

Point prevalence of antimicrobial prescriptions among inpatient in a tertiary level hospital in Nepal

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ABSTRACT

Introduction: Inappropriate use of antimicrobials increases resistance, morbidity, and mortality. Accurate information on the use of antibiotics is crucial to address the problem of antibiotic overuse and resistance. The aim of this study is to explore the antibiotic prescription pattern at inpatient departments of Dhulikhel Hospital.

Method: This prospective point prevalence study was conducted in five inpatient departments by making 25 visits between June 2018 and March 2019. Patient planned to be discharged on the day of visit was included in the study. The details of the patients who received at least one antimicrobial for at least one clinical treatment condition or prophylaxis during the hospital stay was recorded. The data on the antimicrobials received, diagnosis, therapeutic indication according to predefined lists, and markers of prescribing quality were recorded.

Result: Out of 179 patients, 125 patients (69.8%) were prescribed one or more antibiotics. There was noticeable variation in prevalence of antibiotic prescription across the departments, ranging from 59.5%-78.9 %. The top three prescribed antibiotics were third generation cephalosporins 63 (38%), broad spectrum penicillin 49 (29.5%), and metronidazole 19 (11.4%). The patients received antibiotic for non-bacteriological proven infection 66 (52.8%) and only 8 (6.4%) patient received antibiotic for bacteriological proven infection. Culture and sensitivity testing were sent in 45(36%) patients and urine was the most frequent specimen

Conclusion: Study concluded that there is need to further explore factors contributing to the high prevalence of antibiotic use and develop strategies for appropriate antibiotic use in the hospital.

Keywords: antimicrobial prescribing, antimicrobial resistance, ATC classification, antibiotic usage, point prevalence survey

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INTRODUCTION

The role of antibiotics in saving lives is related to their rational use.¹ Irrational use of antibiotics increases the risk of development of antimicrobial resistance (AMR), increasing morbidity, mortality and costs, with costs including additional visits to emergency departments, extra prescriptions for adjuvant therapies as well as prolonged hospital stay, leading to worldwide calls to address this.²

Global overuse of antibiotics has emerged as a major problem, with up to 50% of patients reported to receive unnecessary antibiotics.³ Accurate information on the use of antibiotics is crucial to address the problem of antibiotic overuse and resistance. The World Health Organization (WHO) defined rational use of drug as patients receiving medications appropriate to their clinical needs in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community.⁴ Improvement of the rational use of antimicrobials is encouraged by the WHO through prescription-only use of antibiotics and through educational measures.⁵

The global threat of increasing AMR motivated us to conduct this survey among five selected inpatient wards of Dhulikhel hospital. We used point prevalence method to provide the baseline for antimicrobial prescribing pattern in hospitalized patients. The findings will help build the future strategies to improve the quality of antibiotic prescriptions in our center. In addition, this work will add evidence for policymakers to design strategies and apply interventions to enhance the sensible prescribing of antibiotics among hospitalized patients in Nepal.

METHOD

This prospective point prevalence study was conducted from June 2018 to March 2019 in inpatient wards of Dhulikhel hospital after obtaining approval from Institutional Review Committee of Kathmandu University School of Medical Sciences (IRC-KUSMS). Dhulikhel hospital, a Kathmandu University hospital, is a 475-bedded non-government hospital that is a tertiary care referral center for 2.7 million people from various districts. Patient planned to be discharged from the Internal Medicine, Pediatrics, Surgery, Orthopedics and Gynecology departments on the day of visit was included in the study. These five departments represent 91.2% of all the inpatient bed of our hospital. Patient admitted in critical care unit, patient with malignancy, under dialysis

treatment and, immunocompromised conditions were excluded.

Sample size was calculated with Cochran formula. As the prevalence of antimicrobial prescription is not known in our context, sample size was based on the assumption that the prevalence is 50%. Two tailed test was used and a p-value of 0.05 was considered statistically significant with precision of $\pm 7.5\%$.

$$n = (1.96)^2 * 0.5(1-0.5) / (0.075)^2 = 171$$

Probability proportional to size (PPS) sampling method was applied to enroll a target patient from the cluster of all the five major departments. The treatment cardex of discharged patient was reviewed and the patients who were prescribed any antimicrobial during the hospital stay were identified and the details were noted in the predesigned data collection form. The form included the demographic details of the patient, hospital number, contact number, clinical diagnosis and duration of hospitalization. Antimicrobial information regarding its category was based on Anatomic Therapeutic Chemical Classification (ATC) system from the WHO collaborating Centre for Drug Statistics Methodology.⁶ The number of antibiotics prescribed per individual, their dose, route, frequency, and duration were noted. Number of days after which parenteral antibiotics was switched to oral antibiotics and the continuation of antibiotics after discharge was recorded. Indication of antibiotic used was classified as prophylaxis, Bacteriologically Proven Infection (BPI) and Non-Bacteriologically-Proven Infection (NBPI). In addition, indication of antimicrobials used was classified according to anatomical sites of infection into 10 groups- respiratory, skin, bone and joint, intra-abdominal, urinary tract, otorhinolaryngology, genital, cardiovascular, CNS, eye, and Undefined. Treatment cardex was reviewed regarding the use of generic name and the clarity of the written instruction by the treating physician. Compliance to local protocol if present was also noted. Type of culture and isolated organism was noted if sent by the treating doctors during the patient's hospital stay. The data were entered into a Microsoft Excel spreadsheet as master chart then imported to the latest version of the Statistical Package for the Social Science (SPSS) software (IBM SPSS Statistics 25) and the data were analyzed. Categorical variables were described as frequency (percentage) and mean $\pm$ standard deviation or median with IQR was used for continuous parameters whichever applicable.

RESULT

A total of 179 hospitalized patients were evaluated during the 25 visits to the five major departments. Among them 125 patients (69.8%) were prescribed one or more antibiotics and there was noticeable variation in prevalence of antibiotic prescription across the departments, ranging from 59.5%-78.9 %. (Table 1)

More than half of the patients were female (68%). The median age of the patients was 32 years with IQR from 23 to 48.5 years. Age of majority of patients in the Gynecology/Obstetrics ranged from 17-45 (91.1%) years whereas in Internal Medicine department 73.3% were older than 45 years. Almost equal distribution of participants, from the middle and elderly age group was found in the orthopedics and surgical department.

The median duration of hospital stay was 4 days with Interquartile Range (IQR) from 2 to 5.5. Most of the patient were discharged within 3 days of admission in Gynecology/obstetrics, Pediatrics and Surgery department whereas, in Internal Medicine and Orthopedics department the patient had longer duration of stay.

Out of 125 patients, 75 (60%), 39 (31.2%) and 11 (8.8%) received one antibiotic, two antibiotics and three antibiotics respectively. The average number of antimicrobials prescribed was 1.3 per patient. Out of 125 patients, 99 were started on at least one IV antibiotics for systemic use. Most of them were switched to oral in 1-3 days (51.5%) followed by 4-7 days (28.3%) as mentioned in Table 2.

A total of 166 antibiotics were prescribed to the study population. Out of 166 antibiotics used, the most common route of drug administration was intravenous 130 (78.4%) and the oral route accounting for 36 (21.6%). Fifty-five (33.1%), 47 (28.3%), 33 (19.9%), 18 (10.8%), and 13 (7.9%), antibiotics were prescribed in Gynecological/Obstetrics, Internal Medicine, Surgery, Orthopedic, and Pediatrics, department respectively. Generic name was written in all the cardex. The most common anatomical systems involved for treatment were the genital (36.8%), intra-abdominal (19.2%), skin-joint-bone (15.2%), respiratory tract (8.8%), undefined (7.2%), blood (2.4%), more than one site (2.4%) and CNS (0.8%) respectively. The indication antibiotic use was classified as for prophylaxis, or NBPI as shown in Figure 1.

The 166 total prescription was categorized according to the ATC codes (Table 3). The three most commonly prescribed antibiotics were third generation cephalosporins (J01D) 63 (38%), broad spectrum penicillin (J01C) 49 (29.5%), and metronidazole (J01XD) 19 (11.4%). Culture and sensitivity testing was sent in 45(36%) patients and a total of 55 specimens were sent for testing. Urine was the most frequent specimen followed by blood and body fluids. The result was negative in 37 cases while polymicrobial organism growth was seen in one case. A total of 8 types of organisms were isolated. The predominant organisms isolated were *E. coli* (n=3), MRSA (n=2), *K. pneumoniae* (n=1), and *S. pneumoniae* (n=1).

Table 1. Characteristics, bed occupancy and prevalence of antibiotic use in 5 departments of Dhulikhel Hospital (N=179)

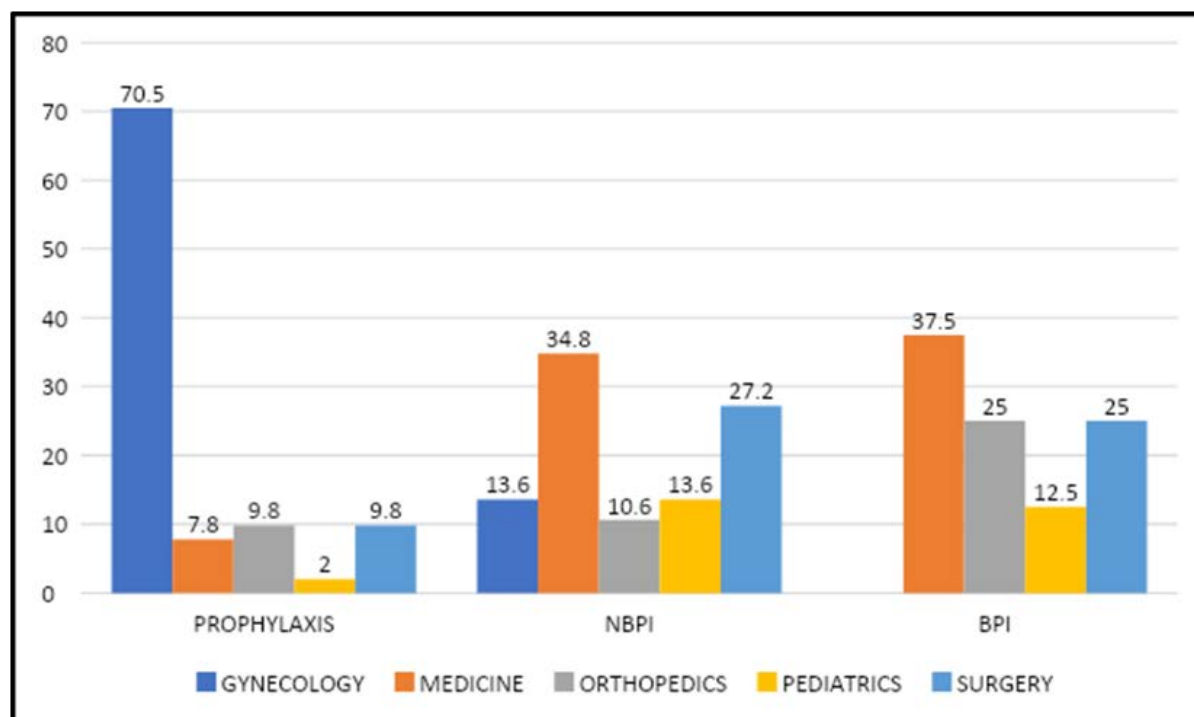
Department	Total beds (n)	Total visits	Total patient	Bed occupancy (percentage of Total patient/ total beds*total visits)	Patients Planned for discharge (n)	Patients on Anti-microbials (n)	Prevalence of Anti- microbial prescription (%)
Gynecology	42	6	190	75.3	57	45	78.9
Medicine	40	5	145	72.5	44	30	68
Orthopedics	40	4	136	85	18	14	77.8
Pediatrics	17	5	39	45.8	18	11	61
Surgery	35	5	172	98.2	42	25	59.5
TOTAL	174	25	682	78.2	179	125	69.8

Table 2. Duration of antimicrobial administration in different departments

Department	Duration of switching of the antibiotic from IV to oral route (n=99)			Antibiotic continued after discharge N= 125 (%)
	1-3 days N (%)	4-7 days N (%)	>7 days N (%)	
Gynecology	24(99.2)	1(0.8)	0	45(100)
Medicine	6(23.1)	12(46.1)	8(30.8)	25(83.3)
Orthopedics	3(21.4)	9(64.3)	2(14.3)	13(92.9)
Pediatrics	5(50.0)	2(20.0)	3(30.0)	9(81.8)
Surgery	13(54.2)	4(16.7)	7(29.1)	20(80)
Total	51(51.5)	28(28.3)	20(20.2)	112(89.6)

Table 3. Antimicrobial prescription pattern and ATC codes in different departments of Dhulikhel Hospital (N=166)

Drugs	Gynecology	Medicine	Orthopedics	Pediatrics	Surgery	Total
J01A	0	3	0	0	0	3(1.8)
Tetracyclines						
J01C	26	5	1	5	12	49(29.5)
B-lactam/ penicillin						
J01D	18	24	14	6	1	63(38)
Other B-lactams						
J01F	0	7	0	1	0	8(4.8)
Macrolides/ Clindamycin						
J01G	0	1	2	1	2	6(3.6)
Aminoglycosides						
J01M	0	2	0	0	11	13(7.8)
Quinolones						
J01XD	11	2	1	0	5	19(11.4)
Metronidazole						
J01XX	0	3	0	0	2	5(3.1)
Linezolid						
Total AB used	55	47	18	13	33	166
%	33.1	28.3	10.8	7.9	19.9	100

**Figure 1. Indications for antimicrobial prescription in different departments of Dhulikhel Hospital (N=125)**

DISCUSSION

Despite availability of clearly defined guidelines for rational antimicrobial usage, the rampant and inappropriate use of antimicrobials is very common. Effective surveillance of antimicrobial usage is invaluable to help rationalize antibiotic prescribing, thereby helping control the emergence of multi-drug resistance microbes, observing the efficiency of policies, identifying targets for quality improvement and informing the policymakers.

In the present study, 69.8% of discharge patient on twenty- five single-day point prevalence surveys had consumed one or more antibiotics. This is much higher than prevalence rates reported in other point prevalence survey studies across the world including the Global PPS (34.4%), Europe (27.4% - 34.4%), and India (40.9%), but comparable with other hospital in Nigeria (69.7%).^{7,8} High rates of antibiotic use observed at Dhulikhel hospital may be due to increased prevalence of infectious disease among patient attending the hospital, presence of hospital acquired infections, suboptimal infection

prevention and control measures, lack of uniform standard protocols for managing infections and the general lack of antimicrobial stewardship. The prevalence rate was even higher than our findings in some other hospital in China (75.3%), which has already resulted in the instigation of antibiotic stewardship strategies to address antibiotic overuse.⁴ Although this study was not designed to evaluate the appropriateness of antibiotic use, it is expected that with high prevalence of antibiotic use, a significant proportion of the use in Dhulikhel hospital may be inappropriate or unnecessary. This finding thus presents an opportunity to further explore on inappropriate antimicrobial prescription in the hospital.

The prevalence of antimicrobial use was highest among Gynecology/Obstetrics patients (78.0%) and lowest among Surgery patients (59.0%). Prophylactic use of antibiotic among Gynecology/Obstetrics patients was high 36(80%) followed by NBPI 9(20%). This may be due to the fact that use of prophylactic antibiotics will reduce the incidence of febrile morbidity, wound infection, endometritis and serious maternal infectious complications following Cesarean section.⁹ In the global Antibiotic Resistance and Prescribing in European Children (ARPEC) PPS study conducted in 2012, involving 226 hospitals from 41 countries, the overall percentage of hospitalized children on antimicrobials was 42.5%, which was much lower in comparison to that in our study in the pediatric ward (61.0%).¹⁰ However, this was similar to PPS study done in six children hospital in India (61.5%).¹¹ This may be due to the similar disease pattern among the children in Nepal and India.

Drug prescribed by generic name was 100% in our finding which is highly recommended by WHO prescribing medications by generic name as a safety precaution for patients because it identifies the drug clearly, enables better information exchange and allows better communication between health care providers.⁴

The top three most commonly prescribed antibiotics were third generation cephalosporins 63 (38%), broad spectrum penicillin 49 (29.5%), and metronidazole 19 (11.4%) similar with a published study in Egypt.¹² The prescribing of third generation cephalosporins was appreciably higher in Internal Medicine ward, Orthopedic ward and Pediatric ward which was also a commonly prescribed antibiotic in Eastern Europe (35.7%) and Asia (28.6%) in the global ARPEC study, as well as in Turkey (18.4%), Italy (20%), Latvia (28%), Iran

(43.5%), Nigeria (21.4%), Pakistan (35.0%) and India (38.9%).^{8,10,11} The high prevalence of use of third generation cephalosporins in the medical ward could be explained by the fact that patients admitted to this ward have a high prevalence of infections, with community acquired infections the most common indication for administering antibiotics and as a surgical prophylaxis in Orthopedic ward. The high consumption of third generation cephalosporins in the pediatric ward could be attributed to the fact that pediatric patients tend to have a high prevalence of serious infections such as pneumonia and meningitis compared to adults. The overall widespread use of third generation cephalosporins in the hospital reflects their tendency to be used for empiric management of serious infections, influenced by the fact that clinicians and nurses find their frequency of dosing convenient. They can be administered once or twice a day and a cost effective compared to the first line agents such as benzyl penicillin, which have to be administered every six hours. This needs to be investigated further. The majority of antibiotics prescribed in Gynecological/Obstetrics and Surgery ward were Beta- lactam and metronidazole which was attribute to a high frequency of mixed anaerobic and aerobic infections in this setting. Surgical prophylaxis was the main indication in this group of patients which is effective in reducing post-operative complications.⁹

Variations in antibiotic use pattern may also be due to difference in the spectrum of diseases and the facilities across countries and regions; however, this needs to be investigated further before any definitive statements can be made. There is also likely to be variation among the departments in the pattern of antibiotic use within the department in Dhulikhel hospital. Overall, the extensive use of broad-spectrum antibiotics in Dhulikhel hospital could be explained by the potential for practitioners to overprescribe antibiotics if they view such practices as a viable way to ensure a speedy recovery.¹³

Another concern is the very high usage of parenteral antibiotics (78.4%) observed in this study which was higher than the previous study done in western Nepal (51.0%), South India (36.0%), and Israel (64.0%).¹⁴ We believe this goes hand in hand with the high use of third generation cephalosporins (ceftriaxone) for which no oral equivalent is currently available. Nevertheless, many physicians and patients consider that parenteral therapy is superior more effective than oral administration.¹⁵ Moreover, the use of

parenteral antibiotics is inevitable in case of life-threatening infections. Most of the IV antibiotics were switched to oral in 1-3 days (51.5%) which was more practice in Gynecology/Obstetric ward (99.2%) due to the reason that high number of antimicrobial prescriptions was for surgical prophylaxis, followed by 4-7 days (28.3%) which was high in Orthopedics ward (64.3%).

The patients were more likely to receive antibiotic for NBPI 66 (52.8%) which was lower than previous study done in one of the teaching hospitals in Western Nepal (62.0%),¹⁴ followed by prophylactic use 51 (40.8%) and only 8 (6.4%) patient received antibiotic for BPI (Table 3). NBPI was the most common indication for antibiotic use in Pediatrics department whereas prophylactic use was high in Gynecology/Obstetrics department.

CONCLUSION

This study indicated a high prevalence of antibiotic use among inpatients in five different wards of Dhulikhel Hospital. To preserve the future effectiveness of antibiotics and reduce harm due to AMR, it is imperative to rationally scrutinize and improve prescribing practice.

Conflict of Interest

None

Funding

None

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