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REVIEW ARTICLE OPEN ACCESS

Molecular detection of ESBL genes in urinary pathogens from hospitalised and community patients in Ogun State, Nigeria

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Abstract
Objectives: The emergence of Extended-Spectrum Beta-Lactamases (ESBL) enzymes in Enterobacteriaceae in hospitals and communities has led to therapeutic failures and increased treatment costs globally. This study isolated and identified ESBL genes from the urine samples of hospitalised patients in two selected hospitals and people living in the Oyan Dam Community, all in Ogun State, Nigeria.
Methods: A total of 416 urine samples were collected and cultured, and the isolates were identified using API 20E. Antibiotic Susceptibility Test was carried out to identify Multi-drug Resistant (MDR) bacteria using the disc diffusion method. ESBL-resistant genes were identified using TEM-1, Sulfhydryl Variable, and Cefotaxime Hydrolysing Capabilities (CTX-M) specific primers.
Results: A total of 167 (40.14%) Gram-negative bacilli were isolated. *Escherichia coli* 104 (62.3%), *Klebsiella pneumoniae* 10 (6.0%), *Klebsiella ozaenae* 21 (12.6%), and other bacteria were identified. A total of 106 (63.5%) isolates were identified as MDR, out of which 75 (70.8%) were *Escherichia coli* and five (4.7%) were *Klebsiella pneumoniae*. The isolates were highly resistant to ceftazidime, cefixime, gentamicin, cefuroxime and ofloxacin. ESBL production was observed in 96 (90.6%), TEM-1 gene 63 (65.6%) was predominant, CTX-M 33 (34.4%) co-existed with TEM and no SHV gene was identified.
Conclusion: This study has revealed that people in their homes may be more predisposed to drug resistance, and this may constitute a public health threat that requires social interventions. *E. coli* and *Klebsiella pneumoniae* isolates *are the most prevalent causative agents in the communities, as with hospital infections*.

Keywords: SHV, TEM, CTX-M, Antibiotic resistance, Enterobacteriaceae, Extended-Spectrum Beta-lactamase

Background

Enterobacteriaceae are Gram-negative bacilli which can be with or without symptoms colonise the urinary tract (1). Enterobacteriaceae are responsible for approximately 80% of Urinary Tract Infections (UTIs) in humans. They cause infection both in the community and in hospitals (2, 3, 4) as reported in hospital and community settings in Osogbo, Nigeria. These include *Escherichia coli (E. coli), Klebsiella species, Proteus species* and *Enterobacter species,* among others, with *E. coli* as the leading cause of UTI (5). Several authors reported that *E. coli* was the most prevalent uropathogen in a facility in Abuja, Ondo and Abakiliki, all in Nigeria (6, 7, 8).

The World Health Organisation refers to infections caused by organisms that confer resistance to several antibiotics as multidrug-resistant organisms. Extended-Spectrum Beta-Lactamases (ESBL) produce enzymes that cause multidrug resistance of

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Enterobacteriaceae. Several genes acquired by ESBL-producing organisms are responsible for the resistance (9). Temoneira (TEM), Sulfhydryl Variable (SHV) and Cefotaxime Hydrolysing Capabilities (CTX-M) variants of ESBL have been reported severally (2, 10), and they are on the increase worldwide (3, 11, 12).

This has led to the non-sustainability of the use of broad-spectrum antibiotics for treatment, since it leads to an increase in resistance (13). This has become of great concern worldwide and a threat to the treatment of both community and hospital-acquired urinary infections (14). Multi-drug resistance affects both developed and developing countries, but is worse in the latter (15). Due to irrational use of antibiotics, this is experienced more in developing countries because there are no polices controlling the use of antibiotics (14, 15). Resistance to antibiotics is mainly reported in Gram-negative bacteria.

Antibacterial resistance varies among the various classes of antibiotics (16). Hospitals are major sources of the emergence and spread of multidrug-resistant bacteria, but there is a paucity of information on antibiotic resistance in natural environments such as water and soil (17). The different resistant patterns observed are a major problem of public health concern (16, 18).

Culture and antibiotic sensitivity of urine samples are key to the diagnosis of urinary tract infections (5). Knowledge of common pathogens and their sensitivity patterns is necessary for the choice of antibiotic therapy (13, 19). There is a great need to identify, genetic type of ESBL genes responsible for the spread of antimicrobial resistance (18, 20).

This research investigated multidrug-resistant ESBL-producing Enterobacteriaceae in community and hospital settings in Ogun State, southwest Nigeria.

Materials and methods

Study Design

This involved a hospital and community-based cross-sectional and experimental design.

Study duration

This study was carried out between June and December 2017.

Study population

The study was carried out among the in-patients of OOUTH, SHI and healthy individuals living in ODC within the ages of 5 and 70 years.

Study Site

The study was conducted in three sites, which include Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, State Hospital Ijaye (SHI), Abeokuta and Oyan Dam Community (ODC), all in Ogun State, Western Nigeria. OOUTH is the only government-owned Tertiary Medical Institution in Ogun State, SHI is a secondary hospital in Ogun State, located in Sokenu, Ijaye, Abeokuta North Local Government Area of Ogun State, while ODC is located near the bank of Oyan water reservoir in Abeokuta North Local Government Area of Ogun State. Oyan water reservoir is situated within the coordinates 07° 15 – 07° 25' N and 03° 06' – 03° 18' E. It is about 20 km Northwest of Abeokuta, the State Capital. The dam was constructed across the Oyan River, a major tributary of the Ogun River. The dam was commissioned on March 29, 1983, and it is operated by the Ogun-Oshun River Basin Development Authority. It was primarily conceived to supply water to Lagos and Abeokuta, but with auxiliary uses in irrigation and power generation. During construction, some villages were submerged, and the displaced people were relocated to three settlement camps. Some of the settlers fish on the lake and grow vegetables along the fertile shoreline as the lake recedes in the dry season (21).

Sample Size Determination

The sample size was determined using the formula of (22):

Kish's method helps adjust for different selection probabilities and response rates among various strata within a population.

$n= Z^2 PQ/e^2$

Z = 1.96 (for 95% confidence level)

P = the frequency of occurrence of an event:

The research conducted in the hospital at Ijaye, Abeokuta, Ogun State, Nigeria, showed the prevalence of ESBL in urine samples of hospitalised patients as 9.6% (23).

P = 0.096

CI = 0.05 (for confidence interval)

Q= 1-P= 1-0.096= 0.904

$n = 1.96^2$ X 0.096 X 0.904/ 0.05^2

3.84 X 0.096 X 0.904/ 0.0025 = 133.30

Preparation of Culture Media

All media used in this study were prepared according to the manufacturer's instructions (Oxoid).

Sterilisation of Culture Media and Other Materials

Sterilisation of culture media, glass petri dish and sterile water used in this study was carried out in an autoclave (model LS-50L, Axiom Medical LtD.UK, Serial number: 16L-1679). The sterilisation was done at $121^{O}C$ temperature, 15 pounds per square inch (PSI) pressure for 15 minutes. The working benches, hot air oven and storage refrigerators were sterilised using 10% Jik solution.

Inclusion Criteria

Inclusion criteria for hospitalised patients and community participants
Any in-patient hospitalised for more than 24 hours in OOUTH and SHI within the ages of 5 and 70 years, whose consent was obtained. Any individual between the age range of 5 and 70 living in the selected community, whose consent was obtained.

Exclusion Criteria
Exclusion Criteria for hospitalised patients and community participants
Non-hospitalised patients in OOUTH and SHI, within the age range of 5 to 70, and inpatients within the ages of 5 and 70 years who had not spent up to 24 hours.
All patient who did not give their consent. Any patient who does not fall between the age range of 5 and 70 years in OOUTH and SHI. Anybody who does not fall within the age range of 5 and 70 years, and anybody living outside the selected community. People whose consent was not obtained.

Sample Collection
The research participants were given labelled, sterile universal bottles with instructions on how to collect mid-stream urine samples. All samples collected were transported to the Laboratory in ice packs and processed within 4 hours of collection in the laboratory (Department of Medical Laboratory Science, Babcock University, Ilishan, Ogun State, Nigeria).

Culture of Urine Samples
Urine samples were cultured on Cysteine Lactose Electrolyte Deficient medium (CLED) and Blood Agar plates using an inoculating loop to deliver 0.02 mL. All incubations were done at 37 ^{0}C for 18 to 24 hours, and the plates were examined for bacterial growth.

Identification of Bacterial Isolates
They were Gram-stained and viewed using the microscope. Biochemical tests were also carried out to identify the isolates. API 20E was used for further identification of the isolates.

Identification of the Isolates Using API 20E
The stock culture was reactivated by sub-culturing on CLED medium to obtain an 18- 24-hour-old culture. A colony of the bacteria was suspended in 5 mL of sterile distilled water. The API 20E test compartments were filled with bacterial suspension as instructed by the manufacturer. Water was put into the supplied tray, with the API 20E test strip placed on it, covered and incubated at 37 °C for 24 hours. The reactions, based on colour to the different biochemical reagents, were noted, matched with the chart provided by the manufacturer and converted to numerical codes. The codes were read with a profile index to identify the bacteria.

Antibacterial Sensitivity Test
The identified bacteria were tested for their sensitivity to different classes of antibiotics using ABTEK brand antibiotics (20). The classes of antibiotics used include: cephems (ceftazidime 30µg, cefuroxime 30µg, cefixime 5µg), aminoglycosides (gentamicin 10µg), fluoroquinolones (ofloxacin 5µg, ciprofloxacin 5µg), beta-lactam/β-lactamase inhibitor combination (Augmentin 30µg) and nitrofurans (nitrofurantoin 300µg).
The Kirby-Bauer method of disc diffusion technique was used in performing the antibiotic sensitivity testing (24), on Mueller Hinton agar using inocula that matched with turbidity of 0.5% Macfarland standard (24). This was done in duplicates and incubated using Medfield Equipment and Scientific England (DNP-9052-1) incubator overnight at 37 °C for 24 hours. The zone of inhibition by the bacteria was measured and recorded. Control was set up simultaneously using *Escherichia coli* ATCC 25922. The average of the zone of inhibition in the duplicate plates was interpreted as sensitive, intermediate and resistant using (25).

Detection of ESBL Genes from the Isolates
All the isolates were resistant to at least three antibiotics; they were termed multidrug-resistant isolates. Three different primers of ESBL types described by (26) was used to detect the presence of ESBL genes Multiplex PCR method in these multidrug-resistant isolates. This technique was carried out using the Solis Biodyne 5X HOT FIREPol Blend Master mix CTX-M, TEM and SHV primers.

Results
A total of 167 (40%) bacteria were identified as Gram-negative bacilli from the sites 63 (37.7%), 49 (29.3%) and 55 (32.9%) from ODC, OOUTH and SHI, respectively. The bacteria isolated include *Escherichia coli* 104(62.3), *Klebsiella pneumoniae* 10(6.0), *Escherichia fergusonii* 5 (3.0), *Klebsiella ozaenae* 21(12.6), *Xenorhabdus luminescens* 6(3.6.), *Hafnia alvei* 4(2.4), *Leclercia adecarboxylate* 2(1.2), *Proteus penneri* 7(4.2), *Enteroobacter agglomeran* 8(4.8). The number of the bacteria in OOUTH, ODC and SHI respectively include; *Escherichia coli* 25(24.0), 35(33.7) and 44(42.3), *Klebsiella pneumoniae;* 4(40.0), 2(20.0) and 4(40.0), *Escherichia fergusonii* 3(60), 1(20) and 1(20), *Klebsiella ozaenae;* 6(28.6), 11(52.4) and 4(19.5), *Xenorhabdus luminescens 1(16.7) and 4 (66.7) Hafnia alvei 2*(50%), *2*(50%) and *Leclercia*

adecarboxylate 3(42.9%), Enteroobacter agglomeran: 4 (50%), 2(25%) and *2 (25%)*

There was a significant difference in the type and number of bacteria identified from the different sites at a p-value of 0.024 (Figure 1).

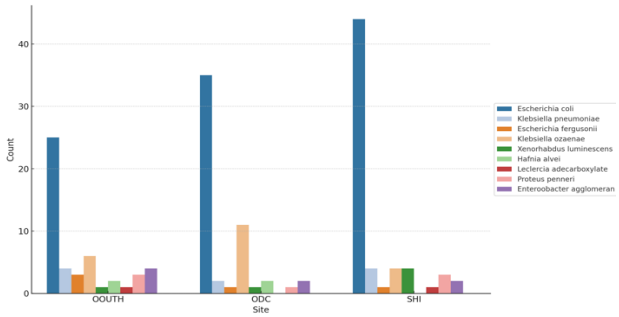

Fig. 1 Frequency Distribution of Bacteria Isolated from Different Sites

All the *K. pneumoniae* were resistant to all the antibiotics tested. Furthermore, *K. ozaenae* are resistant to cefixime 15 (100%), Augmentin 15 (100%), ceftazidime 12 (80%), ciprofloxacin 12 (80%), cefuroxime 11(73.3%), and nitrocefin 11(73.3%). The resistance of *E. coli* ranges between 57.9% and 97.4%. It is interesting to note that the only *E. fergusonii, H. alvei* and *L. adecarboxylate* were 100% resistant to all the antibiotics tested. There was no statistically significant difference in the resistance activity of the multidrug-resistant organisms to the antibiotics used in this study (Supplementary Table 1).

ESBL genes were identified using molecular methods with blaCTX-M, blaSHV, and blaTEM primers. A total of 96 (90.6) blaTEM genes were identified, followed by blaCTX-M 33(31.1). blaCTX-M genes did not exist alone; rather, they co-existed with TEM. Therefore, a total of 33 (31.13%) blaTEM/blaCTX-M were identified. blaTEM genes that existed alone were 63 (59.4%). No blaSHV genes were identified. SHI had the highest percentage of ESBL, followed by ODC. Similarly, blaCTX-M and the combination of blaCTX-M and blaTEM were identified in the same order: 5(15.2%), 25(75.8%) and 3(9.1%) (Figure 2).

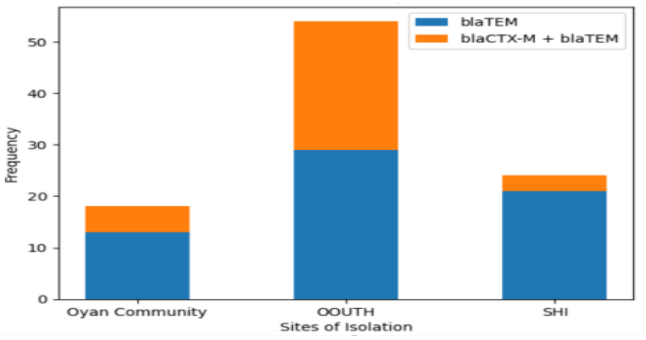

Figure 2: Distribution of the different ESBL genes according to the sites of Isolation

The distribution of ESBL-resistant genes according to age and gender. The gene was more predominant in the age group 16-26, as presented in Figures 3 and 4.

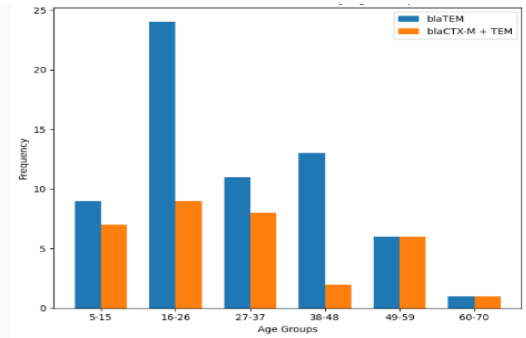

Figure 3: Distribution of ESBL genes according to age

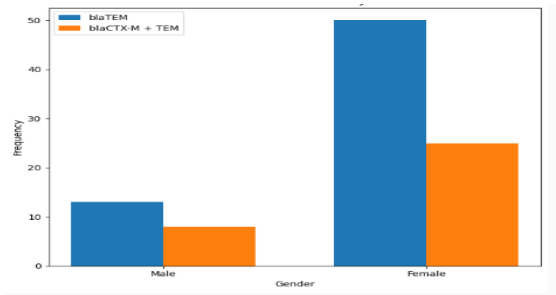

Figure 4: Distribution of ESBL genes according to gender

Klebsiella pneumoniae was observed in this study to harbour the highest percentage of ESBL, as presented in Figure 5.

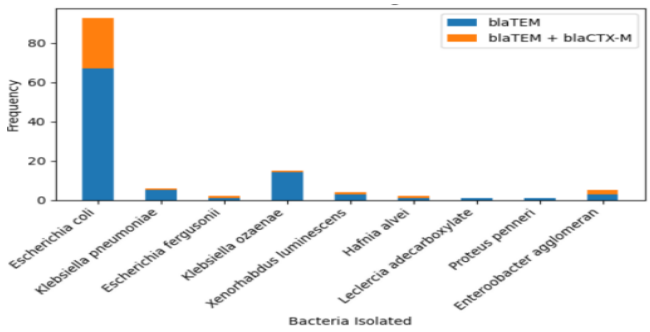

Figure 5: Distribution of ESBL genes among the MDR Bacteria Isolated

Discussions

The prevalence of Gram-negative bacilli obtained in this study is 40%. In the different sites, the prevalence obtained includes 63 (37.7%), 49 (29.3%) and 55 (32.9%) from ODC, OOUTH and SHI, respectively. This strongly indicates that the samples collected from the different hospitals and the Oyan community harbour relatively the same number of Gram-negative bacilli. This further indicates that the participants in this community were carriers of GNB, implying that the participants may pose a big challenge to the community. This finding agrees with a study carried out by (27) in Babcock University, Ogun State, Nigeria, who reported a prevalence of 35% among hospitalised individuals from a similar study. (28) also obtained 33.3% and 29.3% of Gram-negative bacilli from two tertiary hospitals in Osun State, Nigeria. In corroboration, a 43% prevalence was also obtained by (29) from a study carried out in a tertiary hospital in Yobe State, Nigeria.

In contrast, some other authors recorded a higher prevalence in a study carried out among hospitalised patients (30) in Katsina and (31). In a study carried out in two geopolitical zones of Ondo, the prevalence of Gram-negative bacteria was reported as 59.5% and 55.6%, respectively. These are because Gram-negative bacteria are widely implicated as urine pathogens. Elsewhere, (32) reported a lower prevalence of 8.5% in a general hospital population on the day of admission. This lower prevalence compared to that obtained in this present study could probably be because the urine samples were collected on the first day of admission, or the probable acquisition of the bacteria after 24 hours of admission in this present study.

The total prevalence of bacteria in the urine of participants in the Oyan community was 37.7%. Similar studies carried out in different communities reported a prevalence of 52% (33), 58.9% (34), 82.4% (35). (36) recorded a lower prevalence of 25% in a study carried out in a redemption camp, Ogun State. Varying prevalence rates were recorded in urban Nigerian cities such as Ibadan, 57.5% (37), Lagos, 38.6% (38), Jos, 35.5% (39). The prevalence of 77.9% was recorded among Prison inmates in Lafia, Nasarawa State (40). The differences in the community prevalence may be due to geographical location and social amenities of the communities, and the socioeconomic status and occupation of the inhabitants of the different communities. This study showcased that people in their homes may harbour pathogens as much as hospitalised patients, and hence, there is a need to investigate the factors predisposing community members to these pathogenic organisms.

All the *K. pneumoniae* were resistant to all the antibiotics tested. The other pathogens, as well, had varying high resistance to the antibiotics tested in this study. Various research, including

this present study, has confirmed that *Klebsiella pneumoniae* and *Escherichia coli* have been noted worldwide to be the most causative agents of both hospital and community infections. The extreme resistance of *K. pneumoniae* to all the antibiotics may be due to its notable ability to form biofilms and capsules, which protect it from the host immune system and confer antibiotic resistance on it (41, 42). The resistance of *E. coli* ranges between 57.9% and 97.4%. This agrees with the reports of (43) and (31). (44) reported that various Gram-negative bacilli can alter the sensitivity pattern of antibiotics. This resistant pattern exhibited by *K. pneumoniae* in this study is an indication that *K. pneumoniae* is taking the lead in multidrug resistance in hospital and community settings. There is a need to investigate the resistant genes responsible for this extreme resistance.

blaCTX-M and blaTEM were identified in this study. blaCTX-M genes did not exist alone; rather, they co-existed with blaTEM, although some blaTEM genes existed alone. No blaSHV genes were identified. SHI had the highest percentage of ESBL, followed by ODC. This study confirms that SHV ESBL-resistant genes are not present in these sites at the time of this study. The ESBL genes responsible for resistance in these sites are blaCTX-M and blaTEM. also, there is synergy between blaCTX-M and blaTEM in causing resistance among the identified pathogens.

Other studies reported by previous researchers from different locations identified blaTEM at various percentages
(45, *26*). The difference in the various reports of ESBL prevalence may be attributed to geographical variations. The co-existence of blaCTX-M as identified in this study agrees with the report of (46, 47). ESBL genes are responsible for resistance to various antibiotics in these hospital and community settings, and therefore, this has public health implications. The mechanisms by which these resistant genes are transferred to these pathogens are of interest and should be unveiled by further research.

This study indicates that the ESBL-resistant genes were predominant in the age group 16-26 and among females. There is a strong indication that the participants between the ages of 16 and 26 misuse and overuse antibiotics. Presently, in our society, the use of drugs, including antibiotics, by people of this age group is on the increase and therefore is a social and public health concern. Females harbour more urinary pathogens because of their short urethra and are therefore likely to harbour more drug-resistant pathogens. This result is in line with those of (48, 49), who reported that females harboured more ESBL producers than males. This study highlights that the youth are actively misusing drugs and therefore indicates the need for a public health campaign and awareness against the improper use of antibiotics and other drugs. The factors that predispose youth to the misuse of drugs should be investigated in further studies.

Klebsiella pneumoniae was observed in this study to harbour the highest percentage of ESBL in this study. This is a strong indication that *Klebsiella pneumoniae* has shown very extreme resistance. Many authors have widely reported the predominance of *Escherichia coli* in harbouring ESBL genes over Klebsiella *pneumoniae* (50, 26). However, no significant difference was observed in the harbouring of ESBL by the two organisms, which is in line with the report by (51). (44) reported the prevalence of ESBL *E. coli (*39.5%) and *Klebsiella pneumoniae* (44%). Similarly, other studies reported the prevalence as *Escherichia coli* (46.5%) and *Klebsiella pneumoniae* (44.4 %) in India (47), *Escherichia coli (*60%) and *Klebsiella pneumoniae* (40%) in Tehran, Iran (52). *Escherichia coli (*41.5%) and *Klebsiella pneumoniae* (54.4%) in Egypt (53) and *Escherichia coli (*65%) and *Klebsiella pneumoniae* (68.8%) in Khartoum, Sudan (54). The trend of high resistance is changing hands from *Escherichia coli* in harbouring to *Klebsiella pneumoniae* as identified in the present study. This implies that the acquisition of ESBL genes among *Escherichia coli and Klebsiella pneumoniae* varies according to geographical location. The factors that are responsible for this subtle change in trend in antibiotic resistance should be investigated.

Conclusion

This study has revealed that ESBL genes are not limited only to hospitalised patients. People in their homes may also harbour drug-resistant genes, as observed in this study. This is the case of the Oyan Community, which could be a public health threat, until social interventions are made available

List of Abbreviations

API: Analytical Profile Index
CTM: Cefotaxime Hydrolysis Capabilities
ESBL: Extended-Spectrum Beta-Lactamase
GNB: Gram-Negative Bacilli
ODC: Oyan Dam Community
OOUTH: Olabisi Onabanjo University Teaching Hospital
SHI: State Hospital Ijaye
SHV: Sulfhydryl Variabel
TEM: Temoneira
UTI: Urinary Tract Infections
Ml: Millilitre
oC: Degrees Celsius

%: percentage

Declarations

Ethical Clearance and consent to participate

Ethical clearance for this study was obtained from the Olabisi Onabanjo University Teaching Hospital Health Research Ethical Committee (OOUTH/HREC/57/2016). Permission letter for the study with Reference Number SHA/RES/VOL.2/162 was also obtained from the State Hospital, Ijaye, before the commencement of sample collection. Consent of the participants was sought by giving them informed consent forms to declare their willingness to participate in the research. Parents or caregivers gave their consent before children were involved in the study.

Consent for Publication

All the authors gave consent for the publication of the work under the Creative Commons Attribution Non-Commercial 4.0 license.

Availability of Data

Data for this work are available from the authors and may be presented on request.

Conflicts of Interest

The authors declared no conflict of interest.

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No funding was received for this work.

Authors' contributions

OOG: Conceptualisation; Methodology; Investigation; Project administration; Writing – Original Draft. DAM: Supervision; Validation; Writing – Review & Editing. AWA: Formal Analysis; Data Curation; Writing – Review & Editing. OCB: Investigation; Data Curation.

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References

1. Poirel L, Goutines J, Aires-de-Sousa M, Nordmann P. High rate of association of 16S rRNA methylases and carbapenemases in Enterobacteriaceae recovered from hospitalized children in Angola. Antimicrobial agents and chemotherapy. 2018 Apr;62(4):10-128. https://doi.org/10.1128/AAC.00021-18
2. Pitout JD, Chan WW, Church DL. Tackling antimicrobial resistance in lower urinary tract infections: treatment options. Expert review of anti-infective therapy. 2016 Jul 2;14(7):621-32. https://doi.org/10.1080/14787210.2016.1188004
3. Manyahi J, Moyo SJ, Tellevik MG, Ndugulile F, Urassa W, Blomberg B, Langeland N. Detection of CTX-M-15 beta-lactamases in Enterobacteriaceae causing hospital-and community-acquired urinary tract infections as early as 2004, in Dar es Salaam, Tanzania. BMC Infectious Diseases. 2017 Dec;17:1-7. https://doi.org/10.1186/s12879-017-2395-8
4. Hassan AO, Hassan RO, Muhibi MA, Adebimpe WO. A survey of Enterobacteriaceae in hospital and community acquired infections among adults in a tertiary health institution in Southwestern Nigeria. Afr J Microbiol Res. 2012 Jun 28;6(24):5162-7.
5. Delisle G, Quach C, Domingo MC, Boudreault AA, Gourdeau M, Bernatchez H, Lavallée C. Escherichia coli antimicrobial susceptibility profile and cumulative antibiogram to guide empirical treatment of uncomplicated urinary tract infections in women in the province of Québec, 2010–15. Journal of Antimicrobial Chemotherapy. 2016 Dec 1;71(12):3562-7. https://doi.org/10.1093/jac/dkw302
6. Adeleye QA, Ndubuisi EC, Isa FA. Etiologic and Anti-microbial Susceptibility Profiles of Bacterial Urinary Tract Infection and Bacterial Enteritis among Children at a Private Multi-Specialty Healthcare Facility in Abuja, Nigeria: A 5-Year Separate and Comparative Review. Nigerian Journal of Clinical Practice. 2024 Jan 1;27(1):35-46. https://doi.org/10.4103/njcp.njcp_299_23
7. Wilkie ED, Ezeani CV, Olasehinde DO, Oyedemi OT, Alao JO, Oluduro AO, Oyetunde OB. Molecular analysis of multidrug-resistant E. coli in pediatric UTIs: findings from a Nigerian Hospital. The Journal of Infection in Developing Countries. 2024 Feb 29;18(2):1-8. https://doi.org/10.3855/jidc.18520
8. John-Onwe BN, Iroha IR, Moses IB, Onuora AL, Nwigwe JO, Adimora EE, Okolo IO, Uzoeto HO, Ngwu JN, Mohammed ID, Oladimeji AS. Prevalence and multidrug-resistant ESBL-producing E. coli in urinary tract infection cases of HIV patients attending Federal Teaching Hospital, Abakaliki, Nigeria. African Journal of Microbiology Research. 2022 May 31;16(5):196-201. https://doi.org/10.5897/AJMR2022.9624
9. World Health Organization. 2014. Rivers loaded with antibiotic waste. Punch newspaper *Antimicrobial resistance: global report on surveillance*. 2019, May 2;12.
10. Ibrahimagić A, Bedenić B, Kamberović F, Uzunović S. High prevalence of CTX-M-15

and first report of CTX-M-3, CTX-M-22, CTX-M-28 and plasmid-mediated AmpC beta-lactamase producing Enterobacteriaceae causing urinary tract infections in Bosnia and Herzegovina in hospital and community settings. Journal of Infection and Chemotherapy. 2015 May 1;21(5):363-9. https://doi.org/10.1016/j.jiac.2015.01.003

11. Thaden JT, Fowler Jr VG, Sexton DJ, Anderson DJ. Increasing incidence of extended-spectrum β-lactamase-producing Escherichia coli in community hospitals throughout the southeastern United States. infection control & hospital epidemiology. 2016 Jan;37(1):49-54. https://doi.org/10.1017/ice.2015.239
12. Wang Y, Tian GB, Zhang R, Shen Y, Tyrrell JM, Huang X, Zhou H, Lei L, Li HY, Doi Y, Fang Y. Prevalence, risk factors, outcomes, and molecular epidemiology of mcr-1-positive Enterobacteriaceae in patients and healthy adults from China: an epidemiological and clinical study. The Lancet Infectious Diseases. 2017 Apr 1;17(4):390-9. https://doi.org/10.1016/S1473-3099(16)30527-8
13. Zilberberg MD, Nathanson BH, Sulham K, Fan W, Shorr AF. Carbapenem resistance, inappropriate empiric treatment and outcomes among patients hospitalized with Enterobacteriaceae urinary tract infection, pneumonia and sepsis. BMC infectious diseases. 2017 Dec;17:1-3. https://doi.org/10.1186/s12879-017-2383-z
14. Sattar A, Khokhar AR, Abbasi SA, Kaleem F, Faraz A, Faqir F. In Vitro Activity of Tigecycline Against Multi Drug Resistant Bacteria. Annals of PIMS ISSN.;1815:2287.
15. Da Costa PM, Loureiro L, Matos AJ. Transfer of multidrug-resistant bacteria between intermingled ecological niches: the interface between humans, animals and the environment. International journal of environmental research and public health. 2013 Jan;10(1):278-94. https://doi.org/10.3390/ijerph10010278
16. Van Duin D, Paterson D. Multidrug resistant bacteria in the community: trends and lessons learned. Infectious disease clinics of North America. 2016 Jun;30(2):377. https://doi.org/10.1016/j.idc.2016.02.004
17. Arcilla MS, van Hattem JM, Bootsma MC, van Genderen PJ, Goorhuis A, Schultsz C, Stobberingh EE, Verbrugh HA, de Jong MD, Melles DC, Penders J. The carriage of multiresistant bacteria after travel (COMBAT) prospective cohort study: methodology and design. BMC public health. 2014 Dec;14:1-8. https://doi.org/10.1186/1471-2458-14-410
18. Holmes AH, Moore LS, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, Guerin PJ, Piddock LJ. Understanding the mechanisms and drivers of antimicrobial resistance. The Lancet. 2016 Jan 9;387(10014):176-87. https://doi.org/10.1016/S0140-6736(15)00473-0
19. Zalacain M, Biedenbach DJ, Badal RE, Young K, Motyl M, Sahm DF. Pathogen prevalence and antimicrobial susceptibility among Enterobacteriaceae causing hospital-associated intra-abdominal infections in adults in the United States (2012–2013). Clinical Therapeutics. 2016 Jun 1;38(6):1510-21. https://doi.org/10.1016/j.clinthera.2016.04.035
20. Medina E, Pieper DH. Tackling threats and future problems of multidrug-resistant bacteria. How to overcome the antibiotic crisis: facts, challenges, technologies and future perspectives. 2016 Jul 13:3-3. https://doi.org/10.1007/82_2016_492
21. Otuneme OG, Akinkuade FO, Obebe OO, Usiobeigbe OS, Faloye TG, Olasebikan AS, Akinleye WA, Koku OD. A study on the prevalence of Schistosoma haematobium and Schistosoma intercalatum in a rural community of Ogun State, Nigeria. South East Asia Journal of Public Health. 2014;4(1):67-71. https://doi.org/10.3329/seajph.v4i1.21845
22. Kish L. Survey sampling. new york: John wesley & sons. Am Polit Sci Rev. 1965;59(4):1025. https://doi.org/10.1017/S0003055400132113
23. Adeyankinnu FA, Motayo BO, Akinduti A, Akinbo J, Ogiogwa JI, Aboderin BW, Agunlejika RA. A Multicenter Study of Beta-Lactamase Resistant Escherichia coli and Klebsiella pneumoniae Reveals High Level Chromosome Mediated Extended Spectrum β Lactamase Resistance in Ogun State, Nigeria. Interdisciplinary perspectives on infectious diseases. 2014;2014(1):819896. https://doi.org/10.1155/2014/819896
24. Ali M, Garba KA, Abdallah MS. Antibiotic susceptibility profile of bacteria responsible for urinary tract infection (UTI). South Asian journal of biological research (SAJBR). 2018;1(1):12-27.
25. Kassim A, Omuse G, Premji Z, Revathi G. Comparison of Clinical Laboratory Standards Institute and European Committee on Antimicrobial Susceptibility Testing guidelines for the interpretation of antibiotic susceptibility at a University teaching hospital in Nairobi, Kenya: a cross-sectional study. Annals of clinical microbiology and antimicrobials. 2016 Dec;15:1-7. https://doi.org/10.1186/s12941-016-0135-3

26. Mohammed Y, Gadzama GB, Zailani SB, Aboderin AO. Characterization of extended-spectrum beta-lactamase from Escherichia coli and Klebsiella species from North Eastern Nigeria. Journal of clinical and diagnostic research: JCDR. 2016 Feb 1;10(2):DC07. https://doi.org/10.7860/JCDR/2016/16330.7254
27. Elikwu CJ, Shobowale EO, Oluyemi OY, Afolabi DO, Aderinto DA, Onyedibe KI, Solarin AU. The etiology and antimicrobial susceptibility patterns of urinary tract infections at a private Nigerian teaching hospital in South West Nigeria. African Journal of Clinical and Experimental Microbiology. 2017;18(1):21-8. https://doi.org/10.4314/ajcem.v18i1.3
28. Ochada NS, Nasiru IA, Thairu Y, Okanlowan MB, Abdulakeem YO. Antimicrobial susceptibility pattern of urinary pathogens isolated from two tertiary hospitals in Southwestern Nigeria. African Journal of Clinical and Experimental Microbiology. 2015;16(1):12-22. https://doi.org/10.4314/ajcem.v16i1.3
29. Abubakar BM, Abubakar A, Tela UM, Gabchiya MN, Isah MJ, Dogo HM, Panti AA, Ogunyele TT. An appraisal on antibiotic susceptibility of common bacterial pathogens in urinary tract infections at a Nigerian Tertiary Health Center. Arch Int Surg. 2017 Apr 1;7(2):56. https://doi.org/10.4103/ais.ais_17_17
30. Ojokuku HO, Kankara AS, Nasir IA, Olawuyi AO, Alao MB. Phenotypic Profile and Antibiogram of Urinary Tract Pathogens Among Patients Attending a Tertiary Hospital in Katsina State, Nigeria. Journal of Clinical Medicine Research. 2017;4(4):38-43.
31. Ojokuku HO, Kankara AS, Nasir IA, Olawuyi AO, Alao MB. Phenotypic Profile and Antibiogram of Urinary Tract Pathogens Among Patients Attending a Tertiary Hospital in Katsina State, Nigeria. Journal of Clinical Medicine Research. 2017;4(4):38-43.
32. Trevino SE, Babcock HM, Henderson JP, Lane MA, Beekmann SE, Polgreen PM, Marschall J. Perceptions and behaviours of infectious diseases physicians when managing urinary tract infections due to MDR organisms. Journal of Antimicrobial Chemotherapy. 2015 Dec 1;70(12):3397-400. https://doi.org/10.1093/jac/dkv271
33. Akpan I. Asymptomatic and symptomatic urinary tract infection in a Nigerian community. ASSET: An International Journal (Series B)}. 2010 Nov 24;6(1):32-9.
34. Akhtar N, Rahman R, Sultana S, Rahman MR. Antimicrobial sensitivity pattern of bacterial pathogens associated with urinary tract infection. Delta Medical College Journal. 2017 Jul 31;5(2):57-62. https://doi.org/10.3329/dmcj.v5i2.33342
35. Oyeyemi O, Adesanya I, Ogunnowo B, Oyewole I. Uropathogens and diagnostic potential of pH and specific gravity in a rural community of Nigeria. Journal of Coastal Life Medicine. 2015;3(12):975-7. https://doi.org/10.12980/jclm.3.2015j5-212
36. Ayoade F, Moro DD, Ebene OL. Prevalence and antimicrobial susceptibility pattern of asymptomatic urinary tract infections of bacterial and parasitic origins among university students in redemption camp, Ogun state, Nigeria. Open Journal of Medical Microbiology. 2013 Dec 20;3(4):219-26. https://doi.org/10.4236/ojmm.2013.34033
37. Adeyeba OA, Ojeaga SG. Urinary schistosomiasis and concomitant urinary tract pathogens among school children in metropoitan Ibadan, Nigeria. African Journal of Biomedical Research. 2002;5(3). https://doi.org/10.4314/ajbr.v5i3.53993
38. Akinniyi AP, Oluwaseun E, Motayo BO, Adeyokinu AF. Emerging multidrug resistant ampc beta-lactamase and carbapenamase enteric isolates in Abeokuta, Nigeria. Nature and Science. 2012;7(10):70.
39. Ebie MY, Kandakai-Olukemi YT, Ayanbadejo J, Tanyigna KB. Urinary tract infections in a Nigerian military hospital. Nigerian Journal of Microbiology. 2001;15(1):31-7.
40. Mekki AH, Hassan AN, Elsayed DE. Extended spectrum beta lactamases among multi drug resistant Escherichia coli and Klebsiella species causing urinary tract infections in Khartoum. Journal of Bacteriology research. 2010 Aug 23;2(3):18-21.
41. Clegg S, Murphy CN. Epidemiology and virulence of Klebsiella pneumoniae. Urinary Tract Infections: Molecular Pathogenesis and Clinical Management. 2017 Feb 15:435-57. https://doi.org/10.1128/9781555817404.ch18
42. Vuotto C, Longo F, Pascolini C, Donelli G, Balice MP, Libori MF, Tiracchia V, Salvia A, Varaldo PE. Biofilm formation and antibiotic resistance in Klebsiella pneumoniae urinary strains. Journal of applied microbiology. 2017 Oct 1;123(4):1003-18. https://doi.org/10.1111/jam.13533
43. Akbar R, Naeem RA, Shafique M, Sohail M, Naz S. Trends in antimicrobial susceptibility of bacterial isolates from hospitalized patients with urinary tract infection. Pakistan Journal of Medical and Biological Science. 2017;1(2):21-7.
44. Abay GK, Shfare MT, Teklu TG, Kidane KM, Gebremeskel TK, Kahsay AG, Gezae KE, Muthupandian S, Degene TA. Extended-

spectrum β-lactamase production and antimicrobial resistance among Enterobacteriaceae causing clinical infections in Africa: a systematic review and meta-analysis (2012–2020). European Journal of Medical Research. 2025 Dec;30(1):1-4. https://doi.org/10.1186/s40001-024-02267-8
45. Egbebi AO, Famurewa O. Prevalence of extended spectrum beta-lactamase (ESBL) production among Klebsiella isolates in some parts of South West Nigeria.
46. Bali EB, Acik L, Sultan N. Phenotypic and molecular characterization of SHV, TEM, CTX-M and extended-spectrum beta-lactamase produced by Escherichia coli, Acinobacter baumannii and Klebsiella isolates in a Turkish hospital. Afr J Microbiol Res. 2010 Apr 18;4(8):650-4.
47. Olowe OA, Adewumi O, Odewale G, Ojurongbe O, Adefioye OJ. Phenotypic and molecular characterisation of extended-spectrum beta-lactamase producing Escherichia coli obtained from animal fecal samples in Ado Ekiti, Nigeria. Journal of Environmental and Public Health. 2015;2015(1):497980. https://doi.org/10.1155/2015/497980
48. Shakya P, Shrestha D, Maharjan E, Sharma VK, Paudyal R. ESBL production among E. coli and Klebsiella spp. causing urinary tract infection: a hospital based study. The open microbiology journal. 2017 Apr 28;11:23. https://doi.org/10.2174/1874285801711010023
49. Ibeh IN, Florence O, Tery ON. Studies on Escherichia coli associated with diabetic wounds; multi drug resistance and the occurrence of beta lactamase production in south-western Nigeria. Open Access J Sci. 2018;2(6):345-8. https://doi.org/10.15406/oajs.2018.02.00109
50. Yusha'u M, Aliyu H, Kumurya A, Suleiman K. Prevalence of extended spectrum β-lactamases (esbls) among Enterobacteriaceae in Murtala Mohammed specialist hospital, Kano, Nigeria. Bayero Journal of Pure and Applied Sciences. 2010;3(1). https://doi.org/10.4314/bajopas.v3i1.58756
51. Varaiya AY, Dogra JD, Kulkarni MH, Bhalekar PN. Extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in diabetic foot infections. Indian Journal of Pathology and Microbiology. 2008 Jul 1;51(3):370-2. https://doi.org/10.4103/0377-4929.42513
52. Alipourfard I, Nili NY. Antibiogram of Extended Spectrum Beta-lactamase (ESBL) producing Escherichia coli and Klebsiella pneumoniae isolated from Hospital Samples. Bangladesh Journal of Medical Microbiology. 2010;4(1):32-6. https://doi.org/10.3329/bjmm.v4i1.8467
53. Elsayed NY, Awad AM, Omar MM, Desouki DG. Rapid Simultaneous detection of AmpC and ESBLs among Enterobacteriaceae using MastD68C detection set and possible therapeutic options. The Egyptian Journal of Medical Microbiology. 2015 Jul;38(3174):1-2. https://doi.org/10.12816/0024920
54. Ahmed SS, Shariq A, Alsalloom AA, Babikir IH, Alhomoud BN. Uropathogens and their antimicrobial resistance patterns: Relationship with urinary tract infections. International journal of health sciences. 2019 Mar;13(2):48.