http://dx.doi.org/10.5588/pha.21.0044

AMR SUPPLEMENT

Low yield but high levels of multidrug resistance in urinary tract infections in a tertiary hospital, Nepal

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Running title: AMR in UTIs in Nepal

Article submitted 22 April 2021. Final version accepted 21 July 2021.

SUMMARY

SETTING: There are concerns about the occurrence of multidrug resistance (MDR) in patients with urine tract infections (UTI) in Nepal.

OBJECTIVE: To determine culture positivity, trends in MDR among *Escherichia coli and Klebsiella pneumoniae* infections and seasonal changes in culture-positive UTI specimens isolated from 2014 to 2018 at the B P Koirala Institute of Health Sciences, Dharan, Eastern Nepal.

DESIGN: This was a cross-sectional study using secondary laboratory data.

RESULTS: Among 116,417 urine samples tested, 19,671 (16.9%) were culture-positive, with an increasing trend in the number of samples tested and culture positivity. *E. coli* was the most common bacteria (54.3%), followed by *K. pneumoniae* (8.8%). Among *E. coli* and *K. pneumoniae* isolates, MDR was found in respectively 42.5% and 36.0%. MDR was higher in males and people aged >55 years, but showed a decreasing trend over the years. The numbers of isolates increased over the years, with a peak always observed from July to August.

CONCLUSION: Low culture positivity is worrying and requires further work into improving diagnostic protocols. Decreasing trends in MDR are a welcome sign. Information on seasonal changes that peak in July–August can help laboratories better prepare for this time with adequate buffer stocks to ensure culture and antibiotic susceptibility testing.

KEY WORDS: antimicrobial resistance; UTI; uropathogens; seasonality

Urinary tract infections (UTIs) are the most common infections, accounting for 8.1 million visits to healthcare professionals each year. Globally, 150 million people suffer from UTIs, resulting in healthcare expenditure of 6 billion USD per annum.[1] Many studies from South-East Asia have shown that *Escherichia coli* and *Klebsiella pneumoniae* are the most common pathogens isolated from patients with UTIs.[2] A recent study conducted in Eastern Nepal reported an *E. coli* prevalence of 57% among patients with UTI.[3] Another study reported prevalences of respectively 53% and 7% for *E. coli* and *K. pneumoniae* among paediatric patients.[4] A worrying trend has been the increasing rates of multidrug resistance (MDR) in *E. coli* and *K. pneumoniae,* which lead to difficulties in selecting appropriate empirical therapy and achieving treatment success.[5,6]

Antimicrobial resistance (AMR), a major problem for effective treatment of infectious diseases worldwide, is responsible for increased mortality, morbidity, length of hospital stay and increased healthcare costs.[7] Nepal mirrors the global scene of the growing burden of AMR due to widespread and irrational use of antibiotics, along with poor healthcare systems and poor infection control and prevention measures.[8] The National Public Health Laboratory (NPHL) has reported *E. coli* antibiotic resistance rates >50% for cefixime, nalidixic acid, ceftazidime, ciprofloxacin, cotrimoxazole, norfloxacin, ofloxacin and cefotaxime, with increasing trends in AMR between 2006 and 2010.[9]

Organisms exhibiting resistance to three or more classes of antibiotics are considered multidrug-resistant.[10] Understanding MDR patterns in organisms causing UTI in Nepal is imperative to inform clinical practice and improve antibiotic stewardship in relation to appropriate antibiotic use in patients with UTI. The evidence generated will also guide medical professionals in treating patients with UTIs and assist policymakers in developing appropriate AMR guidelines.

This work will help to identify constraints of AMR control activities. In turn, this can help strengthen the national antibiotic resistance programme to focus on the implementation of innovative AMR surveillance, advocate for better resource allocation and improve collaboration between the sub-national and local governments to ensure actions against AMR on the ground.[11] Although previous studies conducted on UTI have documented bacteriological profiles, the trends and seasonality of AMR patterns

among commonly isolated UTI-causing bacteria have not been previously reported in Nepal. We aimed therefore to determine the yield of bacterial growth, the common bacteria causing UTI and the trends in MDR among *E. coli* and *K. pneumoniae* isolates from 2014 to 2018 in patients visiting a tertiary care hospital in Eastern Nepal. We also examined if there was any seasonality in the number of culture-positive specimens isolated.

METHODS

Study design

This was a cross-sectional study involving analysis of secondary data routinely collected in the laboratory.

Setting

Nepal is a landlocked country in South-East Asia, with an estimated population of 29,553,510.[12] The National Action Plan (NAP) on AMR for Nepal recognises the National Public Health Laboratory (NPHL; Kathmandu, Nepal) under the Department of Health Services as a focal point for the surveillance of AMR through the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) platform. The Quality Standards and Regulation Division (QSRD) under the Ministry of Health and Population (MoHP) leads the implementation of the NAP.

This study was conducted at the B P Koirala Institute of Health Sciences (BPKIHS; Dharan, Eastern Nepal), a 813-bed teaching hospital, with over 40,000 admissions per year and a bed occupancy rate of nearly 70%. The average number of patients attending the hospital is 1,000 per day.[13,14]

The Institute has three independent units, Microbiology, Haematology and Biochemistry. The microbiology laboratory is further divided into bacteriology, serology, parasitology, mycology and mycobacteriology. The average number of samples (blood, urine, exudates, stools) received in the bacteriology unit is 48,000 per year, and the average number of urine samples for culture and antibiotic susceptibility testing (AST) is 15,000 per year.[13,14] External quality assessment is done by NPHL every quarter and internal quality control is maintained by monthly testing using

American Type Culture Collection (ATCC) for *Staphylococcus aureus* 25922, *E. coli* 25923 and *K. pneumoniae* 13883 and 70063.

Urine specimens received at the laboratory are inoculated onto cystine lactose electrolyte deficient (CLED) media by using a calibrated loop (0.001/mL). All the media are incubated at 35°C for 18–24 h. With positive urine cultures, the identification of organisms and AST are performed following Clinical And Laboratory Standard Institute (CLSI; Payne, PA, USA) guidelines.[15] Organisms exhibiting resistance to three or more classes of antibiotics are considered multidrug-resistant.[10]

Demographic details, dates of sample testing and reporting results, culture and AST results are documented in the paper-based registers, which are then transcribed electronically using the QLab software (Baltimore, MD, USA) and stored in a database.

Study population and period

We included urine samples of patients with presumptive UTI received for culture and AST at the BPKIHS microbiology laboratory from 1 January 2014 to 31 December 2018.

Data variables and sources of data

Data variables included age, sex, date of culture examination, culture result (positive or negative), organism isolated and AST pattern (resistant, susceptible and intermediate). All data were extracted from the electronic database of the laboratory.

Data analysis and statistics

Data were exported and analysed using Stata v12.1m (StataCorp, College Station, TX, USA). The unit of analysis was the urine sample tested and not the patient, because patients may have been tested multiple times during the study period, possibly for different episodes of UTIs. We assessed the overall culture positivity (proportion culture-positive out of specimens tested) and described the number (proportion) of each organism isolated. We analysed the AST patterns of two key uropathogens (*E. coli* and *K. pneumoniae*) using frequencies and proportions, and presented these as bar charts.

We examined for seasonality using a time-series plot of monthly numbers tested and identified as culture-positive. Seasonal trends were analysed by a seasonal auto-

regressive integrated moving average (SARIMA) model using a time-domain approach.[16,17] We used Gretl software (gretl 1.7.9cvs) according to the following steps: 1) initially, the time-series plot was drawn to identify the pattern of occurrence of culture-confirmed cases per month; 2) a correlogram was drawn to identify the appropriate number of lag periods and moving averages to fit the model; 3) to achieve stationary time series data, seasonal differences with ARIMA were estimated using the augmented Dickey-Fuller test; and 4) among the various postulated combinations of autoregression and moving average models, the model with the best possible fit was estimated using the exact maximum likelihood estimation method. The model that gave the lowest Akaike Information Criteria (AIC) value was considered the best predictive model.

Ethics considerations

Ethics approval was obtained from Ethical Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France (E7/20) and the Institution Review Committee (IRC) at the B P Koirala Institute of Health Sciences, Dharan, Nepal. (IRC/I787/020). Permission to access data was obtained from the department. As we used secondary data without personal identifiers, the need for informed consent was waived by the ethics committees.

RESULTS

A total of 116,417 urine samples tested, of which 19,671 (16.9%) were culture-positive. There was an increasing trend in the number of samples tested, number identified culture-positive and culture positivity over the study period (Figure 1). Most (66.6%) specimens came from female patients. The median age was 32 years (interquartile range [IQR] 22–58), which varied among males (55 years, IQR 25–70) and females (28 years, IQR 22–44). Most of the bacteria (80.1%) isolated were Gram-negative, *E. coli* (54.3%) being the most common, followed by *K. pneumoniae* (8.8%) (Table 1).

Resistance in E.coli

Among 10,630 *E. coli* isolates, 86.5% were resistant to ampicillin and 58.2% were resistant to ciprofloxacin. Resistance to different cephalosporins was also high, ranging

from 53.6% to 78.6%. *E. coli* were least resistant to tigecycline (1.2%), followed by nitrofurantoin (8.1%), amikacin (8.4%), imipenem (12.8%), piperacillin-tazobactam (13.8%), gentamicin (15.7%) and meropenem (31.7%) (Table 2). While there was a decreasing trend in resistance to meropenem (56% in year 2015 to 10.7% in 2018), resistance to imipenem showed an increasing trend (1.3% in year 2015 to 45% in 2018) (Supplementary Figure S1).

Resistance in K. pneumoniae

K. pneumoniae isolates were most resistant to ampicillin (98.4%) and the various cephalosporins (43.6–88.2%), and least resistant to tigecycline (10.9%), followed by imipenem (12.7%), piperacillin-tazobactam (17.8%) and amikacin (19%). Resistance to fluoroquinolones was modest, ranging from 33.8% to 37.5% (Table 3). There was a decreasing trend in resistance to meropenem (37.3% in year 2015 to 19.3% in 2018) and an increasing trend in resistance to imipenem (3.8% in year 2015 to 30.5% in 2018). There was also a decreasing trend in resistance to gentamicin (32.6% in year 2014 to 21.6% in 2018) (Supplementary Figure S2).

Multidrug resistance

Overall, MDR was observed in 42.5% of *E. coli* and 36% of *K. pneumoniae* isolates (Table 4). MDR was higher in males and people aged >55 years, but showed a decreasing trend over the years – the highest levels were seen in 2014–2015 (56–61%) and decreased in 2016–2018 (28.7% to 36.8%).

Seasonality analysis

Month-wise distribution of total of urine samples tested and urine culture positivity during 2014–2018 are shown in Figure 2A and 2B. There was an increasing trend in the numbers of samples tested and culture positivity over the years, and in each year the peak was observed from July to August. Except for 2018, the peak in culture-positive samples coincided with the total number of samples received across all the years. The models which accounted for seasonality (i.e., SARIMA models) had the lowest AIC values, indicating better model fit than models that did not adjust for seasonality (Supplementary Table S1) – confirming the hypothesis of seasonality. Similarly,

residuals (defined as differences between actual values and estimated values derived from the model) were lower in the SARIMA model (Figure 3) than in ARIMA models – again indicating seasonality.

DISCUSSION

This is one of the largest studies from Nepal to assess culture positivity and AST patterns in urine specimens collected from patients with presumptive UTI. This is also the first study from Nepal assessing seasonality in urine specimens examined for culture and AST. We discuss the key findings below.

First, culture positivity of urine samples ranged from 15.4% to 18.9%, with an increasing trend during the study period. This is similar to some previous studies from Nepal which showed culture positivity ranging between 13.8% and 17.4%.[18,19] In contrast, Rizal et al. from Nepal and several studies from India reported higher culture positivity ranging from 46% to 55.8%.[20,21] While we are unclear about the reasons for these differences, we speculate this may have been due to differences in patient populations and clinical criteria used for requesting urine culture.

Second, females accounted for two-thirds of the patients in our study, which is similar to other studies from India (73.6%, 46.6%)[21–23] and Nepal (83.9%, 75%).[18,24] This may be due to a combination of biological female factors (such as proximity of the urethral meatus to the anus, shorter urethra and less acidic pH of the vaginal surface). The age distribution was different among females and males: females were younger, whereas males were relatively older (median age, 28 years vs. 55 years). The age distribution in our study is similar to the study published by Prakash et al. from Meerut, India.[22] In contrast to our findings, other studies have found older people (aged 50–80 years) to be infected.[25,26]

Third, we found that *E. coli* and *K. pneumoniae* were the most common Gram-negative bacteria isolated. This finding is similar to those from a study performed by Dipak B et al.,[27] Lawhale et al.,[28] Joshi et al.[22] and Sokn et al.[29] Among the Gram-positive isolates, *S. aureus* was the most common, followed by methicillin-resistant *S. aureus*, which is similar to reports from other studies.[22,18,28]

Fourth, MDR was high and was reported in respectively 42.8% and 36% of *E. coli* and *K. pneumoniae* isolates – much higher than reports from South Lebanon[29] and

Iran (25.1–27.9%).[30] Most of the previous studies from Nepal reflect similar levels, barring one study by Gurugain et al., which reported MDR of 66.7% in *E.coli*.[31] MDR was also higher in males and older age groups. This is probably due to altered immunity, prostate enlargement, neurogenic bladders and requirements for catheterisation in older age. There was a decreasing trend in MDR over the years, which is heartening, and may reflect better compliance to hospital antibiotic policy and infection control measures. This may also indicate a possible shift in patient profiles – more outpatients investigated for presumed UTI than admitted patients in recent years.

Finally, there was a seasonal trend in the culture-positive urine specimens isolated, and the peak was seen in late summer and the early rainy season (July–August). This may be related to changes in environmental temperature, the relative dehydration in summer and human behaviour at these times such as travel, water consumption and recreational water exposure, which can predispose to many diseases. Seasonality has been reported previously by other researchers from the United Kingdom and Canada.[32,33]

Our study had some strengths. We had a large sample size, with more than 100,000 samples examined over 5 years in the biggest tertiary hospital in Eastern Nepal. Our findings are therefore generalisable to the situation in Eastern Nepal. AST was performed extensively for many available drugs. We had information on the date of culture examination, which enabled the assessment of seasonality in urine cultures. The results are likely to be reliable, as culture and AST was performed per CLSI guidelines in a quality-assured, accredited laboratory. Being an AMR surveillance site, the study laboratory shares an external quality control testing protocol with NPHL, the reference laboratory of Nepal.

There were a few limitations. First, AST was not done consistently for all the antibiotics during the study period because of the unavailability of antibiotics disc. Hence, the proportion of isolates tested for each drug varied, and AST results for some antibiotics may suffer from uncertainty due to small numbers. Second, there was no information on the referring departments and various other baseline clinical characteristics of patients. This would have provided additional insights about factors associated with culture positivity and AMR. Third, there were challenges in extracting the data from the electronic database due to the multiple softwares used during the study

and lack of IT expertise. This caused some problems with the periodic analysis and the generation of antibiograms. Fourth, not all patients with presumptive UTI may have been tested; this, in turn, may not give a true picture of culture positivity. This suggests that clinician practices need to be better aligned with clinical protocols in the hospital, especially when requesting for laboratory tests.

Despite these limitations, our study findings have some important implications. First, information on seasonality may be useful for the hospital to prepare for an increased workload, as well as efficient procurement and antibiotic supply chain management between July and August. Second, there is a need to review the existing electronic databases and the multiple softwares used, and develop an simpler system for periodic data extraction. This should improve analysis of surveillance data and creation of antibiograms. Sharing these antibiograms that show emerging trends in resistance with clinicians is crucial for better antibiotic stewardship. Third, the low yield of culture is worrying, and requires further investigation into improving diagnostic protocols with a view to decreasing the laboratory workload.

In conclusion, although there was an increasing trend in culture positivity among the urine specimens tested, overall positivity remained low. This is worrying, and requires further investigation and surveillance. *E. coli* was the most common micro-organism, followed by *K. pneumoniae*. Both showed an increasing trend in AMR to commonly used antibiotics. While overall levels of MDR were high, there was a decreasing trend over the years, which is a welcome sign. Information on infection seasonality, with a peak in July–August, can help in laboratory preparedness by ensuring there are adequate buffer stocks during that period for culture and AST reagents.

Acknowledgements

This research was conducted through the Structured Operational Research and Training Initiative (SORT IT), a global partnership coordinated by Tropical Disease Research (TDR), the Special Programme for Research and Training in Tropical Diseases at the WHO. The specific SORT IT programme that led to these publications included a partnership of TDR with the WHO Country Office of Nepal and was implemented along with the Tuberculosis Research and Prevention Centre Non-Governmental

Organisation, Yerevan, Armenia; the International Union Against Tuberculosis and Lung Diseases, Paris, France, and South East Asia, New Delhi, India offices; the Damien Foundation, Brussels, Belgium; the Narotam Sekhsaria Foundation, Mumbai, India; Sustainable Health Systems, Freetown, Sierra Leone; the Ministry of Health and Sanitation, Freetown, Sierra Leone; School of Public Health and Community Medicine, B P Koirala Institute of Health Sciences, Dharan, Nepal; the Institute of Medical Research, Bangalore, India; University of Exeter, Exeter, UK; and the University of Washington, Seattle, WA, USA.

Special thanks to all the staff of the Department of Microbiology at the B P Koirala Institute of Health Sciences, Dharan, Nepal, for their constant support; R Das, R Sukhla and B Jaiswal for their support; and Professor A D Harries for his overall edits to improve the English language.

This SORT IT AMR Programme was funded by the National Institute of Health Research, Department of Health & Social Care of the United Kingdom and supported by implementing partners.

Conflict of interests: none declared.

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References

1 Foxman B, et al. Urinary tract infection: self-reported incidence and associated costs. Ann Epidemiol 2000; 10: 509–515.

2 Nuntra S, Carrol CK. Epidemiology and molecular characterization of multidrug-resistant Gram-negative bacteria in Southeast Asia. Antimicrob Resist Infect Control 2016; 5: 15.

3 Shah C, Baral BB, Bahadur Shrestha BL. Virulence factors of uropathogenic *Escherichia coli* (UPEC) and correlation with antimicrobial resistance. BMC Microbiol 2019; 19: 204–208.

4 Shrestha BL, et al. Clinical, etiological and antimicrobial susceptibility profile of pediatric urinary tract infections in a tertiary care hospital of Nepal. BMC Pediatr 2019; 19: 36–44.

5 Kumar A, et al. Antimicrobial susceptibility pattern of urine culture isolates in a tertiary care hospital of Jharkhand, India. Int J Basic Clin Pharmacol 2017; 6 (7): 1733–1739.

6 Sierra-Díaz E, Hernández-Ríos CJ, Bravo-Cuellar A. Antibiotic resistance: microbiological profile of urinary tract infections in Mexico. Cir Cir 2019; 87(2): 176–182.

7 Zakieh R, Ali Afshar T. Antimicrobial susceptibility pattern of urinary tract pathogens. Saudi J Kidney Dis Transpl 2009; 20(2): 251–253.

8 Acharya PK, Wilson T. Antimicrobial resistance in Nepal. Front Med 2019; 6: 105E.

9 Siegel D, et al. Management of MDR organism in health care settings, 2006. The healthcare infection control. Practices Advisory Committee. Atlanta, GA, USA: Centers for Disease Control and Prevention, 2017. http://www.cdc.gov/infection guidelines.mdro

10 Government of Nepal. National Antimicrobial Resistance Containment Action Plan, Nepal, 2016. Kathmandu, Nepal: Government of Nepal, 2016. https://www.flemingfund.org/wpcontent/uploads/3d9bf4b7ab190c600921a99cf1803059.pdf

11 World Health Organization. GLASS | Global antimicrobial resistance surveillance system (GLASS) report [Internet]. Geneva, Switzerland: WHO,

2018. https://www.who.int/glass/resources/publications/early-implementation-report/en/

12 World Bank Country and Lending Groups. World Bank Data Help Desk. New York, NY, USA: World Bank, 2021. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groupsaccess

13 B P Koirala Insitute of Health Sciences. Annual Report and Plan of Action, 2019–2020. Dharan, Nepal: BPIKHS, 2020.

14 Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Document No M100. 27th ed. Wayne, PA, USA: CLSI, 2017.

15 Siriyasatien P, et al. Analysis of significant factors for dengue fever incidence prediction. BMC Bioinformatics 2016; 17: 166.

16 Edson ZM, da Silva EAS. Predicting the number of cases of dengue infection in Ribeirão Preto, São Paulo State, Brazil, using a SARIMA model. Cad Saude Publica 2011; 27(9): 1809–1818.

17 Pradhan B, Pradhan SB. Prevalence of urinary tract infection and antibiotic susceptibility pattern to urinary pathogens in Kathmandu Medical College and Teaching Hospital, Duwakot. Biratnagar J Health Sci 2017; 2(1): 134–137.

18 Subedi N, Pudasaini S. Bacteriological profile and antibiotic sensitivity pattern in patients with urinary tract infection. J Pathol Nepal 2017; 7: 1066–1069.

19 Rijal A, et al. Antibiotic susceptibility of organisms causing urinary tract infection in patients presenting to a teaching hospital. J Nepal Health Res Counc 2012; 10(20): 24–27.

20 Patel BH, et al. 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 Fam Med Prim Care 2019; 8(1): 154–159.

21 Prakash D, Saxena S R. Distribution and antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infection in urban community of Meerut City, India. ISRN Microbiol 2013: 1–13.

22 Kumar A, et al. Antimicrobial susceptibility pattern of urine culture isolates in a tertiary care hospital of Jharkhand, India. Int J Basic Clin Pharmacol 2017; 6(7): 1733–1739.

23 Singh RK, et al. Prevalence of antibiotic sensitivity pattern of uropathogens in patients of different age-groups from western region of Nepal. Int J Med Res Health Sci 2016; 5(9): 1–7.

24 Joshi RD, et al. Isolation of organism and its drug sensitivity patterns in patients in urinary tract infection at Kathmandu Model Hospital. Nepal J Obstetr Gynecol 2018; 24(1): 46–50.

25 Eshwarappa M, et al. Clinico-microbiological profile of urinary tract infection in south India. India Nephrol 2011; 21(1): 31–36.

26 Dipak B, et al. Bacterial uropathogens and their antibiotic sensitivity pattern at a tertiary care hospital in Birgunj, Nepal. J National Medical College 2017; 2(1): 74–77.

27 Lawhale AM, Naikwade R. Recent pattern of sensitivity of most commonly isolated uropathogens from Central India. Int J Res Med Sci 2017 5(8): 3631–3636.

28 Sokhn ES, et al. Antimicrobial susceptibilities and laboratory profiles of *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* isolates as agents of urinary tract infection in Lebanon: paving the way for better diagnostics. Med Sci 2020; 8(3): 32.

29 Moini S, et al. Multidrug-resistant *Escherichia coli* and *Klebsiella pneumoniae* isolated from patients in Kashan, Iran. Microbiol 2015; 8(10): e27517.

30 Guragain N, et al. Extended spectrum beta-lactamase producing Gram-negative bacterial isolates from urine of patients visiting Everest Hospital, Kathmandu, Nepal. Tribhuvan University J Microbiol 2019; 6(1): 26–31.

31 Rosello A, et al. Seasonality of urinary tract infections in the United Kingdom in different age groups: longitudinal analysis of The Health Improvement Network (THIN). Epidemiol Infect 2018; 146: 37–45.

32 Anderson JE. Seasonality of symptomatic bacterial urinary infections in women. J Epidemiol Community Health 1983; 37: 286–290.

Table 1 Number and proportion of bacteria isolated among culture-positive urine specimens examined at B P Koirala Institute of Health Sciences, Dharan, Nepal, 2014–2018 (*n* = 19,671)

Type of organism	*n*	(%)
Gram-positive	3,896	(19.9)
Staphylococcus aureus	2038	(10.3%)
Coagulase-negative *Staphylococcus*	45	(0.2)
Streptococcus species	25	(0.1)
Enterococcus faecalis	1,788	(9.1)
Gram-negative	15,775	(80.1)
Escherichia coli	10,630	(54.3)
Klebsiella pneumoniae	1,721	(8.8)
Klebsiella oxytoca	248	(1.3)
Enterobacter species	428	(2.2)
Acinetobacter *baumanii* complex	1,148	(5.9)
Pseudomonas aeruginosa	692	(3.5)
Citrobacter freundi	580	(3.0)
Citrobacter diversens	46	(0.2)
Proteus mirabilis	154	(0.8)
Proteus vulgaris	73	(0.4)
Morgenella morganii	25	(0.1)
Providencia species	9	(0.0)
Serratia marcescens	7	(0.0)
Missing	14	(0.1)

Table 2 Antibiotic susceptibility patterns in *Escherichia coli* isolated from urine samples examined at B P Koirala Institute of Health Sciences, Dharan, Nepal, 2014–2018 (*n* = 10,630)

	Tested		Susceptible		Intermediate		Resistant	
Drug	*N*	%	*n*	%	*n*	%	*n*	%
Amikacin	5295	49.8	4831	91.2	21	0.4	443	8.4
Ampicillin	6440	60.6	651	13.2	18	0.3	5571	86.5
Cefaperazone sulbactum	14	0.1	2	14.3	1	7.1	11	78.6
Cefepime	1763	16.6	773	43.9	46	2.6	944	53.6
Cefexime	3684	34.7	1221	33.1	29	0.8	2434	66.1
Cefotaxime	4365	41.1	1871	42.9	112	2.6	2382	54.6
Ceftazidime	7087	66.7	2690	38.0	144	2.0	4253	60.0
Ceftriaxone	3801	35.8	1618	42.6	40	1.1	2143	56.4
Ciprofloxacin	4725	44.4	1911	40.4	62	1.3	2752	58.2
Cotrimoxazole	4599	43.3	1964	42.7	8	0.2	2627	57.1
Gentamycin	3628	34.1	3014	83.1	45	1.2	569	15.7
Imipenam	6641	62.5	5682	85.6	111	1.7	848	12.8
Levofloxacin	1668	15.7	750	45.0	51	3.1	867	52.0
Meropenam	3355	31.6	2186	65.2	107	3.2	1062	31.7
Nalidixic acid	5032	47.3	957	19.0	8	0.2	4067	80.8
Nitrofurantoin	9190	86.5	8343	90.8	107	1.2	740	8.1
Norfloxacin	6226	58.6	2615	42.0	66	1.1	3545	56.9
Ofloxacin	4921	46.3	1963	39.9	46	0.9	2912	59.2
Piperacillin tazobactum	2917	27.4	2477	84.9	2	50.0	390	13.8
Tigecycline	1925	18.1	1880	97.7	22	1.1	23	1.2

Table 3 Antibiotic susceptibility patterns in *Klebsiella pneumoniae* isolated from urine samples examined at B P Koirala Institute of Health Sciences, Dharan, Nepal, 2014–2018 (*n* = 1721)

	Tested		Susceptible		Intermediate		Resistant	
Drug	*N*	%	*n*	%	*n*	%	*n*	%
Amikacin	866	50.3	693	80.0	6	0.7	167	19.3
Ampicillin	826	48.0	13	1.6	0	0.0	813	98.4
Cefaperazone sulbactum	17	1.0	2	11.8	0	0.0	15	88.2
Cefepime	250	14.5	139	55.6	2	0.8	109	43.6
Cefexime	673	39.1	269	40.0	4	0.6	400	59.4
Cefotaxime	687	39.9	339	49.3	17	2.5	331	48.2
Ceftazidime	1097	63.7	446	40.7	26	2.4	625	57.0
Ceftriaxone	589	34.2	304	51.6	4	0.7	281	47.7
Ciprofloxacin	768	44.6	475	61.9	5	0.7	288	37.5
Cotrimoxazole	731	42.5	344	47.1	1	0.1	386	52.8
Gentamycin	606	35.2	448	73.9	4	0.7	154	25.4
Imipenam	1090	63.3	942	86.4	10	0.9	138	12.7
Levofloxacin	311	18.1	203	65.3	3	1.0	105	33.8
Meropenam	542	31.5	388	71.6	16	3.0	138	25.5
Nalidixic acid	785	45.6	361	46.0	14	1.8	410	52.2
Nitrofurantoin	1500	87.2	929	61.9	63	4.2	508	33.9
Norfloxacin	975	56.7	631	64.7	7	0.7	337	34.6
Ofloxacin	831	48.3	511	61.5	13	1.6	307	36.9
Piperacillin tazobactum	472	27.4	376	79.7	12	2.5	84	17.8
Tigecycline	331	19.2	264	79.8	31	9.4	36	10.9

Table 4 Factors associated with multidrug-resistance among *Escherichia coli* and *Klebsiella pneumoniae* isolated from urine samples examined at B P Koirala Institute of Health Sciences, Dharan, Nepal, 2014–2018

	E. coli (*n* = 10,630)		*K. pneumoniae* (*n* = 1,721)	
Variable	*n*	%	*n*	%
Total	4547	42.8	620	36.0
Sex*				
Male	1978	58.9	339	56.3
Female	2569	35.3	281	25.1
Age, years†				
<15	458	46.4	46	30.5
15–24	727	31.2	92	22.4
25–34	621	31.1	78	22.9
35–44	472	43.0	57	32.4
45–54	452	46.8	56	43.4
55–64	630	55.1	96	55.8
>65	1185	56.2	195	57.0
Year†				
2014	785	56.4	117	50.7
2015	1121	61.0	112	40.9
2016	769	33.7	146	33.7
2017	916	36.8	106	28.7
2018	956	36.4	139	33.7

* χ^2 $P = 0.0001$.

†P for trend 0.0001.

Figure 1 Annual trend of urine numbers tested, number of samples cultured and culture positivity from 2014 to 2018. Figure1 shows three indicators: number of urine samples tested (the total bar which includes both the green and red portions), number culture-positive (red portion) and percentage that is culture-positive (indicated by the percentages within the red portion).

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Figure 1

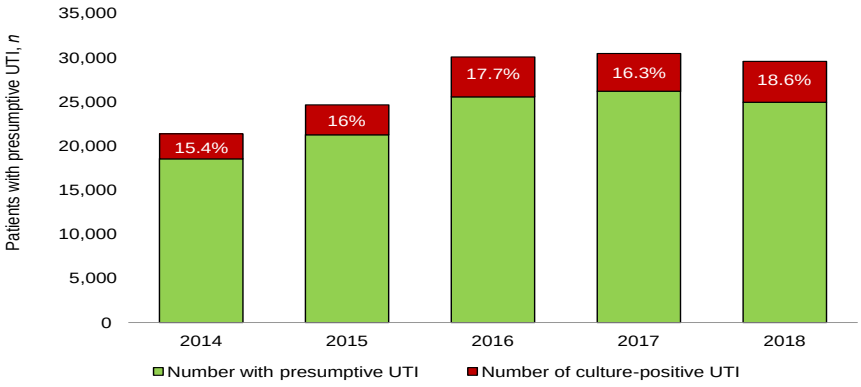

Figure 2 Total number of **A)** urine samples by month, 2014–2018; and **B)** culture-positive urine samples by month, 2014–2018.

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Figure 2

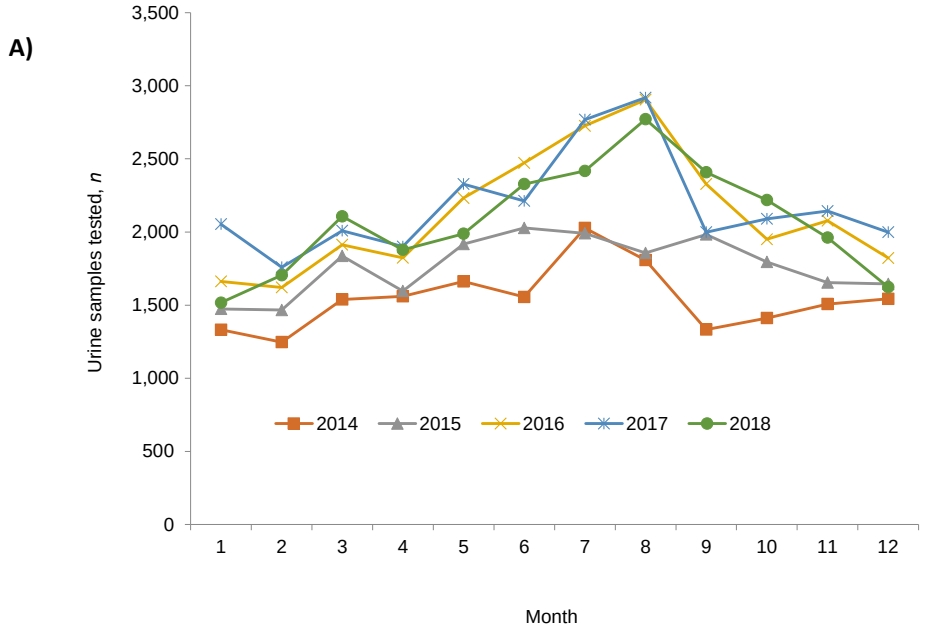

Figure 3 Number of culture-positive urine samples isolated at B P Koirala Institute of Health Sciences, Nepal, 2014–2018 by month (observed vs. fitted with SARIMA model). SARIMA = seasonal auto-regressive integrated moving average.

Figure 3