Prescribing Pattern of Antibiotics among Hospitalized Patients with Urinary Tract Infection

Deepti Shrestha,[1] Jyotshna Sapkota,[2] Rekha Poudel,[1] Rashmi Shakya Gurung,[1] Kiran Aryal[2]

[1]Department of Pharmacology, Nepal Medical College, Attarkhel, Kathmandu, Nepal, [2]Department of Microbiology, Nepal Medical College, Attarkhel, Kathmandu, Nepal.

ABSTRACT

Background: Urinary tract infection is one of the most common bacterial infections worldwide. It has become one of the most common cause for the hospitalization and sepsis. It is generally treated with antimicrobial agents and fluids. This study was conducted to study the prescribing pattern of antibiotic among hospitalized patients with urinary tract infection.

Methods: A descriptive cross-sectional study was conducted in Nepal Medical College Teaching Hospital, Attarkhel, Kathmandu from January 2022 to April 2022. Patients aged 18 years or above of both sex, admitted to various departments with the provisional diagnosis of urinary tract infection prescribed with antibiotics were included in the study.

Results: Out of 146 patients admitted with a diagnosis of urinary tract infection, the most commonly prescribed antibiotics during hospital stay were cephalosporin in 102 (69.9%) patients followed by combination of penicillin and beta-lactamase inhibitors (31, 21.2%) and fluoroquinolones (15, 10.3%). Ceftriaxone (78, 53.4%) alone was the most commonly prescribed antibiotic as empirical therapy followed by combination of piperacillin and tazobactam (22, 15.1%). One hundred and forty four (78.6%) patients were prescribed antibiotics from the watch group followed by the access group (21, 11.5 %). *E. coli* was the most common organism isolated in 29/38 (76.3%) patients.

Conclusions: Cephalosporin was the commonest antibiotic group prescribed in hospitalized patients among which ceftriaxone was commonly prescribed as an empirical therapy. Among AWaRe classification, antibiotics from the watch group were commonly prescribed.

Keywords: Antibiotics; ceftriaxone; urinary tract infection

INTRODUCTION

Urinary tract infection (UTI) is one of the most common cause for the hospitalization and sepsis.[1] About one-third women will have had at least one episode of UTI that requires antimicrobial therapy by the age of 24 years.[2] In Nepalese general hospitals, the UTI cases load ranges from 23.1 to 37.4% of patients.[3] The most common causative organism of UTI are *Escherichia coli (E.coli), Enterococcus, Klebsiella, Pseudomonas* and other *Enterococcus* or *Staphylococcus* species.[4]

Antimicrobial therapy can be prophylactic, preemptive, empirical, definitive or suppressive.[5] Appropriate antimicrobial selection as an empirical therapy is an important factor to treat the patient, as treatment failure can increase the cost and additional morbidity.[4,6]

Misuse or long term use of broad spectrum antimicrobial agents has also become one of the factor for increasing the risk of resistance.[7]

This study was conducted to study the prescribing pattern of antibiotic among hospitalized patients with urinary tract infection in a tertiary care hospital which will help in preparation of national protocol and guidelines for management of hospitalized UTI patients.

METHODS

This cross-sectional study was conducted in Nepal Medical College Teaching Hospital (NMCTH), Attarkhel, Kathmandu from January 2022 to April 2022. Ethical approval was obtained from Nepal Health Research Council (NHRC) and Institutional Ethics Committee of

Correspondence: Dr Deepti Shrestha, Department of Pharmacology, Nepal Medical College, Attarkhel, Kathmandu, Nepal. Email: deepti.shrestha82@gmail.com, Phone: +9779841330082.

Nepal Medical College. Patients aged 18 years or above of both sex, admitted to various departments with the provisional diagnosis of UTI with or without urine culture positive were included in the study. Patients who did not give consent were excluded from the study. The sample size for the study was calculated by using the formula, $n=z^2pq/d^2$

Where, • 'n' is sample size, • 'z' is standard normal deviate; usually set at 1.96, which corresponds to 95% confidence level, • 'p' is the expected proportion in population based on previous studies = 42.8%[8], 'q' is 100-p, i.e.=100-42.8 = 57.2% and • 'd' is confidence interval, i.e. = 5-10% Hence, n = $(1.96)^2X42.8X57.2/8^2$ Therefore, n= 146 patients. Therefore 146 patients were studied in this study.

Informed consent was taken from the patients and were assured about anonymity and confidentiality of the information collected. Data was collected from patient admitted to various departments diagnosed with UTI and antibiotics prescribed by the clinician. Patient demographic, name of the antibiotic/s, number of antibiotic/s used during hospital stay, urine culture and sensitivity report etc was fulfilled in pre designed pro forma. Antibiotics were categorized according to AWaRe classification by WHO.[9]

For urine culture and sensitivity pattern, urine sample was sent to the Microbiology lab, for which following procedure was done by the microbiologists: Urine was collected in sterile wide mouth container. In microbiology lab, urine was inoculated in cystine–lactose–electrolyte-deficient (CLED) Agar for 24 hours. After 24 hours, organism was identified by its cultural characteristics, gram staining and biochemical tests. Antimicrobial susceptibility test was done by disk diffusion method following Clinical and Laboratory Standards Institute (CLSI) guidelines.[10] The data was statistically analyzed using SPSS software version 16.00.

RESULTS

Out of 146 patients admitted with a diagnosis of UTI, more than half were females (98, 67.1%). Most commonly affected age groups range from 18-30 years (40, 27.4%) followed by 51-60 years (25, 17.1%) and 61-70 years (24, 16.4%) as shown in Table 1. Diabetes mellitus (DM) was the commonest risk factor in 36 (24.6%) patients

followed by renal stone (23, 15.7%) and pregnancy (22, 15.1%).

Table 1. Demographic profile of the patients (n=146).	
Parameters	No. (%)
Age (years)	
<30 years	40 (27.4)
31-40	15 (10.3)
41-50	18 (12.3)
51-60	25 (17.1)
61-70	24 (16.4)
70-80	15 (10.3)
>81 years	9 (6.2)
Gender	
Female	98 (67.1)
Male	48 (32.9)
Risk factors*	
None	65 (44.5)
Diabetes mellitus	36 (24.6)
Renal stone	23 (15.7)
Pregnancy	22 (15.1)
BPH	5 (2.7)
Recurrent UTI	2 (1.4)
Catheterization	1 (0.7)

One or more risk factors were present in a patient. BPH-Benign Prostate Hyperplasia

In our study, the average number of antibiotics prescribed per patient during the hospital stay was 1.23±0.53. Most of the antibiotics were given by parenteral route (126, 86.3%) during hospital stay. Duration of injection used was for 3.96±3.24 days.

In our study, the most commonly prescribed antibiotics during hospital stay was cephalosporin in 102 (69.9%) patients followed by combination of penicillin and beta lactamase inhibitors (31, 21.2%) and fluoroquinolones (15, 10.3%) as shown in Table 2.

Ceftriaxone (78, 53.4%) alone was the most commonly used antibiotic as empirical therapy followed by combination of piperacillin and tazobactam (22, 15.1%) and cefixime (15, 10.3%) as shown in figure 1 . Only one (0.7%) patient was prescribed with antibiotic after the culture and sensitivity.

Table 2. Commonly used antibiotic in patients during hospital stay (n=146) and its categorization according to AWaRe classification by WHO.

| Antibiotic prescribed		Frequency (%)	AWaRe category	Total n (%)
Nitrofurantoin		5 (3.4)	Access	5 (3.4)
Aminoglycosides	Amikacin	3 (2.1)	Access	6 (4.1)
	Gentamicin	3 (2.1)	Access	
Penicillin	Ampicillin	1 (0.7)	Access	4 (2.8)
	Amoxicillin	3 (2.1)	Access	
Penicillin and beta lactamase inhibitors	Amoxicillin and clavulanic acid	6 (4.1)	Access	31 (21.2)
	Piperacillin- tazobactam	25 (17.1)	Watch	
Cephalosporin	Cefuroxime	1 (0.7)	Watch	102 (69.9)
	Cefixime	18 (55.5)	Watch	
	Cefotaxime	2 (1.4)	Watch	
	Ceftriaxone	81 (55.5)	Watch	
Fluoroquinolones	Ciprofloxacin	9 (6.2)	Watch	15 (10.3)
	Ofloxacin	1 (0.7)	Watch	
	Levofloxacin	5 (3.4)	Watch	
Others	Meropenem	2 (1.4)	Watch	7 (4.9)
	Imepenem and Cilastin	2 (1.4)	Reserved	
	Colistin	2 (1.4)	Reserved	
	Linezolid	1 (0.7)	Reserved	
Cephalosporin and Beta lactamase inhibitors	Cefoperazone+ sulbactam	10 (6.8)	Not Recommended	13 (8.9)
	Ceftriaxone+tazobactam	2 (1.4)	Not Recommended	
	Cefixime + clavulanic acid	1 (0.7)	Not Recommended	
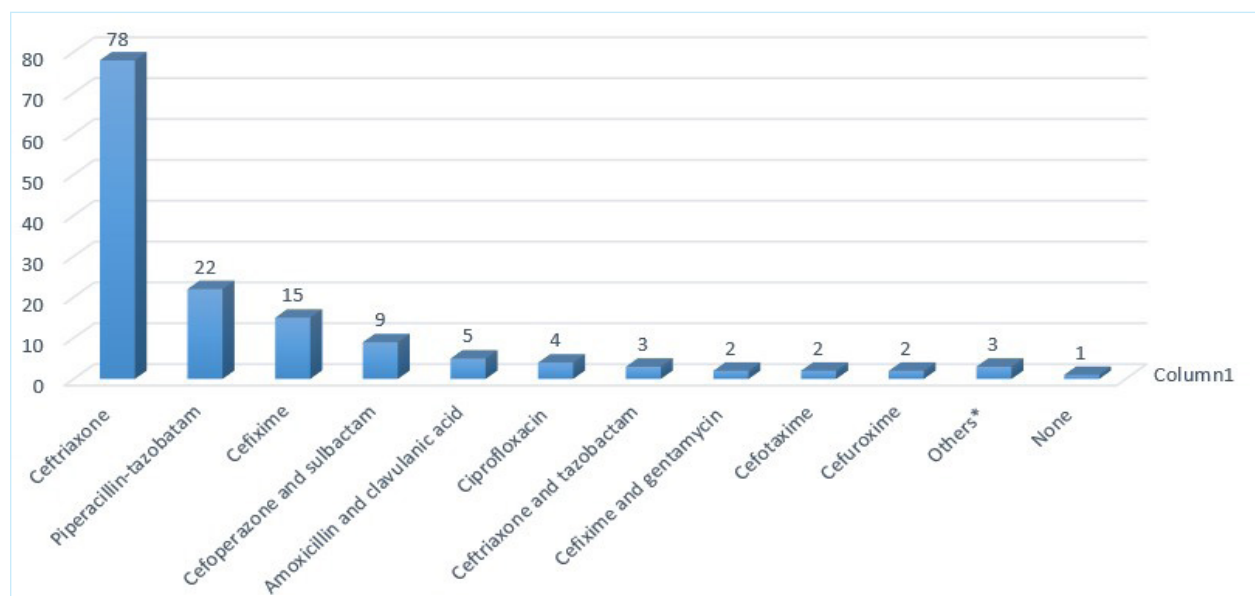
Figure 1. Empirical antibiotics prescribed in hospitalized patients (n=146). Others*- amoxicillin, linezolid, meropenem.

One hundred and forty four (78.6%) patients were prescribed antibiotics from the watch group followed by the access group (21, 11.5 %) and not recommended group (13, 7.1 %) as shown in figure 2. In our study, 76.3% (29/38) culture positive cases, same antibiotic was continued after culture and sensitivity report.
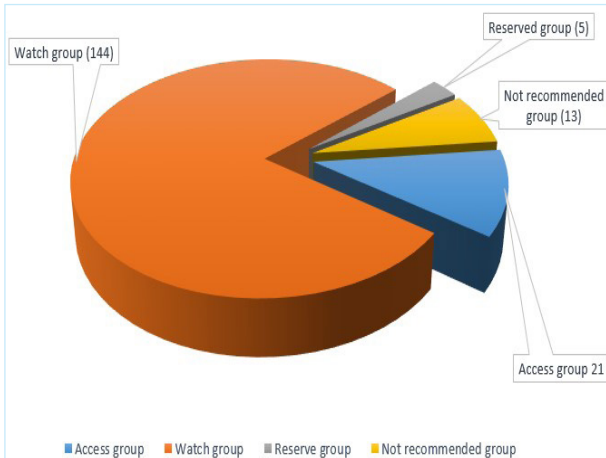

Figure 2. Frequency of antibiotic prescribed in hospitalized patient with UTI by WHO AWaRe classification.

In our study, out of 146 patients, 38 (26%) had significant growth. Among the isolated organism, *E.coli* was the most common isolated organism in 29 (76.3%) patients followed by *Klebsiella pneumoniae* (4, 10.5 %,) and *Pseudomonas aeroginosa* (3, 7.9%) as shown in fig 3.

In our study multiple antibiotics resistant was seen in 17 (58.6%) cases of *E.coli* isolated. *E.coli* showed resistance to antibiotics like Ampicillin, 17 (58.6%), cefotaxime (14, 48.3%), cefixime (14, 48.3%), ceftazidime (13, 44.8%), cotrimoxazole (13, 44.8%) as shown in table 3.
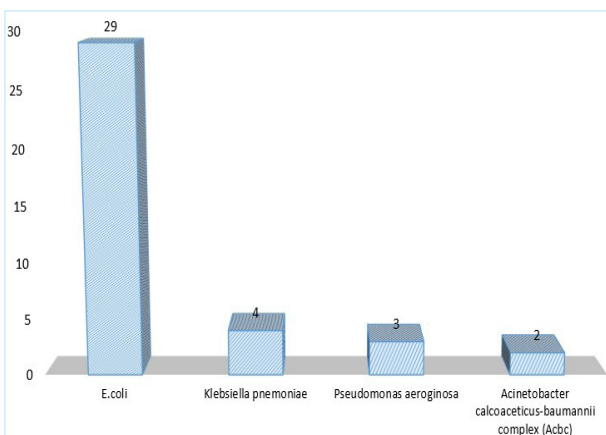

Figure 3. Isolated microorganism in urine culture.

Table 3. Antibiotics sensitive and resistant pattern of E.coli (n=29).

Antibiotics	Sensitive n(%)	Resistant n(%)
Amikacin	28 (96.6)	1 (3.4)
Ampicillin	12 (41.4)	17 (58.6)
Cefotaxime	15 (51.7)	14 (48.3)
Cefixime	15 (51.7)	14 (48.3)
Ceftazidime	16 (55.2)	13 (44.8)
Ciprofloxacin	24 (82.8)	5 (17.2)
Colistin	29 (100)	0 (0)
Cotrimoxazole	16 (55.2)	13 (44.8)
Imepenem	29 (100)	0 (0)
Meropenem	29 (100)	0 (0)
Nitrofurantoin	29 (100)	0 (0)
Ofloxacin	24 (82.8)	5 (17.2)
Piperacillin-tazobactam	28 (96.6)	1 (3.4)
Polymyxin B	29 (100)	0 (0)

DISCUSSION

UTI is among the most common infections worldwide, with substantial morbidity, mortality, and economic burden.[11] Antibiotics are most commonly used for the treatment of UTI. Our study showed that the most common age group was among 18-30 years which is similar to other studies done by Naik et al, Odoki et al and Christy et al in which common age group range from 20-30 years.[12-14] It is found that UTI is common in sexually active age group ie 18-39 years.[15]

This study also revealed that UTI is more common among female. Most of the studies showed that UTI is common among female.[16,17] Between 50% and 60% of adult women will have at least one episode of UTI in their life, and close to 10% of postmenopausal women indicate that they had a UTI in the previous year.[15] Female are more prone to have UTI because of their anatomical structure and hormones.[17] DM, renal stone, pregnancy and BPH were the common risk factors observed in our study. These are the common risk factors for complicated UTI.[4]

The average number of antibiotic prescribed per patient during the hospital stay was 1.23+/-0.539 which is similar to Labi et al study where the mean antibiotic used during hospital stay was 1.7.[18] Atleast one antibiotic was used in all the hospitalized patient during the hospital stay.

During the hospital stay, 126 (86.3%) patients were prescribed with antibiotic by parenteral route with a duration of 3.96+/-3.24. Switch over of parenteral to oral antimicrobial where possible should be there in

order to decrease the unwanted adverse effects and cost burden to the patient.[19]

Cephalosporins were the most commonly prescribed antibiotic during the hospital stay, which is similar to other studies done by Omkar et al and Naik et al where cephalosporin was commonly prescribed antibiotic in 82% and 60.3% of patients respectively for UTI.[20,21] Ceftriaxone as a single antibiotic was most commonly prescribed as an empirical therapy which is similar to the study done by Panday et al and Wiggers et al where ceftriaxone was most commonly prescribed empirically in 53.16% and 49.3% patients.[22,23] UTI is most common infection treated empirically with an antimicrobial therapy and the criteria for the selection of antimicrobial agents should be determined on the basis of the most likely pathogen and its local resistance pattern, antibiotic susceptibility, and antibiotic intolerance/allergy history of previously treated patients.[24,25]

WHO has categorized the antibiotic into AWaRe classification to optimize the use of antimicrobial drugs.[9] In our study it was observed that the watch group of antimicrobial was commonly used. Similar study was seen in study done by Mugada et al in which antibiotic prescribed from the watch group was 53.19%.[26]

Out of 146 urine sample, causative microorganism was isolated in 38 (26%) patients which is similar to study done by Odoki et al, Serretiello et al and Dhungana et al where the positive growth was seen in 32.2%, 21.34% and 21.6% patients respectively.[13,16, 27] Most common organism isolated was *E.coli* in our study which is similar to other studies done by Kushwaha et al, Dhungana et al and Shakya et al.[27,28] In our study *E.coli* showed single or more drug resistance. *E.coli* showed high resistance to ampicillin, cephalosporin and cotrimoxazole. This result is similar to other studies done by Shakya et al and Patel et al.[28,29] Inappropriate prescription, incorrect empirical antibiotics therapy and irrational use of powerful antibiotics have all contributed to antibiotic resistance.[30] Antibiotics should be used very wisely and only when absolutely needed.

CONCLUSIONS

Antibiotics are the most commonly prescribed medicine for UTI. In this study, cephalosporin was the commonest antibiotic group prescribed in hospitalized patient where ceftriaxone was commonly prescribed as an empirical therapy. Among AWaRe classification, antibiotics from the watch group were commonly prescribed. Regular monitoring of antibiotic use in hospitalized patients can be useful for development of guidelines for management of UTI. It is highly recommended that antimicrobial stewardship interventions should be a regular practice in hospitals to reduce the degree of inappropriate antibiotic prescribing and decrease the possible antibiotic resistance.

CONFLICT OF INTEREST

The authors declare no conflict of interest

REFERENCES

1. Komagamine J, Yabuki T, Noritomi D, Okabe T. Prevalence and factors associated with atypical presentation in bacteremic urinary tract infection. Sci Rep 2022; 12, 5197. [Article]

2. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med 2002; 113: 5-13.[Article]

3. Rai GK, Upreti HC, Rai SK, Shah KP, Shrestha RM. Causative agents of urinary tract infections in children and their antibiotic sensitivity pattern: a hospital based study. Nepal Med Coll J 2008; 10: 86–90.[Download PDF]

4. Sabih A, Leslie SW. Complicated urinary tract infections. [Article]

5. Brunton LL, Knollmann BC, Hilal-Dandan RG. Gilman's the pharmacological basis of therapeutics. new York City. 2018: 957-68. [Google Scholar]

6. Alam MF, Cohen D, Butler C et al. The additional costs of antibiotics and re-consultations for antibiotic-resistant Escherichia coli urinary tract infections managed in general practice. Int'l J Antimicrob Agents 2009; 33: 255-7.[Article]

7. WHO. Antibiotic resistance. https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

8. Kattel HP, Acharya J, Mishra SK, Rijal BP, Pokhrel BM. Bacteriology of urinary tract infection among patients attending Tribhuvan University teaching hospital Kathmandu, Nepal. J Nepal Ass Med Lab Sci 2008; 9: 25-9.[Article]

9. WHO. WHO releases the 2021 AWare Classifcation Antibiotics. https://www.who.int/publications/i/item/2021-aware-classification antibiotics/en/

10. Clinical and Laboratory Standards Institute. Performance

Standards for antimicrobial susceptibility testing, (30th edition). Approved Standard. Wayne, PA: Clinical and Laboratory Standards Institute, 2020

11. Huang L, Huang C, Yan Y, Sun L, Li H. Urinary tract infection etiological profiles and antibiotic resistance patterns varied among different age categories: a retrospective study from a tertiary general hospital during a 12-year period. Frontiers in Microbiology. 2022 Jan 27;12:813145.[Article]

12. Naik H, Devi A, Mj S. pattern of antibiotic prescription in urinary tract infection. Indian J Pharm Pharmacol 2016; 3(2); 59-62.[Download PDF]

13. Odoki M, Aliero AA , Tibyangye J et al. Prevalence of bacterial urinary tract infections and associated factors among patients attending hospitals in Bushenyi District, Uganda. Int J Microbiol 2019. [Article]

14. Christy VR, Athinarayanan G , Mariselvam R , Dhasarathan P and Singh R. Epidemiology of urinary tract infection in south India. Biomed Res Clin Prac 2019; 4: 1-5.[Google Scholar]

15. Medina M and Castillo-Pino E. An introduction to the epidemiology and burden of urinary tract infections. Ther Adv Urol 2019; 11: 3–7.[Article]

16. Serretiello E, Veronica Folliero V, Biagio Santella B et al. Trend of bacterial uropathogens and their susceptibility pattern: Study of single academic high-volume center in Italy (2015–2019). Int J Microbiol 2021. [Article]

17. Minardi D, d'Anzeo G, Cantoro D, Conti A, Muzzonigro G. Urinary tract infections in women: etiology and treatment options. Int J Gen Med. 2011; 4:333-43.[Article]

18. Labi AK, Obeng-Nkrumah N, Dayie NT, Egyir B, Sampane-Donkor E, Newman MJ, et al. Antimicrobial use in hospitalized patients: a multicentre point prevalence survey across seven hospitals in Ghana. JAC-Antimicrobial Resistance. 2021 Sep 1;3(3):dlab087.[Article]

19. Cyriac JM., James E. Switch over from intravenous to oral therapy: A concise overview. J Pharmacol Pharmacother 2014; 5(2), 83–7.[Article]

20. Omkar P, Udaykumar P. Prescription pattern and potential drug- drug interactions of patients hospitalised for urinary tract infection in a tertiary care hospital. J Pharm Biol Sci 2016; 11(5): 42-4.

21. Naik SK, Samal S, Sahu SK, Rath B. Antimicrobial prescribing pattern in urinary tract infection in a tertiary care hospital. Natl J Physiol Pharm Pharmacol 2017; 7(12):1318-22.[Download PDF]

22. Panday DR, Amar A, Subedi A, Hussain Md S, Gupta M, Rauniar GP. Antibiotic Usage and its Culture Sensitivity Pattern in Urinary Tract Infections at Tertiary Hospital in Eastern Nepal. Kathmandu Univ Med J. 2017; 60(4):332-5.[Download PDF]

23. Wiggers JB, Sehgal P ,Pinto R, MacFadden D ,Daneman N. The association of adequate empirical treatment and time to recovery from bacteraemic urinary tract infections: a retrospective cohort study. Clin Microbiol and Infect 2019; 25:1253-8.[Article]

24. Khatun SA, Shusmita Shaha S. Prescribing pattern of antimicrobials in urinary tract infection at outpatient department in a tertiary care hospital in Dhaka. J Enam Med Col 2020; 10(1): 23−6.[Download PDF]

25. Gupta K, Hooton TM, Naber KG et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clinic Infect Dis 2011:52 (5). e103-e120. [Article]

26. Mugada V , Mahato V, Andhavaram D, Vajhala SM. Evaluation of prescribing patterns of antibiotics using selected indicators for antimicrobial use in hospitals and the Access, Watch, Reserve (AWaRe) classification by the World Health Organization. Turk J Pharm Sci 2021; 18(3):282-8.[Download PDF]

27. Dhungana JR, Budhathoki A , Poudel G , Basnet J , Shah R. Urinary tract infection among patients visiting Ganesh Man Singh Memorial Hospital and Research Center, Lalitpur, Nepal. Tribhuvan University J Microbiol 2019; 6(1):108-12.[Article]

28. Shakya S, Edwards J, Gupte HA et al. High multidrug resistance in urinary tract infections in a tertiary hospital, Kathmandu, Nepal. Public Health Action 2021; 11: 24-31. [10.5588/pha.21.0035]

29. Patel HB, Soni ST, Bhagyalaxmi A, Patel NM. Causative agents of urinary tract infections and their antimicrobial susceptibility patterns at a referral center in Western India: An audit to help clinicians prevent antibiotic misuse. J Family Med Prim Care 2019; 8(1):154-9.[Article]

30. Acharya KP, Wilson RT. Antimicrobial Resistance in Nepal. Front Med 2019; 6:105.[Article]