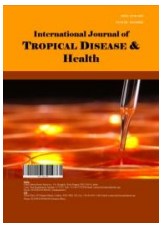

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Prevalence of Carbapenem-Resistance among Enterobacteriaceae Isolated from Patients Attending Uduth Sokoto, North West Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author MUI designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors KM, MKG and SUN managed the analyses of the study. Authors OFA and AA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The major problem threatening the continued success of antimicrobial drugs is the development of resistant organisms. This study was designed to determine the occurrence and prevalence of carbapenem resistance among enterobacteriaceae isolated from in-patients attending Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto, and also to determine the antimicrobial susceptibility patterns of the organisms isolated. The Methodology involves the use of trypticase soy broth containing 10 µg of carbapenem (imipenem) for primary isolation. The secondary isolation involves the use of MacConkey agar and biochemical (Simmon citrate Agar) for identification, and then antimicrobial susceptibility testing by the disk diffusion method. A total of 191 stool samples from male and female in-patients within the range of 2-60 years were screened for the

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gastrointestinal colonization of Carbapenem Resistance Enterobacteriacea (CRE). Data were analysed using Statistical Package for Social Sciences (SPSS) windows version 21. The overall prevalence was 15.7% The prevalence rate was found exclusively in males. The highest prevalence was found within the age group of 30-40 years. *Escherichia coli*, *Klebsiella* species, *Pseudomonas* species and *salmonella* species were the bacteria isolated. The most predominant bacteria isolated were *Escherichia coli*, accounting for 85 (9.4%) resistant strains, *Klebsiella* species accounting for 50 (8%) resistant strain, *Pseudomonas aeruginosa* 21% and *Salmonella* species accounting for 42 (0%) no resistant strain isolated. The misuse of antibiotics is a major factor responsible for the high rate of bacterial resistance. Improvement on the management and personal hygiene, as well as the appropriate use of antibiotics would reduce the prevalence of Nosocomial Carbapenem Resistance (NCR) especially among prolonged hospitalized patients.

Keywords: Resistance; enterobacteriacea; carbapenem; antimicrobial; stool.

1. INTRODUCTION

Antimicrobial agents are substances obtained and purified from other microorganisms microbial organisms (antibiotics), and clinically synthesized agents which can kill or inhibit bacteria growth. Collectively, these natural and synthesized substances are referred to as antimicrobial agents. Depending on the type of the organism targeted these agents are grouped as antibacterial, antifungal, anti-parasitic, or antiviral agents [1,2].

Antimicrobial agents provide some of the most dramatic examples of the advances of modern medicine. Many infectious diseases were once considered incurable and lethal are now amenable to treatment with taking a few pills. The remarkably powerful and specific activity of antimicrobial drugs is due to their selectivity for targets that are either unique to prokaryote and fungal microorganisms or much more important in these organisms than in humans. Among these targets are bacterial and fungal cell wall synthesizing enzymes and bacterial ribosome. The enzymes required for nucleotide synthesis and DNA replication and the machinery of viral replication [3].

The major problem threatening the continued success of antimicrobial drugs is the development of resistant organisms. Microorganisms can adapt to environmental pressures in a variety of effective ways, and their response to antibiotics pressure is no exception.

An inevitable consequence of antimicrobial usage is the selection of resistant microorganisms, perhaps the most obvious example of evolution in action. Overuse and inappropriate use of antibiotics in the patient has fuelled a major increase in the prevalence of multidrug-resistant pathogens [4]. Antibacterial antibiotics are misused by providers in a variety of ways, including use in patients who are unlikely to have bacterial infections, use over unnecessarily prolonged periods, and use of multiple agents or broad-spectrum agents when not needed.

As a result of antibiotic pressure, highly resistant Gram-negative organisms with novel mechanisms of resistance are increasingly reported. Some of these strains have spread over vast geographic areas as a result of patients seeking medical care in different countries. Much larger quantities of antibiotics have been used in agriculture to stimulate growth and prevent infection in farm animals and this has added to the selection pressure that results in resistant organisms [5].

Unfortunately, as the need has grown in recent years, the development of novel drugs has slowed. The most venerable molecular targets of antimicrobial drugs have been identified and, in many cases, crystallized and characterized. Pending the identification of new targets and compounds, it seems likely that over the next decade we will have to rely on currently available families of drugs. In the faces of the continuing development of resistance, considerable effort will be required to maintain the effectiveness of these drug groups [5].

Antimicrobial agents play a central role in the control and management of infectious disease, therefore understanding their mode of action and the mechanism of microorganisms to circumvent antimicrobial activity is important. This is because diagnostic laboratories are expected to design and implement test that measure a pathogen response to antimicrobial activity [1,2].

2. MATERIALS AND METHODS

2.1 Study Area

This study was conducted in the School of Medical Laboratory Science of Usmanu Danfodiyo University Sokoto in collaboration with the pathological department of Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto. The Department of Medical Microbiology in Usmanu Danfodiyo University (UDU) Sokoto and the collaborating Hospital Laboratory at UDUTH had an enabling environment (human and material endowment) to carry out this study. Sokoto State is located in the extreme Northwest of Nigeria, near to the confluence of the Sokoto River and Rima River. With an annual average temperature of 28.3°C (82.3°F), Sokoto is, on the whole, a very hot area. However, the maximum daytime temperature is for most of the year generally under 40°C (104.0°F). The warmest months are February to April when daytime temperatures can exceed 45°C (113°F). The rainy season is from June to October during which showers are a daily occurrence. There are two major seasons, wet and dry which are distinct. Report from the 2007 National population commission indicated that the state had a population of 3.6 million.

The indigenous inhabitants of the study area are mainly Hausa and Fulani. Other ethnic groups resident in the area include Igbo, Yoruba, Nupe, Ebira, Igala, etc. Hausa is the commonly spoken language. Traders from the greater percentage of the population, while the rest are civil servants, farmers, artisan and people of other occupation.

2.2 Study Population

The study population comprises of all patients; male, female and also children preferable in-patient in Usmanu Danfodiyo University Teaching Hospital.

2.3 Study Participants

The participants include patients with prolonged hospitalization and those who are critically ill and exposed to invasive devices.

2.4 Eligibility Criteria

All patients (2 – 60 years) preferable in-patients presenting to the pathological department of UDUTH with prolonged hospitalization, those who are critically ill (those in Intensive Care Unit (ICU) and exposed to invasive devices and patient with a history of non-compliance of drug use, drug abuse and changing regime of drugs. The ICT patients were recruited with the help of the attending clinician and history of noncompliance drug abuse of patients were collected from either the clinician or the patient's family and guardian.

2.5 Exclusion Criteria

The following people are excluded from the study: all children less than 2 years of age and outpatients.

2.6 Sample Size Determination

Calculation of the sample size for this research is based on the findings of 13.8% prevalence of CRE obtained from 108 subjects of a previous study done in Aminu Kano Teaching Hospital (AKTH) Kano –Nigeria [6].

$$N = \frac{Z^2pq}{D^2}$$

Where N is minimum required sample size

Z = previous prevalence = 13.8%

Q = (1-P)

D = 0.05

$$\frac{N = (1.96)^2 \times 0.138 \times (1-0.138)}{(0.05)^2}$$

$$\frac{N = (3.8016) \times 0.138 \times (1-0.138)}{0.0025}$$

$$\frac{0.4569}{0.0025}$$

Attrition rate = 10% of N = 183 x 0.1 = 18.3
N = 183 + 18.3 = 201

2.7 Sample Collection

The sample for this study was collected from in-patient of all age group except children less than 2 years of age; attending Usmanu Danfodiyo University Teaching Hospital Sokoto. A swab stick was given to each patient or the patient guardian, with a verbal description of the process required in getting the stool sample.

2.8 The Instrument of Data Collection

The reference population of study consists of Prolonged Hospitalized in-patients. The selected patients who were willing to participate were interviewed using detailed questionnaires that give information on demographic data, clinical and epidemiologic variables.

2.9 Specimen (stool) Collection

A total of 191 samples were collected from the patients. Collection of the clean stool involves cleaning the external anal sphincter, spreading of the labia (in females) and avoidance of contact with the mouth of the container. They were advised to insert the cotton bulb of the swab stick in the container of the stool.

2.10 Materials

Reagents

5 ml Trypticase Soy Broth

10-ug carbapenem disks (imipenem and Meropenem)

MacConkey agar

Simmons Citrate Agar

2.11 Equipment

Vortex

Forceps,

Sterile loops

2.12 Sample Analysis

2.12.1 Primary culture: procedure

Each sample collected was cultured, aseptically on a primary broth media (Trypticase soy broth). The stool containing swab stick was aseptically inoculated in 5 ml of Trypticase soy broth in a test tube with the subsequent addition of a single 10 ug imipenem antibiotic disc; which act as disinfectants to eliminate contaminate and unnecessary or undesired bacteria isolate, since stool contains a myriad of bacteria species. Each test tube containing the broth inoculated with the rectal swab and 10 ug imipenem antibiotic disc was immediately incubated for 24 hrs at 35°C in ambient air. After 24 hrs of incubation, visual examination of each test tube provided a cloudy broth which is an indication of bacterial growth.

2.12.2 Secondary culture: sub-culturing procedure

After 24 hr each test tube was spun with the centrifuge at 3000 rpm for 5 mins, the supernatant was discarded and the deposit was inoculated aseptically on a secondary culture agar (MacConkey Agar and Salmonella Shigella Agar). By adhering to strict aseptic techniques, the deposit was inoculated on MacConkey agar and Salmonella Shigella Agar simultaneously by using the plate streak method. Each patient sample from the primary culture was subculture on both MacConkey Agar (for the isolation of lactose fermenting) and Salmonella Shigella Agar (for the isolation of *Salmonella* and *Shigella*). The preparation was incubated for 24 hrs at 35°C in ambient air. Discrete colonies, which are small mucoid and pinkish, were isolated on MacConkey agar while on Salmonella Shigella Agar white colonies with black halo centre were isolated.

2.13 Identification by Microscopy

2.13.1 Gram-staining techniques

- A smear was made from the discrete colonies of the culture and heat fixed.
- The slide was placed on a staining rack and flooded with crystal violent for 2 mins.
- The slide was rinsed in distilled water
- The slide was then floated with Lugo's iodine for 2mins.
- The slide was rinsed in distilled water.
- It was decolorized briefly with aceton for 30 seconds and immediately rinsed in water.
- It was then counter stained with neutral red for 2mins and rinsed with water.
- It was allowed to air dry and viewed under the microscope with 100x objectives as described by [7].

2.14 Identification by the use of Biochemical Tests

2.14.1 Citrate utilization tests

Ammonium Dihydrogen Phosphate is the sole source of nitrogen in Simmons Citrate Agar. Dipotassium Phosphate acts as a buffer. Chloride maintains the osmotic balance of the

medium. Sodium Citrate is the sole source of carbon in this medium. Magnesium Sulphate is a cofactor for a variety of metabolic reactions. Bromo thymol Blue is the pH indicator. Organisms that can utilize Ammonium Dihydrogen phosphate and sodium Citrate as their sole source of nitrogen and carbon will grow on this medium and produce a colour change from green (neutral) to blue (alkaline). Agar is the solidifying agent.

2.14.2 Procedure

- Slope preparations of the medium (Simmons Citrate) were made in bijou bottles as recommended by the manufacturer (store at 2-8°C).
- Stile straight wire was used to first streak the slope with a saline suspension of the test organism and then the butt was stabbed.
- The preparation was incubated at 35°C for 48 hours. (Monica, 2002)

3. RESULTS

Table 1. Antibiotics susceptibility testing

Genus	Citrate Utilization Reaction
Escherichia	Negative (Green)
Klebsiella	Positive (Blue)
Salmonella	Positive
Shigella	Negative

3.1 Disc Diffusion Method

Antibiogram, Kirby Bauer's method preparation of standard inoculums and sensitivity plate.

- Three similar colonies of the identified pure isolates were touched with a sterile, wire loop and were emulsified in 5ml of sterile broth.
- The preparation was incubated for 3 hrs at 37°C.
- In a good light match, the turbidity of the suspension was compared to Barium sulphate ($BaSO_4$). Using a sterile swab stick, the inoculum was picked and excess was removed by pressing and rotating the swab stick against the wall of the tube.
- The swab was spread evenly over the surface of a dried nutrient agar in three directions rotating the plate approximately 60° to ensure even distribution.
- The Petri lid dish was placed over the agar and was allowed to dry for 3 mins.
- Ensuring aseptic techniques were adhered to; with the aid of a sterile forceps, the two octal antibiotic discs (Oxoid Diagnostics Lagos) containing imipenem (10 ug) and meropenem (10 ug) each were place on to the inoculated plate about 25 mm from each other.
- The Petri dish was inverted and incubated aerobically at 37°C for 24 hrs [7].

3.2 Determination of Zone of Inhibition

After overnight of incubation at 37°C, the zones of inhibition were measured to the nearest millimeters (mm) by using a millimeter ruler.

3.3 Result Interpretation

Result Interpretation of the antibiotic susceptibility testing is done by comparison of the zone of inhibition of the test and the Breakpoints of the antibiotics provided by an antibiotic susceptibility testing performance standards such as the Clinical Laboratory Standard Institute (CLSI) based in USA or the EUCAST based in England.

In this study, result interpretation was based on the Breakpoints provided by CLSI (2014). The Breakpoints of the antibiotics (imipenem and meropenem) used in this study are illustrated on Table 6.

3.4 Data Analysis

Data were analysed using Statistical Package for Social Sciences (SPSS) windows version 21. Observed differences in data were considered significant if p value less than 0.05.

3.5 Expected Outcomes

The study revealed some bacterial agents which were resistant to Carbapenem and are responsible for Hospital Acquired in patients attending UDUTH.

3.6 Confounding Factors

Inability to exclude patients who have had antimicrobials, as most patients would have sought medical treatment. This may hinder the growth of the bacteria and give a low prevalence for the organisms being evaluated.

3.7 Limitations

Lack of cooperation, Cultural beliefs, Time, Technical expertise and Finance.

3.8 Results

A total of n=191 isolates of Gram-negative rods (*Enterobacteriaceae)* were identified in this study. The highest number of isolates was observed in *E. coli* 85 (44.5%) followed by *K. pneumoniae* 50 (26.2%), *Salmonella* spp. 42 (22.0%) and *Pseudomonas aeruginosa* 14 (7.3%) respectively. The susceptibility of the isolates to both meropenem and imipenem was 91% (Table 2). Table 2 shows the prevalence of carbapenem resistance among members of *Enterobacteriacea* in UDUTH Sokoto. Isolates of *E. coli* shows 9.4% resistance to Meropenem and Imipenem, followed by *K. pneumonia*e (8%), *Salmonella* spp. (0%) and *P. aeruginosa* (21%).

Breakpoint zone diameters of 20-22 mm (for intermediate sensitivity) were employed for both Meropenem (MEM) and Imipenem (IPM). Figures in parenthesis are percentages. The susceptibility of the isolates to Meropenem and Imipenem was 91% and 91%, respectively (Table 2).

The prevalence of carbapenem resistance among the members of Enterobacteriacea in UDUTH is 7.9% for Meropenem (15/191) and for Imipenem is 7.9% (15/191). This indicates the total prevalence of carbapenem resistance among the members of Enterobacteriacea in UDUTH to be 15+15 = 30/191 which is equivalent to 15.7% (Table 2).

The relationship between the type of antibiotics on the patients and zone diameter to imipenem and meropenem are shown in Tables 3 and 4 respectively. Out of the total number of isolates used, 182 were susceptible to various antibiotics with the highest in cephalosporin group IV (56) and lowest in ciprofloxacin oral (8).

The relationship between the type of antibiotics on the patients and zone diameter to imipenem and meropenem are shown on Tables 5 and 6 respectively. Out of the total number of isolates used, 182 were susceptible to various antibiotics with the highest in cephalosporin group IV (56) and lowest in ciprofloxacin oral (8).

Table 2. Susceptibility and prevalence of some members of *Enterobacteriaceae* to Meropenem and Imipenem according to CLSI breakpoints (CLSI 2014)

S/N	Bacterial isolates	No screened	No susceptible to Meropenem (zone ≥ 23 mm in diameter) (%)	No susceptible to Imipenem (zone ≥ 23 mm in diameter) (%)	No resistant to meropenem (zone ≤ 19 mm in diameter)	No resistant to Imipenem (zone ≤ 19 mm in diameter)
1	*E. coli*	85	77 (90%)	77(90%)	8 (9.4%	8 (9.4%)
2	*K. pneumonia*	50	46 (94%)	46 (94%)	4 (8%)	4 (8%)
3	*Salmonella spp.*	42	42 (100%)	42 (100%)	0	0
4	*P. aeruginosa*	14	11 (78%)	11 (78%)	3 (21%)	3 (21%)
	Total	**191**	**175 (91%)**	**175 (91%)**	**15 (7.9%)**	**15 (7.9%)**

Key: S/N = serial number, No = Number

Table 3. The relationship between the type of antibiotics on the patient and zone diameter to Imipenem

Type of antibiotics used	Zone diameter to Imipenem		Total
	Susceptible	Resistance	
Ciprofloxacin IV	18	1	19
Metronidazole IV	15	0	15
Ceftriaxone IV	23	0	23
Cephalosporin Group IV	51	8	61
Amoxicillin Oral	18	0	18
Clindamycin Oral	12	4	16
Gentamycin Oral	12	0	12
Ciprofloxacin Oral	8	0	8
Cephalosporin Groups Oral	18	1	19
Total	**182**	**14**	**191**

Chi-square value: 8.503 P-value: 0.386

Table 4. The relationship between the type of antibiotics on the patient and zone diameter to Meropenem

Type of antibiotics used	Zone diameter to Meropenem			Total
	Susceptible	Intermediate	Resistance	
Ciprofloxacin IV	18	0	1	19
Metronidazole IV	15	0	0	15
Ceftriaxone IV	23	0	0	23
Cephalosporin Group IV	51	1	8	61
Amoxicillin Oral	18	0	0	18
Clindamycin Oral	12	0	4	16
Gentamycin Oral	12	0	0	12
Ciprofloxacin Oral	8	0	0	8
Cephalosporin Groups Oral	18	0	1	19
Total	**182**	**1**	**14**	**191**

Chi-square value: 9.233; P-value: 0903

Table 5 shows the relationship between carbapenems resistant strains and other antibiotics sensitivity. The resistance isolates were screened for multi drug resistance by testing with other antibiotics sensitivity discs such as ceftazidime, cefuroxime, gentamycin, ciprofloxacin, ofloxacin, amoxicillin/clavulanate, nitrofurantoin, and ampicillin, they proved to be resistance to these antibiotics as well. This means the 15 carbapenem resistance isolates are multi-drug resistance. MIC Breakpoints and Interpretive criteria for carbapenems (imipenem and meropenem) {CLSI 2014} is illustrated in Table 6.

4. DISCUSSION

Carbapenemase-producing pathogens cause infections that are difficult to treat and have high mortality rates, due to their appearance in multidrug-resistant pathogens such as *K. pneumoniae*, *P. aeruginosa*, and *Acinetobacter* spp [8,9]. The total percentage of carbapenem resistance among *Enterobacteriaceae* was 15.7%. This study shows 7.9% prevalence for meropenem and imipenem respectively. This is lower to the prevalence rate of 9.7% (meropenem) and 12.4% (ertapenem) reported by Yahaya et al. [10] in Maiduguri, North-Eastern Nigeria and 10.5% (imipenem) and 12.5% (meropenem) documented by Yusuf et al. [11] in Kano among isolates of *Enterobacteriaceae*. Similarly, Rawan et al. [12] and Deogratius et al. [13] also observed a higher prevalence of 12.1% and 22.4% in Gaza strip, Palestine and Sudan. This may be as a result of multiple factors like uncontrolled antibiotic usage, inappropriate dosing regimens, widespread counterfeit and substandard antibiotics.

In contrast, Hyo-jin et al. [14] and Jones et al. [15] recorded much lower prevalence of 1.6% and 0.15% in Korea and Tel Aviv, Israel respectively. These differences could be as a result of restrictions of antibiotics usage in these countries unlike Nigeria where most drugs are available over the counter without prescription by qualified medical personnel.

Table 5. The relationship between Carbapenems resistance strains and other antibiotics sensitivity discs

Sensitivity discs	Zone diameter	Resistance strain			
		E. coli	***K. pnuemoniae***	***Salmonella* spp.**	***P. aeruginosa***
Ceftazidime	6 mm	8	4	0	3
Cefuroxime	6 mm	8	4	0	3
Gentamicin	6 mm	8	4	0	3
Ciprofloxacin	6 mm	8	4	0	3
Ofloxacin	6 mm	8	4	0	3
Amoxycillin	6 mm	8	4	0	3
Nitrofurantoin	6 mm	8	4	0	3
Ampicillin	6 mm	8	4	0	3

Key: 6 mm = resistance

Table 6. MIC Breakpoints and Interpretive criteria for Carbapenems (Imipenem and Meropenem) [CLSI 2014]

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm) S	SDD	I	R	MIC Interpretive Criteria (µg/mL) S	SDD	I	R	Comments
CARBAPENEMS											
(26) Following evaluation of PK-PD properties, limited clinical data, and MIC distributions that include recently described carbapenemase-producing strains, revised interpretive criteria for carbapenems were first published in June 2010 (M100-S20-U) and are listed below. Because of limited treatment options for infections caused by organisms with carbapenem MICs or zone diameters in the intermediate range, clinicians may wish to design carbapenem dosage regimens that use maximum recommended doses and possibly prolonged intravenous infusion regimens, as has been reported in the literature.[14] Consultation with an infectious diseases practitioner is recommended for isolates for which the carbapenem MICs or zone diameter results from disk diffusion testing are in the intermediate or resistant ranges. Until laboratories can implement the current interpretive criteria, the modified Hodge test (MHT) should be performed as described in Table **3C**. After implementation of the current interpretive criteria, the MHT does not need to be performed other than for epidemiological or infection control purposes (refer to Table **3B**). The following information is provided as background on carbapenemases in *Enterobacteriaceae* that are largely responsible for MICs and zone diameters in the intermediate and resistant ranges, and thus the rationale for setting revised carbapenem breakpoints: • The clinical effectiveness of carbapenem treatment of infections produced by isolates for which the carbapenem MIC or disk diffusion test results are within the intermediate (I) range is uncertain due to lack of controlled clinical studies. • Imipenem MICs for *Proteus* spp., *Providencia* spp., and *Morganella morganii* tend to be higher (eg, MICs in the intermediate or resistant range) than meropenem or doripenem MICs. These isolates may have elevated imipenem MICs by mechanisms other than production of carbapenemases.										
B	Doripenem	10 µg	≥23		20–22	≤19	≤1		2	≥4	(27) Interpretive criteria are based on a dosage regimen of 500 mg every 8 h.
B	Ertapenem	10 µg	≥22		19–21	≤18	≤0.5		1	≥2	(28) Interpretive criteria are based on a dosage regimen of 1 g every 24 h.
B	Imipenem	10 µg	≥23		20–22	≤19	≤1		2	≥4	(29) Interpretive criteria are based on a dosage regimen of 500 mg every 6 h or 1 g every 8 h.
B	Meropenem	10 µg	≥23		20–22	≤19	≤1		2	≥4	(30) Interpretive criteria are based on a dosage regimen of 1 g every 8 h.
AMINOGLYCOSIDES											

The susceptibility of some members of *Enterobacteriaceae* to Carbapenems in UDUTH is 91%. This is compared with the findings of Kiffer et al. [16] and Zahedi et al. [17] who reported that overall, worldwide susceptibility to carbapenems is 98% among enterobacteriaceae, whereas Imipenem susceptibility ranges from 60% to 83% for *P. aeruginosa* and *Acinetobacter baumannii*.

The highest prevalence of Carbapenem resistance isolate was *P. aeruginosa* (21%) followed by *E. coli* (9.4%), *K. pneumoniae* (8%) while *Salmonella* spp. shows full susceptibility to carbapenem (imipenem and meropenem). This is similar to the findings of Legese et al. [18] in Ethiopia, East Africa but divergent from the study by Deogratius et al. [13] in Mulago National Referral Hospital Uganda were *Klebsiella* species and *E. coli* had the highest carbapenem resistance rates. This may be due to different antimicrobial treatment protocols for the bacteria mentioned above.

The bacteria isolated from this study cause illnesses such as the Urinary Tract Infection (UTI) and diarrhoea for the prolonged hospitalized patient. Most of these bacteria isolates are affiliated with Hospital Acquired Infection (HAI) which can increase the burden of discomfort or uneasiness for a patient who was in the hospital for long periods or intensive care patient [19,20].

Carbapenemase-producing pathogens cause infections that are difficult to treat and have high mortality rates, due to their appearance in multidrug-resistant pathogens such as *K. pneumoniae*, *P. aeruginosa*, and *Acinetobacter* spp. [21,22,23]. Bush [24] and Bush and Jacoby [25] described these enzymes as species-specific chromosomal carbapenemases. They also reported the appearance of carbapenemase genes that are easily transferred on mobile elements among species. While considered by some to be relatively rare, reports of their occurrence in outbreak settings have steadily

increased. Awareness of their entry into a hospital environment is the first step that clinical microbiologists can take to address this problem. Care in detection is needed because high carbapenem MICs are not always evident. Evaluation of effective antibiotic options and rigorous infection control measures will help in the fight against carbapenemase-producingg organisms.

5. CONCLUSION

From the findings, the total percentage of carbapenem resistance among *Enterobacteriaceae* was 15.7%. Carbapenem resistance was higher in *P. aeruginosa*, amongst all the members of *Enterobacteriaceae* tested while *salmonella* species was completely susceptible to the drugs.

Carbapenemase production among bacterial pathogens in UDUTH Sokoto is on the rise, raising fears of resistance to a multitude of antibiotics in the treatment of clinical infections.

6. RECOMMENDATIONS

Patients in acute care settings who are colonized or infected with Carbapenem Resistance Enterobacteriacea (CRE) should be placed on Contact Precautions. Systems should be in place to identify patients' with a history of CRE.

Health Care Personnel in all settings who care for patients with Multi-Drug Resistance Organisms (MDRO), including CRE, should be educated about preventing transmission of these organisms.

Screening is used to identify unrecognized CRE colonization among epidemiologically-linked contacts of known CRE colonized or infected patients as clinical cultures will usually identify only a fraction of all patients with CRE.

Antimicrobial stewardship is another primary part of MDRO control.

CONSENT

Informed written consent was also obtained from each patient before enrolment into the study.

ETHICAL APPROVAL

Ethical permission was sought from the ethical committee of the selected hospitals before commencing the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Patricia MT. Bailey and Scott's textbook of diagnostic microbiology 13th Ed. By Mosby. Inc. an affiliate of Elsevier Inc. 2014;153-162.
2. Centers for Disease Control and Prevention. Carbapenem-resistant Enterobacteriaceae in healthcare settings; 2016.
   Available:http://www.cdc.gov/hai/organisms/cre/index.html
3. Gajdács M. Commentary: The development of an ideal antibiotic compound: A fairy tale possible reality? J. Infect. 2019;2(2):18-20.
4. Gajdács M, Paulik E, Szabó A. Knowledge, attitude and practice of community pharmacists regarding antibiotic use and infectious diseases: A cross-sectional survey in Hungary (KAPPhA-HU). Antibiotics. 2020;9(2):41.
5. Karn S, Pant ND, Neupane S, Khatiwada S, Basnyat S, Shrestha B. Prevalence of carbapenem resistant bacterial strains isolated from different clinical samples: Study from a tertiary care hospital in Kathmandu, Nepal. J. Biomed. Sci. 2017;3:11–15.
6. Bertram GK. BM and Pharmacology. 12th. Ed USA, LANGE. 2012;789.
7. Cheesbrough M. District laboratory practice in tropical countries. Part 2 Second Edition, Cambridge University Press, Cambridge, United Kingdom. 2002;38.
8. Akujobi CN, Ewuru CP. Detection of extended-spectrum β-lactamases in gram negative bacilli from clinical specimens in a teaching hospital in South Eastern Nigeria. Nig. Med. J. 2010;51:141-146.
9. Najjuka F, Deogratius O, Benon BA, Fred AK, Laban KC. Prevalence and characterization of carbapenem-resistant enterobacteriaceae isolated from Mulago National Referral Hospital, Uganda. PLoS ONE. 2015;10(8).
   DOI: 10.1371/journal.pone.0135745
10. Yahaya M, Sambo BZ, Anthony OO. Characterization of KPC, NDM and VIM type carbapenem resistance *Enterobacteriaceae* from North Eastern,

Nigeria. J. Biosci. and Med. 2015;3:100-107.
Available:http://dx.doi.org/10.4236/jbm.2015.311013

11. Yusuf I, Arzai AH, Getso MI, Sherif A, Haruna M. Emergence of carbapenem resistant *Enterobacteriaceae* in surgical and intensive care units of a hospital with low usage of carbapenem in Kano, North West Nigeria. Antimicro. Resist. and Infect. Cont. 2012;2:75-78.
Available:http://dx.doi.org/10.1186/2047-2994-2-S1-P75
12. Rawan HR, Nahed AA, Abdelraouf AE. Carbapenem resistance among clinical and environmental gram-negative isolates recovered from hospitals in Gaza strip, Palestine. Germs. 2018;8(3):147–154.
DOI: 10.18683/germs.2018.1142
13. Deogratius O, Benon BA, Fred AK, Laban K, Christine FN. Prevalence and characterization of carbapenem-resistant Enterobacteriaceae isolated from Mulago National Referral Hospital, Uganda. PLoS One. 2015;10(8).
DOI: 10.1371/journal.pone.0135745
14. Hyo-Jin L, Jae-Ki C, Sung-Yeon C, et al. Carbapenem-resistant *Enterobacteriaceae*: Prevalence and risk factors in a single community-based hospital in Korea. Infect. Chemo. 2016;48(3):166–173.
DOI: 10.3947/ic.2016.48.3.166
15. Jones SM, Carmeli Y. The impact of a carbapenem-resistant Enterobacteriaceae outbreak on facilitating development of a national infrastructure for infection control in Israel. Clin Infect Dis. 2017;65:2144–2149.
DOI: 10.1093/cid/cix615
16. Kiffer CRV, Mendes C, Kuti JL, Nicolau DP. Pharamacodynamic comparisons of antimicrobials against nosocomial isolates of *Escherichia coli, Klebsiella pneumonia, Acinetobacter spp and Pseudomonas aeruginosa* from MYSTIC surveillance program. South America 2002 Diag. Mic. Infect. Dis. 2004;49:109-116.
17. Zahedi BA, Samadi KH, Ebrahimzadeh LH, Asgharzadeh M, Aghazadeh M. Dissemination of carbapenemases producing gram negative bacteria in the Middle East. Iran J. Microb. 2015;7:226–46. [PMC free article] [PubMed]
18. Legese MH, Weldearegay GM, Asrat D. Extended-spectrum beta-lactamase- and carbapenemase-producing *Enterobacteriaceae* among Ethiopian children. J. Infect. Drug Resist. 2017;10:27-34.
DOI: https://doi.org/10.2147/IDR.S127177
19. Vanegas JM, Parra OL, Jiménez JN. Molecular epidemiology of carbapenem resistant gram-negative bacilli from infected pediatric population in tertiary-care hospitals in Medellín, Colombia: An increasing problem. BMC Infect. Dis. 2016;16:463.
20. Gniadek TJ, Carroll KC, Simner PJ. Carbapenem-resistant non-glucose-fermenting gram-negative bacilli: The missing piece to the puzzle. J. Clin. Micro. 2016;54:1700–10.
21. Bratu S, Landman D, Haag R, Recco R, Eramo A, Alam M, Quale J. Rapid spread of carbapenem-resistant *Klebsiella pneumonia* in New York City: A new threat to our antibiotic armamentarium. Arc. Int. Med. 2005;165:1430-1435.
22. Heudorf U, Büttner B, Hauri AM, et al. Carbapenem-resistant gram-negative bacteria analysis of the data obtained through a mandatory reporting system in the Rhine-Main region, Germany, 2012-2015. GMS Hyg. Infect. Cont. 2016;11:Doc10.
23. Khalifa HO, Soliman AM, Ahmed AM, et al. High carbapenem resistance in clinical gram-negative pathogens isolated in Egypt. Micro. Drug Resist. 2017;23:838–844. [PubMed].
24. Bush K. Recent developments in β-lactamase research and their implications for the future. Rev. Infect. Dis. 1988;10:681-739-743.
25. Bush K, Jacoby GA. Updated functional classification of β-lactamases. Antimic. Agents Chemo. 2010;54:969-976.

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