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STUDY THE COST OF ANTIMICROBIALS THERAPY USED IN POST-OPERATIVE SURGICAL PATIENTS IN TERTIARY CARE HOSPITAL

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ABSTRACT: Background: Antimicrobials are used for prophylaxis and treatment of infections that occur following surgical procedures to reduce the morbidity and mortality associated with surgical site infections (SSIs). A surgical site infection is an infection that occurs after surgery in the part of the body where the surgery took place. These are infections of the tissues, organs, or spaces exposed by surgeons during the performance of an invasive procedure. **Objective:** To assess the cost of antimicrobials therapy used within different types of surgeries. **Methods:** A prospective, non-interventional, observational study in the department of pharmacology for 9 months. Sample size: 330. **Results:** In our study clean 113 (34%), dirty 102 (31%), and clean-contaminated 90 (27%) wound surgeries were the most commonly performed surgeries. Contaminated wound surgeries were the least commonly performed surgeries (8%) in our study. The cost of antimicrobial therapy in patients with clean-contaminated (median-220), contaminated (median-352), or dirty wound surgeries (median-546) was significantly high as compared to clean wound surgeries (median-160). Also the cost of antimicrobial therapy in patients with dirty wound surgeries is significantly high as compared to clean contaminated wound surgeries. **Conclusion:** Total duration of antimicrobial therapy, number, and cost of antimicrobial used was more in clean-contaminated, contaminated, dirty wound surgeries than clean wound surgeries. SSI increases cost, antimicrobial use and resistance. A higher economic burden of antimicrobials was observed in patients with wound infection than those without wound infection.

INTRODUCTION: Antimicrobials are used for prophylaxis and treatment of infections that occur following surgical procedures to reduce the morbidity and mortality associated with surgical site infections (SSIs).

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A surgical site infection is an infection that occurs after surgery in the part of the body where the surgery took place.

While the global estimates of surgical site infection (SSI) have varied from 0.5% to 15%, studies in India have consistently shown higher rates ranging from 23% to 38% [3]. The incidence of SSI may be influenced by pre-operative care, the theatre environment, post-operative care, and the type of surgery [1, 2]. The type of surgeries has been classified by National Research Council (NRC) in four classes: clean, clean-contaminated,

contaminated, and dirty. Clean surgeries are those in which surgical wounds exhibit no infection or inflammation; operations not involving the entry of respiratory, digestive, genital or urinary tracts. *E. g*. hernia repair, hydrocele, breast lump excision, *etc*. Clean-contaminated surgeries involve opening the respiratory, digestive, genital or urinary tracts under controlled conditions and without abnormal contamination. *E.g*. all elective surgeries such as cholecystectomy, appendicectomy, colorectal surgeries, small intestinal surgeries *etc*. Contaminated surgeries are fresh (within 7 h of causal event), include open trauma injuries. Wounds with acute, non-purulent inflammation are included in this class. *E.g.* – penetrating abdominal trauma, large tissue injury, enterotomy during bowel obstruction *etc*.

Dirty surgeries involve old (more than 7 h after causal event) trauma injuries with devitalized tissue and with pre-existing clinical infection or perforated viscera. *E.g*. perforation of gastro-intestinal, biliary or or pharyngeal tract before operation, necrotising soft tissue infections [3, 4].

Antimicrobials used to treat and prevent surgical infections are Beta-lactam antibiotics like penicillins, cephalosporins, aminoglycosides like gentamicin, tobramycin and quinolones like ciprofloxacin, ofloxacin, levofloxacin, imidazoles like metronidazole [5].

Today antimicrobial drugs are one of the most commonly used drugs in clinical practice, and the problems associated with their use are a global problem. There is considerable evidence that antimicrobials are excessively and inappropriately used for the prevention of surgical site infections (SSI). Appropriate antimicrobials selection can reduce both the cost and resistance of antimicrobials. Consequences of surgical site infections are increased cost of treatment, longer duration of hospital stay and increased use of antimicrobials [6, 7]. Hence, it is necessary to improve the appropriate use of antibiotics. Considering these facts, the present study was undertaken to analyze and compare the cost of antimicrobial therapy in different surgical classes.

MATERIALS AND METHODS:

Study Design: A prospective, non-interventional, observational study.

Study Site: General Surgery Wards of a tertiary care hospital.

Study Duration: 9 months - 12-01-2018 to 12-10-2018

Source of Data: Case papers and prescriptions of patients in the surgery ward.

Sample size: 330 Number of patients admitted in 4 surgery wards are approximately 65 per week under all six units. Therefore in one month approximately 260 patients are admitted.

To represent 9 month post-operative surgical patients of different types of surgeries (260*9=2340), sample size calculated using 95% confidence level and 5% confidence interval as per sample size calculator [8] is 330 .

Sampling Technique: Convenient sampling.

Patient Selection:

Inclusion Criteria: Patients undergone surgery and on post-operative antimicrobials therapy, Patients of either gender aged ≥ 18 years.

Exclusion Criteria: Patients of outpatient department in surgery.

Study Procedure: Permission of Head of General Surgery & Ethics committee for Academic Research Project (ECARP) was taken. Patients admitted in all 6 surgery units who were on post-operative antimicrobials treatment were enrolled in the study. Written informed consent was taken from patients or LAR (legally acceptable representative). Cost of each antimicrobial was written in CRF. The cost of each antimicrobial was obtained from the hospital pharmacy if it was prescribed from the hospital pharmacy. If an antibiotic was prescribed from outside the hospital pharmacy then cost will be obtained by M. R. P. (maximum retail price) of drug.

Statistical Analysis: Descriptive statistical terms such as mean, standard deviation, median, percentage etc were used to describe the data which was collected. For comparison of four surgical groups for parameters like duration of antimicrobial therapy, number of antimicrobials prescribed, cost of antimicrobial therapy - Kruskal Wallis test or one way ANOVA followed by Post hoc tukey's test

or Dunn's test as appropriate (SPSS version 23 was used for this).

Results: Total of 330 patients undergone surgical procedures in the surgery department were enrolled during the study period of 9 months and they received total of 731 antimicrobials during their hospital stay. Mean age of the study population was 45.81 ± 14.98 years with range was between 18 and 85 years. Out of 330 patients percentage of male (68.18%) was more than that of female (31.82%).

TABLE 1: PERCENTAGE OF PATIENTS ACCORDING TO TYPE OF SURGERY (AS PER NRC CLASSIFICATION)

Type of surgery	No. of patients (%)
Clean (Class I)	113 (34%)
Clean contaminated (Class II) All elective surgeries	90 (27%)
Contaminated (Class III)	25 (8%)
Dirty (Class IV)	102 (31%)

Table 1 shows the number of patients according to the type of surgeries (as per NRC classification). In our study, clean wound surgeries were the most commonly performed surgeries in 34 % of patients followed by dirty wound surgeries in 31 % of patients. Clean contaminated wound surgeries were the third most commonly performed surgeries (27%) during our study period. Contaminated wound surgeries were the least commonly performed surgeries (8%) in our study.

TABLE 2: COMPARISON OF DURATION OF ANTIMICROBIAL THERAPY BETWEEN DIFFERENT TYPES OF SURGERY

Class	Class I	Class II	Class III	Class IV
Median	5	7	9	11
IQR	4-5.5	5-9	9-11	9-14
Mean±	4.94±	7 ±	9.68±	11.58±
SD	1.39	1.55	1.88	3.21
Range	3-7	5-9	5-14	6-21

TABLE 3: COMPARISON OF P-VALUE OF DURATION OF ANTIMICROBIAL THERAPY BETWEEN DIFFERENT TYPES OF SURGERY

Comparison	P-value
Class I vs Class II, III, IV	< 0.001
Class II vs Class III	<0.001
Class III vs Class IV	<0.001

P-value for comparison among all 4 groups was < 0.001 by kruskal Wallis test followed by Dunn's posthoc test for multiple comparisons.

The total duration of antimicrobial therapy during hospital stay among different surgical classes was significantly longer (p< 0.001) in classes II, III, and IV compared to class I. Also, the total duration of antimicrobials during hospital stay was longer (p< 0.001) in class III compared to Class II and Class IV compared to class III.

TABLE 4: COMPARISION OF NUMBER OF ANTIMICROBIALS USED PER PATIENT BETWEEN DIFFERENT SURGICAL CLASSES

Class	Class I N=113	Class II N=90	Class III N=25	Class IV N=102
Median	2	2	2	2
IQR	1-2.5	2-3	2-3	2-3
Mean ± SD	1.90 ± 0.81	2.42±0.86	2.2±0.82	2.38±0.82
Range	1-4	1-4	1-4	1-4

TABLE 5: COMPARISION OF P VALUE OF NUMBER OF ANTIMICROBIALS USED PER PATIENT BETWEEN DIFFERENT SURGICAL CLASSES

Comparison	P value
Class I vs Class II	< 0.001
Class I vs Class IV	< 0.001

The P value for the comparison among all 4 groups was < 0.001 by kruskal Wallis test followed by Dunn's posthoc test for multiple comparisons.

The number of antimicrobial prescribed per patient was significantly less (P<0.001) in class I as compared to class II and class IV surgeries. **Table 7** shows that the P-value for the comparison among all 4 groups was < 0.001 by the kruskal Wallis test and Dunn's posthoc test for multiple comparisons.

TABLE 6: COMPARISON OF COST OF ANTIMICROBIAL THERAPY (IN RUPEES) BETWEEN DIFFERENT SURGICAL CLASSES

Class	Class I N=113	Class II N=90	Class III N=25	Class IV N=102
Median	160	220	352	546
IQR	99-220.5	133-408.7	190-760.5	368.2-935.2
Mean ± SD	215.5 ± 226	292.5±216.5	476.5±346.6	664.7±474.9
Range	42-2010	60-944	35-1183	126-3120

Cost of antimicrobial therapy in patients of Class II, Class III, Class IV surgeries was significantly high as compared to class I. Also, the cost of antimicrobial therapy in Class IV patients is significantly high compared to class II.

TABLE 7: COMPARISION OF P VALUE OF COST OF ANTIMICROBIAL THERAPY (IN RUPEES) BETWEEN DIFFERENT SURGICAL CLASSES

Comparison	P value
Class I vs Class II	< 0.05
Class I vs Class III	< 0.001
Class I vs Class IV	< 0.001
Class II vs Class IV	<0.001

DISCUSSION: Analysis of the demographic profile of our study shows that the mean age of the patients was 45.81 ± 14.98 years, with a range of 18 to 85 years. Out of all patients percentage of males (68.18%) was more than that of females (31.82%). A similar finding was seen in studies done by Kishore Kumar G. *et al.* [9] where the mean age was 41.51 years and Ramalingam V. *et al.* [10] where the mean age was 44.53 years. We classified the patients according to the type of surgery as per NRC classification as clean (class I), clean-contaminated (class II), contaminated (class III), and dirty (class IV) wound surgeries. In our study clean 113 (34%), dirty 102 (31%), and clean contaminated 90 (27%) wound surgeries were the most commonly performed surgeries **Table 1**. A study done by Chawda *et al.* [11] found that dirty (56.87%) and contaminated (36.69%) wound surgeries were the most commonly performed surgeries.

Our study's mean duration of antimicrobial therapy was 7.92 ± 3.52 days. We found that the total duration of antimicrobial therapy during hospital stay among different surgical classes was significantly longer (p< 0.001) in clean-contaminated (median-7), contaminated (median-9), and dirty (median-11) wound surgeries as compared to clean wound surgeries (median-5). **Table 2** This suggests that patients in clean-contaminated, contaminated, and dirty wound surgeries need more antimicrobial therapy duration compared to clean wound surgeries. However, these figures underestimate the actual duration of antimicrobials as many patients were discharged with further antimicrobials prescribed at discharge, which were not recorded in our study. A study done by Chawda *et al.* [11] found that the duration of antimicrobial therapy was longer (p< 0.001) in contaminated (median-12) and dirty wound surgeries (median-10) as compared to clean wound surgeries (median-8.5). The average number of antimicrobials prescribed per prescription was 2.21 ± 0.86, with a maximum of four antimicrobials per prescription. We also compared the number of antimicrobials used per patient between different surgical classes. The number of antimicrobials prescribed per patient was significantly less (P< 0.001) in clean wound surgeries than in clean-contaminated and dirty wound surgeries **Table 3**. Antimicrobials were prescribed in more numbers and for prolonged duration as infection is more severe in other classes compared to clean wound surgeries. Similar findings were seen in a study done by Chawda et al 11 in which the number of antimicrobials was significantly (P< 0.05) more in number than in other surgical classes.

We compared the cost of antimicrobial therapy between different surgical classes. The cost of antimicrobial therapy in patients with clean-contaminated (median-220), contaminated (median-352), or dirty wound surgeries (median-546) was significantly high as compared to clean wound surgeries (median-160). Also, the cost of antimicrobial therapy in patients with dirty wound surgeries is significantly high as compared to clean contaminated wound surgeries **Table 4**.

This shows that in clean wound surgeries, there is a lower number of antimicrobials and shorter duration of antimicrobials therapy than in other surgical classes. This finding was similar to the study done by Chawda *et al.* [11] in which the cost of antimicrobial therapy was significantly higher in dirty (median-2902) and contaminated wound surgeries (median-2415) (p<0.05) as compared to clean wound surgeries (median-1367). The major limitation of our study was the rate of surgical site infection in different types of surgeries that were evaluated. The incidence of surgical site infection varies concerning different surgical wound classes. The expected surgical site infection rate is 1-2 % in clean wound surgeries, 2-9.5 % in clean-contaminated wound surgeries, 3.4 -13.2% in contaminated wound surgeries and 3.1 to 12.8 % in dirty wound surgeries [1, 2].

Our study did not include the antimicrobials prescribed at discharge, so the actual cost of antimicrobial use will be more than our study's reported cost.

CONCLUSION: Total duration of antimicrobial therapy, number, and cost of antimicrobial used was more in clean-contaminated, contaminated, dirty wound surgeries than clean wound surgeries. SSI increases cost, antimicrobial use and resistance. A higher economic burden of antimicrobials was observed in patients with wound infection than in those without wound infection. Proper sanitation, hygiene, and post-operative care are the utmost important tools to deal with growing resistance to preventing SSI.

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CONFLICT OF INTEREST: None declared

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