



## **Rectal Swabs Demonstrate High Levels of Ciprofloxacin Resistant *Escherichia coli* among Patients Undergoing Prostate Biopsies in San Fernando, Trinidad and Tobago**

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### **Authors' contributions**

*Authors SP and RS designed the study, wrote the protocol, and wrote the first draft of the manuscript. All authors managed the analyses of the study. Authors RS and SP managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Objectives:** To establish the prevalence of ciprofloxacin resistant *Escherichia coli* in the fecal carriage of patients undergoing trans-rectal ultrasound (TRUS) guided prostate biopsy.

**Methodology:** From August 2014 to January 2015, all patients undergoing trans-rectal ultrasound guided prostate biopsy at the San Fernando Hospital had rectal swabbing done. Also, data regarding demographics, recent hospitalization and antibiotic use, prior biopsy, diabetes mellitus and indwelling urinary catheters were prospectively collected. The cultures were incubated in Blood and MacConkey agar and *E. coli* isolates are tested for antibiotic sensitivity using the Kirby-Bauer method and the Microscan automated system. All isolates of *Escherichia coli* were tested for sensitivity to ciprofloxacin and other antibiotics commonly used in urological practice. Patients were followed for 4 weeks post biopsy for complications. Data were recorded in Microsoft Excel and

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analyzed using SPSS version 20.

**Results:** 100 patients had rectal swabs taken, and 70 cultures were positive for *Escherichia coli* with 36 (51%) being resistant to ciprofloxacin and 58% (21/36) of these isolates being multi-drug resistant as defined by resistance to 3 or more classes of antibiotics. Resistance to other antibiotics commonly used in urological practice was also identified: gentamicin 28% (19/67), amoxicillin/clavulanate 34% (24/70), piperacillin/tazobactam 11% (8/70), trimethoprim/sulfamethoxazole 28% (17/61) and ceftriaxone 27% (16/60). There was a trend towards increased resistance among patients with indwelling catheters and recent antibiotic use.

**Conclusion:** There is a high prevalence of ciprofloxacin resistant *Escherichia coli* in the fecal carriage of patients undergoing TRUS guided prostate biopsy and the current prophylaxis policy may need to be revised.

**Keywords:** *E. coli*; Prostate biopsy; rectal swab; Trinidad and Tobago.

## 1. INTRODUCTION

Prostate cancer is a global public health concern and in the Caribbean, mortality rates are the highest in the world [1]. In Trinidad and Tobago, prostate cancer accounts for 38% of cancer related deaths among men (Data – National Cancer Registry). Prostate biopsy is critical in diagnosing prostate cancer and also provides useful prognostic information. It is considered standard of care for biopsies to be done under ultrasound guidance utilizing an extended core template [2].

The San Fernando General Hospital is a tertiary care facility in Southern Trinidad and Tobago with a catchment area of approximately 650,000. The Department of Urology is affiliated with the University of the West Indies and is a Societe Internationale d'Urologie approved training facility. We perform approximately 6-8 prostate biopsies a week. Our current protocol utilizes oral ciprofloxacin as the peri-procedural prophylactic antibiotic of choice. We do not routinely administer enemas. We perform a double sextant pattern of biopsies using an 8 MHz transrectal probe.

Fluoroquinolones are the most commonly prescribed antibiotics for prophylaxis. There has been a temporal rise in the resistance of *E. coli* isolates to fluoroquinolones, coupled with increased post-biopsy infections [3]. This has been attributed to the widespread injudicious use of antibiotics in general medical practice, as well as the agricultural industry. Work at our institution has reported the rate of post biopsy febrile complications of 8% [4] and in this study, we have set about to determine our own rate of ciprofloxacin resistance as the first step to a possible review of our antibiotic protocol.

## 2. MATERIALS AND METHODS

From August 2014 to January 2015, all patients undergoing trans-rectal ultrasound guided prostate biopsy at the San Fernando General Hospital had an anorectal swab taken prior to biopsy. Approval for the study was granted by the institutional Ethics Committee. Data regarding demographics, recent hospitalization and antibiotic use (within the preceding 3 months), prior biopsy, diabetes mellitus and indwelling urinary catheters were prospectively collected.

After informed written consent, patients were placed in the left lateral decubitus position with hips and knees flexed. A cotton tip swab was placed 1½ inch beyond the anal sphincter, rotated 360 degrees and removed. The presence of fecal material on the swab indicated that an adequate specimen was obtained. The specimen was placed in transport medium and sent immediately to the laboratory for processing. The specimens were incubated in Blood and MacConkey agar and bacterial isolates are tested for antibiotic sensitivity (to a panel of 25 antibiotics) using either the Kirby-Bauer disc diffusion method or an automated microbial system (MicroScan, Beckman Coulter). All antimicrobial susceptibility testing and minimum inhibitory concentrations (MICs) were based on the Clinical and Laboratory Standards Institute guidelines. *E. coli* isolates with MIC  $\geq 2$  µg/mL were considered to be resistant to ciprofloxacin. Patients were followed for 4 weeks post biopsy for complications.

Data were recorded in Microsoft Excel and analyzed using SPSS version 20. This study was not powered to determine associations but utilized descriptive statistics.

### 3. RESULTS

The mean age of the study population was 68 years (46-88). During the study period 100 rectal swabs were done of which 70 were positive for *Escherichia coli*. Among the *E. coli* isolates, resistance to ciprofloxacin was recorded in 36 (51%). Overall, 31.4% of *E. coli* isolates were multidrug resistant as defined by non-susceptibility to 3 or more classes of antimicrobials. Of the 36 isolates which were resistant to ciprofloxacin, 21 (58%) were also multidrug resistant while among the 34 isolates which were sensitive to ciprofloxacin, only 1 (3%) was multidrug resistant.

Among commonly used drugs, there was a 34% overall resistance to amoxicillin/clavulanate as well as 28% resistance to gentamicin and trimethoprim/sulphamethoxazole. Overall, resistance was much less common among higher end antibiotics such as the carbapenems. Figs. 1 and 2 summaries overall resistance patterns.

Among ciprofloxacin-resistant isolates, multi-drug resistance was common – 58% were resistant to 3 or more classes of antibiotics. Resistance to antimicrobials commonly recommended as alternatives for prostate biopsy prophylaxis varied from 23% to 94% (Fig. 3).

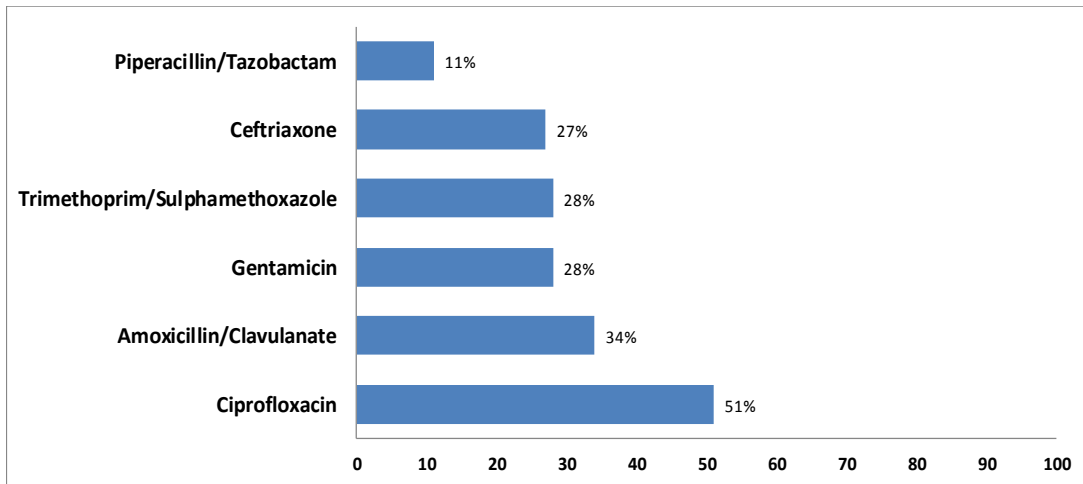


Fig. 1. Resistance patterns of *E. coli* to commonly used antimicrobials

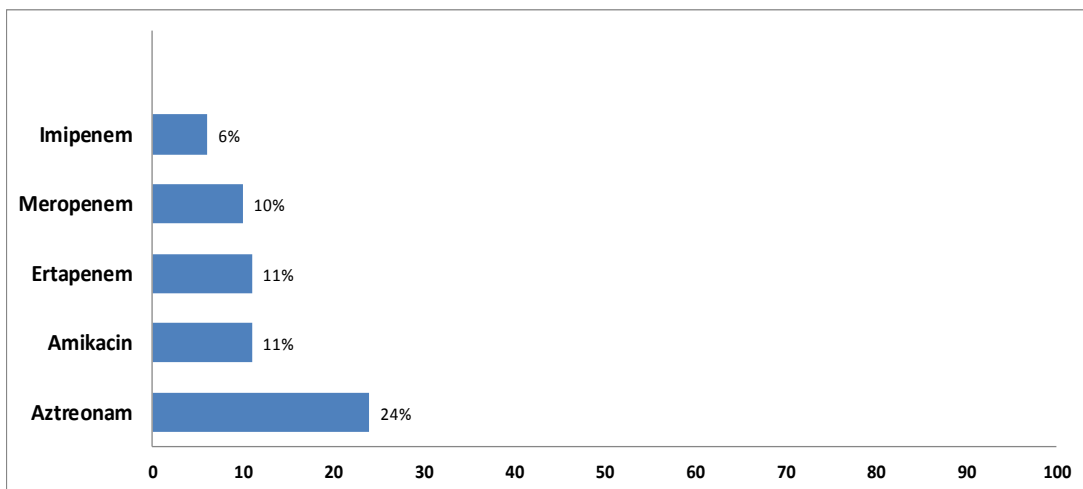
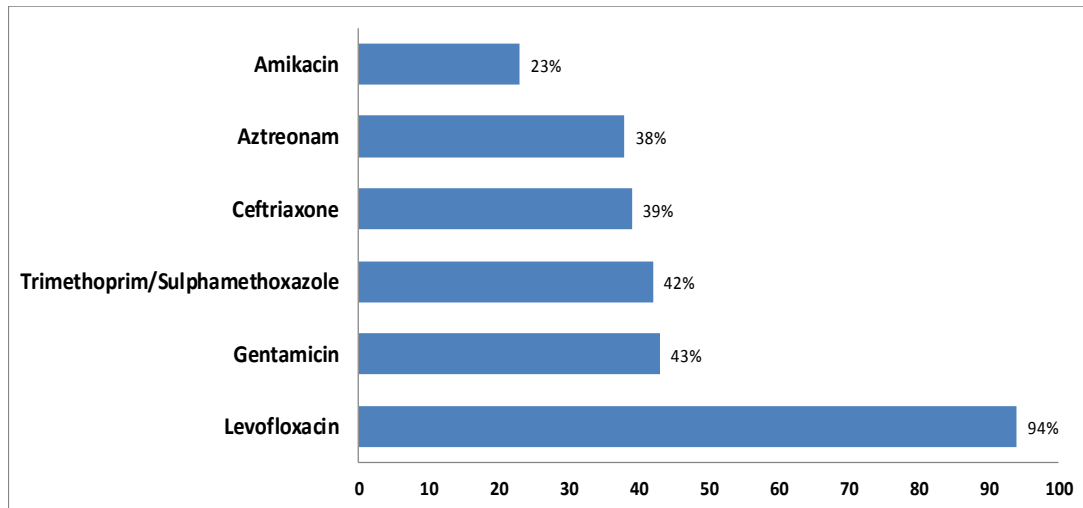


Fig. 2. Resistance patterns of *E. coli* isolates to less commonly used antimicrobials



**Fig. 3. Resistance patterns among ciprofloxacin resistant isolates towards other antibiotics used as alternatives for prophylaxis**

**Table 1. Characteristics of patients harboring *E. coli***

	Total (n/%)	Sensitive (n/%)	Resistant (n/%)
<b>Number of patients</b>	70	34 (48.6)	36 (51.4)
<b>Previous prostate biopsy</b>	13 (18.6)	8 (23.5)	5 (13.9)
<b>Indwelling catheter</b>	9 (12.9)	3 (8.3)	6 (16.2)
<b>Recent antibiotic use</b>	27 (38.6)	10 (29.4)	17 (47.2)
<b>Recent hospitalization</b>	13 (18.6)	6 (17.6)	7 (19.4)
<b>Diabetes mellitus</b>	17 (24.3)	8 (23.5)	9 (25)

Above Table 1 summarizes the characteristics of patients harboring *E. coli*. While this study was not powered to determine associations, there was a trend towards increased resistance among patients with indwelling catheters and recent antibiotic use defined as antibiotics within the last 3 months (Table 1).

There were 5 cases of post biopsy fever among the 70 patients who grew *E. coli* (7.1%) along with sepsis which required hospitalization (1.4%). Of these 6 cases, 50% were ciprofloxacin resistant and 50% ciprofloxacin sensitive.

#### 4. DISCUSSION

Trans-rectal prostate biopsy is an essential component of the management of suspected prostate cancer, but carries the inherent risk of infection. Numerous strategies have been attempted to minimize the risk of post-biopsy sepsis, with the most evidence based being the role of prophylactic antibiotics. Kapoor et al. [5] in

a randomized double-blind controlled trial demonstrated that a single dose of ciprofloxacin administered prior to biopsy reduced the rate of infection to 3% versus 8% in the placebo arm. The American Urological Association (AUA) recommends a single dose of fluoroquinolone, as the agent of choice for the prevention of post-biopsy sepsis, with the caveat that consideration be given to local antibiograms. They further cautioned against using antibiotics for longer than 24 hours [2]. A report on the Global Prevalence Study of Infections in Urology found that worldwide, fluoroquinolones were prescribed to 92.5% of men undergoing prostate biopsies [6].

There has been a temporal rise in the resistance of *E. coli* isolates to fluoroquinolones, coupled with increased post-biopsy infections [3]. This has been attributed to the widespread injudicious use of antibiotics in general medical practice, as well as the agricultural industry. However, urologists are not above reproach. Persaud et al. [7] found that 90% of urologists practicing in the

West Indies used antibiotics much longer than recommend. In fact, contrary to the guidelines, the protocol at our institution includes a 3-day course of ciprofloxacin for prostate biopsy prophylaxis. This has probably contributed to our finding of 51% of *E. coli* isolates being resistant to ciprofloxacin, with many being multi-drug resistant. These results are comparable to other reports from the Caribbean region of high levels of fluoroquinolone resistant bacteria. Hanley et al. [8] reported that 42.8% of uro-pathogenic *E. coli* isolates in St. Kitts were resistant to ciprofloxacin, and Stephenson and Brown [9] found 78% resistant strains in Jamaica.

The AUA White Paper went on to suggested that alternate antimicrobials should be considered if more than 20% of *E. coli* are fluoroquinolone resistant [2]. However, we also found alarmingly high resistance to most of the suggested alternatives, including gentamicin, amoxicillin/clavulanate, trimethoprim/sulfamethoxazole, and ceftriaxone. Only the higher end drugs, including the carbapenems, were found to have acceptable levels of sensitivity. Many centres are utilizing multi-drug prophylaxis, to combat resistance, ensure efficacy and reduce sepsis [10]. While this may be useful in the short term, it has the potential to exacerbate the current global antibiotic resistance crisis. This study would suggest that we should adopt prescription of a carbapenem as routine prophylaxis. Even though Bloomfield et al. [11] reported that using ertapenem for prostate biopsy prophylaxis would not select for carbapenem resistance, their follow up was only for 6 weeks. What will happen after a few years of widespread use, when the bacteria develop increased carbapenem resistance?

It is noteworthy, that not all patients with ciprofloxacin resistant *E. coli* developed infectious complications, and in fact most did not. In our series of 70 patients, we found 7% percent post-biopsy fever in addition to 1 case who was hospitalized for sepsis. These findings were corroborated by Gooden et al. [4] in a larger series at our institution where they found similar rate of hospitalization. Likewise, a Polish study, Adamczyk et al. [12] reported 50.9% ciprofloxacin resistant *E. coli*, and 1% rate of post-biopsy infection. One option is to select at-risk patients for either targeted therapy, or to empirically add another antimicrobial agent to the pre-biopsy preparation. Established risk factors for developing post-biopsy infection and sepsis include diabetes mellitus, previous biopsy, recent

antibiotic use, indwelling catheter, recent travel and hospital workers [3,13]. Due to our small sample size, this study was not powered to provide statistical significance, but we did note trends towards carriage of fluoroquinolone resistant *E. coli* with: an indwelling Foley catheter, recent hospitalization, recent antibiotic use, and diabetes mellitus. Gooden et al. [4] in a study of 233 prostate biopsies at our institution found that diabetes mellitus was a statistically significant risk factor for developing post-biopsy infection.

Recently, there has been a surfeit of studies examining the role of targeted antibiotic prophylaxis for prostate biopsy. Compared to routine empiric approach, the targeted method is more time consuming, costly, and logistically challenging, as it involves extra office visits, rectal swabs, and microbiological culture and sensitivity testing. While it appears logically sound and follows the principles of antibiotic stewardship, there have been contradictory reports of the efficacy of this targeted therapy approach. Singh et al. [14] in a study of 247 Indian men, found ciprofloxacin resistant *E. coli* on 41.7% of the rectal swabs, and using culture directed antibiotic none of these patients developed sepsis. A similar study of 510 men at the Northwestern University, USA did not duplicate these findings [15]. One of the other considerations of the targeted approach is the concern of increased costs. Taylor et al. [16] in a study in Chicago USA, clearly demonstrated that its more cost effective to use the targeted approach, than to treat sepsis following the empiric approach. In their study the incidence of infectious complications was 2.6% in the empirical arm, versus 0% in the targeted arm. We did not attempt to assess costs, though with an infection rate at our institution 3 time that of the Chicago study, it would realistic to assume that a similar cost-effective analysis would favor the targeted approach. We do however acknowledge, that expenses vary across geographic locations and health care models, and a cost analysis at our institution would be warranted to make a definitive pronouncement.

## 5. CONCLUSION

There is a high prevalence of ciprofloxacin resistant *Escherichia coli* in the fecal carriage of patients undergoing TRUS guided prostate biopsy and the current prophylaxis policy may need to be revised.

## CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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