

## An Update on the epidemiology of Extended Spectrum Beta-Lactamases (ESBLs) Producing Organisms in Nigeria

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### ABSTRACT

The significance of extended spectrum beta lactamases (ESBL)-producing organisms in aggravating public health threats, long hospital stays, treatment failures and sometimes death is a very topical issue eliciting great deal of concerns. This study was therefore aimed at providing an expansive update on the epidemiology of ESBL producing organisms in the six geopolitical zones of Nigeria, with a view to providing details of all ESBL producing organisms from different sources including foods, environmental and clinical samples. To achieve this, a literature search was carried out on articles published between 2007 and 2023 through electronic databases including Google Scholar, African Journals Online (AJOL), Scopus and PubMed. The inclusion criterion was that the articles must have been published between 2007 and 2023 in the six geopolitical zones of Nigeria. A total of 252 articles were identified while only 63 studies (10 from north-central, 11 from southwest, 9 from northeast, 10 from southeast, 11 from south-south and 12 from southwest Nigeria) that met the inclusion criteria were used for the study. The prevalence of ESBL producing organisms from the six geopolitical zones were determined to be  $(42.88 \pm 8.28)$ ,  $(30.7 \pm 5.49)$ ,  $(46.57 \pm 5.14)$ ,  $(38.45 \pm 5.14)$ ,  $(32.49 \pm 7.33)$  and  $(30.75 \pm 6.14)$  for North-Central, North-West, North-East, South-East, South-South and South-West respectively. Majority of the studies analyzed used the phenotypic method which is based on double-disc synergy test (DDST) while none of the studies used the minimum inhibition concentration method. The most encountered ESBL producing organism was *Escherichia coli* and this was followed by *Klebsiella* spp. In conclusion, the prevalence of ESBL producing organisms was considerably very high in the six geopolitical zones of Nigeria. This, therefore, highlights the need for establishing programs in Nigeria to educate the populace on the implications of wide epidemiology of ESBL-producing organisms and the best ways to preventing their spread including frequent and thorough hand hygiene.

**Keywords:** Prevalence, ESBL, Gram-negative bacteria, Nigeria, Community

### 1. INTRODUCTION

Extended Spectrum Beta-Lactamases (ESBLs) have been found all over the world and recently works have been done to understand the extent of ESBLs producing Gram negative bacteria (Storberg, 2014). These ESBLs are a group of beta-lactamases that hydrolyzes the extended spectrum cephalosporins, the penicillins and monobactams, but not cephamycins and carbapenems (Khalifa *et al.*, 2019) and are inhibited by beta-lactamase inhibitors such as clavulanic acid, sulbactam and taxobactam (Tanko *et al.*, 2020). The

importance of Extended Spectrum Beta-Lactamase organisms in treatment failure, hospitalization and even death has been well documented (Wellington *et al.*, 2013; Popoola *et al.*, 2024b). This is because these types of organisms have been implicated in several infections including pneumonia, blood stream infections, urinary tract infections, bacteremia, and other intra-abdominal infections (Kotapati *et al.*, 2005, Sun *et al.*, 2006, Canton *et al.*, 2008) and most of these infections are difficult to manage due to the elevated trend of

antibiotics resistance (Afiukwa *et al.*, 2016; Oliveira *et al.*, 2017). Antibiotic resistance is referred to as the resistance of micro-organisms to an antibiotic agent to which they were initially sensitive (Oliveira *et al.*, 2017). Antibiotic resistance is known to be caused by several factors including the efflux pump system, enzymatic inhibition, penicillin-binding proteins (PBP) modifications, porin mutations (Oliveira *et al.*, 2017), and production of enzymes among others. Of these antibiotic resistance mechanisms, production of ESBL has been labelled as a major public health threat (Afiukwa *et al.*, 2016). This may not be unconnected to the fact that the enzymes are the major hydrolyzing agents of ESBL antibiotics (Faith *et al.*, 2003).

What is more deleterious is that genes encoding these enzymes may be located on the plasmid and/or chromosomes (Bradford, 2001; Paterson and Bonomo, 2005; Guenther *et al.*, 2011) thereby making their epidemiology a call for concern. The fact that they could be located on plasmid infers the possibility of easy transferability due to horizontal gene exchange (Paterson and Bonomo, 2005). These plasmids which are known to be extrachromosomal material capable of replicating independently are highly promiscuous and thus making the epidemiology to go far and wide (Paterson and Bonomo, 2005). In order to understand the true epidemiology of ESBL organisms in Nigeria, there is need to ascertain their distribution by states. Hence, this review focused on describing the prevalence of ESBL-producing organisms by states in Nigeria.

## 2. MATERIALS AND METHODS

This descriptive study composed of different articles reported from different states in the six geopolitical zones of Nigeria. A literature search was conducted on Google Scholar using the keywords: ESBL producing organisms, extended spectrum beta-lactamases, states, samples, North-Central, South-West, North-West, South-South, South-East and North-East. The electronic

databases are from Google Scholar, PubMed, African Journals online (AJOL) and Scopus. A total of 252 articles were identified while only 63 studies (10 from North-Central, 11 from South-West, 9 from North-East, 10 from South-East, 11 from South-South and 12 from South-West Nigeria) that met the inclusion criteria were used for the study. These studies were compiled by reviewing the titles and abstract of different articles relating to the objectives of our study. The final 63 articles selected were chosen after reviewing the full details of the articles and the selection was based on the following criteria: reported studies on the prevalence of ESBL-producing organisms in the six geopolitical zones of Nigeria and from different sources. Articles that fell outside the publication years 2007 to 2023 were excluded. Articles with information that was not completely relating to ESBL-producing organisms', retrospective studies, abstracts, review articles, posters, conference proceedings and studies outside Nigeria were excluded.

### 2.1 Data extraction and analysis

Data extracted from the articles included the states where the research was conducted, prevalence of ESBL organisms, sources and author(s). The study did not only assess the community and hospital settings, but it also focused on other non-human sources such as animals and the environment. The average prevalence rates of ESBL organisms for different states were evaluated by dividing the sums of all the prevalence in each region by the number of studies found in such region while the standard error of means was calculated using standard recommended method.

## 3. RESULTS

### 3.1 Distribution of articles describing ESBLs in Nigeria

Nigeria has different geography and climates ranging from arid to humid equatorials. It is located on the western coast of Africa with diverse people having hundreds of languages including the

Yoruba, Igbo, Fulfulde, Hausa, Edo, Ibibio, Tiv and English. This result section is divided into the six geo-political zones in Nigeria. The electronic database searches gave a total of 252 studies. Sixty-three (63) articles from the six geo-political zones in Nigeria were used for this study (North central- 10, North west- 11, North east- 9, South east- 10, South-south- 11 and South west- 12). Majority of the studies reported used the phenotypic method which is based on double-disc synergy test (DDST) and none of the study used minimum inhibition concentration method for the phenotypic detection. See Table 1-6 for a detailed description of the state, prevalent organisms, prevalent ESBLs and sources of organisms

### 3.1.1 North-Central Nigeria

A search was conducted for articles within this region and a total of ten (10) articles were used in the study. All states under this region were analyzed except for Kwara, Niger and Plateau. The prevalence of ESBL-producing organisms from the north-central ranged from 8.0% to 93.2% (see Table 1). *Escherichia coli* has the highest prevalence (93.2%) and *Salmonella typhi* has the lowest prevalence (8.0%) in this region with the sources from both clinical and environmental samples. The average prevalence rate for North-Central Nigeria was evaluated to be (42.88±8.28%)

### 3.1.2 North-West Nigeria

Articles in this geo-political zone of Nigeria were sourced for and a total of eleven (11) articles was used in this study. The prevalence of ESBL-producing organisms from this zone ranged from 2.1% to 62.7% with *Escherichia coli* being the most prevalent (see Table 2). No study was obtained from Jigawa, Katsina and Zamfara in this region with majority of the sources from clinical samples. The average prevalence rate for North-West Nigeria was evaluated to be (30.70±5.49%).

### 3.1.3 North-East Nigeria

A search was conducted for articles within this region and a total of nine (9) articles were used in the study. The prevalence of ESBL-producing organisms from northeast Nigeria ranged from 5.3% to 85.7% (see Table 3). *Escherichia coli* has the highest prevalence in this region with studies from Adamawa, Bauchi, Borno and Gombe except for Taraba and Yobe. The average prevalence rate for North-East Nigeria was evaluated to be (46.57±5.14%)

### 3.1.4 South-East Nigeria

A search was conducted for articles within this region and a total of ten (10) articles were used in the study. At least one study from each of the states in this zone was obtained. The prevalence of ESBL-producing organisms from the south east ranged from 8.1% to 80.0% (see Table 4). *Escherichia coli* has the highest prevalence in this region with the sources from both clinical and environmental samples. The average prevalence rate for South-East Nigeria was evaluated to be (38.45±5.14%)

### 3.1.5 South-south Nigeria

A search was conducted for articles within this region and a total of eleven (11) articles were used in the study. All states under this region were analyzed except for bayelsa. The prevalence of ESBL-producing organisms from the south south ranged from 2.7% to 80.0% (see Table 5). *Klebsiella* spp has the highest prevalence (80.0%) and Gram-negative bacteria having the lowest prevalence (2.7%) in this region with the sources from both clinical and environmental samples. The average prevalence rate for South-South Nigeria was evaluated to be (32.49±7.33%)

### 3.1.6 South-West Nigeria

Articles in this geo-political zone of Nigeria were sourced for and a total of twelve (12) articles was used in this study. The prevalence of ESBL-producing organisms from this zone ranged from 8.3% to 78.9% with *Escherichia coli* being the most

prevalent (see Table 6). At least one study from each of the states in this zone was obtained with majority of the sources from

clinical samples. The average prevalence rate for South-West Nigeria was evaluated to be  $(30.75 \pm 6.14\%)$ .

**Table 1: Prevalence of ESBL organisms in the North-Central of Nigeria**

States	Prev. org.	Prev. ESBL (%)	Source of org.	Reference
Nasarawa	EC	53.5	C/sample	(Abimiku <i>et al.</i> , 2019)
Nasarawa	EC	93.2	P/droppings	(Tama <i>et al.</i> , 2021)
Nasarawa	ST	8.0	C/sample	(Ngolo <i>et al.</i> , 2018)
Nasarawa	EC	47.1	D/handles	(Tsaku <i>et al.</i> , 2019)
Nasarawa	EC	51.4	C/sample	(Nkene <i>et al.</i> , 2020)
Nasarawa	EC	46.8	D/handle	(Alumbugu <i>et al.</i> , 2019)
Nasarawa	EC	66.7	C/sample	(Zakou <i>et al.</i> , 2020)
Benue	PA	10.7	C/sample	(Aernan and Umeh, 2016)
Kogi	SS	27.2	C/sample	(Eze <i>et al.</i> , 2015)
FCT	EC	24.2	C/sample	(Akanbi <i>et al.</i> , 2013)

Prev. org., prevalent organism: EC, *Escherichia coli*; ST, *Salmonella typhi*; PA, *Pseudomonas aeruginosa*; SS, *Salmonella* spp., Prev. ESBL, Prevalence of ESBL, Source of org., source of organism: C/sample, clinical sample; P/droppings, poultry droppings; D/handles, door handles.

**Table 2: Prevalence of ESBL organisms in the North-West of Nigeria**

States	Prev. org.	Prev. ESBL (%)	Source of org.	Reference
Sokoto	EC	28.1	C/sample	(Nuhu <i>et al.</i> , 2015)
Kaduna	KP	35.1	C/sample	(Shetu <i>et al.</i> , 2017)
Kaduna	EC	27.2	W/R water	(Atta <i>et al.</i> , 2022)
Kaduna	KP	11.76	Urine	(Ibtihaj <i>et al.</i> , 2021)
Kano	EC	44.8	C/sample	(Yusha'u <i>et al.</i> , 2010)
Sokoto	EC	2.1	C/sample	(Ungo-kore <i>et al.</i> , 2019)
Sokoto	EC	37.8	C/sample	(Yusuf <i>et al.</i> , 2011)
Sokoto	EC	15.9	C/sample	(Abubakar <i>et al.</i> , 2016)
Kano	EC	52.8	C/sample	(Ibrahim <i>et al.</i> , 2017)
Kano	EC	62.7	C/sample	(Yusuf <i>et al.</i> , 2013)
Kebbi	EC	20.0	Poultry	(Abubakar <i>et al.</i> , 2023)

Prev. org., prevalent organism: EC, *Escherichia coli*; KP, *Klebsiella pneumoniae*, Prev. ESBL, Prevalence of ESBL, Source of org., source of organism: C/sample, clinical sample.

**Table 3: Prevalence of ESBL organisms in the North-East of Nigeria**

States	Prev. org.	Prev. ESBL (%)	Source of org.	Reference
Adamawa	KP	37.8	C/sample	(Sa'id <i>et al.</i> , 2020)
Adamawa	EC	43.5	C/sample	(Tula and Iyoha, 2020)
Bauchi	KP	37.1	C/sample	(Mohammed <i>et al.</i> , 2016)
Bauchi	EC	82.3	C/sample	(Iliyasu <i>et al.</i> , 2018)
Bauchi	EC	41.9	N/notes	(Usman <i>et al.</i> , 2021)
Borno	EC	11.0	P/farm	(Mamza <i>et al.</i> , 2010)
Borno	EC	32.3	P/farm	(Kwoji <i>et al.</i> , 2019)
Gombe	EC	85.7	C/sample	(Garba <i>et al.</i> , 2020)
Gombe	EC/KP	40/54.1	C/sample	(Yarima <i>et al.</i> , 2019)

Prev. org., prevalent organism: EC, *Escherichia coli*; KP, *Klebsiella pneumonia*; SA, *Staphylococcus aureus*, Prev. ESBL, Prevalence of ESBL, Source of org., source of organism: C/sample, clinical sample; N/notes, naira notes; P/farm; poultry farm.

**Table 4: Prevalence of ESBL organisms in the South-East of Nigeria**

States	Prev. org.	Prev. ESBL (%)	Source of org.	Reference
Abia	EC/KS	50.4	C/sample	(Nwosu <i>et al.</i> , 2014)
Abia	EC	80.0	Bev.	(Edward <i>et al.</i> , 2019)
Ebonyi	EC	10.0	C/sample	(Ugbo <i>et al.</i> , 2020)
Anambra	GNB	8.1	F/sample	(Chukwunwejim <i>et al.</i> , 2018)
Anambra	EC	61.0	C/sample	(Ezeanya <i>et al.</i> , 2017)
Enugu	EC	25.2	C/sample	(Iroha <i>et al.</i> , 2008)
Enugu	EC	50.0	C/sample	(Maduakor <i>et al.</i> , 2022)
Imo	EC/PA	45.6	C/sample	(Braide <i>et al.</i> , 2018)
Imo	EC	32.0	Pi/farms	(Akujobi <i>et al.</i> , 2008)
Imo	EC	22.2	P/farm	(Carissa <i>et al.</i> , 2013)

Prev. org., prevalent organism: GNB- Gram Negative Bacteria, EC, *Escherichia coli*; KP, *Klebsiella pneumonia*; KS, *Klebsiella* spp.; PA, *Pseudomonas aeruginosa*, Prev. ESBL, Prevalence of ESBL, Source of org., source of organism: C/sample, clinical sample; Bev., beverages; Pi/farms, piggery farms; P/wastes, poultry wastes.

**Table 5: Prevalence of ESBL organisms in the South-South of Nigeria**

States	Prev. org.	Prev. ESBL (%)	Source of org.	Reference
Akwa-Ibom	PS	19.5	Abattoir	(Ikegbunam <i>et al.</i> , 2012)
Akwa-Ibom	PA	55.7	W/swab	(Oli <i>et al.</i> , 2017)
Akwa-Ibom	EC	35.8	C/sample	(Idang <i>et al.</i> , 2015)
Akwa-Ibom	EC/KP	47.1	C/sample	(Azekhueme <i>et al.</i> , 2015)
Rivers	KP	10.0	C/sample	(Pius <i>et al.</i> , 2019)
Rivers	KS	80.0	C/sample	(Okogeri <i>et al.</i> , 2020)
Rivers	EC/KP	47.1	Urine	(Onanuga <i>et al.</i> , 2019)
Rivers	EC	9.6	C/sample	(Owhorchukwu <i>et al.</i> , 2016)
Delta	KP	40.5	C/sample	(Egbule and Odih, 2021)
Cross River	SS	9.4	F/sample	(Oghenevo <i>et al.</i> , 2016)
Edo	GNB	2.7	C/sample	(Omoriege <i>et al.</i> , 2010)

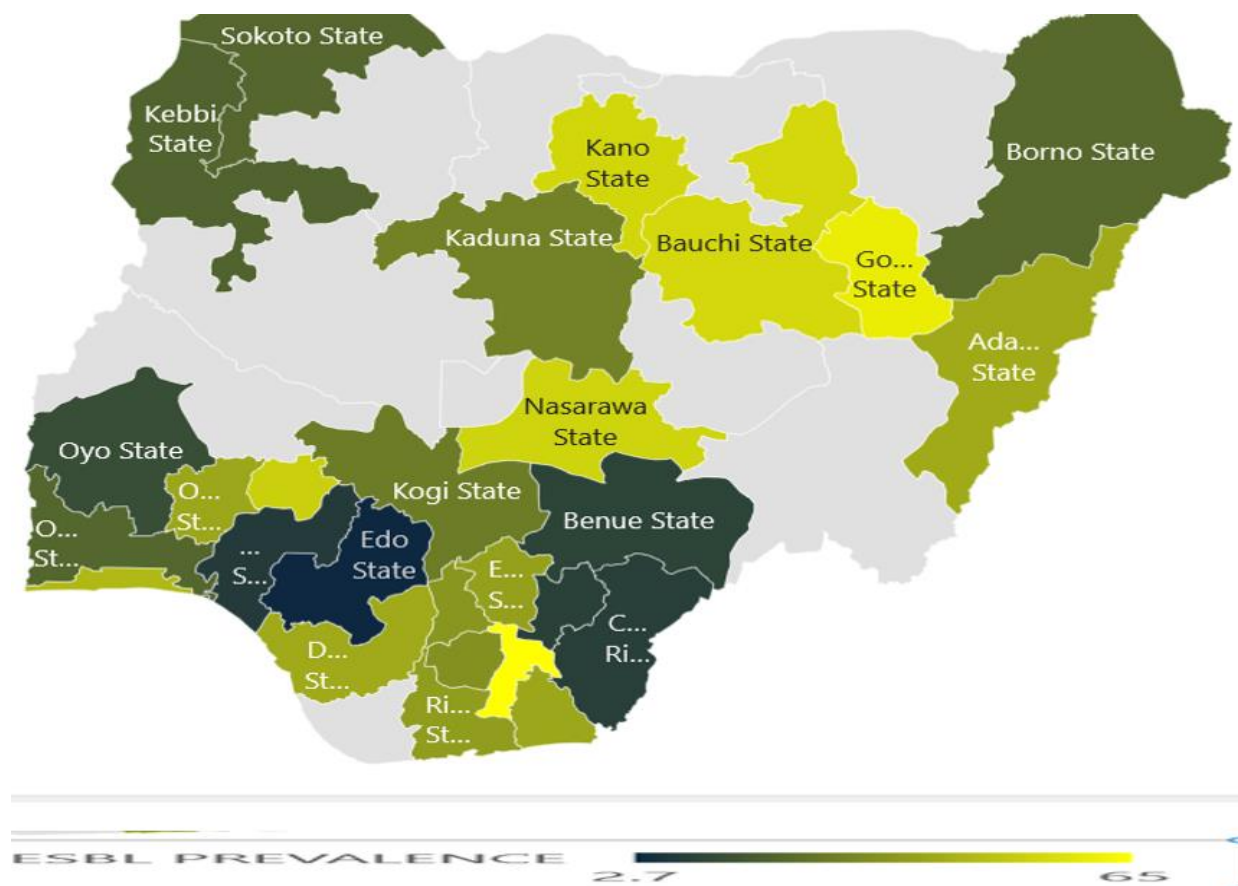
Prev. org., prevalent organism: EC, *Escherichia coli*; KP, *Klebsiella pneumonia*; KS, *Klebsiella* spp.; PA, *Pseudomonas aeruginosa*; PS, *Proteus* spp. SS. *Salmonella* spp.; GNB, Gram negative bacteria, Prev. ESBL, Prevalence of ESBL, Source of org., source of organism: C/sample, clinical sample; W/swab, Wound swab.

**Table 6: Prevalence of ESBL organisms in the South-West of Nigeria**

States	Prev. org.	Prev. ESBL (%)	Source of org.	Reference
Ogun	BS	33.3	C/sample	(Umeokoli <i>et al.</i> , 2020)
Ogun	EC	9.9	C/sample	(Obebe <i>et al.</i> , 2014)
Ogun	SS	19.4	W/waters	(Banjo and Ohue, 2017)
Ekiti	EC	23.8	F/sample	(Omolayo and Adenike, 2019)
Ekiti	EC	78.9	AFS	(Olowe <i>et al.</i> , 2015)
Osun	KS	51.0	Sputum	(Abike <i>et al.</i> , 2018)
Lagos	EC/KP	52.1	C/sample	(Raji <i>et al.</i> , 2015)
Osun	EC	27.8	F/sample	(Adefioye <i>et al.</i> , 2021)
Lagos	EC/KP	37.3	C/sample	(Raji <i>et al.</i> , 2013)
Oyo	PA	9.3	C/sample	(Aibinu <i>et al.</i> , 2007)
Ondo	EC/KP	8.3	U/FS	(Deji-Agboola <i>et al.</i> , 2020)
Oyo	KP	17.9	W/sample	(Falodun <i>et al.</i> , 2018)

Prev. org., prevalent organism: EC, *Escherichia coli*; KP, *Klebsiella pneumonia*; KS, *Klebsiella* spp.; PA, *Pseudomonas aeruginosa*; SS. *Salmonella* spp.; BS, *Burkholderia* spp, Prev. ESBL, Prevalence of ESBL.

Source of org., source of organism: C/sample, clinical sample; W/waters, waste waters; F/sample, faecal sample; AFS, animal faecal sample; U/FS, urine/faecal sample.



**Figure 1:** A map showing the prevalence of ESBL-producing organisms in Nigeria

#### 4. DISCUSSION

The ubiquitous presence of ESBL-producing organisms in different environmental sources beyond hospital settings and even other animate subjects like insects has been well documented (Iroha *et al.*, 2009; Popoola *et al.*, 2019; Tanko *et al.*, 2020; Popoola *et al.*, 2022; Popoola *et al.*, 2023; Popoola *et al.*, 2024a; Popoola *et al.*, 2024b). In this study, the prevalence of ESBL-producing Gram-negative bacteria was found to range between 30.7 - 46.57 %. This observation is contradictory to that reported by Tanko *et al.* (2020) where they documented prevalence rate of 7.5- 82.3%. The

decrease in the highest prevalence rate in this review may be interpreted to be that works are ongoing on the education of the populace on proper usage of antibiotics and hygienic practices which are two of the ways by which the spread of these organisms in Nigeria can be circumvented.

The fact that the two most prevalent regions with highest ESBL producing organisms falls in the northern region (North-East and North-Central) may be directly linked to low literacy rate in that region of Nigeria, which has been reported to be due to poverty, insecurity, and cultural factors like child marriage and religious extremism. These

observations are consistent with that of Tanko *et al.* (2020) and Iroha *et al.* (2009) where they documented similar findings. These factors contribute to low awareness on the meaning and even indiscriminate use of antibiotics and thus subsequently heightening antibiotics resistance and consequently the spread of ESBL-producing organisms. Consequently, the higher prevalence rate found in the southern part of Nigeria may be ascribed to misuse and lack of stringent measures on antibiotics usage which galvanize the uninformed educated on self-treatment that causes selective pressure that triggers antibiotics resistance (Popoola *et al.*, 2024a). Our review also implicated that more studies on ESBL has been carried out in the southern part of Nigeria than in the northern part as revealed by the number of articles obtained in each geo-political zone and the number of states evaluated. The southwest had the highest number of studies while the northeast had the least number.

Furthermore, it was found that *Escherichia coli* was the most frequently isolated bacteria in the majority of the studies except for studies from the south-south where *Klebsiella* spp was the most isolated bacteria and this remark which corroborate that of Egbule and Odih (2020) is a testament to the fact that ESBLs are found in large number of different Gram-negative bacteria species (Hassan and Abdalhamid, 2014). However, in another study from south-south, *Pseudomonas aeruginosa* had the second highest prevalence (55.7%) and this serves as a pointer that all Gram-negative bacteria and not just *E. coli* and *Klebsiella* species should be screened for ESBL production. Majority of the studies in this

review employed the double-disc synergy test (DDST) phenotypic approach to detect ESBL while none of the studies used the minimum inhibition concentration method despite the availability of several methods that can be used for screening ESBL including the ESBL E-test with cloxacillin on Mueller-Hinton agar (MHA), combined disk method, Cica-Beta test, vitek 2 system, among others (Rawat and Nair, 2010; Sahni *et al.*, 2018; Salihu *et al.*, 2020). It is thus imperative to further educate researchers on the need to use other methods and even compare methods in order not to under/over-estimate prevalence rates. According to this review's findings, most of the samples utilized in the studies that were analyzed were clinical samples with environmental samples coming in second and relatively few multicenter samples. Although numerous research has reported the production of ESBL in Gram-negative bacteria in various zones in Nigeria, the prevalence and number of cases in some areas are still unknown. This could be due to scarce resources, the high cost of materials as well as inadequate facilities for research in those locations.

Thus, to effectively limit the development and spread of this menace, extensive infection control measures along with meticulous monitoring of these organisms utilizing various phenotypic and molecular techniques are essential. Also, subsequent investigations should be carried out in regions where limited research has been done. Ultimately, researchers, laboratory scientists, clinicians and patients should all work together to combat antimicrobial resistance and ESBL producing



organisms in an all-encompassing manner. This is necessary to avert the impacts posed by antibiotics resistance to achieving sustainable development goals related to health, in addition to having far-reaching implications for equality, clean water, economic growth, poverty alleviation, hunger eradication, food production, among other important developments.

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