## REVIEW

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# Prevalence, antimicrobial susceptibility and genotypic characteristics of *Staphylococcus aureus* in Tanzania: a systematic review

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## Abstract

**Background:** Data on the prevalence, genotypes and antibiotic resistance patterns of colonizing and infectionassociated *Staphylococcus aureus* (*S. aureus*) strains both in humans and animals in Tanzania are scarce. Given the wide range of infections caused by *S. aureus* and the rise of methicillin-resistant *S. aureus* (MRSA) globally, this review aims at collecting published data on *S. aureus* bacterium to improve our understanding of its epidemiology in Tanzania.

**Main body:** We carried out a systematic review of scientific studies reporting on prevalence, antibiotic resistance and genotyping data pertaining to *S. aureus* in human and animal infection and colonization. The literature extracted from electronic databases such as PubMed and Google Scholar was screened for eligibility and relevant articles were included. The review is limited to manuscripts published in English language between the years 2010 and 2020. A total of 45 studies conducted in 7 of the 9 administrative zones in Tanzania were reviewed to gather data on *S. aureus* prevalence in humans and animals. Prevalence in humans ranged from 1 to 60%. Antibiotic resistance patterns of *S. aureus* isolated from colonized humans showed high resistance rates against co-trimoxazole (46%) and erythromycin (41%) as compared to reports from studies conducted outside Africa. The review suggests an increased MRSA prevalence of up to 26% as compared to 6–16% reported in previous years. Genotypic data reviewed suggested that MRSA predominantly belonged to ST88. The prevalence of *S. aureus* in animal studies ranged from 33 to 49%, with 4 to 35% of MRSA isolates. Most studies reported low antibiotic resistance levels, with the exception of penicillin (85%) and ampicillin (73%).

**Conclusion:** The prevalence of *S. aureus* and MRSA in Tanzania is rising, although clear variations between different geographic areas could be observed. Non-susceptibility to commonly prescribed antibiotics in community-associated *S. aureus* is of concern. Research strategies to ameliorate our knowledge on *S. aureus* epidemiology should employ regular antibiotic resistance surveillance, antimicrobial stewardship as well as genotypic characterization.

Keywords: Staphylococcus aureus, Prevalence, Antimicrobial resistance, Genotyping, Infection, Colonization, Tanzania

## Background

Antimicrobial resistance (AMR) is a global concern estimated to account for approximately 700,000 deaths each year (O'Neill 2016). If no appropriate measures are

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taken to slowdown the progression of this epidemic it is estimated that by 2050 it will cost the world around 10 million lives per annum (O'Neill 2016). The lack of development of new antimicrobial agents in the pipeline further emphasizes the necessity to reduce dependency on antibiotics by implementing infection control strategies (O'Neill 2016; WHO 2014).

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According to the 2014 World Health Organization (WHO) report, most regions stated over 50% bacterial resistance against third-generation antibiotics, particularly methicillin-resistant *S. aureus* (MRSA) clones in hospitals (WHO 2014). Furthermore in 2017, the WHO listed antibiotic-resistant bacteria including *Staphylococcus aureus* (*S. aureus*) as a priority bacterium to guide research, discovery and development of new antibiotics (WHO 2017). The report further recommended special attention to be directed towards the identified resistant bacteria due to their ability to rapidly develop resistance against multiple antibiotic classes hence limiting therapeutic options (WHO 2017).

Staphylococcus aureus is an old bacterium discovered in the eighteenth century, antibiotic resistance in the bacterium against penicillin was described in the 1950's, the penicillin-resistant staphylococci inactivates penicillin function by an enzyme called penicillinase or beta-lactamase which degrades the  $\beta$ -lactam ring in penicillin, thus altering the shape of penicillin and preventing its binding to the penicillin binding proteins (Haddadin et al. 2002). Following penicillin failure in treating S. aureus infections, methicillin was introduced. Methicillin was particularly effective upon its introduction into clinical therapy due to its ability to resist the action of  $\beta$ -lactamase. However, methicillin resistance in S. aureus was also reported only a year after its introduction. Strains of S. aureus resistant to methicillin or oxacillin or other  $\beta$ -lactam compounds are still termed MRSA, only to honour the historic role of methicillin that used to effectively treat staphylococcal infections, and it is to methicillin that the resistance was first described (Jevons 1961). Several terms are used to describe different MRSA strains associated with outbreaks in different settings based on strains' genomic background and level of virulence (Zetola et al. 2005). MRSA strains associated with hospital-acquired infections are commonly abbreviated to HA-MRSA, while strains causing community-associated infection are abbreviated to CA-MRSA and those associated with livestock are abbreviated as LA-MRSA.

*Staphylococcus aureus* is both a commensal and potentially harmful pathogen in humans and animals. The bacterium can give rise to a variety of infections ranging from mild skin and soft tissue infections to more serious and complex diseases such as pneumonia, septicaemia, infective endocarditis and other deep-seated infections (e.g. osteomyelitis) in humans as well as mastitis and necrotic infections in a variety of animal hosts. *Staphylococcus aureus* can also colonize the skin and approximately 30% of the human population is found to be transiently colonized if nasal swabs are examined microbiologically.

High levels of MRSA have been reported across Africa, ranging between 43 and 72%, as reported in Cameroon, South Africa and Ethiopia (Founou et al. 2017). The vast majority of clinical S. aureus/MRSA data in Africa is associated with hospital acquired infection (HAI) affecting individuals with healthcare-related risk such as hospitalization, surgery and underlying chronic diseases (David 2010). Information on community-acquired S. aureus/MRSA infections (CAI) causing diseases in people with no healthcare-associated risk is also available on the continent even though to a lesser extent. Moreover, very limited data on livestock acquired S. aureus/ MRSA infections (LAI) whereby S. aureus clones of animal origins colonize or cause infections in humans have been published in Africa (Founou et al. 2017). Further information on the antibiotic-resistant clones occurring in both human and animal are very limited, hindering comprehensive understanding of the epidemiology of the bacterium (Lozano et al. 2016).

Tanzania, a developing country located along the East African coast, housing a population of about 57 million people, of which 36% is engaged in livestock keeping as the major source of livelihood. The potential for humananimal contact is very high, especially in tribes that cohabit with their animals such as Maasai people. The aim of this review is to summarize literature reporting on the prevalence, antibiotic resistance of *S. aureus* in Tanzania. Furthermore, reported genotypic characterization of *S. aureus* will be reviewed to provide a more nuanced profile of *S. aureus* genetic diversity in colonization and infections both in animal and human hosts as well as their possible relationship.

### Main text

### Methods

## Eligibility criteria

A systematic review of Tanzanian scientific studies reporting on prevalence, antimicrobial resistance and genotypic characterization of *S. aureus* from human and animal sources published between 2010 and 2020 was performed. Information sought for in the publications included commensal and clinical *S. aureus* recovered from different infections including invasive and noninvasive. Animal studies reporting on *S. aureus* recovered from animals and their products were also considered. All studies that recovered less than five *S. aureus* isolates as well as publications that were written in a language other than English were excluded from this review.

## Information sources and search strategies

PubMed database was researched in November 2018 and February 2021 by a librarian using Boolean operators "AND" and "OR" to identify studies fitting our inclusion criteria. The following search terms were used "*Staphylococcus aureus* OR *S. aureus* AND antimicrobial susceptibility OR antibiotic resistance AND prevalence AND Tanzania." Additionally search words such as "Molecular typing AND *S. aureus* AND antibiotic resistance AND Tanzania" and "*Staphylococcus aureus* OR *S. aureus* AND antimicrobial susceptibility OR antibiotic resistance AND prevalence AND Tanzania" were used in Google scholar to identify eligible articles. The bibliographies of all eligible documents were hand-searched for additional publications eligible for review.

## Data extraction and appraisal process

The Joana Briggs Institute checklist was applied to appraise and review the quality of each study accessed by two independent reviewers. A data extraction form was designed to capture required information such as author, year of publication, study period, methodology, MRSA identification strategies, S. aureus and MRSA prevalence, antibiotic resistance patterns as well as genotypic information. Two reviewers were involved in the process whereby the first reviewer (TM) extracted the information and the second reviewer (TK) double checked the information to eliminate possible bias. All disagreement raised during the critical appraisal process were resolved through reviewers discussions. All extracted literature was analysed using reference manager ENDNOTEX7. This study followed the standardized scientific writing format of the Preferred Reporting Items for systematic reviews and meta-analyses (PRISMA) guidelines. The study has not taken on any meta-analysis due to the heterogeneity of the studies under review; nevertheless, mean resistance rates and prevalence were calculated to help present the results better.

### Scope of the study

This review is limited to prevalence, antibiotic resistance patterns and genetic typing information [i.e. specified resistance and virulence genes, Staphylococcus protein A (*spa*) typing and multi-locus sequence typing] of *S. aureus* retrieved from human and animal hosts.

### Results

PubMed search resulted in 18 eligible articles followed by an additional 13 articles included from the Google scholar search. Rigorous reference list review supplemented another 14 eligible publications making a total of 45 (Fig. 1).

Data concerning *S. aureus* prevalence, antimicrobial resistance and genotyping were extracted from studies performed in 7 zones of the 9 administrative zones in Tanzania. Table 1 describes the distribution of the published articles review in their consecutive zones. The



**Table 1** Distribution of the reviewed S. aureus Studies by zone inTanzania

Zone	Human	Animal	Human and animal
Eastern Zone	15	2	1
Lake Zone	15	-	-
Northern Zone	5	1	-
Central	1	-	-
Zanzibar	2	1	-
East and lake Zone	1	-	-
Lake and Western Zone	1	-	-
Total	40	4	1

majority of the publications reviewed were from regions in the eastern and lake zones (i.e. 40% and 33%, respectively), showing lack of *S. aureus* researched data in the other parts of the country.

The majority of the publications were reported in the Eastern and Lake Zones. *S. aureus* data of animal origin have been poorly represented throughout the country.

Database searched

## Prevalence, antibiotic resistance and genotyping of *S. aureus* isolated from humans

A total of 45 studies reported on prevalence, antimicrobial resistance and genetic characteristics of *S. aureus* in humans published between 2010 and 2020 in Tanzania as indicated in Table 1.

### Prevalence of S. aureus in humans

*Staphylococcus aureus* prevalence was reported in 39 human-related studies, reporting a prevalence ranging from 6 to 69%. Higher infection rates were typically observed in SSTI's, nevertheless the bacterium was also implicated in other infections. Furthermore, it was notably observed that *S. aureus* colonization ranged around 10–60% in the three different zones that reported on colonization. The summary of *S. aureus* prevalence in colonization and different infections in human, as well as the geographic distributions reported in Tanzania between 2010 and 2020, is summarized in Table 2.

## Antibiotic resistance in human S. aureus isolates

The primary method for establishing *S. aureus* antibiogram in the reviewed work was done phenotypically using the *Kirby-Bauer* disc diffusion test along with Clinical Laboratory Standard Institute (CLSI) guidelines. *Kirby-Bauer* is an antimicrobial susceptibility test based on the size of inhibition zones of microbial growth in a lawn culture around discs impregnated with the antimicrobial drug (Hudzicki 2009).

Twenty-four studies contributed information on antibiotic susceptibility of *S. aureus* bacteria. MRSA in most cases was identified by resistance against cefoxitin; however, one study used methicillin as their identification disc. As summarized in Table 3, extremely high resistance rates against  $\beta$ -lactams, i.e. penicillin (87–99%) and ampicillin (67–92%), were observed.

Apart from high resistance to the reported  $\beta$ -lactams, trimethoprim/sulphamethoxazole (co-trimoxazole) and erythromycin showed average resistance of 54% and 47%, respectively. Notably individual analysis of antibiotics susceptibility in isolates collected from colonization showed lower rates of resistance compared to *S. aureus* isolated from clinical infections, as summarized in Table 3.

Resistance rates of 50% (co-trimoxazole), 45% (clindamycin), 37% (erythromycin) and 32% (gentamicin) were observed in SSTIs. Unlike in commensal and SSTIrelated isolates, blood born *S. aureus* showed higher resistance variation against most commonly used antibiotics (i.e. erythromycin, gentamicin, co-trimoxazole and clindamycin) ranging from 42 to 66%.

MRSA detection in all reported reviewed studies had an average prevalence of 21%, nevertheless 7 studies reported on specific resistance patterns of MRSA isolates sighting higher rates against other antibiotics (clindamycin, erythromycin and co-trimoxazole) ranging from 50 to 100% (Joachim et al. 2018, 2017; Geofrey et al. 2015; Moyo et al. 2014; Moremi et al. 2014) apart from the expected  $\beta$ -lactams antibiotic resistance.

Even though most articles reported 100% susceptibility to vancomycin, Geofrey et al. 2015; Kayange et al. 2010; Seni et al. 2019a observed vancomycin resistance of above 10% in their respective studies (not demonstrated in Table 3).

### Genotypic characterization of human S. aureus isolates

Five human-related studies were reviewed (summarized in Table 4). MSSA genotypic characterization by Staphylococcal protein A (spa) typing in one of the studies revealed 13 different spa types including one new spa type t10779. The most common spa types were t714 and t148 (associated with ST72) followed by t084 (ST15 and ST18) and t223 (ST 22). Furthermore, spa types t314 (ST121), t084 (ST15 and ST18) and t223 were reported to be shared by human and animal isolates in this study (Katakweba et al. 2016). In a more recent study whereby patients were swabbed for S. aureus carriage on admission, after their hospital stay as well as wound swabs for those who had SSTIs, the study further swabbed HCW attending the patients in question. Taking these groups into consideration 60 S. aureus were characterized by MLST, as in the other studies ST distribution was diverse. Eight STs were detected in the 17 isolates from admission of which ST8 (4/17) and ST5 (4/17) were dominant. Nine STs were detected among 13 acquired isolates typed of which ST152 (3/13) and ST5 (2/13) were predominant. Moreover in the 12S. aureus SSTI isolates, eight STs were detected predominated by ST152 (3). Subsequently in a study which used the whole genome sequencing and multi-locus sequence typing (MLST) in their analysis reported 13 different sequence types predominated by ST8 (23%) followed by ST1 (13.3%) and ST152 (10%) (Kumburu et al. 2017). Unfortunately, the limited number of publications on genotypic MSSA data could not reveal dominance in any particular identified strain.

MRSA characterization was reported in three of the five publications (Moremi et al. 2019, 2012; Kumburu et al. 2017; Moremi et al. 2019) screened for the *mecA* resistance conferring gene as well as the Panton–Valentine leukocidin (*pvl*) virulence gene by conventional PCR technique. All analysed 24 MRSA isolates harboured the *mecA* gene hence concordantly agreeing 100% with the phenotypic results. Of note 16.7% of the isolates also harboured the *pvl* gene. Further characterization of the isolates by MLST and *spa* typing was done. These typing methods categorized the isolates

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S. no	Prevalence S. aureus % (n)	Prevalence MRSA % ( <i>n</i> )	Population	Source of S. aureus isolates	Location	References
-	41.4% (157)	37.6% (59)	Healthcare workers adults male and female from June 2016 to October 2016	Nasal carriage	Dar es Salaam (Eastern zone)	Joachim et al. (2018)
5	N	11.8% in ICU patients and 2.1% in ICU HCW	ICU patients (male and female of all age groups) and ICU HCW from October 2012 to March 2013	Nasal carriage	Dar es Salaam (Eastern zone)	Geofrey et al. (2015)
m	34.5% (89) in swabs collected on admission 20% (4) in swabs collected 48 h after admission	24.7% (22) from samples on admission, and 50% (2) in samples collected after 48 h	Patients admitted to emer- gency or medical ward aged 5 and above	Nasal carriage	Dar es Salaam (Eastern zone)	Joachim et al. (2017)
4	40% (114)	8.3% (12)	Healthy children < 5years From April 2010 to June 2010	Nasal carriage	Dar es Salaam (Eastern zone)	Moyo et al. (2014)
Ŋ	Overall 23.2% (223), whereby 26.2% (95), detected in children with acute respiratory infection and 21.4% (128) were detected in children without acute respiratory infection	ц	Children 2–10 years old aged with axillary temperature of ≤ 38 °C Dar es Salaam from April to August 2008 (DSM) and June to December 2008 (Ifakara)	Nasal carriage	Dar es Salaam and Morogoro (Eastern zone)	Chochua et al. (2016)
Q	13.2% (138)	R	Healthy children < 5years born after mass distribution of Azithromycin for trachoma control. The study was con- ducted in 2014	Nasal carriage	Kilosa, Morogoro (Eastern zone)	Bloch et al. (201 <i>7</i> )
~	22% (22)	09%	100 nasal swabs from healthy individuals with no epidemiological connection were collected within urban and peri-urban Morogoro Municipalities	Nasal carriage	Morogoro (Eastern zone)	Katakweba et al. (2016)
$\infty$	13.2% (245)	23.3% (57)	Male and female of all age groups who were subjected to microbiology testing between January 2005 and December 2009 (Retrospec- tive study)	Bacteremia	Dar es Salaam (Eastern zone)	Moyo et al. (2010)
0	28% (12)	Х	Male and female sickle cell anaemic patients of all age groups seeking healthcare at MNH from January 2006 to December 2008	Bacteremia	Dar es Salaam (Eastern zone)	Makani et al. (2015)

Table	e 2 (continued)					
S. no	Prevalence S. aureus % (n)	Prevalence MRSA % (n)	Population	Source of S. aureus isolates	Location	References
10	In blood 36.5% (27), and in pus swabs 52.3% (132)	۳	Neonates aged 3–26 days suspected with neonatal sep- sis. Study duration October 2009–January 2010	Bacteremia and wound swabs	Dar es Salaam (Eastern zone)	Mhada et al. (2012)
	12.2% (18)	44.4% (8)	100 participants (male and female aged 18–80 years) with clinical evidence of Surgical site infection. Dura- tion from September 2011 to February 2012	Wound infections	Dar es Salaam (Eastern zone)	Manyahi et al. (2014)
12	71.4% (132)	0.8% (1)	Skin and soft tissue infections patients of all age groups	Wound infections	Bagamoyo (Eastern zone)	Kazimoto et al. (2018)
13	48.3% (131)	ЖХ	Asymptomatic otitis media (OM)-associated bacteria found in patients living with HIV	Ear colonization	Morogoro (Eastern zone)	Mwambete and Eulambius (2018)
4	Overall 28.4% (57/201) whereby the distribution was 56.3% (40/71) in blood samples, 20.4% (7/34) in pus samples, 23.1% (3/13) and 7.5% (6/80) in urine and spu- tum samples respectively	٣Z	Patients of all age groups pre- senting different infections. The study was conducted between July and November 2019. About 201 clinical samples were included in the study	Bacteremia, wound infection, urinary tract infection and pulmonary infection	Dar es Salaam (Eastern Zone) and Mwanza (Lake Zone)	Mikomangwa et al. (2020)
15	22.7% (5) in Blood culture 9.3% (8) in endocervical culture	53.8 (7/13)	197 qualified woman aged between 20–35 years admit- ted in the maternity wards between Dec. 2017 and April 2018 for postnatal care with clinical diagnosis of puerperal sepsis at MNH	Blood samples and Endocer- vical swabs	Eastern Zone	Kiponza et al. (2019)
16	The overall carriage rate of S. aureus was 21.0% (66). 47% (31) were from preclinical students while 53% (35) from clinical students	1.5% (1)	Healthy students (clinical and Pre clinical) aged 18 years and above. Study duration Febru- ary to June 2013	Nasal carriage	Mwanza (Lake zone)	Okamo et al. (2016)

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Tabl	e 2 (continued)						
S. no	Prevalence S. aureus % (n)	Prevalence MRSA % ( <i>n</i> )	Population	Source of S. aureus isolates	Location	References	
1	<ul> <li>13.9% (129) in patients screened on admission</li> <li>9.6% (29.301) aqured SA after their hospital stay</li> <li>7.7% (11/143) in HCW</li> <li>21.1% (12/57) in patients who developed SSI during their hospital stay</li> </ul>	<ul> <li>- 5.4% (7/129) in patients screened on admission</li> <li>- 10.3% (3/29) acquired MRSA</li> <li>- 1.4% (2/143) in HCW</li> <li>- 3.5% (2/57) in SSI patients</li> </ul>	930 patients were enrolled between Dec.2014 and Sep.2015 from two healthcare centres in Mwanza, Nasal swabs were collected on admission ad discharge, addi- tionally wound swabs were collected in patients who had developed SSI during their hospital stay. Subse- quently nasal swabs from HCW attending the enrolled patients were collected for analysis	Nasal carriage and wound infections	Mwanza (Lake Zone)	Moremi et al. (2019)	
18	21.5%	28% (9)	300 neonates with clinical neonatal sepsis	Bacteremia	Mwanza (Lake zone)	Kayange et al. (2010)	
19	14.8% (8)	50% (4)	402 malnourished children aged < five years Study duration September 2012January 2013	Bacteremia	Mwanza (Lake zone)	Ahmed et al. (2017)	
20	17.0% (23)	34.7% (8)	950 children aged < 5 years with signs and symp- toms of blood stream infec- tions were enrolled from 4 Healthcare facilities including district, regional and referral hospitals with in Mwanza. Study was conducted between July 2016 and October 2017	Bacteremia	Mwanza (Lake Zone)	Seni et al. (2019a)	
21	13.7% (29)	79% (23)	Patients of all age groups and gender with lower limb ulcers seen at the surgical ward or outpatient department from November 2010 to April 2012	Wound infection	Mwanza (Lake zone)	Mbunda et al. (2012)	
22	8.9%(18)	44.4% (8)	Patients of all age groups with chronic lower limb ulcers seen at the surgical ward. 300 wound infection were swabbed between November 2011 and Echniary 2012	Wound infection	Mwanza (Lake zone)	Moremi et al. (2014)	

Tabl	e 2 (continued)					
S. no	Prevalence S. aureus % (n)	Prevalence MRSA % ( <i>n</i> )	Population	Source of S. aureus isolates	Location	References
23	28.6% (18)	19% (3)	65 patients of all age groups who underwent major surgery at BMC between July 2009 and June 2010	Surgical site wound infection	Mwanza (Lake zone)	Mawalla et al. (2011)
24	27.3% (6)	16.7% (1)	Woman aged 14–44 years whohave developed surgical site infections after having undergone a caesarean Sections 345 woman were swabbed between October 2011 and February 2012	Surgical site wound infection	Mwanza (Lake zone)	Mpogoro et al. (2014)
25	29.2% (7)	ж	162 patients of all age group and gender who underwent major limb amputations at BMC between March 2008 and February 2010. 24 of the participants had surgical site infections out of which differ- ent bacteria were recovered as the cause of infection	Surgical wound infection	Mwanza (Lake zone)	Chalya et al. (2012)
26	59.3%	Ϋ́	All patients of all age groups and gender presenting with animal-related injuries at the BMC between September 2007 and August 2011. Post- operative wound infection was the most commonest complication reported lead by <i>S. aureus</i> infections	Surgical site wound infections	Mwanza (Lake zone)	Gilyoma et al. (2013)
27	Overall prevalence 16.1 (25) out of which 28% (7) were iso- lated in HIV positive patients and 72%(18) in HIV negative patients	Ϋ́	The study was done to com- pare magnitude of bacterial resistance to co-trimoxazole/ other antimicrobials among isolates from HIV infected patients on co-trimoxazole prophylaxis and those not on prophylaxis and non-HIV patients attending BMC between January and Octo- ber 2012	Urine and wound swabs	Mwanza (Lake zone)	Marwa et al. (2015)

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S. no	Prevalence S. aureus % (n)	Prevalence MRSA % (n)	Population	Source of S. aureus isolates	Location	References
28	18.2% (34)	41.2% (14)	301 patients aged > 1 year who presented with ear dis- charge for more than 6 weeks and tympanic membrane perforation at the ENT depart- ment between October 2013 and March 2014 were recruited into the study	Ear infection	Mwanza (Lake zone)	Mushi et al. (2016)
29	Overall 22.8% (100) Blood 80% (80) Pus swabs 18% (18) Other infections 2% (2)	Only 78 were subjected to AST.34.6% (27) were MRSA	A total of 3330 microbio- logical culture results scripts representing non-repetitive specimens reported between June 2013 and May 2015 were retrieved and analysed for pathogens and their susceptibility patterns using STATA-11 software	Bacteremia, wound infection, urinary tract infection and pulmonary infection	Mwanza (Lake zone)	Moremi et al. (2016)
30	8.7% (28)	Ϋ́	1828 pregnant woman with significant bacteriuria seek- ing healthcare at different healthcare facilities within the north-western part of the country. The woman were recruited from dispensaries, health centres, district and regional/referral Hospitals	Urinary infection	Mwanza, Shinyanga, Tabora (Lake and Western Zones)	Seni et al. (2019b)
1	69.25	28.5%	74 Patients aged between 8–20 years undergoing surgi- cal treatment at BMC. Majority of the patients were male with history of abuse	Bone fragments collected during surgery	Mwanza (Lake Zone)	Silago et al. (2020)
32	55.3% (68)	Ч	Primary school children (aged 6–15 years) from 4 schools in Moshi municipality assessed/ self-reported respiratory tract infection symptoms. The community-based study was conducted between January and March 2014	Nasal and Throat swabs	Moshi (Northern zone)	Ngocho et al. (2015)

Table 2 (continued)

Table	2 (continued)					
S. no	Prevalence S. aureus % (n)	Prevalence MRSA % ( <i>n</i> )	Population	Source of S. aureus isolates	Location	References
33	66% (103) at 6 weeks, 36% (47) at 3 months and 24% (33) at 6 months. 38% (17) mothers were colonized by <i>S. aureus</i> parallel to their children	X	Children born to HIV positive mothers attending RCH clin- ics to establish prevalence and influence of nasal phar- yngeal bacterial colonization on children. Wasal swabs from children were taken at 6 weeks ( $n = 130$ ) months con- secutively. Mothers (45) of the infants were also swabbed at 3- and 6-month visits (Study duration 2005–2009	Nasal carriage	Moshi (Northern zone)	Kinabo et al. (2013)
34	16% (23)	щ	Patients presenting with SSI, infected diabetic wounds, infected wounds due to trauma, and patients with other infected wounds admit- ted in surgical ward (study duration July 2013 to June 2014)	Wound infections	Moshi (Northern zone)	Kassam et al. (2017)
35	9.3% (35) of which 82.9 (29) were from wound infections, 11% (4) from blood samples and 6% (2) from sputum samples	Only 22 isolates were sub- jected to AST. 27.3% (6) were MRSA	People admitted to the medi- cal or surgical wards at KCMC between 2013 and 2015. The study collected stool, sputum, blood and wound/pus sam- ples from patients of all age groups to describe causative agents of different infections	Wound infection Bloodinfection Bronchial infection	Moshi (Northern zone)	Kumburu et al. (2017)
36	9.1% (6)	Ť	A total of 867 patients aged between 2–5 years with fever above 37 °C were enrolled between January and Octo- ber 2013. 373 urine samples were collected and 66 tested positive for UTI. All <i>S. aureus</i> isolates were recovered from UTI patients	Urinary tract infection	Tanga (Korogwe) (Northern zone)	Mahende et al. (2014)

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lable	(continued)					
S. no	Prevalence S. aureus % (n)	Prevalence MRSA % ( <i>n</i> )	Population	Source of S. aureus isolates	Location	References
37	17% (17)	R	Children aged 0–12 years dis- missed from the hospital with pneumonia diagnosis. 100 children were enrolled in the attempt to characterize aeti- ology of community-acquired pneumonia. (Study duration August 2014–April 2015)	Blood infection	ltigi (Central zone)	Caggiano et al. (2017)
80	11.3% (9)	9%0	Febrile adults and children seeking care at the Mnazi mmoja hospital between March 2012– April 2013	Blood infection	Zanzibar	Onken et al. (2015)
39	6.3% (5)	9%0	Febrile patients seeking outpatient healthcare at 3 dif- ferent district hospitals (Wete, Chake Chake, and Mkoani) on Pemba island between March 2009 to December 2010	Blood infection	Zanzibar	Thriemer et al. (201 <i>2</i> )
NR Not	reported					

Table 2 (continued)

## **Table 3** Antimicrobial resistance rates of S. aureus in humans

Antibiotic (N*)	(% range)	Mean resistance ( <i>n/N</i> *)	(%)	References
Resistance rates in <i>S. aureus</i> isolates from human colonization				
Penicillin(420)	(96–100)	(416/420)	(99%)	Joachim et al. (2018), Geofrey et al. (2015), Joachim et al. (2017), Moremi et al. (2019)
Ampicillin (151)	(84–100)	(133/151)	(88%)	Katakweba et al. (2016), Okamo et al. (2016), Ngocho et al. (2015)
Tetracycline (381)	(9–95)	(103/381)	(27%)	Geofrey et al. (2015), Moyo et al. (2014), Katakweba et al. (2016), Okamo et al. (2016), Moremi et al. (2019)
Erythromycin (402)	(19–100)	(163/402)	(41%)	Joachim et al. (2018), Geofrey et al. (2015), Okamo et al. (2016), Moremi et al. (2019)
Gentamicin (540)	(9–34)	(105/540)	(21%)	Joachim et al. (2018), Joachim et al. (2017), Moyo et al. (2014), Katakweba et al. (2016), Moremi et al. (2019), Ngocho et al. (2015)
Co-trimoxazole (443)	(14–66)	(205/443)	(46%)	Joachim et al. (2018), Geofrey et al. (2015), Moyo et al. (2014), Katakweba et al. (2016), Moremi et al. (2019)
Ciprofloxacin (233)	(4-11)	(15/233)	(6%)	Joachim et al. (2017), Moyo et al. (2014)
Clindamycin (336)	(9–76)	(33/336)	(9.8%)	Joachim et al. (2018), Geofrey et al. (2015), Moremi et al. (2019)
Cefoxitin (546)	(2–100)	(103/546)	(19%)	Joachim et al. (2018, Geofrey et al. (2015), Moyo et al. (2014), Okamo et al. (2016), Moremi et al. (2019)
Resistance rates in <i>S. aureus</i> isolates from invasive (blood-borne) infections				
Penicillin (46)	(23–80)	(40/46)	(87%)	Kayange et al. (2010), Onken et al. (2015), Thriemer et al. (2012)
Ampicillin (50)	(85–100)	(46/50)	(92%)	Mhada et al. (2012, Seni et al. (2019a)
Erythromycin (60)	(20–66)	(38/60)	(63%)	Kayange et al. (2010), Seni et al. (2019a, Thriemer et al. (2012)
Gentamicin (50)	(26–56)	(21/50)	(42%)	Mhada et al. (2012), Seni et al. (2019a)
Co-trimoxazole (69)	(22–96)	(46/69)	(66%)	Kayange et al. (2010), Seni et al. (2019a), Onken et al. (2015), Thriemer et al. (2012)
Clindamycin (32)	(44)	(14/32)	(44%)	Kayange et al. (2010)
Methicillin (245)	(23)	(57/245)	(23%)	Moyo et al. (2010)
Cefoxitin (69)	(0-32)	(17/69)	(25%)	Kayange et al. (2010; Seni et al. (2019a), Onken et al. (2015), Thriemer et al. (2012)
Resistance rates in <i>S. aureus</i> isolates from non-invasive infections				
Penicillin (202)	(30–100)	(183/202)	(91%)	Manyahi et al. (2014), Kazimoto et al. (2018), Moremi et al. (2014), Marwa et al. (2015), Moremi et al. (2012)
Ampicillin (263)	(47–88)	(177/263)	(67%)	Mhada et al. (2012), Mwambete and Eulambius (2018)
Tetracycline (67)	(6–45)	(14/67)	(21%)	Marwa et al. (2015), Mushi et al. (2016), Moremi et al. (2012)
Erythromycin (221)	(14–46)	(81/221)	(37%)	Moremi et al. (2014), Marwa et al. (2015), Mushi et al. (2016), Moremi et al. (2012)
Gentamicin (339)	(11–52)	(110/339)	(32%)	Mhada et al. (2012), Mwambete and Eulambius (2018), Moremi et al. (2014), Mushi et al. (2016), Moremi et al. (2012)
Co-trimoxazole (232)	(43–74)	(115/232)	(50%)	Mwambete and Eulambius (2018), Moremi et al. (2014), Marwa et al. (2015), Mushi et al. (2016) Seni et al. (2019b), Moremi et al. (2012)
Ciprofloxacin (187)	(4–25)	(20/187)	(17%)	Mwambete and Eulambius (2018), Marwa et al. (2015), Mushi et al. (2016)
Clindamycin (42)	(21–63)	(19/42)	(45%)	Moremi et al. (2014), Moremi et al. (2012)
Cefoxitin (226)	(1–100)	(55/226)	(24%)	Manyahi et al. (2014), Kazimoto et al. (2018), Moremi et al. (2014), Mushi et al. (2016), Moremi et al. (2012)

Host	Sample type	Resistant gene	Virulence factor	spa Type	MLST	References
Human	Wound, pus, nasal swabs (24 MRSA strains from previ- ous studies)	mecA (100%)	pvl (16.7%)	t7231, t690, t064, t104,t1855, t7237 t186, t667	ST88, ST1719, ST8,ST1820	Moremi et al. (2012)
Human	Blood, sputum, wound/pus	mecA (33.3%)	<i>pvl</i> (16.7%), tst (6.7%) both in non <i>mecA</i> isolates	ND	ST8, ST1, ST152, ST1719, ST15, ST1847, ST188, ST22, ST239, ST30, ST5, ST580, ST6, ST97	Kumburu et al. (2018)
Human	Nasal swabs	<i>mecA</i> and <i>mecC</i> (None detected)	NS	t714, t148, t084, t002, t223, t314, t311, t015, t451, t690, t1849, t2030, t10779*	ST15, ST18, ST72, ST22, ST5, ST121, ST231, ST45, ST8	Katakweba et al. (2016)
Pig	Nasal swab	<i>mecA</i> and <i>mecC</i> (None detected)	NS	t131	ST80	Katakweba et al. (2016)
Dog	Nasal swabs	<i>mecA</i> and <i>mecC</i> (None detected)	NS	t084, t127, t223, t314, t267, t508, t1476	ST15, ST18, ST1, ST22, ST121,	Katakweba et al. (2016)
Human	Nasal and SSTI swabs	<i>Mec A</i> (exact information disclosed)	pvl (8.3%)	t148,t355, t002, t4353, t095, t223, t311, t690, t1257	ST88, ST3118, ST152, ST5, ST72, ST508, ST22, ST4266 <sup>*</sup> , ST612	Moremi et al. (2019)
Human	Nasal, SSTI swabs	dfrA, dfrG and dfrK. dfrG detected by (37%)	NS	ND	ND	Nurjadi et al. (2014)

 Table 4
 S. aureus genetic diversity as described by the reviewed publications

ND Not done, NS not screened

in four sequence types. ST88 predominated by 52.2% (n = 13), followed by ST1719 at 29.2% (n = 7), ST8 and ST 1820 were assigned to 3 and 1 isolates, respectively. Of the 4 pvl positive isolates three belonged to ST88 and one to ST1820 (a single locus variant of ST 88). All isolates were ultimately divided into two clonal complexes, i.e. CC8 and CC88 (Moremi et al. 2012). In a subsequent study by Moremi et al. (2019) whereby conventional PCR methods were used so screen for mecA and pvl an account on the characterization of some of the MRSA analysed was given. The study reported that one MRSA from a healthcare worker nasal carriage belongs to ST88 and was pvl positive; furthermore, they reported that 2 SSTI-related MRSA were characterized to belong to ST612 (Moremi et al. 2019). Kumburu et al. (2018) on the other hand characterized MRSA using whole genome sequencing method. Of the 30 isolates analysed, 33.3% (n = 10) were confirmed to harbour the mecA resistance conferring gene. Among the identified 10 MRSA, 6 belonged to ST8 and 2 belonged to ST239, the remaining two had unknown sequence type. Furthermore, none of the MRSA strains harboured the *pvl* or toxin shock syndrome (*tst*) virulence genes (Moremi et al. 2016).

Nurjadi et al. 2014 while researching on trimethoprim resistance genes in *S. aureus* isolated from Sub-Saharan Africa determined that 100% of the Tanzanian *S. aureus* in the study which were pheno-typically trimethoprim resistant in fact harboured trimethoprim conferring resistance genes (Nurjadi et al. 2014).

## Prevalence, antibiotic resistance and genotyping of *S. aureus* isolated from animals

As indicated in Table 5, few studies (n=5) have reported on prevalence, antimicrobial resistance and genetic characteristics of *S. aureus* in animals published between 2010 and 2018 in Tanzania.

## Prevalence of S. aureus in animals

Five publication reported on prevalence of *S. aureus* in animals whereby the most examined sample in animals was milk (n = 4). Prevalence of *S. aureus* varied in different geographic areas. Kashoma et al. (2018) and Mohammed et al. (2018) reported the highest prevalence at 49% and 41% in Morogoro, respectively. Suleiman and Mdegela (2018) did not fall far back when observing a prevalence of 37% describing subclinical mastitis in cows on Unguja Island. The lowest prevalence of 33% was recorded in a study aiming at assessing raw milk quality in Arusha and Meru District (Ngasala et al.

Tablé	e 5 S. aureus prevalence in	animal-related samples				
S. no	Prevalence S. aureus % (n)	Prevalence MRSA % (n)	Population	Source of S. aureus isolates	Location	References
	Milk: 49% (49) Cow nasal swabs: 28% (37)	Milk: 35% (17) Cow nasal swabs: 16% (6)	The study was carried out in 3 dairy farms (A, B and C) that belonged to Sokoine University of Agriculture. All farms were located within the same climatic zone. All 3 farms carried out mixed animal farming	Milk samples and cow nasal swabs	Morogoro (Eastern zone)	Kashoma et al. (2018)
7	41% (48)	4% (3)	The study involved 18 of the 29 Wards within Morogoro Municipality. In each of the selected wards, sales points and local shops where raw milk is sold were randomly selected. A total of 117 milk samples. The study was conducted between January and June 2015	Milk samples	Morogoro (Eastern zone)	Mohammed et al. (2018)
m	37% (217)	Ř	Study conducted between January and July 2014 on Unguja Island to establish prevalence of subclinical mastitis in smallholder dairy cows and pattern of antimicrobial susceptibility of major mastitis pathogens	Milk samples	Unguja (Zanzibar)	Suleiman and Mdegela (2018)
4	33% (30)	Ч	105 milk samples from smallholder dairy farmers, milk vendors and retailers were taken within Arusha City and Meru District to assess the quality of raw milk and stakeholders' awareness on milk- borne health risks and factors for poor milk hygiene	Milk samples	Arusha city and Meru district (Northern zone)	Ngasala et al. (2015
2	Pig nasal swabs 4% (4) Dog nasal swabs 11% (11)	Pig swabs: 0% Dog nasal swabs: 0%	100 pigs and 100 dogs dwelling in urban and peri-urban Morogoro Municipality	Nasal swabs	Morogoro (Eastern zone)	Katakweba et al. (2016)

NR Not reported

2015). Generally prevalence of *S. aureus* seemed to be much lower in swabs taken from nasal cavities. Kashoma et al. (2018) who took nasal swabs from cows observed a *S. aureus* prevalence of 28% whereas Katakweba et al. (2016) observed a prevalence of 4% and 11% in pig and dog nasal swabs, respectively.

MRSA detection in milk-associated studies varied tremendously ranging from 4 to 35% (Mohammed et al. 2018; Kashoma et al. 2018), even though both studies were conducted in Morogoro township. Furthermore, MRSA prevalence in isolates recovered from cow nasal cavities was repowered at 16% (Suleiman and Mdegela 2018), whereas no MRSA was detected in pigs and dogs nasal swabs (Kashoma et al. 2018).

### Antibiotic resistance in animal originated S. aureus isolates

Four studies described antibiotic resistance in *S. aureus* using different antibiotic pallets which included cephalexin, gentamicin, kanamycin, neomycin, tetracycline, streptomycin, amoxicillin, cephalexin, clindamycin, vancomycin, ampicillin, co-trimoxazole, oxacillin and cefoxitin. This review, however, focused on the most reported antibiotics in this area as indicated in Table 6.

Most of the reviewed studies reported low antibiotic resistance levels with exception of penicillin and ampicillin which showed mean resistances rates of 85% and 73%, respectively. Suleiman and Mdegela (2018) also further observed resistance against amoxicillin and cephalexin at a rate of 47% and 30%, which was unfortunately not reported by any of the other reviewed studies. Moreover, Tetracycline, co-trimoxazole and cephalexin were reported to have a resistance proportion of 30%, 32% and 30%, respectively.

MRSA detection in all studies was confirmed by resistance against cefoxitin and/or oxacillin, whereby mean resistance rates of 10% and 17% were observed, respectively. An average of 8% resistance against vancomycin was observed, reported in 3/5 studies as described in (Table 6).

# Genotypic characterization of animal originated S. aureus isolates

Genotypic data retrieved from 2 of the 5 studies were reviewed. In both, real-time- PCR (qPCR) was used to confirm *S. aureus* as well as screening for *mecA* resistance conferring gene. Katakweba et al. (2016) additionally screened for *mecC*, a recently discovered *mecA* homologue said to have the potential to be mis-categorized as methicillin-sensitive *S. aureus* (MSSA). None of the two resistance conferring genes were detected in this study; however, *S. aureus* was confirmed in 4 pigs and 11 dog samples, respectively. Further *spa* typing of the pig originating MSSA characterized them

Table 6 Antimicrobial resistance rates of S. aureus in animals \*

Antibiotic (N*)	Range %	Mean resistance ( <i>n/N</i> *)	(%)	References
Resistance rates in different studies in animals				
Penicillin(265)	(72–88)	(225/265)	(85%)	Mohammed et al. (2018), Suleiman and Mdegela (2018)
Ampicillin (99)	(62–100)	(72/99)	(73%)	Katakweba et al. (2016), Kashoma et al. (2018)
Tetracycline (364)	(16–73)	(110/364)	(30%)	Katakweba et al. (2016), Mohammed et al. (2018), Kashoma et al. (2018), Suleiman and Mdegela (2018)
Erythromycin (301)	(5–23)	(28/301)	(9%)	Kashoma et al. (2018), Suleiman and Mde- gela (2018)
Gentamicin (99)	(6–25)	(4/99)	(4%)	Katakweba et al. (2016), Kashoma et al. (2018)
Co-trimoxazole (132)	(22–40)	(42/132)	(32%)	Mohammed et al. (2018), Kashoma et al. (2018)
Vancomycin (132)	(2–11)	(10/132)	(8%)	Katakweba et al. (2016), Mohammed et al. (2018), Kashoma et al. (2018)
Amoxicillin (217)*	(47)	(102/217)	(47%)	Suleiman and Mdegela (2018)
Cephalexin (217)*	(30)	(64/217)	(30%)	Suleiman and Mdegela (2018)
Oxacillin (147)	(0-34)	(25/147)	(17%)	Katakweba et al. (2016), Mohammed et al. (2018), Kashoma et al. (2018)
Cefoxitin (132)	(4–17)	(13/132)	(10%)	Mohammed et al. (2018), Kashoma et al. (2018)

\* Reported in only one study

as spa type t131 associated with ST80. Additionally isolates of dog origin were characterized as spa types t314 (ST121), t084 (ST15 and ST18) and t223 (ST22) all of which were also identified in human nasal isolates reported in the same study.

In the study by Mohammed et al. (2018), both coagulase positive (n=46) and coagulase negative (n=2) *S. aureus* were detected in their milk samples. *mecA* gene was detected in two coagulase positive and one coagulase negative *S. aureus* isolate making this study the first in Tanzania to report on coagulase negative *S. aureus* harbouring the *mecA* gene. Of the 3 MRSA isolates phenotypically detected in the study, one was genotypically coagulase negative *S. aureus* characterized as *spa* type t2603, whereas the other two MRSA's were *spa* un-typable.

## Discussion

The publications under review showed that *S. aureus* was isolated in a number of infections including SSTI's, bloodstream, otitis media, respiratory tract and urinary tract infections staying true to characteristically causing a wide range of infections.

This review observed a *S. aureus* average prevalence ranging from 1 to 45% in human (Fig. 2). However, particularly higher infection rates were typically observed in SSTI's.



**Fig. 2** Distribution of *S. aureus* prevalence in colonization and clinical infections in humans. Based on reviewed publications in Tanzania from 2010 to 2020, slight zonal variations in prevalence of different infections could be observed. Blood born *S. aureus* was more prevalent in the Lake zone. Collectively the review revealed that *S. aureus* was most frequently implicated in association with SSTIs. Prevalence of *S. aureus* in human colonization in all reported zones was generally less than 30% with exception to the northern zone where the prevalence was uncharacteristically high

Furthermore, it was notably observed that *S. aureus* colonization ranged between 28 and 45% (Fig. 2) indicative of considerable circulation of both hospital- and community-associated *S. aureus* in the country. Considering the wide range of infections *S. aureus* can cause especially in various vulnerable populations such as children, elderly and the immune compromised individuals which was also observed in this review, there is need to emphasize the necessity to establish a reliable and sustainable surveillance system to monitor the *S. aureus* bacterium countrywide.

This review discovered that the antibiotic resistance patterns in colonization strains recorded uncharacteristically high proportions. Mean resistance rates of 41%, 27% and 46% against erythromycin, co-trimoxazole and tetracycline could be observed, respectively, whereas resistance rates of the same antibiotics reported in colonization strains in Europe and some parts of Asia did not exceed 20% (Heijer et al. 2013; Lestari et al. 2008). Contrary to resistance pattern in clinical S. aureus observed in this review were in accordance with other reports around Africa (Shittu and Lin 2006; Onwubiko and Sadiq 2011). As in many parts recorded resistance against  $\beta$ lactams was high. Resistance rates ranging from 30 to 65% against erythromycin, gentamicin, co-trimoxazole and clindamycin were also described in this review. The affected antibiotics are readily available in the community and also commonly used for empirical treatment of different cases of bacterial suspected infections. A notable presence of resistance against these antibiotics is an indication of their failure in treatment and a need for broader class antibiotics which are expensive and not accessible for most Tanzanians.

The two zones that reported on MRSA prevalence showed immense variation in their studies; however, on average prevalence was reported to be around 26% (Fig. 2). More than a third of the included studies reported prevalence above 25%. This shows that MRSA prevalence has risen in the last 10 years. Abdulgader's review on MRSA prevalence on the African continent categorized Tanzania as belonging to countries with low MRSA prevalence ranging from 6 to 16% between the years 2001 and 2009 (Abdulgader et al. 2015). This observed abrupt increase should be taken seriously by employing active antibiotic stewardship as well as directing more research efforts towards understanding and preventing the spread of these strains.

A wide spectrum of MSSA *spa types* and sequence types (ST) were identified in the reviewed studies. With the limited information gathered no dominance could be reported. Nevertheless, most *pvl* positive MSSA clones associate with skin infections identified in this review belonged to ST152 which concurs with the findings from

other African-based studies (Ruffing et al. 2017). Genetic characterization of MRSA strains has managed to categorize them into five predominant sequence types, i.e. ST8, ST1719, ST 1820, ST239, ST612 and ST88. Most characterized MRSA were pvl negative consistent with the findings by Abdulgader et al. (2015) who suggested that Africa is predominated by pvl negative MRSA belonging to ST88. Even though some important information was apparent in this review, data concerning MSSA and MRSA genotyping is still limited, Kumburu et al. (2018) was the only study that reported on other virulence factors apart from *pvl*, hence the scarcity of knowledge on S. aureus virulence factors circulating in our communities. Furthermore, genotypic characterization studies predominantly focused on screening for the *mecA* gene; the  $\beta$ -lactam-associated resistance gene, neglecting other resistant markers for other commonly used antibiotic in the country. Katakweba et al. (2016) was the only study that screened for *mecC* gene; a *mecA* homologue which has been identified in other studies to be associated with causing infection in humans with animal contact (Petersen et al. 2013). This homologue can easily be misdiagnosed as MSSA hence causing consequences on patient management as well as on antimicrobial resistance surveillance strategies. In order to make informed decisions about disease prevention and management, there is a need for extended surveillance as well as genotypic based research in Tanzania.

Studies reporting on prevalence, antimicrobial resistance and genetic characteristics of *S. aureus* in animals published between 2010 and 2020 in Tanzania were few; only 5 studies were included in this review, scantly representing a small area in the country. As in human, animal *S. aureus* isolates seem to harbour highly resistance rates against to penicillin and ampicillin antibiotics. Mean resistance rates against oxacillin (17%) and tetracycline (30%) were further able to describe the effects of overusing oxytetracycline previously stated as the most used antibiotic in the livestock keeping business in Tanzania (Caudell et al. 2017).

*Staphylococcus aureus* is one of the leading causes of bovine mastitis which explains the fact that the majority of publications included in this review concerning *S. aureus* in animals addressed the pathogen in clinical and sub-clinical mastitis or in regards to milk production quality. This has been instrumental in the reviews failure to make a link in describing either animals or humans acting as potential *S. aureus* reservoir for each other, as well as the effect of such in both public and animal health. Very few studies on genomic *S. aureus* characterization were available for review and did not suffice in showing such linkage. Even so one publication reported on the

genetic characteristics managed to confirm *S. aureus* strains belonging to the same *spa* type found to colonize both dogs and humans. Unfortunately, the humans and animals involved in this study were epidemiologically unrelated hence making it impossible to link the two. These findings nevertheless present a clear possibility for the *S. aureus* strain to infect across host species.

The primary method for establishing S. aureus antibiogram in the reviewed work was done phenotypically by using the Kirby-Bauer disc diffusion test along with CLSI guidelines. This method has been reported to have inherent shortcomings such as being highly dependent on experimental conditions that may affect end results (Reller et al. 2009). With this fact in mind the Kirby Bauer antibiogram results would have to be confirmed by another test of a different principle to prevent over reporting of resistance, particularly in the confirmation of MRSA and Vancomycin resistant S. aureus strains. In this review, four studies had MRSA confirmed genotypically which showed 100% agreement with the phenotypic Kirby-Bauer disc diffusion test. This agreement between the methods should encourage the use of the Kirby-Bauer disc diffusion test as an antibiotic sensitivity monitoring strategy in the country, since it is the most available and affordable method in the Tanzanian setting.

Information about prevalence, antibiotic susceptibility and genotypic characteristics of S. aureus originating from different hosts and sources in Tanzania still remains scarce. It is evident that the majority of the publications included in this review are from research institutions or tertiary hospitals affiliated to universities with health-related focuses hence most information could be derived from three focal points MNH in Dar es Salaam, BMC Mwanza and, KCMC Moshi, respectively (i.e. Northern, Lake and Eastern zones). According to the Tanzania National Bureau of Statistics the focal regions represented in this review earn higher income per capital compared to the zones whereby no information could be gathered. This implies that most of the data obtained for review are based in relatively well to do regions (Tanzania National Bureau of Statistics 2018). No published data between 2010 and 2020 on the epidemiology of S. aureus were available for the southern and western parts of the country, which are home to some of the most impoverished regions in Tanzania (refer to Fig. 3). It is well known that poverty struck areas also face other challenges as poor healthcare facilities and access, lack of basic needs such as food, proper housing and sanitation, which in turn leaves the population ridden by different infectious diseases (Alvarez-Uria et al. 2016). Furthermore, since the income gained by the poor is mainly for subsistence,



the tendency to resort to self-treatment and or consulting traditional healer is very high (Green et al. 2015) all of which are known indicators associated with driving antibiotic resistance (Byarugaba 2004).

## Limitations

The data from this review cannot be generalized as true prevalence, antibiotic resistance patterns or genotypic characterization of *S. aureus* bacterium in Tanzania, there is lack of *S. aureus* studies representation from other zones. High inter-study variations such as type of specimen analysed, objective of studies, time frame as well as methods employed including criteria set for resistance/MRSA confirmation may have influenced the outcome. Methods used to genetically characterize *S. aureus* in this review were very divergent from simple PCR to whole genome sequencing. The data collected in these methods had different focuses which made comparing the results between studies difficult. Since the main objective in characterizing *S. aureus* or any other bacteria for that matter is understanding the genetic similarities and differences in conferring antibiotic resistance, strain type as well as virulence factors, it would therefore be useful to have a common guideline that allowing inter-laboratory comparability to gather more reliable and holistic data meant to guide treatment and infection prevention strategies in the country.

## Conclusions

With the insight this review has given it is evident that prevalence of *S. aureus* and MRSA in Tanzania is rising, although clear variations between different geographic areas could be observed. Furthermore, non-susceptibility to commonly prescribed antibiotics in community-associated *S. aureus* is also of concern hence the need to emphasize further collection of inf epidemiology (susceptibility patterns and genotypic characterization) data of all bacteria of public health and animal health importance in Tanzania to gain a comprehensive description of the burden of the bacteria as well as enable proper strategies guiding empirical infections treatment and management in the country.

### Abbreviations

AMR: Antimicrobial resistance; AST: Antibiotic susceptibility testing; BMC: Bugando medical centre; CAI: Community-acquired infection; CLSI: Clinical laboratory standard institute; CNS: Coagulase negative Staphylococcus; HAI: Hospital acquired infection; HCW: Healthcare workers; ICU: Intensive care unit; KCMC: Kilimanjaro Christian Medical Centre; LAI: Livestock acquired infections; MLST: Multi-locus sequence typing; MNH: Muhimbili National Hospital; MRSA: Methicillin-resistant *Staphylococcus aureus*; MSSA: Methicillin-sensitive *Staphylococcus aureus*; ND: Not done; NR: Not reported; NS: Not Screened; OM: Otitis media; RCH: Reproductive and child health; Spa: Staphylococcus protein A; SSI: Surgical site infection; SSTI's: Skin and soft tissue infections.

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### Authors' contributions

TM and TK were responsible for the concept, design, reviewing studies for the manuscript: JM contributed in literature search strategies and data extraction method: MB, RM and MM took part in revising important contents of the manuscript: TM drafted the manuscript: TK and SLB critically reviewed the manuscript for publication. All authors read and approved the final manuscript.

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### Availability of data and materials

Not applicable.

### Declarations

**Ethics approval and consent to participate** Not applicable.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare that they have no competing interests.

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#### References

- Abdulgader SM, Shittu AO, Nicol MP, Kaba M (2015) Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* in Africa: a systematic review. Front Microbiol 6:348
- Ahmed M, Mirambo MM, Mushi MF, Hokororo A, Mshana SE (2017) Bacteremia caused by multidrug-resistant bacteria among hospitalized malnourished children in Mwanza, Tanzania: a cross sectional study. BMC Res Notes 10(1):62
- Alvarez-Uria G, Gandra S, Laxminarayan R (2016) Poverty and prevalence of antimicrobial resistance in invasive isolates. Int J Infect Dis 52:59–61
- Bloch EM, West SK, Mabula K, Weaver J, Mrango Z, Munoz B et al (2017) Antibiotic resistance in young children in Kilosa District, Tanzania 4 years after mass distribution of azithromycin for trachoma control. Am J Trop Med Hyg 97(3):815–818
- Byarugaba DK (2004) A view on antimicrobial resistance in developing countries and responsible risk factors. Int J Antimicrob Agents 24(2):105–110
- Caggiano S, Ullmann N, De Vitis E, Trivelli M, Mariani C, Podagrosi M et al (2017) Factors that negatively affect the prognosis of pediatric communityacquired pneumonia in district hospital in Tanzania. Int J Mol Sci 18(3):623
- Caudell MAQM, Subbiah M, Call DRRC, Roulette JW et al (2017) Antimicrobial use and veterinary care among agro-pastoralists in Northern Tanzania. PLoS ONE 12(1):e0170328
- Chalya PL, Mabula JB, Dass RM, Ngayomela IH, Chandika AB, Mbelenge N et al (2012) Major limb amputations: a tertiary hospital experience in northwestern Tanzania. J Orthop Surg Res 7:18
- Chochua S, D'Acremont V, Hanke C, Alfa D, Shak J, Kilowoko M et al (2016) Increased nasopharyngeal density and concurrent carriage of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are associated with pneumonia in febrile children. PLoS ONE 11(12):725
- David MZ (2010) Community-associated methicillin-resistant *Staphylococ-cus aureus*: epidemiology and clinical consequences of an emerging epidemic. Clin Microbiol Rev 23:616–687
- den Heijer CD, van Bijnen EM, Paget WJ, Pringle M, Goossens H, Bruggeman CA et al (2013) Prevalence and resistance of commensal *Staphylococcus*

*aureus*, including meticillin-resistant *S. aureus*, in nine European countries: a cross-sectional study. Lancet Infect Dis 13(5):409–415

Founou RC, Founou LL, Essack SY (2017) Clinical and economic impact of antibiotic resistance in developing countries: a systematic review and meta-analysis. PLoS ONE 12(12):e0189621

Geofrey A, Abade A, Aboud S (2015) Methicillin-resistant *Staphylococcus aureus* (MRSA) colonization among intensive care unit (ICU) patients and health care workers at Muhimbili national hospital Dar Es Salaam, Tanzania. Pan Afr Med J. https://doi.org/10.11604/pamj.2015.21.211.420

Gilyoma JM, Mabula JB, Chalya PL (2013) Animal-related injuries in a resourcelimited setting: experiences from a Tertiary health institution in northwestern Tanzania. World J Emerg Surg 8(1):7

Green JA, Norris P, Bukhari NI (2015) Self-medication, home remedies, and spiritual healing: common responses to everyday symptoms in Pakistan AU—Anwar, Mudassir. Health Psychol Behav Med 3(1):281–295

Haddadin AS, Fappiano SA, Lipsett PA (2002) Methicillin resistant Staphylococcus aureus (MRSA) in the intensive care unit. Postgrad Med J 78(921):385–392

Hudzicki J (2009) Disk diffusion susceptibility test protocol. Kirby-Bauer. Amecan Society for Microbiology, Washington

Jevons MP (1961) "Celbenin"—resistant Staphylococci. Br Med J 1(5219):124–125

Joachim A, Moyo SJ, Nkinda L, Majigo M, Mmbaga E, Mbembati N et al (2017) Prevalence of methicillin-resistant *Staphylococcus aureus* carriage on admission among patients attending regional hospitals in Dar es Salaam, Tanzania. BMC Res Notes 10(1):417

Joachim A, Moyo SJ, Nkinda L, Majigo M, Rugarabamu S, Mkashabani EG et al (2018) Nasal carriage of methicillin-resistant *Staphylococcus aureus* among health care workers in tertiary and regional Hospitals in Dar es Salam, Tanzania. Int J Microbiol 2018:7

Kashoma IP, Lalata EP, Maiga CJ, Mtemela BO, Medardus JJ (2018) Prevalence and antimicrobial susceptibility profiles of *Staphylococcus aureus* from cow's milk, nasal and environmental swabs in selected dairy farms in Morogoro Tanzania. Tanzan Vet J 30(2):61–75

Kassam NA, Damian DJ, Kajeguka D, Nyombi B, Kibiki GS (2017) Spectrum and antibiogram of bacteria isolated from patients presenting with infected wounds in a Tertiary Hospital, northern Tanzania. BMC Res Notes 10(1):757

Katakweba AS, Muhairwa AP, Espinosa-Gongora C, Guardabassi L, Mtambo MM, Olsen JE (2016) spa typing and antimicrobial resistance of *Staphylococcus aureus* from healthy humans, pigs and dogs in Tanzania. J Infect Dev Ctries 10(2):143–148

Kayange N, Kamugisha E, Mwizamholya DL, Jeremiah S, Mshana SE (2010) Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza-Tanzania. BMC Pediatr 10(1):1

Kazimoto T, Abdulla S, Bategereza L, Juma O, Mhimbira F, Weisser M et al (2018) Causative agents and antimicrobial resistance patterns of human skin and soft tissue infections in Bagamoyo, Tanzania. Acta Trop 186:102–106

Kinabo GD, van der Ven A, Msuya LJ, Shayo AM, Schimana W, Ndaro A et al (2013) Dynamics of nasopharyngeal bacterial colonisation in HIV-exposed young infants in Tanzania. Trop Med Int Health TM IH 18(3):286–295

Kiponza R, Balandya B, Majigo MV, Matee M (2019) Laboratory confirmed puerperal sepsis in a national referral hospital in Tanzania: etiological agents and their susceptibility to commonly prescribed antibiotics. BMC Infect Dis 19(1):690

Kumburu HH, Sonda T, Mmbaga BT, Alifrangis M, Lund O, Kibiki G et al (2017) Patterns of infections, aetiological agents and antimicrobial resistance at a tertiary care hospital in northern Tanzania. Trop Med Int Health TM IH 22(4):454–464

Kumburu HH, Sonda T, Leekitcharoenphon P, van Zwetselaar M, Lukjancenko O, Alifrangis M, et al (2018) Hospital epidemiology of methicillin-resistant staphylococcus aureus in a tertiary care hospital in Moshi, Tanzania, as determined by whole genome sequencing. BioMed Res Int 2018:2087693

Lestari ES, Severin JA, Filius PMG, Kuntaman K, Duerink DO, Hadi U, Wahjono H, Verbrugh HA (2008) Antimicrobial resistance among commensal isolates of *Escherichia coli* and *Staphylococcus aureus* in the Indonesian population inside and outside hospitals. Eur J Clin Microbiol Infect Dis 27:45–51

Lozano C, Gharsa H, Ben Slama K, Zarazaga M, Torres C (2016) *Staphylococcus aureus* in animals and food: methicillin resistance, prevalence and population structure. A review in the African continent. Microorganisms  $4(1){:}12\,$ 

Mahende C, Ngasala B, Lusingu J, Butichi A, Lushino P, Lemnge M et al (2014) Aetiology of acute febrile episodes in children attending Korogwe District Hospital in north-eastern Tanzania. PLoS ONE 9(8):e104197

Makani J, Mgaya J, Balandya E, Msami K, Soka D, Cox SE et al (2015) Bacteraemia in sickle cell anaemia is associated with low haemoglobin: a report of 890 admissions to a tertiary hospital in Tanzania. Br J Haematol 171(2):273–276

Manyahi J, Matee MI, Majigo M, Moyo S, Mshana SE, Lyamuya EF (2014) Predominance of multi-drug resistant bacterial pathogens causing surgical site infections in Muhimbili National Hospital, Tanzania. BMC Res Notes 7:500

Marwa KJ, Mushi MF, Konje E, Alele PE, Kidola J, Mirambo MM (2015) Resistance to cotrimoxazole and other antimicrobials among isolates from HIV/ AIDS and Non-HIV/AIDS patients at Bugando Medical Centre, Mwanza, Tanzania. AIDS Res Treat 2015:8

Mawalla B, Mshana SE, Chalya PL, Imirzalioglu C, Mahalu W (2011) Predictors of surgical site infections among patients undergoing major surgery at Bugando Medical Centre in Northwestern Tanzania. BMC Surg 11:1–7

Mbunda F, McHembe MD, Chalya PL, Rambau P, Mshana SE, Kidenya BR et al (2012) Experiences with surgical treatment of chronic lower limb ulcers at a tertiary hospital in northwestern Tanzania: a prospective review of 300 cases. BMC Dermatol 12:17

Mhada TV, Fredrick F, Matee MI, Massawe A (2012) Neonatal sepsis at Muhimbili national hospital, Dar es Salaam, Tanzania; aetiology, antimicrobial sensitivity pattern and clinical outcome. BMC Public Health 12:904

Mikomangwa WP, Bwire GM, Kilonzi M, Mlyuka H, Mutagonda RF, Kibanga W et al (2020) The existence of high bacterial resistance to some reserved antibiotics in tertiary hospitals in Tanzania: a call to revisit their use. Infect Drug Resist 13:1831–1838

Mohammed J, Ziwa MH, Hounmanou YMG, Kisanga A, Tuntufye HN (2018) Molecular typing and antimicrobial susceptibility of methicillin-Resistant *Staphylococcus aureus* isolated from bovine milk in Tanzania. Hindawi Int J Microbiol 2018:1–6

Moremi N, Mshana SE, Kamugisha E, Kataraihya J, Tappe D, Vogel U et al (2012) Predominance of methicillin resistant *Staphylococcus aureus*—ST88 and new ST1797 causing wound infection and abscesses. J Infect Dev Ctries 6(8):620–625

Moremi N, Mushi MF, Fidelis M, Chalya P, Mirambo M, Mshana SE (2014) Predominance of multi-resistant gram-negative bacteria colonizing chronic lower limb ulcers (CLLUs) at Bugando Medical Center. BMC Res Notes 7(1):211

Moremi N, Claus H, Mshana SE (2016) Antimicrobial resistance pattern: a report of microbiological cultures at a tertiary hospital in Tanzania. BMC Infect Dis 16(1):756

Moremi N, Claus H, Vogel U, Mshana SE (2019) The role of patients and healthcare workers *Staphylococcus aureus* nasal colonization in occurrence of surgical site infection among patients admitted in two centers in Tanzania. Antimicrob Resist Infect Control 8:102

Moyo S, Aboud S, Kasubi M, Maselle SY (2010) Bacteria isolated from bloodstream infections at a tertiary hospital in Dar es Salaam, Tanzania– antimicrobial resistance of isolates. S Afr Med J S Afr Tydskr Geneeskd 100(12):835–838

Moyo SJ, Aboud S, Blomberg B, Mkopi N, Kasubi M, Manji K et al (2014) High nasal carriage of methicillin-resistant *Staphylococcus aureus* among healthy Tanzanian under-5 children. Microb Drug Resist (larchmont NY) 20:82–88

Mpogoro FJ, Mshana SE, Mirambo MM, Kidenya BR, Gumodoka B, Imirzalioglu C (2014) Incidence and predictors of surgical site infections following caesarean sections at Bugando Medical Centre, Mwanza, Tanzania. Antimicrob Resist Infect Control 3:25

Mushi MF, Mwalutende AE, Gilyoma JM, Chalya PL, Seni J, Mirambo MM et al (2016) Predictors of disease complications and treatment outcome among patients with chronic suppurative otitis media attending a tertiary hospital, Mwanza Tanzania. BMC Ear Nose Throat Disord 16:1

Mwambete KD, Eulambius M (2018) High prevalence of antibiotic-resistant otitis media-associated bacterial flora of asymptomatic people living with HIV at Morogoro Hospital, Tanzania. J Int Assoc Provid AIDS Care 17:2325958218759761

- Ngasala JHNH, Madundo M, Mtambo A (2015) Assessment of raw milk quality and stakeholders' awareness on milk-borne health risks in Arusha City and Meru District, Tanzania. Trop Anim Health Prod 47:927–932
- Ngocho JSAC, Sariko M, Mmbaga BT, Kibiki GS (2015) Bacterial etiology of respiratory tract infections among ambulatory school children in Moshi Municipality, Tanzania. Sci J Public Health 3(5):625–632
- Nurjadi D, Olalekan AO, Layer F, Shittu AO, Alabi A, Ghebremedhin B et al (2014) Emergence of trimethoprim resistance gene dfrG in *Staphylococcus aureus* causing human infection and colonization in sub-Saharan Africa and its import to Europe. J Antimicrob Chemother 69(9):2361–2368
- Okamo B, Moremi N, Seni J, Mirambo MM, Kidenya BR, Mshana SE (2016) Prevalence and antimicrobial susceptibility profiles of *Staphylococcus aureus* nasal carriage among pre-clinical and clinical medical students in a Tanzanian University. BMC Res Notes 9(1):1–6
- O'Neill J (2016) Tackling drug-resistant infections globally: final report and recommendations
- Onken A, Said AK, Jorstad M, Jenum PA, Blomberg B (2015) Prevalence and antimicrobial resistance of microbes causing bloodstream infections in Unguja, Zanzibar. PLoS ONE 10(12):e0145632
- Onwubiko NE, Sadiq NM (2011) Antibiotic sensitivity pattern of *Staphylococcus aureus* from clinical isolates in a tertiary health institution in Kano, Northwestern Nigeria. Pan Afr Med J 8(4):1–7
- Petersen A, Stegger M, Heltberg O, Christensen J, Zeuthen A, Knudsen LK et al (2013) Epidemiology of methicillin-resistant *Staphylococcus aureus* carrying the novel *mecC* gene in Denmark corroborates a zoonotic reservoir with transmission to humans. Clin Microbiol Infect 19(1):E16–E22
- Reller LB, Weinstein M, Jorgensen JH, Ferraro MJ (2009) Antimicrobial susceptibility testing: a review of general principles and contemporary practices. Clin Infect Dis 49(11):1749–1755
- Ruffing U, Alabi A, Kazimoto T, Vubil DC, Akulenko R, Abdulla S et al (2017) Community-associated *Staphylococcus aureus* from sub-Saharan Africa and Germany: a cross-sectional geographic correlation study. Sci Rep 7(1):154
- Seni J, Mwakyoma AA, Mashuda F, Marando R, Ahmed M, DeVinney R et al (2019a) Deciphering risk factors for blood stream infections, bacteria species and antimicrobial resistance profiles among children under five years of age in North-Western Tanzania: a multicentre study in a cascade of referral health care system. BMC Pediatr 19(1):32

- Seni J, Tito JN, Makoye SJ, Mbena H, Alfred HS, van der Meer F et al (2019b) Multicentre evaluation of significant bacteriuria among pregnant women in the cascade of referral healthcare system in North-western Tanzania: bacterial pathogens, antimicrobial resistance profiles and predictors. J Glob Antimicrob Resist 17:173–179
- Shittu AO, Lin J (2006) Antimicrobial susceptibility patterns and characterization of clinical isolates of *Staphylococcus aureus* in KwaZulu-Natal province, South Africa. BMC Infect Dis 6:125
- Silago V, Mushi MF, Remi BA, Mwayi A, Swetala S, Mtemisika CI et al (2020) Methicillin resistant *Staphylococcus aureus* causing osteomyelitis in a tertiary hospital, Mwanza, Tanzania. J Orthop Surg Res 15(1):95
- Suleiman R (2018) Local and regional variations in conditions for agriculture and food security in Tanzania: a review
- Suleiman TSKE, Mdegela RH (2018) Prevalence of bovine subclinical mastitis and antibiotic susceptibility patterns of major mastitis pathogens isolated in Unguja island of Zanzibar, Tanzania. Trop Anim Health Prod 50(2):259–266
- Tanzania National Bureau of Statistics (2018) Highlights for the third quarter (July–September) gross domestic product. United republic of Tanzania, National Bureau of Statistics Ministry of Finance and Planning
- Thriemer K, Ley B, Ame S, von Seidlein L, Pak GD, Chang NY et al (2012) The burden of invasive bacterial infections in Pemba, Zanzibar. PLoS ONE 7(2):e30350
- WHO (2014) Antimicrobial resistance: Global report on surveillance Geneva. WHO, Geneva
- WHO (2017) Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. WHO, Geneva
- Zetola N, Francis JS, Nuermberger EL, Bishai WR (2005) Community-acquired meticillin-resistant *Staphylococcus aureus*: an emerging threat. Lancet Infect Dis 5(5):275–286

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