Original Article

Evaluation of Suspected Adverse Drug Reaction and Prescribing Patterns of Perioperative Antimicrobials in Major Surgical Patients of Tertiary Care Hospital of Bihar

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ABSTRACT

Introduction: The purpose of giving antibiotics prophylactically is to prevent development of infections at the incision site. Despite a lack of adequate number of studies on prescribing pattern of antibiotics in India, sudden development and spread of antibiotic resistance could be expected due to high utilization of antibiotics. This data recommends us to conduct a survey on prescribing pattern of antibiotics in healthcare facilities of India particularly in departments like surgery where risk of infection with resistant bacteria is high.

Aims/ objective: To evaluate suspected adverse drug reaction and prescribing patterns of perioperative antimicrobials in major surgical patients of tertiary care hospital of Bihar.

Materials and Method: ADR symptoms were classified with symptom organ class (SOC) from the MedDRA (Medical Dictionary for Regulatory Activities). Causality of ADRs with antibiotics was done using WHO- Uppsala Monitoring Center (WHO-UMC). Analysis was done based on World Health Organization (WHO) prescribing indicators, frequency of utilization of different antibiotics, percentage of antibiotic used under generic or branded drugs, proportion of fixed dose combinations (FDC) that were approved or not approved by DCGI (drug controller general of India) and proportion of drugs prescribed from national list of essential medicine at the time of data collection.

Results: Most of the antibiotics were prescribed by their generic name (68.73%). Average amount of antibiotic/ prescription in this study was found to be 1.94. Most of the patients have received at least one antibiotic at one moment or another. The percentage of antibiotics prescribed from NLEM (National list of essential medicine) were found to be 81.57%. Metronidazole, ceftriaxone, and amoxicillin plus clavulanic acid were the most commonly perioperatively used antibiotics. ADRs were more frequently reported from patients who were prescribed with antibiotics of reserve and watch category.

Conclusion: This scenario recommends us to develop strict policies and regulation on antibiotic prescription to achieve the target of stopping the trend of rising resistance to antibiotics and promotion of rational use of antibiotics.

Keywords: Antibiotics, Prescriptions, Adverse Drug Reactions, Perioperative.

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INTRODUCTION

There have been drastic changes in the pharmacotherapy of infectious disease since the discovery of antibiotics. But emerging resistance is becoming major problem in the current era due to misuse and overuse of antibiotics. Apart from misuse and overuse, there are many other reasons for this crisis such as lack of development of new antibiotics by pharmaceutical companies because of less financial incentives and complicated regulatory requirements. [1-4]

Major contributors to emergence and spread of antibiotic resistance are poor availability and implementation of stewardship policy, prescribing guidelines and limited resources. Following local prescribing guidelines before prescribing antibiotics for a specific diagnosis can lead to both effective pharmacotherapy and better utilization of antibiotics. So, hospital should have its own prescribing guidelines based of Development of local prescribing guidelines based on result of active antibiotic surveillance and survey of resistance patterns. [5]

The purpose of giving antibiotics prophylactically is to prevent development of infections at the incision site. The process of selecting and prescribing antibiotics is based on guess of the likely causative organism(s), presence of any active infection, patient demographic and clinical characteristics, resistance pattern in the bacteria, and category of wound (i.e., dirty vs. clean). [6] Based on the suggestions of the American Society of Health-System Pharmacists (ASHP) and the clinical practice guidelines of the Society for Healthcare Epidemiology of America,

prophylactic antibiotic administration is usually begun within 60 minutes after surgery and continued for 24 hours after surgery.[6,7] It has been shown by several studies that the timing of administration of perioperative prophylactic antibiotics is essential for successful prevention of surgical site infections (SSI). Administration of these antibiotics near the site of surgical incision helps us to confirm that effective plasma and tissue concentrations are achieved for antibiotic. [6-8]

Adverse drug reactions (ADRs) are any unwanted/uncomfortable effects from medication that result in physical, mental, or functional injuries.[9] ADRs reported by hospitalized patients are related with rise in morbidity and mortality, longer duration of hospitalization, and rise in medical expense.[10] For this reason, it has been recommended by multiple studies that ADRs are a major public health problem. [11]

Many cross-sectional studies have surveyed on the frequency, pattern, and level of severity of ADRs, but many of these studies have been done in USA or Europe. Reporting of ADRs due to antibiotics are limited in Asian countries.[12-14]

Despite a lack of adequate number of studies on prescribing pattern of antibiotics in India, sudden development and spread of antibiotic resistance could be expected due to high utilization of antibiotics. This data recommends us to conduct a survey on prescribing pattern of antibiotics in healthcare facilities of India particularly in departments like surgery where risk of infection with resistant bacteria is high.[15] The current situation on antibiotic resistance is poor as earlier studies from the surgery department that was related to 716 isolates from 2568 patients revealed that 69% of E. coli and 41% of Klebsiella pneumoniae isolates were producers of extended-spectrum beta-lactamases. Those isolates showed higher pattern of resistance to fluoroquinolones and beta-lactam antibiotics but were susceptible to imipenem and piperacillin-tazobactam. Methicillin-resistant Staphylococcus aureus (MRSA) revealed higher pattern of resistance to ciprofloxacin, co-trimoxazole, and levofloxacin.[16]

Peri-operative antibiotic prophylaxis (PAP) is the restricted number of doses of antibiotics that are administered along with preoperative preparation, both intra-operatively and post-operatively, in an aseptic condition and wound care after surgery with aim of preventing the suspected surgical site infections.[17] It is recommended to stop PAPs after 24 hour of operation, when there is no known infection.[18] Thus, it is necessary to analyse the contents of the PAP and assessment of antibiotic prescription based on the diagnosis.

Thus, the aim of the current study was to evaluate suspected adverse drug reaction and prescribing patterns of perioperative antimicrobials in major surgical patients of tertiary care hospital of Bihar.

MATERIALS AND METHODS

This was an observational and prospective study carried out in indoor patients of various surgical departments in tertiary care hospital of eastern India from October 2021 to October 2022. This study was started after getting permission by the institutional ethics committee and taking written informed consent from study participants.

Inclusion Criteria

Patients of age greater than 18 years of either sex; patients being planned for major surgical procedures, patients being planned for surgery in departments of surgery, orthopaedics, urology, gynaecology, and ENT.

Exclusion Criteria

Patients being planned for surgery in departments of paediatric surgery, neurosurgery, cardiothoracic vascular surgery (CTVS), ophthalmology; medicolegal case or in case of death of the patient before hospital discharge; if the patients who has taken discharge against medical advice; patients being referred to other centres; patients with incomplete data and pregnancy or lactation.

With anticipated 2000 maximum number of surgeries in one year and with 95% confidence level and 5% margin of error, minimum number of patients was found to be 323. So, data was collected from 350 patients. Of which 14 patients were excluded as per our inclusion and exclusion criteria. So, analysis was done on remaining 336 patients.

Information such as baseline demographic and clinical parameters, indication for surgery written by treating surgeon and prescriptions of antibiotics were collected from patients' file. Relevant laboratory data and filled suspected adverse drug reaction reporting form were also collected. ADR symptoms were classified with symptom organ class (SOC) from the MedDRA (Medical Dictionary for Regulatory Activities). [19] Causality of ADRs with antibiotics was done using WHO- Uppsala Monitoring Center (WHO-UMC). [20]

Analysis was done based on following parameters:

- World Health Organization (WHO) prescribing indicators[21]
- Frequency of utilization of different antibiotics
- Percentage of antibiotic used under generic or branded drugs
- Proportion of fixed dose combinations (FDC) that were approved or not approved by DCGI (drug controller general of India) at the time of data collection
- Proportion of drugs prescribed from national list of essential medicine at the time of data collection

Statistical Analysis

Data recorded was revealed in tabular form and analysed using Microsoft excel 365 software. Descriptive analysis was done to interpret the results using numbered analysis.

RESULTS

Table 1: Patients baseline demographic and clinical characteristics

Parameters	Number of patients (%)
Total number of patients	336
Mean age in years ± SD	36.87 ± 14.78
Gender Male (%) Female (%)	 151 (44.94) 185 (55.06)
Preoperative length of stay in days (mean ± SD)	1.87 ± 1.43
Postoperative length of stay in days (mean ± SD)	4.16 ± 1.29
Duration of Surgery (mean ± SD)	104.53 ± 41.72
Departments	
General Surgery	147 (43.75)
Gynaecology	73 (27.72)
ENT	66 (19.64)
Orthopaedics	43 (12.80)
Urology	7 (2.08)

SD = Standard deviation

Table 2: Analysis of antibiotic usage using WHO prescribing indicators

Prescribing Indicators	Value
Average number of drugs prescribed per prescription	5.26
Average number of antibiotics prescribed per prescription	1.94
Percentage of antibiotics prescribed by generic name	68.73 %
Percentage of antibiotics prescribed by intravenous route	78.36 %
Percentage of antibiotics prescribed from essential medicine list	85.65 %
Percentage of antibiotics prescribed from national list of essential medicine (NLEM)	81.57 %

Table 3: Frequency of prescribing of different antibiotics during preoperative period

Antibiotics	Number of antibiotics prescribed	Percentage of antibiotics prescribed
Metronidazole	181	25.89
Ceftriaxone	131	18.74
Amoxicillin + Clavulanate	128	18.31
Clindamycin	53	7.58
Cefotaxime	39	5.58
Cefixime	34	4.86
Gentamicin	33	4.72
Amikacin	31	4.43
Meropenem	23	3.29
Levofloxacin	13	1.86
Piperacillin + Tazobactam	11	1.57
Ciprofloxacin	9	1.29
Linezolid	7	1.00
Ampicillin + Sulbactam	3	0.43
Ofloxacin	3	0.43
Total	699	100.00

Table 4: Frequency of prescribing of different antibiotics during intraoperative period

Antibiotics	Number of antibiotics prescribed	Percentage of antibiotics prescribed
Gentamicin	16	55.17
Ceftriaxone	7	24.14
Cefotaxime	6	20.69
Total	29	100.00

Table 5: Frequency of prescribing of different antibiotics during postoperative period

Antibiotics	Number of antibiotics prescribed	Percentage of antibiotics prescribed
Metronidazole	203	21.97
Amoxicillin + Clavulanate	167	18.07
Ceftriaxone	151	16.34
Clindamycin	71	7.68
Cefixime	67	7.25
Gentamicin	58	6.28
Cefotaxime	44	4.76
Meropenem	34	3.68
Amikacin	30	3.25
Ciprofloxacin	24	2.6
Levofloxacin	23	2.49
Linezolid	19	2.06
Piperacillin + Tazobactam	16	1.73
Doxycycline	7	0.76
Ampicillin + Sulbactam	5	0.54
Ofloxacin	5	0.54
Total	924	100.00

DISCUSSION

In our study, the patients took admission for different diagnosis such as acute appendicitis, acute cholecystitis, acute tonsillitis, myomas of uterus, dysfunctional uterine bleeding (DUB), bone fractures, osteoarthritis etc. According to baseline demographic data, male to female ratio was 0.82 contradictory to Akter SF et al where it was 1.8113.[22] This may be due to inclusion of patients whose surgeries were done in department of gynaecology. The mean age of study participant was 36.87 years and the most common age group of patients was middle aged group (36- 55 years). This result of the study is similar with research of Sharma and Goel where the average age was 45.33 ± 19.01 years.[23] Similar results were also found in the research of Bhataia et al.[24] This is the common trend because this age group is considered to be most productive age group and is actively engaged in socioeconomic works, which may add up to their stress and aging makes them more prone to disorders that may require surgical interventions.[24]

Most of the patients were recruited from wards of department of general surgery (43.75 %) followed by department of gynaecology (27.72%). This result was like research of Alemkere G where patients from department of general surgery were 60.1% followed by department of gynaecology with 24.8% of study participants.[25] Similarly, SG kamath et al have found a that 32.47% of patients were from department of general surgery.[26] However in the research of Rehan HS et al, most of the patients have taken admission under department of general surgery (30%) followed by department of orthopaedics (26%).[27]

Table 6: Frequency of ADRs and their distribution into different causality categories

Antibiotic	Total number of prescriptions	Number of ADR	Number of ADR per Prescription	Organ/Organ System affected by ADR or Type of ADR according to MedDRA coding
Metronidazole	384	85	22.14	Skin and subcutaneous tissue (17), Gastrointestinal (63), Nervous system (5)
Amoxicillin + Clavulanate	295	47	15.93	Skin and subcutaneous tissue (22), Gastrointestinal (17), Allergic (6)
Ceftriaxone	289	49	16.96	Skin and subcutaneous tissue (21), Gastrointestinal (19), Allergic (4), Others (5)
Clindamycin	124	27	21.77	Skin and subcutaneous tissue (16), Allergic (5), Blood and Lymphatic System (3), Others (3)
Cefixime	101	13	12.87	Skin and subcutaneous tissue (6), Gastrointestinal (4), Allergic (3)
Gentamicin	107	27	25.23	Skin and subcutaneous tissue (16), Gastrointestinal (5), Renal and Urinary (5)
Cefotaxime	89	17	19.10	Skin and subcutaneous tissue (7), Gastrointestinal (5), Allergic (5)
Meropenem	57	11	19.30	Skin and subcutaneous tissue (5), Gastrointestinal (2), Allergic (4)

Amikacin	61	14	22.95	Skin and subcutaneous tissue (8), Gastrointestinal (3), Renal and Urinary (3)
Ciprofloxacin	33	6	18.18	Skin and subcutaneous tissue (3), Gastrointestinal (2), Nervous system (1)
Levofloxacin	36	6	16.67	Skin and subcutaneous tissue (3), Gastrointestinal (3)
Linezolid	26	5	19.23	Blood and lymphatic system (5)
Piperacillin + Tazobactam	27	6	22.22	Skin and subcutaneous tissue (4), Gastrointestinal (1), Allergic (1)
Doxycycline	7	2	28.57	Gastrointestinal (2)
Ampicillin + Sulbactam	8	2	25.00	Gastrointestinal (2)
Ofloxacin	8	1	12.50	Nervous system (1)

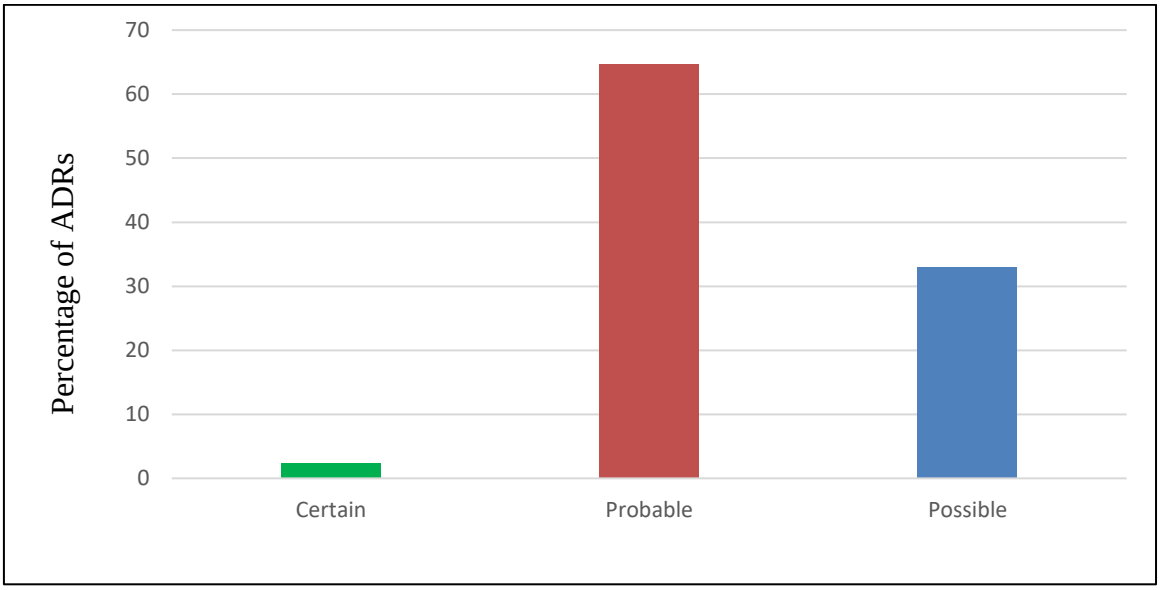

Figure 1: Distribution of ADRs into WHO-UMC causality categories

In this study, most common operations were abdominal surgeries. This result was not similar to study of Patel DJ et al where they have reported that most common operations were urological surgeries (30.5%) and cases of abdominal surgeries were only 37 (18.5%).[28] Many procedures of abdominal surgeries like exploratory laparotomies, appendectomies and cholecystectomies under laparoscopy were found in this study.

Most of the antibiotics were prescribed by their generic name (68.73%). This result is similar with study Bhataia et al where assessment on 5627 total medicine formulations was done and 98.51% (5534) have been found out being prescribed by official/generic names.[24] According to WHO standard, percentage of drugs prescribed by generic name should be 100%. Promoting generic prescribing could result in more rational use of drugs and will also lead to reduction in cost of therapy. [29] Average amount of antibiotic/ prescription in this study was found to be 1.94. Most of the patients have received at least one antibiotic at one moment or another. This is consistent with finding of Bhansali et al and Kumar R et al.[30,31] But this is much greater than the other similar studies done in India in which utilization of antibiotics was reported to be among 20% to 67% of the patients only.[24,30] Similar research outside India have reported that percentage of patients receiving at least one antibiotic were in the range of 20% to 42%.[32] The greater number of antibiotics per patient suggest that most of the antibiotics were utilized for prophylaxis indication rather than indication of definitive pharmacotherapy and that they were used as empirical therapy to minimize the risk of any or all types of infection. The percentage of antibiotics prescribed from NLEM (National list of essential medicine) were found to be 81.57%. This result was also consistent with essential drug list of the hospital.

Overall, the metronidazole was most commonly perioperatively used antibiotic in the study. It was also the most common antibiotic used preoperatively in the study followed by ceftriaxone and amoxicillin plus clavulanic acid. The finding was consistent with the study of Agrawal et al., where metronidazole was also most commonly used

antibiotic.[33] Metronidazole was predominantly utilized for anaerobic coverage.[32] In this study, nearly all the patients were prescribed prophylactic antibiotic preoperatively which was consistent with the study done in Kerala and Ahmadabad. [34,35]

Although, third generation cephalosporins were commonly used antibiotics for surgical prophylaxis in our study, use of first generation antibiotic is recommended by recent guidelines for this indication.[36, 37] First-generation cephalosporins particularly cefazolin are considered as the most suitable antibiotics for surgical prophylaxis because of their spectrum that covers staphylococcus species and most of gram-negative bacilli together with desired pharmacokinetic properties, easy administration and lower cost. But the choice of antibiotics is usually influenced by the local resistance pattern, experience of treating surgeon at the hospital setting and availability of antibiotics in government pharmacy or medical store.

We have found very few prescriptions that were based on report of culture and sensitivity tests. Prescribing antibiotics without any evidence from culture and sensitivity tests is one of the major concerns that could result in rise in resistance, treatment failure and poor patient compliance. So, this scenario recommends us to develop strict policies and regulation on antibiotic prescription to achieve the target of stopping the trend of rising resistance to antibiotics and promotion of rational use of antibiotics. [38]

ADRs were more frequently reported from patients who were prescribed with antibiotics of reserve and watch category. In earlier studies, antibiotics were the main cause of cutaneous ADRs. [39] In another research, antibiotics were reported to be associated with 48% of delayed cutaneous ADRs, 20% of which were causally related to glycopeptides and sulfonamides.[40] Penicillin, third-generation cephalosporins, quinolones, and glycopeptides were the most common antibiotics associated with the development of ADRs related to skin and subcutaneous-related. This different trends in the type of antibiotic associated with ADRs may be due to different social, geographical, and ethnic background among various study.[41] Further studies are needed to investigate on the mechanisms behind development of ADR by antibiotics.

CONCLUSION

Metronidazole, ceftriaxone, and amoxicillin plus clavulanic acid were the most commonly perioperatively used antibiotics in our study. ADRs were more frequently reported from patients who were prescribed with antibiotics of reserve and watch category. Further studies are needed to investigate on the mechanisms behind development of ADR by antibiotics. This scenario also recommends us to develop strict policies and regulation on antibiotic prescription to achieve the target of stopping the trend of rising resistance to antibiotics and promotion of rational use of antibiotics.

REFERENCES

1. Gould IM, Bal AM. New antibiotic agents in the pipeline and how they can overcome microbial resistance. Virulence. 2013;4(2):185–191.

2. Sengupta S, Chattopadhyay MK, Grossart HP. The multifaceted roles of antibiotics and antibiotic resistance in nature. Front Microbiol. 2013;4:47.

3. Read AF, Woods RJ. Antibiotic resistance management. Evol Med Public Health. 2014;2014(1):147.

4. The antibiotic alarm. Nature. 2013;495(7440):141

5. Machowska A, Sparrentoft J, Dhakaita SK, StålsbyLundborg C, Sharma M. Perioperative antibiotic prescribing in surgery departments of two private sector hospitals in Madhya Pradesh, India. Perioper Med (Lond). 2019 Sep 10;8:10. doi: 10.1186/s13741-019-0121-3.

6. Dale B, E-Patchen D, Keith O, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013;14(1):73–156.

7. Deverick A, Kelly P, Berríos-Torres S, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol 2014;35(6):605–627.

8. James S, Barbara B, Walter H, et al. Timing of antimicrobial prophylaxis and the risk of surgical site infections: results from the trial to reduce antimicrobial prophylaxis errors. Ann Surg 2009; 250(1):10–6

9. Bates D. W. Incidence of adverse drug events and potential adverse drug events. Implications for prevention. ADE Prevention Study Group. Journal of the American Medical Association. 274(1):29–34. doi: 10.1001/jama.274.1.29.

10. Classen D. C. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. Journal of the American Medical Association. 277(4):301–306. doi: 10.1001/jama.277.4.301.

11. Lacoste-Roussillon C. Incidence of serious adverse drug reactions in general practice: A prospective study. Clinical Pharmacology & Therapeutics. 2001;69(6):458–462. doi: 10.1067/mcp.2001.116145.

12. Trubiano J. A., Cairns K. A., Evans J. A., et al. The prevalence and impact of antimicrobial allergies and adverse drug reactions at an Australian tertiary centre. BMC Infectious Diseases. 2015;15(1) doi: 10.1186/s12879-015-1303-3.

13. Jha A. K., Kuperman G. J., Rittenberg E., Teich J. M., Bates D. W. Identifying hospital admissions due to adverse drug events using a computer-based monitor. Pharmacoepidemiology and Drug Safety. 2001;10(2):113–119. doi: 10.1002/pds.568.

14. Evans R. S., Lloyd J. F., Stoddard G. J., Nebeker J. R., Samore M. H. Risk Factors for Adverse Drug Events: A 10-Year Analysis. Annals of Pharmacotherapy. 2005;39(7-8):1161–1168. doi: 10.1345/aph.1E642.

15. Hawkey PM. Prevalence and clonality of extended-spectrum beta-lactamases in Asia. Clin Microbiol Infect. 2008;14(Suppl 1):159–165. doi: 10.1111/j.1469-0691.2007.01855.x.

16. Pathak A, Marothi Y, Kekre V, Mahadik K, Macaden R, Lundborg CS. High prevalence of extended-spectrum beta-lactamase-producing pathogens: results of a surveillance study in

two hospitals in Ujjain, India. Infect Drug Resist. 2012;5:65–73. doi: 10.2147/IDR.S30043.

17. Hohmann C, Eickhoff C, Radziwill R, Schulz M. Adherence to guidelines for antibiotic prophylaxis in surgery patients in German hospitals: a multicentre evaluation involving pharmacy interns. Infection. 2012;40(2):131–137. doi: 10.1007/s15010-011-0204-7.

18. Crader MF, Bhimji SS. Preoperative Antibiotic Prophylaxis. Treasure Island: StatPearls; 2018.

19. Ozcan G., Aykac E., Kasap Y., Nemutlu N. T., Sen E., Aydinkarahaliloglu N. D. Adverse Drug Reaction Reporting Pattern in Turkey: Analysis of the National Database in the Context of the First Pharmacovigilance Legislation. *Drugs - Real World Outcomes*. 2016;3(1):33–43. doi: 10.1007/s40801-015-0054-1.

20. Helling M., Venulet J. Drug recording and classification by the WHO research centre for international monitoring of adverse reactions to drugs. *Methods of Information in Medicine*. 1974;13(3):169–178.

21. Ofori-Asenso R. A closer look at the World Health Organization's prescribing indicators. J Pharmacol Pharmacother. 2016 Jan-Mar;7(1):51-4. doi: 10.4103/0976-500X.179352. PMID: 27127400

22. Akter 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.

23. Sharma 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):23-27.

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

25. Alemkere 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.

26. Kamath 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.

27. Rehan 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):30-36.

28. Patel 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.

29. Goodman 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.

30. Bhansali 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.

31. Kumar 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.

32. Bhabhor 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.

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

34. Tourmousoglou 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.

35. 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.

36. Scotish 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].

37. World Health Organization. Guidelines for Safe Surgery: Safe Surgery Saves Lives. Geneva: World Health Organization; 2009. Available from: https://www.who.int/publications/i/item/9789241598552

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

39. Doshi K., Yegnanarayan R., Gokhale N. A Retrospective Study of Drug Induced Cutaneous Adverse Reactions (CADR) in Patients Attending Tertiary Care Hospital. *Current Drug Safety*. 2016;11(999):1–1. doi: 10.2174/1574886311666160724213109.

40. Trubiano J. A., Aung A. K., Nguyen M., et al. A Comparative Analysis Between Antibiotic- and Nonantibiotic-Associated Delayed Cutaneous Adverse Drug Reactions. *The Journal of Allergy and Clinical Immunology: In Practice*. 2016;4(6):1187–1193. doi: 10.1016/j.jaip.2016.04.026.

41. Eliasson E. Ethnicity and adverse drug reactions. *BMJ*. 2006;332(7551):1163–1164. doi: 10.1136/bmj.332.7551.1163.

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