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Urinary Tract Infections Associated with Escherichia Coli: A 2005 to 2009 Clinical Assessment of Trends in Fluoroquinolones Activities in Maiduguri-City, Nigeria

John David OHIEKU[1*] and Rilwanu Aminu MAGAJI[1]
[1]Department of Clinical Pharmacy and Pharmacy Administration, Faculty of Pharmacy, University of Maiduguri, P.M.B. 1069, Maiduguri, Borno State, Nigeria.

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ABSTRACT

Urinary Tract Infections caused by *Escherichia coli* were investigated for infectivity patterns, trends in sensitivity to fluoroquinolones, multi-fluoroquinolone resistant pattern and the fluoroquinolones' inter-activities relation. 1590 patients (785/805 male/female) with clinical symptoms suggestive of UTI and confirmed with microbiological assay of the mid-stream of early morning urine specimens were surveyed. Isolated pathogens were cultured and sensitivity tests were performed. UTI cases increased by 17.7% between 2005 and 2009 with *Escherichia coli* accounting for 41% and showing an increase from 5.7% in 2005 to 28.0% in 2009 and a significant correlation ($P<0.05$). *E. coli*-UTIs were higher in females (56.6%) than males (43.4%). Pathogen's susceptibility to agents varied but the activities of ciprofloxacin, ofloxacin, pefloxacin and nalidixic acid against *E. coli* recorded significant yearly decrease ($P<0.05$). The overall susceptibilities of *E. coli* were 71%, 58%, 48%, 34% and 15% for ofloxacin, ciprofloxacin, pefloxacin, norfloxacin and nalidixic acid respectively. About 35% of ciprofloxacin-resistant *E. coli* indicated sensitivity to ofloxacin whereas only 20% was the converse. Multi-fluoroquinolones-resistant cases (282, 43.6%) were observed in *E. coli* which increased from 30.2% in 2006 to 57.5% in 2009. The study observed a rapid and progressive loss of activities of quinolones, increasing multi-fluoroquinolone-resistant, high resistance rates and poor inter-activities relations between the fluoroquinolones against *E. coli* in the region.

INTRODUCTION

Urinary tract infections are common bacterial infections that affect the urethra, bladder, ureter or the kidney which require appropriate antibiotic interventions to prevent complications and further damages to these organs. A global infection burden rate of 150 million cases are estimated per annum (Stamm et al., 2001) while approximately 8 million physician visits per year are attributed to UTI in the USA (Warren et al., 1999). When untreated or poorly managed, serious life threatening complications like pyelonephritis resulting to permanent scar and damage to the kidneys occur in addition to bloodstream infections and other infections elsewhere in the body (University of Maryland Medical Center, UMMC, 2011). UTI occurring during pregnancy may present a potential risk for kidney infection as well as affecting the health of the mother and the child. Both the genito-urinary tracts of male and female subjects may be affected alike but gender related specific risk factors like shortness of urethra, pregnancy and menopausal status put the female gender at higher prevalence rates than their male counterpart (Harrington and Hooton, 2000). Medical conditions like diabetes, kidney disorders, sickle cell disease, immune system problems and urinary tract abnormalities as well as age related urinary incontinence can increase the risk of the disease (UMMC, 2011). UTI is common at all ages but the elderly people, children and sexually active people may be at higher risk than other population group (UMMC, 2011). Although many agents including β-lactams, fluoroquinolones and nitrofurantoin may be used in the management of UTI base on their tolerability, spectrum of activities and pharmacokinetic profile (Neu 1992), the trimetoprim-sulphamethoxazole combination has been favored for many years (UMMC, 2011). But with the increasing report of resistance development to these agents in many regions (Willize *et al*., 2011), the fluoroquinolones are now becoming widely used as a standard alternative to trimetoprim-

* *Corresponding Author*
E-mail: joni.dav@hotmail.co.uk
Tel: +234 803 604 0798

sulphamethoxazole and has even overtaken trimetoprim-sulphamethoxazole as the most commonly prescribed antibiotic in some areas (UMMC, 2011). Their ability to achieve inhibitory urinary concentrations that significantly exceed serum levels and eradicate aerobic gram-negative flora with minimal effect on the vaginal and fecal anaerobic flora made them to provide the best long-term cures for uncomplicated urinary tract infections (Neu 1992).

The quinolones which has nalidixic acid as the basic structure are synthetic chemotherapeutic agents that have made remarkable impact in bacterial chemotherapy (Nelson *et al*., 2007) with the fluorinated ones having a broaden activities and effectiveness in the treatment of a wide variety of infectious diseases (William, 2006). Agents like ciprofloxacin, ofloxacin, norfloxacin, pefloxacin and lomefloxacin regarded as second generation quinolones have an expanded gram-negative, some gram-positive as well as atypical bacterial pathogens are indicated in the treatment of both uncomplicated and complicated urinary tract infections, pyelonephritis, sexually transmitted disease, prostatitis, skin and soft tissue infections (Dana *et al*., 2000). Other agents like levofloxacin, gatifloxacin, sparfloxacin and moxifloxacin additionally have increased gram-positive activities making them useful in the chemotherapy of community acquired pneumonia, acute sinusitis and acute exacerbation of chronic bronchitis (Dana *et al*., 2000). But the fourth generation ones like trovafloxacin, clinafloxacin and gemifloxacin have additional activity against anaerobic bacteria (Ambrose *et al*., 1997; Dana *et al*., 2000). Many factors including their wide spectrum continue to justify their increased utilization in any given region. For example, they have multiple modes of activity that make them effective against wide range of pathogens, particularly those of gram positive, gram negative, atypical bacteria and anaerobes (Appelbaum and Hunter, 2000). They also have long half-lives which allow for once or twice daily dosing (Dana *et al*., 2000). Their high oral absorption profile from the gastrointestinal tract and high bioavailability as well as a serum concentration that compares well with those of intravenous administration continue to favor their frequent orderings (Borcherding *et al*., 1996; Turnidge, 1999; Hooper, 2000). The fluoroquinolones also have large volume of distribution and concentrate in tissues at levels that exceed serum drug concentration and leading to high concentration in tissues of renal, lung, prostate, bronchial, nasal, gall bladder and genital tract (Stein, 1996) making them useful in the treatment of infections in these areas. They are effective in the treatment of urinary tract infection including infection caused by multi-drug resistant *Pseudomonas spp*. Williams (2006) also reported their effectiveness in sexually transmitted diseases caused by neisseria, hemophillus and chlamydia spp. Most fluoroquinolones may achieve adequate systemic concentrations making them of relevant in the treatment of typhoid fever, and soft tissues, bones, intra-abdominal and respiratory tract infections (Henry, 2004). Uncomplicated urinary tract infections are most times treated empirically, particularly in areas where clinicians can recognize resistance patterns of uropathogens in the community. But this can pose challenges in most other places, thereby making it difficult for most appropriate antimicrobial agent to be chosen. Antibiotic selection for urinary tract infection can depend on many factors such as the allergy history of patients, treatment cost, tolerability of the treatment, previous antibiotic therapy, and the prevalence of resistance in the community. All these factors appeared to favor fluoroquinolones use in many regions.

However, the fluoroquinolones have been overused in many quarters leading to the development of resistant of both gram positive and gram negative bacteria (Acar and Golstein, 1997) since they are capable of preventing access of the drug to the target sites through the reduction in entry into the cell or by pumping the drug out of the cell (Bast, *et al*., 2000; Broskey *et al*., 2000); although the mutation of the genes that encode for DNA gyrase and topoisomerase IV can change the enzyme structure to inhibit binding at their sites of action (Hooper, 1998). Experts recommended that physician should obtained information on local resistance rates, and ongoing local, regional and national surveillance be conducted to monitor changes is susceptibility to uropathogens and suitability of empiric therapy recommended (Warren *et al*., 1999).

AIMS AND OBJECTIVES

The study was aimed at investigating trends in urinary tract infection caused by *E. coli* in the region, the changing patterns of the activities of the fluoroquinolones against UTI *E. coli* pathogens, trends in the multi-fluoroquinolone-resistances and to investigate the inter-activity relations of the fluoroquinolones from 2005 to 2009.

MATERIALS AND METHODS

Sampling

1590 cases of urinary tract infections comprising of 785 and 805 females aged below 1year to 95 years were investigated between 2005 and 2009 in individuals suspected to have UTI following the presented clinical signs and symptoms and confirmed with microbiological assay of the mid-stream catch of early morning urine specimens.

Urine culture and Sensitivity Assay

Midstream urine samples were obtained from patients with suspected urinary tract infection into clean urine specimen bottle previously sterilized. Urine samples were inoculated on Cystein Lactose Electrolyte Deficient (CLED) agar and blood agar; and incubated at 37^{o}C for 48 hours. Pathogens were isolated and identified using gram staining, morphology and biochemical characters. Only samples with CFU greater than 10^{5} /milliliter were considered to be significant bacteruria as determined by the Laboratory medical microbiologist. Antimicrobial sensitivities were performed with nalidixic acid and fluoroquinolones agents like norfloxacin, pefloxacin, ciprofloxacin and ofloxacin using the Kirby Bauer Disc Diffusion Method in accordance with the Clinical Laboratory Standards Institute (CLSI).

Statistical analysis

Chi square was performed to determine the level of significant difference between the activities of two or more agents at 95% confidence interval.

RESULTS AND DISCUSSION

UTI associated with E. coli

The distribution of isolated *E. coli* in urine specimens from 2005 to 2009 (Table 1) indicated that the pathogen accounted for 647 (41%) out of the 1590 isolated pathogens. UTI cases caused by *E. coli* were observed to peak in 2009 and recorded significant correlation (P=0.048) in its yearly increase. Though a worldwide range of 75-90% *E. coli* association UTI etiological pathogen is reported (Zakaria, 2009), this value is lower than the result obtained in India (51%), Gaza Strip (52%), Ethiopia (48%), Canada (54%), Karachi (53%) and Sapele (Nigeria) (45.7%) where *E. coli* pathogens were similarly reported as the predominant bacteria causing UTI (Gupta *et al.*, 2002; Sabir *et al.*, 2004; Zakaria, 2005; Fantahm and Bayel, 2009; Orhiosefe *et al.*, 2009; Karlowsky *et al.*, 2011).

The age distribution of patients with *E. coli* associated UTI is as shown in Figure1. The distribution is multimodal with the mean and standard deviation of 38.71 ± 24.42 years for the male patients while that of the female patients is skewed toward lower frequency of higher age group with a mean and standard deviation of 26.76 ± 16.17 years. However, the mean age and standard deviation of the general population (combine male and female subjects) is 33.03 ± 21.00 years Although UTI case caused by *E. coli* were slightly higher in male children than the female who are under 10 years of age (Fig 1), the preponderance of the disease is higher in female than male for those between 10 to 50 years before a reversal in trends were observed. These results may have illustrated the interplay of age and/or gender related risk factors influencing the course of the disease.

The UTI incidences caused by *E. coli* in all were higher among the females (56.6%) than the males (43.4%) since many factors including those of closer anatomical structure of women urethra to the anus, diaphragm use, sexual behavior, new sex partner, pregnancy and post-menopausal women are known gender related risk factors that impact the course of the disease in women than men (UMMC, 2011). Although catheter associated UTI have been reported among the geriatric age group as specific male related risk factors capable of causing UTI by many authors (UMMC, 2011), however its relationship in causing higher cases of *E. coli* UTI in male patients who are above 50 years than the female of similar age peers could not be verified in this study.

This rising incidences of *E. coli* in urogenital infections in this zone which may partly be explained by increasing environmental and health related factors as well as the increasing antibiotics resistance is not surprising since many similar pathogens isolated from other infectious sites in the region have similarly been reported to be on the increase and have shown high resistance to several antibacterial agents (Ohieku and Nnolim 2010a, 2010b; Ohieku *et al.*, 2010a, 2010b; Ohieku et al, 2011), thereby necessitating increased hospital visits arising from resurged conditions, therapeutic failures or transfer of pathogenic bacteria from one site to the other.

Table. 1: Gender distribution pattern of isolated uropathogenic *E. coli* from 2005 to 2009

Urinary Pathogens	Gender	Number and Percentage (%) Isolated per Year					Total (%)
		2005	2006	2007	2008	2009	
E. coli	Male	19	60	53	57	92	281
	Female	18	79	65	115	89	366
	Total	37	139 (21.5)	118	172	181	647
	(%)	(5.7)		(18.2)	(26.6)	(28.0)	(100)

Table. 2: Quinolones activities against isolated uropathogenic *E. coli* between 2005 and 2009

Antibiotics	Percentage activities (%) of antibiotics against *E. coli* (n=number of tested pathogens)					
	2005	2006	2007	2008	2009	Total (%)
Ciprofloxacin	**62.5%**, n=40	**73.6%**, n=140	**62.6%**, n=115	**56.8%**, n=169	**42.9%**, n=177	**57.5%**, n=641
Ofloxacin	**58.3%**, n=36	**89.1%**, n=137	**72.4%**, n=105	**70.7%**, n=140	**55.0%**, n=149	**70.5%**, n=567
Pefloxacin	**60.5%**, n=38	**57.5%**, n=134	**61.4%**, n=101	**39.6%**, n=154	**37.7%**, n=154	**48.4%**, n=581
Norfloxacin	**66.7%**, n=3	**50.0%**, n=9	**55.5%**, n=9	**37.8%**, n=37	**11.1%**, n=18	**34.2%**, n=76
Nalidixic acid	**35.1%**, n=37	**16.5%**, n=121	**15.5%**, n=97	**13.8%**, n=130	**9.3%**, n=150	**15.0%**, n=535
Total	**n=154**	**n=541**	**n=427**	**n=630**	**n=648**	**n=2400**

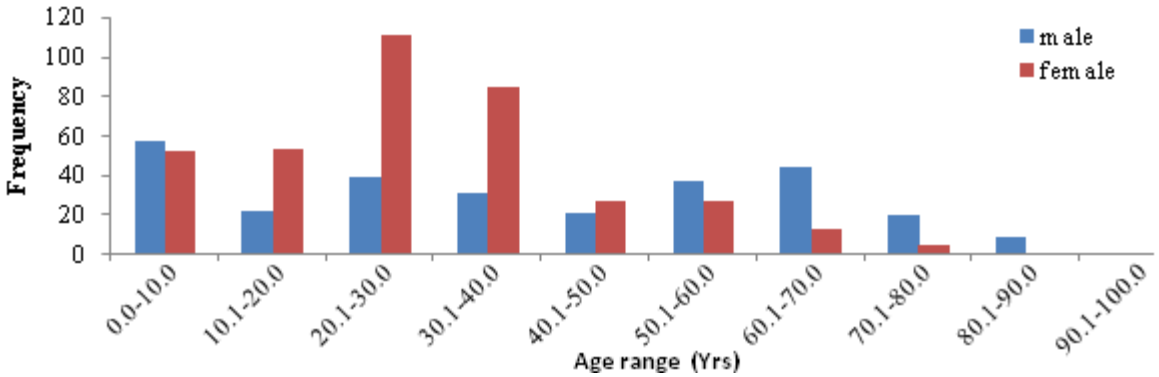

Fig. 1: Distribution of age of patients with UTI associated with *E. coli* between 2005 and 2009.

Quinolones activities pattern against Uropathogenic *E. coli*

The susceptibilities and resistances of each quinolone to uropathogenic *E. coli* from 2005 to 2009 are as shown in Table 2 and Figure 2 respectively. The activities (susceptibilities) of both ofloxacin and ciprofloxacin were observed to peak in 2006 before progressive decrease in their activities that indicated significant regression ($P<0.05$) were observed (Table 2). However, while pefloxacin recorded activities peak in 2007, that of norfloxacin were observed in 2005. The results further showed that ciprofloxacin recorded 30.7% loss in activities between 2006 and 2007 as against the 34.1% recorded with ofloxacin during similar periods. The ciprofloxacin activity change from 62.5% in 2005 to 42.9% in 2009 indicated significant difference ($X^2 = 5.04$, $P<0.05$). Similarly, the 22.8% loss in activities recorded between 2006 and 2009 with pefloxacin were found to be significant ($X^2=11.3$; $P<0.005$) during these two periods but norfloxacin and nalidixic acid activities respectively drop by 55.6% and 25.8% between 2005 and 2009. Despite the ofloxacin's 34% loss in activities from 2006 to 2009, the agent was still determined to be the most active drug even when it was the most resisted agent in recent times and is consistent with results from other regions in the country. For example, ofloxacin was similarly determined to be the most active fluoroquinolone in Ibadan, Nigeria (Idowu and Adelola, 2007) where resistance rates were lower than this study but the resistance rates obtained in Iran for ofloxacin and ciprofloxacin (Nakhjavani *et al*., 2007) were higher than this present study. The higher activities of ofloxacin against UTI-associated *E. coli* found to be significantly different from that of ciprofloxacin ($X^2=18.85$; $P< 0.005$). These results was similarly consistent with results from other places like USA and Canada where ofloxacin was reported to show the highest activities against *E. coli* (Jones and Hoban, 1994). However, the activities of norfloxacin were determined to be higher than ciprofloxacin and pefloxacin in those regions. In contrast to our findings, the activities of ciprofloxacin were reported to be higher than ofloxacin in Sapele, Nigeria (Orhiosefe *et al*., 2009). These variations are naturally attributable to differences in the degree of previous overuse or misuse in these regions (Acar and Goldstein, 1997). The results indicated that most fluoro-quinolones (except ofloxacin) showed low activities against *E. coli*.

Trends in annual resistance changes of UTI *E. coli* to individual quinolones

The results of trends in resistance pattern of individual quinolone to *E. coli* from 2005-2009 is as shown in Figure 2. These results further demonstrated that most agents are fast becoming resistance to UTI caused by *E. coli* in the region. In particular, the progressive increase in resistances recorded with *E. coli* against ciprofloxacin, norfloxacin and ofloxacin (Fig 2) were significantly correlated ($P = 0.011$, 0.028 and 0.037 respectively) from year 2006 to 2009 with resistance reaching high record of 57.1%, 45%, 62.3%, 89.9% and 90.7% respectively for ciprofloxacin, ofloxacin, pefloxacin, norfloxacin and nalidixic acid in 2009 (Fig 2). However, nalidixic acid is near plateau stage in its resistance changes between 2006 and 2009. When changes in resistance growth rates of UTI *E. coli* against the fluoroquinolones were compared between year 2005 and year 2009 (Fig 2), the results indicated significant difference ($P< 0.05$) for pefloxacin, and norfloxacin only but changes occurring with pefloxacin were not found to be significant. However resistance trend of *E. coli* against ciprofloxacin (Fig 2) when compared with reported changes occurring elsewhere in the world was found to be much higher than the stepwise increase of 4.1% to 15% in Gaza Strip between 2000 and 2004, 5% to 12.9% changes in South-East Austria between 2002 and 2006, and 3.3% to 15.3% changes in Turkey between 1999 and 2004 (Zakaria, 2009). In Sweden, only 9% increase in pathogen's resistance to ciprofloxacin were recorded over a period of three decades (Kronva, 2010) while a change from 3% to 17.1% of ciprofloxacin-resistant *E. coli* was reported between 2000-2010 in USA (Sanchez *et al*., 2012). Many reasons including those of inappropriate prescribing of antibiotics, poor antibiotics control strategies, self medication, and poor habit of performing necessary culture testing continue to account for the increasing resistance to ciprofloxacin in many regions of the world (Zakaria, 2009). The resistance change for all the fluoroquinolones from 29.5% in 2005 to 56.2% in 2009 (representing 26.7% increase) were found to be significant ($P<0.005$) and also showed significant correlation ($P = 0.018$) during these periods. These results are worrisome particularly when compared with the slow resistance growth of pathogenic *E. coli* to the quinolones in other regions. For example, an increment of *E. coli* resistance to quinolones from 1.9% to 7.7% between 2002 and 2009 was reported (Wiles *et al*., 2010; Institute of Environmental Science and Research Limited, 2011). Similarly, *E. coli* resistance increase of about 10-12% were reported between 2001 and 2005 in two separate regions of Saudi Arabia (Hanan., 2007; Akhtar *et al*., 2010). Orhiosefe *et al* (2009) also reported a 9.7% increase in *E. coli* resistance in Sapele, Nigeria. As low as 0.7% resistance growth were reported over a decade in Australia. Fluoroquinolones resistance increase is also as low as 1.2% in Norway (Grude, 2008). Furthermore, when the cumulative activities of each agent was computed from 2005 to 2009 (Fig 4), the results showed that resistance rate has out-grown susceptibilities rate for pefloxacin, norfloxacin and nalidixic acid with ciprofloxacin approaching similar status. Only ofloxacin was found to have shown a clear deviation from this pattern. As observed, *E. coli* recorded an overall resistance rate of 42.5% against ciprofloxacin during the period (Fig 4). This value is similarly much higher than the 4.5% reported resistant values of *E. coli* in Russia (Leonid and Vlamidir, 2006) and in other regions of the world like UK (2.3%), France (1.7%), US and Canada (5.5%), Poland (6.7%), Germany (7.7%), South Korea (14.3%), Spain (14.7%), Madagascar (15%) and Bangladesh (26%) (Naber *et al*., 2008; Schito *et al*., 2009; Wagenlehner *et al*., 2010; Palou *et al*., 2011; Neuzillet *et al*., 2011). In contrast, the result of this present study is lower than the 45.5% cases reported in North East areas of Pakistan (Khalil and Imran, 2008). Resistance rates greater than 10% of *E. coli* against ciprofloxacin was reported in Spain and Italy (Schito *et al*., 2009).

Ofloxacin recorded the least resistance growth among the fluoroquinolones (Table 2, Figures 2 and 4) and changes occurring with it between year 2005 and year 2009 were not found to be significant (P >0.05) although the agent recorded high resistances changes between 2006 and 2009 while norfloxacin was the highest resisted agent by the pathogen. Resistance of uropathogenic *E. coli* has been attributed to clonal spread of resistant plasmid but other environmental factors like the lack of antibiotic policies and the poor enforcement of relevant regulations regarding antibiotics, which make them readily available to the public for misuse and in the hands of unskilled business people and non-professionals, as well as increase in their prescription and their irrational usage may be contributing to their rapid increase in resistance development. These high changing patterns in UTI drug resistance in the region underscore the need for a reassessment of local empiric choices and continuous monitoring of resistance since such choices may not be reliable.

Age related percentage resistance pattern of quinolones to E. coli between 2005 and 2009

The relationship between age and percentage resistance pattern to *E. coli* of some of the studied quinolones is as shown in Figure 5.

The results showed that the proportions of resistance to uropathogenic *E.coli* with respect to age for ciprofloxacin, ofloxacin, nalidixic acid peaked in those who are 50-60 years before declining resistance (P< 0.05) proportion were observed.

Apart from those who are under 10 years of age, age related percentage resistances were significant (P<0.05) for ciprofloxacin and ofloxacin but not for pefloxacin while nalidixic acid seems to show age dependent percentage resistance pattern up to 60 years.

The result may be of value in guiding clinicians in the future use of these agents among several age strata in the study area.

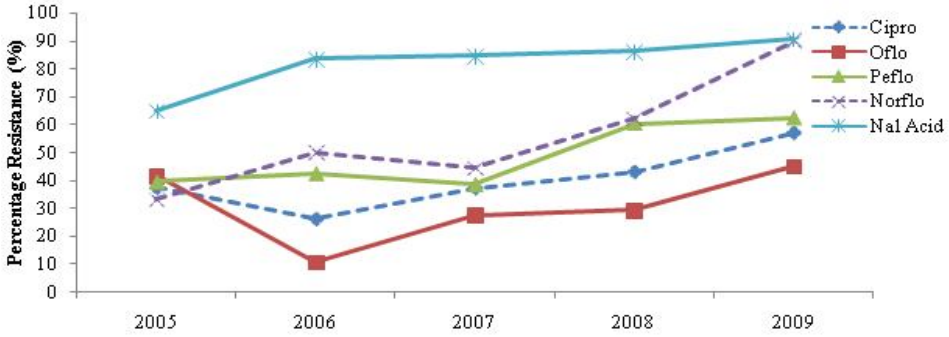

Fig. 2: Trends in resistance pattern of quinolones to E.coli from 2005-2009.

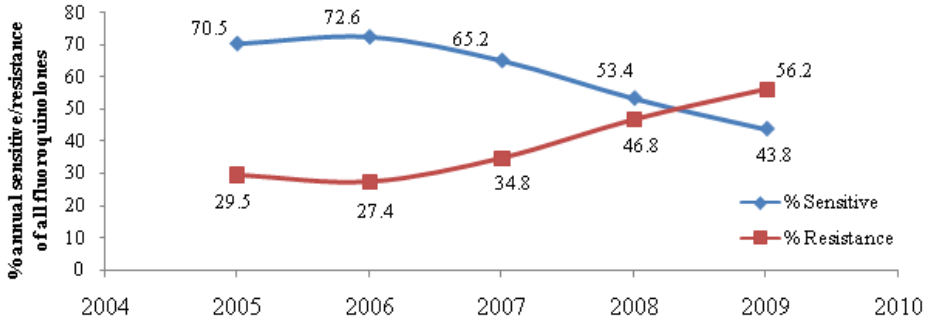

Fig. 3: Annual trends in combined resistances and susceptibilities of all the fluoroquinolones (excluding Nalidixic acid) to uropathogenic *E. coli* isolates.

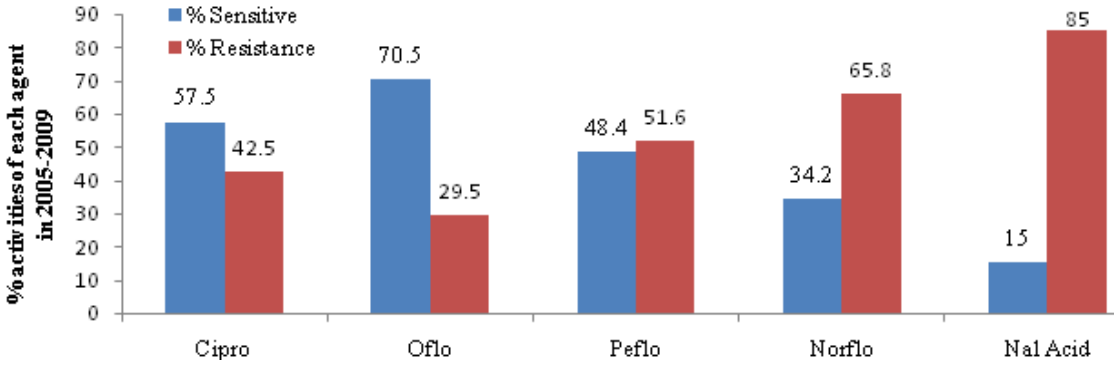

Fig. 4: Percentage total susceptibility and Resistance of *E. coli* to each agent from 2005 to 2009

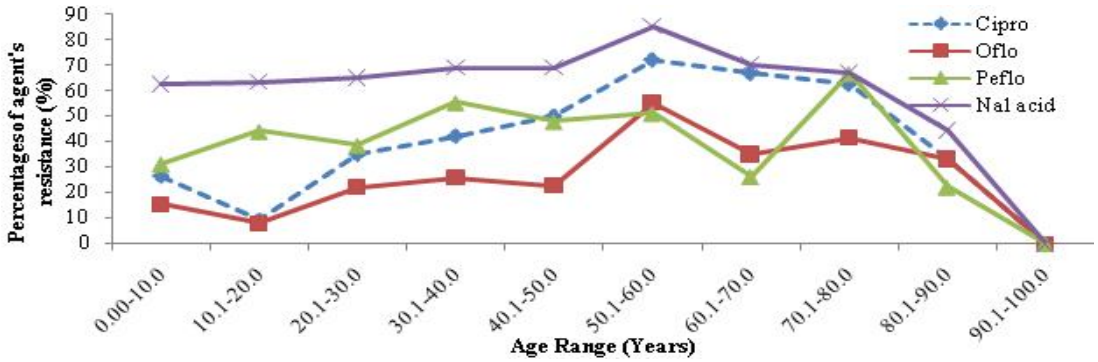

Fig. 5: Percentage resistance pattern of the quinolones with respect to age.

Table. 3: Cross tabulation of overall activities of all Quinolones to resistant uropathogenic *E. coli*.

	Nos (%) of Resistant *E. coli* that are sensitive to other quinolones			
No. of *E.coli* Resistant to quinolones:	**Nal. acid**	**Pefloxacin**	**Ciprofloxacin**	**Ofloxacin**
Nalidixic acid (n=412)	XXX	161 (39.1%)	227 (55.1%)	270 (65.5%)
Pefloxacin (n=299)	6 (2.0%)	XXX	83 (27.8%)	136 (45.5%)
Ciprofloxacin (n=259)	7 (2.7%)	22 (8.5%)	XXX	92 (35.5%)
Ofloxacin (n=160)	7 (4.4%)	22 (13.8%)	32 (20.0%)	XXX

Table. 4: Pattern of Multi-fluoroquinolone-resistant *E.coli* **.

	2005	**2006**	**2007**	**2008**	**2009**	**Total**
Escherichia coli	18 (48.6%) n=37	42 (30.2%) n=139	41(34.7%) n=118	76 (44.2%) n=172	104(57.5%) n=181	282 (43.6%) n=647

**This is defined in this study as resistance of *E. coli* to 2 or more of the 4 used fluoroquinolone (excluding nalidixic acid).

Inter-activities relation of the quinolones against E. coli

When E. coli was found to be resistant to one quinolone agent, the activities of other fluoroquinolones were compared with this resistant strain (Table 3).

The clinical relevant is to search for suitable therapeutic options among the quinolone group of drugs in order to guide their empirical uses. The results showed that the higher activities recorded with ofloxacin against nalidixic acid-resistant and pefloxacin-resistant E. coli (being 65% and 45% respectively) over that of ciprofloxacin (55% and 27.8% respectively) (Table 3) indicated a significant difference (P<0.005 each) between them but pefloxacin indicated low activities (39%) against nalidixic acid-resistant E. coli. High levels of cross-resistivity of the pathogen may have accounted for the low activities of pefloxacin (13.8%) and ciprofloxacin (20.0%) against ofloxacin-resistant E. coli since many bacteria have special abilities of expressing resistance traits which they spread through the transfer of resistance plasmid gene against similar or dissimilar agents (Acar and Goldstein, 1997).

The pattern of this results showed no deviation from the higher activities recorded with ofloxacin against nalidixic acid-resistant and pefloxacin-resistant bacteraemic E. coli isolates in blood specimens of patients over ciprofloxacin earlier reported in the zone during a similar period (Ohieku et al., 2011) although much higher activities of ofloxacin are recorded than this present study.

Neither pefloxacin nor ofloxacin also indicated good activities against ciprofloxacin-resistant E. coli (being 8.5% and 35.5% respectively) and only about 13.8% and 20.0% of ofloxacin-resistant E. coli are susceptible to pefloxacin and ciprofloxacin respectively. These results have serious clinical implications in the region since high levels of cross resistance may both affect their empiric choices and even when therapeutic failures is encountered with one fluoroquinolone agent, getting effective alternative may be difficult.

Pattern of Multi-fluoroquinolone Resistant *E. coli*

E. coli multi-Fluoroquinolone-resistant cases (excluding nalidixic acid) (Table 4) indicated a significant and progressive increase from 30.2% in 2006 to 57.5% in 2009. This rising pattern is again of concern not only because it creates circumstances that limit empirical choice of agents in the region but also because curtailing resistance *E. coli* may require a herculean tasks. It also showed that the region may gradually be approaching a period when all the available quinolones agents currently in use in the region will no longer be relevant in chemotherapy. There is also a fear of experiencing negative health consequences and outcomes if no drastic measures are placed to halt these rising trends of resistant pathogen since it implies that as more agents become inactive, patients may be faced with increased morbidity and mortality, increased hospital visits, high treatment cost, increased duration of stay on health facilities, increased economic loss in term of wages and increased environmental problems in the region.

CONCLUSION

Many treatment guidelines and authors have suggested that fluoroquinolones be reserved when dealing with the routine treatment of uncomplicated UTI so as to safeguard the occurrence of resistances against them. Co-trimoxazole is still the preferred

choice for this purpose in many regions where their resistances have not exceeded 10-20%. But previous report of co-trimoxazole activities against *E. coli* and other pathogens isolated from many infectious sites in the region have shown values as high as 80-100% resistances (Ohieku and Nnolim 2010a, 2010b; Ohieku *et al*., 2010a, 2010b) making the agent to have little or no chemotherapeutic relevance in clinical practice in the region. The worries today are that the fluoroquinolones which now serve as the alternative agents in the region are fast losing their clinical application and rapidly following similar trends with agents that have lost their chemotherapeutic relevance. It is hopeful that appropriate antibiotics policies will be of immense therapeutic benefits in the region.

The worries today are that the fluoroquinolones which now serve as the alternative agents in the region are fast losing their clinical application and rapidly following similar trends with agents that have lost their chemotherapeutic relevance.

This underscores the need for immediate local antibiotic policies. We also suggest that it is time to introduce other quinolones that are effective, safe, and affordable in the region since the currently available agents appeared to have been over used leading to increasing resistance and limited empiric application.

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