Less is more: single dose versus extended antibiotic prophylaxis for transperineal prostate biopsy

Maxwell Sandberg, MD,[1] Wyatt Whitman, MD,[1] Janmejay Hingu, MD,[1] Parth Thakker, MD,[1] Anita Rong,[2] Caleb Bercu,[2] Jacob Greenberg, MD,[3] Ronald Davis III, MD,[1] Ashok Hemal, MD,[1] Matvey Tsivian, MD[1]

[1]Department of Urology, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, USA
[2]Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA
[3]Department of Urology, Tulane Medical Center, New Orleans, Louisiana, USA

SANDBERG M, WHITMAN W, HINGU J, THAKKER P, RONG A, BERCU C, GREENBERG J, DAVIS III R, HEMAL A, TSIVIAN M. Less is more: single dose versus extended antibiotic prophylaxis for transperineal prostate biopsy. *Can J Urol* 2023; 30(4):11599-11604.

Introduction: *There is an ongoing debate as to the appropriate regimen of antibiotic prophylaxis with transperineal (TP) biopsy. The objective of this study was to report the rate of infection following TP biopsy at a high-volume institution and assess the impact of single dose antibiotics at the time of biopsy versus outpatient antibiotics in preventing postprocedural infections.*

Materials and methods: *Records of men undergoing TP prostate biopsy from 2012 to 2022 were reviewed. Patients were divided into two groups, those who received single dose intravenous (IV) antibiotics at the time of biopsy (n = 440) and those who received both IV antibiotics at the time of biopsy and outpatient antibiotics before/after biopsy (n = 327). Post biopsy infection was defined as at least one of the following: fever (≥ 38.3°C) with/without symptoms of urinary tract infection or positive urine culture (> 105 colony forming units) within 72 hours post biopsy. The rates of infection were compared between the two groups.*

Results: *A total of 767 biopsies were included in the study. Infection rate post TP biopsy was 1.83% (n = 14). The infection rate for patients with single dose prophylaxis was 2.05% (n = 9) and 1.53% (n = 5) for those that received the extended antibiotic regimen. No significant difference in infection rates between the different antibiotic regimens was found (p = 0.597).*

Conclusions: *Overall rates of infection after TP prostate biopsy are very low. Our data indicate that single dose and extended regimen of antibiotic prophylaxis show similar infection rates. These findings support antibiotic stewardship and encourage further research into the appropriate regimen of prophylaxis for TP prostate biopsy.*

Key Words: cancer, prostate, transperineal, biopsy, antibiotics, infection

Introduction

Transperineal (TP) ultrasound guided approach to prostate biopsy is becoming increasingly popular and the technique is well described.[1] As compared to the transrectal (TR) approach for biopsy, TP technique avoids fecal contamination of the sampling needle and thus is believed to have a lower rate of post biopsy infection. Another reason for the expanding popularity of the TP approach is its cancer detection rates that are reported to be potentially superior to the traditional TR biopsy of the prostate.[2-4] Further, and perhaps more importantly, more evidence is evolving that TP biopsy has a low rate of infection and sepsis, especially compared to the TR method, a longstanding issue for men undergoing prostate biopsy.[5,6] Despite suggested lower infection rates, guidelines on antibiotic prophylaxis for men undergoing TP biopsy are not well established.

Emerging evidence suggests that antibiotic prophylaxis may not be required in most men

Accepted for publication July 2023

Address correspondence to Dr. Maxwell Sandberg, 994 W 2nd Street, Unit 386, Winston-Salem, NC 27101 USA

undergoing TP biopsy.[7-9] These data, however, are immature and not universally accepted in clinical practice. Nationally, practice patterns for antibiotic prophylaxis, duration, and agents are not well known. Further, as noted in a recent metanalysis by Basourakos et al, much of the literature on antibiotic prophylaxis for TP biopsy centers around single-arm cohort studies where no antibiotics were used, but there is a paucity of studies comparing different antibiotic regimens against one another.[7] With increased emphasis on antibiotic stewardship and rising prevalence of multi drug resistant organisms, establishing evidence-based guidelines for antibiotic prophylaxis are warranted.

The purpose of this study is to compare infection rates following TP prostate biopsy using single dose perioperative antibiotics at the time of biopsy versus a combination regimen of extended perioperative antibiotics (at the time of biopsy and outpatient).

Materials and methods

We retrospectively reviewed records of patients who underwent TP prostate biopsy at our institution between 2012-2022. Data accuracy was then verified by a second abstractor. Patients were excluded if they had a pre-biopsy positive urine culture (n = 1) or if the TP biopsy was aborted (n = 3). Study design is shown in Figure 1. All TP prostate biopsies were performed under TR ultrasound guidance with sedation or general anesthesia in dorsal lithotomy using a brachytherapy grid template. Patients followed up with their urologist after the procedure in clinic. Antibiotic choice and method of administration (intravenous (IV) versus outpatient) were at the physician's discretion. Patients were divided into two groups for statistical analysis based on the method of antibiotic prophylaxis they received for their TP biopsy. Every patient received a

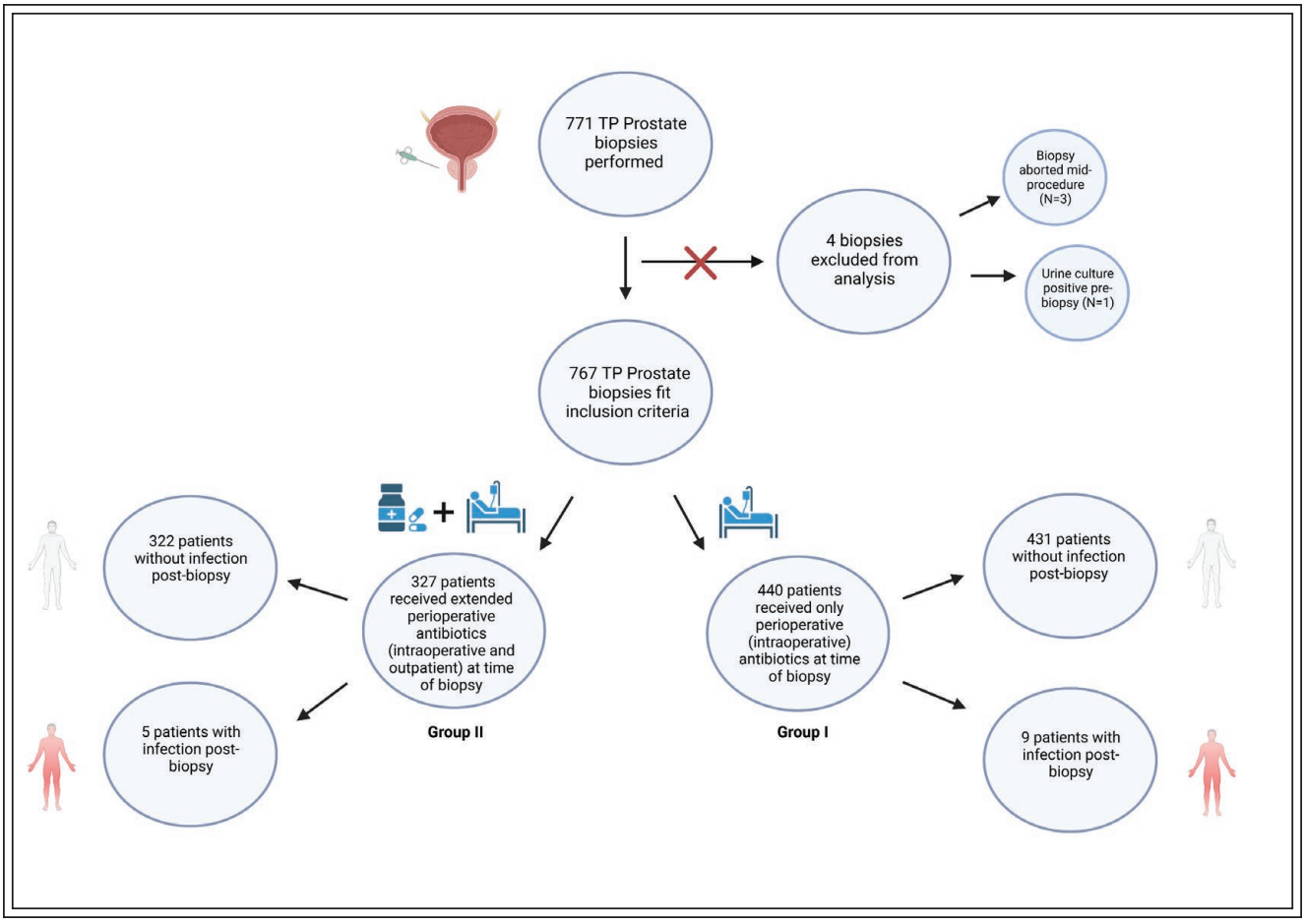

Figure 1. Prism diagram. There were 767 total patients who met the inclusion criteria for this retrospective analysis. From this, patients were divided into either group I (only perioperative antibiotics) or group II (extended perioperative antibiotics). Figure created using BioRender.com

TABLE 1. **Descriptive statistics of the study group**

Variable	Total population	Group I	Group II	p value
# Patients	767	440	327	-
Age	67.5 (61.7-71.8)	67.5 (61.5-72.4)	67.6 (61.7-71.7)	0.924
Body mass index	28.1 (25.2-31.1)	27.9 (25.2-31)	28.3 (25.3-31.4)	0.600
Cores taken	16 (15-19)	16 (14-19)	17 (16-21)	< 0.001
Mean number prior biopsies	0.9 (± 1.1)	0.9 (0.1.1)	0.9 (1.1)	0.301
# Prior positive biopsy	218 (28%)	138 (31 %)	80 (24 %)	0.036
# Active surveillance	260 (33.9%)	150 (341%)	110 (33.6%)	0.896
Mean PSA	3.5 (± 5.7)	3.7 (± 5.0)	3.4 (± 6.1)	0.711
# Infection	14 (1.8%)	9 (2.1%)	5 (1.5%)	0.597

Patient demographic variables are listed on the left. Cohorts are broken down by the total population, group I who only received perioperative antibiotics, and group II who received extended perioperative antibiotics (intraoperatively and outpatient). Variables with '#' are listed as total numbers for each cohort with percentages in parentheses. Mean variables are listed with standard deviation in parentheses. All other variables are medians with interquartile ranges in parentheses.

single dose of perioperative IV antibiotics at the time of biopsy. Upon chart review, a subset of these patients also received extended perioperative antibiotics (at the time of biopsy and outpatient). Group I (IV; n = 440) was defined as patients who received only perioperative antibiotics at the time of TP biopsy and group II (extended regimen; n = 327) received both perioperative antibiotics at the time of TP biopsy and extended perioperative antibiotics outpatient. No discernment was made between those who received

TABLE 2. **Antibiotic usage for transperineal prostate biopsy**

Antibiotic choice	Total population	Group I	Group II		p value
			Intraop	Outpatient	
Ceftriaxone	627 (81.7%)	366 (83.2%)	261 (79.8%)	-	0.194
Cefazolin	104 (13.6%)	56 (12.7%)	48 (14.7%)	-	0.435
Gentamycin	9 (1.7%)	6 (1.4%)	3 (0.9%)	-	-
Ciprofloxacin	8 (1.0%)	2 (0.5%)	6 (1.8%)	257 (78.6%)	-
Piperacillin/tazobactam	1 (0.1%)	1 (0.2%)	0 (0%)	-	-
Clindamycin	2 (0.3%)	1 (0.2%)	1 (0.3%)	-	-
Combination of any 2 antibiotics intraop	16 (2.6%)	8 (1.8%)	8 (2.5%)	-	-
TMP/SMX	-	-	-	68 (20.8%)	-
Ciprofloxacin and TMP/SMX	-	-	-	2 (0.6%)	-

Antibiotic names are listed. Each column is a specific cohort of patients. Group I are those patients that only received perioperative IV antibiotics. Group II patients received extended perioperative antibiotics. P values are comparing the intraoperative antibiotic usage between group I and group II to ensure allotment was similar for the two most used agents. Any column with a '-' means no value existed and/or calculation was done for that antibiotic(s).

outpatient antibiotics before versus after TP biopsy. Moreover, when assigning groups to patients, specific names and classes of antibiotics used were documented but did not affect group assignment.

Infection was defined as least one of the following: fever (≥ 38.3°C) with/without symptoms of urinary tract infection (UTI) or positive urine culture (> 10^5 colony forming units) within 72 hours post biopsy. Demographic and clinical variables were summarized with descriptive statistics in Table 1. This included age, body mass index (BMI), prostate-specific antigen (PSA), cores taken, prior biopsy history, and active surveillance. Specific antibiotics administered were also recorded and listed in Table 2. Demographic and clinical data are presented as median (interquartile range, IQR) and number (percent) unless otherwise specified. Univariate comparisons were performed using t-test and chi-square tests as appropriate. For perioperative antibiotics, only ceftriaxone and cefazolin were included in the final analysis as most patients received one of these IV. Similarly, for outpatient antibiotics only ciprofloxacin and trimethoprim/sulfamethoxazole (TMP/SMX) were included in final analysis as these were the most used agents. All statistical analysis was completed using SPSS v27 (IBM, Chicago, IL, USA).

Results

A total of 767 patients underwent prostate biopsy and were included in this analysis. Every patient (n = 767) received IV perioperative antibiotic prophylaxis. There were 440 patients in group I (single dose) and 327 patients in group II (extended prophylaxis). Groups I and II differed significantly with regards to the number of cores taken at biopsy and history of prior positive biopsy. For the overall cohort, 14 patients had an infection post TP biopsy with an infection rate of 1.8%. Further, for all patients fitting the definition of infection, 7/14 (50%) had a positive urine culture post TP biopsy. Causative agents of infection and antimicrobial resistance profiles are provided in Figure 2. Of all infections, there were 2/14 (0.3%) who required readmission to the hospital for sepsis. Both patients had a positive blood culture and one of these patients also had a concomitant positive urine culture post TP biopsy. Infection occurred in 9 and 5 patients in group I and II, respectively (2.1% versus 1.5%, p = 0.597). No other significant differences between groups I and II were found. Full descriptive statistics are listed in Table 1.

Perioperative antibiotics administered are listed in Table 2. Cefazolin and ceftriaxone were the most common agents used for perioperative IV administration. For patients in the extended perioperative group (group II) most patients received either ciprofloxacin or TMP/SMX orally as their outpatient antibiotics. The type of perioperative IV antibiotic allotment between group I and group II was not significantly different (p = 0.194; p = 0.435). There was also no difference in infection rates between those who received ceftriaxone and those receiving cefazolin IV perioperatively (p = 0.555). Lastly, no difference existed in infection rates within group II (extended perioperative antibiotics) based on whether patients took ciprofloxacin or TMP/SMX as their outpatient antibiotic agent (p = 0.954). Comparison of infection rate based on antibiotic choice both for inpatient and outpatient prophylaxis is shown in Figure 3.

Figure 2. Culture positive bacteria and antibiogram. There were 7 total patients who had a culture positive infection, of which 6 had available data on the infectious microbe and local antibiogram. Each row corresponds to a specific bacterium. For bacteria that were the infectious agent for multiple patients, each color represents a unique patient antibiogram. Check marks represent susceptibility and "X" is resistance. Figure created using BioRender.com

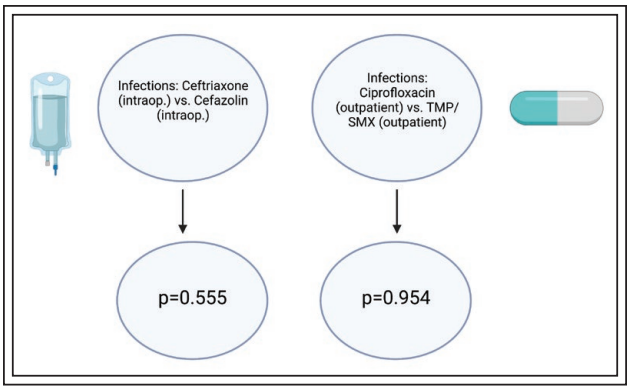

Figure 3. Infection rate based on antibiotic choice. Rate of infection was compared between the two most used IV intraoperative antibiotic agents in the study (left panel). No significant difference in infection rate existed. Rate of infection was also compared between the two most used outpatient antibiotics in the study (right panel). No significant difference in infection existed. Figure created using BioRender.com

Discussion

In this study we examined the differences in infection rates after TP prostate biopsy between single dose and extended antimicrobial prophylaxis and found no significant difference, arguing in favor of limiting the prophylaxis duration. The findings of this study have potential for clinically significant implications for urologists performing TP prostate biopsy. The rate of antibiotic resistant bacteria is rising. A recent study examining UTI and resistant pathogens found that 92% of all urine samples cultured positive for UTI had resistance to at least one antibiotic and 80% were multidrug resistant.[10] The authors have further shown that increasing provider use of fluoroquinolones is a direct contributor to the rise in fluoroquinolone resistant bacteraemic Escherichia (E.) Coli.[10] In urologic literature, a recent study describes rates of ciprofloxacin resistant rectal flora in patients undergoing TR prostate biopsy.[11] The authors found 48% of all patients who had infection after their biopsy harbored ciprofloxacin-resistant bacteria on their preoperative rectal swab.[11] Similarly, Labi et al recently published on the incidence of fluoroquinolone resistant E. coli and Klebsiella (K.) pneumoniae and extended spectrum beta-lactamase (ESBL) resistance using pre-biopsy rectal cultures in men undergoing TR prostate biopsy.[12] They found 86.4% of all patients had fluroquinolone resistant E. Coli or K. pneumoniae and 62.6% had ESBL producing E. Coli or K. pneumoniae.[12] Antibiotic resistant bugs pose a global health threat moving forward. This emphasizes the need for antibiotic stewardship in urologic practice. Our data suggest that extended antibiotic prophylaxis may not be necessary for patients undergoing TP prostate biopsy.

Our findings add to the existing literature. Pepdjonovic et al analyzed 577 patients undergoing TP prostate biopsy with single dose cefazolin at the start of biopsy as antibiotic prophylaxis[13] and found no patients who required readmission to the hospital following TP biopsy and just one who developed prostatitis that needed to be treated with oral antibiotics post-biopsy.[13] This is in line with our results, albeit the endpoints are substantially different (readmission versus clinical infection). In our study 2/14 (0.3%) patients required readmission. Vyas et al utilized Amikacin during anesthesia induction and outpatient antibiotics with ciprofloxacin following biopsy and saw no readmissions for urosepsis.[14] Pepe and Aragona used levofloxacin 500 mg daily for 3 days beginning the day before TP prostate biopsy in 3000 men and found 37 cases of UTI and no sepsis cases.[15] Despite differences in study designs, the rates of infection after TP prostate biopsy appear to be overall low and our results are in line with the literature.

In our study, which included a wide range of antibiotics, the choice of agent did not affect infection rate. Further, no significant difference existed in infections between perioperative IV agents and extended perioperative outpatient agents. Basourakous et al have reported that fluoroquinolones alone or in combination with another antibiotic are most often used by urologists performing TP prostate biopsy, followed by aminoglycosides as the second most utilized.[7] In the paper by Pepdjonovic et al, the authors argue that cefazolin is a superior antibiotic to fluoroquinolones due to rising rates of fluoroquinolone resistance.[13] Our study included patients receiving prophylaxis against skin flora microbes as well as agents covering gram-negative bacteria. In theory, providers should opt for skin flora coverage and not gram-negative coverage in antibiotic administration for TP biopsy. While this is not wrong, there are studies examining the use of a range of antibiotics covering for skin flora and/or gram-negative bacteria in prostate biopsy which show many ways for effective prophylaxis.[16-19] Moreover, our study dates to when TP prostate biopsy was a relatively new procedure at our institution and all antibiotics were at provider discretion. Further, there were three culture proven infections with gram negative bacteria in the cohort, Figure 2. The antimicrobial of choice, if used, should

be guided by the local antibiogram, and in the interest of antibiotic stewardship, skin flora prophylaxis is appropriate under most circumstances, but there are instances where gram-negative coverage is justifiable at provider discretion. It is also worth saying that literature is starting to emerge that antibiotic prophylaxis may not be needed at all when performing TP biopsy. Recent papers by Pirola et al, Jacewicz et al, and Castellani et al seem to point towards this.[9,20,21] This is certainly an interesting area for research, but all our patients received some form of antibiotic prophylaxis and so we cannot comment on this.

There are several limitations that need to be considered when interpreting the results of this study. For one, this is a retrospective analysis subject to all inherent biases of this study design. Second, the definition of post biopsy infections varies in the literature making comparisons challenging. Lastly, the results of our study may not be applicable to TP biopsies performed in the office as in our cohort all the procedures were carried out in an operating room setting.

Conclusions

In summary, in this single institution series we found a low overall rate of infection after TP biopsy. Further, we found no significant difference in rates of infection after TP prostate biopsy with use of single dose versus extended antibiotic prophylaxis. Our data add to the available evidence arguing that limiting antimicrobial prophylaxis is safe in most patients undergoing TP prostate biopsy. □

References

1. Thomson A, Li M, Grummet J, Sengupta S. Transperineal prostate biopsy: A review of technique. *Transl Androl Urol* 2020;9(6):3009-3017.
2. Huang GL, Kang CH, Lee WC, Chiang PH. Comparisons of cancer detection rate and complications between transrectal and transperineal prostate biopsy approaches - A single center preliminary study. *BMC Urol* 2019;19(1):101.
3. Di Franco CA, Jallous H, Porru D et al. A retrospective comparison between transrectal and transperineal prostate biopsy in the detection of prostate cancer. *Arch Ital Urol Androl* 2017;89(1):55-59.
4. Shen PF, Zhu YC, Wei WR et al. The results of transperineal versus transrectal prostate biopsy: A systematic review and meta-analysis. *Asian J Androl* 2012;14(2):310-312.
5. Skouteris VM, Crawford ED, Mouraviev V et al. Transrectal ultrasound-guided versus transperineal mapping prostate biopsy: complication comparison. *Rev Urol* 2018;20(1):19-25.
6. Grummet JP, Weerakoon M, Huang S et al. Sepsis and "superbugs": should we favour the transperineal over the transrectal approach for prostate biopsy? *BJU Int* 2014;114(3):384-388.
7. Basourakos SP, Alshak MN, Lewicki PJ et al. Role of prophylactic antibiotics in transperineal prostate biopsy: A systematic review and meta-analysis. *Eur Urol Open Sci* 2022:37:53-63.
8. John JB, MacCormick A, MacDonagh R, Speakman MJ, Vennam R, Burns-Cox N. Complications following local anaesthetic transperineal prostate biopsies without antibiotic prophylaxis: An institution's experience. *J Clin Urol* 2022;15(5):385-390.
9. Castellani D, Pirola GM, Law YXT et al. Infection rate after transperineal prostate biopsy with and without prophylactic antibiotics: Results from a systematic review and meta-analysis of comparative studies. *J Urol* 2022;207(1):25-34.
10. Cuevas O, Oteo J, Lázaro E et al. Significant ecological impact on the progression of fluoroquinolone resistance in Escherichia coli with increased community use of moxifloxacin, levofloxacin and amoxicillin/clavulanic acid. *J Antimicrob Chemother* 2011; 66(3):664-669.
11. Taylor S, Margolick J, Abughosh Z et al. Ciprofloxacin resistance in the faecal carriage of patients undergoing transrectal ultrasound guided prostate biopsy. *BJU Int* 2013;111(6):946-953.
12. Labi AK, Obeng-Nkrumah N, Dayie NTKD et al. Occurrence and significance of fluoroquinolone-resistant and ESBL-producing Escherichia coli and Klebsiella pneumoniae complex of the rectal flora in Ghanaian patients undergoing prostate biopsy. *JAC Antimicrob Resist* 2022;4(6):dlac113.
13. Pepdjonovic L, Tan GH, Huang S et al. Zero hospital admissions for infection after 577 transperineal prostate biopsies using single-dose cephazolin prophylaxis. *World J Urol* 2017;35(8):1199-1203.
14. Vyas L, Acher P, Kinsella J et al. Indications, results and safety profile of transperineal sector biopsies (TPSB) of the prostate: A single centre experience of 634 cases. *BJU Int* 2014;114(1):32-37.
15. Pepe P, Aragona F. Morbidity after transperineal prostate biopsy in 3000 patients undergoing 12 vs 18 vs more than 24 needle cores. *Urology* 2013;81(6):1142-1146.
16. Odo C, Afogu EN, Odoemene CA et al. Prophylactic role of ciprofloxacin and ceftriaxone in prostate biopsy-related infection: randomized comparative study of bacterial spectrum and antibiotic sensitivities. *Afr J Urol* 2021;27(1):157.
17. Wenzel M, von Hardenberg J, Welte MN et al. Monoprophylaxis with cephalosporins for transrectal prostate biopsy after the fluoroquinolone-era: A multi-institutional comparison of severe infectious complications. *Front Oncol* 2021;11:684144.
18. Luong B, Danforth T, Visnjevac O, Suraf M, Duff M, Chevli KK. Reduction in hospital admissions with the addition of prophylactic intramuscular ceftriaxone before transrectal ultrasonography-guided prostate biopsies. *Urology* 2015;85(3):511-516.
19. Baba K, Sekine Y, Miyazawa Y et al. Assessment of antimicrobiral prophylaxis in transperineal prostate biopsy: A single-center retrospective study of 485 cases. *J Infect Chemother* 2018;24(8): 637-640.
20. Pirola GM, Gubbiotti M, Rubilotta E et al. Is antibiotic prophylaxis still mandatory for transperineal prostate biopsy? Results of a comparative study. *Prostate Int* 2022;10(1):34-37.
21. Jacewicz M, Günzel K, Rud E et al. Antibiotic prophylaxis versus no antibiotic prophylaxis in transperineal prostate biopsies (NORAPP): a randomised, open-label, non-inferiority trial. *Lancet Infect Dis* 2022;22(10):1465-1471.