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Urinary tract infections in pregnancy caused by carbapenem-resistant *Enterobacteriaceae* in University of Calabar Teaching Hospital, Nigeria: An emerging therapeutic threat

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Abstract:

Background: Severe infections caused by carbapenem-resistant *Enterobacteriaceae* (CRE) have mortality rate exceeding 50%. On the strength of this, this study sought to determine the prevalence of urinary tract infection (UTI) in pregnancy caused by CRE and associated risk factors in University of Calabar Teaching Hospital (UCTH), Nigeria, with the aim of making recommendations that can stem the tide of UTI caused by this bacterial strain in the hospital.

Methodology: This was a descriptive cross-sectional study of 349 consecutively selected pregnant women attending antenatal clinic of UCTH, Calabar, Nigeria, between September 2020 and August 2021. Demographic/clinical data and risk factors were collected with semi-structured interviewer-administered questionnaire. Voided mid-stream urine (MSU) sample was collected from each participant and transported to the medical microbiology laboratory of the hospital for microbiological analysis using conventional culture and biochemical identification methods. Antimicrobial susceptibility test (AST) on each isolate was performed by the disk diffusion technique against selected antibiotics. Phenotypic carbapenemase production from presumptive carbapenem resistant isolates following AST was confirmed by the modified Hodge test (MHT). Data analysis was done on SPSS version 19.0. Association of risk factors with prevalence of UTI caused by CRE was determined using Chi square or Fisher Exact test, with $p < 0.05$ considered statistically significant.

Results: The prevalence of UTI among the pregnant women was 10.0% (35/349), with prevalence of 6.6% for *Escherichia coli* (23/349) and 3.5% (12/349) for *Klebsiella pneumoniae*. Antibiotic susceptibility test result showed that piperacillin-tazobactam was the most active antibiotic *in vitro*, with 82.9% isolates sensitive to it while sensitivity to imipenem (60.0%) and meropenem (40.0%) was low. A total 17 (48.6%) of the 35 isolates were resistant to carbapenems in the AST and 12 (34.3%) were carbapenemase-producing strains on MHT while 5 (14.3%) were non-carbapenemase-mediated resistance (NCMR). None of the demographic characteristics or risk factors analysed was significantly associated with UTI caused by CRE in the pregnant women ($p > 0.05$).

Conclusion: To stem the rising trend of UTIs in pregnancy caused by carbapenem resistant uropathogens, pregnant women receiving antenatal care in UCTH, Calabar should be routinely screened for UTI and offered appropriate treatment if indicated based on microbiological test results

Keywords: UTI; Pregnancy, *Enterobacteriaceae*, carbapenem-resistant, emerging threat

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Infections des voies urinaires pendant la grossesse causée par des *Entérobactéries* résistantes aux carbapénèmes à l'hôpital universitaire de Calabar, Nigéria: une menace thérapeutique émergente

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Résumé:

Contexte: Les infections graves causées par des entérobactéries résistantes aux carbapénèmes (CRE) ont un taux de mortalité supérieur à 50 %. Forte de ces éléments, cette étude a cherché à déterminer la prévalence des infections des voies urinaires (IVU) pendant la grossesse causée par la CRE et les facteurs de risque associés à l'hôpital universitaire de Calabar (UCTH), au Nigeria, dans le but de formuler des recommandations qui peuvent endiguer la marée d'infections urinaires causées par cette souche bactérienne à l'hôpital.

Méthodologie: Il s'agit d'une étude transversale descriptive portant sur 349 femmes enceintes sélectionnées consécutivement fréquentant la clinique prénatale de l'UCTH, Calabar, Nigeria, entre septembre 2020 et août 2021. Les données démographiques/cliniques et les facteurs de risque ont été collectés à l'aide d'un questionnaire semi-structuré administré par un intervieweur. Un échantillon d'urine mi-jet (MSU) a été collecté auprès de chaque participant et transporté au laboratoire de microbiologie médicale de l'hôpital pour analyse microbiologique à l'aide de méthodes de culture et d'identification biochimiques conventionnelles. Le test de sensibilité aux antimicrobiens (AST) sur chaque isolat a été réalisé par la technique de diffusion sur disque contre des antibiotiques sélectionnés. La production phénotypique de carbapénémase à partir d'isolats présumés résistants aux carbapénèmes après AST a été confirmée par le test de Hodge modifié (MHT). L'analyse des données a été effectuée sur SPSS version 19.0. L'association des facteurs de risque avec la prévalence des infections urinaires causées par la CRE a été déterminée à l'aide du test du Chi carré ou de Fisher Exact, avec $p < 0,05$ considéré comme statistiquement significatif.

Résultats: La prévalence des infections urinaires chez les femmes enceintes était de 10,0% (35/349), avec une prévalence de 6,6% pour *Escherichia coli* (23/349) et de 3,5% (12/349) pour *Klebsiella pneumoniae*. Les résultats du test de sensibilité aux antibiotiques ont montré que l'association pipéracilline-tazobactam était l'antibiotique le plus actif in vitro, avec 82,9% des isolats qui y étaient sensibles, tandis que la sensibilité à l'imipénème (60,0%) et au méropénème (40,0%) était faible. Au total, 17 (48,6%) des 35 isolats étaient résistants aux carbapénèmes dans l'AST et 12 (34,3%) étaient des souches productrices de carbapénémase sur MHT, tandis que 5 (14,3%) étaient des souches non médiées par la carbapénémase (NCMR). Aucune des caractéristiques démographiques ou des facteurs de risque analysés n'était associée de manière significative aux infections urinaires causées par la CRE chez les femmes enceintes ($p > 0,05$).

Conclusion: Pour endiguer la tendance croissante des infections urinaires pendant la grossesse causée par des uropathogènes résistants aux carbapénèmes, les femmes enceintes recevant des soins prénatals à l'UCTH de Calabar devraient être systématiquement dépistées pour les infections urinaires et se voir proposer un traitement approprié si cela est indiqué sur la base des résultats des tests microbiologiques.

Mots-clés: IVU; Grossesse; *Enterobacteriaceae*; résistantes aux carbapénèmes; menace émergente

Introduction:

The rapid spread of multidrug-resistant bacteria has become a public health concern, particularly in countries where the spread of carbapenem-resistant microorganisms is endemic (1). Severe infections caused by carbapenem-resistant *Enterobacteriaceae* (CRE) have mortality rate exceeding 50% (2-4). As part of their virulent factors, microorganisms causing urinary tract infections (UTIs) produce enzymes that hydrolyze therapeutic agents rendering them ineffective for treatment of conditions related to them. Carbapenemases production is one of such mechanisms of antibiotic resistance amongst species of *Enterobacteriaceae* and Gram-negative non-fermenters such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (5), which are common isolates of UTIs.

Urinary tract infections in pregnancy are common worldwide and if untreated can lead to poor perinatal and maternal outcomes (6). A combined effects of hormonal and physiological changes occurring during pregnancy predispose pregnant women to UTIs. Carba-

penemases constitute a group of β -lactam hydrolyzing enzymes that break down the carbapenem class of antibiotics. This class of antibiotics has broad spectrum activities and is reserved for the treatment of serious infections arising from multidrug resistant organisms (7). The carbapenem class of antibiotics is readily the drugs of choice for the treatment of infections caused by Gram-negative bacteria producing extended spectrum β -lactamases (ESBLs), a group of enzymes that hydrolyzes third generation cephalosporins and aztreonams but inhibited by β -lactamases inhibitor antibiotics such as clavulanic acid (8).

There is association between ESBL-production and resistance to other classes of antibiotics (9). This turn of events further causes serious therapeutic difficulties in the management of infections caused by ESBL-producing organisms which often culminates in poor treatment outcomes. Persistence of this trend of carbapenem resistance will further compound the problem associated with antibiotic management of serious infections caused by ESBL-producing Gram-negative bacteria. This study is intended to determine the prevalence

of UTI caused by CRE and other Gram-negative bacteria, and associated risk factors, with the aim of promoting and implementing prevention and control measures in the wards and antenatal clinic (ANC) of the hospital.

Materials and method:

Study design, setting and period:

This was a descriptive cross-sectional study carried out among pregnant women attending the ANC of the University of Calabar Teaching Hospital (UCTH), Calabar, Cross River State, Nigeria between 22nd September, 2020 and 14th August, 2021. Cross River State is located in the south-south geopolitical zone of Nigeria and embedded in the Niger Delta region. In 2015, it has a total projected of 3,756,403 and a population density of 170 person/Km². It has component units of 18 local government areas. The main occupation of the people includes farming, fishing and petty trading except for those in the few urban towns who are either civil servants or artisans.

The UCTH is a 260-bed tertiary facility located in Calabar the seat of Government of Cross River State, Nigeria. The hospital is patronized by inhabitants of the State and adjoining States and countries. It has several departments and units including the department of Obstetrics and Gynaecology in charge care of women care and child-bearing related conditions.

Ethical approval:

Ethical approval was given by the University of Calabar Teaching Hospital Health Research Ethical Committee. Informed consent was also obtained from each participant before the study was conducted, with assurance of safety, confidentiality of data, freedom to opt out of the study without any consequence, and assurance of no cost on the part of the participants.

Study participants and sample size:

The participants included in this study were consenting pregnant women attending the antenatal clinic and those with obstetric referrals to the hospital. The sample size was determined using the sample size formula for proportion (10), $n = Z^2pq/d^2$, where n is the calculated sample size, Z is 1.96 (95% confidence interval), p is 7.7% (0.077), obtained from the prevalence of UTI in UCTH, Calabar in a previous study (11), q is 1-p, and d is the acceptable margin of error for proportion (which was taken as 0.03 or 3%). This gave the calculated sample size of 303.36, which was adjusted for 15% non-response/attrition, to give the desired sample size of 349.

Method of sampling and data collection:

A total of 349 participants who met the

inclusion criteria were consecutively recruited from the ANC over the period of study. All eligible participants for the study were enlisted on their first antenatal visit only. Semi-structured interviewer-administered questionnaires were used to collect socio-demographic data from the participants. The questionnaire consisted of 5 sections which, collected information on participant's demographics, social lifestyle, obstetric, medical and drug history, respectively.

Sample collection:

Each participant was given a sterile appropriately labeled universal container and instructed to collect a clean-catch mid-stream urine specimen after adequate instruction on how to do this. The urine specimens were transported to the medical microbiology laboratory of the hospital for analysis

Urine microscopy:

The urine samples were first examined macroscopically for colour and consistency. A drop of well-mixed uncentrifuged urine sample was then made on a clean grease-free glass slide and covered with cover slip to make a thin film. The thin film of urine was then examined, using light microscope at x10 and x40 for pus cells, epithelial cells, bacteria and were reported on count per high power field (hpf).

Culture isolation and bacterial identification:

Each urine sample was well-mixed by gently tilting the sample bottle after which a loopful was inoculated on Cysteine Lactose Electrolytes Deficient (CLED) media plate using a standard wire-loop (0.005mm diameter) and incubated at 37°C for ≥ 16 hours in ambient air to yield discrete colonies.

Significant bacteriuria was determined from each culture plate when there are $\geq 10^5$ CFU/ml of urine (≥ 500 colonies on a culture plate). Discrete colonies from plates with significant bacteriuria were examined for colony morphology and Gram-staining reaction, and bacteria isolates were identified to species level using conventional biochemical test scheme (12).

Antibiotic susceptibility test:

Antibiotic susceptibility testing of each isolated bacterial species was done using the Kirby Bauer disk diffusion technique according to the Clinical and Laboratory Standard Institute (CLSI) guidelines (13), against 7 selected antibiotics (Oxoid, UK); amoxicillin-clavulanic (20+10 μ g), piperacillin-tazobactam (110 μ g), ceftriaxone (30 μ g), ciprofloxacin (30 μ g), imipenem (10 μ g) and meropenem (10 μ g).

Inoculum suspension of bacterial isolates and the control strain (*E. coli* ATCC 25922) were separately made in sterile normal

saline, and the turbidity adjusted to match that of 0.5 McFarland standard. The inoculum suspensions were inoculated on separate Mueller Hinton (MH) agar plates to make thin homogeneous lawns using sterile swab sticks. Antibiotic sensitivity discs were then placed on the inoculated MH agar plate and incubated at 35°C for 18 hours in ambient air. The diameter of zone of inhibition around each antibiotic disc was measured using a metre ruler and interpreted as sensitive, intermediate sensitive or resistant based on stipulated breakpoints according to the CLSI criteria (13).

Phenotypic screening for carbapenemase production:

Enterobacteriaceae species (or miscellaneous Gram-negative bacterial isolates) with diameter of zones of inhibition ≤ 21 mm to at least one carbapenem (imipenem or meropenem) in the AST were considered to be resistant to carbapenem and presumptive carbapenemase-producing isolates, which were confirmed by the modified Hodge test (13).

Phenotypic confirmation of carbapenemases using modified Hodges test (MHT):

An inoculum suspension of *Escherichia coli* (ATCC 25922) was prepared and the turbidity adjusted to match that of 0.5 McFarland standard. The suspension was inoculated on MH agar plate to make a thin uniform lawn. A meropenem disk (10 μ g) was placed in the centre of the lawn. Suspensions of the test bacterial isolates and the control strains (MHT positive *Klebsiella pneumoniae* ATCC1705 and MHT negative *Klebsiella pneumoniae* ATCC1706) were separately prepared and their turbidity adjusted to match 0.5McFarland standard and each was then used to make a straight-line streak from the edge of the meropenem disk at the centre outwards to the edge of the MH agar plate. The plates were incubated for ≥ 16 hours at 35°C in ambient air.

Carbapenemase-producing (MHT positive) isolate displayed a 'clover-leaf' like indentation of the zone of inhibition due to the growth of *E. coli* (ATCC 25922) along the line of streak of the isolate as a result of inactivation of meropenem by the isolate. MHT negative isolate did not show these indentations.

Statistical analysis of data:

The data were analysed using SPSS version 19.0 (SPSS, Chicago, Illinois, USA). Chi-square test was used to assess differences between proportions, and *p* value <0.05 was considered to be the statistical significance.

Results:

Sociodemographic characteristics of the study participants:

A total of 349 participants were included in the study and their socio-demographic characteristics are detailed in Table 1. Majority of the study participants (170, 48.7%) were in the age group 30-34 years, closely followed by those in age group 24-29 years (103, 29.5%). The mean age of the participants is 29.5 ± 6.3 years.

Most participants (145, 41.5%) were business women while 2 (0.6%) were farmers. Majority, (260, 75.5%) had tertiary education with only 8 (2.3%) having primary education. Over half of the participants (182, 52.1%) were indigenes of Cross River State while 165 (48.4%) were non-indigenes of the State. Majority of the participants (208, 59.6%) were low-income earners, with monthly income of 20,000-50,000 Nigeria Naira, and only 18 (5.2%) earned 100,000.00 Naira or more.

Obstetrics and medical history of the study participants:

Table 2 shows that majority of the participants (189, 54.2%) were primigravida and 6 (1.7%) were multiparous (Para⁴). Most of the participants (190, 54.4%) were in the 25-40 weeks gestation, 113 (32.4%) were in 13-24 weeks gestation and only 1 (0.3%) was post-date/post-term. Majority of participants (296, 84.8%) admitted to having obstetric care and hospital delivery in their previous confinements whereas 37 (10.6%) were cared for and delivered by traditional birth attendants.

A total of 30 (8.6%) participants had history of contraceptive use, 11 (3.2%) used oral contraceptives and 19 (5.4%) used injectable contraceptives, while 319 (91.4%) have no history of contraceptive use. Fifteen (4.3%) participants had positive history of painful micturition with vaginal discharge during the last menstrual period (LMP), 5 (1.7%) had painful micturition without discharge during LMP, 41 (11.7%) had painful micturition in the index pregnancy at the time of sample collection, while there was no history of painful micturition in 288 (82.5%) in the index pregnancy before or during sample collection.

Most participants (223, 92.6%) had no sugar in urine while 26 (7.4%) had glycosuria. A total of 66 participants (19.1%) had fever in present pregnancy.

Table 1: Frequency distribution of socio-demographic characteristics of the student participants

Socio-demographic variables	Number (%)
Age group (years)	
<16	1 (0.3)
16-19	1 (0.3)
20-23	23 (6.6)
24-29	103 (29.5)
30-34	170 (48.7)
35-39	42 (12.0)
>40	9 (2.6)
Mean age (years)	29.5 ± 6.3
Occupation	97 (27.8)
Civil Servant	145 (41.5)
Business	2 (0.6)
Farming	71 (20.3)
Others	34 (9.7)
Unemployed (No Reliable Income)	
Religion	
Christian	344 (98.6)
Muslim	5 (1.4)
Others	0
State of origin	
Cross Rivers	182 (52.1)
Other States	165 (48.4)
Non-Nigerian	2 (0.6)
Monthly Income Level (₦)	
<20000	55(15.7)
20-50000	208(59.6)
60000-100,000	68(19.5)
>100,000	18(5.2)
Educational Level	
No Formal	0
Primary	8 (2.3)
Secondary	81 (23.2)
Tertiary	260 (74.5)

There was no history of smoking in majority of participants (348, 99.7%) but 1 (0.3%) participant admitted to occasional smoking. No history of alcohol consumption in 278 (79.7%), 69 (19.7%) participants consumed alcohol occasionally while 2 (0.6%) were habitual alcohol consumers.

Most of the participants (315, 90.3%) had not used antibiotics in the index pregnancy but 34 (9.7%) had used antibiotics, with 21 (6.0%) being inappropriate use (no medical prescription) while 13 (3.7%) were appropriately prescribed by medical doctor. There was no use of steroidal drug in 319 (91.4%) while 30 (8.6%) admitted to using steroidal contraceptives prior to index pregnancy.

Prevalence of UTI and uropathogenic isolates from the study participants:

Out of the 349 participants included in the study, urine samples of 314 (89.9%) yielded no growth of bacterial uropathogens while 35 (10.0%) yielded significant growth of Gram-negative uropathogenic bacilli, thus giv-

ing a UTI prevalence of 10.0% among the participants. The bacterial uropathogens isolated were *Escherichia coli* in 23 participants (6.6%) and *Klebsiella pneumoniae* in 12 participants (3.5%).

Antimicrobial susceptibility of uropathogenic isolates:

The result of the AST shows that piperacillin-tazobactam was most active *in vitro* on the isolates, with 29 of 35 (82.9%) isolates sensitive to it, followed by ciprofloxacin (26, 74.3%), ceftazidime (25, 71.4%), ceftriaxone (25, 71.4%), imipenem (21, 60.0%), amoxicillin-clavulanate (18, 51.4%) and meropenem (14, 40.0%) (Table 3).

A total of 17 (48.6%) urinary isolates were resistant to carbapenems (resistance to imipenem and/or meropenem), 12 (34.3%) of which were carbapenemase-producing on modified Hodge test, while 5 (14.3%) were non-carbapenemase-mediated antibiotic resistance (NCOMR) (Fig 1).

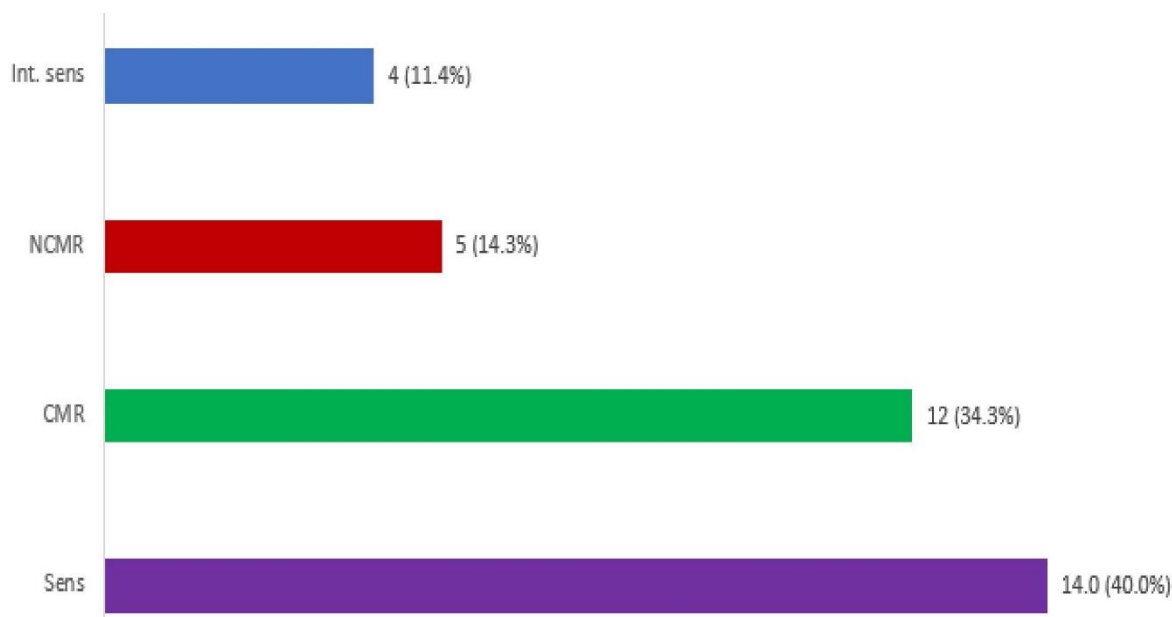
Table 2: Obstetrics and medical history of the student participants

Obstetrics and medical variables	Number (%)
Parity	
Primigravida	189 (54.2)
2	96 (27.5)
3	40 (11.5)
4	19 (5.4)
> 4	5 (1.4)
Gestation age of present pregnancy (weeks)	
< 2	1 (0.3)
2-12	44 (12.6)
13-24	113 (32.4)
25-40	190 (54.4)
≥ 40	1 (0.3)
Place of previous deliveries	
Hospital	296 (84.8)
Traditional Birth Attendants	37 (10.6)
Home	15 (4.3)
Never had previous delivery	1 (0.3)
Previous use of contraceptives	
No	319 (91.4)
Yes (Oral)	11 (3.2)
Yes (Injectable)	19 (5.4)
History of painful micturition with/without discharge	
None	288 (82.5)
Yes (≤5 days with discharge during LMP)	15 (4.4)
Yes (≤5 days without discharge during LMP)	5 (1.4)
Presently manifesting ± discharge	41 (11.7)
History of sugar in urine	
Yes	26 (7.4)
No	323 (92.6)
History of fever in current pregnancy	
Yes	66 (18.9)
No	283 (81.1)
Smoking status	
No	348 (99.7)
Yes (Occasionally)	1 (0.3)
Alcohol use	
No	278 (79.7)
Yes (Occasionally)	69 (19.7)
Yes (1 Unit daily)	1 (0.3)
Yes (>1 Unit daily)	1 (0.3)
History of antibiotic use	
No	315 (90.3)
Yes (≤ 4 weeks ago unprescribed)	15 (4.3)
Yes (≤ 4 weeks ago prescribed but abused)	6 (1.7)
Yes (Presently and prescribed)	13 (3.7)
Presently on steroidal drug	
No	319 (91.4)
Yes	30 (8.6)

Table 3: Antibiotic susceptibility of uropathogenic isolates causing urinary tract infections among the student participants

Degree of susceptibility	Antibiotics (n, /%)						
	IMP	CRO	AUG	CIP	TZP	CAZ	MERO
Resistant	11 (31.4)	7 (20)	9 (25.7)	5 (14.3)	5 (14.3)	8 (22.9)	17 (48.6)
Intermediate sensitive	3 (8.6)	3 (8.6)	8 (22.9)	4 (11.4)	1 (2.9)	2 (5.9)	4 (11.4)
Sensitive	21 (60.0)	25 (71.4)	18 (51.4)	26 (74.3)	29 (82.9)	25 (71.4)	14 (40.0)

IMP= Imipenem, CRO= Ceftriaxone, AUG= Amoxicillin/Clavulanate, CIP= Ciprofloxacin, TZP= Piperacillin/Tazobactam, CAZ= Ceftazidime, MERO= Meropenem.



Sens=Sensitive; Int sens = intermediate sensitivity; NCMR = non-carbapenemase resistance; CMS=carbapenemase producing

Fig 1: Susceptibility of urinary bacterial isolates to carbapenems

Risk factors associated with UTI caused by CRE amongst the study participants:

Regarding risk of UTI caused by CRE in Table 4, none of the factor analysed was a significant risk factor for UTI in pregnancy caused by CRE

Discussion:

Physiological and hormonal changes that occur in the course of pregnancy, the short female urethra with proximity to the anal verge and urinary tract instrumentation are among the major factors predisposing pregnant women to acquiring UTI (13). The prevalence of UTI among pregnant women in the study was 10.0%, which is similar to 15.8% reported in Kano (14) and 13.5% reported in Saudi Arabia (13). However, this prevalence is far lower than the prevalence of 56.7% reported in Ile-Ife (15), 31.0% in Ogun State (16), and 61.0% in Akure, Nigeria (17). These variations may be due to prevalent factors bordering on environmental, economic and socio-cultural differences between study locations.

Piperacillin-tazobactam had the highest *in vitro* activity (82.9% sensitivity) against the CRE isolates, which agrees with the report of a study in Lagos (9). However, sensitivity of the CRE isolates to meropenem (48.6%) and

imipenem (31.4%) was low, which is at variance with the study in Lagos (9), where *in vitro* sensitivity of 99.2% and 93.4% were reported for imipenem and meropenem respectively against the tested organisms. The reason for this variation may be due to differences in 'selection pressure' for antibiotics at the different locations of study.

The prevalence of phenotypic carbapenem resistance in this study among the *Enterobacteriaceae* isolates was 46.8% (17/35) with 34.3% (12/35) being carbapenemase-mediated resistance and 14.3% (5/35) non-carbapenemase-mediated resistance. Carbapenemases production remains a major factor in the spread of carbapenem resistance. Rising antimicrobial resistance to carbapenems creates difficulties in the management of severe infections caused by Gram-negative bacteria as carbapenems remain the drug of choice for the management of such conditions.

In our study, none of the variables tested was identified as significant risk factor associated with UTI in pregnancy caused by CRE, which disagrees with the study by Belete et al., (13) which reported socioeconomic factors, level of education and sexual activities as major reasons for acquiring multi-resistant Gram-negative organisms.

Table 4: Analysis of risk factors associated with urinary tract infection caused by carbapenemase-resistant *Enterobacteriaceae* among study participants

Risk factors	CRE (%) (n=17)	Non-CRE (%) (n=18)	χ^2	OR (95% CI)	p value
Parity					
Primigravida	8 (47.1)	10 (55.6)	7.018	NA	0.0713
2	4 (23.5)	7 (38.9)			
3	5 (29.4)	0			
4	0	1 (5.6)			
Gestation of index pregnancy (weeks)					
2-12	3 (17.6)	4 (22.2)	1.258	NA	0.7391
13-24	3 (17.6)	4 (22.2)			
25-40	10 (58.9)	10 (55.6)			
Postdate	1 (5.9)	0			
Place of previous delivery					
Hospital	10 (58.9)	10 (55.6)	0.06239	NA	0.9693
Traditional Birth Attendant	5 (29.5)	6 (33.3)			
Home	2 (11.8)	2 (11.1)			
History of contraceptive use					
No	9 (52.9)	10 (55.6)	0.024	0.90 (0.238-3.41)	0.8767
Yes	8 (47.1)	8 (44.4)			
Painful micturition ± discharge					
No	13 (76.5)	14 (77.8)	1.152	NA	0.562
Yes (≥ 2wks post LMP)	1 (5.9)	0			
Yes (currently)	3 (17.6)	4 (22.2)			
History of sugar in urine					
No	14 (82.4)	16 (88.9)	0.0048	0.583 (0.085-4.011)	0.6581
Yes	3 (17.6)	2 (11.1)			
History of fever in pregnancy					
No	14 (82.4)	13 (72.2)	0.0965	1.795 (0.36-9.06)	0.6906
Yes	3 (17.6)	5 (27.8)			
Alcohol consumption					
No	17 (100.0)	14 (77.8)	2.352	10.862 (0.539-219.1)	0.1039
Yes	0	4 (22.2)			
History of antibiotic use					
No	16 (94.1)	18 (100.0)	0.0008	0.297 (0.011-7.82)	0.4857
Yes (presently)	1 (5.9)	0			
Present steroidal drug use					
No	15 (88.2)	17 (94.4)	0.00268	0.4412 (0.036-5.37)	0.6026
Yes	2 (11.8)	1 (5.6)			

χ^2 =Chi square; OR=Odd ratio; CI=Confidence interval; NA=Not applicable; LMP=last menstrual period

Conclusion:

The prevalence of UTI in this study was 10.0% (35/349), with prevalence of 6.6% for *E. coli* and 3.5% for *K. pneumoniae*. Piperacillin-tazobactam was most active antibiotic *in vitro* while sensitivity to imipenem and meropenem was low, with 48.6% of the isolates resistant to the carbapenems, mainly through carbapenemase production (34.3%). This situation will create obvious difficulties in antibiotic management of severe infections caused by Gram-negative bacteria particularly ESBL-producing strains since carbapenems have been the antibiotic class of choice for treatment of severe infections caused by these organisms.

To stem this rising trend of UTIs in pregnancy caused by CRE, pregnant women receiving antenatal care in UCTH, Calabar should be screened for UTI and offered appro-

prate treatment if required based on microbiological analysis of their urine samples.

Contributions of authors:

The study was conceptualized by OGI and IUC. All authors were involved in the literature searches. IAA analysed the data, while OGI, USN and EUE wrote the manuscript. EUE, AAI and IUC edited the final copy of the manuscript which was read and approved by all the authors.

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