Moremi *et al. BMC Res Notes (2021) 14:77*
https://doi.org/10.1186/s13104-021-05495-x

BMC Research Notes

RESEARCH NOTE

Open Access

Extended-spectrum β-lactamase $bla_{\text{CTX-M-1}}$ group in gram-negative bacteria colonizing patients admitted at Mazimbu hospital and Morogoro Regional hospital in Morogoro, Tanzania

Nyambura Moremi[1], Vitus Silago[2*] , Erick G. Mselewa[2], Ashery P. Chifwaguzi[2], Mariam M. Mirambo[1], Martha F. Mushi[1], Lucas Matemba[3], Jeremiah Seni[2] and Stephen E. Mshana[2]

Abstract

Objective: The objective of this study was to determine the proportion of extended spectrum β-lactamase producing gram-negative bacteria (ESBL-GNB) colonizing patients admitted at Mazimbu hospital and Morogoro Regional hospital, in Morogoro, Tanzania. Rectal colonization with ESBL-GNB increases the risks of developing bacterial infections by extra-intestinal pathogenic ESBL-GNB.

Results: Of the 285 patients investigated, 123 (43.2%) carried ESBL-GNB in their intestines. Five of the 123 ESBL positive patients were colonized with two different bacteria, making a total of 128 ESBL producing isolates. *Escherichia coli* (n = 95, 74.2%) formed the majority of ESBL isolates. The proportion of CTX-M-1 group genes among ESBL isolates tested was 94.9% (93/98). History of antibiotic use (OR: 1.83, 95% CI: 1.1–3.2, P = 0.03), being on antibiotic treatment (OR: 2.61, 95% CI: 1.5–4.53, P = 0.001), duration of hospital stay (OR: 1.2, 95% CI: 1.1–1.3, P < 0.001) and history of previous admission (OR: 2.24, 95% CI: 1.2–4.1, P = 0.009) independently predicted ESBL-GNB carriage.

Keywords: Antimicrobial stewardship, ESBL colonization, ESBL genes, Infection prevention and control

Introduction

Extended spectrum beta-lactamases (ESBLs) production, is the commonest mechanism of resistance to multiple broad-spectrum beta-lactams among gram-negative bacteria mainly members of the family Enterobacteriaceae [1, 2]. ESBL enzymes hydrolyze beta-lactam ring of the beta-lactams making these antibiotics ineffective against ESBL producing bacteria [3]. The $bla_{\text{CTX-M}}$ group out of other ESBL groups, is the commonest reported group of ESBL genes in different part of the World including in Tanzania [2, 4–7]. CTX-M enzymes effectively hydrolyzes third generation cephalosporins (3GCs) e.g., ceftriaxone and cefotaxime but not oxyimino-cephalosporins e.g., ceftazidime [8]. Although, some CTX-M members; CTX-M-15, -16 and -19 have been reported to hydrolyze ceftazidime activity [9–11].

Colonization with ESBL producing gram-negative bacteria (ESBL-GNB) increases the risk of developing multidrug resistant (MDR) bacterial infections e.g., bloodstream infection, urinary tract infection or wound infection [12]. Infections with MDR bacteria are associated with increased days of hospitalization, healthcare

*Correspondence: vsilago.silago2@gmail.com
[2] Department of Microbiology and Immunology, Weill Bugando School of Medicine, Catholic University of Health and Allied Sciences-Bugando, P. O. Box 1464, Mwanza, Tanzania
Full list of author information is available at the end of the article

© The Author(s) 2021. This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

costs and mortalities from treatment failure and/or limited therapeutic options [13].

In Tanzania, previous studies from national and zonal referral hospitals have reported magnitudes of rectal/intestinal carriage of ESBL producing gram-negative bacteria (ESBL-GNB) ranging from 15% to 59.7% among hospitalized patients [14–17]. ESBL producing *E. coli* (ESBL-EC) and ESBL producing *K. pneumoniae* (ESBL-KP) are frequently reported with proportion ranging from 30% to 68.7% and 28.2% to 77.1%, respectively [14, 15, 17]. The magnitude of ESBL rectal colonization and associated factors among hospitalized patients in other tiers of the healthcare facilities like regional and district hospitals has not been well studied in developing countries including Tanzania. The objectives of this study was to determine the magnitude and factors associated with rectal colonization with ESBL producing gram-negative bacteria (ESBL-GNB) among hospitalized patients at Mazimbu hospital and Morogoro Regional hospital in Morogoro, Tanzania. Therefore, this study's findings provide baseline information to improve measures of infections prevention and control (IPC).

Main text

Methods

Study design, population, duration and settings

This cross-sectional analytical study was conducted among patients admitted at Mazimbu hospital (~ 30 beds capacity) and Morogoro Regional hospital (~ 450 beds capacity) in Morogoro region, Tanzania between May and July 2017. A minimum sample size of 280 was obtained using Kish and Leslie formula (1965) and a prevalence of 24% [5]. Participants stayed ≥ 24 h in hospital wards were eligible to be enrolled in this study. A standardized data collection tool was used to collect socio-demographic and clinical associated data relevant to study's objectives.

Sample collections and laboratory procedures

Sterile swabs (Mast Diagnostica GmbH, Germany) in Amies transport media were used to collect a single time rectal swab from participants. Then, transported to Microbiology laboratory at Morogoro Regional hospital within 4 h of collection for laboratory analysis. Screening of presumptive ESBL-GNB was done by direct inoculation of rectal swab samples on MacConkey agar (MCA; Oxoid, UK) plates supplemented with 2 μg/ml cefotaxime (MCA-C) incubated in ambient air at 37 °C for 24 h [18, 19]. CHROMagar ESBL plates (BD BBL™ CHROMagar™ ESBL, Germany) were used for primary identification while physiological and biochemical characteristics (lactose fermentation; production of CO_2, H_2S, indole, urease and oxidase; motility; and utilization of citrate) were used for secondary identification of isolates to species level as reported [20]. Discs combination method (ceftazidime 30 μg and cefotaxime 30 μg with and without clavulanic acid 10 μg) was used for phenotypic confirmation of ESBL production in *E. coli*, *K. pneumoniae* and *K. oxytoca* as recommended by Clinical and Laboratory Standards Institutes (CLSI) [21]. All isolates were archived in vials containing 20% glycerol in brain heart infusion (BHI; Oxoid, UK) broth and stored at − 40 °C untill molecular analysis.

Determination of minimum inhibitory concentration (MIC) of cefotaxime

The minimum inhibitory concentrations (MICs) of ESBL-GNB to cefotaxime were determined using agar incorporation method [22, 23] on Mueller Hinton agar (MHA; Oxoid, UK) plates supplemented with 4 μg/mL, 8 μg/mL and 16 μg/mL cefotaxime. Inoculated plates were incubated in ambient air at 37 °C for 18–24 h. The MICs were recorded as greater than the highest concentration tested or the lowest concentration when no growth occurs on any of the agar plates.

DNA extraction and molecular detection of $bla_{CTX\text{-}M\text{-}1}$ group

Out of 128 isolates, 98 ESBL-GNB (73 *E. coli*, 18 *K. pneumoniae* and 7 *K. oxytoca*) were selected and successful recovered for molecular characterization of the $bla_{CTX\text{-}M\text{-}1}$ group. Selection of isolates for molecular characterization was limited by the availability of PCR reagents. The isolates were sub-cultured on plain MCA (Oxoid, UK) plates followed by crude DNA extraction using boiling method as previously described [24]. Out of five major phylogenetic groups of CTX-M genes (CTX-M-1, CTX-M-2, CTX-M-8, CTX-M-9, and CTX-M-25), we chose to test only for CTX-M-1 due to predominance of its members especially the $bla_{CTX\text{-}M\text{-}15}$ and from insufficient resources. PCR amplifications of the $bla_{CTX\text{-}M\text{-}1}$ group was carried out in thermal cycler machine (PCR Gene AmpR System) with primers CTX-M3G-F (5′-GTTACAATGTGTGAGAAGCAG) and CTX-M3G-R (5′-CCGTTTCCGCTATTACAAAC) and procedures reported previous [25]. PCR products were electrophoresed (at 110 V for 90 min) by using 2% agarose gel which was stained by SBR-Safe DNA gel stain (ThermoFisher Scientific, UK) and visualized under UV light.

Quality control

Known ESBL-GNB from [26] and *E. coli* ATCC 25922 were used as control organisms.

Data analysis

STATA software version 13.0 was used for data analysis as per objectives of this study.

Results

Socio-demographic and clinical characteristics of study participants

A total of 285 patients with median age (IQR: interquartile range) of 18 (3–34) years were enrolled with the majority (53%, n = 151) being males (Table 1).

Carriage of ESBL-GNB, MICs, and harboring of $bla_{CTX\text{-}M\text{-}1}$ group in ESBL-GNB

Of the 285 patients investigated, 123 (43.2%) were colonized by ESBL-GNB whereby five patients had two ESBL-GNB isolated from single rectal swab making a total of 128 isolates (Fig. 1). Of 128 ESBL confirmed isolates, 123 (96.1%) had a MIC of ≥ 16 μg/mL while the remaining 5 isolates had a MIC of ≥ 4 μg/mL. Ninety-nine ESBL-GNB tested, 93 (94.9%) carried $bla_{CTX\text{-}M\text{-}1}$ group genes while the remaining five (all were *Escherichia coli*) had no $bla_{CTX\text{-}M\text{-}1}$ group genes.

Factors associated with rectal colonization by ESBL-GNB

On multivariable logistic regression analysis controlled by age and sex: history of antibiotic use (OR: 1.83, 95% CI: 1.1–3.2, P = 0.03), being on antibiotic treatment (OR: 2.61, 95% CI: 1.5–4.53, P = 0.001), duration of

Table 1 Socio-demographic and clinical characteristics of study participants

Variables	Frequency (n)/median (IQR)	Percentage (%)
Median age (IQR) in years	18 (3–34)	–
Median days (IQR) of hospital stay	1 (1–3)	–
Median days (IQR) of antibiotic exposure	2 (1–3)	–
Gender		
Males	151	53
Females	134	47
Hospital of admission		
MH	29	10.2
MRH	256	89.8
Admitted ward during enrollment		
Medical	205	71.9
Surgical	80	28.1
Antibiotics use past three months		
No	148	51.9
Yes	137	48.1
Antibiotics use at enrollment		
No	107	37.5
Yes	178	62.5
On β-lactams during sampling		
No	12	6.7
Yes	166	93.3
Type of antibiotics used during sampling		
Ciprofloxacin/gentamicin	12	6.7
Penicillins	95	53.4
Cephalosporins	71	39.9
History of admission		
No	203	71.2
Yes	82	28.2
Livestock keeping		
No	253	88.8
Yes	32	11.2
HIV status		
Negative	283	99.3
Positive	2	0.7

MH Mazimbu Hospital, *MRH* Morogoro Regional Hospital

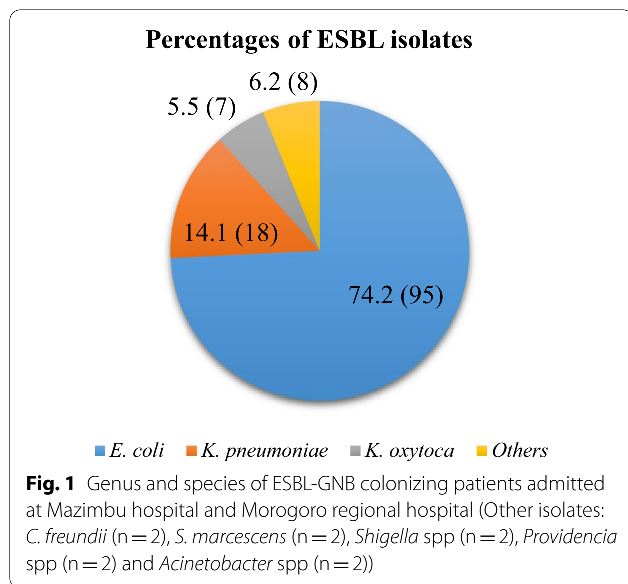

Fig. 1 Genus and species of ESBL-GNB colonizing patients admitted at Mazimbu hospital and Morogoro regional hospital (Other isolates: *C. freundii* (n = 2), *S. marcescens* (n = 2), *Shigella* spp (n = 2), *Providencia* spp (n = 2) and *Acinetobacter* spp (n = 2))

hospital stay (OR: 1.2, 95% CI: 1.1–1.3, P < 0.001) and history of previous hospital admission (OR: 2.24, 95% CI: 1.2–4.1, P = 0.009) were independently found to predict ESBL-PE GNB carriage (Table 2).

Discussion

This study identified a high carriage of ESBL-GNB in Morogoro regional hospital and Mazimbu hospital. The overall prevalence (43.2%) observed in this study is comparable to a study in Gabon [27]. Although the carriage in our study is relatively lower compared to (50.4%) a study conducted at Tanzanian National Hospital, Muhimbili National hospital (MNH), in Dar es Salaam [28]. Being a national referral hospital, MNH receives patients with multiple antibiotics exposure from other healthcare facilities mainly regional and zonal referral hospitals, increasing the risk of carriage of ESBL-GNB.

E. coli followed by *K. pneumoniae* are predominant ESBL producers colonizing patients. Similar findings were reported previous in Ethiopia, Turkey and other regions of Tanzania [15, 16, 29, 30]. Pathogenic potential of *E. coli* (e.g., *E. coli* ST131) and *K. pneumoniae* (e.g., *K. pneumoniae* ST14), and frequent acquisition of conjugative plasmids encoding for antimicrobial resistance genes (ARGs i.e., ESBL genes) facilitates rapid exchange and dissemination of ARGs in *E. coli* and *K. pneumoniae* [31]. These isolates, ESBL-GNB, colonizing patients are potentially shaded of to contaminate patient's immediate inanimate surroundings as previous reported [32, 33]. Thus increasing the risk of exogenous source of acquiring of healthcare associated infections (HCAIs) from

Table 2 Factors associated with ESBL-GNB colonization

Variable	All participants (N = 285)	ESBL-GNB positive colonization N = 123 (%)	Univariable (*P* value)	Multivariable OR (95%CI)	*P* value
Median age (IQR) in years	19 (IQR: 3–33)	17 (IQR: 3–33)	0.929	0.99 [0.99–1.01]	1.000
Median (IQR) days in hospital	1 (IQR: 1–2)	2 (IQR: 1–4)	< 0.001	1.20 [1.08–1.33]	< 0.001
Antibiotic use past 3 months					
No	148	49 (33.1)	< 0.001	1	0.009
Yes	137	74 (54.0)		2.16 [1.22–3.84]	
Gender					
Females	134	51 (38.1)	0.102	1	0.443
Males	151	72 (47.7)		0.81 [0.47–1.39]	
Type of ward of admission					
Medical	205	91 (44.4)	0.502	1	0.526
Surgical	80	32 (40.0)		1.24 [0.64–2.39]	
On antibiotic use during sampling					
No	107	28 (26.2)	< 0.001	1	0.008
Yes	178	95 (53.4)		2.20 [1.23–3.95]	
Hospital admission past 3 months					
No	203	70 (34.5)	< 0.001	1	0.013
Yes	82	53 (64.6)		2.17 [1.17–4.01]	
Livestock keeping					
No	253	112 (44.2)	0.287	1	0.122
Yes	32	11 (34.4)		0.51 [0.22–1.19]	

ESBL-GNB among vulnerable patients (immunocompromised and critically ill) associated with increased mortality from treatment failures and limited antibiotic therapeutic options [34, 35]. Therefore, this study's findings alert for the strengthening of infections prevention and control measures and AMR surveillance in line with the Tanzania National Action Plan in order to combat AMR in the country in all tiers of health facilities [36].

This study found high proportion (94.9%) of ESBL-GNB carrying CTX-M-1 group genes colonizing patients. The CTX-M-1 group genes particularly $bla_{\text{CTX-M-15}}$ are predominantly reported in clinical, colonization and environment isolates in Tanzania and elsewhere [6–8, 15, 16, 37]. Horizontal gene transfer (HGT) of mobile genetic elements (MGEs) including plasmids, transposons, and intergrons facilitates rapid dissemination and spreading of CTX-M-1 group genes, mostly in *E. coli* and *Klebsiella* spp., [8, 38–40] in the hospital environment. These findings hint the possibility of the common genetic elements or resistant strains carrying CTX-M-1 genes in healthcare facilities in Tanzania, necessitating the strengthening of IPC and antimicrobial stewardship in Tanzania.

Hospital admission, previous and current antibiotic use, and longer hospital stay significantly predicted carriage of ESBL-GNB. These findings are in consistency with other studies [5, 16, 27]. Hospital admission and longer stays increases the odds of being exposed to antibiotics mostly beta-lactams i.e., ampicillin and ceftriaxone as they make first- and second-lines of therapy [41]. Therefore, increasing antimicrobial selection pressure favoring the proliferation of resistant bacterial strains colonizing patients' gastro-intestinal tracts as observed in this study [42, 43].

Antibiotic exposure creates essential pressure which select the small fraction of resistant bacteria of the intestinal microbiota therefore giving rise to the emergency and establishment of an entirely resistant population of bacteria [42]. With poor IPC practices especially in low- and middle-income countries, these superbugs may be cross-transmitted between patients resulting to subsequent invasive infections such as BSIs, UTIs and SSTIs. Presence of these bacteria in the gut and environment may also result in exchange of resistance genes to the highly virulent bacteria making the infection difficult to treat hence high morbidity and mortality [42].

Limitations

From limited funds and resources: ESBL isolates were conventionally identified to possible genus and species; agar dilution method was used to determine MICs for cefotaxime only; and other ESBL alleles contributing about 5–10% of ESBL genes in our setting and genetic relatedness of ESBL isolates were not determined.

Abbreviations

ATCC: American Type Culture Collection; BSIs: Bloodstream infections; CI: Confidence interval; DNA: Deoxyribose nucleic acid; ESBL: Extended spectrum beta lactamase; ESBL-EC: Extended spectrum beta lactamase producing *Escherichia coli*; ESBL-GNB: Extended spectrum beta lactamase producing gram negative bacteria; ESBL-KP: Extended spectrum beta lactamase producing *Klebsiella pneumonia*; GNB: Gram negative bacteria; HIV: Human immunodeficiency virus; IPC: Infection prevention and control; IQR: Interquartile range; MCA: MacConkey agar; MCA-C: MacConkey agar supplemented with cefotaxime 2 µg/mL; MIC: Minimum inhibitory concentration; MRRH: Morogoro Regional Referral Hospital; OR: Odd ratio; PCR: Polymerase chain reaction; SSTIs: Skin and soft tissue infections; UTI: Urinary tract infections.

Acknowledgements

The authors acknowledge the assistance provided by the administration and health care workers of Morogoro regional hospital and Mazimbu District hospital.

Authors' contributions

NM, VS, MMM and SEM conceived and designed this study; EM, NM, and VS collected data and samples for this study; NM, VS, JS, EM, AC, MFM and LM performed laboratory procedures; NM, VS, and SEM analyzed and interpreted data; NM and VS wrote the first draft of the manuscript which was critically reviewed by JS and SEM. All authors read and approved the final manuscript.

Funding

The research was supported by grant from World Health Organization AGISAR Pilot Projects to SEM. Funder had no any role in conducting this study.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available in the department of Microbiology and Immunology repository of the Catholic University of Health and Allied Sciences-Bugando. The data can be obtained upon request to the Director of Research and Innovation of the Catholic University of Health and Allied Sciences.

Ethics approval and consent to participate

The protocols for the study were reviewed and approved by the Joint CUHAS/BMC ethics and scientific review committee (CREC/019/2014). Permissions were sought from administration of the Morogoro regional hospital and Mazimbu hospital. All participants aged above 18 years signed an informed written consent forms whereas for participants aged below 18 years their parents/caretakers consented on their behalf.

Consent for publication

Not applicable.

Competing interests

Authors declare no competing interests exist.

Author details

[1] Quality Assurance & Training Centre, National Health Laboratory, P. O. Box 9083, Dar Es Salaam, Tanzania. [2] Department of Microbiology and Immunology, Weill Bugando School of Medicine, Catholic University of Health and Allied Sciences-Bugando, P. O. Box 1464, Mwanza, Tanzania. [3] National Institute for Medical Research, P. O. Box 805, Dodoma, Tanzania.

Received: 15 December 2020 Accepted: 16 February 2021
Published online: 27 February 2021

References

1. Teklu DS, Negeri AA, Legese MH, Bedada TL, Woldemariam HK, Tullu KD. Extended-spectrum beta-lactamase production and multi-drug resistance among Enterobacteriaceae isolated in Addis Ababa, Ethiopia. Antimicrob Resist Infect Contr. 2019;8(1):39.

2. Shaikh S, Fatima J, Shakil S, Rizvi SMD, Kamal MA. Antibiotic resistance and extended spectrum beta-lactamases: types, epidemiology and treatment. Saudi J Biol Sci. 2015;22(1):90–101.
3. Van Bambeke F, Mingeot-Leclercq M-P, Glupczynski Y, Tulkens PM. Mechanisms of action. Infect Dis. 2017;2:1162–80.
4. Moremi N, Claus H, Vogel U, Mshana SE. Faecal carriage of CTX-M extended-spectrum beta-lactamase-producing Enterobacteriaceae among street children dwelling in Mwanza city, Tanzania. PLoS ONE. 2017;12(9):e0184592.
5. Moremi N, Claus H, Rutta L, Frosch M, Vogel U, Mshana S. High carriage rate of extended-spectrum beta-lactamase-producing Enterobacteriaceae among patients admitted for surgery in Tanzanian hospitals with a low rate of endogenous surgical site infections. J Hosp Infect. 2018;100(1):47–53.
6. Moremi N, Manda EV, Falgenhauer L, Ghosh H, Imirzalioglu C, Matee M, Chakraborty T, Mshana SE. Predominance of CTX-M-15 among ESBL producers from environment and fish gut from the shores of Lake Victoria in Mwanza, Tanzania. Front Microbiol. 1862;2016:7.
7. Mshana SE, Falgenhauer L, Mirambo MM, Mushi MF, Moremi N, Julius R, Seni J, Imirzalioglu C, Matee M, Chakraborty T. Predictors of bla CTX-M-15 in varieties of *Escherichia coli* genotypes from humans in community settings in Mwanza, Tanzania. BMC Infect Dis. 2016;16(1):187.
8. Zhao W-H, Hu Z-Q. Epidemiology and genetics of CTX-M extended-spectrum β-lactamases in gram-negative bacteria. Crit Rev Microbiol. 2013;39(1):79–101.
9. Poirel L, Gniadkowski M, Nordmann P. Biochemical analysis of the ceftazidime-hydrolysing extended-spectrum β-lactamase CTX-M-15 and of its structurally related β-lactamase CTX-M-3. J Antimicrob Chemother. 2002;50(6):1031–4.
10. Bonnet R, Dutour C, Sampaio J, Chanal C, Sirot D, Labia R, De Champs C, Sirot J. Novel cefotaximase (CTX-M-16) with increased catalytic efficiency due to substitution Asp-240→ Gly. Antimicrob Agents Chemother. 2001;45(8):2269–75.
11. Poirel L, Naas T, Le Thomas I, Karim A, Bingen E, Nordmann P. CTX-M-type extended-spectrum β-lactamase that hydrolyzes ceftazidime through a single amino acid substitution in the omega loop. Antimicrob Agents Chemother. 2001;45(12):3355–61.
12. Cheikh A, Belefquih B, Chajai Y, Cheikhaoui Y, El Hassani A, Benouda A. Enterobacteriaceae producing extended-spectrum β-lactamases (ESBLs) colonization as a risk factor for developing ESBL infections in pediatric cardiac surgery patients: "retrospective cohort study." BMC Infect Dis. 2017;17(1):1–6.
13. Peters L, Olson L, Khu DT, Linnros S, Le NK, Hanberger H, Hoang NT, Tran DM, Larsson M. Multiple antibiotic resistance as a risk factor for mortality and prolonged hospital stay: a cohort study among neonatal intensive care patients with hospital-acquired infections caused by gram-negative bacteria in Vietnam. PLoS ONE. 2019;14(5):e0215666.
14. Nelson E, Kayega J, Seni J, Mushi MF, Kidenya BR, Hokororo A, Zuechner A, Kihunrwa A, Mshana SE. Evaluation of existence and transmission of extended spectrum beta lactamase producing bacteria from post-delivery women to neonates at Bugando Medical Center, Mwanza-Tanzania. BMC Res Notes. 2014;7(1):279.
15. Marando R, Seni J, Mirambo MM, Falgenhauer L, Moremi N, Mushi MF, Kayange N, Manyama F, Imirzalioglu C, Chakraborty T. Predictors of the extended-spectrum-beta lactamases producing Enterobacteriaceae neonatal sepsis at a tertiary hospital, Tanzania. Int J Med Microbiol. 2018;308(7):803–11.
16. Tellevik MG, Blomberg B, Kommedal Ø, Maselle SY, Langeland N, Moyo SJ. High prevalence of faecal carriage of ESBL-producing Enterobacteriaceae among children in Dar es Salaam, Tanzania. PLoS ONE. 2016;11(12):e0168064.
17. Kibwana UO, Magijo M, Kamori D, Manyahi J. High fecal carriage of extended beta lactamase producing Enterobacteriaceae among adult patients admitted in Referral Hospitals in Dar es salaam, Tanzania. BMC Infect Dis. 2019;20:557.
18. Nyambura Moremi HC, Vogel U, Mshana SE. Faecal carriage of CTX-M extended-spectrum beta-lactamase-producing Enterobacteriaceae among street children dwelling in Mwanza city, Tanzania. PLoS ONE. 2017;12(9):e0184592.
19. Rao SP, Rama PS, Gurushanthappa V, Manipura R, Srinivasan K. Extended-spectrum beta-lactamases producing *Escherichia coli* and *Klebsiella pneumoniaei*: a multi-centric study across Karnataka. J Lab Phys. 2014;6(01):007–13.
20. Koneman EW, Allen SD, Janda W, Schreckenberger P, Winn W. Diagnostic microbiology. The nonfermentative gram-negative bacilli. Philedelphia: Lippincott-Raven Publishers; 1997. p. 253–320.
21. CLSI C. Performance standards for antimicrobial susceptibility testing. Clinical Lab Standards Institute 2016.
22. Andrews JM. Determination of minimum inhibitory concentrations. J Antimicrob Chemother. 2001;48(Suppl_1):5–16.
23. Wiegand I, Hilpert K, Hancock RE. Agar and broth dilution methods to determine the minimal inhibitory concentration (MIC) of antimicrobial substances. Nat Protoc. 2008;3(2):163.
24. Dashti AA, Jadaon MM, Abdulsamad AM, Dashti HM. Heat treatment of bacteria: a simple method of DNA extraction for molecular techniques. Kuwait Med J. 2009;41(2):117–22.
25. Pagani L, Dell'Amico E, Migliavacca R, D'Andrea MM, Giacobone E, Amicosante G, Romero E, Rossolini GM. Multiple CTX-M-type extended-spectrum β-lactamases in nosocomial isolates of Enterobacteriaceae from a hospital in northern Italy. J Clin Microbiol. 2003;41(9):4264–9.
26. Mshana SE, Falgenhauer L, Mirambo MM, Mushi MF, Moremi N, Julius R, Seni J, Imirzalioglu C, Matee M, Chakraborty T. Predictors of bl a CTX-M-15 in varieties of *Escherichia coli* genotypes from humans in community settings in Mwanza, Tanzania. BMC Infect Dis. 2016;16(1):187.
27. Schaumburg F, Alabi A, Kokou C, Grobusch MP, Köck R, Kaba H, Becker K, Adegnika AA, Kremsner PG, Peters G. High burden of extended-spectrum β-lactamase-producing Enterobacteriaceae in Gabon. J Antimicrob Chemother. 2013;68(9):2140–3.
28. Tellevik MG, Blomberg B, Kommedal Ø, Maselle SY, Langeland N, Moyo SJ. High prevalence of faecal carriage of ESBL-producing Enterobacteriaceae among children in Dar es Salaam, Tanzania. PLoS ONE. 2016;11(12):e0168024.
29. Desta K, Woldeamanuel Y, Azazh A, Mohammod H, Desalegn D, Shimelis D, Gulilat D, Lamisso B, Makonnen E, Worku A: High gastrointestinal colonization rate with extended-Spectrum β-lactamase-producing Enterobacteriaceae in hospitalized patients: emergence of Carbapenemase-Producing K. pneumoniae in Ethiopia. *PloS one* 2016, 11(8).
30. ERDOĞAN DÇ, Cömert F, SEPETCİ EA, Köktürk F, Külah C: Fecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella spp. in a Turkish community. *Turkish journal of medical sciences* 2017, 47(1):172–179.
31. Isendahl J, Turlej-Rogacka A, Manjuba C, Rodrigues A, Giske CG, Naucler P. Fecal carriage of ESBL-producing *E. coli* and *K. pneumoniae* in children in Guinea-Bissau: a hospital-based cross-sectional study. PLoS ONE. 2012;7(12):e58981.
32. Moremi N, Claus H, Silago V, Kabage P, Abednego R, Matee M, Vogel U, Mshana S. Hospital surface contamination with antimicrobial-resistant gram-negative organisms in Tanzanian regional and tertiary hospitals: the need to improve environmental cleaning. J Hosp Infect. 2019;102(1):98–100.
33. Silago V, Kovacs D, Msanga DR, Seni J, Matthews L, Oravcová K, Zadoks RN, Lupindu AM, Hoza AS, Mshana SE. Bacteremia in critical care units at Bugando Medical Centre, Mwanza, Tanzania: the role of colonization and contaminated cots and mothers' hands in cross-transmission of multidrug resistant gram-negative bacteria. Antimicrob Resist Infect Contr. 2020;9:1–14.
34. Organization WH. Water, sanitation and hygiene in health care facilities: status in low and middle income countries and way forward. 2015.
35. Bouzid M, Cumming O, Hunter PR. What is the impact of water sanitation and hygiene in healthcare facilities on care seeking behaviour and patient satisfaction? A systematic review of the evidence from low-income and middle-income countries. BMJ Glob Health. 2018;3(3):e000648.
36. URT. The National Action Plan on Antimicrobial Resistance (2017–2022). In. The United Republic of Tanzania (URT): The Ministry of Health Community Development Gender Elderly and Children (MHCDGEC), Ministry of Agriculture, Livestock and Fisheries (MALF); 2017.
37. Mugnaioli C, Luzzaro F, De Luca F, Brigante G, Perilli M, Amicosante G, Stefani S, Toniolo A, Rossolini GM. CTX-M-type extended-spectrum β-lactamases in Italy: molecular epidemiology of an emerging countrywide problem. Antimicrob Agents Chemother. 2006;50(8):2700–6.

38. Peerayeh SN, Eslami M, Memariani M, Siadat SD. High prevalence of blaCTX-M-1 group extended-spectrum β-lactamase genes in *Escherichia coli* isolates from Tehran. Jundishapur J Microbiol 2013;6(7).
39. Rossolini G, Dandrea M, Mugnaioli C. The spread of CTX-M-type extended-spectrum β-lactamases. Clin Microbiol Infect. 2008;14:33–41.
40. Eckert C, Gautier V, Arlet G. DNA sequence analysis of the genetic environment of various bla CTX-M genes. J Antimicrob Chemother. 2006;57(1):14–23.
41. Ministry of Health T. Standard Treatment Guidelines & National Essential Medicines List-Tanzania Mainland. 2017.
42. Karam G, Chastre J, Wilcox MH, Vincent J-L. Antibiotic strategies in the era of multidrug resistance. Crit Care. 2016;20(1):136.
43. Meyer E, Gastmeier P, Deja M, Schwab F. Antibiotic consumption and resistance: data from Europe and Germany. Int J Med Microbiol. 2013;303(6–7):388–95.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions