



A Drug Utilization Study of Antimicrobials in Major Surgical Patients in Tertiary Care Teaching Hospital- A Prospective Observational Study

Authors

Dr Vidisha Vivek Parulekar^{1*}, Dr Vandana Avinash Badar²,
Dr Vartika Gupta³, Dr Priti Garate⁴

^{1,3,4}Resident, Department of Pharmacology, Indira Gandhi Government Medical College, Nagpur

²Associate Professor, Department of Pharmacology, Indira Gandhi Government Medical College, Nagpur

*Corresponding Author

Dr Vidisha Vivek Parulekar

Resident, Department of Pharmacology, Indira Gandhi Government Medical College, Nagpur, India

Abstract

Introduction: Surgical site infection (SSI) is the most common post-operative complication and represents a significant burden in terms of patient morbidity and mortality, and cost to health services around the world. Appropriate antibiotic prophylaxis has been shown to be effective in reducing the incidence of surgical site infections as studies suggest that 40-60% of these infections are preventable.

Aims: To evaluate and compare the utilization pattern of antimicrobial agents (AMA) in surgical prophylaxis use in preoperative, intraoperative and post-operative wards of different specialities.

Settings and Design: It is a cross-sectional observational study conducted patients admitted to surgery, orthopaedics, ENT and gynaecology wards in tertiary teaching care hospital.

Methods and Material: The study duration was from November 2016-November 2018 (2 years). The data was collected time to time from all the medical records of the patient. The study protocol was approved by the Institutional Ethics Committee.

Statistical Analysis Used: Data was collected and compiled using Microsoft Excel 2010 and then analysed by calculating simple proportions, frequency and percentage of various parameters.

Results: Out of 386 patients, it was observed that female patients (55.69%) were more than male (44.60%) patients. The majority of surgical wounds were clean (39.11%) and most common antimicrobial used pre-operatively was metronidazole (29.24%) and in the intraoperative and postoperative period was gentamicin (54.28%). Number of DDD for inj.amoxicillin-clavulanic acid 1.2g was 274.4.

Conclusions: After observing the trend of use of antibiotics, there is a clear need for the development of prescribing guidelines and educational initiatives to encourage the appropriate use of antimicrobials in surgical period. Also, there is scope for improving prescribing habits among the fraternity and minimizing incidence of resistance to antimicrobials.

Keywords: surgical site infection, pre-operative, intra-operative, post-operative, antibiotic prophylaxis.

Introduction

Surgical site infection (SSI) is the most common post-operative complication and represents a

significant burden in terms of patient morbidity and mortality, and cost to health services around the world. They are the second commonest

nosocomial infection accounting for approximately one quarter of 2 million hospital acquired infections in USA annually¹. Between 1.9% and 2.7% of all surgical patients, more than 500,000 per year, are diagnosed with SSI leading to an estimate of 8000 annual deaths^{2,3,4,5}.

Antibiotic consumption in humans is increasing globally. The greatest increase between 2000 and 2010 was in low- and middle-income countries, but in general, high-income countries still use more antibiotics per capita. Growing economic prosperity and rising incomes, as well as expanding insurance coverage, have increased antibiotic consumption. Inappropriate use of broad spectrum antimicrobials leads to decrease in sensitivity of antimicrobials against microorganisms. With increasing multidrug resistance and limited availability of newer agents, there is urgent need for vigilant surveillance, stringent infection control practices, as well as rational antibiotic prescription.

In India, there are National Treatment guidelines for Antimicrobial use in infectious diseases given by National Centre for disease Control (NCDC), Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India (2016)⁶ and Treatment Guidelines for Antimicrobial Use in Common Syndromes given by Indian Council of Medical Research (ICMR), Department of Health Research, New Delhi, 2017⁷.

Antibiotic prophylaxis can protect the patients from post-operative infections by abating the bacterial load present within the surgical site at the time of operation⁸. Hence, prophylactic antibiotics should be administered before giving an incision to any intra-operative patient.

Appropriate antibiotic prophylaxis has been shown to be effective in reducing the incidence of surgical site infections as studies suggest that 40-60% of these infections are preventable⁹. Also it results in good hospital functioning, which leads to increase in patient's satisfaction, maintains high reputation for the hospital, fewer hospitalizations, lesser incidence of re-surgeries and re-admissions

and less cost for care and treatment, as well as lesser numbers of claims and compensations¹. Also there are very few studies which describe the utilization of drugs postoperatively.

Therefore, the present study was conducted to analyse the rationality and drug utilization patterns of antimicrobials in perioperative surgical inpatients and to compare with the standard treatment guidelines (National treatment guidelines for antimicrobials) and also calculate the defined daily dosing (DDD) of antimicrobials as per WHO ATC-DDD criteria.

Subjects and Methods

The study was prospective observational conducted in indoor patients of various surgical departments in Tertiary care teaching institute in central India from November 2016-November 2018 (2 years). The study did not involve any interview of the patients admitted. The study protocol was approved by the Institutional Ethics Committee prior to the commencement of the study. *The inclusion criteria* was patients above 18years, of either gender, patient undergoing major surgeries, patient receiving in-patient care in departments of surgery, gynecology, orthopedics and ENT, patients having comorbidities like diabetes, hypertension, malnutrition, COPD, TB, HIV, obesity, smoking and alcohol abuse. *The exclusion criteria* was pregnancy and lactation, medico-legal cases, patient receiving in-patient care in cardiothoracic, ophthalmic, neurosurgical, pediatric surgical, obstetrics departments, any patient who dies post-operatively before being discharged, patient who absconded/discharged against medical advice, patient referred to other hospitals, incomplete data. The data from 386 surgical in-patients was collected from their prescriptions & peri-operative notes admitted in departments of general surgery (4 units, 5 wards- 3 male ward and 2 female ward and 1 surgical intensive care unit [SICU]), gynecology (3 units and 5 wards), orthopedics (3 units and 2 wards-one male and one female ward) and ENT (2 units and 2 wards- one male and one

female ward). The in-charge authority of surgical departments was notified and permission was taken.

Demographic analysis of data was done. Data was analysed according to classification of wound by CDC (Centers for Disease Control and Prevention) into clean, clean-contaminated, contaminated and dirty surgical wounds¹⁰ and as per type of surgery into abdominal, gynecology, head and neck, musculoskeletal etc.

Following parameters like WHO prescribing indicators¹¹, most common AMA used in clean, clean-contaminated, contaminated and dirty

surgical wounds, percentage of AMAs used as generic drugs, branded drugs, fixed dose combinations (FDCs) and DCGI (Drug Controller General of India) approved FDCs and route of administration of AMAs used peri-operatively were also included.

To measure the degree to which practices adhere to rational therapy as well as standard treatment guidelines, percentage of AMA prescribed from an essential medicine list (EML) or National list of essential medicine (NLEM) was calculated with following formula.

$$\text{Percentage calculated (\%)} = \frac{\text{No. of products prescribed which are in essential drug list} \times 100}{\text{Total number of drugs prescribed}}$$

From the prescription data of commonly prescribed groups of drugs, the amounts of drugs consumed were converted into the number of

DDD as per the 2010 version of ATC/DDD index¹².

$$\text{No of DDD} = \frac{\text{No. of items issued} \times \text{Amount of the drug per item}}{\text{WHO recommended DDD of drug}}$$

Comparison with standard treatment guidelines such as National treatment guidelines for antimicrobial use in infectious diseases by NCDC⁶ and Treatment Guidelines for Antimicrobial Use in Common Syndromes by ICMR⁷ were also included.

Statistical Analysis

Data was collected and compiled using Microsoft Excel 2010 and then analysed by calculating simple proportions, frequency and percentage of various parameters. Suitable graphs, charts and photographs were added. A brief interpretation was included in the results below every table. Sample Size was calculated by using software Open Epi, Version 3, an open source calculator and was 386 considering population size (N) that

is the total number of major operations done in surgical OT, gynecology OT, ENT OT and orthopedics OT for last one year i.e. from February 2016 to February 2017 as 3971 and prevalence as 50%.

Results

In our study, 386 patients were followed up till the postoperative period. It was observed that female to male ratio of 1.21 as shown in Figure 1. The age-wise distribution of data was categorized in Figure 2.

Figure 1 Gender-wise distribution of data

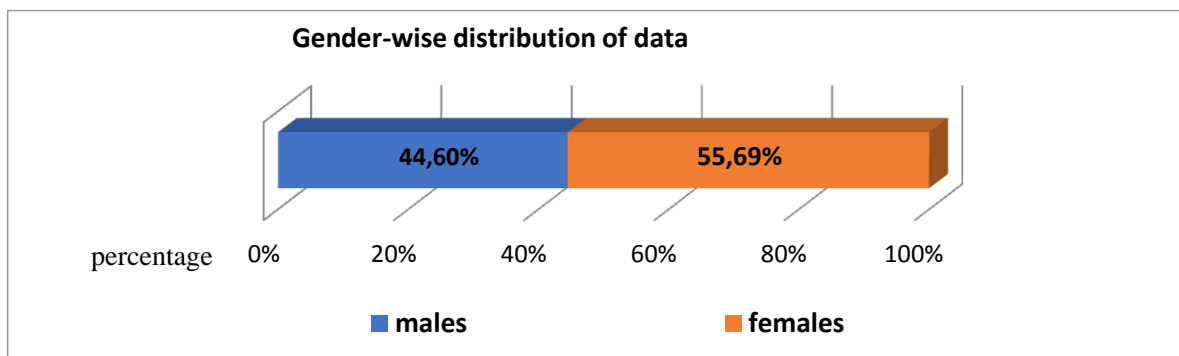
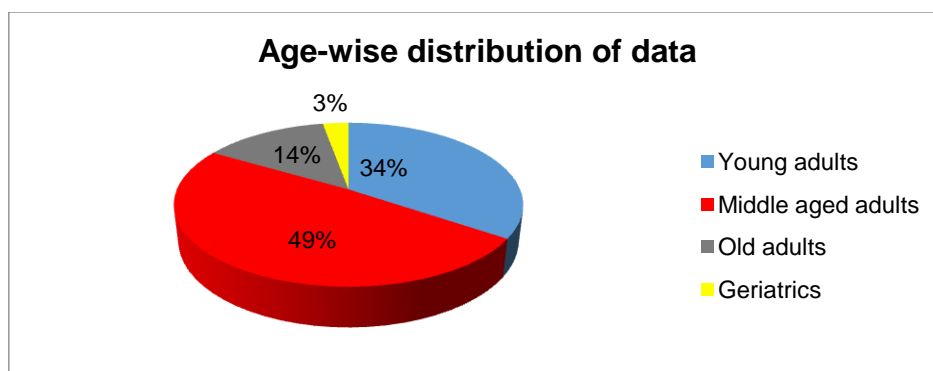
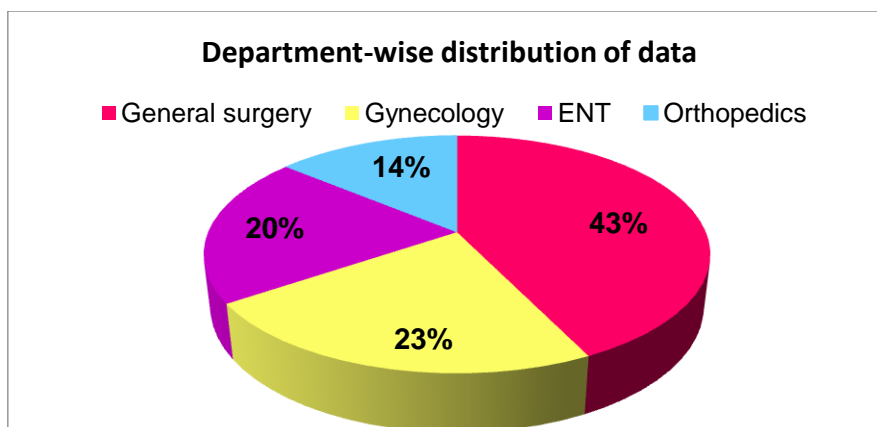


Figure 2 Age-wise distribution of data



In figure 3, department-wise distribution of data is shown. Four departments were involved in the study with majority of cases from general surgery department (43%).

Figure 3 Department-wise distribution of data



The data was analysed according to the type of surgical wound as shown in Table 1.

Table 1 Classification of surgical wound

Classification of surgical wound (n=386)		
Type of surgical wound	No of patients	Percentage of patients (%)
1- clean	151	39.11
2- clean-contaminated	120	31.08
3- contaminated	75	19.43
4- dirty	40	10.36

The common surgeries associated with clean surgical wound were operations of head and neck

surgeries like tonsillectomy, modified radical mastoidectomy and musculoskeletal surgeries like

fracture fixations or arthroplasties, hernia repair surgeries. Clean-contaminated surgical wounds included operations like gynaecological operative procedures such as myomectomies, hysteroscopies, hysterectomies etc; urological surgeries such as lithotripsy, pyloolithotomy, nephrectomy. Contaminated surgical wounds comprised of rectal surgeries like haemorrhoidectomies, fistulectomies and

abdominal surgeries. Dirty surgical wounds included exploratory laparotomy for intra-abdominal abscess or perforation peritonitis and scrotal surgeries like chylocoele or pycocele.

As shown in Table 2; majority of study cases were of abdominal surgery with 24.61%, followed by gynecology surgery with 22.79% and head and neck surgeries with 20.46%.

Table 2 Type of surgery

Type of surgery (n=386)		
Type of surgery	No of patients	Percentage of patients (%)
Abdominal surgery	95	24.61
Gynecology surgery	88	22.79
Head and neck surgery	79	20.46
Musculoskeletal surgery	54	13.98
Rectal surgery	26	6.73
Hernia repair surgery	18	4.66
Scrotal surgery	12	3.10
Urological surgery	10	2.59
Breast surgery	4	1.03

On evaluation of WHO prescribing parameters it was seen that the average number of AMA

prescribed per prescription was 1.8 as shown in Table 3.

Table 3 WHO prescribing parameters

Total drugs prescribed	3059
Percentage of AMA used by generic name/prescription	79.56%
Average number of drugs/prescription	4.854922
Average number of AMA/prescription	1.8
Percentage of AMA prescribed for Intravenous route	81.09%
Percentage of AMA prescribed from Essential medicine list (EML)	97.14%
Percentage of AMA prescribed from National list of essential medicine (NLEM)	90.64%
Average duration of SICU stay	5.26
Average duration of hospital stay	11.36

AMA – Antimicrobials

The total antimicrobials prescribed at pre-operative, intra-operative and post-operative stage were 660, 35 and 844 respectively. Most common AMA used pre-operatively, intraoperatively and postoperatively was metronidazole (29.24%), gentamicin (54.28%) and metronidazole (26.52%)

respectively. Apart from amoxicillin-clavulanic acid, other fixed dose combinations seen were Piperacillin +Tazobactam 2.25g and 4.5g, Ampicillin 1g+ Sulbactam 0.5g as shown in Table 4.

Table 4 AMA prescribed during peri-operative period

AMA prescribed at preoperative stage (n=660)		
AMA	No of antibiotics prescribed	Percentage of antibiotics prescribed (%)
*Cap.amoxicillin-clavulanic acid 625mg	38	5.75
inj.amikacin 1g	17	2.57
inj.amikacin 500mg	14	2.12
*inj.Augmentin (amoxicillin/clavulanic acid) 1.2g	104	15.75
*inj.ampicillin 1g+ sulbactam 0.5g	4	0.60
inj.cefotaxime 1g	47	7.12
inj.ceftriaxone 1g	137	20.75
inj.ciprofloxacin 200mg	14	2.12
inj.gentamicin 80mg	38	5.75
inj.levofloxacin 500mg	4	0.60
inj.meropenem 1g	22	3.33
inj.metronidazole 100mg	24	3.63
inj.metronidazole 250mg	18	2.72
inj.metronidazole 500mg	147	22.27
inj.ofloxacin 200 mg	4	0.60
*inj.piptaz (piperacillin/tazobactam) 4.5g	4	0.60
moxifloxacin drops 0.5%	8	1.21
T.cefixime 200mg	4	0.60
T.metronidazole 500 mg	4	0.60
T.albendazole 400mg	4	0.60
T.moxifloxacin 400 mg	4	0.60
AMA prescribed at intra-operative stage (n=35)		
inj.cefotaxime 1g	8	22.85
inj.ceftriaxone 1g	8	22.85
inj.gentamicin 80mg	19	54.28
AMA prescribed at postoperative stage (n=841)		
*Cap.amoxicillin-clavulanic acid 625mg	39	4.6
inj.amikacin 500mg	19	2.25
inj.amikacin 1g	11	1.32
*inj.Augmentin (amoxicillin/clavulanic acid) 1.2g	138	16.56
*inj.ampicillin 1g+ sulbactam 0.5g	4	0.48
inj.cefotaxime 1g	54	6.48
inj.ceftriaxone 1g	157	18.84
inj.ciprofloxacin 100mg	20	2.4
inj.ciprofloxacin 500mg	3	0.36
inj.ciprofloxacin 200mg	8	0.96
inj.gentamicin 80mg	57	6.84
inj.levofloxacin 750mg	3	0.36
inj.levofloxacin 500mg	8	0.96
inj.meropenem 1g	25	3
inj.metronidazole 100mg	40	4.8
inj.metronidazole 250mg	20	2.4
inj.metronidazole 500mg	161	19.32
inj.ofloxacin 200 mg	4	0.48
*inj.piptaz (piperacillin/tazobactam) 4.5g	34	4.04
inj. teicoplanin 400mg	8	0.96
moxifloxacin drops 0.5%	8	0.96
T.ciprofloxacin 500mg	8	0.96
T.doxycycline 100 mg	4	0.48
T.moxifloxacin 400 mg	4	0.48

Figure 4 AMA used in clean surgical wounds

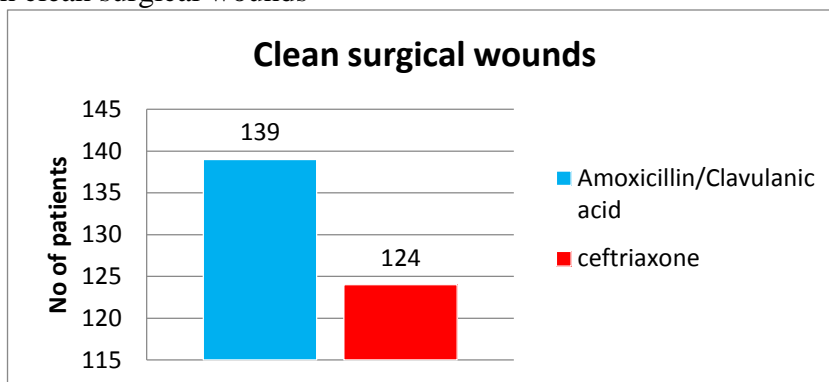


Figure 5 AMA used in clean contaminated surgical wounds

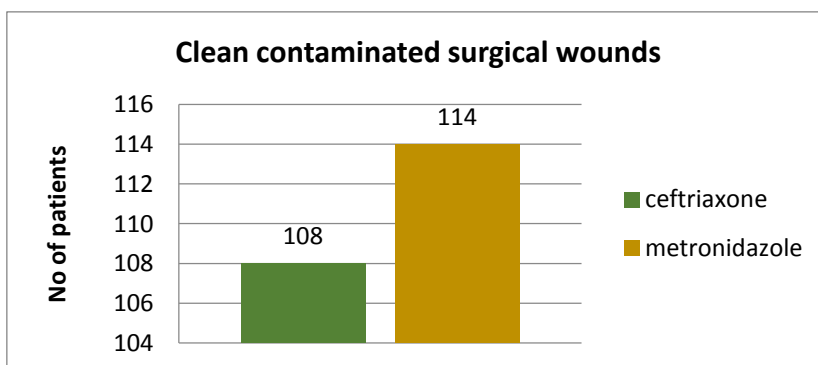


Figure 6 AMA used in contaminated surgical wound

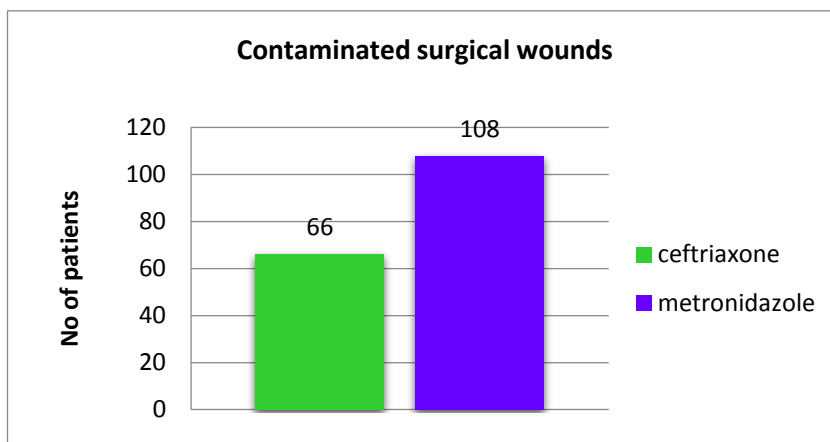
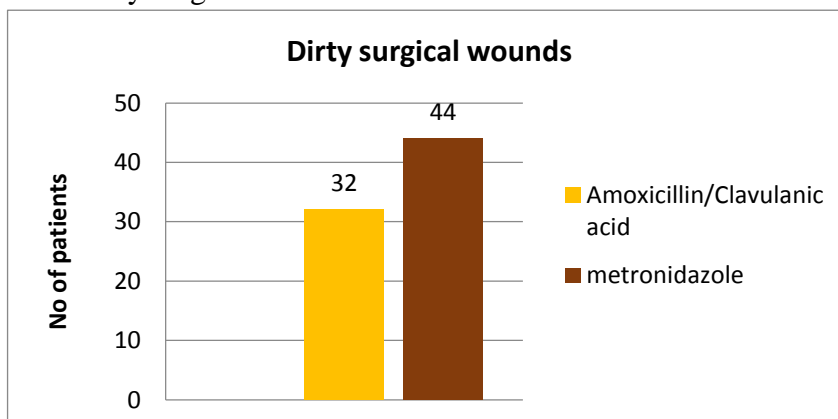


Figure 7 AMA used in dirty surgical wounds



Maximum number of drugs were prescribed by generic name (79.89%). 13.76% of drugs were fixed dose combinations as shown in table 5.

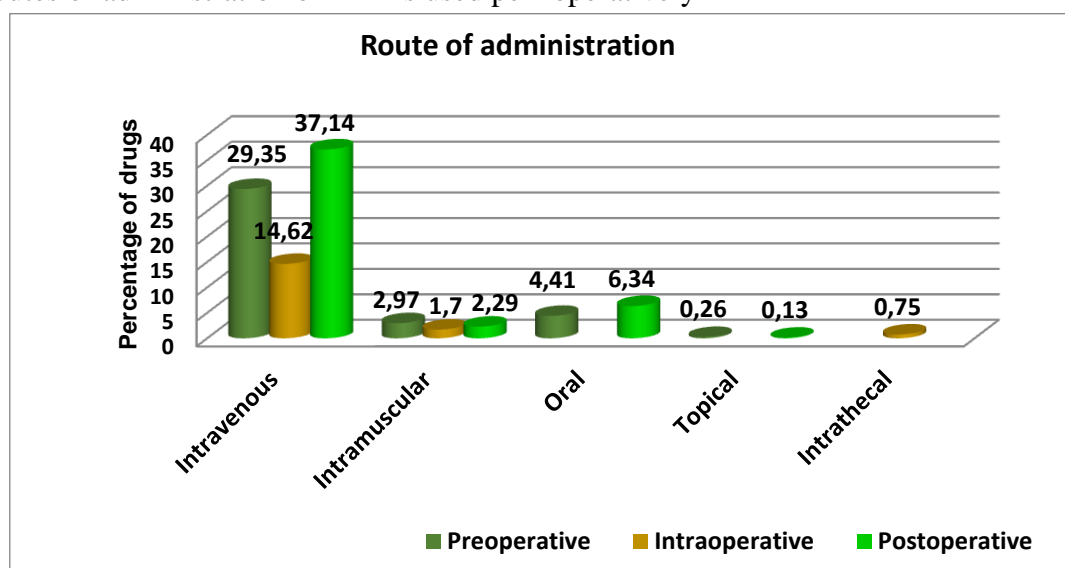
Table 5 Use of generic drugs, branded drugs & fixed dose combinations

Use of generic drugs, branded drugs & fixed dose combinations (n=3059)		
Drugs	Number	Percentage (%)
Generic drugs	2444	79.89
Branded drugs	615	20.10
Fixed dose combinations	421	13.76
FDC approved by DCGI	338	80.28
FDC approved by WHO	318	75.53

FDC- Fixed dose combinations, DCGI- Drug Controller General of India.

Maximum study medications were prescribed by intravenous route in peri-operative period (81.03%) as shown in Figure 8.

Figure 8 Routes of administration of AMAs used peri-operatively



For the common 3 AMAs used in the perioperative period, ATC code has been mentioned and number of DDD calculated as shown in Table 6.

Table 6 -ATC-DDD classification

DRUG	ATC CODE	WHO recommended DDD	No. of DDD
Inj amoxicillin with clavulanic acid(1.2g)	J01CR02	3 g	274.4
Inj ceftriaxone(1g)	J01DD04	2 g	528
Inj.metronidazole (500 mg)	J01XD01	1.5 g	325.3

Discussion

In this study, the patients were admitted for various diagnosis like acute appendicitis, acute cholecystitis, acute tonsillitis, uterine myomas, dysfunctional uterine bleeding, fractures, osteoarthritis etc. According to demographic data, male to female ratio is 0.82 as oppose to Akter SF et al where it was 1.81¹³. This is due to inclusion of cases operated in department of gynecology. The average age was 41.84 years and the most

common age group was middle aged adults (36-55years) with 49%. This finding of our study is in consistent with study by Sharma and Goel where the mean age was 45.33 ± 19.01 years¹⁴. Similar results were also seen in the Bhataia et al¹⁵ and Khan M L et al¹⁶ study. This is the usual trend as this is the productive age group and is actively involved in socioeconomic activities, which may lead to stress and age factor making them

vulnerable to diseases that may need surgical interventions¹⁵.

Maximum number of cases were taken from wards of general surgery department (43%) followed by gynaecology (14%) department. This finding was similar to study by *Alemkere G* where participants from general surgery were 60.1% followed by gynaecology cases with 24.8%¹⁷. Also, *SG kamath et al* noted a same finding with 32.47% of cases from general surgery department¹⁸. However in study by *Rehan HS et al*, most patients were admitted under General surgery department (30%) followed by orthopedics department (26%)¹⁹.

As per the CDC classification of surgical wounds, it was observed in our study that clean surgeries were the dominating ones with 39.11%. Similar finding was noted in the study by *Sozen H et al* (n=340) on perioperative antibiotic prophylaxis. They noted that clean surgeries were 31.8%²⁰. This might be because majority of cases were of hernia repair surgeries (hernioplasty), modified radical mastoidectomies, open reduction and internal fixations of fractures with nail or plate or pins or screws, total hip and knee arthroplasties, hemiarthroplasties, tonsillectomies and modified radical mastectomies which belonged to clean surgeries.

In our study, most common surgeries were abdominal surgeries with 24.61%. This finding was not consistent with *Patel DJ et al* where they found out that commonest surgeries were urological procedures (30.5%) and abdominal surgeries were only 18.5% (37 cases)²¹. Many cases of abdominal surgeries like exploratory laparotomies, laparoscopic appendectomies, laparoscopic cholecystectomies were observed in our study.

Majority of AMA were prescribed by generic name (79.56%). This finding is consistent with *Bhataia et al* where 5627 total medicine formulations were studied and 98.51% (5534) were found out to be prescribed by official/generic names¹⁵. Percentage of drugs prescribed by generic name according to the WHO standard

should be 100%. Increasing generic prescribing would rationalize the use and reduce the cost of drugs. It also reduces confusion while prescribing²². Average number of AMA/prescription in our study was 1.8. All patients received an antimicrobial drug at one time or the other. This is similar to *Bhansali et al*²³ and *Kumar R et al*²⁴ study But this is much higher than the other Indian studies which reports the use of AMA in 20% to 67% of the patients only^{15,23}. Similar studies abroad indicate a range of 20% to 42% of patients receiving antimicrobial drugs²⁵. The higher number of AMA per patient indicates that more and more antimicrobial were used for prophylaxis purpose rather than definitive treatment purpose and that they are used blanket therapy to prevent any or all types of infection. The percentage of AMAs prescribed from National list of essential medicine (NLEM) were 90.64%. This finding was consistent with essential drug list of our hospital.

Overall the most common AMAs used peri-operatively was metronidazole in our study. Also the most common antimicrobial used pre-operatively in our study was metronidazole followed by ceftriaxone with and amoxicillin-clavulanic acid. Similarly in *Agrawal et al* study, metronidazole topped the list²⁶. Metronidazole is used predominantly to cover up for all the anaerobic infections²⁵. In our study, all patients were given preoperative prophylactic antimicrobial which was similar to study done in *Kerala*²⁷ and *Ahemadabad*²⁸.

Though in our study third generation cephalosporins were most commonly used for surgical prophylaxis, recent guidelines recommend the use of first generation cephalosporins as surgical antibiotic prophylaxis^{29,30}. First-generation cephalosporins particularly cefazolin are the most suitable agents for surgical prophylaxis due to their spectrum that includes *Staphylococcus* species and gram-negative bacilli along with desirable pharmacokinetic characteristics, ease of administration and low cost. But local resistance

pattern, surgeon's own experience at hospital setting and availability of AMAs in our own government medical store might influence the choice of anti-microbial.

In our study amoxicillin and clavulanic acid found to have used in 44.7%, 54.4% and 50% of clean, clean contaminated and dirty surgical wounds respectively. The high rate of infection with amoxicillin and clavulanic acid in our study demonstrates need for updating the β -lactam inhibitor combinations as prophylaxis in surgery³¹. But in *Chandrasekaran et al* study cefuroxime was used in 68.42% of clean surgical wounds, cefaperazone/sulbactam was most frequently used as 27.08% in clean-contaminated and 26.77% of contaminated cases as single dose administration of first and second generation cephalosporin is sufficient for optimal prevention of surgical site infections in absence of high rate of resistance³¹. Dirty wounds and Clean- contaminated wounds have more chances of getting infected as compared to clean wounds and contaminated ones have the highest rate of infection²⁹. Hence it was seen that more number of AMAs were used in dirty and clean - contaminated wounds.

Very few prescriptions were based on laboratory culture sensitivity reports. According to *ICMR guidelines*, in culture confirmed cases of SSI, antimicrobials should be based on Lab AST reports⁷. Also prescription of antibiotics without evidence of culture and sensitivity tests is another major problem that results in poor patient compliance. Strict antibiotic prescription policies have to be developed and target must be aimed to minimize the incidence of resistance to antimicrobial agents and also to promote infection control practices and rational antibiotic utilization³².

80.28% and 75.53% of FDCs prescribed in our study were approved by DCGI and WHO respectively. This indicates the rational prescribing pattern.

In table 6, ATC-DDD classification of 3 most common AMAs. The DDD is the assumed

average maintenance dose per day for a drug used for its main indication in adults. The DDD does not necessarily reflect the recommended or actual dose used³³. The objective of ATC/DDD system is to serve as tool for drug utilization research, to favor improvement in drug use³⁴.

The AMA use in our study does not align with the national guidelines for surgical prophylaxis and as the preference in the use of antimicrobials was due to availability of free drugs from hospital supply and hospital standard operating procedures. Selection of antimicrobial agent is done taking into consideration various aspects like site of surgery, spectrum and pharmacokinetic profile. No universal surgical antimicrobial prophylaxis guideline can be implemented basis solely on the type of surgical wound as the occurrence of SSIs is also influenced by other factors such as site and length of the procedure, overall health of the patient, i.e., glucose levels, weight of the patients, etc³⁰. The guidelines for prophylaxis are based on the evidence obtained from controlled clinical trials. These guidelines encourage the utilization of older narrow spectrum antimicrobials³⁵.

Limitations of the study

The limitations of the current study include the involvement of small number of patients which did not give complete overview among the different departments. Further studies involving different departments encompassing super-speciality and oncology surgical patients should be established.

Conclusion

The present study illustrates the pattern and type of antimicrobial use in surgical departments of tertiary care hospital. It also highlights the use of drugs by generic name, use of drugs from the NLEM and EML with metronidazole being the most commonly used antimicrobial. There is lack of alignment in drug use when we compare with national guidelines. After observing the trend of use of antimicrobials, there is a clear need for the development of prescribing guidelines and

educational initiatives to encourage the appropriate use of antimicrobials and analgesics in surgical period. Also, there is scope for improving prescribing habits among the fraternity and minimizing incidence of resistance to antimicrobials. A periodic survey by hospital infection control committee is essential. Awareness regarding antimicrobial resistance, timing and duration of surgical antimicrobial prophylaxis, optimal post-operative pain management should be imparted to all the prescribers.

Author's contribution

All authors have contributed equally in developing the concept of the study, data collection, data analysis, and drafting the manuscript.

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Conflict of interest

Declared none.

References

¹Stone PW. Economic burden of healthcare-associated infections: an American perspective. Expert review of pharmacoeconomics & outcomes research. 2009 Oct 1;9(5):417-22.

²Meeks DW, Lally KP, Carrick MM, Lew DF, Thomas EJ, Doyle PD, Kao LS. Compliance with guidelines to prevent surgical site infections: as simple as 1-2-3?. The American Journal of Surgery. 2011 Jan 1;201(1):76-83.

³CDC. Data from National Hospital Discharge Survey. 2010. Available at : <https://www.cdc.gov/nchs/data/nhds/4procedures/>

2010pro_numberpercentage.pdf. Accessed September 2018.

⁴Mu Y, Edwards JR, Horan TC, Berrios-Torres SI, Fridkin SK. Improving risk-adjusted measures of surgical site infection for the National Healthcare Safety Network. Infection Control & Hospital Epidemiology. 2011 Oct;32(10):970-86.

⁵Klevens RM, Edwards JR, Richards Jr CL, Horan TC, Gaynes RP, Pollock DA, Cardo DM. Estimating health care-associated infections and deaths in US hospitals, 2002. Public health reports. 2007 Mar;122(2):160-6.

⁶National Treatment Guidelines for Antimicrobial Use in Infectious Diseases (2016) http://pbhealth.gov.in/AMR_guideline7001495889.pdf

⁷Treatment Guidelines for Antimicrobial Use in Common Syndromes [Internet]. New Delhi; 2017 [cited 28 November 2018]. Available from: https://www.icmr.nic.in/sites/default/files/guidelines/treatment_guidelines_for_antimicrobial.pdf

⁸Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. Clinical infectious diseases. 2006 Aug 1;43(3):322-30.

⁹Hawn MT, Vick CC, Richman J, Holman W, Deierhoi RJ, Graham LA, Henderson WG, Itani KM. Surgical site infection prevention: time to move beyond the surgical care improvement program. Annals of surgery. 2011 Sep 1;254(3):494-501.

¹⁰Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR, Hospital Infection Control Practices Advisory Committee. Guideline for prevention of surgical site infection, 1999. Infection Control & Hospital Epidemiology. 1999 Apr;20(4):247-80.

¹¹WHO. How to investigate drug use in health facilities: selected drug indicators, action program on essential drugs (DAP), Geneva, 1993. Available at: <http://apps.who.int/medicinedocs/en/d/Js2289e/>. Accessed on 19 September 2018.

¹²WHOCC - Purpose of the ATC/DDD system [Internet]. Available from: https://www.whooc.no/atc_ddd_methodology/purpose_of_the_atc_ddd_system/

¹³Akter SF, Rani MF, Rahman JA, Nordin MS, Satwi S, Awang MB. Antimicrobial use and factors influencing prescribing in medical wards of a tertiary care hospital in Malaysia. *Int J Sci Environ Technol.* 2012;1(4):274-84.

¹⁴Sharma P, Goel D. Utilization assessment of antimicrobial prophylaxis in surgical patients at tertiary care teaching hospital. *Saudi Journal for Health Sciences.* 2018 Jan 1;7(1):23.

¹⁵Bhataia S, Mathur S, Sankhla S, Kumar M, Sharma M. *International Journal of Pharma and Bio Sciences* ISSN 2016 April; 7(2):332 – 338.

¹⁶Khan MLZ, Arain A, Qureshi FA. Patient's selection in limited resources a stimulus for improving care. *PJS2008*, 24, (4), 35-8.

¹⁷Alemkere G. Antibiotic usage in surgical prophylaxis: A prospective observational study in the surgical ward of Nekemte referral hospital. *PLoS one.* 2018 Sep 13;13(9):e0203523.

¹⁸Kamath SG, Varun HV, Rani DU, Aithal S and Patil UN: Prescribing patterns of antimicrobials in surgical departments in a Tertiary Care Hospital in South India. *Int J Pharm Sci Res* 2014; 5(3): 1051-58

¹⁹Rehan HS, Kakkar AK, Goel S. Pattern of surgical antibiotic prophylaxis in a tertiary care teaching hospital in India. *International journal of infection control.* 2010;6(2).

²⁰Sozen H, Cetinkaya M, Sahan MU, Caylak SD, Hazer DB, Canbek UM, Koca YS, Baldemir E. Cost and efficacy of perioperative antibiotic prophylaxis in a state hospital in Turkey. *Acta Medica.* 2013 Jan 1;29:455-60.

²¹Patel DJ, Chhaiya SB, Mehta DS. Drug utilization study-pattern of use of anti-microbial drugs among post-operative patients in department of general surgery at a tertiary care hospital. *Int J Basic Clin Pharmacol* 2017;6:1482-5.

²²Goodman L, Gilman A, Brunton L, Hilal-Dandan R, Knollmann B, Buxton I. Principles of

Prescription Order Writing and Patient Compliance : Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York [i 11 pozostałych]: McGraw-Hill Education; 2018.

²³Bhansali NB, Gosai TR, Dholaria NK, Suthar SD, Chacko J,Chavda DA, et al. Drug utilization study in post-operative patients in surgical ward of a tertiary hospital attached with medical college. *Der Pharm Lett.* 2013; 5(1):251-7.

²⁴Kumar R, Kohli Kamlesh, Sidhu D. S., Kaur Navjot, Mala Chandra, Garg Monique. An indepth study of drugs prescribing pattern in the Surgery Department of a Tertiary Care Teaching Institute in Northern India. *Int J Basic ClinPharmacol.* 2014 Aug; 3(4):681-686.

²⁵Bhabhor P, Hotchandani H. An Antibacterial Drug Utilization Study at Surgical Units of Shree Sayaji General Hospital, Vadodara, Gujarat, India. *The Internet J Pharmacol.* 2012;10(1):1-11.

²⁶Agrawal JM, Patel NM, Vaniya HV, Trivedi HR, Balat JD. Drug utilization study in post-operative patients in obstetrics and gynaecology ward of a tertiary care teaching hospital. *J Clin Exp Res.* 2014;2:103-109.

²⁷Tourmousoglou CE, Yiannakopoulou EC, Kalapothaki V, Bramis J, St. Papadopoulos J. Adherence to guidelines for antibiotic prophylaxis in general surgery: A critical appraisal. *J Antimicrob Chemother* 2008;61:214- 8.

²⁸ Khan AK, Mirshad PV, Rashed MR, Banu G. A study on the usage pattern of antimicrobial agents for the prevention of surgical site infections (SSIs) in a tertiary care teaching hospital. *J Clin Diagn Res* 2013;7:671- 4.

²⁹Scottish Intercollegiate Guidelines Network. Updated April 2014 Antibiotic Prophylaxis in Surgery – A National Clinical Guideline; 2008. Available from: <http://www.sign.ac.uk/pdf/sign104>. [Last accessed on 2018 Nov 5].

³⁰World Health Organization. Guidelines for Safe Surgery: Safe Surgery Saves Lives. Geneva: World Health Organization; 2009. Available from:

http://www.who.int/patientsafety/safesurgery/tools_resources/9789241598552/en/. [Last accessed on 2018 Nov 5].

³¹Chandrasekaran K, Saeed K, Gandhiraj D, Mohanta GP, Rajasekaran A. Study on Adherence to Prophylactic Antimicrobials Use Guidelines in Surgical Wards of an Indian Private Corporate Hospital. *International Journal of Pharmaceutical Research and Allied Sciences*. 2016 Jan 1;5(2):280-92.

³²Divyashree L, Bhushan A and Tejaswini K. Drug utilisation study in gynaecological post-operative cases: a retrospective study. *EJPMR*.2017;4(04):418-423.

³³Rode S and Salankar H: Analysis of antimicrobial usage pattern: a retrospective observational study. *Int J Pharm Sci & Res* 2018; 9(3): 1231-36. doi: 10.13040/IJPSR.0975-8232.9(3).1231-36.

³⁴Ali H, Zafar F, Alam S, Beg AE, Bushra R, Manzoor A, Naqvi GR, Yasmeen R, Shafiq Y, Tariq A, Zubair S. Drug utilization and prescribing pattern of antibiotics in a tertiary care setups; trends and practices. *Pakistan journal of pharmaceutical sciences*. 2018 Mar 2;31.

³⁵R. Revathi, N. Saralaand A. Bhaskaran. Prescribing Pattern of Antimicrobials in Patients during Post-Operative Period – An Observational Study.*British Journal of Medicine & Medical Research*. 2015;5(10):1213-1219.