Bacteriology and Antibiogram of Urinary Tract Infection Among Female Patients in a Tertiary Health Facility in South Eastern Nigeria

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Received: August 04, 2017 Revised: October 05, 2017 Accepted: October 11, 2017

Abstract:

Background:

Urinary Tract Infection (UTI) is a common contagion among men and women with the incidence relatively higher among women due to their differing anatomy. An understanding of the kind of pathogens implicated in urinary tract infections as well as antibiotic susceptibility profiling may help the clinician make rationally correct empirical choice in their treatment.

Objective:

This study is aimed at determining the type and antibiotic susceptibility pattern of bacterial uropathogens isolated from female patients attending Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH), Awka, Nigeria.

Method:

Two hundred and forty patients with clinically diagnosed UTI and who were on at least 5 days’ antibiotic holiday were recruited into the study. Their demographic characteristics were captured using pre-tested questionnaire. Their clean catch mid-stream urine samples were collected using sterile universal container and sent to the Microbiology Department for processing. Within 30 minutes of samples collection, the specimens were cultured and the isolates were identified, after 24 h of incubation, using standard microbiological techniques. Antibiotic susceptibility tests were done with standard antibiotic discs using the Kirby–bauer disc diffusion method.

Results:

Out of the 240 urine samples, 89.17% yielded significant bacteriuria. The pathogens implicated were Escherichia coli (28.5%),

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Staphylococcus aureus (28.0%), Salmonella spp (22.8%) and Pseudomonas aeruginosa (20.5%). HIV status, patients age, pregnancy status and marital status all significantly affected bacteriuria rate (p value < 0.05), while patients’ location (sub-urban/rural dwelling), and level of education did not (p value > 0.05). The pattern of microbial resistance to antibiotics suggests that ceftazidime, fosfomycin and cefoxitin may not be used as first-line agents in the empirical treatment of UTIs rather; levofloxacin, meropenem or aztreonam should be considered. Levofloxacin was significantly effective against all the isolates and may be administered empirically while waiting for the culture result (Mean % susceptibility was 79.85).

**Conclusion:**

E. coli and S. aureus were the predominant pathogens in the study and many were resistant to the commonly prescribed antibiotics and so leave the clinicians with only few alternative drugs for UTIs treatment. Routine surveillance and monitoring studies need to be constantly conducted to update clinicians on the prevalent pathogens and the rational and empirical treatment of UTIs. Aggressive and consistent health education using every possible media is also recommended to combat the menace of drug resistance occasioned by inappropriate antibiotic use.

**Keywords:** Bacteriology, Antibiogram, Urinary tract infection, Bacteriuria, Uropathogens.

**1. INTRODUCTION**

Urinary Tract Infections (UTIs) have been proven to be the most encountered bacterial infection in humans [1, 2], affecting all age groups and gender in both the community and hospital settings [3, 4]. About 50% of all females will experience at least an episode of UTI during their lifetime [5]. Asymptomatic bacteriuria and urinary tract infection (UTI) are common among adult men and women; although the incidence is higher among women due to their anatomy [6, 7]. They also have a higher prevalence among women during pregnancy and in very sexually active females [8]. Asymptomatic bacteriuria denotes significant bacteriuria (> 10^5 CFU/mL of urine) without clinical symptoms of urinary tract infections (such as frequent urination, painful urination or fever) or other abnormal findings. The bacteriuria should not be due to contamination from urine sample collection.

UTI is an infection that affects any part of the urinary tract from the bladder to the kidney. It is not classified as a sexually transmitted infection [9] although sexual activity is known to be a risk factor [10]. Symptoms include frequent and/or painful urination, a feeling to urinate despite having an empty bladder, fever and flank pain. At times, the urine may contain pus and/or appear bloody. UTI is a risk factor for pyelonephritis, preterm delivery and miscarriages among pregnant women, and is associated with impaired renal function and end-stage renal disease among pediatric patients [11].

Antibiotic resistance in the treatment of UTI and other bacterial infections constitute a major public health problem especially in the developing countries. Irrational and indiscriminate use of antibiotics as well as fake and substandard drugs, including antibiotics is common in these countries [12, 13]. In view of these and attendant tendency for changes in bacteriological profile, it is worthwhile that the degree of susceptibility and resistance of these uropathogens to various antibiotics be known to clinicians for effective treatment of infections they cause and to avoid antibiotic misuse. This study is aimed at determining the type and level of drug susceptibility of bacterial uropathogens isolated from female patients with symptomatic UTI and attending a tertiary health care institution in south-east Nigeria. This will help reduce irrational use of antibiotics and development of resistance.

**2. MATERIALS AND METHODS**

**2.1. Study Area and Study Population**

This study was carried out at Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH), Awka, Nigeria; an Anambra State owned 150 bedded Hospital serving over 2 million populations. The study population comprised symptomatic female patient aged 12-56 years who presented at the pediatric, obstetrics and gynecology and antenatal out-patient clinics of the hospital between May 1” and July 31” 2016. Participants were recruited consecutively after their verbal informed consents were obtained or that of their legal care-givers.

All the media used in the study were products of HiMedia Laboratories Pvt. Ltd, Mumbai, India while the antibiotic discs were from Oxoid, England.

**2.2. Sample Size and Sample Technique**

The minimum sampling size was determined using the statistical formula:
N = \frac{(Z^2pq)}{D^2}

\text{where} \\
q = (1-p) \\
N = \text{Sample Size} \\
p = \text{Prevalence Rate in \%} \\
Z = \text{Confidence interval of 95\% which is equivalent to Confidence of 1.96} \\
D = \text{Desired level of Size Significance (5\%)}

The prevalence of UTI in a similar hospital in South-east Nigeria was reported as 2.0\% [14].

So, N = 30.12. Four study groups (Pregnant HIV positive, Pregnant HIV negative, Non-pregnant HIV positive and Non-pregnant HIV negative) were used with each group having a population of 60 subjects. A total sample size of 240 was chosen.

2.3. Study Design and Sample Collection

This is a cross-sectional hospital based study. Patients with clinical manifestations of UTI who gave consent were included in the study, while those with clinical manifestations but are on antibiotics within the past five days were excluded.

Clean catch mid-stream urine was collected, from each consenting patient in a 20 mL calibrated sterile screw-capped universal containers which were distributed to the patients. Each specimen was appropriately labeled, transported to the Microbiology Laboratory of the Department of Pharmaceutical Microbiology and Biotechnology, Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University, Agulu, Nigeria and analyzed within 30 minutes of collection. Prior to sample collection, all patients or their legal care-givers were well instructed by the recruiting pediatrician and gynaecologist on how to collect clean catch mid-stream urine. Urine samples were collected from a total of 240 pregnant and non-pregnant females.

2.4. Sample Processing and Culture

On arrival at the laboratory, MacConkey agar, Mannitol salt agar, Cetrimide agar and Salmonella-Shigella agar were prepared according to their manufacturers’ specifications and sterilized in the autoclave by heating at 121°\text{C} for 15 minutes. The sterilized media were poured aseptically into previously labeled sterile petri-dishes and allowed to solidify. Each urine sample was aseptically inoculated (in triplicate) onto the MacConkey agar plates, Mannitol salt agar plates, Salmonella-Shigella agar and Cetrimide agar plates. The inoculated agar plates were incubated at 37°\text{C} for 24 h.

2.5. Identification of Isolates and Antibiogram Study

Identification of bacterial isolates was done on the basis of their cultural, Gram and biochemical characteristics while the antibiotic susceptibility of pure cultures of confirmed isolates was performed on Mueller-Hinton Agar using the standard Kirby-Bauer disc diffusion method. Briefly, standardized overnight culture of each isolate was prepared by inoculating 3-5 pure colonies of each isolate into 3 ml sterile nutrient broths in test tubes and adjusting to match 0.5 McFarland turbidity standards. The microbial suspensions were streaked on to the Mueller-Hinton Agar plates using a sterile wire loop and allowed to dry and diffuse for about 5 minutes. The antibiotic discs (Ceftazidime 30µg, Cefuroxime 30µg, Meropenem 10µg, Fosfomycin 50µg, Cefoxitin 30µg, Azithromycin 15µg, Levofloxacin 5µg, Ceftriaxone/Sulbactam (30/15µg), Aztreonam 30µg, Ceftriaxone 30µg.) were aseptically picked and placed on to the surface of the microorganisms seeded agar plates. The plates were incubated for 24 h at 37 °\text{C}. The inhibition zones created by each antibiotic against each isolate were measured and recorded in millimeter (IZD in mm) as Inhibition Zone Diameter. Susceptibility/resistance was interpreted according to Clinical and Laboratory Standard Institute (CLSI) guidelines [15].

2.6. Data Analysis and Interpretation

The data were analysed using GraphPad Prism version 5.00 for Windows, GraphPad Software, Inc. San Diego California USA, www.graphpad.com. One-Way Analysis of Variance (ANOVA) was used to establish the mean differences in prevalence of the isolates among various age groups while the Chi Square checked for the relative risks of UTI in relation to pregnancy status, HIV status, marital status, educational levels and urban/rural dwellers. Two-Way Analysis of Variance (ANOVA) was used to establish the mean differences in susceptibility of the isolates to the
commercial antibiotics. Bonferroni post-tests were used to compare the effects of the individual drugs on the isolates. All P values reported are for a two-tailed test. The significance level was chosen at p<0.05.

2.7. Ethical Approval and Compliance with Ethical Standards

Ethical approval for the study was obtained from the ethical committee of COOUTH, Awka with reference number COOUTH/AA/VOL.1.006. All necessary international, national, and/or institutional ethical guideline were followed and the study protocols obeyed the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The participants or their legal care-givers gave a verbal consent to participate in the study after the reasons for the study were explained to them. No information on the participants’ names was collected. The urine sample containers and questionnaires for data collection were identified with study identification numbers.

3. RESULTS

Table 1 shows that at the time of the study, most of the UTI patients (47.92%) encountered were from rural communities. However, correlation analysis did not show that rural dwelling significantly correlate (p > 0.05) with the incidence of bacterial UTI. Age, marital status and educational levels also did not correlate (p > 0.05). There were significant differences in the incidence of bacterial UTI among the age groups and in the marital status of the study participants (p < 0.05).

Table 1. Characteristics of study participants (N = 240).

| Variable                     | Number of Subjects Tested | Number (%) with Significant Bacteriuria | Chi-Square (X²) p Value | Correlation (% Bacteriuria) P Value |
|------------------------------|---------------------------|----------------------------------------|-------------------------|-----------------------------------|
| Location (Residence)         |                           |                                        |                         |                                   |
| Urban                        | 40                        | 32 (80.00)                             | p value = 0.0691        | 0.0962                            |
| Sub-Urban                    | 85                        | 75 (88.24)                             |                         |                                   |
| Rural                        | 115                       | 107 (93.04)                            |                         |                                   |
| Age Group (Years)*           |                           |                                        |                         |                                   |
| 12 – 16                      | 19                        | 16 (84.21)                             |                         | 0.1674                            |
| 17 – 21                      | 20                        | 17 (85.00)                             |                         |                                   |
| 22 – 26                      | 54                        | 47 (87.04)                             |                         |                                   |
| 27 -31                       | 50                        | 49 (98.00)                             |                         |                                   |
| 32 - 36                      | 65                        | 60 (92.31)                             |                         |                                   |
| 37 – 41                      | 20                        | 17 (85.00)                             |                         |                                   |
| 42 - 46                      | 4                         | 2 (50.00)                              |                         |                                   |
| 47 - 51                      | 3                         | 2 (66.67)                              |                         |                                   |
| 52 – 56                      | 5                         | 4 (80.00)                              |                         |                                   |
| Highest Education Completed  |                           |                                        |                         |                                   |
| No formal education          | 31                        | 29 (93.55)                             | p value = 0.0816        | 0.0517                            |
| First School leaving         | 52                        | 48 (92.31)                             |                         |                                   |
| Senior Secondary Certificate (or equivalent) | 84 | 77 (91.67) | ANOVA p value < 0.0001 |   |
| Tertiary Education           | 51                        | 44 (86.27)                             |                         |                                   |
| Higher degree                | 22                        | 16 (72.73)                             |                         |                                   |
| Marital Status*              |                           |                                        |                         |                                   |
| Single                       | 125                       | 118 (94.40)                            | p value < 0.0001        | 0.9192                            |
| Widowed                      | 15                        | 9 (60.00)                              |                         |                                   |
| Divorced                     | 12                        | 7 (58.33)                              |                         |                                   |
| Still Married                | 88                        | 80 (90.91)                             |                         |                                   |

Also, it can be observed that the incidence of UTI increased from urban to rural dwelling and also increased with increasing age of the participants until it picked at age 27-31. It was observed that the incidence of UTI decreased with increase in the level of formal education acquired, although this was not significant (p > 0.05). Marital Status significantly affected outcome (bacteriuria) – may be due to sexual habits.

We evaluated a total of 240 patients with symptoms and sign of UTI. Out of this, 214 (89.17%) yielded significant bacteriuria (Table 2). *E. coli* (28.5%) and *Staphylococcus aureus* (28.0%) were the most common isolates in the cases
of UTI in the study. However, there was no significant difference (p > 0.05) in the rate of occurrence of all the isolates (E. coli, S. aureus, Salmonella spp and P. aeruginosa).

Table 2. Frequency of occurrence of the Isolates.

| Organism           | Number of Isolates | Incidence Rate (%) | HIV Status* | Patients Age (yrs.)* | Pregnancy Status* |
|--------------------|--------------------|--------------------|-------------|---------------------|-------------------|
|                    |                    |                    | Positive (n = 120) | Negative (n = 120) |                   |
| E. coli            | 61                 | 28.5               | 46           | 15                  | 3 4 15 16 14 5 0 1 3 45 16 |
| S. aureus          | 60                 | 28.0               | 31           | 29                  | 6 4 14 15 16 5 0 0 0 33 27 |
| Salmonella spp     | 49                 | 22.8               | 36           | 13                  | 3 5 9 11 15 4 1 1 0 38 11 |
| P. aeruginosa      | 44                 | 20.5               | 32           | 12                  | 4 4 9 7 15 3 1 0 1 34 10 |
| TOTAL              | 214                | 100                | 145          | 69                  | 16 17 47 49 60 17 2 2 4 136 78 |

From the antibiogram study, (Table 3) it can be observed that the carbapenems, monobactam, macrolide and fluoroquinolones (Meropenem, Aztreonam, Azithromycin and Levofloxacin respectively) performed better than the rest of the antibiotics tested with the fluoroquinolone proving to be the most ideal drug in the management of bacteria UTI in the study centre. It was observed that the Escherichia coli isolates responded worst to the commercial antibiotics tested (mean % susceptibility = 22.05%). A Two-Way ANOVA of the susceptibility of the isolates to the drugs shows that the kind of antibiotic used extremely affected the microbial susceptibility and accounted for 79.87% of the total variance with a p value of < 0.0001. It is therefore inferred that the antibiotic type significantly affected the microbial susceptibility. Also, the kind of bacterial isolate accounted for only 6.00% of the total variance with a p value = 0.0211. This also showed that the isolate type significantly affected the effects of the drugs.

Table 3. Drug Susceptibility profile of Isolates.

| Bacterial Isolate | % Susceptibility | Mean% Susceptibility | ANOVA |
|-------------------|------------------|----------------------|-------|
|                   | CAZ | FOX | FOS | CXM | CEF | C/S | MEM | ATM | HVX | LVD |         |         |       |
| Salmonella spp    | 0.0 | 0.0 | 3.3 | 5.0 | 23.0 | 39.3 | 74  | 78.7 | 49.2 | 86.9 | 35.94   |         |       |
| P. aeruginosa     | 0.0 | 0.0 | 6.1 | 14.3| 18.4 | 37.0 | 86  | 71.4 | 61.2 | 81.6 | 37.60   |         |       |
| Escherichia coli  | 0.0 | 13.3| 3.6 | 3.3 | 8.3  | 17.0 | 37  | 75.0 | 5.0  | 60.0 | 22.05   |         |       |
| Staphylococcus aureus | 0.0 | 0.0 | 0.0 | 14.0| 23.0 | 43.2 | 59.1| 59.1 | 73.0 | 90.9 | 36.23   |         |       |
| Mean % Susceptibility | 0.00 | 2.75 | 9.15 | 18.18 | 34.13 | 64.03 | 71.05 | 47.1 | 79.85 |         | p value = 0.0001 |       |

Key: CAZ = Ceftazidime, FOX = Cefoxitin, FOS = Fosfomycin, CXM = Cefuroxime, CEF = Ceftriaxone, C/S = Ceftriaxone/Sulbactam, MEM = Meropenem, ATM = Aztreonam, HVX = Azithromycin, LVD = Levofloxacin

Bonferroni post-tests analysis showed that there was a significant difference in the effect of Meropenem on the Salmonella spp and P. aeruginosa isolates (p <0.01) and on S. aureus isolates (p < 0.05) compared with the effects of Cefazidime. Also, effects of Aztreonam on the Salmonella spp and P. aeruginosa isolates compared with the effects of Cefazidime (p <0.01). A comparison of Azithromycin and Cefazidime showed a significant difference for the Salmonella spp and P. aeruginosa (p <0.01) and for S. aureus (p < 0.05) isolates. Same effects were observed between Meropenem and Cefoxitin. Aztreonam was significantly better than Cefoxitin on the Salmonella spp and P. aeruginosa isolates (p <0.01). Azithromycin was significantly better than Cefoxitin against Salmonella spp and P. aeruginosa isolates (p < 0.05) and against S. aureus isolates (p<0.05). Same was also true of Azithromycin compared to Fosfomycin. Meropenem was significantly better than Fosfomycin against Salmonella spp and P. aeruginosa isolates (p < 0.01) and against S. aureus isolates (p <0.05). Aztreonam was significantly better than Fosfomycin against Salmonella spp and P. aeruginosa isolates (p < 0.01). Same was also true of Meropenem and Azithromycin compared to Cefuroxime. Meropenem and Aztreonam were significantly better than Ceftriaxone against P. aeruginosa isolates (p < 0.05). Only Levofloxacin showed a significantly better effect on all the isolates (Salmonella spp, P. aeruginosa, Escherichia coli and S. aureus) p < 0.05 compared to most drugs used. Escherichia coli (especially) and S. aureus isolates showed significantly higher resistance to several of the commercial antibiotics (p >0.05).

4. DISCUSSION

The study centre is a state owned tertiary hospital located in Awka, the state capital and is engaged in research and training of medical and nursing students and specialist doctors. The state capital, Awka, is surrounded by several rural
The incidence of resistant *Escherichia coli* in the study center has been reported by other researchers [31, 32] who demonstrated the presence of ESBL producing *Escherichia coli*.

5. STRENGTHS AND LIMITATIONS OF THE STUDY

Hitherto, clinicians had relied on the information on drug detailing as given by drug companies’ sales representatives for the treatment of UTI in the study centre and not on empirical evidence of susceptibility of the isolates. Also, epidemiological data on the microbial isolates in cases of UTI has been lacking. This study, therefore, provides a first-hand information or documentation on both scientific evidence of microbial susceptibility of the isolates as well as the microbial etiology of UTI in the study centre. This study is of international importance knowing that the world is a global village where people can migrate from one country to another with the attendant possibility of
spreading resistant strains of microbes. A knowledge of the susceptibility profile as offered by this study will help clinicians offer objective treatment of UTI and so reduce intercontinental spread of resistant microbial strain.

However, the study did not provide the molecular bases of resistance to the commercial antibiotics. It also did not establish the presence of extended beta-lactamase producing isolates as a possible cause of resistance to the antibiotics.

CONCLUSION

In this study, *E. coli* and *S. aureus* were the predominant pathogens. The bacterial isolates were resistant to the commonly prescribed drugs and so left the clinicians with only few alternative drugs for UTIs treatment. The pattern of microbial resistance to antibiotics suggests that Ceftazidime, Fosfomycin and Cefoxitin may not be the appropriate first-line agents in the empirical treatment of UTIs, instead; Levofoxacin, Meropenem or Aztreonam may be considered. More studies on this topic will substantiate this finding. Routine surveillance and monitoring studies need to be constantly conducted to update clinicians on the prevalent pathogens and the rational and empirical treatment of UTIs. Aggressive and consistent health education using all possible social media is also recommended to combat the menace of drug resistance occasioned by inappropriate antibiotic use.

AUTHORS’ CONTRIBUTIONS

CEE conceptualized the study and participated in drafting of the manuscript, ANO did statistical analysis and assisted in designing the study as well as drafting of the manuscript, VBA implemented the study (acquisition of data) and interpreted the data, GUE participated in drafting of the manuscript. IUE, OSE and KNO assisted in designing the study, did clinical diagnosis and patient selection/recruitment, CBO revised the draft critically for intellectual content. GOE and IME revised the draft critically for intellectual content and gave final approval of the version to be submitted.

FUNDING

This study was not covered by any grant but was self-financed.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval for the study was obtained from the ethical committee of COOUTH, Awka with reference number COOUTH/AA/VOL.1.006. The participants or their legal care-givers gave a verbal consent to participate in the study after the reasons for the study were explained to them. No information on the participants’ names was collected. The urine sample containers and questionnaires for data collection were identified with study identification numbers.

HUMAN AND ANIMAL RIGHTS

All necessary international, national, and/or institutional ethical guideline were followed and the study protocols obeyed the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

Angus Nnamdi OLI, Vivian Beka AKABUEZE, Obiora Shedrack EJIOFOR, Charlotte Blanche OGUEJIOFOR, Chijioke Elias EZEUUDU, Ifeoma Mercy EKEJINDU, George Ogonna EMECHEBE, Kenneth Nchekwube OKEKE and Ifeanyichukwu Uzoma EZEJIALU are natives of the State where the study center is located. Obiora Shedrack EJIOFOR, Ifeanyichukwu Uzoma EZEJIALU, George Ogonna EMECHEBE, Kenneth Nchekwube OKEKE are also employees in the study centre. George Uchenna ELEJE declares no conflict of interest.

ACKNOWLEDGEMENTS

The authors wish to thank the study participants and the management of COOUTH, Awka for moral support and permission to conduct the study.

REFERENCES

[1] Demilie T, Beyene G, Melaku S, Tsegaye W. Urinary bacterial profile and antibiotic susceptibility pattern among pregnant women in north west ethiopia. Ethiop J Health Sci 2012; 22(2): 121-8.
Bacteriology and Antibiotic of Urinary

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[PMID: 22876076]

[2] Parveen SS, Reddy SV, Rama Rao MV, Janardhan Rao R. "Uropathogens and their drug susceptibility patterns among pregnant women in a teaching hospital. Amn Biol Res 2011; 2(5): 516-21.

[3] Ahmed E, Shahid HM, Ikhliaqae SS, Ejaz M. Urinary tract bacterial pathogens and their sensitivity pattern J Rawalpindi Med Coll (JRMC). 2014; 18: pp. (2)263-6.

[4] Omigie O, Okoror L, Umolu P, Ikhuog G. Increasing resistance to quinolones: A four-year prospective study of urinary tract infection pathogens. Int J Gen Med 2009; 2: 171-5. [PMID: 20360901]

[5] Al-Badr A, Al-Shaikh G. Recurrent urinary tract infections management in women: A review. Sultan Qaboos Univ Med J 2013; 13(3): 359-67. [http://dx.doi.org/10.12816/0003256] [PMID: 23984019]

[6] Rowe T A, Juthani-Meha M. Urinary tract infection in older adults Aging Health 2013. Available at: http://doi.org/10.2217/age.13.38 [http://dx.doi.org/10.2217/age.13.38]

[7] Vasudevan R. Emergence of UTI causing Staphylococcus aureus as a superbug: Has the pathogen reduced the options of antimicrobial agents for treatment. EC Microbiol 2015; 1: 88-112.

[8] Verstraehen H, Verhelst R, Vaneechoutte M, Temmerman M. The epidemiology of bacterial vaginosis in relation to sexual behaviour. BMC Infect Dis 2010; 10: 81. [http://dx.doi.org/10.1186/1471-2334-10-81] [PMID: 20353563]

[9] Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol 2015; 13(5): 269-84. [http://dx.doi.org/10.1038/nrmicro3432] [PMID: 25853778]

[10] Lee-Ellen C. Copstead-Kirkhorn, Jacquelyn L, Banasik Study Guide for Pathophysiology (5 ed) Elsevier Health Sciences. 2013; p. 272.

[11] Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med 2002; 113(11)(Suppl. 1A): 55-135. [http://dx.doi.org/10.1016/S0002-9343(02)01054-9] [PMID: 12113866]

[12] Abubakar E M. Antimicrobial Susceptibility pattern of pathogenic bacteria causing urinary tract infection at specialist hospital Yola Adamawa state Nigeria. J Clin Med Res 2009; 1(1): 001-8.

[13] Wilson JM, Fenoff R. The health and economic effects of counterfeit pharmaceuticals in Africa anti-counterfeiting and product protection program backgrounder series global edge business review 2011. Available at: http://royfenoff.com/Global_Edge_Business_Review_Article.pdf

[14] Anozie OB, Lawani OL, Esike CU, Mamah E, Ajah LO. Prevalence and common microbial isolates of urinary tract infection in pregnancy; A four year review in a tertiary health institution in abakaliki, south-east Nigeria. J Clin Med Res 2016; 4(2): 25-8.

[15] CLSI. Performance standards for antimicrobial disk tests; Approved Standards. 25th Edition. Clinical and Laboratory Standards Institute (CLSI) Document M2-A9. Wayne. 2016; 26.(1)

[16] O’Donnell O. Access to health care in developing countries: Breaking down demand side barriers. Cad Saude Publica 2007; 23(12): 2820-34. [http://dx.doi.org/10.1590/S0102-311X2007001200003] [PMID: 18157324]

[17] Emily H, Claudia B. Global educational expansion and socio-economic development: An assessment of findings from the social sciences. World Dev 2005; 33(3): 335-54. [http://dx.doi.org/10.1016/j.worlddev.2004.10.001]

[18] Francesco B. Identifying the role of education in socio-economic development. International Conference on Human and Economic Resources. Izmir. 2006; pp. 193-206.

[19] Avasarala KA, Ahmed SM, Nandagiri S, Tadisetty S. Epidemiological differences of lower urinary tract symptoms among female subpopulations and group level interventions. Indian J Urol 2008; 24(4): 498-503. [http://dx.doi.org/10.4103/0017-5140-44256] [PMID: 19468505]

[20] Debalke Serkadis, Cheneke Waqtola, Tassew Haimanot, Awol Mohammed. Urinary tract infection among antiretroviral therapy users and nonusers in Jimma University specialized hospital, Jimma, Ethiopia. Int J Microbiol 2014; 2014: 6. Article ID 968716 [http://dx.doi.org/10.1155/2014/968716]

[21] Johnson EK. Urinary tract infections in pregnancy: Practice essentials, pathophysiology, etiology medscape 2016. Available at: http://emedicine.medscape.com/article/452604-overview Accessed on 24th March 2017

[22] Foxman B. The epidemiology of urinary tract infection. Nat Rev Urol 2010; 7(12): 653-60. [http://dx.doi.org/10.1038/nrurol.2010.190] [PMID: 21139641]

[23] Oli AN, Okafor CI, Ibezim EC, Akuijobi CN, Osunwuzo MC. The prevalence and bacteriology of asymptomatic bacteriuria among antenatal patients in Nnamdi Azikiwe University Teaching Hospital Nnewi; South Eastern Nigeria. Niger J Clin Pract 2010; 13(4): 409-12. [PMID: 21220855]

[24] Sheela DA, Rajkumar J. Investigation of bacterial pathogens responsible for urinary tract infection in human subjects. J Med Sci 2012; 12: 234-8.
Subramaniam J, Eswara S, Yesudhason B. Association of urinary tract infection in married women presenting with urinary incontinence in a hospital based population. J Clin Diagn Res 2016; 10(3): DC10-3. [http://dx.doi.org/10.7860/JCDR/2016/16547.7390] [PMID: 27134871]

Al-Mathkhury HJ, Abdul-Ghaffar SN. Urinary tract infections caused by *staphylococcus aureus* DNA in comparison to the candida albicans DNA. N Am J Med Sci 2011; 3(12): 565-9. [http://dx.doi.org/10.4297/najms.2011.3562] [PMID: 22363080]

Levison ME, Kaye D. Treatment of complicated urinary tract infections with an emphasis on drug-resistant gram-negative uropathogens. Curr Infect Dis Rep 2013; 15(2): 109-15. [http://dx.doi.org/10.1007/s11908-013-0315-7] [PMID: 23378123]

Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol 2015; 13(5): 269-84. [http://dx.doi.org/10.1038/nrmicro3432] [PMID: 25853778]

Castañeda-García A, Blázquez J, Rodríguez-Rojas A. Molecular mechanisms and clinical impact of acquired and intrinsic fosfomycin resistance. Antibiotics (Basel) 2013; 2(2): 217-36. [http://dx.doi.org/10.3390/antibiotics2020217] [PMID: 25853778]

Giske CG. Contemporary resistance trends and mechanisms for the old antibiotics colistin, temocillin, fosfomycin, mecillinam and nitrofurantoin. Clin Microbiol Infect 2015; 21(10): 899-905. [http://dx.doi.org/10.1016/j.cmi.2015.05.022] [PMID: 26027916]

Ejiofor SO, Edeh AD, Ezeudu CE, Gugu TH, Oli AN. Multi-drug resistant acute otitis media amongst children attending outpatient clinic in Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Awka, South-East Nigeria. Adv Microbiol 2016; 6: 495-501. [http://dx.doi.org/10.4236/aim.2016.67049]

Oli AN, Eze DE, Gugu TH, Ezemo I, Maduagwu UN, lhekerereme CP. Multi-antibiotic resistant extended-spectrum beta-lactamase producing bacteria pose a challenge to the effective treatment of wound and skin infections. Pan Afr Med J 2017; 27: 66. [http://dx.doi.org/10.11604/pamj.2017.27.66.10226]