

# Pattern of Antibiotics Use for Prophylaxis and Treatment among Patients Who Undergone Major Surgery at Nekemte Referral Hospital, West Ethiopia

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## Abstract

**Background:** Appropriate use of antimicrobial agents is vitally important from clinical perspectives and is essential if the usefulness of antibiotic is to be preserved and the further spread of resistance is to be limited. Antibiotics are one of the pillars of modern medical care and play a major role both in prophylaxis and treatment of infectious diseases. However, their misuse is a worldwide problem with the extent of the problem being greater in the developing countries.

**Objective:** To assess antibiotics use for prophylaxis and treatment among patients who undergone major surgery in Nekemte Referral Hospital.

**Methods:** A retrospective cross-sectional study was conducted on 228 medical records of patients who undergone major surgery at Nekemte Referral Hospital during February 2017 to February 2018. Stratified random sampling technique was used for this study. Data was collected by using a pre-tested structured questionnaire from March, 2018 to May, 2018 and then analyzed using statistical package for social science (SPSS) version 20.0 software.

**Result:** Out of 228 patients who undergone major surgery 177 patients were male and 51 patients were females. Based on age group classification <20 (21.1%) was mostly affected. The most common diagnosis was appendectomy (32.9%) followed benign prostate hyperplasia (20.2%). The most frequently prescribed antibiotics drugs was ceftriaxone (52.88%), followed by Metronidazole (29.58%) for treatment and for prophylaxis ceftriaxone (71.96%) followed metronidazole (17.56%). The most used class of drug for prophylaxis was cephalosporin (72.45%) and Nitro imidazole (17.35%); and for treatment cephalosporin (56.81%) followed by Nitro imidazole (29.58%).

**Conclusion:** Generally, this study indicated that underwent surgical procedures by majority of patients were appendectomy and benign prostate hyperplasia. Mostly prescribed antibiotics in the patients who undergone major surgery were ceftriaxone followed by Metronidazole. In general, this study result indicated some level of inappropriateness which high light need for intervention.

**Keywords:** Antibiotics; Major surgery; Resistance; Prophylaxis; Treatment; Ethiopia

## Introduction

Antibiotics are one of the pillars of modern medical care and plays major role both in prophylaxis and treatment of infectious diseases. The issues of their availability, selection, and proper use are of critical importance to the global community. Antibiotic misuses are however, a worldwide problem with the extent of the problem being greater in the developing countries through their purchase (without prescription) in local pharmacies and drug stores, and through inappropriate prescribing habits and an over-Zealous desire to treat severe infections [1].

Prophylactic antibiotics are widely used in surgical procedures and account for substantial antibiotic use in many hospitals. The purpose of SAP is to reduce the prevalence of postoperative wound infection (about 5% of surgical cases overall) at or around the surgical site. By preventing surgical site infections, prophylactic antimicrobial agents have the potential to decrease patient morbidity and hospitalization costs for many surgical procedures that pose significant risk of infection. However, the benefits of prophylaxis are controversial, prophylaxis is not justified for some surgical procedures (e.g., urologic operations in patients with sterile urine). Consequently, the inappropriate or indiscriminate use of prophylactic antibiotics can increase the risk of

drug toxicity, selection of resistant organisms, and costs [2].

Serious morbidity and mortalities are associated with post-operative wound infections. They have an enormous impact on patient's quality of life and contribute substantially to the financial cost of patient care. The use of preoperative antibiotics has become an essential component of the standard of care in virtually all surgical procedures, and has resulted in a reduced risk of the post-operative infection when sound and appropriate principles of prophylaxis are applied [3].

In 1960s it was reported that pathogens are present during surgery

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regardless of how aseptic the surgery might appear. Moreover, the correlation between prophylactic antibiotics and post-operative wound infections were demonstrated. Therefore, antibiotic prophylaxis now used in almost all surgical procedures, the preoperative administration of antibiotics because it can act at the time when the wound is potentially contaminated that the use of antibiotics after 3-4 hours of a bacterial incision is unsuitable [4].

Previous studies have demonstrated that antibiotics must be active against major anticipated pathogens and must have reached sufficient concentration in the tissue or body fluids at risk by the time of bacterial challenges. If prophylactic therapy is to be maximally effective in reducing the infection rate of potentially contaminated surgery. The need for continuing antibiotic prophylaxis of operation, however, has been uncertain [5].

Different studies had indicated that there is high proportion of inappropriate antibiotics use for patients who admitted at surgical ward and these studies have also suggested reasons for inappropriateness as an excessive duration of treatment, incorrect timing of administration, inadequate antibacterial spectrum of the drugs used, and unnecessary combination of two antibiotics [6-16].

The increase resistance rate of many important pathogens to currently most available antibiotic has been recognized as an important and potentially life threatening problem. This problem is promoted in part by irrational antibiotics prescribing behavior and usage. Medically inappropriate, ineffective and economically inefficient use of pharmaceuticals is common health care systems problem throughout the world especially in the developing countries [10].

This study aimed at identifying inappropriate use of antibiotics for prophylaxis and treatment at surgical ward which serve as a baseline data for health authority and policy maker and it helps in developing strategies or essential drug list guideline for rational use of drugs at the hospital level as well as for improvement of hospital service.

## Methods

### Study setting

The study was conducted in Nekemte referral hospital, Nekemte town, Eastern Wollega zone, Oromia regional state which is located at 331 km from west of Addis Ababa. NRH was established in 1932 (1924 E.C) by Swedish missionary. It has a different department and wards like outpatient department (OPD), medical wards, gynecology and obstetrics ward, pediatrics ward and surgical ward. It delivers diversified health services and clinics including the emergency services, eye clinic, dental clinic, mother and child health (MCH), psychiatry clinic, laboratory, radiology, pharmacy, physiotherapy and follow up of chronic disease. The study was conducted from March 20/2018 to May 5/2018.

### Study design

Retrospective cross-sectional study on assessment of drug use was conducted using patients' medical card.

Source population: All medical records of patients, who undergone major surgery from February 2017-February 2018.

Study population: A medical record of Patients with antibiotics prescription in major surgery which get chance of selection.

### Eligibility criteria

**Inclusion criteria:** All patients who undergone major surgery from

February, 2017 to February, 2018 at NRH

**Exclusion criteria:** Patient cards with incomplete information for the study.

**Sample size:** The minimum statistically required sample size was calculated by using the following formula.

$$N = \frac{Z^2 P(1-P)}{D^2}$$

$$D^2$$

Where:

N=Sample size required

P=Prevalence rate of antibiotics

Z=The standard normal Confidence at interval of 95% =1.96

D=The margin of sampling error tolerated

Since there is no prevalence rate for prescription pattern, 50% was taken to get maximum sample size with confidence interval of

95% margin of error therefore, the sample size was:

$$n = \frac{(1.96)^2 0.5 (0.5)}{(0.05)^2} = 384$$

Since the total number of patients who undergone major surgeries are less than 10,000 the following correctional formula was used.

$$n_f = \frac{n}{1 + \frac{n}{N}}$$

Where: n=initial sample size which was 384

nf= desired sample size

N= population size 560 (total number of patients who who undergone major surgery at NRH from February 2017-February 2018)

Therefore,  $n_f = \frac{n}{(1+n/N)} = \frac{384}{(1+384/560)} = 228$ .

**Sampling technique:** Stratified random sampling method was conducted to select more representative sample. There are seven therapeutic indication of major surgery in NRH during study period, to calculate sample allocated to each stratum proportionate allocation was used. Then a simple random sampling was done depending on the type of allocation.

Proportionate allocation:

$$n_i = \frac{n}{N} * N_i$$

Where:

n<sub>i</sub> is sample size of the i<sup>th</sup> stratum

N<sub>i</sub> is population size of the i<sup>th</sup> stratum

### Study variables

**Independent variables:** Age, Sex, Diagnosis, residence, number of antibiotics used, duration of hospital stay.

**Dependent variables:** Appropriateness of antibiotic use.

**Data collection procedure:** Relevant information about each patient like demographic factors, type of diagnosis, medication history (antibiotics used for prophylaxis and treatment including

other medication used), other comorbid conditions, durations of hospitalization stay and condition of discharge were recorded using well-structured data collection format through reviewing medical records of patients. Other supplementary information was obtained from register. Appropriateness of antibiotic use was checked by using the Ethiopian Standard Guidelines for general hospitals [17].

**Data quality control:** To maximize accuracy of this study, data collection format was validated with its objective and developed enough to assess the objective of the study. This data collection format was pre-tested on 5% [18] of patient's cards from the same source population before starting actual data collection. Patient's cards which used for pre-testing is not used in study. In addition, regular checkup for completeness and consistency of the data was made on daily basis. To check the consistency, data were entered in two different SPSS programs (double method).

### Data analysis and presentation

Data entry and analysis was carried out using statistical package for social science (SPSS) version 20.0. Descriptive statistics were used for statistical analysis. The result was analyzed and presented using tables and graphs. Data available was interpreted and discussed with the results of similar studies.

### Ethical consideration

Ethical clearance was obtained from Wollega University, College of Health Sciences Ethical Review Committee. A formal letter was written to the NRH in order to get permission to conduct the study and Official permission was granted from the hospital administration. To ensure confidentiality, name and other identifiers of patients and prescribers were not recorded on the data abstraction formats.

### Result

#### Socio-demographic characteristics

A total of 228 patients' medical records that undergone major surgery and took antibiotics drugs were analyzed. The majority of the patients were less than 20 years, 48 (21.1%) and 21-30 years, 45 (19.7%). But inappropriateness of antibiotics used for treatment was higher in age between 51-60 years and above 60 years. And also the prevalence of inappropriateness is higher in antibiotics used for treatment (43.4%) than for prophylaxis (27.6%) (Table 1).

#### Therapeutic indication

Out of 228 patients who undergone major surgery at NRH from February 2017 to February 2018, the most frequently diagnosed disease for which antibiotic indicated were appendectomy 75 (32.9%) followed by Benign prostate hyperplasia 46 (20.2%) (Table 2).

#### Total antibiotics used for surgical prophylaxis and treatment

As shown below in the Table 3, the most commonly prescribed antibiotics for patients who undergone major surgery for both Prophylaxis and Treatment Were Ceftriaxone 71.96% and 52.88% respectively, followed by Metronidazole (Table 3).

#### Prescribed antibiotic drug regimens (single/multiple drugs) for prophylaxis and treatments

228 patients were treated with different regiment of antibiotics drugs. The numbers of patients who were treated with monotherapy for prophylaxis were 160 (70.2%) and for the treatment were 85 (37.3%).

No.	Socio-demographic characteristics	Frequency N (%)	Inappropriateness of antibiotic used	
			For Prophylaxis N (%)	For Treatment N (%)
<b>Age group (year)</b>				
1	< 20	48 (21.1)	11 (22.9)	20 (41.7)
	21-30	45 (19.7)	11 (24.4)	17 (37.8)
	31-40	34 (14.9)	8 (23.5)	13 (38.2)
	41-50	42 (18.4)	12 (28.6)	18 (42.8)
	51-60	28 (12.3)	10 (35.7)	16 (57.1)
	>60	31 (13.6)	11 (35.5)	15 (48.4)
	Total	228 (100)	63 (27.6)	99 (43.4)
<b>Sex</b>				
2	Male	177 (77.6)	48 (27.1)	79 (44.6)
	Female	51 (22.4)	15 (29.4)	20 (39.2)
<b>Residence</b>				
3	Urban	89 (39.0)	22 (24.7)	34 (38.2)
	Rural	139 (61.0)	41 (29.5)	65 (46.8)
N- is the number of patient				

**Table 1:** Socio-demographic characteristics cross tabulation with inappropriateness of antibiotic used for patients who undergone major surgery at surgical ward of NRH from February 2017 to February 2018 n=228.

Diagnosis	Frequency	Percentage (%)
Appendectomy	75	32.9
BPH	46	20.2
LBO	32	14
Inguinal hernia	24	10.5
SBO	23	10.1
GS	16	7
Cholecystectomy	12	5.3
Total	228	100

**Table 2:** Types of diagnosis of major surgery at NRH from February 2017 to February 2018.

Drug name	Prophylaxis	Treatment
	No of patients N (%)	No of patients N (%)
Ceftriaxone	213 (71.96%)	202 (52.88%)
Metronidazole	52 (17.56%)	113 (29.58%)
Cloxacillin	11 (3.71%)	14 (3.66%)
Ampicillin	20 (6.76%)	21 (5.5%)
Gentamycin	0	14 (3.66%)
Cephalexin	0	15 (3.93%)
Norflaxacillin	0	3 (0.79%)
Total	296 (100%)	382 (100%)

**Table 3:** Total antibiotics used for surgical prophylaxis and treatment at NRH for a patient who undergone major surgery from February 2017 to February 2018.

From antibiotic combinations, combinations of two drugs prescribed for prophylaxis were 68 (29.80%), and for the treatment were 130 (57.00%) patients (Figure 1).

#### Appropriateness of antibiotics

Appropriate antibiotics used for prophylaxis were 165 (72.37%) and appropriate antibiotics used for treatment where 129 (56.58%) (Table 4).

### Single prescribed antibiotics

As shown below in Table 5, the most frequently prescribed antibiotics are ceftriaxone; for prophylaxis 98.75% (N=158) and for treatment 96.5% (N=83) (Table 6).

### Combination of antibiotics used for prophylaxis and treatment

According to the result in Table 6 below, antibiotics combination regimen used for prophylaxis was Ceftriaxone+Metronidazole (57.4%), Metronidazole+Ampicillin (19.1%), Ceftriaxone+cloxacillin (16.2%), Ampicillin+Ceftriaxone (7.4%).

For treatment; Ceftriaxone+Metronidazole (76.8%), Metronidazole+Ampicillin (3.6%), Ceftriaxone+cloxacillin (8%), Ampicillin+Ceftriaxone (2.2%), Ampicillin+Gentamicin+Cephalexin (8%) and Ampicillin+Ceftriaxone+Metronidazole (1.45%) (Table 6).

### Class of antibiotic prescribed

This study indicate that most prescribed antibiotic classes were cephalosporin 213 (72.45%), followed by nitroimidazole 51 (17.35%) for prophylaxis and cephalosporin 217 (56.81%), and nitroimidazole 113 (24.26%) for treatment respectively (Table 7).

### Presence of other comorbid conditions and other medications taken, duration of hospital stay and condition of discharge

As shown in the table below, 36.4% patients had other comorbid conditions and 32.9% patient have taken other medication in addition to antibiotics. Duration of Hospital stay was <10 days for 76.3%

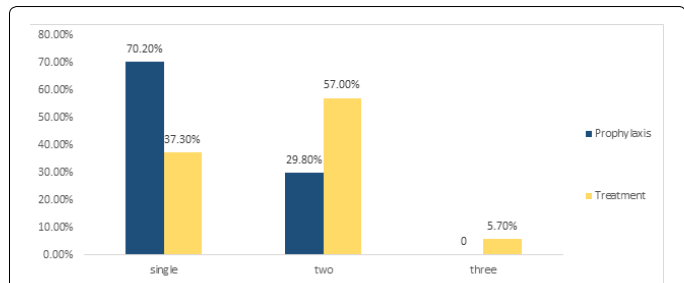


Figure 1: Prescribed antibiotic drugs regimen (single/multiple drugs) for prophylaxis and treatments at surgical ward of NRH from February 2017 to February 2018.

Reason for use	Appropriateness	Frequency	Percentage (%)	
Prophylaxis	Appropriate	165	72.37	
	Inappropriate	inappropriate choice	40	17.54
		unnecessary combination	23	10.09
		Total	63	27.63
Treatment	Appropriate	129	56.58	
	Inappropriate	Excessive duration	27	11.84
		Short duration	9	3.94
		inappropriate choice	45	19.74
		unnecessary combination	18	7.9
		Total	99	43.42

Table 4: The appropriateness of antibiotic used for patients who undergone major surgery at NRH from February 2017 to February 2018.

Drug name	Prophylaxis No of patients N (%)	Treatment No of patients N (%)	Total N (%)
Ceftriaxone	158 (98.75%)	83 (96.5%)	241 (97.97)
Ampicillin	2 (1.25%)	0	2 (0.81)
Norflaxacillin	0	3 (3.5%)	3 (1.22)
Total	160 (100%)	86 (100%)	246 (100)

Table 5: Single prescribed antibiotics for patients who undergone major surgery at NRH from February 2017 to February 2018.

	Antibiotic combination	Frequency	Percentage (%)
For prophylaxis	Ceftriaxone+Metronidazole	39	57.4
	Ampicillin+Ceftriaxone	5	7.4
	Metronidazole+Ampicillin	13	19.1
	Ceftriaxone+cloxacillin	11	16.2
	Total	68	100
For treatment	Ceftriaxone+Metronidazole	106	76.8
	Metronidazole+Ampicillin	5	3.6
	Ceftriaxone+cloxacillin	11	8
	Ampicillin+Ceftriaxone	3	2.2
	Ampicillin+Ceftriaxone+Metronidazole	2	1.45
	Ampicillin+Gentamicin+Cephalexin	11	8
Total	138	100	

Table 6: Combination of antibiotics used for prophylaxis and treatment for patients who undergone major surgery at NRH from February 2017 to February 2018.

Class of antibiotic	For prophylaxis N (%)	For treatment N (%)	Total (%)
Cephalosporin's	213 (72.45)	217 (56.81)	430 (63.61)
Nitroimidazole	51 (17.35)	113 (29.58)	164 (24.26)
Penicillin's	30 (10.2)	35 (9.16)	65 (9.62)
Aminoglycosides	0	14 (3.66)	14 (2.07)
Fluoroquinolones	0	3 (0.79)	3 (0.44)
Total	294 (100)	382 (100)	676 (100)

Table 7: Class of antibiotic used for prophylaxis and treatments for patient who undergone major surgery in NRH from February 2017 to February 2018

patients, 11-20 days for 21.9%, and >20 days for 1.8%. And Condition of discharge for patients who undergone major surgeries were 90.8% improved (Table 8).

This study indicate that duration of hospital stay was higher (>11 days) for 75.93% patients who receive antibiotics inappropriately. And also this study found that 10.5% of condition of discharge for patient who undergone major surgery was death, out of this 70.83% of patients has taken antibiotics inappropriately. Special attention needed to be given for patients with other comorbid conditions and taking other medications in addition to antibiotics (Table 8).

### Discussion

This study identified that the prevalence of appendectomy was found to be 32.9%, which has no more difference with study done in Italian general hospital (37.68%). But prevalence of Cholecystectomy



No.	Variables	Frequency N (%)	Inappropriateness of antibiotic use	
			For prophylaxis N (%)	For treatment N (%)
1	Comorbid conditions available	83 (36.4)	27 (32.5)	42 (50.6)
2	Took Other medications	75 (32.9)	26 (34.7)	39 (52)
3	Duration of Hospital stay			
	<10	174 (76.3)	35 (20.1)	58 (33.3)
	Nov-20	50 (21.9)	26 (52)	39 (78)
	>20	4 (1.8)	2 (50)	2 (50)
4	Condition of discharge			
	Improved	204 (89.5)	54 (26.5)	82 (40.2)
	Died	24 (10.5)	9 (37.5)	17 (70.83)

**Table 8:** Medication and disease related factors cross tabulation with inappropriateness of antibiotic used for patients who undergone major surgery at NRH from February 2017 to February 2018.

was 5.3 % which is very low than result of study in same hospital (Italian general hospital) (49.27%) [8]. According to this study Benign prostate hyperplasia were (20.2%) which was very different with study done in Department of Surgery, Rangpur Medical College Hospital, Rangpur, BPH which was (42%) [19]. The reason for the difference could be because the study done Rangpur Medical College Hospital mainly deals with study of major surgery associated with obstructive jaundice.

In this study the prevalence of inguinal hernia found to be 10.5% which was almost similar with the study done in a tertiary care teaching rural hospital in India (10.36%) [16]. In this study the prevalence of genitourinary systems found to be 7 % which had no more difference with the study done in secondary health-care level in the Kyrgyz republic (13.9%) [20]. Out of 228 patients, small bowel obstruction was done for 23 (10.1 %) and large bowel obstruction 32 (14.0%) which was very different with study done in Adama Hospital Medical College [21] small bowel obstruction (64 %) and large bowel obstruction (36.0 %).

In this study from the prescribed antibiotic drugs ceftriaxone was 52.88% for treatment which was different with study done in Navy Hospital, Jakarta, Indonesia 87.8% but, gentamycin use was similar in the same hospitals 3.66% and 3.7% respectively [13]. In this study (for treatment) the metronidazole prescribed were (29.58%), cloxacillin (3.66%), ampicillin (5.5%) and gentamycin (3.66%) When we compare with study done in Manipal Teaching Hospital, Pokhara, Nepal [12] the most commonly used individual antibiotics were preparation of ampicillin and cloxacillin (54.64) followed by metronidazole (31.95), ampicillin (18.34) and gentamicin (16.37), which was different but there is no more difference in case of metronidazole.

In current study the most prescribed antibiotic were ceftriaxone (71.96%), Metronidazole (17.56%) and ampicillin (6.76%) for prophylaxis respectively which was different with study done in Orthopedics and Traumatology Surgical Unit of a Tertiary Care Teaching Hospital in Addis Ababa [22] the most frequently prescribed antimicrobial agent used for prophylaxis was ceftriaxone (70%), cloxacillin (9%) and Metronidazole (7%) was used. However, ceftriaxone was almost similarly prescribed. The prophylactic antimicrobial regimens included both single as well as combination regimens; single regimens in prophylaxis took the lion's share. In this study the most commonly prescribed regimen among the combination regimens was ceftriaxone plus Metronidazole (57.4%), and metronidazole plus

ampicillin (19.1%).

Combination of antibiotic are prescribed to reduce risk of wound infection and to prevent infection situation of a gross contamination. In this study the most prescribed combination antibiotic drugs for treatment were ceftriaxone plus Metronidazole 106 (76.8%) followed by cloxacillin plus ceftriaxone 11 (4.8%), ampicillin plus gentamycin plus cephalixin 11 (4.8%), and ceftriaxone plus Metronidazole plus ampicillin 2 (0.9%) which was very different with study done in Manipal Teaching Hospital, Pokhara, Nepal [23] the most commonly used antibiotic regimens were: ampicillin and cloxacillin combination preparation (27.22%), ampicillin and cloxacillin combination along with metronidazole (5.13), ampicillin, metronidazole and gentamicin (2.76%) and Metronidazole plus cloxacillin (2.56%). The difference for antibiotic utilization could be because of difference on the type of common surgery in current study and the study done in Manipal Teaching Hospital.

The most common class of antibiotics used for patient who undergone major surgery for prophylaxis were cephalosporin 213 (31.51%), followed by Nitro imidazole 51 (7.54%) and penicillin 30 (4.44%). Similarly a study done in Medicine surgical inpatient wards of Basaweswara Medical College Hospital [6] the most prescribed antibiotics were 3<sup>rd</sup> Generation Cephalosporin's 108 (40.7%), followed by Aminoglycoside 11 (4.2%), Fluoroquinolones 11 (4.2%), and Penicillin 9 (3.4%).

The numbers of patients who were treated with monotherapy of antibiotic drugs for prophylaxis were 160 (70.2%) and for the treatment 85 (37.3%) and from antibiotic combinations, two drugs combination prescribed for prophylaxis were 68 (29.8%), and for the treatment 130 (57.0%) patients, and three drugs combination for treatment were prescribed 13 (5.7%), which was different with study done in Medicine surgical inpatient wards of Basaweswara Medical College Hospital [6] which majority of them are on single antibiotics 73 (45.1%), two antibiotics 75 (46.3%) and three antibiotics 14 (8.6%) for prophylaxis. The reason for the difference could be because of difference in study design as the study done in Basaweswara Medical College Hospital was a prospective study.

According to this study appropriately used antibiotic for prophylaxis were 72.37% which was very similar with study done in 21 public hospitals in Italy which were 72.6% [18]. This study also found that antibiotic therapy for treatment was inappropriate in 43.42% of patients. This finding was completely in agreement with the published data indicating that as many as 41% to 91% of all antibiotic prescriptions in hospitals are inappropriate [24]. Similar findings were also reported by another study from Brazil where rational antibiotic use was only 45.7% [25].

Limitation of this study was that the study design we used was retrospective study which is often subject to biases (errors that affect the observations of an investigation); for example, in the collection of data it is difficult to evaluate how the patients took their medication and if there is any unwanted effect of the drugs. Being retrospective study also made us not to study important variables including education level, adherence, patient-health worker communication and provider and health system related factors. Another limitation was the small sample size that we have used and that this study included only one referral hospital of the country.

## Conclusion

Generally, this study indicated that underwent surgical procedures by majority of patients were appendectomy and benign prostate

hyperplasia. Mostly prescribed antibiotics in the patients who undergone major surgery were ceftriaxone followed by Metronidazole. But since ceftriaxone is broad spectrum antibiotics it has higher chance to cause more drug resistant bacteria, thus we recommend the use of cefazolin which is a first line agent for prophylaxis for most surgical cases. Additionally, the result of this study indicated some level of inappropriateness which highlights the need for intervention. The role of clinical pharmacist by studying the prescribing patterns was useful as it helps to assess if the right prophylactic therapy and postoperative treatment is being followed in the hospital.

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#### Competing Interests

No competing interests between authors.

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