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Research Article

Urogenital Colonization and Characterization of Extended Spectrum Beta-Lactamase-Producing Gram-Negative Isolates from Infertile Women at Selected Hospitals in Ibadan, Nigeria

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ABSTRACT

Antimicrobial resistance as a result of Extended Spectrum Beta-Lactamase production among Gram- negative bacteria to commonly prescribed antibiotics is increasing all over the world. ESBL production among urinary-pathogens may predispose women to treatment failure as a result of resistance to antibiotics and increases the risk for various reproductive dysfunctions that can precipitate infertility. In this study, ESBL-producing gram negative isolates from urine and high vaginal swab of infertile women were investigated for a period of one year (2020 and 2021). Urine and high vaginal swabs were taken from 140 infertile women (mean age of 26 and 33) for cases of primary and secondary infertility respectively. Standard microbiological analysis including microscopy, culture and sensitivity using the VITEK-2 automated compact system and disk diffusion method were employed. Detection of ESBL phenotypes among the isolates was conducted using double disc synergy test. Klebsiella pneumoniae, *Escherichia coli* and *Pseudomonas aeruginosa* were identified as follows and in this respective proportion (72%, 64%, 43%) with Klebsiella pneumoniae being the most prevalent. ESBL-production was detected in 62.9% of isolates with multi-drug resistance potential. The overall prevalence of Carbapenem sensitivity was high for all isolates except for Escherichia coli with 50% resistance expressed. Infertile women had a significant colonization of ESBL-producing pathogen in their urinary tract, may suffer the risk of transmission of infection to the reproductive tract; an important risk factor for reproductive dysfunctions to be addressed. These findings emphasized the need to embrace regular periodic surveillance of antimicrobial resistance and access to molecular screening towards treatment of bacterial infections.

Keywords: *Infertile women; Uro-genital; Antimicrobial resistance; Extended-spectrum, beta-lactamase (ESBL), Escherichia coli; Klebsiella pneumoniae; Pseudomonas aeruginosa, Carbapenem sensitivity, Gram-negative bacteria.*

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INTRODUCTION

Infertility has been known as a complex human health problem causing serious, social and emotional trauma globally especially in developing countries such as Nigeria. The psychological problem associated with cases of infertility cannot be over-emphasized; it is capable of altering the quality of life in couples facing the condition particularly on the woman. Infertility affects over 100million people all over the world; about 2% to 10% of women within the reproductive age (20-44years) experience primary or secondary infertility problems. Higher percentage of these cases are prevalent in developing countries.(Jalilian, Kooshkiforooshani, Ahmadi, and Nankali, 2019).

A couple is generally considered clinically infertile when there is failure to conceive and produce offspring after at least twelve months of regular and unprotected sexual activity.((Ruggeri, Cannas, Cubeddu, Molicotti, Piras, Dessole, and Zanetti, 2016)). Globally, a substantial number of couples seek fertility treatment as a result of multiple factors that may include congenital and hormonal disorders, environmental hazards, age, tubal factors, ovarian factors, male factors among other factors that may be unknown. All the factors mentioned here have been proven as causes of impairments to reproductive functions both in male and female. ((Alawan, Khamees, Tahir, and Ail El-Deweny, 2020)). Among other factors that is well established is

microbial infections of the reproductive tract, it is widely accepted that the impact of bacterial and parasitic infections involving Chlamydia trachomatis, Neisseria gonorrhoeae, Ureaplasma urealyticum, Gardnerella vaginalis and Trichomonas vaginalis on human reproductive functions is detrimental leading to pelvic inflammatory diseases (PID), ectopic pregnancies and infertility. ((Madziyire, Magwali, Chikwasha, and Mhlanga, 2021)). Among other species, are pathogens of the genito-urinary tract both in men and women, these may include *Escherichia coli, E. faecalis, Staphylococcus aureus, Proteus vulgaris, Pseudomonas aeruginosa, Streptococcus specie, Candida specie and etc*.These organisms are readily found in the human urogenital tract and may be responsible for serious damage to the female reproductive tract, such as postpartum uterine diseases, abortion and infertility. ((Ruggeri et al., 2016)).

Uro-genital infections can be described as an infection caused by the presence, growth and multiplication of micro-organisms anywhere within the urinary and genital tracts. Uro-genital infections are perhaps reported as a very common bacterial infection in women than men and it account for significant morbidity and high cost of treatment. Among young women of reproductive age, the incidence of genito-urinary tract infections is greater than 50% episodes in a year with about 30% of women having recurrent infections ((Perslev, Msemo, Minja, Møller, Theander, Lusingu, Bygbjerg, Nielsen, and Schmiegelow, 2019)). For most women, uro-genital infections usually begin in the lower part of the urinary system with no observable symptoms. Some of the urogenital pathogens reaches the female reproductive tract either through heamatogenus spreador may ascend the reproductive tract after sexual intimacy or parturition (Alawan et al,2020). The higher prevalence of urinary tract infections in women is in connection with the differences in the body anatomy of the male and female urinary tracts. The male urethra is between 3-4cm in length while the female urethra is shorter, measuring up to 2cm in length (Perslev et al., 2019)). Urinary tract infection is one of the most prevalent and very familiar bacterial infections posing serious health problems in both sexes, but the impact of complications and sequelae are most severe in women and neonates.(Perslev et al,2019). In 2007, United States of America alone estimated 10.5million hospital visit for urinary tract infection symptoms consisting 0.9% of all visits (Ali et al,2019). A publication by the Unplanned Admission Consensus Committee (2016) reported that between 2013 and 2014, the NHS has expended over $400 millions on the treatment of thousands of emergency cases by urinary tract infections. Most of the urinary tract infections are presented asymptomatically that is without symptoms initially and if undiagnosed and untreated; it can increase the risk of severe reproductive dysfunctions that may include chronic pelvic pain, pelvic inflammatory diseases, ectopic pregnancy, abortions and tubal factor infertility among others. (Onoh et al;2019). When these pathogens reach the uterus, the host resistance to damages is dependent on the balance between the host defense systems and virulence potential of the pathogen which may include intrinsic ability to produce resistance mechanisms to treatment either by mutation or acquired through the production of hydrolytic enzymes.(Arzanlou et al; 2017).

Microscopy, Culture and Sensitivity of mid stream urine and high vaginal and endocervical swabs is the key laboratory test for definitive diagnosis of urinary tract infections. (Peter, ojo kehinde, 2021). This is a very reliable diagnostic measure that can confirm the causal pathogen and also guide and indicate the correct antibiotic treatment. However, the WHO Quality Standard (WHO, 2016) explains that culture may not be required in all cases though, but the culture of urine and high vaginal swab is required to determine effective antibiotic therapy against the target strain of bacteria implicated in the UTI especially for women who suffers recurrent infections otherwise resistance to empiric treatment may be unavoidable. Hence, prompt and accurate diagnosis of UTIs is very crucial to reducing the course of illness as well as to prevent the progression of the infection towards the upper urinary and genital tract. (Peter, ojo kehinde; 2021). Clinical signs and symptoms of genito-urinary tract infections include:-frequent urination,painful urination(dysuria),Urgency (inability to hold urine for long),Nocturia (waking up overnight to urinate), Foul smelling urine, Subrapubic pain (low back pain), heamaturia (blood in the urine), Vagina discharge (offensive),Vagina itching and so on among others. Furthermore, signs of a more serious infection may include fever, malaise, and generalized pain (Simon-oke et al, 2019)
Antibiotics have been employed over the years to combat diverse bacterial infections but currently their efficacy has been reduced as a result of microbial resistance to treatment. According to the World Health Organization (WHO 2017), increasing antimicrobial resistance is a problem so notorious that it threatens the achievements of new generation of antibiotic in the effective treatment of bacterial infections. The use of broad spectrum antibiotics such as Co-amoxiclav, Quinolones and Cephalosporins in place of narrow-spectrum antibiotics as Trimethoprim or Nitrofurantoin should be discontinued due to the risk of developing resistant UTIs pathogen (Giwa et al, 2018). Recently, the increase of antimicrobial resistance among uro-genital pathogens has become so challenging, complicating the choice of antibiotics. Previous studies all over the world have suggested an increase in the emergence of multi drug resistant (MDR) uropathogens owing to lack of periodic updates as regards appropriate periodic data on true epidemiological survey and microbiology of UTIs from our regional hospitals (Simon-Oke et al, 2021).

Therapeutic regimen that are commonly followed by clinicians to begin initial therapy for patients to treat variety of infections are not frequently reviewed and updated and of course current epidemiology and patterns of local antibiotic resistance may not be reflected. For example, the guidelines for the treatment of UTIs in Taiwan has been published since the year 2000 by the infectious Diseases Society of Taiwan, and up till now the guidelines are yet to be updated and are still being used by hospitals across the country in Taiwan (Guidelines for antimicrobial therapy of UTI in Taiwan). This shows that the current epidemiological survey of UTIs within the community is yet to be taken into considerations.(Winkelman et al, 2016). In Nigeria, inappropriate antibiotic prescription by practitioners following empiric therapy without standard diagnostic tests, self medication by patients, incomplete treatment course and

manufacturer-based antibiotic quality are possible risk factors for the prevalence of antimicrobial resistance. Other factors that precipitates the spread of antibiotics treatment failure according to previous studies among the nations is related to distribution of resistance genes according to geographical area, rate of antibiotic consumption and prescription pattern. (Arzanlou et al, 2017).

The development of multi-drug resistant mutants has been extensively reported among pregnant women in many countries resulting into serious obstetric complications. (Ali, Muhammad et al, 2019). Moreover, reports have also showed high prevalence of UTIs among the elderly (women above the age of sixty) and who are menopausal are at risk of developing urinary tract infections owing to the fact that the female hormone 'Oestrogen' has become deficient, this in turn causes atrophic changes within the uro-genital tract. (Onoh et al; 2019). Similar studies has just been completed on the impact of genito-urinary infections on male fertility as it is reported to reduce sperm viability and cause morphological alterations.(Vitus Silage et al, 2020). However, the production of Extended- Spectrum Beta-Lactamases (ESBLs) which are known to be plasmid-borne hydrolytic enzymes capable of inactivating B-lactams rings of almost all currently prescribed beta-lactam antibiotics including Carbapenems. is the common antibiotic resistance mechanism among Gram-negative bacteria ever studied (Giwa et al; 2018). *Escherichia coli, Klebsiella pneumoniae., Citrobacter* species., *Enterobacter* species., *Acinetobacter* sp ecies and *Pseudomonas aeruginosa* are common ESBL producers among Gram-negative bacteria (GNB) causing genito-urinary infections(Tufa et al; 2020). About 75% of ESBL genes variants detected so far among ESBL- producing gram negative bacteria isolated from clinical isolates (Sonda et al; 2018) is the *blaCTX-M gene.* However, very little data is established on the incidence of ESBL producing Gram-negative bacteria in the microbiological screening of genito-urinary pathogen in the clinical management of infertility cases. Meanwhile, the work of Melania et al; (2016) gave a clue to the pathophysiology of urinary pathogens as it was reported that the colonization of the uro-genital tract by some pathogenic bacteria such as ***E.coli*** has been associated with the release of pro-inflammatory cytokines, and a direct relationship between elevated (interleukins) IL-beta and IL-8 and unknown causes of female infertility was demonstrated in an in-vivo experiment.(Ruggeri et al; 2016)

Therefore, this presents study reports on the magnitude of urogenital infections caused by Gram-negative bacteria, detection of *blaCTX-M;* a common encoding resistance gene among ESBL-producing gram-negative bacteria enhancing antimicrobial resistance and consequent treatment failure leading to the migration of the pathogens to the reproductive tracts to cause impairments. The high rate of ESBL producing gram negative isolates from infertile women will emphasize the need for regular and periodic surveillance on true epidemiology of uro-genital infections in various geographical location and advocate for access to molecular screening of isolates in the management of bacterial infection in fertility cases among human population.

The study objective is to determine the prevalence of urogenital colonization with ESBL-producing gram-negative bacteria revealing the estimates about epidemiology of ESBL in cases of infertility among women and also to detect the beta-lactamase encoding genes for the resistance. This will have implications for clinicians and researchers in the selection of antibiotic for the treatment of urogenital infections.

MATERIALS AND METHODS

Ethical Consideration: Written informed consent was obtained from all study participants. An official approval of this research was humbly sought from the Medical Research Ethics Review Board of the University College hospital, Ibadan and Oyo state hospital Management board in charge of Adeoyo Maternity hospitals, Yemetu, Ibadan before the commencement of this study. Laboratory results were made available to participants and their clinicians for effective management.

Study Design:-This is a hospital-based laboratory study, conducted in Six months between May and October 2020 involving 152 presumptive infertile women attending gynecological clinics in selected hospitals, Ibadan (whose male partners were medically considered fertile). A simple questionnaire was used to collect socio-demographic data and clinical characteristics of the consented participants.

Study Population: the study population consisted of 152 women presenting for fertility treatment in the selected fertility clinics were enrolled for the study. The mean age of the participants was taken as 26years. Inclusion criteria was that the women were of reproductive age (18-48) and consenting to participate in the study.

Study sites: The study was carried out at selected fertility clinics in Ibadan (University College Hospital and ADEOYO Maternity State Hospital) in Oyo State, South-western Nigeria.

Exclusion Criteria: Non –consenting women and women who have reached menopause were excluded from study and those that were menstruating as at the time of specimen collection during the study.

Sample collection: Mid-stream urine specimens and High vagina swabs were aseptically collected into a wide mouth, clean, sterile and universal bottles after voluntary consent was taken. Patients were instructed to thoroughly observe hand and vulva hygiene using clean water and non-antiseptic soap before the urine is collected. High Vagina Swabs were taken using a sterile swab sticks by rotating them along the walls of the vagina and in the cervix for about 10 seconds.

Laboratory Protocol.: Urine cultures were seeded on Mac-Conkey and Blood agar plates while high vagina swabs were cultured on chocolate agar, incubated at 37^0C for 24hours. Significant colonies were isolated using an inoculating loop and subsequently subculture as pure isolate on agar slants for further identification. Further identification and characterization of isolates were Gram`s staining,

Microscopic examination, motility test, biochemical testes and sensitivity tests towards various antimicrobials using disc diffusion method of Bauer-kirby.

Identification of ESBL phenotypes: ESBL phenotypes were confirmed by using a double disc diffusion method according to the Clinical and Laboratory Standard Institute (2018). Discrete colonies from the plates were picked and transferred into 1mL of normal saline to turbidity adjusted to 0.5 McFarland standard. A lawn culture of inoculums was spread out on a Mueller-Hilton agar plate. Consequently**,** ceftazidime-clavulanate and ceftazidime plain discs were plated out on Muller Hilton Agar plate with the bacterial isolates. Plates were incubated at 370C for 24 hours. Zones of inhibitions of ≥ 5mm between ceftazidime-clavulanic acid and ceftazidime plain was interpreted as ESBL producer (Mansouri et al, 2019)

Molecular characterization of blaCTX-M gene from ESBL producing gram negative bacteria: Boiling treatment method was used to extract bacterial DNA with slight modification. A suspension of freshly grown bacteria from 2 colonies was made into DNase/RNase free tubes containing 500 µL of sterile de-ionized water, vortexed and boiled at 100C for 10minutes was achieved. Tubes were subjected to centrifugation at 12000rpm for 10 minutes to obtain 5 µL of supernatant of each test bacterium for PCR.

PCR was carried out to detect ESBL phenotype production by Gram negative isolates so as to determine the variants of blaCTX-M gene as reported by (Sonda et al., 2018). CTX-M3G; forward primer: 5'-GTTACAATGTGTGAGAAGCAG-3' and 5'-CCGTTTCCGCTATTACAAAC-3' reverse primers were incorporated. Briefly, PCR amplification was performed on a Thermocycler machine as explained by (Monstein et al.,2017) PCR were initially conditioned to denature at 94^0C for 5 minutes and cycles: 1; denaturation at 94^0C for 60seconds, 2; annealing at 55^0C for 30 seconds and 3; extension at 72^0C for 60 seconds and final extension at 72^0C for 5 minutes. End-PCR products were then visualized under Ultra Violet illumination on gel electrophoresis by using 2% agarose gel stained with redsafe. Adding7.5 µL of redafe into 150 ml of TBE suspended with 3g of agarose powder).Bla-CTX-M gene with band size of1000bp was annotated as an Amplicon, (Figure 1). *E.coli* ATCC 25922 was employed as negative control organisms using 2% agarose gel stained with redafe.

Statistical analysis; The frequency of isolation of the various gram negative isolate for the primary and secondary infertility cases among the participants was done using simple percentile. All observed differences between the two groups was tested for statistical significance with chi square test

RESULTS

The demographic and clinical profile in table 1 showed that a total of 152 reproductive age women with mean age of 26years(18-46) and 33years (18-48) were enrolled in the study. As shown, a higher proportion of women were of secondary infertility as compared with the primary infertility cases. Higher percentage of both cases admitted previous history of urinary tract infection as itching and vagina discharge at the time of the study.

Table 1
Demographic characteristics and clinical profile of enrolled participants

Characteristics	Primary infertility n=61	Secondary infertility n=79(56.4%)
Age (mean)	26(18-45)	33 (18-48)
Occupation		
Housewife	17	30
Public servant	08	19
Student	05	10
Self employed	31	20
History of Previous UTIs		
Itching	23	26
Vaginal Discharge	23	19
Low pelvic pain	06	11
Painful urination	05	13
No symptom	02	10

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Table 2
Prevalence of bacterial species isolated in relation to type of fertility and specimen

Isolates	Pry infertility		Secondary Infertility	
	Urine	HVS	Urine	HVS
Klebsiella Spp.	15	10	16	20
Escherichia coli	13	08	15	17
Pseudomonas spp.	08	10	14	10
Acinectobacter spp.	11	06	10	08
Proteu mirabilis.	08	06	09	06
Total	55	40	64	61

Multiple microbial populations of Gram-negative bacteria were cultured from urine and high vaginal swabs of both cases. A total of 55 and 64 of bacterial isolates were isolated from urine samples of primary and secondary infertility cases respectively, while a total of 40 and 61 were isolated from the HVS of both cases of primary and secondary infertility respectively. Apparently, a little difference was observed in the rate of isolation of organisms between the primary and secondary infertility cases. As reflected in table 2, no significant difference was obtained in the prevalent species of organisms isolated. The prevalent bacterial isolates in the two cases were *Klebsiella pneumoniae, E.coli and Pseudomonas aeruginosa* with 54.1% of women having primary infertility and 45.9% of women with secondary infertility harbouring the pathogens in their urine and high vagina canal.

As shown in Table 3, a total of Two hundred and Seven isolates were obtained from the clinical samples collected of which One hundred and Nine was obtained from Urine and Ninety Eight were isolated from HVS. The total no of ESBL positive isolates was Eighty Eight with Fifty Two (47.7%) from Urine and Thirty six (36.7%) from HVS. The result here

indicates that, about 50% of all the gram negative isolates from urine and high vaginal swabs of infertile women were ESBL-producers and hence, it can be considered as significant.

Characterization of ESBL positive bacteria using API 20E identification kit: ESBL-producing bacteria obtained from urine and HVS were identified to be 88 in number as revealed by using API 20E identification kit, this showed that 45% of the total ESBL-producing bacteria prevalent in the two cases were identified as *Klebsiella pneumonie and E.coli*. Hence, the remaining 4 isolates were identified as*Pseudomonas aeruginosa, Acinetobacter baummani and Enterobacter cloacae as seen in Table 2 above. This* shows that the prevalent gram negative isolates in the urogenital tract of women with cases of infertility were identified with ESBL-production that may likely enhance their resistance to antibiotic treatment. However, the pattern of antibiotic resistance among the bacterial isolates is shown in Table 4.

Figure 1 shows that all the five ESBL-producing bacteria were resistant to AMC, except Escherichia coli that was significantly resistant to cefpodoxime with 100%. The percentage resistance to SXT, CTX, and CIP were 68%,40% and 53% respectively. All the isolates were found to be sensitive to Ertapenem with 62.9 % except *Escherichia coli* that showed 50% resistance.

Table 5 shows that ESBL-producing isolates were isolated from the two cases of infertility. More than half(52.3%) of all isolates screened for molecular characteristics harbored *bla-CTX-M* encoding gene for AMR.

Table 3.
Distribution of ESBL- Positive among total isolates for each the samples

Sample Source	No of isolates	No of ESBL positive	No of ESBL negative	P% of ESBL positive
Urine	109	52	57	47.7
HVS	98	36	62	36.7
Total	207	88	119	42.5

Table 4.
Percentage of resistance of isolate to various antibiotics.

Bacterial isolates	**AMC**	**CPD**	**CTX**	**CRO**	**CIP**	**SXT**	**GEN**	**ETP**
Klebsiella pneumonia	73.6	37.2	46.9	38.5	56.8	69.1	78.3	11.7
Escherichia coli	85.5	100	93.1	40.2	45.7	65.7	32.8	48.6
Proteus mirabilis	53.7	25.6	23.3	41.4	42.6	14.7	I6.9	12.1
Pseudomonas aeruginosa	76.7	52.7	48.7	14.6	56.3	68.4	65.8	13.8
Acinetobacter baummannii	75.4	26.3	37.9	52.2	65.2	65.4	43.6	10.5
Total %	72.9	48.4	50.0	.2	53.3	56.7	46.5	20.2

KEYS:- *AMC-amoxicillin-clavulanate, CPD- cefpodoxime, CTX –cefotaxime, CRO- cefriaxone, CIP- ciprofloxacin, SXT-trimethoprim-sulfamethoxazole, GEN- gentamicin, ETP- ertapenem.*

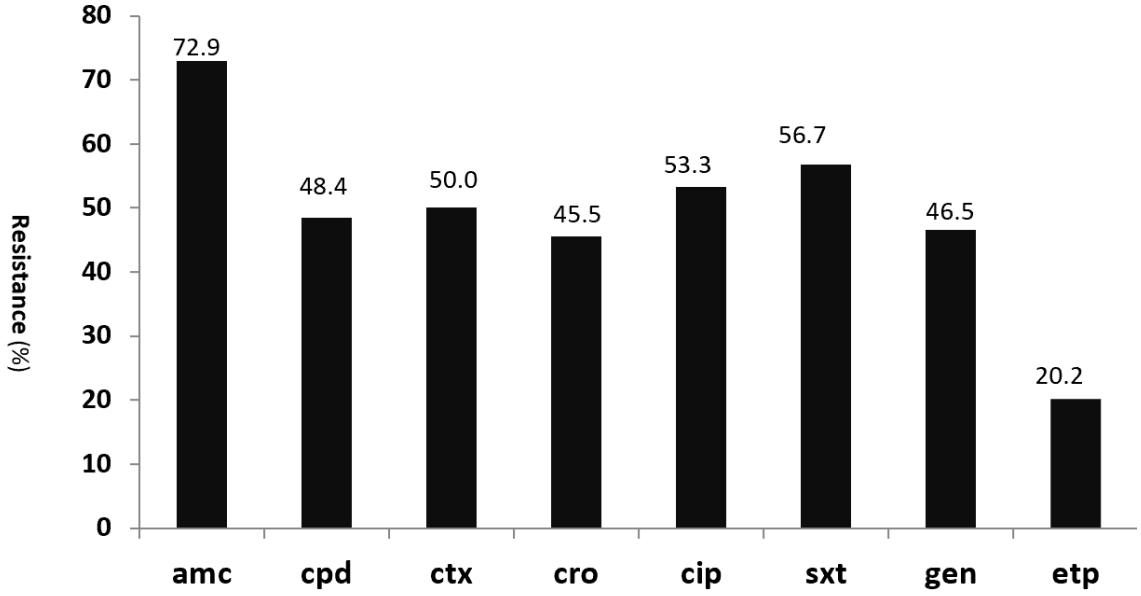

Figure 1
Resistance of ESBL-producing isolates from Urine and HVS from infertile women
KEYS:- ***AMC-amoxicillin-clavulanate, CPD-cefpodoxime, CTX–cefotaxime, CRO-cefriaxone, CIP- ciprofloxacin, SXT- trimethoprim-sulfamethoxazole, GEN- gentamicin, ETP- ertapenem***

Table 5.
ESBL-genotypes of ESBL- producing isolates from urine and high vaginal swab of participants.(n=88)

Bacterial agents	Pattern of ESBL genotype	Type of infertility	No of isolates	Percentage
E. coli	bla-CTX-M	1 and 2	15	17.1
Klebsiella pneumoniae	bla-CTX-M	1 and 2	12	13.6
Acinetobacter baummannii	Bla- CTX-M	2 only	10	11.4
Pseudomonas aeruginosa	Bla-CTX-M	1 and 2	9	10.2
Proteus mirabilis	Nil	1 and 2	29	32.9
Other isolates	Nil	1 and 2	25	28.4

DISCUSSION

The study was designed to investigate the colonization and prevalence of ESBL-producing gram negative bacteria in the urogenital tract of infertile women and so we hypothesized a relationship between higher rate of colonization with ESBL-producing pathogens and resistance to commonly prescribed antibiotics. However, there was a significant rate of urogenital colonization with ESBL- producing gram negative pathogens. *Klebsiella pneumonia, E.coli and Pseudomonas aeruginosa* were the prevalent pathogens isolated from urine and high vagina swab of the infertile women; there was a moderately significant difference between the cases of primary and secondary infertility in the rates of isolation of these pathogens.

In Nigeria, there has been a paucity of information on the role of urogenital infections in cases of women infertility. However, extensive literatures has been reported on rather, the impact on fertility by the colonization of women reproductive tract with major sexually transmitted infections by *Neisseria gonorrhea, Treponema palladium, Ureaplasma urealyticum and Chlamydia trachomatis among others* as causal pathogens of pelvic inflammatory diseases(PID) resulting into chronic pelvic pain, abortions and infertility.(Ruggeri et al,2016). The rate of isolation of bacteria pathogen in this study is higher for secondary infertility cases as conformed with the work of (Vitus Silago et al, 2020) on bacteriospermia. However, available reports revealed that most cases of secondary infertility in Africa are traceable to previous infections and in this study 50%-80% of women with secondary infertility in agreement with their findings, had at least an episode of urinary tract infection as evidenced by symptoms. Furthermore, our findings of high rate of urogenital colonization by gram negative pathogens in this study is suggestive of a continuing prevalence of untreated or antimicrobial treatment failure of urinary tract infections. This explains the intrinsic ability of gram negative bacteria to inactivate the potency of B-lactam antibiotics by the production of hydrolytic enzymes in the variant of Extended spectrum beta-lactamases (bla-CTX-M) genes that was detected in more than 50% of the isolates. This also agrees with the work of (Banjo et al, 2020). Consequently, many of the infections of the reproductive tract may have been as a result of upward progression of the pathogen either through sexual intercourse or abortions, among other factors.

The present study also revealed that the higher percentage of isolated organisms in both cases were resistant to common antibiotics except for few (20.2%) that were resistant to Ertapenem (carbapenems); a new generation of antibiotics closely formulated in relation to recent antimicrobial resistance challenges. The challenge here is that, due to restricted supply chain and limited financial resources challenges, common to most of the human population caught in the web of infertility usually among low and medium income earners as revealed by the demographic ratings in this study, carbepenems are often unavailalble or are too expensive to afford. On the other hand, the emergence of new strains that may be resistant to carbapenems is inevitable over time, therefore it is pertinent to have a periodic surveillance to establish a reliable database on the identification and resistance patterns of clinical isolates to available antibiotics therapy where appropriate.

In conclusion, the detection of ESBL- producing bacteria among the Uro-genital isolates from infertile women is an indication towards the emergence of multidrug resistant strains taking advantage to migrate upward to infect the reproductive structures. With reference to this impact, primary healthcare providers especially on fertility cases, can use these data as a reliable template in the medical intervention towards the management of infertility among women. There is need to incorporate molecular typing revealing the genotypic characteristics of AMR surveillance in our hospitals so as to better understand the spread of AMR and effective antibiotic use. However, more studies are essential towards the validation of the claims of the study.

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