

## CIPROFLOXACIN RESISTANCE AMONG MEMBERS OF ENTEROBACTERIACEAE FAMILY IN LAFIA, NASARAWA STATE, NIGERIA

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### ABSTRACT

Ciprofloxacin is known to be a very effective and a commonly used drug in the treatment of Enterobacteriaceae infections, an increasing trend of resistance to the drug has been noted. This work sought to determine the prevalence of Ciprofloxacin resistance in clinical isolates of some selected members of the Enterobacteriaceae family, and to determine the general degree of susceptibility of some enterobacterial isolates to some other antibiotics. Fifty (50) clinical enterobacterial isolates of *E. coli* (30), *Enterobacter* spp (10) and *Proteus* spp (10) were sampled from Agu hospital using purposive sampling technique and subjected to antimicrobial susceptibility test using the agar disc diffusion technique. Prevalence of Ciprofloxacin resistance among the isolates was 16% (8). Three (10%) of *E. coli*, 4 (40%) of *Enterobacter* spp and 1(10%) *Proteus* spp were resistant to Ciprofloxacin. High susceptibility to Ciprofloxacin-resistant isolates was demonstrated with Ampicillin (87.5%), to a lesser degree 62.5% with Gentamicin and Nalidixic acid and moderately 50.0% for Peflaxine. This suggests that frequent exposure to antibiotics is a major predisposing factor for resistance and there are indications of their spread among other species other than *E. coli*, *Enterobacter* and *Proteus*.

**Keywords:** Ciprofloxacin, resistance, enterobacteriaceae and antibiotics.

### INTRODUCTION

Ciprofloxacin is known to be a very effective and a commonly used drug in the treatment of enterobacterial infections. However, an increasing trend of resistance to the drug has been noted (Lautenbach et al., 2002). Consequently this resistance leads to failure in treatment. Antimicrobial resistance result in increased morbidity, mortality and cost of health care (David et al., 1997). With respect to the problem of increasing Ciprofloxacin resistance, physicians need to be practically informed of the possibility of treatment failure when prescribing Ciprofloxacin for infections due to members of the Enterobacteriaceae.

Ciprofloxacin is a broad spectrum antibacterial agent which was brought to medical light as a result of the therapeutic advance of the 1980s (David et al., 2002). It is a fluoroquinolone which has a hundred fold greater antimicrobial activities than its parent compound, Nalidixic acid. The drug is highly active against members of the Enterobacteriaceae, such as *E. coli*, *Klebsiella* spp, *Enterobacter* spp, *Proteus* spp, *Salmonella* spp, *Shigella* spp, *Yersinia* spp, *Serratia* spp, and *Erwinia* spp, (Patrick et al., 1995). These microorganisms are aetiological agents of gastrointestinal tract, urinary tract, skin and respiratory tract infections (Prescott et al., 2002). It is known that members of the Enterobacteriaceae family are associated with serious health problems in plants, animals and humans (Prescott et al., 2002). Although medical effort by means of chemotherapy has been continually used to provide treatment for infections caused by members of Enterobacteriaceae family, but some of these microorganisms are increasingly becoming resistant to several antimicrobial agents (Patrick et al., 1995).

Resistance to Ciprofloxacin was largely due to the fact that resistance *E. coli* mutants are difficult to be selected in vitro and plasmid-mediated resistance to the quinolone was unknown even after 30 years of Nalidixic acid usage (David et al., 2002). Recently, Enterobacteriaceae members with multiple mutations that diminish the affinity of DNA gyrase and topoisomerase IV target as well as plasmid-mediated resistance to the quinolone (of which Ciprofloxacin is the most active) have been reported (Linda et al., 1998), with mechanisms of resistance being the acquisition of new genes and

chromosomal changes in DNA gyrase. Cases of resistance of Ciprofloxacin have been reported from various parts of the world. In the Netherlands, the incidence of ciprofloxacin resistance *Enterobacter cloacae* and *E. coli* increased from <0.5% to 2.7% and <0.5% to 64.0% respectively from 1996 to 1999 (Alex et al., 2001). In England, an increased from 7.0% to 14.0% of resistance to ciprofloxacin was observed in a multi-resistant *Salmonella typhimurium* (Threlfall et al., 1997). In Nigeria, 21.7% resistance rate was reported by Daini et al. (2005) from Ibadan. Okoli, (2006) reported 10.5% Ciprofloxacin resistance by *Escherichia coli* from Imo state, Nigeria.

This work was aimed to determine the prevalence of Ciprofloxacin resistance in clinical isolates of some selected members of the Enterobacteriaceae family, and to determine the general degree of susceptibility of some enterobacterial isolates to some other antibiotics.

**MATERIALS AND METHODS**

**Sample Collection:** A total of 50 clinical isolates were obtained from the Agu Hospital, Lafia in Nasarawa State. The isolates consisted of the following members of Enterobacteriaceae: *Escherichia coli* (30 isolates), *Enterobacter spp* (10 isolates) and *Proteus spp* (10 isolates). The isolates were then subjected to antimicrobial susceptibility test.

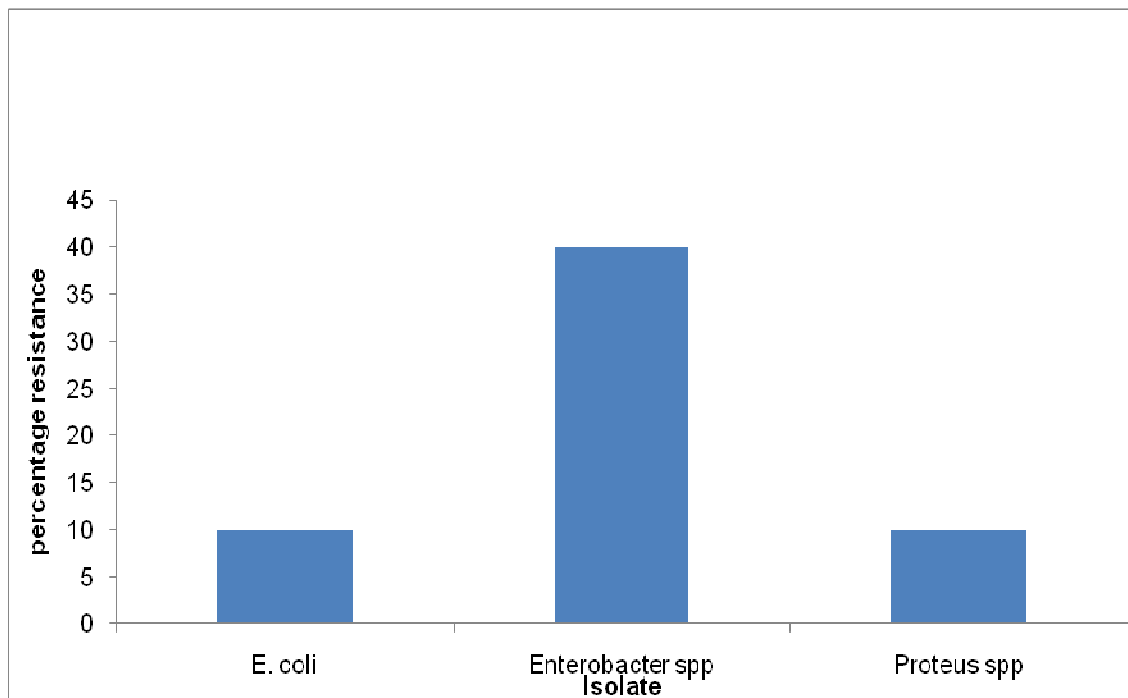
**Antimicrobial Susceptibility Test:** The isolates were screened for antimicrobial susceptibility, using the agar disk diffusion method by Kirby-Bauer, (1966), according to the guidelines recommended by the CLSI (2005). The surface of agar plates were uniformly streaked with the test organisms. Disc impregnated with known concentration of antimicrobial agents were then placed on the plates using a pair of sterile forceps. The plates were incubated aerobically at 37 °C for 24 hours. Susceptibility data were determined by measuring the diameters of the zones of inhibition to the nearest whole millimeter, using a transparent ruler according to the interpretation chart of the Kirby-Bauer sensitivity test method (Prescott et al., 2002; Okoli, 2006). The zones were interpreted as resistant or sensitive.

The following discs (Optun laboratories) containing specific concentrations of antibiotics were used: Ampicilin (30 mcg), Augmentin (30 mcg), Ceporex (10 mcg), Gentamicin (10 mcg), Ciprofloxacin (10 mcg), Nalidixic acid (30 mcg), Septrin (30 mcg), Streptomycin (30 mcg), Peflacin (10 mcg) and Tarivid (10 mcg) respectively.

**RESULTS AND DISCUSSION**

Out of the isolates 50 enterobacterial isolates tested, 3 (10%) of *E. coli*, 4 (40%) of *Enterobacter spp* and 1 (10%) of *Proteus spp* were resistant to Ciprofloxacin as seen in Figure 1 below

**Figure I.** Percentage resistance of Enterobacterial isolates to Ciprofloxacin



A total of 8 (16%) of the isolates tested were resistant to Ciprofloxacin. Further details are presented below.

**Table 1.** The invitro antimicrobial susceptibility pattern of three members of Enterobacteriaceae to ciprofloxacin

Isolate	No. of isolates tested	No. Sensitive	No. Resistant
Escherichia spp	30	27 (90%)	3 (10%)
Enterobacter spp	10	6 (60%)	4 (40%)
Proteus spp	10	9 (90%)	1 (10%)
Total	50	42 (84%)	8 (16%)

Among the other antimicrobial agents tested, 16 (32%) of the 50 isolates were sensitive to Streptomycin, 26 (52%) to Peflacin, 23 (46%) to Septrin, 34 (68%) to Ampicillin, 19 (38%) to Tarivid, 16 (32%) to Ceporex, 27 (54%) to Gentamicin, 19 (38%) to Augmentin and 28 (56%) were sensitive to Nalidixic acid as seen in table 2 below

**Table 2.** An invitro susceptibility pattern of Enterobacteriaceae isolates to nine antibiotics.

Isolates No.	Streptomycin	Peflacin	Septrin	Ampicillin	Tarivid	Ceporex	Gentamicin	Augmentin	Nalidixic acid
<i>E. coli</i> (30)	10 (33%)	15 (50%)	12 (40%)	18 (60%)	8 (26%)	7 (23%)	18 (60%)	5 (16%)	16 (53%)
<i>Enterobacter spp.</i> (10)	2 (20%)	3 (30%)	8 (80%)	9 (90%)	4 (40%)	3 (30%)	7 (70%)	6 (60%)	7 (70%)
<i>Proteus spp.</i> (10)	4 (40%)	8 (80%)	3 (30%)	7 (70%)	7 (70%)	6 (60%)	2 (20%)	8 (80%)	5 (50%)
Total 50	16 (32%)	26(52%)	23 (46%)	34 (68%)	19 (38%)	16 (32%)	27 (54%)	19 (38%)	28 (56%)

The antimicrobial susceptibility pattern of the Ciprofloxacin-resistant *Enterobacteriaceae* isolates were as follows; 3 (37.5%) of the isolates were resistant to Streptomycin, 4 (50%) to Peflacin, 2 (25%) to Septrin, Gentamicin, Augmentin and Tarivid, 7 (87.5%) to Ampicillin, 5 (62.5%) were resistant to Ceporex and Nalidixic as shown in table 3.

**Table 3.** An invitro Antimicrobial susceptibility pattern to ciprofloxacin- resistant Enterobacteriaceae

Isolates	Resistance number	STREPTOM -YCIN	Peflacin	Septrin	Ampicillin	Tarivid	Ceporex	Gentamicin	Augmentin	Nalidixic
<i>E. coli</i>	3	2 (66.7%)	1 (33.3%)	0 (0.0%)	3 (10.0%)	0 (0.0%)	2 (66.7%)	0 (0.0%)	2 (66.7%)	2 (66.7%)
<i>Enterobacter spp.</i>	4	1 (25.0%)	2 (50.0%)	1 (25.0%)	3 (75.0%)	2 (50.0%)	2 (50.0%)	1 (25.0%)	0 (0.0%)	3 (75.0%)
<i>Proteus spp.</i>	1	0 (0.0%)	1 (100%)	1 (100%)	1 (100%)	0 (0.0%)	1 (100%)	1 (100%)	0 (0.0%)	0 (0.0%)
Total	8	3 (37.5%)	4 (50%)	2 (25%)	7 (87.5%)	2 (25%)	5 (62.5%)	2 (25%)	2 (25%)	5 (62.5%)

A prevalence of 16% resistance was recorded for ciprofloxacin in this study. This result differs significantly from the finding of Daini et al. (2005) who obtained a higher resistance of 21.7% among some isolates of Enterobacteriaceae

in Ibadan, Nigeria. These variations could probably be due to the difference in drug exposure as well as patients attitude toward drugs. However, the resistance obtained for *E. coli* in this study was 10%, which is in consonance with the findings of Okoli (2006), who recorded a prevalence of 10.5% resistance among some isolates of *E. coli* in Imo state, Nigeria. The Ciprofloxacin resistance among members of the Enterobacteriaceae family tested were in the order; *Enterobacter* spp > *E. coli* > *Proteus* spp. Resistance was expected to be very low in gentamicin, ampicillin and augmentin, as these drugs are known to be effective against the Enterobacteriaceae members. However, significant resistance was displayed to these drugs as 46%, 32% and 62% respectively. This finding may probably be attributed to frequent exposure to these antimicrobial agents.

Ciprofloxacin-resistant isolates showed significantly higher resistance to Ampicillin (87.5%), slightly high to Ceporex (62.5%) and Nalidixic acid (62.5%) and moderately resistant to Peflacin (50%). This may likely be linked to indiscriminate use of the antimicrobial agents. High instances of resistance recorded in this study were because it was in an urban area, suggesting frequent exposure and indiscriminate use of these drugs as a major predisposing factor for resistance. Resistance was found to be relatively low in Streptomycin (37.5%), Septrin (25%), Tarivid (25%), Gentamicin (25%) and Augmentin (25%) by the Ciprofloxacin-resistant isolates tested. Less exposure to these drugs may account to low resistance, which may be due to discouraged use of the drugs coupled with the intravenously route of administration leading to restriction of indiscriminate use of these antibiotics (Cheesbrough, 2000; Kayser et al., 2005). This shows that ciprofloxacin, streptomycin, peflacin, septrin, Ampicillin, Tarivid, Ceporex, Gentmentin and Nalidixic acid could be used as drugs of choice against infections caused by the three members of Enterobacteriaceae earlier mentioned.

## CONCLUSION

In conclusion, it is significant to mention that prevalence of Ciprofloxacin resistance in clinical isolates of *E. coli*, *Enterobacter* and *Proteus* species is relatively low (16%) compared to 21.7% reported by Daini et al. (2005) in Ibadan, Nigeria. The study has indicated that frequent exposure and indiscriminate use of antimicrobial agents are considered as major predisposing factors for resistance among some members of Enterobacteriaceae in Lafia, Nigeria.

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