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# Prophylactic role of ciprofloxacin and ceftriaxone in prostate biopsy-related infection: randomized comparative study of bacterial spectrum and antibiotic sensitivities

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## Abstract

**Background:** The mainstay for the diagnosis of prostate cancer is transrectal ultrasound-guided prostate biopsy. However, prostate biopsy is associated with a significant risk of complications including urinary tract infection. This study aims to compare the bacterial profile and antibiotic susceptibility pattern in urinary tract infection after prostate biopsy between patients on 2 different antimicrobial prophylactic regimens.

**Methods:** This was a comparative cross-sectional study done at the urology unit of our institution, over 13 months. Fifty-six patients who met the inclusion criteria made up the study population and were randomly assigned to two groups. Those in group 1 (28) received intravenous ciprofloxacin (Juhel) 400 mg at induction of anesthesia, while those in group 2 (28) received intravenous ceftriaxone (Rocephin) 1 g at induction of anesthesia. All patients received bisacodyl (dulcolax) rectal suppositories 20 mg nocte starting 2 nights before the procedure as well as intravenous metronidazole (Juhel) at induction of anesthesia. Urine samples were taken for urine culture and sensitivity three days after biopsy. Isolated organisms and their antibiotics sensitivities were documented. Statistical analysis was done using SPSS version 21.0 with the level of significance set at  $P < 0.05$ .

**Results:** In group 1 the prevalence of urinary tract infection was 61%. *Escherichia coli* was isolated in 11 (64.71%) cases, *Klebsiella species* in 3 (17.65%), *staphylococcus aureus* in 1 (5.88%), *Proteus species* in 1 (5.88%), and non-hemolytic *streptococcus species* in 1 (5.88%). In this group, all isolated bacterial organisms were resistant to ciprofloxacin. In group 2 the prevalence of urinary tract infection was 43%. *Klebsiella spp* was isolated in 6 (50%) cases, *Pseudomonas aeruginosa* in 3 (25%), *E. coli* in 2 (16.67%), *Staphylococcus* in 1 (8.33%). In group 2 all isolated bacterial organisms were resistant to ceftriaxone.

**Conclusion:** Ciprofloxacin and ceftriaxone are both associated with a high rate of urinary tract infection when used as prophylaxis for prostate biopsy. The bacterial etiology of prostate biopsy-related urinary tract infection is dependent on the prophylactic antibiotics used. Based on the high rate of urinary tract infection associated with the use of either ciprofloxacin or ceftriaxone, we recommend a combination of both drugs as prophylaxis for prostate biopsy.

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**Keywords:** Prostate biopsy, Fluoroquinolone resistance, Post-biopsy urine culture

## 1 Background

Prostate cancer is a major health concern world over, being the second most common neoplasm in men and the sixth commonest cause of cancer-related death in the entire world [1]. It is the most common non-cutaneous cancer detected among men [2]. In Nigeria earlier study put the hospital incidence and annual death rate at 127/100,000 and 20,000, respectively [3].

Transrectal ultrasound (TRUS)-guided prostate biopsy is the gold standard technique for prostate cancer diagnosis and among the commonest procedure performed by urologists. However, in our facility digitally guided prostate biopsy is still widely practiced due to the non-availability of rectal ultrasound probes. Extended-core protocol is currently the recommended technique for prostate biopsy, and this involves taking 10–12 cores [4]. A Nigerian study has shown that 10-core biopsy protocol improves cancer detection without increasing the rate of complication [5]. Prostate biopsy is indicated in men with raised serum levels of prostate-specific antigen (PSA), an abnormal digital rectal examination (DRE), or a combination of the two [2].

Complications are common following transrectal prostate biopsy occurring in up to 70% of patients undergoing this procedure though most are minor [6]. These complications could be traumatic (hematuria, hematochezia, hematospermia) or infective (fever, urinary tract infection, or septicemia). Earlier studies in Nigeria had noted infective complications to occur in 3.8 to 19% of cases [7–10].

To reduce infective complications antibiotic prophylaxis is recommended for all patients going for prostate biopsy [11]. This is based on the fact that 16 to 100% of cases of biopsies without antibiotic prophylaxis present with either asymptomatic bacteriuria or transient bacteremia, increasing the risk for complications such as urinary tract infections, sepsis, and Fournier's gangrene [11]. The antibiotics for prophylaxis should have activity for bacteria from the flora of the skin, rectum, and genitourinary tract. Aerobic and anaerobic organisms are commonly introduced into the prostatic tissue and blood when performing transrectal biopsies; therefore, drugs used for prophylaxis must have activity against both aerobic and anaerobic organisms. The most common organisms are the gut commensals, viz. *Escherichia coli*, *Streptococcus faecalis*, and *Bacteroides species* [12]. It has been reported that the causative pathogen in urinary tract infection after a transrectal

prostate biopsy was mainly *E. coli* with a high resistance rate to fluoroquinolones [13]. The widespread use of fluoroquinolones to treat urinary tract infections has increased the rate of fluoroquinolone-resistant *E. coli*. Given this rising resistance of *E. coli* to fluoroquinolones, there is a need to try other antibiotics with good activity against expected bacteria flora encountered during prostate biopsy.

The aim of this study was to compare the bacterial profile and antibiotic susceptibility pattern in urinary tract infection after prostate biopsy between patients on 2 different antimicrobial prophylactic regimens.

## 2 Methods

This was a comparative cross-sectional study done at the urology unit of a tertiary hospital, over 13 months (April 2019–April 2020). A sample size of 56 was determined using Fisher's formula,

$$nf = n/(I + n/N)^{14}$$

where  $nf$  = desired sample size when the population is < 10,000,  $n$  = desired sample size when the population is > 10,000,  $N$  = estimated population size. In FETHA, the urology units do an average of 8 cases of prostate biopsies per month (unpublished data from the hospital). So in one year, the estimated population size is 96.

$$n = 2Z^2pq/d^2.$$

where  $Z$  = standard normal deviation, usually at 1.96 (95% confidence level),  $P$  = prevalence. According to a study done by Stephen Odunayo Ikuero et al. in Lagos Nigeria, the prevalence rate of cancer of the prostate is 1.046% [15].

Inclusion criteria were elevated prostate-specific antigen (PSA) level greater than 4 ng/ml, abnormal digital rectal examination (DRE), or elevated PSA and abnormal DRE. Excluded from the study were patients with symptomatic urinary tract infection or suspected prostatitis, diabetics with poor glycemic control, those with acquired immunodeficiency syndrome, those with hypersensitivity to ciprofloxacin or ceftriaxone, and patients on a urethral catheter.

Ethical approval was obtained from the ethics committee of our institution, and written informed consent was obtained from each patient.

The patients were randomly assigned to two groups. Those in group 1 (28) received intravenous ciprofloxacin (Juhel) 400 mg at induction of anesthesia, while those in group 2 (28) received intravenous ceftriaxone (Rocephin)

1 g at induction of anesthesia. Patients in both groups received bisacodyl (dulcolax) rectal suppositories 20 mg nocte starting 2 nights before the procedure as well as intravenous metronidazole (Juhel) at induction of anesthesia.

All patients included in the study had pre-biopsy-negative urine culture results. The patients underwent digitally guided 10-core transrectal prostate biopsy on an out-patient basis. The procedure was performed using a semiautomatic 18G, spring-loaded biopsy needle device (AUTO-CUT/Egemen). The procedures were performed in the day-case theater by a single urologist with the patient in the left lateral position under low-dose saddle block [16]. The benefits of saddle block include: good anesthesia, paralysis of the anal sphincter, absence of lower limb paralysis, or appreciable drop in systolic blood pressure [16]. This technique is, therefore, ideal for day-case procedure but requires the services of an anesthetist. Local peri-prostatic block unlike saddle anesthesia does not require the services of an anesthetist, but is not feasible in our facility because the procedure requires a transrectal probe which we currently do not have.

Urine samples were taken for culture and sensitivity three days after the biopsy. During the outpatient visit on the third day after the biopsy, a clean catch mid-stream urine sample was collected and sent to the microbiology laboratory within 30 min. The samples were inoculated on blood agar for colony counting and MacConkey agar for cultural characteristics. Antimicrobial susceptibility testing was done on Mueller–Hinton agar according to clinical laboratory standard institute (CLSI) [17]. Positive urine culture refers to colony count of > 100,000 colony-forming units (CFU) /ml [18]. Isolated organisms and their antibiotic sensitivities were documented. Data obtained from the study were analyzed using Statistical Package for Social Sciences (SPSS) version 21. The mean differences between continuous variables were compared using independent Student’s t test or Mann–Whitney test depending on whether variables are normally distributed or not. Associations between categorical variables were tested using Fisher’s exact test. The level of significance was set at  $P < 0.05$ .

### 3 Results

Comparison of the mean for age, the median for prostate volume, and PSA between the two groups showed no statistically significant difference (Table 1).

The prevalence of urinary tract infection was 61% in group 1 and 43% in group 2; however, this difference in infection rate was not statistically significant (Table 2). In group 1 *Escherichia coli* was isolated in 11(64.71%) cases, *Klebsiella species* in 3(17.65%), *staphylococcus aureus* in 1(5.88%), *Proteus species* in 1(5.88%), and non-hemolytic *streptococcus species* in 1(5.88%) (Table 3 and Fig. 1). In this group, all isolated bacterial organisms were resistant to ciprofloxacin (Table 3). All isolated organisms in this group were, however, sensitive to either cephalosporins (ceftriaxone, cefpodoxime, ceftazidime) except in three instances. Two out of the eleven (18.8%)-isolated *E. coli* were resistant to these cephalosporins, while one out of the three (33.33%) cases of *Klebsiella spp* was resistant to cephalosporins. Therefore, 82.35% of organisms isolated in this group were sensitive to cephalosporin.

In group 2 *Klebsiella spp* was isolated in 6(50%) cases, *Pseudomonas aeruginosa* in 3(25%), *E. coli* in 2(16.67%), *Staphylococcus* in 1(8.33%) (Table 4 and Fig. 1b). In group 2 all isolated bacterial organisms were resistant to ceftriaxone (Table 4). In half (50%) of the cases where *Klebsiella spp* were isolated, this organism was resistant to all antibiotics except meropenem (Table 4). In two out of 3 instances (66.66%) where *Pseudomonas aeruginosa* was isolated, this organism was resistant to all antibiotics used including imipenem and meropenem (Table 4). The remaining isolated organisms were sensitive to

**Table 2** Chi-square test analysis showing the level of association in the presence of positive post-biopsy urine culture between group 1 and group 2

	n (%)		X <sup>2</sup>	P-value
	Group 1	Group 2		
Positive urine culture				
Yes	17 (61)	12 (43)	1.788	0.181
No	11 (39)	16 (57)		

**Table 1** The comparison of mean for age, median for prostate volumes, and serum PSA between the two groups

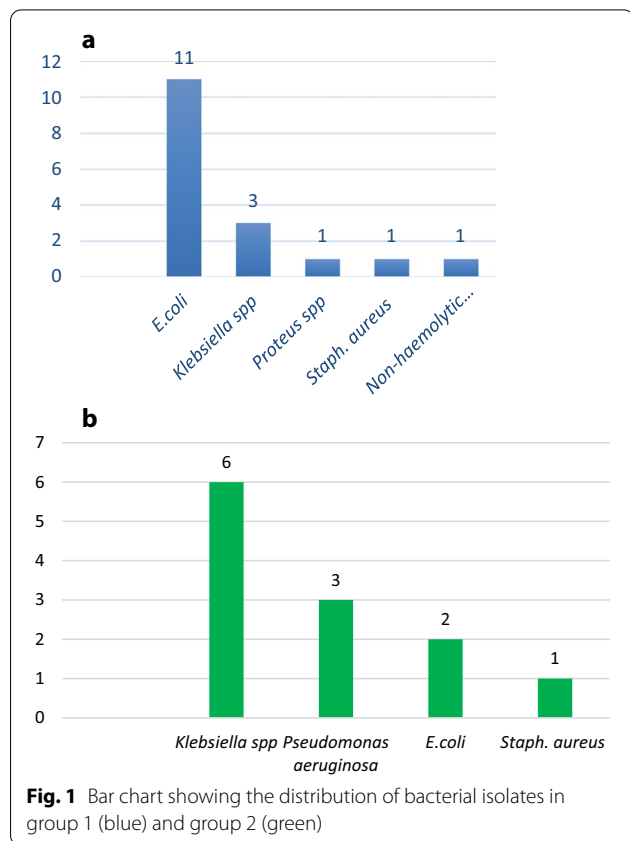
Variable	Group 1 (n = 28) Mean ± SD	Group 2 (n = 28) Mean ± SD	t-value	P-value
Age (years)	70.32 ± 9.02	73.25 ± 8.79	– 1.230	0.224
Variable	Group 1 (n = 28) (Mean rank)	Group 2 (n = 28) (Mean rank)	z-value	P-value
PSA (ng/ml)	27.36	29.64	– 0.524	0.600
Prostate Volume (ml)	31.66	25.34	– 1.450	0.147

**Table 3** Bacterial isolates in group 1 and antibiotic sensitivity pattern from urine culture

Cultured organism	Frequency	Sensitive antibiotics	Resistant antibiotics
<i>E. coli</i>	11	Cefpodoxime, ceftriaxone, nitrofurantoin, ceftazidime, gentamicin, augmentin, cefepime, piperacillin + tazobactam	Levofloxacin, ofloxacin, ciprofloxacin, Ceftazidime, ceftriaxone, Cefuroxime
<i>Klebsilla spp</i>	3	Cefpodoxime, ceftriaxone, cefoxitin, cefpodoxime, gentamicin, augmentin	Levofloxacin, ofloxacin, ciprofloxacin, nitrofurantoin, Ceftriaxone, ceftazidime
<i>Staphylococcus aureus</i>	1	Cefoxitin, amikacin, ceftriaxone	Ciprofloxacin, levofloxacin, ofloxacin, vancomycin
<i>Proteus spp</i>	1	Ceftriaxone, nitrofurantoin, imipenem, meropenem	Ciprofloxacin, levofloxacin, gentamicin
Non-hemolytic strep	1	Ceftriaxone, erythromycin	Levofloxacin, ampicillin, ciprofloxacin

**Table 4** Bacterial isolates in group 2 (test group) and antibiotic sensitivity pattern from urine culture

Cultured organisms	Frequency	Sensitive antibiotics	Resistant antibiotics
<i>Klebsiella spp</i>	6	Ceftazidime, cefepime, gentamicin, meropenem	Augmentin, ceftriaxone, levofloxacin, ciprofloxacin, ceftriaxone, ofloxacin,
<i>Pseudomonas aeruginosa</i>	3	None	Augmentin, ceftriaxone, levofloxacin, ciprofloxacin, ceftriaxone, ofloxacin, meropenem, cefepime, ceftazidime, cefoxitin
<i>E. coli</i>	2	Augmentin, ceftazidime,	Cefoxitin, ofloxacin, cefuroxime, cefepime, ceftriaxone, gentamicin, ciprofloxacin,
<i>Staph. Aureus</i>	1	Ciprofloxacin, levofloxacin, amoxicillin, erythromycin, gentamicin	Ceftriaxone



ceftazidime, cefepime, augmentin, gentamicin, meropenem, imipenem, ciprofloxacin, and levofloxacin (Table 4).

**4 Discussion**

Several approaches have been employed by urologists in an attempt to reduce prostate biopsy-related infection. Key among these approaches is the use of prophylactic antibiotics which is a standard recommendation for all patients undergoing prostate biopsy. This is based on the fact that 16 to 100% of cases of biopsy without antibiotic prophylaxis presented with either asymptomatic bacteriuria or transient bacteremia, increasing the risk for complications such as urinary tract infections, sepsis, and Fournier’s gangrene [11]. *Escherichia coli* (*E. coli*) is the commonest pathogen implicated in post-TRUS biopsy sepsis, accounting for 75–90% infective complications in published series [16, 19]. However, the rate of fluoroquinolone resistance in prostate biopsy-related infection is worrisome as previous studies have shown that the rate of fluoroquinolone-resistant *E. coli* in the post-biopsy bloodstream and urine infections was 62% and 88%, respectively [19, 20]. Consequently, the use of fluoroquinolone antimicrobial as prophylaxis before a prostate biopsy is a significant risk factor for subsequent *E. coli* infection [21, 22].

In our center ciprofloxacin with metronidazole has been the standard of care for prophylaxis during prostate biopsy. However, based on the reports of increasing resistance to fluoroquinolone we introduced ceftriaxone and metronidazole as prophylactic antibiotics.

Positive post-biopsy urine cultures were identified in 17(60.71%) patients in group 1, and all the isolated organisms in this group were resistant to ciprofloxacin the prophylactic antibiotics used. The commonest offending organism is *E. coli* with 100% resistance to ciprofloxacin. This observation was similar to earlier reports by Williamson et al., Marino et al., and Williamson et al. [16, 19, 20] and also support the suggestion that the use of fluoroquinolone for prophylaxis in prostate biopsy is a risk factor for subsequent *E. coli* infection [21, 22].

Of note in this study is the fact that 82.35% of cultured organisms in group 1 were sensitive to ceftriaxone. This is fairly high and therefore ceftriaxone may be used for empiric treatment of post-prostate biopsy UTI caused by *E. coli*. This observation is in agreement with the suggestion by Lee et al. that fluoroquinolone-resistant *E. coli* is susceptible to ceftriaxone [23].

Positive post-biopsy urine cultures were identified in 12(42.86%) patients in group 2, with all the isolated organisms being resistant to ceftriaxone the prophylactic antibiotic used. In this group (Table 4 and Fig. 1) the most commonly isolated organism was *Klebsiella* species (6/50%); this differed from earlier studies that cited *E. coli* as the commonest organism causing post-prostate biopsy infection [10, 16, 19, 24]. Though group 2 patients had fewer positive urine cultures result (12) compared to group 1 (17), the difference was not statistically significant ( $P=0.181$ ).

Forty-one percent (41%,5/7) of the isolated organisms in group 2 were resistant to at least 3 different antimicrobial classes and therefore are multi-drug resistant [25]. Fifty percent (3/6) of *Pseudomonas spp* cultured and 66.66% of *Klebsiella spp* cultured belonged to this category. The cultured organisms were similar between the 2 groups; however, the prevalence of the offending organisms differed. In group 1, the most commonly isolated organism was *E. coli*, while in group 2 the most commonly isolated organism was *Klebsiella spp*. This is most likely due to the varying susceptibility of the cultured organisms to the different prophylactic antibiotics used in the respective groups. A critical look at the prevalence of organisms cultured in the two groups (Fig. 1) will suggest that ceftriaxone has greater activity against *E. coli* and was able to reduce infection by this organism to 16.67% of the total in group 2, while ciprofloxacin has greater activity against *Klebsiella spp* and was able to keep infection by this organism to 17.65% of the total.

A look at Table 3 showed that all isolated organisms except three *E. coli* isolates were sensitive to a cephalosporin (ceftazidime, cefuroxime, or ceftriaxone); therefore, a combination of cephalosporin, e.g., ceftazidime and ciprofloxacin, would have reduced positive urine culture in this group to 3 out 28 (10.71%). Similarly, a look at Table 4 showed that all the isolated organisms except one (*Pseudomonas spp*) were sensitive to ceftazidime or a fluoroquinolone (ciprofloxacin/levofloxacin). Therefore, a combination of ceftazidime and ciprofloxacin would have reduced positive urine culture in this group to 1 out 28 (3.57%). This observation is supported by prior studies that suggested the use of augmented antimicrobial prophylaxis for prostate biopsy. Described augmented regimens include the addition of a second antimicrobial such as gentamicin, cephalosporin, or piperacillin/tazobactam to a fluoroquinolone [26]. One American study had demonstrated the place of augmented prophylaxis by showing that single-agent antimicrobial prophylaxis including ciprofloxacin, ceftriaxone, or augmentin was associated with significantly more infections than ciprofloxacin plus an additional agent such as ceftriaxone [19]. This assertion is demonstrated in the present study using ciprofloxacin and ceftriaxone with a 60.7% and 43% prevalence of post-biopsy UTI, respectively.

## 5 Conclusions

Ciprofloxacin and ceftriaxone are both associated with a high rate of urinary tract infection when used as prophylaxis for prostate biopsy. The bacterial etiology of prostate biopsy-related urinary tract infection is dependent on the prophylactic antibiotics used.

### Abbreviations

DRE: Digital rectal examination; *E. coli*: Escherichia coli; PSA: Prostate-specific antigen; SPP: Species; SPSS: Statistical Package for Social Sciences; TRUS: Transrectal ultrasound; UTI: Urinary tract infection.

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None.

### Authors' contributions

CO and ENA participated in conceptualization of the work, carried out acquisition, analysis, interpretation of data, and drafted the first manuscript. CAO, AOO, TUM, and EAO reviewed the data analysis and contributed to subsequent drafts of manuscript. CJO, UUN, AOU participated in literature search, reviewed the analysis, and critically revised the manuscript. All authors read and approved the final manuscript.

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### Availability of data and materials

Primary data are available in a secured storage.

## Declarations

### Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of Alex-Ekwueme Federal University Teaching Hospital, Abakaliki, Ebonyi State. Ethical approval number is FETHA/REC/VOL 2/2018/059. A written informed consent was obtained from each patient included in the study.

### Competing interests

All authors have no competing interest.

### Consent for publication

Not applicable.

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