OCCURRENCE OF MULTIDRUG RESISTANCE *ESCHERICHIA COLI* AND OTHER BACTERIA SPECIES ASSOCIATED WITH URINARY TRACT INFECTION IN TWO GEOPOLITICAL ZONES OF ONDO STATE, NIGERIA

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Abstract

Urinary tract infection (UTI) is a common bacterial infection known to affect different parts of the urinary tract of both male and female. *Escherichia coli* has been found to be responsible for causing 80% to 90% of the infection. An investigation was carried out to determine the prevalence of bacteria, especially *E.coli* implicated in UTI, and to ascertain their antibiotics susceptibility pattern. Early morning mid-stream urine samples were collected from 250 patients aged 18 to 60 years, between March and July of 2016 from 5 major Hospitals in the study location. The isolates were identified using standard microbiological methods and susceptibility tests were carried out using ten antibiotics. Results showed that 65(30.7%) of the isolates were *E. coli*. Followed by *Pseudomonas aeruginosa* 45(21.2%), *Klebsiella pneumoniae* 42(19.8%), *Staphylococcus aureus* 32(15.1%) and *Proteus mirabilis* 28(13.2%). The percentages of resistance of *E. coli* isolates to antimicrobial agents were chloramphenicol (64.9%), sparfloxacin (59.5%), ciprofloxacin (73.0%), septrin (73.0%), amoxacillin (91.9%), augmentin (83.8%), gentamycin (48.7%), perfloxacin (40.5%), ofloxacin (40.5%) and streptomycin (54.1%). The need for constant antimicrobial susceptibility surveillance by health managements system that will help clinicians to provide safe and effective therapy is advocated.

Key words: Uropathogen, *Escherichia coli,* Urinary tract infection

INTRODUCTION

Urinary tract infection is one of the most frequent bacterial infectious diseases that affect both inpatient and outpatients around the world [1], and is one of the most common diseases that affect people of all ages from neonate to adulthood and globally [2, 3]. UTI is more common among females than male with about 60% of women having at least one episode in their lifetime [4]. This is due to shorter urethra in females which is more readily transverse by microorganisms [5]. The highest incidence of UTI occurs mostly in child bearing age due to the fact of high increase in sexual activity and aging. Gupta [6] reported that about 150 million people are diagnosed with urinary tract infection each year.

Escherichia coli have been found to be responsible for 90% of the first urinary tract infections in young women [7]. They are known as a component of the intestinal microflora of human or warm blooded animals [8], which can exist as commensal, it also exist in a symbiotic state providing resistance against pathogenic organisms or it can be pathogenic and cause diseases of the intestinal and extra intestinal sites

Over 150 million people experienced an episode of UTI yearly and this is costing the world economy over 6 billion US dollars in treatment and workloss [6]. Studies that have being carried out in Enugu, Yola, Zaria and Ile-Ife showed that the same etiological agent was isolated in Nigeria. The prevalence rate of urinary tract infection in Yola was 67.2% and 77% in Enugu [9]. Olowu [10] reported an incidence of 28.1% in a population of 2780 outpatients at Lagos University Teaching Hospital while Aiyegoro [11] reported 11.96% in Ile-Ife. The common bacteria associated with urinary tract infections aside *E. coli* are *Klebsiella*, *Pseudomonas, Proteus* and also the Gram positive organism like *Stappylococci* sp, *Enterococci* sp. *Candida albicans* has been isolated in patients with underlying physiological debilitation [12].

Commensal strains of *E. coli* can also cause diseases in immunocompromised hosts, the pathogenic and commensal *E. coli* are classified into four main phylogenetic groups: A, B1, B2 and D [13]. The phylogenetic group A and B1 consists mainly of the commensal strains that are found in large intestine of humans and animals, but they do not naturally carry any known virulence factor [14]. Whereas, the phylogenetic group B2 and to a lesser extent the group D consist of pathogenic strains that normally carry virulence–associated genes, which are mostly associated with extra-intestinal diseases. The pathogenic *E. coli* strains causes enteric or diarrhoegenic disease, urinary tract infection and blood infection. The aim of this study is to isolate and identify microorganisms that are associated with urinary tract infection and to assess the antibiotic susceptibility pattern of the isolates.

MATERIALS AND METHODS

Sample collection

A total of 250 urine samples were collected from volunteers (between the ages of 18 and 60 years) that visited the General Hospital, Ikare-Akoko; Federal Medical Center Owo; Adekunle Ajasin University Health Center Akungba-Akoko and Union Diagnostic Center, Akure, Ondo State, Nigeria between March and July of 2016.

Culture and identification of isolates

Each sample was inoculated on MacConkey agar, Eosin Methelene Blue (EMB) agar and Cystine Lactose Electrolyte Deficient (CLED) agar plates and incubated at 37^0C for 24 hours. The identification and characterization of isolated bacteria were done by Gram staining, followed by microscopic examination and biochemical tests such as indole production, citrate utilization and phenol red lactose broth tests.

Susceptibility test

Antimicrobial sensitivity testing of all the isolates was performed using disk diffusion method according to [15]. Clinical samples were inoculated on Mueller Hinton plates and spread evenly to form a lawn culture, after which, the antibiotic discs were placed on the surface and incubated at 37^0C for 24 hours. The antibiotics used include: cotrimoxazole (30ug), chloramphenicol (30ug), sparfloxacin (10ug), ciprofloxacin (10ug), amoxacillin (10ug), augmentin (30ug), gentamycin (10ug), perfloxacin (10ug), ofloxacin (10ug) and streptomycin (30ug).

RESULTS

A total of 212 (84.8%) of urine samples yielded significant growth, out of 155 (62%) females that participated, 150(96.8%) showed positive culture, while 62(65.3%) showed positive culture out of 95(38%) males that participated (Table 1). Five different uropathogens were isolated *E.coli* was predominant 65(26%) followed by, *Pseudomonas aeruginosa* 45(18.0%), *Klebsiella pneumonia* 42(16.8%), *Staphylococcus aureus* 32(12.8%), and *Proteus mirabilis* 28(11.2%). Thirty eight (15.2%) samples had no bacteria growth (Table 2). The frequency of bacteria isolated from male and female volunteers was shown in Table 3.

Distribution according to age group revealed that the highest rate of infection occurred in age group 18-45 and the least infection was recorded in volunteers above 46 years (Table 1). The antimicrobial drugs used on the uropathogenic *E.coli* isolated showed that ofloxacin (40.5%) and perfloxacin (40.5%) were the most efficient drugs of choice *in vitro*. This was because they showed high efficacy on the isolates than any other antimicrobials used in this study, this was followed by gentamycin (48.7%). The bacteria showed high degree of resistance to amoxicillin (91.9%), augmentin (83.8%), ciprofloxacin (73.0%), cotrimoxazole (73.0%), chloramphenicol (64.9%) sparfloxacin (59.5%) and streptomycin (54.1%) (Table 5) *Pseudomonas aeruginosa* isolated in this study were resistant to chloramphenicol, sparfloxacin, cotrimoxazole, amoxicillin,

augmentin, perfloxacin and streptomycin, but were sensitive to gentamycin, ofloxacin and ciprofloxacin (Table 5). The resistance pattern of *K. pneumonia*, *S. aureus* and *P. mirabilis* were also shown in Table 4, the zone of inhibition was 15 to 40mm.

Table 1: Age and Sex distribution of volunteers with significant bacteriuria

Age (years)	Males	Females	Total	Total Percentage
18-45	39	95	134	63.2%
46-60	23	55	78	36.8%
Total	62	150	212	100%
	29.2%	70.8%	84.8%	

N= 250

Table 2: Prevalence of microorganisms isolated from urine of patients

Organisms isolated	Number of isolates	Percentage (%)
Escherichia coli	65	26.0
Pseudomonas aeruginosa	45	18.0
Klebsiella pneumonia	42	16.8
Staphylococcus aureus	32	12.8
Proteus mirabilis	28	11.2
No bacteria growth	38	15.2
Total	**250**	**100**

Table 3: Frequency of isolated bacteria from positive cultures of volunteers

Bacteria isolates	Female	Male	Total (%)
Escherichia coli	49(75.4%)	16(24.6%)	65(30.7)
Pseudomonas aeruginosa	32(71.1%)	13(28.9%)	45(21.2)
Klebsiella pneumonia	28(66.7%)	14(33.3%)	42(19.8)
Staphylococcus aureus	26(81.3%)	6(18.8%)	32(15.1)
Proteus mirabilis	12(42.9)%	16(57.1%)	28(13.2)
Total	**147(69.3%)**	**65(30.7%)**	**212(100)**

Table 4: Antimicrobial sensitivity pattern showing resistance to bacterial agents

Isolates	CH	SP	CPX	SXT	AM	AU	CN	PEF	OFX	S
Escherichia coli	64.9	59.5	73.0	73.0	91.9	83.8	48.7	40.5	40.5	54.1
Pseudomonas auriginosa	65	80	30	55	70	65	25	50	30	65
Klebsiella pneumonia	50	57.1	50	78.6	78.6	71.4	64.3	35.7	14.3	85.7
Staphylococcus aureus	58.3	66.7	50	58.3	33.3	41.7	41.7	50.0	25.0	66.7
Proteus mirabilis	80	50	30	70	80	80	20	60	30	70

CH=Chloramphenicol, SP=Sparfloxacin, CPX=Ciprofloxacin, SXT=Septrin , AM=Amoxacillin, AU=Augmentin, CN=Gentamycin , PEF= Perfloxacin , OFX=Ofloxacin, S=Streptomycin

DISCUSSION

Out of 250 patients (155 females and 95 males between the ages of 18 – 60years), that participated in this study, 212(84.8%) urine samples had significant bacteriuria. This was higher than the study on profile of urinary tract infection and quinolones resistance among *E.coli* and *Klebsiella* spp isolated by Namratha [16], who reported the prevalence of 62%. Also prevalence of 67.2% was reported in Yola [9], 60% reported in Lafia [17], 22% in Ibadan [18], 77.9% in Enugu [19] and 35.5% in Jos [20] all in Nigeria. The high prevalence observed might be due to factors like peer group influence, promiscuity, pregnancy, low socio-economic status that are common among Nigerian young men and women [17].

This study revealed that *E. coli* was one of the predominant organisms incriminated in urinary tract infection. Out of 212 positive isolates *E. coli* had 65(30.7%) followed by *P. aeruginosa* 45(21.2%), *K. pneumonia* 42(19.8%), *S. aureus* 32(15.1%) and *P. mirabilis* 28(13.2%). The pattern and frequency of occurrence of the bacterial isolates found in this study is similar to those reported by other workers. Alausa and Onile [21] reported in their study that *Escherichia coli* was the most commonly isolated pathogens in significant bacteriuria. Also, Bishara [22] in Israel agreed with this statement, the authors reported that *E. coli* was responsible for 52% of cases of urinary tract infection, *Klebsiella* spp.(14%), *Proteus* species (95%) and *Enterococcus* spp. was 4 %. A variant result was observed in a study in Ile-Ife Southwestern Nigeria by Okonko [23] where *S. aureus* 11(28.9%) was second to *E. coli* 13(42.1%), *Klebsiella* spp 7(18.4%) and *Pseudomonas* spp 2(5.3%). A variant was also observed in a tertiary hospital in Abuja, Central Nigeria, where Iregbu and Nwajiobi-Princewill [24] proved that *E.coli* and *Klebsiella* spp were the two predominant uropathogens 323(37%) and 202(25%) respectively, *P. aeruginosa* 75(8.4%), *Proteus* spp 67(7.5%) and *S. aureus* 60(6.8%). The same trend of *E. coli* leading other uropathogens was reported by [25, 26].

The frequency of urinary tract infections in female was 150(70.8%) and the occurrence in male was 62(29.3%). This finding was in agreement with studies carried out by [27, 23]. This also correlates with other studies by [28, 29] where urinary tract infection was higher in females compared to males. Anochie [30] reported a predominance of female patients in a study carried out to determine the influence of instruction about the method of urine collection and storage on the prevalence of urinary tract infection. Similar findings were reported by Olowu [10]. The author reported that urinary tract infection was more frequent in women than men [9, 31, 32]. Okafor [33] reported 20.7% cases of urinary tract infection in males which was similar to 29.3% cases reported in this study.

The higher incidence of urinary tract infection in females has been attributed to the shorter female urethra and its close proximity to the anus that make it easier for enteric flora to colonize this area [34, 35]. Other contributory factors may include the use of contraceptives, childbirth and menopause [36, 37].

The highest rate of infection (UTI) was recorded in volunteers between the age group 18-45 and

the least infection (UTI) was recorded in volunteers above 46 years, this is in agreement with the study conducted by Ani and Mgbechi [38]. The high incidence of urinary tract infection between the ages of 18-45 years is due to high sexual activities and multiple sex partners among the age group.

The antibiotic resistant *E coli* isolated from urinary tract infections are on high increase and this is a serious problem. Many of the isolated strains are multi-resistance [39, 40]. In this study 54.1% of the *E coli* isolates were noted to have multiple resistance, they are resistant to more than six antibiotics. The antibiotic sensitivity test of this study shows that ofloxacin and perfloxacin were the most efficient antibiotics *in vitro* testing followed by gentamycin and sparfloxacin, meanwhile most of the organisms are highly resistance to amoxicillin followed by augmentin ciprofloxacin, septrin and chloramphenicol. Sensitivity test in this study revealed that ofloxacin and perfloxacin have the highest efficacy in vitro (59.5%) and (59.5%) respectively, this is in agreement with [41] where ofloxacin had (70.5%) as the most effective among antimicrobials. In this study 91.9% resistance to amoxicillin was found, and this is in agreement with the report of [42]. The authors reported 95% resistance to amoxicillin, also Datta [43] reported 88.57% and 100% resistance to amoxicillin was reported by Xavier and Amutha [44].
The percentages of the pathogens resistance varied between 91.9% and 40.5%. In this study, the isolates have demonstrated extremely high percentage of multidrug resistance phenotype. The rate of resistance to Septrin found is higher than those reported by others [45, 46]. Septrin or trimethoprim alone has been used widely in treating urinary tract infections caused by *E. coli* for decades. This study shows low efficacy of septrin also Ciprofloxacin resistance in this study is found to be higher than that reported in previous studies [47].
Current study shows that resistance to Ciprofloxacin is on high increase and if urgent measures are not taken to put the situation under control the need for search of new drugs to combat bacterial infection will arise in Nigeria, meanwhile few ciprofloxacin resistance strains were found in other countries [48].
The high level of resistance seen in Amoxicillin, Augmentin, Septrin, Ciprofloxacin, Chloramphenicol and Sparfloxacin is most likely due to selective pressure that results from uncontrolled and inappropriate use of these agents in our hospitals and in this country as a whole, this is promoted by poverty, lack of awareness about the usage of drugs, lack of antibiotic policy and also the readily availability of antibiotics sold over the counter in Nigeria. The high rate of antimicrobial resistance has pose a problem in the medical sector, 54.1% of our *Escherichia coli* population were noted to be multiple resistance.

In this study *Pseudomonas aeruginosa* isolated were resistant to chloramphenicol, sparfloxaxin, septrin, amoxicillin, augmentin, perfloxacin and streptomycin, but were sensitive to gentamycin, ofloxacin and ciprofloxacin. Olowu and Oyetunji [49] also reported multi-resistance in *Pseudomonas aeruginosa* in their study of nosocomial urinary tract infection. *Klebsiella pneumonia* showed high level of resistance to most of the antibiotics used a resistance of 78.6% was seen against amoxicillin, 85.7% were seen against streptomycin, 71.4% were resistance to

augmentin and 64.3% to gentamycin while 14.3?% were resistance to ofloxacin this result was similar to that reported by Aiyegoro *et al* [11].

Staphylococcus aureus had a resistance pattern of 58.3% to Chloramphenicol, 66.7% to sparfloxacin, 50% to ciprofloxacin, 58.3% to cotrimoxazole,50.0% to perfloxacin, 66.7% to streptomycin this is contrary to [50] report which presented a report in which 67.3% of Staphylococcus spp were resistance to cloxacillin, 64.9% to amoxicillin,51.8% to augmentin, 70.2% to tetracycline,48.8% to erythromycin, 36.9% to cotrimoxazole, 11.9% to chloramphenicol and 1.8% to gentamycin in a study in Ibadan Nigeria

CONCLUSION

The choice of drugs in the treatment of urinary tract infection (UTI) is quite narrow due to the wide -scale resistance that the UTI pathogens exhibited. *E. coli* remains the most frequent bacteria isolate. There is the need for constant antimicrobial sensitivity surveillance which will help clinicians to provide safe and effective therapy. The role of personal hygiene to curtail its spread cannot be overemphasized.

REFERENCES

1. Basu, S.,Mukherjee,S.K.,Hazra,A. and Mukherjee, M.(2013). "Molecular characterization of uropathogenic Escherichia coli: nalidixic acid and ciprofloxacin resistance, virulent factors and phylogenetic background. *Journal of Clincal and Diagnostic Research*.7(12): 2727-2731.
2. Chang, S.L and Shortliffe, L.D. (2006). Pediatric urinary tract infections. *Pediatr Clin North Am* 53:379-400.
3. Kucheria, R., Dasgupta, P., Sacks, S.H., Khan, M.S. and Sheerin, N.S.(2005). Urinary tract infections: new insights into a common problem. *Postgrad Med J*.81:83-6.
4. Foxman, B., Barlow, R., D'Arcy, H., Gillespie, B. and Sobel, J.D. (2000) Urinary tract infection: self-reported incidence and associated costs. *Ann Epidemiol* 10: 509-515.
5. Uehling, D.T.(1995). Vaginal mucosa immunization in recurrent urinary tract infections. *Infect. Urology vol 57-61*.
6. Gupta, K. (2001). Increasing antimicrobial resistance and the management of uncomplicated community acquired urinary tract infections. *Int. J. Antimicrob. Agents.* 135: 41-50.
7. Geo, F.B., Janet, S.B. and Stephen, A.M. (2001). Urinary tract infections.Enteric gram negative rods (Enterobacteriaceae). *Jawetz, Melnik and Adelberg's Medical Microbiology.* 22nd Edition. Pp 221.
8. Bettelheim, K.A. (1997). *Escherichia coli* in the normal flora of humans and animals. *In Escherichia coli: Mechanisms of Virulence. Edited by M. Sussman. Cambridge, UK: Cambridge, University Press. pp. 85-109.*

9. El-Mahmood, M.A. (2008). Antimicrobial susceptibility pattern of pathogenic bacteria causing urinary tract infection in a specialist hospital in Yola, Adamawa state. *Journal of ClinicalMedicine and Research* 1(1):001-008.

10. Olowu, W.A.(1996). Symptomatic bacteriuria in children.*Nig. Med Pract.*27: 76-80.

11. Aiyegoro, O.A., Igbinosa O.O., Ogunmwonyi, I.N., Odjadjare, E.E., Igbinosa, O.E and Okoh, A.I. (2007). Incidence of urinary tract infections (UTI) among children and adolescents in Ile-Ife, Nigeria. *African journal of Microbiology Research* pp 013-019.

12. Moore, K.N., Day, R.A. and Albers, M. (2002). Pathogenesis of urinary tract infections: a review. *Journal Clinical Nurse*. 11(5): 568-74.

13. Clermont, O, Bonacorsi, S, and Bingen, E. (2000) Rapid and simple determination of the *Escherichia coli* phylogenetic group. *Appl Environ Microbiol* 66: 4555-4558.

14. Johnson, J.R, Delavari, P, Kuskowski, M. and Stell, A.L. (2001). Phylogenetic distribution of extraintestinal virulence-associated traits in *Escherichia coli*. *J Infect Dis.*183: 78-88.

15. Clinical and Laboratory Standards Institute. (2014). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Third Informal Supplement. *CLSL Document Wayne,PA* M100-S23.

16. Namratha, W.N. (2015). Profile of Urinary Tract Infection and quinolones resistance among *Escherichia coli* and *Klebsiella* species isolates. *Int. J. Curr. Microbiol. App. Sci* 4(7):749-756.

17. Kolawole, A.S., Kolawole, O.M., Kandaki-Olukemi, Y., Babatunde, S.K., Durowade, K.A. and Kolawole, C.F.(2009). Prevalence of urinary tract infections (UTI) among patients attending Dalhatu Araf Specialist Hospital, Lafia, Nasarawa State,Nigeria. *Int. J. Med. Sci.*1(1):163-167.

18. Okesola, A.O. and Oni, A.A. (2009). Antimicrobial resistance among common bacterial pathogens in south western Nigeria. *American-Eurasian J.Agric. Environ. Sci*. 5(3): 327-330

19. Mbata, T.I. (2007). Prevalence and antibiogram of UTIs among prison immates in Nigeria.*Int. J. Microbiol*. 3(2): 6-12.

20. Ebie, M., Kandki-Olukemi, Y.T., Ayanbadejo, J. and Tanyigna, K.B. (2001). Urinary tract infections in a Nigerian Military Hospital. *Niger. J.Microbiol*. 15(1):31-37.

21. Alausa, K.O and Onile, B.A. (1984). The epidemiological pattern of bacterial septicaemia at the University College Hospital, Ibadan. *Nig Med. J.* 14: 55-62.

22. Bishara, J, Leibovic, L, Huniner, D, Drucker, M, Samra, Z, Konisberger, H. and Fitlik, S. (1997). Five years prospective study of bacteraemic urinary tract infection in a single institution. *Evr. J. Clin . Microbiol. Infect.Dis.* 16 (8): 563-567.

23. Okonko, I.O., Donbraye-Emmanuel, O.B., Ijandipe, L.A., Ogun, A.A., Adedeji, A.O. and Udeze, A.O.(2009). Antibiotics Sensitivity and Resistance Patterns of Uropathogens to Nitrofurantoin and Nalidixic Acid in Pregnant Women with Urinary Tract Infections in Ibadan, Nigeria. *Middle-East Journal of Scientific Research* 4(2):105-109.

24. Iregbu, K.C. and Nwajiobi-Princewill, P.I. (2013). Urinary Tract Infections in a Tertiary Hospital in Abuja, Nigeria. *African Journal Clinical Experimental Microbiology*, 14(3):169-173

25. Yabaya, A., Lucy, M. and Maimuna, H. (2012). Bacteria associated with urinary tract infections and their Susceptibility pattern to routine antibiotics. *Journal of medical and applied biosciences* 4(62):1360.

26. Mubanga, P., Steinberg, W.J. and Van Rooyen, F.C. (2015). Antimicrobial susceptibility profile of uropathogens in Maluti Adventist Hospital patients. *Afr J Prm Health Care Fam Med. Art* 7(1): 800.

27. Ibadin, O.M., Peada, O. and Abel, U.G. (2006). Urinary tract infection in Adolescent/ Young Adult Nigerians with Acquired Human Immuno Deficiency Disease in Benin City. *A peer review journal of Biomedical Sciences* 5(2):55-60.

28. Swetha, V.V., Rao, U.S., Prakask, P.H. and Subbarayudu, S.(2014). Aerobic Bacteriological Profile of Urinary Tract Infections in a Tertiary Care Hospital. *Int J Curr Microbiol App* Sci 3(3):120-125

29. Kibret, M. and Abera, B. (2014). Prevalence and antibiogram of bacterial isolates from urinary tract infections at Dessie Health Research Laboratory, Ethopia. *Asian pac J Trop Biomed* 4(2):164-168.

30. Anochie, I.C, Nkanginieme, K.E.O. and Eke F.U. (2001). The influence of instruction about the method of urine collections and storage on the prevalence of urinary tract infection. *Nig. J. Paediatr.* 28(2): 39-42.

31. Ahmad, S. (2012). Pattern of urinary tract infection in Kashmir and antimicrobial susceptibility. *Bangladesh Med Res Counc Bull* 38:79-83.

32. Randrianirina, F., Soares, J.L., Carod, J.F., Ratsima, E., Thonnier, V., Combe, P., Grosjean, P. and Talarmin,A.J.(2007).Antimicrobial resistance among uropathogens that cause community acquired urinary tract infections in Antananarivo, Madagascar. *AntimicrobChemother* 59(2):309-312.

33. Okafor, H.V, Okoro, B.A and Ibe, B.C. (1993). Prevalence of asymptomatic bacteriuria among nursery school children. *Nig. J. Paediatr.* 20: 84-88.

34. Dai, B., Liu, Y., Jia, J.and Mei, C. (2010). Long-term antibiotics for the prevention of recurrent urinary tract infection in children: a systematic review and meta-analysis. *Archives of Disease in Childhood* .95(7):499–508.

35. Salvatore, S., Cattoni, E., Siesto, G., Serati, M., Sorice, P. and Torella, M.(2011). Urinary tract infections in women. *European journal of Obstetrics, Gynecology, and Reproductive Biology* 156(2):131–6.

36. Phipps, S, Lim, Y.N, McClinton, S, Barry, C, Rane A, and N'Dow, J. (2006). Short term urinary catheter policies following urogenital surgery in adults. In Phipps, Simon."Cochrane Database of Systematic Reviews". *Cochrane Database Syst Rev*; (2):43-74.

37. Dielubanza, E.J. and Schaeffer, A.J. (2011). Urinary tract infections in women. *The Medical clinics of North America*;95(1): 27–41.

38. Ani, O.C. and Mgbechi, E.K. (2008). Prevalence of urinary tract infections (UTI) in sexually active women of Abakaliki, Ebonyi State, Nigeria. *Animal Research International* 5(2): 876-887.

39. Al-Assil, B., Mahfoud, M. and Hamzeh, A. R. (2013). Resistance trends and risk factors of extended-spectrum b-lactamases in Escherichia coli infections in Aleppo, Syria. *Am J Infect Control* 41, 597–600.

40. Ma, K. L. and Wang, C. X. (2013). Analysis of the spectrum and antibiotic resistance of uropathogens in vitro: results based on a retrospective study from a tertiary hospital. *Am J Infect Control* 41, 601–606.

41. John, D.O. and Rilwanu, A.M. (2013). Urinary Tract Infections Associated with *Escherichia Coli*: A 2005 to 2009 Clinical Assessment of Trends in Fluoroquinolones Activities in Maiduguri-City, Nigeria. *Journal of Applied Pharmaceutical*. 3(8): 84-91.

42. Mittal, S., Sharma, M, and Chaudhary, U. (2014). Study of virulence factors of uropathogenic *Escherichia coli* and its antibiotic susceptibility pattern. *Indian J Pathol Microbiol*. 57:61-64

43. Datta, P., Gupta, V. and Sidhu, S. (2014). Extended spectrum beta lactamase positive uropathogenic *E. coli* – epidemiological factors and resistance. *Br J Med Practic*. 7(2):a718

44. Xavier, A.M. and Amutha, S.(2016). Antibiotic resistance, RAPD-PCR Typing of Multidrug Resistant strains of Escherichia coli from Urinary Tract Infections (UTI). *Journal of clinical and diagnostic research dol.* 10(3):5-9.

45. Valdivieso, F., Trucco, O., Prado, V., Diaz, M.C., and Ojeda, A. (1999). Antimicrobial resistance of agents causing urinary tract infections in 11 Chilean hospital. *PRONARES Project. Rev. Med. Chil*., 127(9): 1033-1040.

46. Zhanel, G.G., Karlowsky, J.A., Harding, G.K.M., Carrie, A, Mazzulli, T. and Low, D.E. (2000). A Canadian national surveillance study of urinary tract isolates from outpatients: comparison of the activities of trimethoprim-sulfamethoxazole, ampicillin, mecillinam, nitrofurantoin and ciprofloxacin. *Antimicrob. Agents Chemother*. 44: 1089-1092.

47. Sahm, D.F., Thornsberry, C., Mayfield, D.C., Jones, M.E. and Karlowsky, J.A.(2001).Multidrug-resistant urinary tract isolates of *Escherichia coli*:prevalence and patient demographics in the United States in 2000. *Antimicrob. Agents Chemother* 45:1402-1406

48. Diekema, D.J., Boots, B.J., Miller, T.E., Vaughn, R.F., Woolson, J.W., Yankey, E.J.,Ernst, S.D., Flach, M.M., Ward, C.L., Franciscus, M.A., Pfaller, T.M and Doebbeling, B.N.(2004). Antimicrobial resistance trends and outbreak frequency in United States hospitals. *Clin. Infect. Dis* 38: 78-85.

49. Olowu, W.A and Oyetunji, T.G. (2003). Nosocomial significant bacteriuria prevalence and pattern of bacterial pathogens among children hospitalized for non-infective urinary tract disorders. *West Afr. J. Med*. 22 (1): 72-75.

50. Ako-Nai, A.K., Adeyemi, F.M., Aboderin, O.A. and Kassim, O.O. (2005). Antibiotic resistance profile of staphylococci from clinical sources recovered from infants. *Afr. J. Biotechnol*. 4(8): 816-822.