

DRUG UTILIZATION EVALUATION OF PRE-OPERATIVE ANTIMICROBIALS USED IN SURGERY DEPARTMENT AT A TERTIARY HOSPITAL

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ABSTRACT

The use of antimicrobial agents need to be evaluated since misuse of antimicrobials may lead to increased adverse effects, resistance to antimicrobials, making illnesses more serious, and increasing expenses of health services. The aim of this study was to assess the Drug Utilization Evaluation of pre-operative antimicrobials used in the surgery department at a tertiary care hospital. This prospective observational study was carried out with 181 patients who had undergone various surgeries in the General Surgery department of Muthoot Healthcare Kozhencherry from November 2018 to May 2019. In this study it was found that the majority of surgeries were performed in males and the age group of 61-80 years. Most of the subjects had

undergone incision and drainage. The most commonly and efficiently used preoperative antibiotic and antiprotozoal agent was the fixed dose combination of Cefoperazone-Sulbactam (56.35%) and Metronidazole respectively. Drug utilization evaluation of antimicrobials are essential as it highlights the importance of assessing optimal drug use and provides a strong basis for therapeutic decision making.

KEYWORDS: ANTIMICROBIALS; DUE; PRE-OPERATIVE;
CEFOPERAZONE-SULBACTAM; METRONIDAZOLE.

INTRODUCTION

Drug Utilization Evaluation (DUE) helps in assessing the actual process of medication prescribing, administration, or dispensing. It involves a comprehensive review of patients' prescription and medication data before, during and after dispensing in order to assure appropriate therapeutic decision-making and positive outcome. Identification of drug use errors and problems that contribute to rational drug therapy can be achieved through DUE.^[1] Our study basically focuses on the DUE of preoperative antimicrobials used in a general surgery department in a tertiary care hospital. The use of antimicrobials is an area of problems that may increase the hospital stay of patients. Here we analyze whether the use of antimicrobials is according to the guidelines.

Antibiotics have 2 indications in surgery:

- To treat established infections.
- To prevent postoperative infections.^[2]

The main classes of antibiotics are:

- Beta-Lactams: Penicillins, Cephalosporins
- Macrolides
- Fluoroquinolones
- Tetracyclines
- Aminoglycosides.^[4]

Surgical antimicrobial prophylaxis may be defined as a brief course of antibiotic given just before surgery. Surgical site infection increases the hospital stay this may be due to the increase in the risk of morbidity and mortality. Prophylaxis has the potential to shorten hospital stay and fasten return to normal activity after discharge from the hospital.^[1] Judicious use of antibiotics may help in decreasing the morbidity associated with SSI, but inappropriate antibiotic use may lead to antibiotic resistance. Assessment of current antimicrobial utilization patterns is an important step toward promoting the appropriate use of antimicrobial agents, and in India, there is inadequate information and standard guidelines for antimicrobial prophylaxis.^[4] Poor adherence to the guidelines has been reported by various studies, specifically in the area of the antimicrobial selection, timing and the duration of the antimicrobial prophylaxis.^[5]

The goals of prophylactic antimicrobial administration of antimicrobial agents to surgical patients are:

- To reduce incidence of surgical site infection.
- Use antibiotics in a manner that is supported by incidence of effectiveness.
- Minimize the effect of antibiotics on the patient's normal bacterial flora.
- Minimize adverse effects.
- Cause minimal change to the patient's host defenses.^[2]

The following is a direct quote from the current American Heart Association guidelines which indicates about the use of antibiotics as prophylactic agent;

“An antibiotic for prophylaxis should be administered in a single dose before the procedure. If the dosage of antibiotic is inadvertently not administered before the procedure, the dosage may be administered up to 2 hours after the procedure. However, administration of the dosage after the procedure should be considered only when the patient did not receive the pre-procedure dose”.^[6]

Surgical site infection (SSI) is a postoperative complication and an important part of nosocomial infection.^[7] SSIs are the second-most common nosocomial infection accounting for approximately one quarter of 2 million hospital-acquired infections in the United States annually.^[4] The rate of occurrence of surgical site infections in clean surgeries is 1-5%, in clean-contaminated surgeries 6-9%, in contaminated surgeries 13-20%.^[5] Preoperative antibiotic therapy can reduce the incidence of surgical site infections. The most common organisms causing surgical site infections are MRSA, *Staphylococcus epidermidis*, enteric gram+ve cocci, gram-ve bacilli and anaerobes.^[8]

The selection of an appropriate antimicrobial agent for a specific patient should take into account the characteristics of the ideal agent, the comparative efficacy of the antimicrobial agent for the procedure, the safety profile, and the patient's medication allergies.^[9]

The Guidelines for Prevention of Nosocomial Infection proposed by the Brazilian Society of Infectious Diseases suggests that, antibiotic use in surgical prophylaxis should have parenteral presentation, minimal toxicity and cost, be a weak inducer of resistance and possess activity against most pathogens causing surgical site infection in the institution. The Consensus of Rational Use of Antimicrobial Agents, first-generation cephalosporins are the choice of antimicrobials with the nearest profile for most surgical specialties. In India the

prevalence of use of antimicrobial agents varies from 24-67%. The use of antimicrobial agents before, during and after surgery is done to prevent postoperative complications.^[8]

MATERIALS AND METHOD

STUDY DESIGN

Prospective Observational Study.

STUDY SITE

The study was conducted at the General Surgery Department of Muthoot Healthcare Hospital Pvt Ltd., Kozhencherry, Pathanamthitta, Kerala after obtaining the approval from the Institutional Ethical Committee of the hospital.

STUDY PERIOD

6 months (November 2018- April 2019)

SAMPLE SIZE

A sample size of 181 patients who were undergoing the respective surgeries of the inclusion criteria and were under antimicrobial treatment were selected. The sample size was calculated using the standard statistical formula.

STUDY APPROVAL

This study was approved by the Institutional Ethical Committee of the MUTHOOT HEALTHCARE, KOZHENCHERRY.

STUDY SUBJECTS

All the patients under the general surgery department of the hospital during the study period who were eligible for enrollment as well as patients who met the criteria were enrolled.

STUDY CRITERIA

□ Inclusion Criteria

- Patients undergoing following surgeries ; Laparoscopic appendectomy, laparoscopic and open hernioplasty, thyroidectomy, lipoma excision, breast lump excision, circumcision, laparoscopic and open cholecystectomy, video assisted anal fistula treatment, infected sebaceous cyst incision and drainage, slough excision-bedsore, stapler hemorrhoidectomy and fistulectomy.

- Patients of any age and either sex getting admitted in the study site during the study period who have been prescribed with antimicrobials and are willing to participate are included in the study.
- **Exclusion Criteria**
- Patients in whom antimicrobials are not prescribed, those with immuno-compromised disorders and those receiving immuno-compromised drugs.
- Patients with uncontrolled diabetes mellitus.
- Patients who discontinue their treatment, who are not in compliance with the treatment and those who are not willing to participate in the study are excluded.

SOURCE OF DATA

The data required for our study was collected from the hospital.

Pre-designed data collection form:

- Patient demographics
- Medical History
- Medication history
- Treatment regimen
- Culture and sensitivity reports

STUDY PROCEDURE

- A prospective observational study was conducted at the General Surgery Department of Muthoot Healthcare Hospital Pvt Ltd., Kozhencherry, Kerala for a period of 6 months. For this study 181 patients were enrolled based on the inclusion and exclusion criteria.
- All subjects were provided with a brief introduction regarding the study and the confidentiality of the data.
- A written Informed Consent printed in their understandable language was obtained from the patient or care-giver, if the subject was unable to give the same.
- Relevant information was collected according to the approved pre-designed data collection form.
- Data of each subject was individually screened to assess the drug utilization pattern of antimicrobials used in pre-operative patients.
- Data was then statistically analyzed.

DATA ANALYSIS

The data collected was entered as well as analyzed in Microsoft excel -2010 version and results were analysed as tabular form and percentages. Paired T-test was used for analysis of data.

RESULT AND DISCUSSION

In the six month study, 181 eligible patients were enrolled as per the inclusion and exclusion criteria. The results are as follows.

TABLE 1: DISTRIBUTION OF PATIENTS BASED ON AGE GROUP.

AGE GROUP	FREQUENCY	PERCENTAGE (%)
<20	16	8.83
20-40	25	13.8
41-60	59	32.59
61-80	74	40.88
>80	7	3.86
Total	181	100

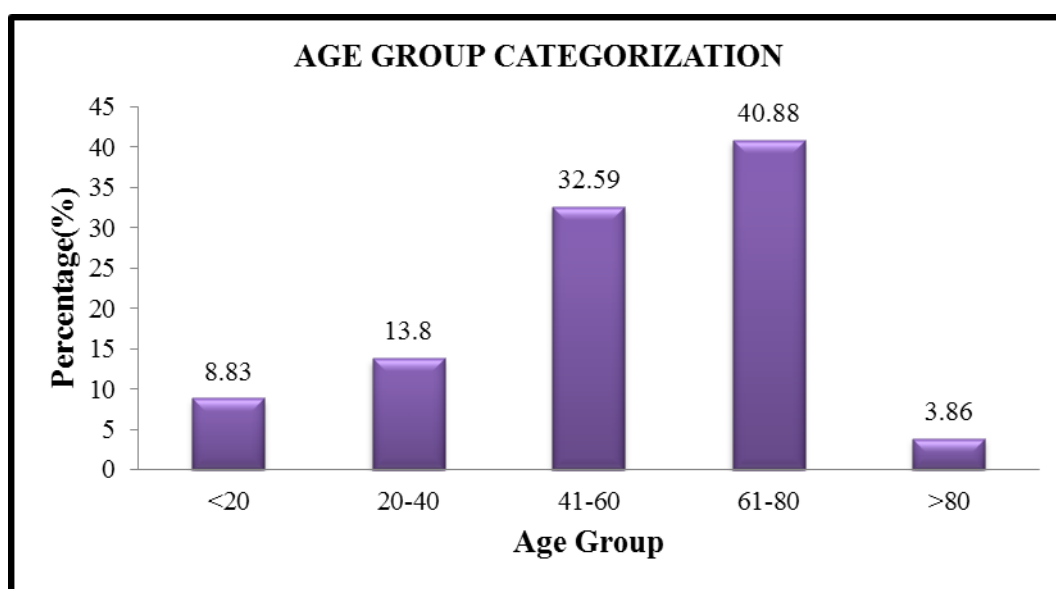
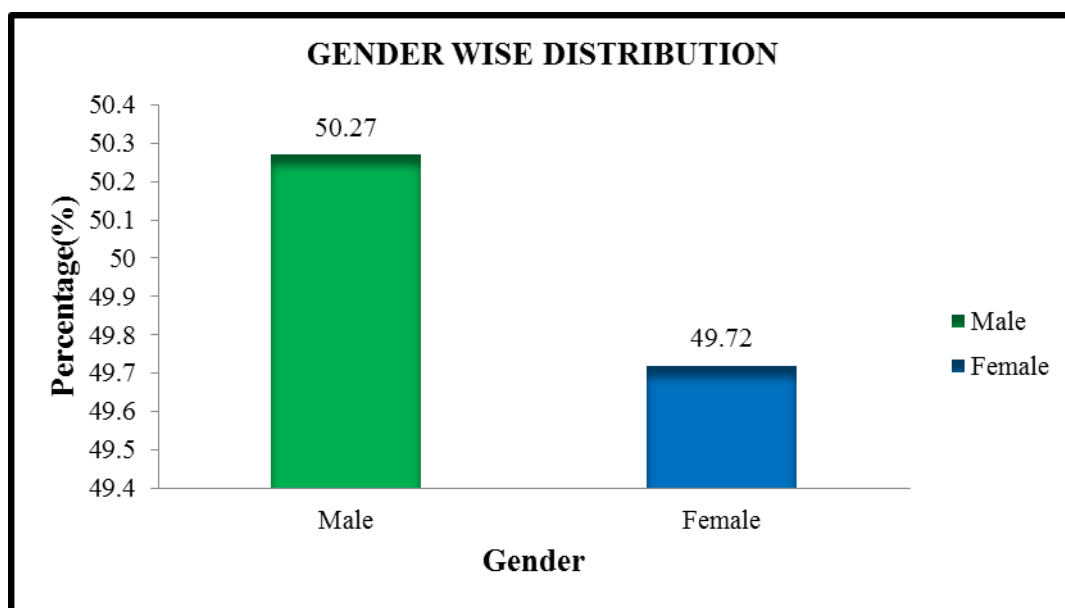


FIGURE 1: DISTRIBUTION OF PATIENTS BASED ON AGE GROUP.

Age wise distribution of the patients were analysed and it was found that 8.83% of the surgeries performed were in the age group of less than 20 years, followed by 13.8% in the age group of 20-40 years, 32.59% in the age group of 41-60 years, 40.88% in the age group of 61-80 years and 3.86% in the age group above 80 years.

TABLE 2: DISTRIBUTION OF PATIENTS BASED ON GENDER.

GENDER	FREQUENCY	PERCENTAGE
Male	91	50.27
Female	90	49.72
Total	181	100

**FIGURE 2: DISTRIBUTION OF PATIENTS BASED ON GENDER.**

The study result shows that 50.27% of the patients were male and 49.72% were female.

TABLE 3: DISTRIBUTION OF PATIENTS BASED ON BODY MASS INDEX.

BMI CATEGORY	FREQUENCY	PERCENTAGE (%)
<18.5: Underweight	6	3.31
18.5-24.9: Normal	98	54.1
25-29.9: Overweight	60	33.1
≥30: Obese	17	9.39
TOTAL	181	100

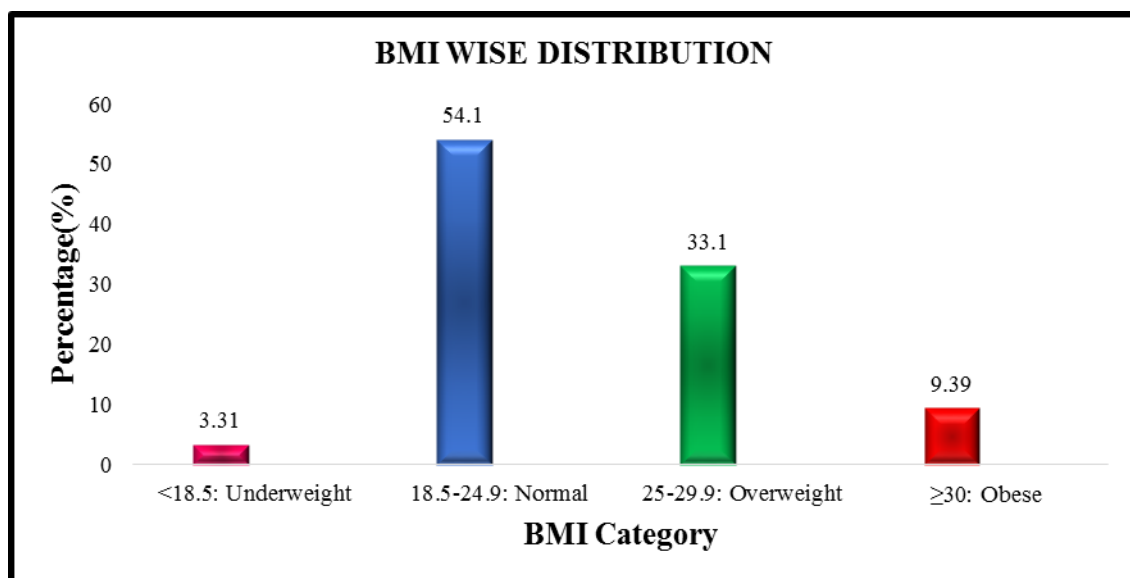


FIGURE 3: DISTRIBUTION OF PATIENTS BASED ON BODY MASS INDEX.

BMI distribution of the patients were analysed and it was found that 3.31% of the patients were underweight, followed by 54.1% had normal weight, 33.1% were overweight, 9.39% were obese.

TABLE 4: DISTRIBUTION OF PATIENTS BASED ON SURGICAL PROCEDURES UNDERGONE.

NAME OF SURGERY	FREQUENCY	PERCENTAGE (%)
Lipoma excision	3	1.65
Circumcision	8	4.41
Thyroidectomy	11	6.07
Cholecystectomy	13	7.18
Slough excision	14	7.73
Appendectomy	15	8.28
Breast Lump Excision	15	8.28
Haemorrhidectomy	15	8.28
Fistulectomy	17	9.39
Hernioplasty	28	15.46
Incision & Drainage	42	23.2
Total	181	100

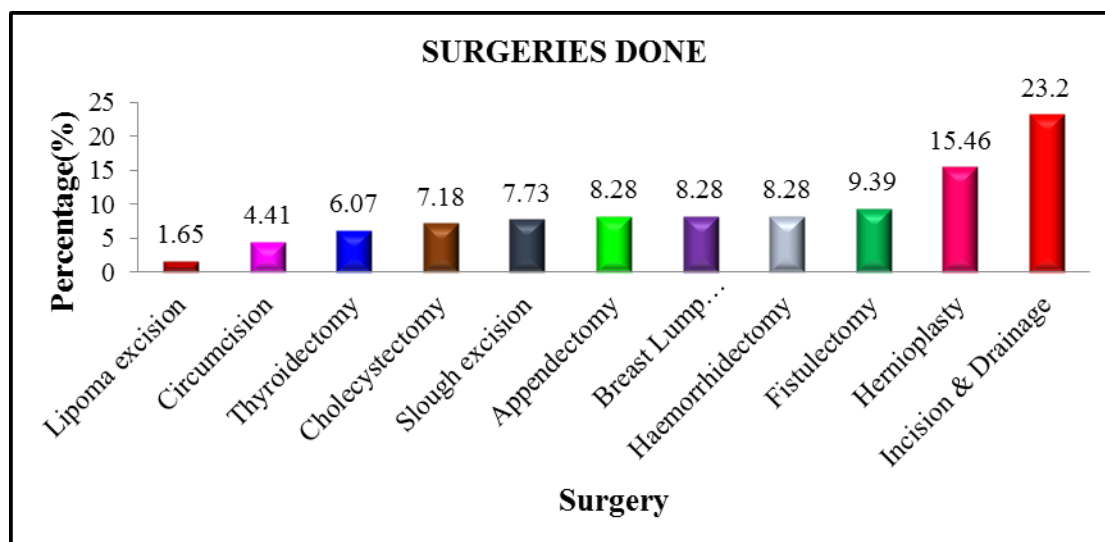


FIGURE 4: DISTRIBUTION OF PATIENTS BASED ON SURGICAL PROCEDURES UNDERGONE.

In the study on analysing the number of surgeries performed in the study population it was noted that 1.65% surgeries done were lipoma excision, 4.41% surgeries were circumcision, 6.07% surgeries were thyroidectomy, 7.18% surgeries were cholecystectomy, 7.73% surgeries were slough excision, 8.28% surgeries were appendectomy and breast lump excision each, 9.39% surgeries were fistulectomy, 15.46% surgeries were hernioplasty and 23.2% surgeries done were incision & drainage. (Figure 4)

TABLE 5: ASSESSMENT OF PREOPERATIVE ANTIMICROBIAL USAGE.

ANTIMICROBIAL USED	FREQUENCY	PERCENTAGE(%)
Antibiotic	153	84.53
Antifungal	0	0
Antiprotozoal	0	0
Antiviral	0	0
Antibiotic + Antiprotozoal	28	15.46
Total	181	100

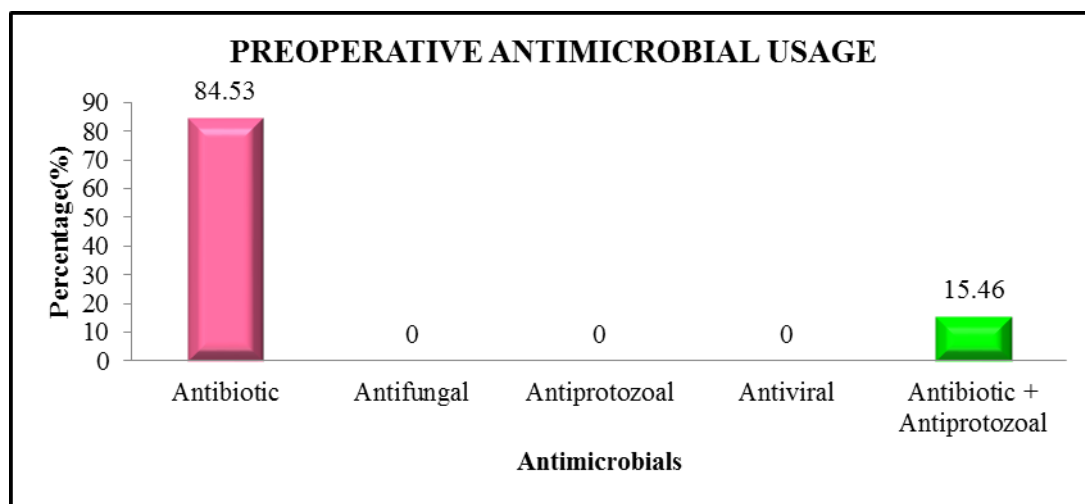


FIGURE 5: ASSESSMENT OF PREOPERATIVE ANTIMICROBIAL USAGE.

On analyzing the study population receiving preoperative antimicrobials, it was found that 84.53% of the population received only antibiotics, 15.46% received a combination of an antibiotic and an antiprotozoal and none of the patients received antifungal, antiprotozoal and an antiviral. (Figure5)

TABLE 6: ASSESSMENT OF PREOPERATIVE ANTIBIOTIC USAGE.

ANTIBIOTICS	FREQUENCY	PERCENTAGE (%)
Cephalosporins	158	87.2
Penicillins	21	11.6
Fluroquinolones	1	0.55
Sulfonamides	0	0
Tetracyclines	0	0
Aminoglycosides	0	0
Macrolides	0	0
Cephalosporins + Penicillins	103	56.9
Cephalosporins+Fluroquinolone	1	0.55

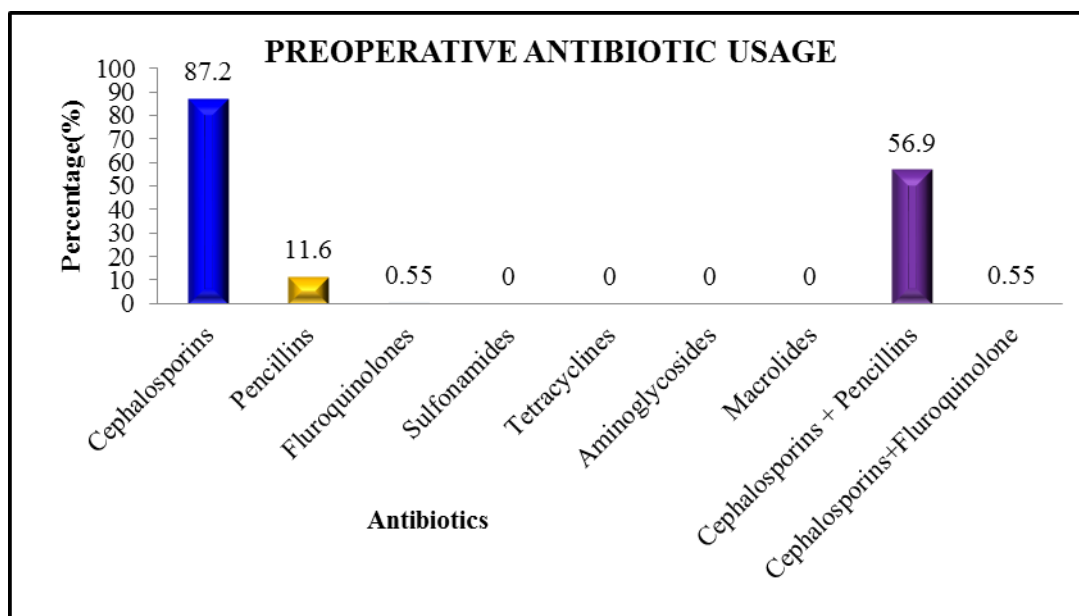


FIGURE 6: ASSESSMENT OF PREOPERATIVE ANTIBIOTIC USAGE.

On analysing the study population for antibiotic usage, it was found that 87.2% of the patients received only cephalosporins, 11.6% received only penicillins, 0.55% received Fluroquinolones, 56.9% received a combination of cephalosporins and penicillin, and none of the patients received sulphonamides, tetracyclines, aminoglycosides and macrolides. (Figure 6)

TABLE 7: COMMONLY USED PREOPERATIVE ANTIMICROBIAL AGENTS.

ANTIMICROBIAL CLASS	DRUG USED
Penicillin	Piperacillin+Tazobactam
Fluroquinolones	Ciprofloxacin
Antiprotozoal	Metronidazole

TABLE 8: ASSESSMENT OF PREOPERATIVE CEPHALOSPORIN USAGE.

CEPHALOSPORINS	FREQUENCY	PERCENTAGE(%)
Cefoperazone+Sulbactam	102	56.35
Ceftriaxone	44	24.3
Cefpirome	10	5.52
Ceftriaxone+Tazobactam	1	0.55

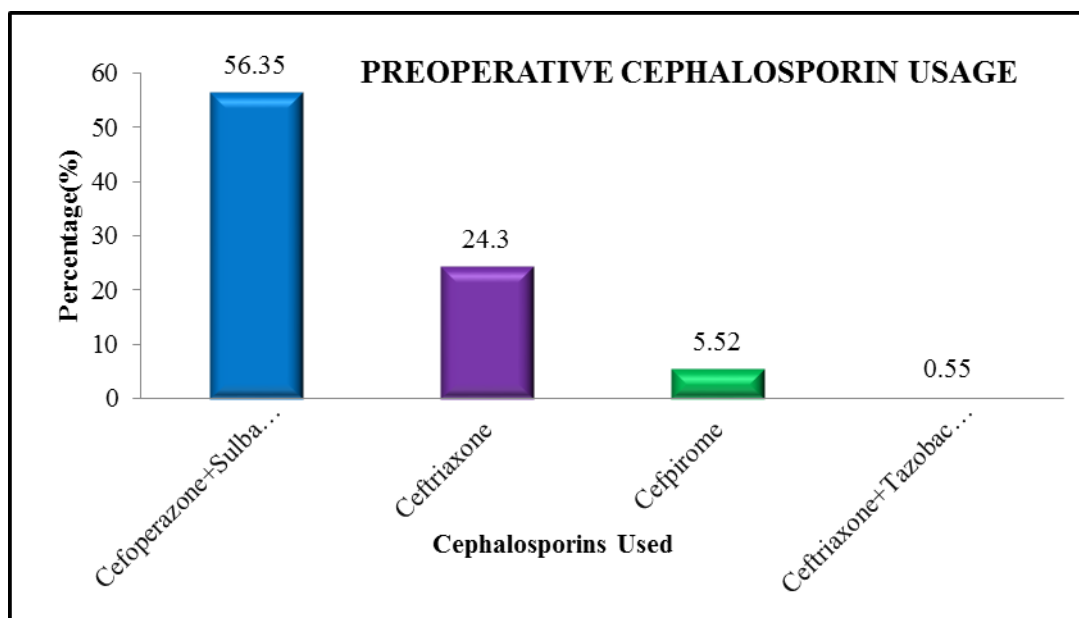


FIGURE 7: ASSESSMENT OF PREOPERATIVE CEPHALOSPORIN USAGE.

Here, on analysing the study population receiving cephalosporins pre-operatively, it was found that, 56.35% of the patients have been treated with a combination of Cefoperazone and Sulbactam, followed by 24.3% with Ceftriaxone 5.52% with cefpirome and 0.55% with a combination of Ceftriaxone and tazobactam.

TABLE 9: ASSESSMENT OF PREOPERATIVE CEPHALOSPORINS USED IN EACH SURGERY.

SURGICAL PROCEDURE	NUMBER OF CASES	NUMBER OF CEFOPERZONE-SULBACTUM	NUMBER OF CEFTRIAZONE
Lipoma excision	3	0	3
Circumcision	8	2	6
Thyroidectomy	11	9	2
Cholecystectomy	13	6	2
Slough excision	14	5	4
Appendectomy	15	10	3
Breast Lump Excision	15	13	1
Hemorrhoidectomy	15	9	5
Fistulectomy	17	12	5
Hernioplasty	28	23	5
Incision & Drainage	42	14	8

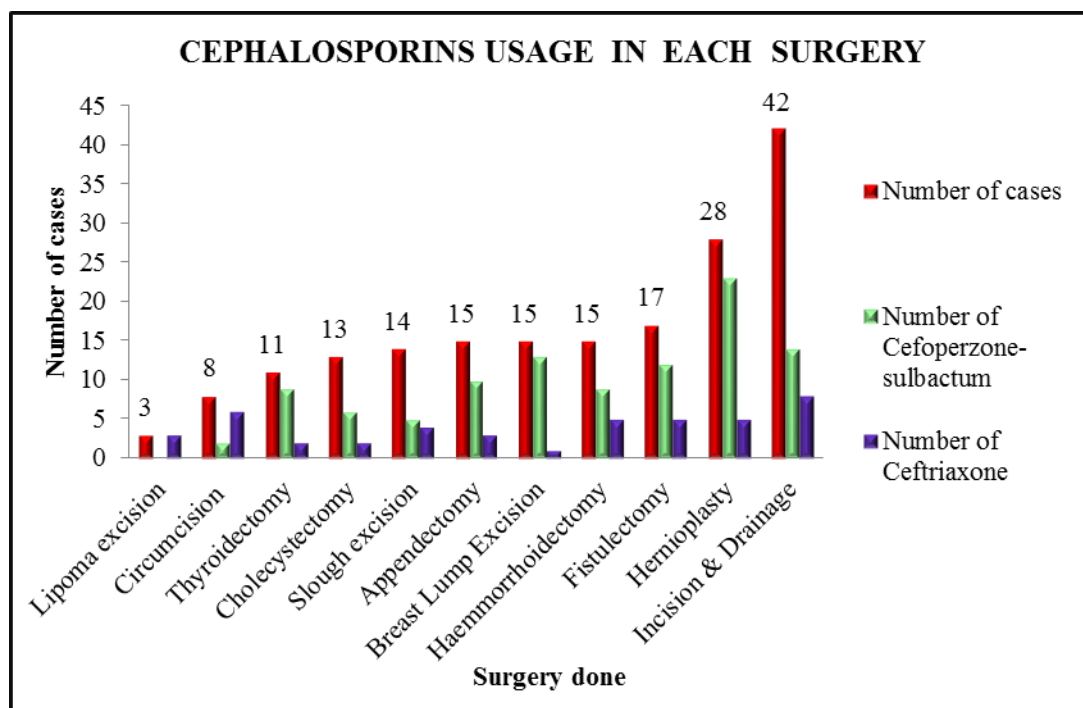


FIGURE 8: ASSESSMENT OF PREOPERATIVE CEPHALOSPORINS USED IN EACH SURGERY.

On analyzing the use of Cefoperazone-Sulbactam combination and Ceftriaxone in each surgery we found out that, the former said antibiotic was used for none of the lipoma excision case, 2 of the circumcision, 9 case of thyroidectomy, 6 cases of cholecystectomy, 5 cases of slough excision, 10 cases of appendectomy, 13 cases of breast lump excision, 9 cases of hemorrhoidectomy, 12 cases of fistulectomy, 23 cases of hernioplasty and 14 cases of Incision & drainage. The antibiotic Ceftriaxone was used for 3 case of lipoma excision, 6 case of circumcision, 2 cases of thyroidectomy, 2 cases of cholecystectomy, 4 cases of slough excision, 3 cases of appendectomy, 1 cases of breast lump excision, 5 cases of hemorrhoidectomy, 5 cases of fistulectomy, 5 cases of hernioplasty and 8 cases of Incision & drainage. (Figure 8)

DISCUSSION

The study was conducted to evaluate the drug use pattern of antimicrobials used in preoperative patients admitted in the general surgery department of Muthoot Healthcare, Kozhenchery.

AGE WISE DISTRIBUTION

Age wise distribution was analyzed and found that most of the surgeries were in the age group of 61-80 years followed by 41-60 years which agrees with the common concept of age related issues, chronic illness, weakened body system functioning even which may be the same in many countries. Similar study conducted by Hussain M *et al.*, (2014) also found that most prescriptions were in the age group of 46-60 years.^[15] A study conducted by Kamarajah SK *et al.*, (2017) the median age of patients was 57 and majority were male (55%).^[16]

SEX WISE DISTRIBUTION

The study was conducted by analyzing the medical reports of 181 patients in which the analysis on gender categorization revealed that the overall study population was predominantly male population (50.27%). The female population was found to be on average 49.72%. In Indian scenario, female populations are reluctant to utilize health care facilities even if they are critically ill and especially if they are from lower socioeconomic strata. In a similar study conducted by Shankar RP *et al.*, (2003) noted that the majority of patients were males.^[17]

BMI WISE DISTRIBUTION

In the study conducted the BMI analysis shows that the patients with normal BMI (54.1%) had to undergo the surgery most followed by the patients with overweight BMI (33.1%) which shows that the people have good knowledge on diet management. In a similar study conducted by Kamarajah SK *et al.*, (2017) out of 368 patients taken, 33% were of normal weight, 31% were overweight, and 35% were obese.^[16]

SURGICAL PROCEDURE DISTRIBUTION

In this study, the most commonly performed surgery is Incision & Drainage (23.2%) followed by hernioplasty (15.46%). In a similar study conducted by Kamata S I *et al.*, (2011) noted that majority of surgeries were hernioplasty followed by appendectomy.^[18] In a similar study conducted by Sane R M *et al.*, (2017) the majority of surgeries in patients were hernioplasty followed by haemorrhoidectomy.^[3]

PREOPERATIVE ANTIMICROBIAL USAGE

In this study preoperative prophylaxis was mostly done with the use of antibiotics (84.53%) or combination of antibiotic and antiprotozoal may be used (15.46%). Almost all patients (181) received preoperative antimicrobials intravenously. None of the antifungal,

antiprotozoal or antiviral agents were used alone for prophylaxis. The antimicrobials were administered half an hour before the incision.

In our study the most commonly prescribed antimicrobial agent was combination of third generation cephalosporin & beta lactamase inhibitors antibiotics, combination of Cefoperazone and Sulbactam and in 15.46% of cases Metronidazole was also administered intravenously along with Cefoperazone and Sulbactam for better coverage. In our study combination of Piperacillin and Tazobactam were used in 11.6% of cases.

In a similar study conducted by VenuGopal D *et al.*, (2014) also found that cephalosporins were mostly prescribed for preoperative patients.^[19]

In a similar study conducted by Afzal Khan A.K *et al.*, (2013) also suggest that third generation cephalosporins were prescribed as preoperative antimicrobials.^[6]

In a study conducted by Abebe FA *et al.*, (2012) reveals that Ceftriaxone was majorly used for preoperative prophylaxis. In our study Ceftriaxone (24.3%) is the second most used preoperative antibiotic.^[1]

In our study the use of Cefoperazone –Sulbactam in each surgery were found to as in follows: lipoma excision-0, circumcision-2, thyroidectomy-9, cholecystectomy-6, slough excision-5, appendectomy- 10, breast lump excision-13, haemorrhoidectomy-9, fistulectomy-12, hernioplasty-23, incision & drainage-14. Similarly the use of Ceftriaxone was found to be: lipoma excision-3, circumcision, thyroidectomy-2, cholecystectomy-2, slough excision-4, appendectomy-3, breast lump excision-1, haemorrhoidectomy-5, fistulectomy-5, hernioplasty-5, incision & drainage-8.

In a study conducted, it was found that, the most frequently used agents for gastroduodenal procedures were first generation and second-generation cephalosporins. No differences in efficacy between first- and second-generation cephalosporins were found.

As per the ASHP guideline, the second-generation cephalosporins with anaerobic activity and a first-generation cephalosporin plus Metronidazole are the recommended agents on the basis of cost and tolerability for appendectomy. For hernioplasty and herniorrhaphy, the recommended regimen is a single dose of a first-generation cephalosporin (Cefazolin). A single dose of second-generation cephalosporin with both aerobic and anaerobic activities

(Cefoxitin or Cefotetan) or Cefazolin plus Metronidazole is recommended for colon procedures.

Cephalosporins are the most widely used antibiotic for surgical prophylaxis for various surgeries due to its featured antimicrobial activities. It is considered the choice of antibiotic or surgical prophylaxis as it shows least allergic reactions when compared to other higher antibiotics. Third generation cephalosporins are widely used in our study as it has activity against both gram positive as well as gram negative bacterias. Cefoperazone differs from other 3rd generation cephalosporins in having stronger activity on *Pseudomonas*.

CONCLUSION

The effective prescribing of antimicrobials is based upon the availability, safety, efficacy, cost, spectrum of activity, target specified action, least subject resistance and allergic reactions to the patient population. Drug utilization review of antimicrobial agents is essential among health care professionals as it highlights the importance of assessing optimal drug use. The study was conducted prospectively by using a sample size of 181 patients with the aim of evaluating the drug utilization pattern of antimicrobials in preoperative as well as postoperative patients admitted in the general surgery department for a study period of 6 months. To conclude our study, defines that, in pre-operative patients as prophylaxis were administered with antibiotics the most, which is then followed by the combined dose of antibiotics and antiprotozoal intravenously. The most commonly used antibiotics were third generation cephalosporins, i.e, Cefoperazone -Sulbactam combination and Ceftriaxone and among Penicillins, was a fixed dose combination of Piperacillin / tazobactam. The most commonly used antiprotozoal was Mentronidazole. From the study an attempt was made to use WHO prescribing guidelines and this study clearly shows that prescribing pattern was in accordance with the standard guidelines. Hence the prescribing pattern of antimicrobial agents need to be evaluated continuously on the basis of WHO prescribing guidelines which helps in therapeutic decision making and promoting the effective, non-profit based drug therapy which can improve the patient satisfaction by providing expected therapeutic outcome.

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CONFLICTS OF INTEREST: NIL.**REFERENCES**

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