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Pattern of Antimicrobial Utilization for Surgical Prophylaxis to Prevent Surgical Site Infection in Tertiary Care Teaching Hospital

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Abstract:

Background: *Surgical site infections (SSIs) are the second most common nosocomial infections and have adverse impact on patient. Despite proved effectiveness of surgical antimicrobial prophylaxis in reducing morbidity and mortality use is often inappropriate. However, this inappropriate use of antimicrobial agents (AMAs) leads to emergence of resistance. The objective of this study is to evaluate the pattern of surgical antimicrobial prophylaxis in our hospital to decrease SSIs and to suggest corrective measures.*

Material and Methods: *201 medical records of general surgery department were analysed retrospectively for five parameters of rational surgical antimicrobial prophylaxis like (i) selection (ii) timing of pre-operative dose, (iii) intra-operative dose, (iv) duration of post-operative prophylaxis and (v) unnecessary use of antimicrobial agents (AMA) were evaluated using ASHP (American Society of Health-System Pharmacists) guidelines.*

Results: *Total 201 patients were prescribed AMA for surgical prophylaxis. The most frequent use of AMA was third generation cephalosporin and metronidazole. With regards to pre-operative dose 33.83% patients received AMAs 12 hours before surgery while no patient received intra-operative AMA. The duration of the postoperative prophylaxis extended more than 48 hours in 89.55% cases during their hospital stay. 11.94% and 35.32% cases were given unnecessary AMA in pre-operative and post-operative period respectively. 89.55% cases received AMA for long prophylaxis*

Conclusion: *Current study revealed there is inappropriate use of AMA to prevent SSIs such as mistake in selection of AMA, excessive dosing and prolonged prophylactic use of AMA.*

Keyword - Surgical site infection, antimicrobial prophylaxis, retrospective

Introduction:

Nosocomial infections are common with incidence rate of 4.5 to 7.1% globally while it range from 11 to 83% in India.[1,3] Surgical site infections (SSI) are complications associated with surgery and is the second common cause of nosocomial infection.[1,2] SSI is the major cause of prolonged hospital stay, increase morbidity, mortality and health care cost. Prevention by proper hygiene, use of sterile instruments and good surgical technique to minimise tissue damage and devascularisation are often the only measures needed.[1,5,18]

Surgical antimicrobial prophylaxis (SAP) refer to brief course of antimicrobial agents (AMAs) initiated just before surgery to prevent SSI.[1,2,4,5] It is different from treating infection. It is widely accepted and established practice in surgery since 1960s. However despite its effectiveness for surgical prophylaxis, its adoption is sub-optimal and use is inappropriate.[1,4,5] It is observed that extensive, prolonged and often combined use of AMAs is made for SAP practically after all surgeries. Such misuse is particularly rampant in developing countries because of unreliable infection control measures.[2,3,16] SAP with single dose of AMA is enough for clean surgery, except in patients with comorbid condition like diabetes mellitus.[5,19] The selection of AMA, dose, timing and duration of SAP is often crucial. SAP should not be initiated early and is not continued for more than 24 hours after surgery. To ensure effective blood

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and tissue levels of AMA during surgery, oral drugs are given 1 hour before and intravenous (i.v.) just before anaesthesia/incision.[6-8] In prolonged surgeries, i.v. dose is repeated intra-operatively. Post-operative dose after 4 hours of wound closure is recommended only in contaminated and dirty surgeries, or it may be continued for 5 days.[4,8,10] Prolonged post-operative dose does not add any benefit but foster resistance, toxicity, super-infection, increase morbidity, mortality and health care cost.[6,15]

Many studies in India and Maharashtra reported inappropriate use of AMAs for surgical prophylaxis.[2,3,16,24] Hence, the objective of this study is to examine prevalent practice of SAP in this hospital, to suggest corrective measures or strategies of rational AMA use to prevent SSI. Presently few studies exist across this area.

Material and Methods:

This was the retrospective study. Medical records of patients who were admitted in General Surgery Ward in tertiary care hospital of Maharashtra from 10/11/2016 to 10/01/2017 and who underwent minor/major surgeries were evaluated. The data was collected randomly from medical record (MR) section during the period from 01/06/2017 to 31/08/2017. Total 230 records were evaluated, 201 were included in the study and 29 records were excluded for reasons like referral to other centre, improper documentation and discharge against medical advice. Finally 201 case records were processed. The consent of chief of MR section was taken prior to study.

Five parameters of rational SAP like (i) selection (ii) timing of pre-operative dose, (iii) intra-operative dose if any (iv) duration of post-operative prophylaxis (v) unnecessary use of antimicrobial agents (AMA), were evaluated using ASHP guidelines along with demographic/medical/surgical data, type of surgery/wound class[1,4] length of stay in hospital.

Preferred parenteral drug for SAP is cefazolin 2gm i.v. (30mg/kg). If MRSA is suspected, then vancomycin 1gm i.v. (20mg/kg), metronidazole 500mg i.v. if anaerobes and clindamycin 600mg (20mg/kg) if penicillin allergy. For oral administration cephalexin/cefadroxil/amoxicillin 2gm (50mg/kg) is given as single dose 1 hour before surgery. In penicillin allergy clindamycin 600mg (200mg/kg) or azithromycin/clarithromycin 500mg (15mg/kg) is used.[4,5]

The data was in percentage and mean ± SD and was analysed using SPSS software 21.

Results:

A total of 201 surgical case records of patients who underwent surgery and met inclusion criteria were selected. Out of selected cases 61.7% were men and 38.3% were women. The mean age (mean ± SD) was 35.83 ± 18.7 years. The mean duration of hospital stay was 6.75 ± 4.77 days and median stay length was 5 days [Table 1].

Table 1: Demographic and surgical data of patients (n = 201)

Patients characteristics	Values (n=201)
Mean age ± SD years	35.83 years ± 18.7
Men	124 (61.7 %)
Women	77 (38.3 %)
Median stay	05 days
Pre-operative stay (mean ± SD) days	0.75 ± 1.79
Post-operative stay (mean ± SD) days	6.09 ± 4.40
Number of comorbidities	
Hypertension	06 (2.99%)
Diabetes Mellitus	03 (1.49%)
Hypertension + Diabetes Mellitus	03 (1.49%)
Hepatitis B	03 (1.49%)
HIV	01 (0.49%)
Hypothyroid	01 (0.49%)
Epilepsy	01 (0.49%)
Type of procedure	
Abdominal	90 (44.77%)
Lump/cyst	37 (18.40%)
Urogenital	17 (8.46%)
Hepatobiliary	05 (2.49%)
Miscellaneous	52 (25.87%)
Type of surgery	

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Elective	150 (74.63%)
Emergency	51 (25.37%)
Wound Class:	
Clean	46 (22.88 %)
Clean contaminated	103 (51.24 %)
Contaminated	41 (20.40 %)
Dirty	10 (04.98 %)

Comorbidities like Hypertension, Diabetes Mellitus, Hypertension + Diabetes Mellitus, Hepatitis B, HIV, Hypothyroid and Epilepsy were present in 02.99%, 01.49%, 01.49%, 01.49%, 0.49%, 0.49% and 0.49% patient respectively [Table 1].

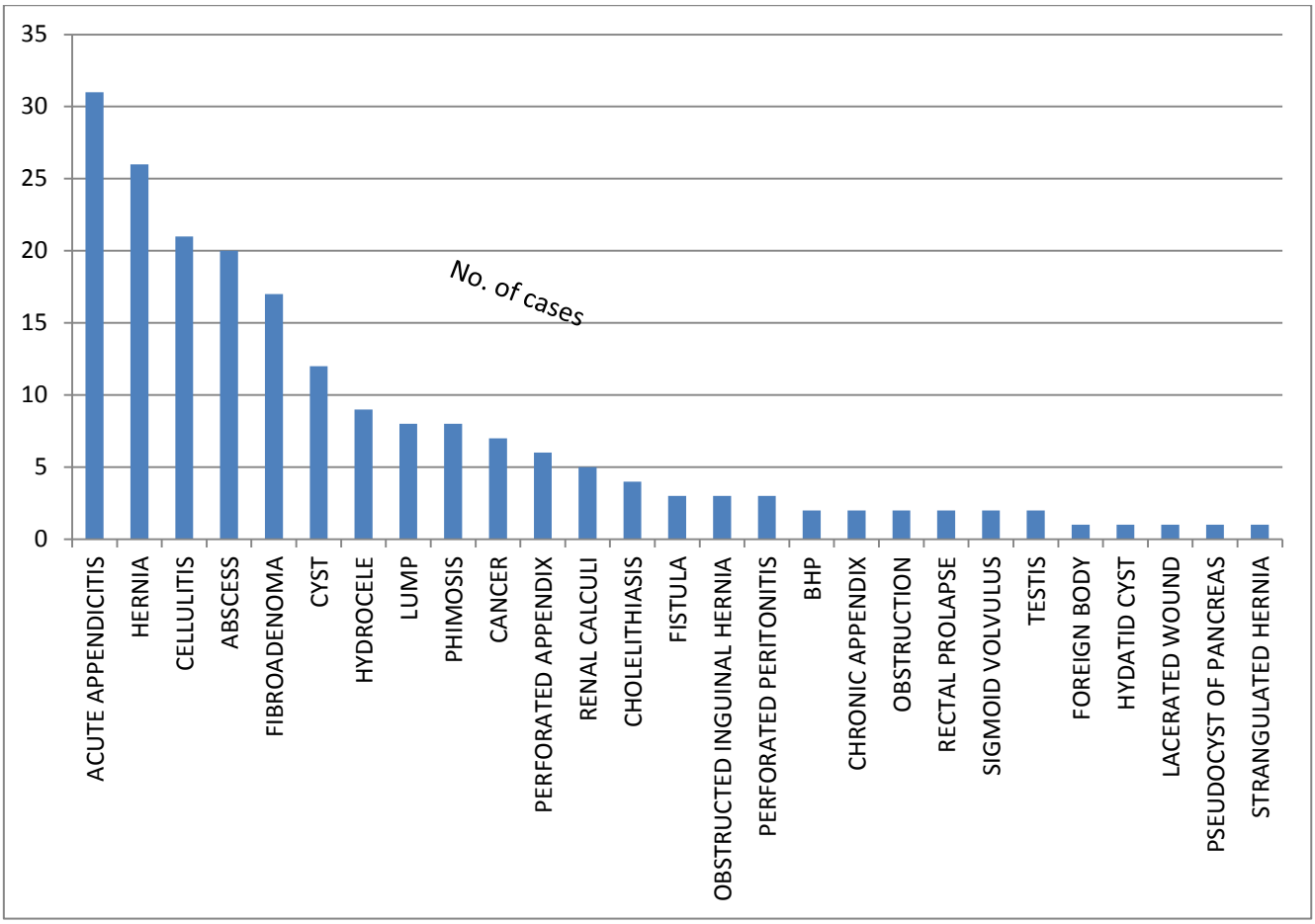

Fig: 1 Diagnosis of the patients who underwent surgery

In this study, out of 201 cases 74.63% were elective surgeries, whereas 25.37% were emergency surgeries. Under type of surgical procedures 44.77% were abdominal surgeries, 18.47% were excision of lump/cyst, 08.46% were urogenital surgeries, 02.49% were hepatobiliary, while miscellaneous surgeries were 25.87%. In wound class clean surgeries were 46 (22.88%) while clean contaminated, contaminated and dirty surgeries were 92 (45.77 %), 52 (25.87 %) and 10 (04.98 %) respectively [Table 1]. Appendicectomy was the most frequent surgical procedure which was performed (19.40%) followed by hernia repair (14.92%) [Fig1].

Patients who underwent minor or major surgery, 28.86% didn't received preoperative antimicrobial agents. 57.21% patients received preoperative injectable antimicrobial agents while 13.93% received oral antimicrobial prophylaxis [Table 2].

Most commonly used antimicrobial agent in pre-operative period was combination of i.v. Ceftriaxone 1gm + metronidazole 500mg infusion in 13.93% patients followed by i.v. Cefotaxime 1gm + metronidazole 500mg infusion in 12.93% patients which was followed by i.v. Cefotaxime 1gm in 08.95% patients, while 7.96% patients received Tab. Cotrimoxazole DS. Combination of three AMA i.e. Inj. Cefotaxime 1g + Inj. Metronidazole 500mg infusion + Inj. Amikacin 500mg was administered in 05.47% patient, these were the cases of acute appendicitis, abscess, cellulitis, haemoperitoneum, obstructed inguinal hernia [Table 2].

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Table 2: SAP utilization

Name of AMA	Number of cases (%)	
	Pre-operative (n=201)	Post-operative (n=201)
Single AMA		
Inj.Ceftriaxone 1gm	10 (4.97%)	07 (3.48%)
Inj.Cefotaxime 1gm	18 (8.95%)	32 (15.92%)
Inj.Ciprofloxacin 200mg infusion	01 (0.49%)	0
Inj.Amoxiclav 1.2 gm	03 (1.49%)	01 (0.49%)
Inj.Metronidazole 500mg infusion	0	01 (0.49%)
Cap.Amox	07 (3.48%)	0
Tab.Cotrimoxazole DS	16 (7.96%)	0
Tab.Ciprofloxacin 500mg	02 (0.99%)	0
Syp.Amoxicillin	01 (0.49%)	0
Combination of 2 AMA		
Inj.Cefotaxime 1g + Inj.Metronidazole 500mg infusion	26 (12.93%)	44 (21.89%)
Inj.Ceftriaxone 1g + Inj.Metronidazole 500mg infusion	28 (13.93%)	41 (20.39%)
Inj.Amoxiclav 1.2gm + Inj.Metronidazole 500mg infusion	02 (0.99%)	07 (3.48%)
Inj.Amoxiclav 1.2g + Inj.Amikacin 500mg	06 (2.98%)	04 (1.99%)
Inj.Cefotaxime 1g + Inj.Amikacin 500mg	05 (2.48%)	23 (11.44%)
Inj.Ciprofloxacin 200mg infusion + Inj.Metronidazole 500mg infusion	01 (0.49%)	0
Inj.Piperacillin-Tazobactam 4.5g + Inj.Metronidazole 500mg infusion	0	03 (1.49%)
Inj.Meropenem + Inj.Metronidazole 500mg infusion	0	01 (0.49%)
Tab.Cotrimoxazole DS + Tab.Metronidazole 400mg	01 (0.49%)	0
Cap.Amoxicillin + Tab.Metronidazole	01 (0.49%)	0
Tab.Ciprofloxacin 500mg + Tab.Metronidazole 400mg	0	05 (2.48%)
Combination of 3 AMA		
Inj.Amoxiclav 1.2g + Inj.Amikacin 500mg + Inj.Metronidazole 500mg infusion	01 (0.49%)	0
Inj.Cefotaxime 1g + Inj.Metronidazole 500mg infusion + Inj.Amikacin 500mg	11 (5.47%)	15 (7.46%)
Inj.Ceftriaxone 1g + Inj.Metronidazole 500mg infusion + Inj.Amikacin 500mg	03 (1.49%)	05 (2.48%)
Inj.Piperacillin-Tazobactam 4.5g + Inj.Metronidazole 500mg infusion + Inj.Amikacin 500mg	0	04 (1.99%)
Inj.Ciprofloxacin 200mg infusion + Inj.Metronidazole 500mg infusion + Inj.Amikacin 500mg	0	01 (0.49%)
Inj.Ceftriaxone 1g + Inj.Metronidazole 500mg infusion + Inj.Levofloxacin 400mg	0	01 (0.49%)
Inj.Meropenem + Inj.Metronidazole 500mg infusion + Inj.Ciprofloxacin 200mg infusion	0	01 (0.49%)
Inj.Ceftriaxone 1gm + Inj.Amikacin 500mg + Tab.Moxifloxacin 400mg	0	01 (0.49%)
Inj.Ceftriaxone 1gm + Inj.Ciprofloxacin 200mg infusion + Tab.Moxifloxacin 400mg	0	01 (0.49%)
Combination of 4 AMA		
Inj.Aztreonam + Inj.Meropenem + Inj.Levofloxacin 400mg + Inj.Metronidazole 500mg infusion	0	01 (0.49%)
Inj.Piperacillin-Tazobactam 4.5g + Inj.Metronidazole 500mg infusion + Inj.Amikacin 500mg + Tab.Moxifloxacin 400mg	0	01 (0.49%)
Inj.Ceftriaxone 1gm + Inj.Metronidazole 500mg infusion + Inj.Amikacin 500mg + Tab.Moxifloxacin 400mg	0	01 (0.49%)
Unnecessary SAP		
	24 (11.94%)	71 (35.32%)

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Selection of SAP		
Narrow spectrum AMA	04	03
Broad spectrum AMA	01	01
Combination of AMA	11	19
Duration of SAP		
< 24 hours	126 (62.68%)	03 (1.49%)
> 24 hours	17 (8.46%)	198 (98.50%)

With regards to timing of antimicrobial administration, 33.83% patients received AMAs 12 hours before surgery. 28.86% received AMA 1 day before surgery while 08.46% received AMA for more than 24 hours prior to surgery. Intra-operative AMA was not administered. The duration of postoperative prophylaxis extended more than 48 hours in 89.55% cases during their hospital stay. Only 10.45% patients received the antimicrobials for less than 48 hours [Table 3].

Table 3: Duration for which antimicrobial agents (AMAs) were used in each patient in pre-operative and post-operative period (n = 201)

Duration for which AMAs were used	Pre-operative period (No. of cases)	Post-operative period (No. of cases)
Less than 12 hours	68 (33.83)	0
1 day	58 (28.86)	03 (1.49)
2 days	10 (4.97)	18 (8.95)
3 to 5 days	03 (1.49)	109 (54.22)
6 to 10 days	03 (1.49)	45 (22.38)
11 to 15 days	01 (0.49)	13 (6.47)
16 to 20 days	0	07 (3.48)
21 to 25 days	0	06 (2.98)

Postoperative intravenous antimicrobials were not used in 5 cases, which were instead given oral drugs i.e. combination of ciprofloxacin 500mg and metronidazole 400mg tablet. Most common antimicrobial agent preferred post-operatively was combination of i.v. cefotaxime 1G and metronidazole 500mg infusion in 21.89% patients, followed by i.v. ceftriaxone 1G + metronidazole 500mg infusion in 20.39% patients. 15.92% patients received single AMA i.e. i.v. cefotaxime 1G. Most preferred combination of three AMAs was Inj.Cefotaxime 1G + Inj.Metronidazole 500mg infusion + Inj. Amikacin 500mg in 7.46% patients, followed by Inj. Ceftriaxone 1g + Inj. Metronidazole 500mg infusion + Inj. Amikacin 500mg in 2.48% patients and Inj.Piperacillin-Tazobactam4.5G + Inj. Metronidazole 500mg infusion + Inj.Amikacin 500mg in 1.99% patients. Combination of 4 AMAs was also used in 3 patients; one was operated for right inguinal obstructed hernia with jejunal perforation, second underwent emergency exploratory laparotomy (resection anastomosis with hernia repair) for obstructed inguinal hernia and third had open subtotal cholecystectomy with drain in situ for cholelithiasis with cholecystitis [Table 2].

Discussion:

Total 201 medical records including 61.7% men and 38.3% women of surgery department who underwent surgical procedures were evaluated with regard to compliance with American Society of Health-System Pharmacists (ASHP) guidelines.[5,9] The study was aimed to assess practice of SAP (SAP) at this tertiary care hospital.

Medical records were evaluated for selection of AMA, timing of pre-operative dose, intra-operative dose, duration of post-operative prophylaxis and unnecessary use of AMA along with patients' demographic data and details of surgical procedures.

In this study 22.88% medical records belonged to clean or elective surgeries and yet 9.45% case records mentioned use of SAP before surgery.[5,19,26] The reason may be comorbid conditions like diabetes mellitus or immunocompromised host, but in many case records proper history regarding past diseases or treatment was lacking.[2] 51.24% cases belonged to clean contaminated category which was in agreement with Napolitano F et al.[11]

Intravenous route (i.v.) was used in 57.21% patients prior to incision to have reliable and predictable serum and tissue concentration. Combination of 3rd generation cephalosporin i.e. cefotaxime/ceftriaxone with metronidazole was commonly used while oral route was used in 13.93% patients. These findings were in agreement with study by Afzal Khan A.K. et al.[2]

In 11.94% pre-operative cases, AMA prophylaxis was not needed/indicated. This finding was higher than the study of Mohamoud SA et al[25] and lesser than study of Alavi SM et.al[23] while in 35.32% cases post-operative AMA

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prophylaxis was of longer duration which exceed 5 days. These findings are lower than the study of Kulkarni RA et.al[21]

Wrong selection of AMA was noticed in 25 (12.44%) cases in pre-operative period while in 66 (32.84%) cases in post-operative period. Such wrong selection of AMA was noticed in other studies in and outside India.[2,3,20,21,24]

There was excessive and inappropriate use of i.v. ceftriaxone/cefotaxime despite availability of guidelines. IV ceftriaxone/cefotaxime are recommended as a single agent in high risk biliary surgeries or in combination with metronidazole in colorectal surgeries. As per SAP principle, narrow spectrum AMA effective against likely pathogen i.e. staphylococcus aureus (S.aureus) should be used. Use of broad spectrum single agent or combination of antimicrobial agents give rise to lack of response or resistance and increase cost. SAP guidelines recommend i.v. cefazoline 2gm (30mg/kg).[5,19,21]

There was use of broad spectrum AMAs and unnecessary AMA combinations. There is a false belief that such practices are more effective in prevention of SSI.[5,15,19,25] Non-availability of hospital supplies of AMA at that point of time of surgery may have contribute to inappropriate selection, but in spite of availability most surgeon fail to act as per guidelines. Another cause may be lack of awareness about presence or existence of guidelines.[6,17,20]

The selection of AMA was empirical based on surgeons' experience. Local resistance pattern were not considered while prescribing AMAs, this was in consistent with Khade A et.al.[24] 3rd generation cephalosporins were used along with metronidazole and amikacin in 09.94% cases to cover anaerobes and gram negative bacteria respectively, however studies shows no significant difference in efficacy by addition of aminoglycoside to third generation cephalosporins as both have gram negative cover providing no additional benefit.[5,10,16,21] Meropenem is a broad spectrum AMA; it has activity against gram positive, gram negative organism, aerobic and anaerobic bacteria still it was used along with metronidazole and levofloxacin in 3 (01.49%) patients. Anaerobes are moderately susceptible to Levofloxacin, which was seen combined with metronidazole in 2 (0.99%) cases. Piperacillin-tazabactam have activity against gram positive and negative bacteria, yet we found its use along with amikacin in 4 (1.99%) cases.[4] This was the wastage of AMA.

Pre-operative dose is ideally administered 60min before incision as per guidelines but this is not properly documented in case records,[11,16] therefore AMA administration 12 hour before was considered as pre-operative test dose which was given in 33.83% cases. Findings were similar to study by Kulkarni RA et.al.[21]

Intra-operative use of AMA in prolong surgeries lasting more than 4 hours or in case of heavy blood loss during surgery was not properly documented. Such incomplete and unclear documentation has been reported by other researchers.[2]

There were 37.31% procedures where AMA was started right at the time of admission empirically. In 28.86% cases 1 day prior, 6.46 % cases 2 to 5 day prior, 1.98 % cases 6 to 15 days prior to surgical procedures. Duration of post-operative SAP was prolonged (more than 5 days) in 35.32% cases which was the main concern. This is the common feature across many studies.[12-15] SAP for less than 36 to 48 hours is given only to 10.44% of cases. This was in contrast with guidelines which deny use of AMAs after 24 to 48 hours.[5,17] Empirical AMA administration for 1 to 5 days in 64.66% patients, continued for 5 to 10days in 22.38% cases, for 10 to 20 days in 9.95 % patients and more than 20 days in 2.98% cases that too using or changing different AMA with no rationale. Again this was misuse of AMA, as nowhere there was mention of infective condition, sending specimen for culture and sensitivity or changing AMA after arrival of culture and sensitivity reports, so as to change over from empirical to definitive treatment. The documentation about AMA in brand names like Tazar, Tazobac, Monocef, Taxim, Augmentin was rampant which was in agreement with Khade A et al.[16,24]

Limitations: This was a retrospective single institutional study using small sample size.

Conclusion:

There was inappropriate i.e. irrational use of AMA for SAP. This is global phenomenon, as similar findings were reported by studies across world. In this hospital antimicrobial used for SAP was not reasonable with regard to timing of pre-operative dosing and needlessly extended post-operatively utilizing baseless antimicrobial combinations. Corrective measures against such irrational practices will be formulation of local hospital SAP guidelines using evidence based medicines, formation and implementation of hospital antibiotic policy, educating and training surgeons on SAP, ensuring strict aseptic measures in surgeries, promoting good surgical techniques, regular intervention to surveillance of SAP, committee supervising SAP practices for prevention of SSI, compulsory clear and complete documentation of medical records by surgeon to help future researchers in this area are needed.

Conflict of interest: None

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Abbreviations:

AMA: Antimicrobial Agents
ASHP: American Society of Health-System Pharmacists
SAP: Surgical Antimicrobial Prophylaxis
MR section: Medical Record Section
i.v.: intravenous
g/gm: gram
mg: milligram

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