Preliminary insights into the occurrence of similar clones of extended-spectrum beta-lactamase-producing bacteria in humans, animals and the environment in Tanzania: A systematic review and meta-analysis between 2005 and 2016

J. Seni1,2 | N. Moremi1 | M. Matee3 | F. van der Meer4 | R. Devinney2 | S. E. Mshana1 | J. D. D Pitout2

1Department of Microbiology and Immunology, Catholic University of Health and Allied Sciences, Mwanza, Tanzania
2Department of Microbiology, Immunology and Infectious Diseases, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada
3Department of Microbiology and Immunology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
4Faculty of Veterinary Medicine: Ecosystem and Public Health, University of Calgary, Calgary, AB, Canada

Correspondence
Jeremiah Seni, Department of Microbiology and Immunology, Catholic University of Health and Allied Sciences, Mwanza, Tanzania. Email: senij80@gmail.com

Summary
The emergence and spread of extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBL-PE) are complex and of the public health concern across the globe. This review aimed at assessing the ESBL-PE clones circulating in humans, animals and the environment to provide evidence-based insights for combating ESBL-PE using One Health approach. Systematic search from Medline/PubMed, Google Scholar and African Journals Online was carried out and retrieved nine eligible articles (of 131) based on phenotypic and genotypic detection of ESBL-PE between 2005 and 2016 in Tanzania. Analysis was performed using STATA 11.0 software to delineate the prevalence of ESBL-PE, phenotypic resistance profiles and clones circulating in the three interfaces. The overall prevalence of ESBL-PE in the three interfaces was 22.6% (95% CI: 21.1–24.2) with the predominance of Escherichia coli (E. coli) strains (51.6%). The majority of ESBL-PE were resistant to the commonly used antimicrobials such as trimethoprim–sulfamethoxazole and tetracycline/doxycycline, 38%–55% were resistant to ciprofloxacin and all were sensitive to meropenem/imipenem. ESBL-PE infections were more associated with deaths compared to non-ESBL-PE infections. Strikingly, E. coli ST38, ST131 and ST2852 were found to intersect variably across the three interfaces. The predominant allele, blaCTX-M-15, was found mostly in the conjugative IncF plasmids connoting transmission potential. The high prevalence of ESBL-PE and shared clones across the three interfaces, including the global E. coli ST131 clone, indicates wide and inter-compartmental spread that calls for One Health genomic-driven studies to track the resistome flow.

KEYWORDS
clones, extended-spectrum beta-lactamase, one health, Tanzania

1 INTRODUCTION

Antimicrobial resistance (AMR) is a complex global matter, which adversely affects human health (WHO, 2014). The worldwide spread of multi-drug-resistant (MDR) bacterial strains in livestock and companion animals that share the same clones with strains from humans and the environmental sources poses controversies among scientists regarding their transmission and evolution (Ewers, Bethe, Semmler, Guenther, & Wieler, 2012). Irrational use of antimicrobial agents in both humans and food animals and use of antimicrobial
agents as growth promoter as well as unregulated antimicrobial dispos- al to the environment have been pointed out as the predominant factors driving the persistence of AMR (El Salabi, Walsh, & Chouchni, 2013; Kummerer, 2003; Martinez, 2009; Wegener, 2003).

Extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBL-PE) resists beta-lactam antibiotics by producing beta-lactamase enzymes that are encoded by different gene variants including TEM, SHV and CTX-M types (Pitout & Laupland, 2008; Sturenburg & Mack, 2003), limiting antimicrobial therapeutic potential of these agents. Moreover, coresistance with non-beta-lactam antibiotics such as aminoglycosides and fluoroquinolones has been reported to complicate antimicrobial therapeutic options for both enteric and extra-intestinal infections (Pitout & Laupland, 2008; Storberg, 2014). The burden of ESBL-associated infections is growing with noticeable regional variations, and higher ESBL-PE rates have been reported in Asia, Middle East and Latin America, whereas the rates in North America and European countries have remained below 10%, with a few exceptions in some countries (Hoban et al., 2012; Morrissey et al., 2013; Sturenburg & Mack, 2003). Available limited local data from the African continent also show a continuous rise in ESBL-PE rates in most countries (Storberg, 2014). The CTX-M types of beta-lactamases, notably the \( \text{bla}_{\text{CTX-M-15}} \), have been observed to be the most common ESBL alleles (Pitout & Laupland, 2008). It has recently emerged as a worldwide allele in isolates causing infections in the healthcare and community settings, but also colonizing animals and birds (Nicolas-Chanoine, Bertrand, & Madec, 2014).

The ESBL-PE burden among humans and animals has been widely described in Tanzania (Lupindu et al., 2014; Madoshi et al., 2016; Sonda et al., 2016), as opposed to their occurrence in the environmental sources (Lyimo, Buza, Subbiah, Smith, & Call, 2016). There is high faecal carriage of ESBL strains among children and in the general population, which in turn may partly explain their involvement in fatal sepsis among vulnerable children population in this country (Blomberg et al., 2005; Kayange, Kamugisha, Mwizamholya, Jeremiah, & Mshana, 2010; Mhada, Fredrick, Matee, & Massawe, 2012). Moreover, previous studies which evaluated AMR in the three interfaces were not specifically focused on ESBL-PE (Lupindu et al., 2015; Shah, Colquhoun, Nikuli, & Sorum, 2012). Therefore, there is limited information on the linkage between ESBL-PE in humans, animals and environmental interfaces in Tanzania. In the present review, the aim was to examine whether there is existence of similar clones of ESBL-PE in humans, animals and environmental interfaces in Tanzania. To address this, a review of available literature was carried out to establish the prevalence of ESBL-PE and ascertain whether there are similar ESBL clones circulating between humans, animals and the environment, as a crucial starting point for specific interventions.

## 2 MATERIALS AND METHODS

### 2.1 Literature search and selection criteria

Literature search of articles on ESBL-PE in humans, animals and the environment in Tanzania was carried out by two researchers (JS and NM) from Medline/PubMed, Google Scholar and African Journals Online (AJOL) from October to December 2016. Whenever there was a discordance finding, consensus was reached by involving a third researcher (SEM). Abstracts and titles of 131 articles published in English from 1946 to 2016 were retrieved using exact key words (“AMR” AND “Tanzania”) as recommended by the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Table S1) (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group 2009), and all articles on AMR searched have been attached (Table S2). We used Medline/PubMed search strategy to retrieve 72 abstracts and titles. This was followed by specific search using key words (“ESBL OR [extended-spectrum beta-lactamase]” AND (“Human” OR “Animal” OR “Environment”) AND (“Tanzania”)), which in turn enabled us to retrieve more 59 abstracts and titles (48 from Medline/PubMed and 11 from Google Scholar/AJOL). A total of 116 full-text articles were retrieved for in-depth assessment of eligibility. Studies which included both phenotypic and genotypic ESBL detection from humans, animals and environmental sources were considered eligible for the final systematic review and meta-analysis. Moreover, review articles, laboratory-based studies focusing only on resistance genes transfer, and studies conducted during outbreaks were excluded (Figure 1).

Articles were further assessed for quality and strength of evidence, and graded as high, middle or low based on criteria stipulated before with some minor modifications (Hedin & Källestål, 2004; Storberg, 2014) (Table 1). Therefore, articles included in the final analysis (n = 9) contained information on the prevalence of ESBL-PE, circulating ESBL clones, phenotypic resistance profiles markers and proportions of ESBL strains expressing \( \text{bla}_{\text{CTX-M-15}} \) (Table 1).

### 2.2 Data extraction, quality assessment and data analysis

Information extracted from the articles was author names, year of publication, journal name, study duration, study site/region, study population (humans, animals and environment), types of samples,
ESBL diagnostic methods, sample size, number of ESBL-PE-positive isolates, ESBL bacterial species, phenotypic resistance to trimethoprim–sulfamethoxazole (1.25/23.75 μg), tetracycline/doxycycline (30 μg), gentamicin (10 μg), ciprofloxacin (5 μg) and meropenem/imipenem (10 μg), ESBL genotypes (blaCTX-M-15 allele), ESBL clones (sequence types), location of ESBL gene, predictors of ESBL and outcome of ESBL attributable infections in humans.

Two strategies were employed in assessing potential bias in eligible studies, and as a result, two studies (Doijad et al., 2015; Mshana, Gerwing, et al., 2011) were excluded because they were conducted during an outbreak involving one strain of Enterobacter spp. Also, five studies were excluded because they included only genotypic detection of ESBL (Lyimo et al., 2016; Madoshi et al., 2016; Doijad et al., 2015; Mshana, Gerwing, et al., 2011; Sato et al., 2009), inclusion of these studies would have resulted into involvement of ESBL strains containing ESBL genes which are not expressed phenotypically (Figure 1). Nevertheless, contributions of these studies were appraised and discussed in this review.

Meta-analysis was performed using STATA software version 11.0 (College Station, Texas, USA) to get the proportions of ESBL-PE among humans, animals and in the environmental sources, and their respective 95% confidence intervals. The random-effects meta-analysis model was used to calculate the pooled (weighted) proportion of ESBL, and the I² statistic was used as measure of inconsistency in delineation of heterogeneity across studies. A value of 0% was used as a measure of no observed heterogeneity, whereas increasing values indicate increasing heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). Percentages of resistance to the five antimicrobial agents among ESBL-PE were pooled and their means determined respectively. The proportion of ESBL-PE expressing blaCTX-M-15 was done using two-sample test of proportions, after computing the proportions of blaCTX-M-15 in each of the three categories.

Ethical approval was sought and provided from the Joint Catholic University of Health and Allied Sciences (CUHAS)/Bugando Medical Centre (BMC) Research and Ethical Committee (CREC/123/2016).

3 | RESULTS

3.1 | Prevalence of ESBL in humans, animals and the environment

The overall prevalence of ESBL in the three interfaces was found to be 22.62% (95% CI: 21.08–24.16) (Blomberg et al., 2005; Moremi et al., 2016; Mshana, Imirzalioglu, et al., 2011; Mshana et al., 2013, 2016; Ndugulile, Jureen, Harthug, Urassa, & Langeland, 2005; Onken, Said, Jorstad, Jenum, & Blomberg, 2015; Seni et al., 2016; Tellevik et al., 2016). The lowest and highest ESBL prevalence were 0.90% (95% CI: 0.46–1.34) and 53.40% (95% CI: 41.96–64.84), respectively (Blomberg et al., 2005; Moremi et al., 2016) (Figure 2).

3.2 | ESBL-producing bacterial species from humans, animals and the environment in Tanzania

With regard to ESBL-PE species, E. coli and Klebsiella species were the predominant bacterial species (93.2%) compared to other bacterial
| Author and year | Journal | Duration | Region | Population | Settings | Samples | ESBL diagnostic methods | Sample size | ESBL positive | Number typed | Prevalence of ESBL (%) | Grade |
|-----------------|---------|----------|--------|------------|----------|---------|-------------------------|-------------|---------------|-------------|---------------------|-------|
| Ndugulile et al. (2005) | BMC Infect Dis. 2005; 5:86 | October 2002–April 2003 | Dar es salaam | Humans | Hospital based | Urine & pus | Disc diffusion method, E test, PCR, PFGE and Sequencing | 50 | 11 | 11 | 22.0 | Medium |
| Blomberg et al. (2005) | J Clin Microbiol 2005; 43(2):745–9 | August 2001–August 2002 | Dar es salaam | Humans | Hospital based | Blood | Disc diffusion method, E test, PCR and Sequencing | 1798 | 16 | 19 | 0.9 | High |
| Mshana, Imirzalioglu, et al. (2011) | Clin Microbiol Infect 2011; 17: 1279–1282 | Not indicated | Mwanza | Humans | Hospital based | Blood, wound swab, urine & pus | Disc diffusion method, PCR and Sequencing | 800 | 110 | 32 | 13.8 | High |
| Mshana et al. (2013) | BMC Infect Dis. 2013; 13:466 | April 2009–March 2010 | Mwanza | Humans | Hospital based | Blood, wound swab, urine & pus | Disc diffusion method, PCR and Sequencing | 1260 | 103 | 92 | 8.2 | High |
| Onken et al. (2015) | PLoS One. 2015;10(12) | March 2012–April 2013 | Unguja | Humans | Hospital based | Blood | Disc diffusion method, E test, VITEK system, MALDI-TOF, and PCR | 469 | 5 | 4 | 1.1 | Low |
| Seni et al. (2016) | Front. Microbiol. 2016; 7:142 | August 2014–September 2014 | Mwanza | Animals | Community based | Rectal swabs | Mac Conkey with 2 mg/L of CTX, ESBLCHROMagar, Disc diffusion method, VITEK-2 compact system and WGS | 600 | 130 | 25 | 21.7 | High |
| Mshana et al. (2016) | BMC Infect Dis. 2016; 16:187 | June 2014–September 2014 | Mwanza | Humans | Community based | Rectal swabs | ESBL CHROMagar, Disc approximation method, VITEK-2 compact system, PCR and WGS | 334 | 55 | 42 | 16.5 | High |

(Continues)
species, which accounted for only 6.8% (Blomberg et al., 2005; Moremi et al., 2016; Mshana et al., 2013, 2016; Mshana, Imirzalioglu, et al., 2011; Ndugulile et al., 2005; Onken et al., 2015; Seni et al., 2016; Tellevik et al., 2016) (Figure 3).

### 3.3 Predictors and outcomes of ESBL-associated infections/colonization in humans and animals

Of the nine articles included, four analysed factors associated with ESBL-PE infections/colonization (Blomberg et al., 2005; Mshana et al., 2016; Seni et al., 2016; Tellevik et al., 2016). In domestic animals, exotic breed type was significantly associated with ESBL carriage compared to local type whereas (Seni et al., 2016) in humans, history of admission, history of previous antibiotics use, longer duration from admission to culture, HIV-positive individuals and isolates from tertiary hospitals were significantly associated with ESBL (Blomberg et al., 2005; Mshana et al., 2016; Tellevik et al., 2016).

Two studies described the outcomes among patients with ESBL-PE attributable infections; all of them indicated that patients suffering from ESBL-PE infections were more likely to die compared to those suffering from non-ESBL-PE infections 71% versus 39% and 60% versus 36%, respectively (Blomberg et al., 2005; Onken et al., 2015).

### 3.4 Antimicrobial resistance patterns of ESBL bacterial isolates to non-beta-lactam agents

High-resistance trends of ESBL-PE to the non-beta-lactam antimicrobials were observed in all three interfaces (Blomberg et al., 2005; Moremi et al., 2016; Mshana et al., 2013, 2016; Mshana, Imirzalioglu, et al., 2011; Ndugulile et al., 2005; Onken et al., 2015; Seni et al., 2016; Tellevik et al., 2016). In all cases, human isolates exhibited more resistance to the four antimicrobials compared to animals’ and environmental isolates. The majority (60%) of ESBL-PE were resistant to the commonly used antimicrobials such as trimethoprim–sulfamethoxazole and tetracycline/doxycycline, 38%–55% were resistant to ciprofloxacin and between 46% and 75% were resistant to gentamicin. Fortunately, all tested ESBL-PE isolates were sensitive to meropenem/imipenem (Blomberg et al., 2005; Moremi et al., 2016; Mshana et al., 2013, 2016; Mshana, Imirzalioglu, et al., 2011; Ndugulile et al., 2005; Onken et al., 2015; Seni et al., 2016; Tellevik et al., 2016) (Figure 4).

### 3.5 ESBL alleles/genes and clones circulating between humans, animals and the environment

All but one study (Onken et al., 2015) evaluated the ESBL alleles/genes. Over three quarters (78.8%) of ESBL-PE from humans, animals and environment expressed blαCTX-M-15 alleles. This was relatively lower in humans (72.5%) compared to animals (90.9%) and environment (92.3%) (Blomberg et al., 2005; Moremi et al., 2016; Mshana et al., 2013, 2016; Mshana, Imirzalioglu, et al., 2011; Ndugulile et al., 2005; Onken et al., 2015; Seni et al., 2016; Tellevik et al., 2016) (Table 2).
E. coli sequence types (STs) (Moremi et al., 2016; Mshana et al., 2016; Mshana, Imirzalioglu, et al., 2011; Seni et al., 2016). In humans, E. coli ST131 was the commonest followed by ST38 (Mshana et al., 2016; Mshana, Imirzalioglu, et al., 2011) and ST617 predominated in animals (Seni et al., 2016). A quarter of the isolates expressed unique STs (Moremi et al., 2016; Mshana et al., 2016; Mshana, Imirzalioglu, et al., 2011; Seni et al., 2016). Strikingly, E. coli ST131, ST38 and ST2852 were the only clones found to circulate in both three interfaces (Moremi et al., 2016; Mshana et al., 2016; Mshana, Imirzalioglu, et al., 2011; Seni et al., 2016) (Figure 5). Klebsiella pneumoniae (K. pneumoniae) isolates in humans showed predominance of ST14 and ST48 (in 28 of 92 isolates) (Mshana et al., 2013). Other STs found were ST101, ST147 and ST348 in humans, two ST37 in fish and one ST280 from soil/environmental source (Moremi et al., 2016; Mshana et al., 2013).

**FIGURE 2** Prevalence of extended-spectrum beta-lactamase (ESBL) in humans, animals and the environment in Tanzania. Mid-point of each horizontal line segment shows the prevalence estimate of ESBL in each study, whereas rhombic mark shows the pooled prevalence from all nine studies included. Moremi et al. (a) and Moremi et al. (b) is one study but divided into two purposely to represent fish and environmental sources of ESBL, respectively.

**FIGURE 3** Proportions of bacterial species among extended-spectrum beta-lactamase-producing bacterial isolates (N = 709). Others: Enterobacter spp. (25); Citrobacter spp. (13); Proteus spp. (9), Salmonella spp. (1)

**FIGURE 4** Antimicrobial resistance of extended-spectrum beta-lactamase bacterial isolates to non-beta-lactam agents. TMP-SXT: trimethoprim–sulfamethoxazole; TET/DOXY: tetracycline/doxycycline; GENT: gentamicin; CIPRO: ciprofloxacin. Tetracycline/doxycycline resistance was not tested in two studies (Mshana, Imirzalioglu, et al., 2011; Onken et al., 2015); ciprofloxacin resistance was not tested in one study (Blomberg et al., 2005); and meropenem/imipenem resistance was not tested in two studies (Ndugulile et al., 2005; Seni et al., 2016).
TABLE 2 The proportion of extended-spectrum beta-lactamase bacterial isolates expressing bla_{CTX-M-15} in humans, animals and the environment in Tanzania

| Group                        | Proportion (95% confidence interval) |
|------------------------------|--------------------------------------|
| Isolates from humans         | 72.5 (68.5–76.5)                     |
| Isolates from animals        | 90.9 (81.5–100.3)                    |
| Isolates from the environment| 92.3 (77.8–106.8)                    |
| All isolates                 | 78.8 (75.3–82.28)                    |

FIGURE 5 Multiple *Escherichia coli* clones circulating between humans, animals and the environment in Tanzania. This figure was based on four articles which detected extended-spectrum beta-lactamase-producing Enterobacteriaceae sequence types (Moremi et al., 2016; Mshana et al., 2016; Mshana, Imirzalioglu, et al., 2011; Seni et al., 2016)

4 | DISCUSSION

In this review, the overall ESBL-PE prevalence pooled from the three interfaces was found to be 22.6%, which is within the range of ESBL prevalence in other African countries such as Kenya, Algeria and Cameroon irrespective of the categories (Kiiru, Kariuki, Goddeeris, & Butaye, 2012; Storberg, 2014). However, this overall prevalence is lower compared to 42% reported among humans in East African hospitals (Sonda et al., 2016). Prevalence in the later may be accounted by the fact that these ESBL bacterial isolates were from patients in the hospitals where MDR bacteria prevail. This is also supported by two studies in Uganda where the proportions of ESBL-producing bacteria isolated from inpatients and outpatients were over 75% and 5.3%, respectively (Najjuka, Kateete, Kajumbula, Joloba, & Essack, 2016; Seni et al., 2016).

As it has been reported in other studies done outside African continent (Friedmann et al., 2009; Pasricha et al., 2013), carriage of ESBL-PE in this review was predicted by history of previous use of antimicrobial agents and longer hospitalization (Blomberg et al., 2005; Mshana et al., 2016; Tellevik et al., 2016), and exotic bred in domestic animals (Seni et al., 2016). Infections caused by ESBL-PE contributed to more deaths than non-ESBL infections as previously reported and reiterated in the current review (Blomberg et al., 2005; Kayange et al., 2010; Onken et al., 2015). The plausible explanation of this may be due to the severity of infections caused by MDR bacteria (both were blood stream infections), immune status of patients and antimicrobial therapeutic challenges in managing infections attributable to these strains. This calls for up-scaling of diagnostic services and setting up AMR surveillance systems, as many patients are probably succumbing from MDR infections unnoticed due to the absence of antimicrobial testing diagnostic services in most regions across Tanzania.

Data from this review found a significant number of ESBL-PE resistant non-beta-lactam antibiotics. More than 60% of the ESBL-PE isolated from humans, animals and the environment were resistant to trimethoprim–sulfamethoxazole and tetracycline/doxycycline, agents which are widely available and less costly in Tanzania and therefore more likely to be abused. In this review, the resistance to ciprofloxacin and gentamicin ranged from 46% to 75%. Despite of the established evidence that ESBL isolates tend to coresist, other classes of antimicrobials such as aminoglycosides (Doi & Arakawa, 2007), abuse of sulphur and tetracyclines in animals and human medicine (Sarmah, Meyer, & Boxall, 2006), and their longer persistence in the environment when disposed inappropriately (Kay, Blackwell, & Boxall, 2004; Monteiro & Boxall, 2010) might have allowed the selection of resistant strains and subsequent spread in the three interfaces. Similar to this review, a recent review from Kenya and another study from Uganda showed that there is no resistance to meropenem/imipenem (Kiiru et al., 2012; Najjuka et al., 2016). Moreover, studies in Kenya and Uganda also showed that piperacillin–tazobactam was effective in 60%–73% of isolates connoting its potential therapeutic alternative in the management of ESBL attributable infections (Kiiru et al., 2012; Najjuka et al., 2016).

In this review *E. coli* and *K. pneumoniae* were predominant ESBL-PE; an observation previously reported within and outside the African continent (Lautenbach, Patel, Bilker, Edelstein, & Fishman, 2001; Sonda et al., 2016; Storberg, 2014). The worldwide pandemic clone *E. coli* ST131 (Nicolas-Chanoine et al., 2008, 2014) predominated in this review (Moremi et al., 2016; Mshana et al., 2016; Mshana, Imirzalioglu, et al., 2011; Seni et al., 2016). Similar to the previous study carried out in three European countries to establish the clonality of ESBL-*E. coli* strains from drinking water sources in Tanzania, and clinical isolates in the North, West and South African countries such as Tunisia, Nigeria and South Africa (Lyimo et al., 2016; Storberg, 2014). However, this was different from bla_{CTX-M-14} in flamingos exported to Japan from Tanzania and bla_{CTX-M-15} in a nearby East African country, Kenya in
urine specimens (Sato et al., 2009; Storberg, 2014). The observed variations among African countries point out the role played by other factors apart geographical location in the spread of resistant genes. ESBL-PE strains expressing $\beta$-lactamases have been previously reported to cause outbreak among neonates in Tanzania with case fatality rate of 35%, connoting an impending threat if AMR surveillance to guide specific control and preventive measures is not in place in the hospitals (Mshana, Gerwing, et al., 2011).

As opposed to $E. coli$ ST131 in humans, $E. coli$ STs 617, 1303 and 2852 in animals and $E. coli$ ST2852 in the environment predominated, connoting genotypic diversity of the strains across the three interfaces. Surprisingly, the global ST131 previously reported (Mathers, Peirano, & Pitout, 2015; Nicolas-Chanoine et al., 2014; Price et al., 2013), as well as ST38 and ST2852 were found intersecting in the three interfaces calling for multisectoral genomic-based strategic intervention using One Health approach to combat the situation. Preponderance of occurrence of $E. coli$ ST131 in humans as opposed to the animals and environmental sources was reiterated in this review, and also cautioned in another study in Tanzania (Madoshi et al., 2016). Despite the fact that none of the ESBL isolates were resistant to meropenem/imipenem in the present review, existence of the $E. coli$ ST131 clone underscores a need for continuous AMR surveillance for potential occurrence of strains expressing carbapenemases in the future (Peirano et al., 2014). Moreover, a previous study in Tanzania showed existence of carbapenemase genes among Gram-negative bacteria, reiterating further the need to monitor unprecedented phenotypic expression of these genes in the future (Mushi, Mshana, Imirzalioglu, & Bwanga, 2014).

The current review found more than 75% of the expressed ESBL genes in humans, animals and environmental isolates were located in conjugative IncF and IncY plasmids, with IncF plasmids cutting across all three interfaces. Similar observations have been observed in $E. coli$ isolates from humans, animals and environmental sources in Europe, USA and other countries around the globe (Carattoli, 2009; Johnson et al., 2016; Wu et al., 2013). Although this review could not establish the transmission routes shared in the three interfaces, the similarity of the conjugative plasmids observed hint to the possibility of strong epidemiological link of the typed ESBL isolates, which worthy further scrutiny in the follow-up studies.

4.1 Limitation of the review

In this review, only nine articles fulfilled the eligibility criteria (of 131 articles), this limited in-depth analysis of the dynamics of transmission of the circulating genotypes. Nevertheless, common genotypes in the three interfaces were shown to guide future studies on infection prevention and control strategies. Also, only a limited number of research articles in animal and environment categories were involved in the final analysis due to scarcity of the appropriate articles. Furthermore, the proportions of ESBL within each of the respective bacterial species could not be calculated due to the nature of reporting, because majority of studies reported the overall prevalence of ESBL, i.e. number of ESBL-PE over total population (humans, animals and environmental samples).

5 CONCLUSIONS

Approximately 23% of humans, animals and environmental samples harbour ESBL-PE strains. The evidence of shared ESBL $\beta$-lactamase al- lele occurring in conjugative IncF plasmids, as well as ST38, ST131 and ST2852 clones in the three interfaces calls for One Health genomic-driven approaches to identify the resistome flow and subsequently prevent negative impacts attributable to ESBL-PE infections. In the light of these findings, ESBL transmission dynamics in the three interfaces and economic impacts should be potential areas for future research.

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CONFLICT OF INTEREST

All authors have no any competing interests and have agreed the manuscript to be submitted.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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