for Gram-positive and Gram-negative bacteria [25]. Respective disks for Gram-positive bacteria included were penicillin G (10µg), erythromycin (15µg), clindamycin (2µg), ciprofloxacin (5µg), gentamicin (10µg), gentamicin (120µg–high level for *Enterococcus* spp), trimethoprim-sulfamethoxazole (1.25µg/23.7µg), and chloramphenicol (30µg). Antibiotic discs for Gram-negative bacteria included were ampicillin (10µg), ciprofloxacin (5µg), gentamicin (10µg), amikacin (30µg), ceftriaxone (30µg), ceftazidime (10µg), and cefepime (10µg), trimethoprim/sulfamethoxazole (1.25µg/23.7µg), piperacillin/tazobactam (100/10µg), and meropenem (10µg).[25] Detection of the four key AMR phenotypes (MRSA, ESBL, CarbR, and MDR) were conducted based on the CLSI and other standard guidelines.[25,26]

Quality Control of Data and Laboratory Procedures

The study used a standard data collection tool which captured key parameters available in the hospital and laboratory information systems (eHMIS/DISA). Data consistence was ensured using unique patients' registration numbers, and was reviewed at the end of each day. The study deployed both sterility and performance tests for Gram staining, bacteria culture, biochemical identification tests and AST using American Type Culture Collection (ATCC) strains. Two representative bacteria from Gram positive and negative used were *Staphylococcus aureus* ATCC 25923 and *Escherichia coli* ATCC 25922, respectively. These strains were also used for quality control of Methicillin-sensitive *Staphylococcus aureus* and non-ESBL Gram negative bacteria, respectively. *Staphylococcus aureus* ATCC 43300 and *Klebsiella pneumoniae* ATCC 700603 were used quality control of Methicillin resistant *Staphylococcus aureus* (MRSA)

and ESBL Gram negative bacteria, respectively. Finally, two in-house *Pseudomonas aeruginosa* strains were used for quality control of CarbR and carbapenem-sensitive Gram-negative strains.[25]

Data Management

Data cleaning and consistence checks were done using Microsoft Excel, and data analysis was done using STATA version 15.0. Descriptive analysis was performed on continuous variables and categorical variables using measures of central tendencies and frequencies (percentages), respectively. Pearson chi-square test and one-sample test of proportion were used to assess distribution and statistical differences between categorical variables. Logistic regression analysis was used to assess the association between dependent variable (MDR SSTIs) and independent variables like age, gender, residence, referral status, inpatient/outpatient, department, payment category, SSTIs site, SSTIs type and fever (among others), using odds ratio and 95% confidence interval. Independent variables with a p-value of <0.05 on bivariate analysis were subjected to multivariate logistic regression analysis to ascertain the independent predictors of MDR SSTIs using a p-value cut-off of <0.05. The WHONET software was used for bacterial isolate listings and generation of hospital-wide antibiograms (https://whonet.org/). Only ≥29 bacterial isolates per species were subjected to antibiogram generation, those less than 29 were combined together as "Other Gram-positive bacteria" and "Other Gram-negative bacteria" to avoid undue exaggeration of susceptibility profiles.

Study Approvals, Permission and Ethical Considerations

Waiver of consent was sought from CUHAS/BMC Research and Ethical Review Committee through the BMC management and the BMC Antimicrobial Stewardship/Resistance Surveillance Committee within a previously approved SMART project (CREC/615/2022). Approval of research information to be used by a graduate student was sought and provided (CREC/680/2023). Permission to conduct the study was sought from the BMC Director General. Patients' information was strictly kept confidential using anonymous codes, and disclosed only to the research team and attending health practitioners. This study did not cause any adverse effects or unintended harm on the patients as it was conducted as part and parcel of routine SSTIs patients' management at BMC. Results from culture and AST were promptly communicated to the attending doctors to guide patient management based on the BMC management guidelines and Tanzania Standard Treatment Guidelines.[27]

Results

Socio-Demographic and Clinical Characteristics Among SSTIs Patients

A total of 614 patients were included in the study, with 54.4% (334/614) being male. The patients' median [IQR] age was 34 [IQR 14–54] years, with 46.25% (284/614) being residents of Mwanza. A total of 353 (57.49%) were outpatients. The most common SSTIs category was surgical site infections, 184/614 (30.0%), Table 1. Patients were further divided into four groups based on the departments, namely, adult surgical patients, 48.1% (295/614); adult medical patients, 34.7% (213/614), obstetrics and gynecology (OBGY) patients, 9.1% (56/614) and pediatric patients, 8.1% (50/614). All surgical patients in this study were exposed to antibiotics previously (notably a combination of beta lactam antibiotic + aminoglycoside or metronidazole) based on the type of the SSTIs and the anatomical site involved.

Laboratory Confirmed SSTIs and Bacterial Species Implicated

The proportion of laboratory confirmed SSTIs among 614 patients' samples analyzed was 72.48% (n=445). The highest laboratory-confirmed SSTIs were in adult surgical patients (75.9%), and the lowest were found among OBGY patients (50.0%), Table 2.

A total of 586 pathogens were detected from 445 clinical samples analyzed. Approximately 31.2% (139/445) had mixed growth [89.93% (125/139) had two bacteria species, 8.63% (12/139) had three bacteria species, and 1.44% (2/139) had four bacteria species]. During WHONET analysis, six isolates' variables were incompatible with the software system, and therefore, a total of 580 isolates were subjected to WHONET analysis. The most prevalent bacteria species were *Staphylococcus aureus*, 17.07% (99/580), *Escherichia coli*, 17.07% (99/580), and *Klebsiella* spp. 16.55% (96/580). Other notable bacteria species included *Pseudomonas aeruginosa* 13.96% (81/580), and *Acinetobacter* spp. 12.93% (75/580), Table 3.

Table 1 Socio Demographic and Clinical Characteristics of SSTI Patients

Variables	Frequency (n)	Percent (%)
Gender		
Male	334	54.40
Female	280	45.60
Residence		
Mwanza	284	46.25
Out of Mwanza	330	53.75
Referral		
Self-referred patient	523	85.18
Referred patient	91	14.82
Inpatient/Outpatient status		
Outpatient	353	57.49
Inpatient	261	42.51
Payment		
NHIF	290	47.23
Cash	233	37.95
Waiver	67	10.91
Other health insurances	24	3.91
SSTIs category		
Traumatic and SSIs[¥]	305	49.67
Chronic lower limb ulcers	171	27.85
Folliculitis, abscess, swelling and necrotic tissue fasciitis[£]	121	19.71
Congenital anomalies	17	2.77
SSTI site		
Lower extremities	248	40.39
Abdomen	96	15.64
Head and neck	84	13.68
Pelvic	63	10.26
Back	31	5.05
Skin	28	4.56
Upper extremities	23	3.75
Thoracic	16	2.61
Breasts	8	1.30
Trunk	8	1.30
Upper and lower extremities	6	0.98
Others*	3	0.49
Fever		
No	505	82.25
Yes	109	17.75

Notes: [¥]Traumatic wound and SSI: traumatic wound (121) and SSI (184). [£]Swelling (48), abscess (41), folliculitis and skin rashes (22), necrotic tissue fasciitis (10) * perianal areas (3).
Abbreviations: NHIF, National Insurance Fund; SSTIs, Skin and soft tissue infections.

Antibiograms Profiling Among Bacteria Species Implicating in SSTIs

Staphylococcus aureus showed predominantly low sensitivity to penicillin G (1.0%) and erythromycin (37.8%), moderately sensitivity to cefoxitin (70.6%) connoting methicillin sensitive *Staphylococcus aureus*, and highly sensitivity to gentamicin (87.9%) and chloramphenicol (97.1%). Gram-negative Enterobacterales showed low sensitivity to ampicillin, trimethoprim-sulphamethoxazole and ceftriaxone (7.5% to 41.4%), moderate sensitivity to gentamicin (56.9% to

Table 2 Proportion of Laboratory Confirmed SSTIs in the Four Patients' Departments

Patients' Department	Samples Taken	Frequency of Laboratory Confirmed SSTIs (n)	Percentage (%)
Adult surgical patients	295	224	75.9
Adult medical patients	213	159	74.6
Pediatrics patients	50	34	68.0
OBGY patients	56	28	50.0
Total	**614**	**445**	**72.5**

Abbreviations: NHIF, National Insurance Fund; OBGY, Obstetrics and Gynecology; SSTIs, Skin and soft tissue infections.

70.7%) and high sensitivity to piperacillin-tazobactam, meropenem and amikacin (80.0% to 98.9%). However, unlike Enterobacterales, *Acinetobacter* spp. showed moderate sensitivity to piperacillin-tazobactam, meropenem and amikacin (Supplementary Table).

Antimicrobial Resistant Phenotypes Among Bacteria Species Causing SSTIs

All 586 bacteria species isolated were subjected to AMR and MDR phenotypes analysis, and 300 isolates were Enterobacterales, and of them, 47.3% (142/300) were found to be ESBL producers. Out of 456 gram-negative bacteria, 12.9% (59/456) were CarbR. Methicillin-resistant *Staphylococcus aureus* (MRSA) was identified in 29.4% (30/102) of the *S. aureus*. Inducible clindamycin resistance was observed in 34.3% (35/102) of the *S. aureus* isolates. The overall MDR among all bacterial isolates was 56.68% (297/586). The overall MDR was significantly higher among gram-negative bacteria than gram-positive bacteria, 39.8% (233/586) versus 10.9% (64/586; p-value<0.001). The predominant MDR organisms were *E. coli* 13.65% (80/586), *K. pneumoniae* 10.41% (61/586), *S. aureus* 9.39% (55/586), and *Acinetobacter* spp. 7.68% (45/586).

Association of Predictor Variables and SSTIs MDR Phenotype

The overall MDR SSTIs among patients were 40.9% (251/614). On bivariate logistic regression analysis, referred patients, inpatients, and those who were given waivers for their treatment were significantly associated with SSTIs MDR phenotypes. However, on multivariate logistic regression analysis, only inpatients were found to be independently associated with MDR SSTIs [OR (95% CI); p-value] = 1.86 (1.33–2.59); p-value<0.001], Table 3.

Table 3 Association of Socio-Demographic and Clinical Characteristics and the MDR Phenotype

Variable		Multi Drug Resistance (MDR) SSTIs						
		Total	Negative, n (%)	Positive, n (%)	Bivariate Regression		Multivariate Regression	
					OR (95% CI)	*p-value*	OR (95% CI)	*p-value*
Age (years)	Children ≤5	89	59 (66.3)	30 (33.7)	1			
	Adolescent (6–17)	86	61 (70.9)	25 (29.1)	0.81 (0.42–1.53)	0.509		
	Adult (≥18)	439	243 (55.4)	196 (44.6)	1.59 (0.98–2.56)	0.059		
Gender	Female	280	174 (62.1)	106 (37.9)	1			
	Male	334	189 (56.6)	145 (43.4)	1.26 (0.91–1.74)	0.163		

(*Continued*)

Table 3 (Continued).

Variable		Multi Drug Resistance (MDR) SSTIs						
		Total	Negative, n (%)	Positive, n (%)	Bivariate Regression		Multivariate Regression	
					OR (95% CI)	*p-value*	OR (95% CI)	*p-value*
Residence	Mwanza	284	171 (62.1)	113 (37.9)	1			
	Other regions	330	192 (58.2)	138 (41.8)	1.09 (0.79–1.50)	0.610		
Referral status	Self-referred	523	319 (61.0)	204 (39.0)	1			
	Referral	91	44 (48.4)	47 (51.6)	1.67 (1.07–2.61)	0.025	1.44 (0.90–2.31)	0.126
Admission status	Outpatient	353	233 (66.0)	120 (34.0)	1			
	Inpatient	261	130 (49.8)	131 (50.2)	1.96 (1.41–2.71)	<0.0001	1.86 (1.33–2.59)	<0.001
Payment modalities	Insurances	314	196 (62.4)	118 (37.6)	1			
	Cash	233	135 (57.9)	98 (42.1)	1.21 (0.85–1.70)	0.289	1.05 (0.73–1.51)	0.797
	Waiver	67	32 (47.8)	35 (52.2)	1.82 (1.07–3.09)	0.028	1.66 (0.97–2.86)	0.065
Departments	OBGY	50	27 (54.0)	23 (46.0)	1			
	Surgical	295	179 (60.7)	116 (39.3)	0.76 (0.42–1.39)	0.374		
	Medical	213	118 (55.4)	95 (44.6)	0.95 (0.51–1.75)	0.858		
	Pediatric	56	39 (69.6)	37 (36.4)	0.51 (0.23–1.13)	0.099		
SSTIs category	Congenital deformities	17	8 (47.1)	9(52.9)	1			
	Traumatic and SSIs	305	165 (54.1)	140 (45.9)	0.75 (0.28–2.01)	0.572		
	Chronic lower limb ulcers	171	107 (62.6)	64 (37.4)	0.53 (0.19–1.45)	0.216		
	Folliculitis, abscess and necrotizing fasciitis	121	83 (68.6)	38 (31.4)	0.41 (0.15–1.14)	0.086		
Fever	No	505	302 (59.8)	203 (40.2)	1			
	Yes	109	61 (56.0)	48 (44.0)	1.17 (0.77–1.78)	0.460		

Abbreviations: MDR, Multi-drug resistance; NHIF, National Insurance Fund; SSTIs, Skin and soft tissue infections; OBGY, Obstetrics and Gynecology.

Discussion

The current study has shed light on the significant burden of MDR pathogen SSTIs, an area currently overlooked by the Tanzania NAP-AMR. The proportion of laboratory confirmed SSTIs, bacterial species, AMR phenotypes have been determined. Furthermore, risk factors associated with MDR pathogens among patients with SSTIs is detailed. These findings underscore the urgency of revisiting treatment guidelines and advocating for the inclusion of SSTIs in the ongoing AMR surveillance in Tanzania.

Laboratory Confirmed SSTIs and Implicated Bacteria Species

The proportion of laboratory-confirmed SSTIs (72.5%) in this study was similar to other previous studies (67.7% in patients with chronic lower limb ulcers in Tanzania), 68.8% in patients with surgical site infections in Uganda, and 73% in patients with SSTIs in India, connoting similar epidemiological predispositions in LMICs.[6,13,28] A relatively higher proportion (96.8%) was previously reported in Bagamoyo, Tanzania because of inclusion of Coagulase negative *Staphylococci* (CoNS) which in contrast to the current study were regarded as contaminants based on global standard guidelines.[29] However, lower proportions of laboratory confirmed SSTIs were reported in Mwanza, Tanzania (10.9%) and 9.72% in a systematic review involving 11 studies in Ethiopia.[11,19] Lower proportions in the latter two studies could

be related to involvement of a homogenous population of women post-caesarian sections in contrast to heterogenous patient populations in other previous studies. Regardless of the populations, there is a progressive increasing on trend of laboratory confirmed SSTIs in Tanzania underscoring a need to include SSTIs in the Tanzania NAP-AMR surveillance to monitor this group of patients and guide specific responsive measures.

Similar to previous studies in the same region, *S. aureus, E. coli*, and *K. pneumoniae* were found to be the most common bacterial species in the current study.[11–13] Predominance of these species may be related to anatomical distribution of microbiota colonizing non-sterile sites of the body with *S. aureus* being skin microbiota, while *E. coli* and *K. pneumoniae* being gut microbiota. These altogether result into endogenous infections or transmission from other people in case stringent personal protective gears are not adhered by patients themselves, care takers or health care workers. On the other hand, exposed wounds among patients with SSTIs can create potential niches for contamination with environmental bacteria, and this may explain the role of *Pseudomonas aeruginosa* and *Acinetobacter* spp., which ranked 4th and 5th in this study. Other previous studies have also explained a similar association between infections with both endogenous and exogenous sources.[30–32] Therefore, our results underscore the significance of adopting both hygiene and sanitation measures, in conjunction with thorough environmental decontamination to disrupt the transmission chain of bacteria that contribute to SSTIs.

AMR and the MDR Phenotypes Among Bacteria Implicated in SSTIs

A higher proportion of ESBL producing Enterobacterales (47%) was found in this study than 35.0% previously reported in 2014 in the same region connoting a rising burden of resistant pathogens.[13] The rising proportion of ESBLs could be attributed to the inherent resistance mechanisms exhibited by GNB bacteria owing to their outer membrane, efflux pumps, antimicrobial degrading enzyme production, and mutations in porin proteins, which collectively render many antimicrobials less effective.[33,34] Also, this significant rise may be associated with irrational use of 3rd generation cephalosporins in LMICs (Tanzania inclusive) which is rampant and which inadeptly creates antimicrobial selective pressure and dissemination of ESBL resistant strains.[35,36] On the other hand, resistance to agents like carbapenems which are very expensive, and whose prescription is stringent was shown to be low in this study (12.7%) similar to 15.6% for Enterobacterales in the previous study and in another similar study in Italy.[13,32] It should be reiterated that despite this low CarbR to Enterobacterales, CarbR to *Pseudomonas aeruginosa* and *Acinetobacter* spp., in this study, another similar study in Tanzania and in other countries was alarmingly high.[8,37] Inherent resistant mechanisms to the two pathogens account for this trend, and hence, a pivotal need to prioritize screen strategies for vulnerable surgical patients against these pathogens to ensure favorable management outcomes.[32]

Approximately one-third of *Staphylococcus aureus* strains were MRSA, indicating a gradual decrease from 44.4% in a similar study previously conducted in the same hospital between 2011 and 2012.[13] The decrease may be associated with difference in the cell envelope structures of *Staphylococcus aureus* which are more liable to destruction by antimicrobials compared to Gram negative bacteria, together with on-going comprehensive infection prevention and control (IPC) measures implemented at BMC as part and parcel of the national-wide AMR surveillance. Our findings, therefore, emphasize the need to strengthen AMR surveillance involving large the number of patients and bacterial isolates so as not to erroneously conclude on high ESBL and MRSA proportions as reported in two previous studies in the same hospital.[11,12] Of all the isolates, approximately 57% were MDR, with MDR gram-negative bacteria accounted for the majority of strains, similar to previous studies in Tanzania and Uganda.[6,8] Admitted patients had 1.96 increased odds of having MDR SSTIs compared to outpatients' due to the fact that health-care associated infections are MDR in nature due to exposure of patients to antibiotics and exposure to environmental bacteria to antiseptics, disinfectants, and other antimicrobial agents, which altogether create antimicrobial selective pressure and drive the MDR burden. Furthermore, our findings are similar to a recent meta-analysis across African countries in terms of the spectrum of the dominant bacterial pathogens (*S. aureus E. coli, K. pneumoniae, P. aeruginosa* and *A. baumannii*), and the dominant AMR phenotypes (MRSA: 48.0%; 3rd generation cephalosporin resistance) (range: 60.0% −70.0%); and CarbR (<20.0%), which altogether connote similar socio-demographic, economic and clinical predisposition.[38]

Antibiograms and Its Significance in the SSTIs Treatment Guidelines at BMC

There were notably low sensitivities to ampicillin, trimethoprim/sulfamethoxazole and third generation cephalosporins among Gram negative bacteria; and penicillin G and erythromycin for Gram positive bacteria similar to previous studies in India, Uganda, and Tanzania.[6,13,28] Decreased sensitivities may be attributed to the frequent use of these antibiotics as empirical antimicrobial therapeutic options and non-prescription misuse of these agents. In addition, ceftriaxone is commonly used in Tanzania for prophylaxis in surgical patients. There was moderate sensitivity to ciprofloxacin and high sensitivity to gentamicin, piperacillin/tazobactam, amikacin and meropenem for Gram negative bacteria. High sensitivity of Gram negative bacteria to amikacin and meropenem is not surprising as these antibiotics are categorized as Reserve in the Access Watch and Reserve (AWaRe) classification of antibiotics and are closely monitored with prescriptions guided by culture and AST results as per Tanzania Standard Treatment Guidelines and the National Essential Medicines List for Tanzania Mainland (STG/NEMLIT., 2021).[27] These strategies reduce excessive use of these antibiotics in both community and healthcare settings, indirectly decrease AMR, and increase their longevity.[21,27] On the other hand, moderate-to-high sensitivity was shown for cefoxitin (a surrogate marker of cloxacillin), clindamycin, gentamicin and chloramphenicol for Gram positive bacteria. High sensitivity against gentamicin and chloramphenicol may be due to their less frequent use related to their injection administration route and the fact that they are not indicated for children and older patients. Therefore, based on this hospital-wide antibiograms generated from SSTIs AMR surveillance, the first-line agent for Gram-negative bacteria is recommended to be ciprofloxacin, whereas for Gram-positive bacteria, either cloxacillin or ciprofloxacin can be judiciously used. The second line for Gram-negative bacteria is recommended to be gentamicin and/or piperacillin-tazobactam, whereas for Gram-positive bacteria, it is recommended to be gentamicin and/or clindamycin or chloramphenicol. The third line for Gram negative bacteria is recommended to be meropenem. We did not screen Gram positive bacteria against vancomycin because we used disk diffusion method and not the recommended minimum inhibitory concentration methods. However, based on other studies, local and global guidelines, vancomycin is still recommended as the third line and strengthening AMR surveillance to this reserve agent in Tanzania is highly recommended.[27,39] We therefore, envisage to incorporate these findings in the revised BMC hospital formulary and treatment guidelines so as to expedite evidence-based specific management of patients with SSTIs in Tanzania. The similarities in the burden of SSTIs in this study to other studies across African countries underscore regional-wide concerted efforts to combat AMR threat by leveraging existing resources (humans, material and financial resources) and systems through harmonization of the continental-wide policy guidelines based on these prevailing evidence.[38,40]

Study Limitations

Firstly, the study did not address anaerobic bacteria pathogens which also play a significant role, especially in deep-seated SSTIs due to limited standardized in-house detection methods. Secondly, we have created only one hospital-wide antibiogram and not department-specific antibiograms as there were few patients with SSTIs in pediatrics and OBGY departments. Future studies should be extended to at least a year to cater not only for the limited number of isolates for department/unit-specific antibiograms' generations, but also address annual seasonal variations. Thirdly, molecular characterization of the dominant AMR phenotypes (MRSA, ESBL and CarbR) to decipher transmission dynamics in the context of IPC guidance was not performed as this was outside the primary scope of the current study. All bacteria pathogens were kept for further research (including molecular characterization of the dominant AMR phenotypes). Nevertheless, our findings have created a crucial baseline platform where continuous SSTIs AMR surveillance data can be collected and subsequently allow sub-analysis at department and unit-specific levels.

Conclusions

Approximately three-quarter of patients at BMC in Mwanza, Tanzania, have laboratory-confirmed SSTIs, which are remarkably caused by MDR pathogens in admitted patients. There was high sensitivity to gentamicin and chloramphenicol in Gram-positive bacteria, and piperacillin/tazobactam, meropenem, and amikacin in Gram-negative bacteria. Revisiting SSTIs antimicrobial treatment options in this setting, and the need to include SSTIs in the ongoing AMR surveillance in Tanzania are reiterated in these findings. There is a need to continue with this established SSTIs AMR

surveillance so as to get more data for antibiogram sub-analysis at the department levels. The high MDR burden among admitted patients emphasizes on strengthening of robust antimicrobial stewardship programs and infection control measures in this hospital. Finally, molecular characterization of the dominant AMR phenotypes (MRSA, ESBL and CarbR) to decipher transmission dynamics in the context of IPC guidance is recommended in future studies.

Abbreviations

AWaRe, Access Watch and Reserve classification of antibiotics; AMR, antimicrobial resistance; AST, antimicrobial susceptibility testing; ATCC, American Type Culture Collection; BMC, Bugando Medical Centre; CarbR, Carbapenem resistance; CLSI, Clinical and Laboratory Standards Institute; CUHAS, Catholic University of Health and Allied Sciences; ESBL, extended-spectrum beta-lactamase; IPC, Infection prevention and control; IQR, Interquartile range; LMIC, Low- and middle-income countries; MDR, Multi-drug resistance; SD, Standard deviations; SSTIs, Skin and soft tissue infections; MRSA, Methicillin resistant *Staphylococcus aureus*; NAP-AMR, National Action Plan on Antimicrobial Resistance; STG/NEMLIT, Standard Treatment Guidelines and the National Essential Medicines.

Data Sharing Statement

The dataset used is available from the corresponding author upon request.

Ethical Approval

This study was granted research and ethical approval by the CUHAS/BMC Research and Ethical Review Committee (CREC/615/2022 and CREC/680/2023) to the SMART program and BNJ, respectively. It was conducted in accordance with the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, from conception, study design, execution, acquisition of data, analysis and interpretation. They took part in critically revising the manuscript, and gave final approval of the version to be published. They have also agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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