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Antimicrobial resistance trends of *Escherichia coli* and *Staphylococcus aureus* isolated from clinical blood cultures in Namibia: a nine-year (2011-2019) retrospective study

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Abstract

Background Due to inadequate data on the antimicrobial resistance situation among the two predominant bacteremia-causing pathogens, the objective was to analyze the nine-year antimicrobial resistance trends of *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*) from blood cultures.

Methods A nine-year countrywide register data (2011–2019) covering all microbiological specimen tests performed at the Namibia Institute of Pathology (NIP) were analyzed. Antimicrobial susceptibility testing (AST) was performed by disk diffusion and VITEK-2, along with Quality Control parallels to validate AST results. This was interpreted in accordance with the prevailing CLSI breakpoints. Data analysis included descriptive statistics and chi-square, Multiple Antibiotic Resistance (MAR) Index and Mann-Kendall trend tests ($\alpha = 0.05$).

Results The original findings comprised 30,266 bacterial organisms isolated from 37,765 blood cultures. After adjusting for putative contaminants, the Gram-negative bacterial species (GNB) group comprised most of the major findings, including *E. coli* (15.2%), *K. pneumoniae* (13.2%), *S. enterica* (3.2%), and *P. aeruginosa* (2.8%). *S. aureus* (15.3%) and *E. faecalis* (6.5%) comprised the majority of gram-positive bacterial (GPB) organisms. *E. coli* and *S. aureus* were commonly isolated from the 15–59 and 0–4 age groups, respectively. Significant upward trends (for amoxicillin-clavulanate and 3rd generation cephalosporins) and downward trends (oxacillin and gentamicin) were found. In 2019, the following resistance to *E. coli* were observed: ceftriaxone (37%), ciprofloxacin (29.4%), gentamicin (18.8%), and meropenem (0.9%). In 2019, *S. aureus* resistance to oxacillin was 18.8%. The proportions of ESBLs increased from 22.1% ($n = 79$) to 42% ($n = 116$) (ss:1.75, $p = 0.03$). Whilst methicillin-resistant *S. aureus* (MRSA) reduced from 47.2% to 18.8% in 2019 (ss: −2.05, $p = 0.03$). The proportion of multi-drug resistant *E. coli* increased to 47.8% ($p < 0.01$), whilst extensive-drug resistant *E. coli* decreased to 3% ($p = 0.04$) and no potential pan-drug resistant organisms were found.

Conclusions To our knowledge, this is the first study to provide a 9-year insight into the trends of antimicrobial resistance in clinical blood culture isolates in Namibia. ESBLs showed an increasing trend, whilst MRSAs declined due to potential improvements in infection prevention & control (IPC) and antimicrobial stewardship. Resistance levels

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of above 20% to critical antimicrobials (i.e. amoxicillin-clavulanate, ceftriaxone, ciprofloxacin, and erythromycin) is worrying for the management of bloodstream infections caused by ESBLs or MRSAs. Overall, this study serves as a baseline for future surveillance work and highlights the continuous need for AST-guided therapy.

Keywords Antimicrobial resistance, Antibiotic, ESBL, MRSA, Blood cultures

Background

In 2019, an estimated 4.95 million (95% uncertainty interval: 3.62- 6.57) deaths associated with bacterial antimicrobial resistance (AMR) occurred globally, with about 1.07 million (0.847–1.340) of these occurring in sub-Saharan Africa [1]. Bloodstream infections (BSI's) involving methicillin-resistant *Staphylococcus aureus* and gram-negatives such as *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Enterobacter sp.* have previously been associated with high mortality [2, 3]. Recently, the causative agents and antimicrobial susceptibility profiles of bacteremia have undergone shifts [4, 5]. In Namibia, the blood culture AMR data over the years remain unpublished.

The 2015 global action plan on antimicrobial resistance calls for international and national efforts aimed at combating AMR [6]. Strengthening surveillance systems is recognized as one of the key strategies in combating AMR [6–8]. Namibia is enrolled in the Global Antimicrobial Surveillance System (GLASS) but annual surveillance data is lacking [9, 10].

In general, the WHO reports that information on the incidence and prevalence of antimicrobial resistance is lacking and is urgently required [11, 12]. Similarly, historic and current AMR trend data from Namibia remain limited. It therefore becomes difficult to comprehensively understand and estimate both the current and future national burden of AMR. This is necessary for the formulation of evidence-based policies and AMR combating strategies.

The objective of this study was to analyse the 9-year antimicrobial resistance trends of *S. aureus* and *E. coli* from blood cultures within the Namibian setting. This analyzes contributes to the knowledge gap in AMR and provides guidance for future AMR prevention and surveillance actions.

Methods

Study setting

A countrywide retrospective record review was performed using laboratory data obtained from the Namibia Institute of Pathology (NIP), the national public health laboratory. Healthcare provision was majorly provided by the government, with about 85% of the population serviced by public health facilities and non-profit private facilities http://www.aho.afro.who.int. The network of NIP laboratories across the country provides laboratory services to patients from all tiers of the public health system (1 referral and 4 intermediate hospitals; 30 district hospitals; 44 health centers; 265 clinics; 1150 outreach points).

The dataset extracted from the NIP database included information on all specimens during January 2011-December 2019. The data included the patient's date of birth and gender, specimen type and collection date, the microbiological culture result and the antimicrobial sensitivity testing (AST) result of the isolate.

Study population

The focus of this study was on nationwide blood culture *E. coli* and *S. aureus* isolates with AST results.

Laboratory procedures and information management

Microbiological cultures and AST were performed in accordance with the prevailing Clinical Laboratory Standards Institute (CLSI) guidelines, https://clsi.org/standards/products/microbiology/documents/m100/. Aerobic blood culture bottles were incubated for 5 days using the automated BACTEC (Becton Dickinson, MD, USA) or manual incubation bottles (Oxoid Ltd., Hampshire, United Kingdom) and cultured for 48 hours on blood or MacConkey agar. The performance of automated or manual practices was dependent on the resources and equipment available in each laboratory, although all adhered to the CLSI guidelines. Gram staining and sub-culturing were only performed for visually positive cultures (1 CFU/ml), before the identification of *E. coli* and *S. aureus* with 10S or 20E GNB Analytical Profile Index (API) kits (bioMériuex, Mercy l'Etoile, France). AST was performed with either VITEK®2XL or the Kirby Bauer disk diffusion on Mueller Hinton agar with 0.5 McFarland standardized suspensions. Zone interpretations were made in accordance with prevailing CLSI breakpoints [13]. The isolates were evaluated against 20 (*E.* coli) and 22 (*S. aureus*) antimicrobials, which are tabulated in Additional file 1. All the procedures were validated and performed with Quality Control (QC) parallels, *E. coli* ATCC25922 and *S. aureus* ATCC29213. The results were captured and stored in MEDITECH (https://ehr.meditech.com/) - a centralized Laboratory Information Management System.

Data processing

Data cleaning

The data was checked for completeness, where the missing variables were recorded as "NA". The age of the

patient was calculated from the date of birth and the specimen collection date. Age was also assigned as "NA" if the specimen collection date preceded the date of birth (i.e. negative age). De-duplication could not be done on the database, as there is no unique patient identifier for individuals in the Namibian healthcare system.

Data analysis

Categorical variables (type of specimen, microbe identity, age, and sex of patients) were given as frequencies (n) and percentages (%) of their respective totals in tables or graphs. Culture positivity was calculated as a fraction of the number of culture positives (numerator) over the total cultures (positives and negatives). The positivity rate was also recalculated by excluding putative contaminants (e.g. *Staphylococcus epidermidis, S. hominis, S. haemolyticus*, *Micrococcus* spp, *Bacillus* spp., and diphtheroids).

AST results were given as the proportion of resistant isolates (n) and percentage resistant (%R) with its 95% confidence interval (95% CI) for each isolate-antimicrobial combination. The frequency and resistance were given for each successive year.

The weighted mean percentage resistance and standard deviation were calculated to provide an understanding of the overall antimicrobial susceptibility pattern. Trends (increases and/or decreases) were determined using Mann-Kendall trend analysis for non-parametric data with a significance set at an alpha value of 0.05. Multiple Antibiotic Resistance Index was determined as per the formula $MAR_{index}=a$ (number of resistant antimicrobials)$\div b$ (total number of antimicrobials tested against isolate). An index of ≤0.2 represents less exposure of the isolate to antimicrobials and > 0.2 indicates a high-risk contamination source [14]. Putative extended-spectrum beta-lactamase (ESBL) producing *E. coli* was defined as any isolate showing resistance to any 3rd generation cephalosporin (e.g. ceftriaxone, cefotaxime, and ceftazidime). Multi-drug resistant (MDR), extensively-drug resistant (XDR), and pan-drug resistant (PDR) definitions by Magiorakos *et.al* (2012) [15] were applied to the *E. coli* dataset, except that XDR and potential PDR were applied if at least 7 antimicrobial classes were tested for the isolate (Additional file 1). Phenotypic oxacillin resistance was used as a proxy for methicillin-resistant *Staphylococcus aureus* (MRSA). An MRSA was considered as an MDR by virtue of being an MRSA, without additional resistance analysis of other classes. The antimicrobial classes applied for the classifications of MDR, XDR, and PDR are given in Additional file 1.

The data cleaning, conversion and analyses were achieved with Microsoft® Excel 2021, BacLink-WHONET 2021 https://whonet.org and R version 4.4.2 (packages: ggplot, dplyr, tidyr, Kendall, trend and survey).

Table 1 Proportions of bacteria identified from blood cultures (*N* = 37,765) based on original reports (*N* = 30,266) and adjusted data (*N* = 15,288), (2011 – 2019)

	Original N	Original %	Adjusted[#] N	Adjusted[#] %
Gram-negative bacteria	**8090**	**26.8**	**8090**	**52.9**
Escherichia coli	2319	7.7	2319	15.2
Klebsiella pneumoniae ss. pneumoniae	2011	6.6	2011	13.2
Salmonella enterica	491	1.6	491	3.2
Pseudomonas aeruginosa	430	1.4	430	2.8
Enterobacter cloacae	285	0.9	285	1.8
Klebsiella oxytoca	225	0.7	225	1.5
Acinetobacter baumannii	200	0.7	200	1.3
Other gram-negative bacterial species	2129	7	2129	13.9
Gram-positive bacteria	**22062**	**72.9**	**7084**	**46.3**
Staphylococcus aureus sS. aureus	2341	7.7	2341	15.3
Enterococcus faecalis	987	3.2	987	6.5
Coagulase negative staphylococcal species	13435	44.4	Excluded	Excluded
Diphtheroids, *Bacillus* spp., *Micrococcus* spp.	1543	5.1	Excluded	Excluded
Other gram-positive bacterial species	3756	12.4	3756	24.6
Other bacterial species/ groups	**114**	**0.38**	**114**	**0.7**
Anaerobic organisms	68	0.2	68	0.4
Several bacterial species present	23	0.07	23	0.15
Mycobacterial organisms	23	0.07	23	0.15
Total	**30266**	**100**	**15288**	**100**

[#] Excluding coagulase negative staphylococci (*Staphylococcus epidermidis, S. hominis, S. haemolyticus*), *diphtheroids, Bacillus spp,* and *Micrococcus spp*

Results

Microbial profile: blood culture findings

A total of 37,765 blood cultures were collected between 2011 and 2019. A minimum of 2,582 and a maximum of 5,948 blood culture specimens were recorded in the years 2014 and 2011 respectively (Additional file 2).

Overall, 30,266 bacterial isolates were identified from the 37,765 blood cultures (Table 1). Additionally, in 23 of the blood cultures, there were several bacterial species present. Gram-positive and gram-negative organisms constituted 72.9% and 26.8% of the culture findings, respectively. The proportions of anaerobes, cultures with multiple bacterial species, and mycobacterial organisms constituted the remaining total of 0.38%.

While analyzing the bacterial findings, a high proportion of coagulase-negative staphylococci (CNS, e.g. *S. epidermidis, S. hominis,* and *S. haemolyticus*), as well as diphtheroids, *Bacillus* spp and *Micrococcus* spp was noted. They comprised 67.8% of all gram-positive and 49.5% of all findings respectively (Table 1). While *S.*

epidermidis and CNS have previously been described also as contaminants in clinical specimens [16–18], we also performed the data analysis without them and the other above mentioned skin-related microbes. Hence, the adjusted proportions reduced to 52.9% and 46.3% for gram-negatives and gram-positives, respectively (Table 1). The original bacterial culture positivity rate of 80.1% (30,266/37,765) was also reduced to 40.5% (15,288/37,765) after the adjustment.

Based on the adjusted reports (Table 1) the most common pathogens in decreasing order were, *S. aureus* ($n=2341$, 15.3%), *E. coli* (2319, 15.2%), *Klebsiella pneumoniae* (2011, 13.2%), *Salmonella enterica* (491, 3.2%), *Pseudomonas aeruginosa* (430, 2.8%), *Enterobacter cloacae* (285, 1.8%), *Klebsiella oxytoca* (225, 1.5%) and *Acinetobacter baumanii* (200, 1.3%). The 9-year average of *E. coli* and *S. aureus* isolates was 258 (minimum: 184 – maximum: 357) and 260 (min: 196 – max: 484) respectively. The categories "other gram-negative/positive bacterial species" were comprised of different species, each with a prevalence below 1% in the samples. Additional file 2 provides a detailed analysis of the yearly counts and percentages of these isolates.

Table 2 Demographic background information on blood cultures positive for *Escherichia coli* and *Staphylococcus aureus* in 2011–2019, Namibia

	E. coli (N = 2,319)		S. aureus (N = 2,341)		χ^2, *p-value*
	n	%	n	%	
Year					
2011	357	15.4	484	21	2.1, 0.98
2012	228	9.8	257	11	
2013	260	11.2	296	13	
2014	208	9	196	8.4	
2015	184	7.9	222	9.5	
2016	256	11	214	9.1	
2017	298	12.9	250	11	
2018	252	10.9	208	8.9	
2019	276	11.9	214	9.1	
Sex					
Female	1231	54.5	1073	47	1.13, 0.57
Male	1027	45.5	1203	53	
NA[1]	61	2.6	65	2.8	
Sex ratio (f/m)	1.2		0.89		
Age					
< 5	694	32.8	1035	48	9.8, 0.04
5 - 14	109	5.1	198	9.1	
15 - 59	958	45.2	798	37	
60 >	358	16.9	135	6.2	
NA[1]	200	8.6	175	7.5	
median	30	-	8	-	
IQR	48	-	34	-	

[1] Missing information

IQR – Interquartile range

Escherichia coli and *Staphylococcus aureus* blood culture distribution

For the total period (2011–2019), the two main bacteria species isolated were *S. aureus* (2341, 15.3%) and *E. coli* (2319, 15.2%). The 9-year average of *S. aureus* and *E. coli* isolates was 260 (min: 196 – max: 484, %: 8.4–20.7) and 258 (min: 184 – max: 357, %: 7.9–15.4), respectively. The highest number of isolations for both bacterial species was collected in 2011. Thereafter, for each of the successive years, the isolate counts either increased or decreased by ±5% (i.e. percentage change) from the previous year's count, for both organisms (min- max:184–298; %: 7.9–12.9) (Table 2). There was no difference in the year-to-year frequency of isolates (p=0.98), nor differences in the sex distribution (p=0.57) for both *E. coli* and *S. aureus*. Among *E. coli,* 45.2% (958/2,319) of the isolates were from the age category of 15–59 whilst *S. aureus* were mainly (48%, 1,035/2,341) from the less than 5 age group. Hence, the age differences between the pathogens were statistically significant (*p-value*: 0.04).

Antimicrobial resistance trend analysis and multi-drug-resistant organisms

Escherichia coli: In 2019, the antimicrobial resistance levels in decreasing order of resistance were: ampicillin (83.6%), trimethoprim-sulfamethoxazole (79.1%), cefuroxime (43.7%), ceftriaxone (37%), ceftazidime (32.7%), amoxicillin-clavulanic acid (AMC, 32.6%), ciprofloxacin (29.4%), cefepime (19.3), gentamicin (18.8%), ertapenem (1.1%), amikacin (1.1%), and meropenem (0.9%). In-depth trend analysis for the years 2011–2019 showed a significant positive trend (i.e. increasing resistance) for amoxicillin-clavulanic acid (sens-slope (ss): 2.2, *p-value: 0.04*) (Fig. 1), with a weighted mean resistance (wmR) of 28.3% (95% CI:24.3–32.3) (Additional file 3).

The MAR indices of the *E. coli* isolates ranged between 0 to 1, with 43.8% (1,020 isolates) having an index of greater than 0.2 (*not shown*). As shown in Fig. 2, the MDR minimum was 9.6% ($n=22$) in 2012 and maximum of 47.8% ($n=132$) in 2019. The overall MDR trend significantly increased (ss: 14, $p<0.01$). The proportions of XDR's were highest in 2013 (16.9%, $n=44$) and lowest (1.6%, $n=4$) in 2018. The reducing trend was confirmed by sens-slope of –3.7 (*p:0.04*) (Additional file 4). The proportions of putative ESBLs have increased, from 22.1% ($n=79$) to 42% ($n=116$) (ss:1.75, $p=0.03$). Resistance to all antimicrobials was generally higher in the ESBL groups, particularly with amoxicillin-clavulanate (63.3% vs 14.6%), piperacillin-tazobactam (27.2% vs 4.4%), ciprofloxacin (68.3% vs 9.4%), gentamicin (62.6% vs 12.7%) and cefepime (90.8% vs 32.1%) (Fig. 3).

Staphylococcus aureus: In 2019, the antimicrobial resistance levels in decreasing order were: trimethoprim-sulfamethoxazole (73.5%), erythromycin (21.6%),

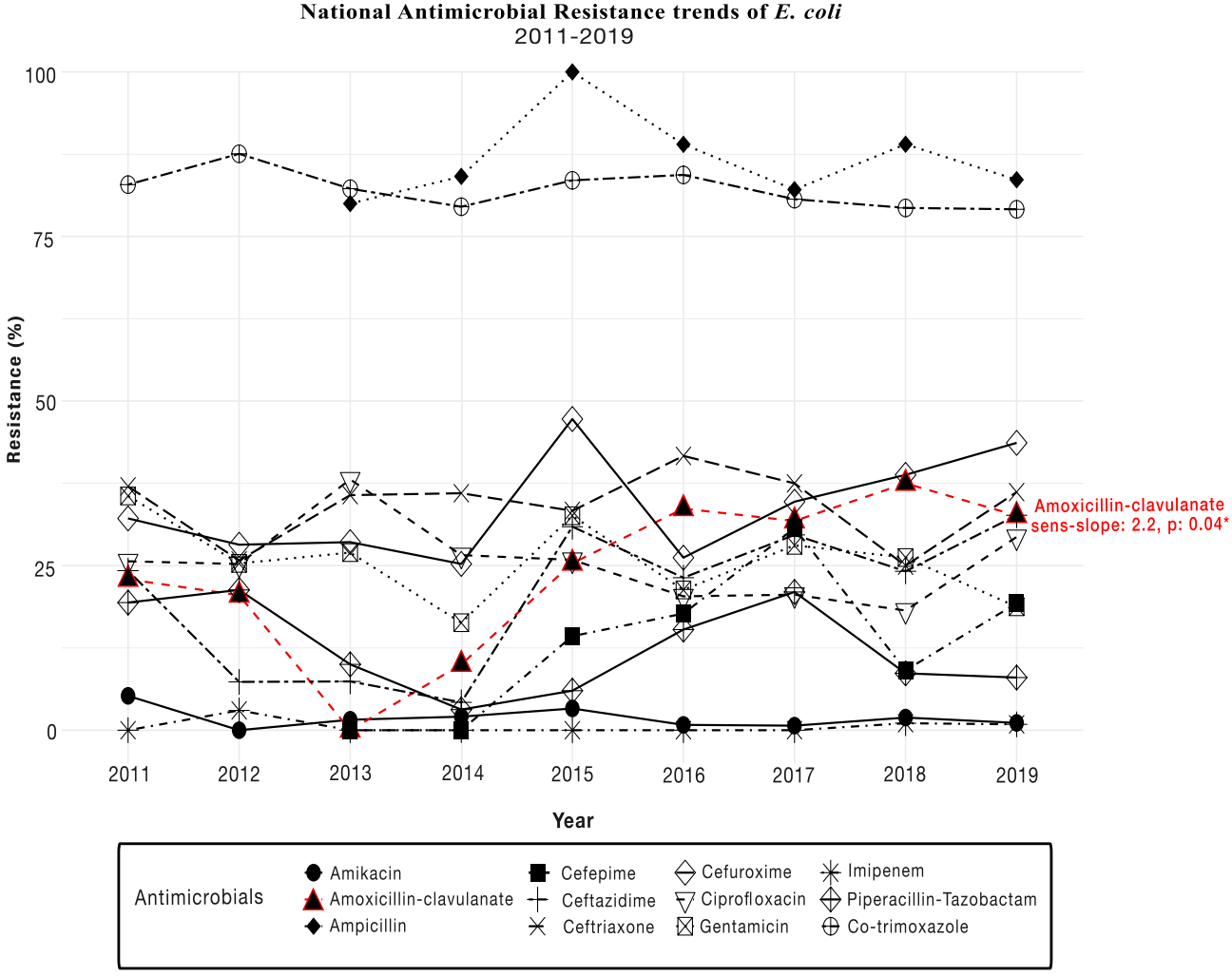

Fig. 1 Resistance prevalence and trend analysis (sens-slope) of *E. coli* to various antimicrobials, 2011–2019

oxacillin (18.8%), clindamycin (9.6%), gentamicin (9.5%), tetracycline (8.5%), ciprofloxacin (6.9%) and vancomycin (3%), teicoplanin (0%). Overall, significant declining antimicrobial resistance trends were noted for gentamicin (ss: −2.4, *p: 0.02*), oxacillin (ss: −2.0, *p: 0.03*) and trimethoprim-sulfamethoxazole (ss: −1.7, *p: 0.04*) (Fig. 4). For other antimicrobials, the sens-slope and p-values are provided in Additional file 5.

In our setting, cefoxitin as an MRSA screening antibiotic has only been reported between 2016 and 2019 in less than 30 isolates. Oxacillin was tested against ~200 isolates per annum and was thus used as the indicator for MRSA prevalence instead of cefoxitin. Among *S. aureus,* 37% ($n = 366$) of the isolates had a MAR index of greater than 0.2 (not shown). From 2011 - 2019, the proportion of MRSA significantly declined from 47.2% to 18.8% (*p: 0.01*). Large differences were noticed between the MRSA and non-MRSA groups for penicillin/novobiocin (87.7% vs 54.5%), ciprofloxacin (40.9% vs 3.6%), erythromycin (59.5% vs 15.5%), moxifloxacin (23.7% vs 0%), ofloxacin (39.4% vs 11.9%) and vancomycin (3.6% vs 2.3%) (Fig. 3).

Discussion

This is the first report on the antimicrobial resistance situation among bacteria isolated from clinical blood cultures in Namibia. The initial high (80.1%) blood culture positivity rate was halved to 40.5% after adjusting for putative contaminants. The adjusted blood culture positivity rate in our study was almost similar to the one-third positivity rate reported by Towns *et.al* [19] in the guidelines on blood cultures. High positivity rates have been associated with hospitalizations, neonatal populations [20, 21] and contamination of the blood culture bottle with skin microflora especially when aseptic sampling techniques are not strictly followed [22]. The high proportion of putative skin-related bacterial contaminants among our original reports suggests contamination in our setting also, speculatively due to quality of practise during specimen collection. Indirect evidence for this

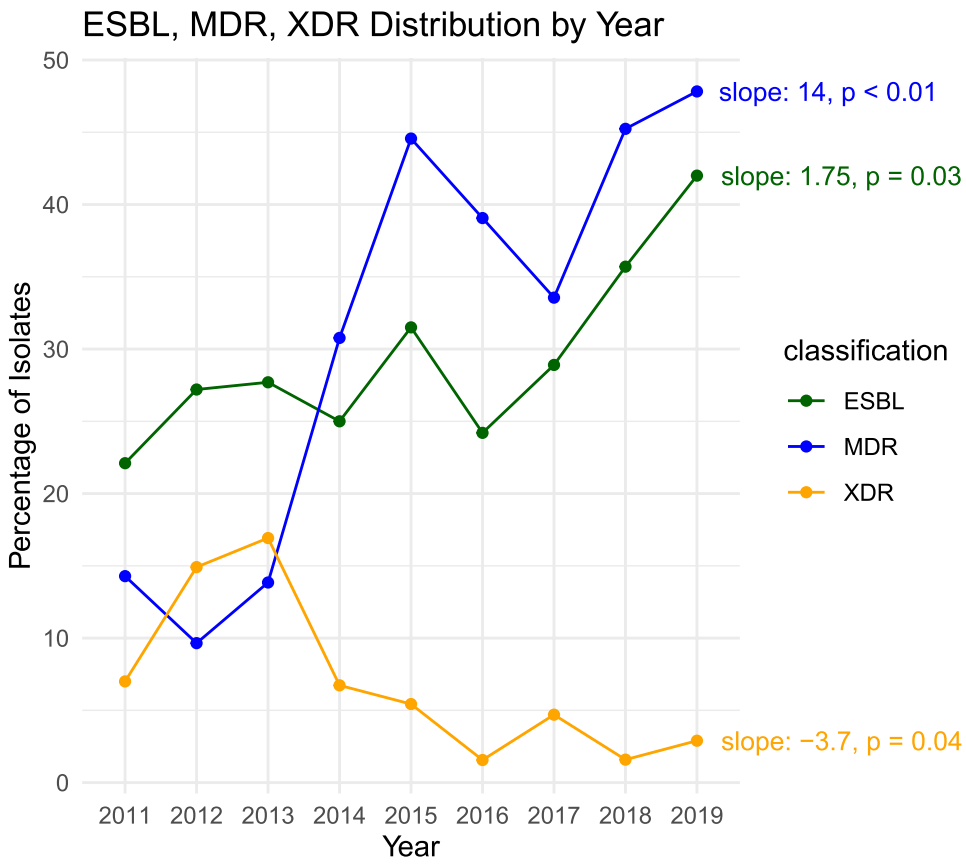

Fig. 2 Distribution of *E. coli* isolates showing extended-spectrum-ß-lactamase (ESBL, *N* = 677), multi-drug resistance (MDR, *N* = 701) and extensively-drug resistance (XDR, *N* = 157) during the period 2011–2019. The corresponding absolute counts, percentages and Mann Kendall trend analysis are provided in Additional file 4

may be found in a study by Sheehama et al. (2024), which reported that almost half of the public healthcare workers in Namibia do not know the laboratory specimen rejection criteria [23]. After adjustment, Gram-negative bacteria (GNB's) were the predominant pathogens in our setting; this is comparable to rates generally recovered from blood cultures [22].

In our study, the *E. coli* resistance to penicillin and sulfamethaxazole-trimethoprim was > 80%. This is comparable to studies from the same country and was previously discussed [24, 25]. Amoxicillin-clavulanate (AMC) (ss:2.2, $p = 0.04$) and cephalosporins (wmr: 21–33%, ss: > 0.5, $p > 0.1$) have also shown increasing trends over the 9 years. The increasing AMC trend is comparable to the findings reported in Spain [26], while Zimbabwe was higher (40.2%) in 2017 [27]. AMC resistance was as high as 80% among nosocomial isolates in Benin, as well as among ESBL producing *E. coli* in Turkey [28, 29] The observed median cephalosporin resistance is comparable to the several median resistance found by systematic reviews in Africa [5, 30–32], as well as those reported globally by GLASS. Inter-country resistance variations have also been observed. For example, ceftazidime resistance ranged from 5%-95% [1, 33]. This highlights the importance of country specific resistance detection and surveillance, as the drivers for resistance are multifactorial and may vary between even neighbouring countries [34–36].

Ciprofloxacin and gentamicin resistance was approximately 25% in 2019. In general, comparable trends of resistance to fluoroquinolones and aminoglycosides [37–40] have previously been reported. An earlier study by Haindongo et.al., (2022) on UTI *E. coli* isolates from Namibia corroborates the findings in this bacteremic *E. coli* study [24]. Ciprofloxacin resistance showed a declining trend (ss:-0.1, *p:0.47*). The decrease in the trend may not represent actual decreases but may be due to the reduction in the number of isolates tested for the particular antimicrobials, year-to-year. The decrease is potentially also due to the coincidental shift from ciprofloxacin to nitrofurantoin as the empirical regimen for UTI management in Namibia [41] and elsewhere [42, 43].

Singu *et. al* (2024) has attributed gentamicin therapy failure in Namibia to prolonged treatment, low birthweight and elevated C-reactive proteins among neonates. Thus, microbiological susceptibility to gentamicin should

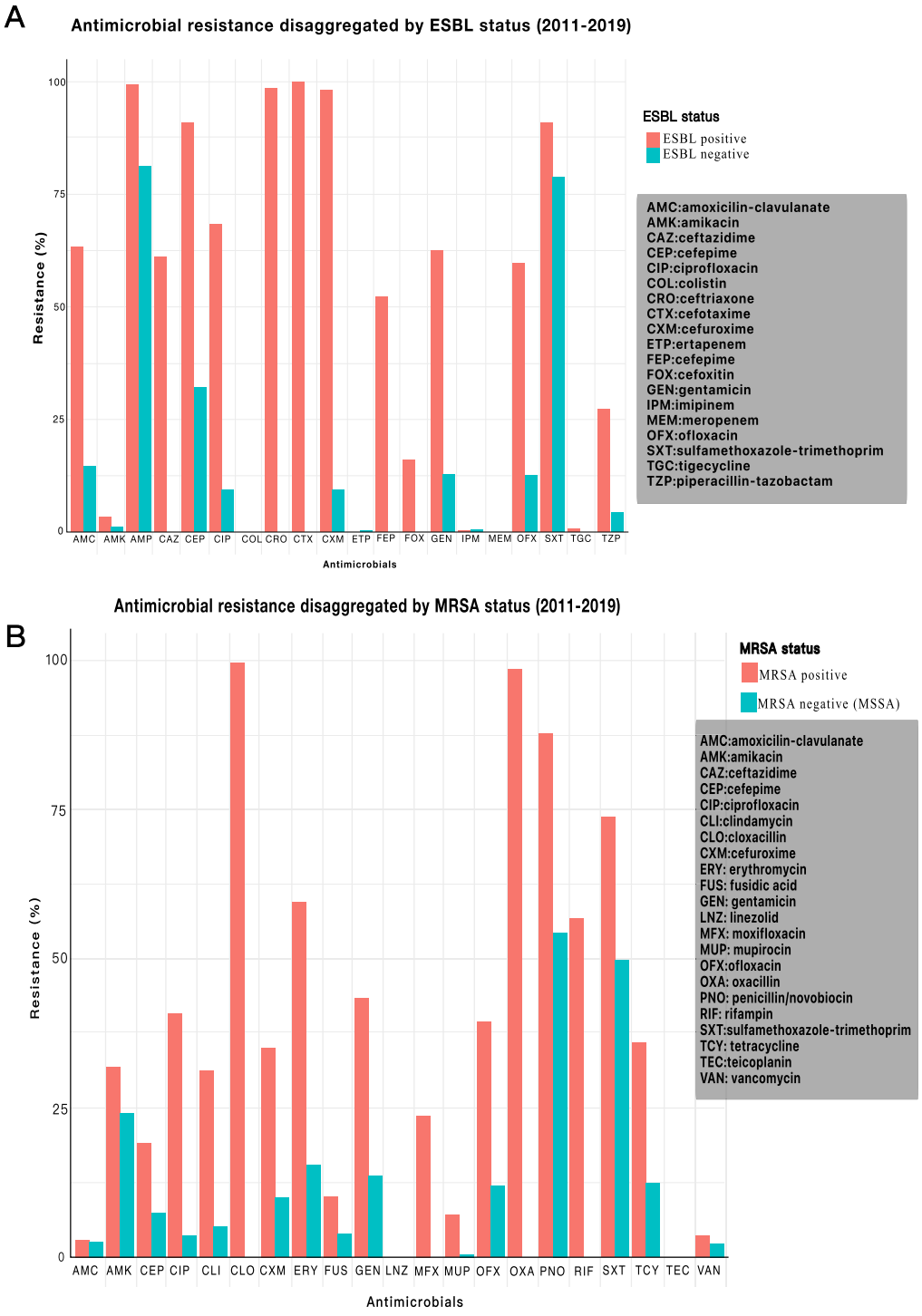

Fig. 3 Overall antimicrobial resistance (2011–2019) disaggregated by ESBL (Panel **A**) and MRSA (Panel **B**) status

be considered along with the parameters described by Singu *et.*al (2024) in future studies aimed at successful gentamicin treatment outcomes [44].

The Namibia Standard Treatment Guidelines (NSTG) currently recommends the use of intravenous amoxicillin-clavulanate (AMC), ceftriaxone, ciprofloxacin and gentamicin for sepsis management [45]. Antimicrobial use (AMU) data in Namibia has not been published in the public sector but, the private sector medical aid claims data showed increased consumption of AMC, cefuroxime, clarithromycin and ciprofloxacin [46]. Speculatively, there may equally be widespread usage of the NSTG recommended antimicrobials as alternatives to

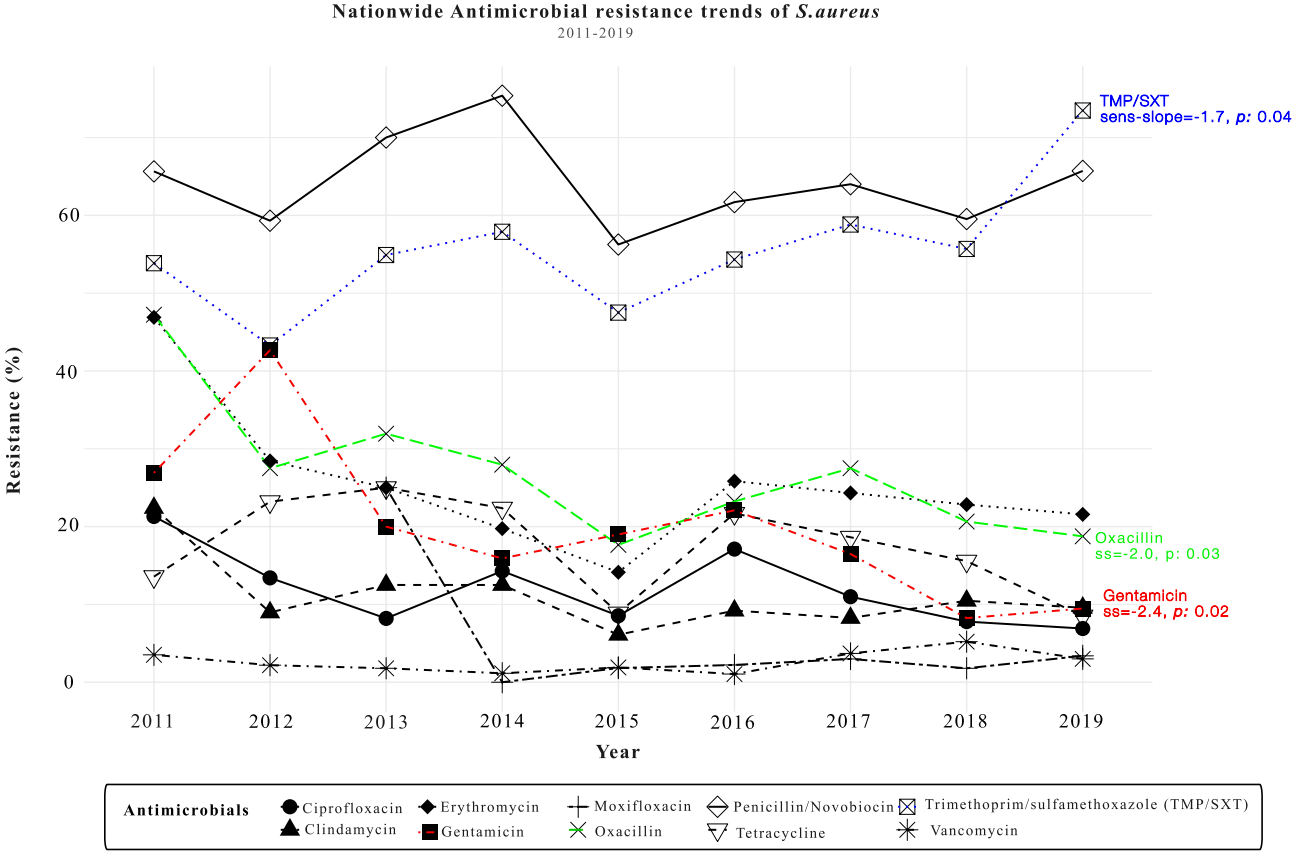

Fig. 4 Resistance prevalence and trend analysis (sens-slope) of *S. aureus* to various antimicrobials, 2011–2019

amoxicillin. Hence, the dynamics of AMU-AMR cannot be established in our setting.

The study also revealed 1.1% and 0.9% resistance to ertapenem and meropenem, respectively. Haindongo's systematic review in African countries also reported low resistance to carbapenemes in South Africa, Uganda, Kenya, and Ghana, except for a 4% imipenem resistance rate in Uganda (Kajumbula et al. 2018) [25]. Global increases in the prevalence of carbapenem-resistant *E. coli* have been reported, particularly amongst phylogroup B and ST131 strain [47–49].

Our study found an *E. coli* MDR prevalence of 47.8%. Our MDR prevalence is comparable to that reported in Egypt (47.83%), and Eritrea (42.9%) [50, 51]. Multiple surveillance studies across Europe, America and the Asia Pacific region reported an MDR frequency of 10.7% [52]. Another multicenter study has reported an overall frequency of 37.4%, especially when ST131 strain predominates [53]. Molecular analysis and typing of strains in Namibia is therefore critical for an enhanced understanding of our AMR dynamics and patterns.

MRSA rates (oxacillin resistance) displayed a statistically significant decline to 18.7% in 2019 (slope: −2.05, $p = 0.03$). Our MRSA rate is lower than that reported in Italy (34%), Slovakia (27%) and Spain (23%) in 2019. Sharp declines from 16% (2011) to 3.9% (2022) have been reported in Germany [54]. Another consideration is the reduction in the number of isolates from 484 in 2011 to 214 in 2019. This variation could be explained by possible technical errors in culture-taking, reporting practices and shift to cefoxitin as a screening agent. The use of oxacillin or cefoxitin has different performances depending on the underlying mechanims (*mecA* or *mecC*) [55, 56]. Due to this variation, both CLSI and EUCAST have offered warnings around MRSA detections. The former recommends *mecA* and PBP2a detection as definitive rather.

Nevertheless, the phenomenon of MRSA rate reduction is not unique to Namibia and was parallelly reported in the US and Europe [57–60]. Reductions have alternatively been credited to improved infection, prevention and control (IPC) measures and prevention of device and procedure related infections [57, 59].

Erythromycin resistance was about two times higher (21.5%) than clindamycin (9.6%) resistance among *S.aureus*. This is somewhat comparable to the erythromycin resistance findings in India (12.1% – 23.8%) and Pakistan (24%) and Ethiopia (30.3%), except that our study does not report on the results of the D-test [61–63]. The variation in resistance between erythromycin and clindamycin suggests the possibility of inducible

clindamycin resistance (MLSBi) due to the presence of *erm* genes in our setting.

Our study found a 3% resistance to vancomycin among *S. aureus*. This resistance was 3.6% and 2.3% in MRSAs and MSSAs, respectively. High vancomycin resistance has also been reported across Ethiopia [64], whilst Brazil has reported on vancomycin resistance among MSSAs [65]. The main detection method in all these settings has been disk diffusion testing. Vancomycin testing by disk diffusion is however not recommended by CLSI, nor EUCAST, as it has been found to overestimate resistance. In the absence of any additional verification, this finding needs to be considered with caution. As vancomycin-resistant *S. aureus* (VRSA) is a priority pathogen, there is a need for reliable and acceptable MIC detection methods to quantify the true extent of the problem [66].

Our study harbors several limitations. Firstly, the main limitation hampering the interpretation of the findings is the unstandardized national blood culture collection practices. The indications for taking blood cultures may be too strict. For example, only severely ill or hospitalized patients have specimens taken for analysis. Blood culture performance and utilization parameters, which consider optimized collection processes, patient selection, and blood culture rates are more informative [67, 68].

Secondly, there is unstandardized reporting of AST findings. ESBLs were inferred from 3rd generation cephalosporins because double or combination disc diffusion results are not recorded. Hence, molecularly the definition of a classical ESBL (SHV, TEM, CTX) is somewhat met but cannot be separated from ampC producers which may exhibit the same resistance profile.

Thirdly, the lack of epidemiological and clinical data such as the setting of acquisition, hospital unit, admission characteristics and clinical diagnosis makes sub-analysis impossible [24]. The District and Health Information System 2 (DHIS2) and MEDITECH are the main health and laboratory information management systems in the Namibian public health institutions, respectively. However, the absence of a unique patient identifier makes it impossible to harmonize the two systems. Consequently, it becomes impossible to apply the first isolate rule on microbiological AST data (i.e. de-duplication of records).

Lastly, the variation in the number of annual isolates, blood culture positivity and AST test coverage may point to some technical or quality problems. It is difficult to ascertain if there were actual increases or reductions without background information, such as bloodstream infection rates and the underlying/catchment population.

Conclusions

To our knowledge, this is the first study to provide a 9-year insight into the microbial epidemiology, antimicrobial resistance situation, and trend analysis of BSI in Namibia. Almost half of bacteremic *E. coli* cases were from individuals aged 15–59 years, and *S. aureus* cases were mostly from children aged 0–4 years. Overall resistance levels of above 20% are worrying for amoxicillin-clavulanate, 3rd generation cephalosporins, ciprofloxacin and gentamicin among bacteremic *E. coli* isolates. This may worsen due to ESBLs and MDRs which have concerningly demonstrated an upward trend. MRSAs have declined due to possible improvements in IPC and AMR stewardship, but they may still present challenges to therapeutic management. Overall, this study serves as a baseline for future surveillance work and highlights the need for AST-guided therapy, along with in-depth molecular analysis.

Supplementary information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

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Author contributions

All authors initiated the study. The formal data analysis was done by EH and all authors have contributed to the writing and editing of the manuscript. All authors have also approved the manuscript.

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Data availability

Limited datasets, without any personal or identifiable information, used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval

Hence, the Ethics Committee of the Ministry of Health & Social Services has approved the study and gave a waiver of consent and participation (Ref: 17/3/3EHH) due to the retrospective nature of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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