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PHARMACOECONOMIC STUDY OF PROPHYLACTIC ANTIBIOTICS USED IN THE PREVENTION OF SURGICAL SITE INFECTION IN THE SURGERY DEPARTMENT OF GSVM MEDICAL COLLEGE, KANPUR

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Abstract:
Introduction: A pharmaco-economic analysis is the act of breaking down cost summaries into their constituents and studying and reporting them. Costs are compared to disclose and report on conditions subject to improvements.
Aims & Objectives: to analyze the frequency of different antibiotics used for the prevention of SSIs in study subjects, to assess the total cost of illness associated and to assess the cost minimization analysis associated with Prophylactic antibiotics used for the prevention of SSI.
Material & Methods: An observational prospective study was conducted by the Department of Pharmacology in collaboration with the Department of Surgery, G.S.V.M Medical College, Kanpur from February 2023 to June2024. All their basic personal details and prescribed antibiotics for SSIs were collected and entered in predesigned proforma, Cost minimization analysis was also calculated.
Results: Overall, this analysis concluded that antibiotic prophylaxis decreased the incidence of SSIs after elective surgery in most patients while noting a high infection rate in gastrointestinal surgery like appendectomy, gastric, small, and large surgeries. The study concluded that antibiotic prophylaxis with a longer duration and broader spectrum significantly reduces the incidence of SSI in high-risk patients, resulting in a substantial reduction in antibiotic costs as well as hospitalization expenses.
Conclusion: However, while the economic analysis indicates that prophylactic antibiotics are generally cost-effective, the findings also underscore the complexity of balancing clinical benefits with long-term costs. In conclusion, prophylactic antibiotics, when used judiciously, can be a cost-effective strategy for preventing SSIs in surgical patients.

Keywords: Pharmaco-economic Evaluation, Prophylactic antibiotic, Surgical Site Infection, Cost

INTRODUCTION:

A pharmaco-economic analysis is the act of breaking down cost summaries into their constituents and studying and reporting them. Costs are compared to disclose and report on conditions subject to improvements. Cost Analysis in Pharmacology is known as Pharmacoeconomics (PE).

Surgical site infections (SSIs) remain a significant concern in surgical practice, leading to increased morbidity, prolonged hospital stays, and higher healthcare costs. In adults, SSIs represent a significant financial burden and are associated with increased length of hospitalization, re-admission, and mortality. It has been reported that patients who develop SSIs have a mortality rate that is 2- 11 times higher than that of patients who do not develop SSIs, and the mortality rate for SSIs is up to 6%[1].

A widely accepted wound classification system has been developed by the National Academy of Sciences and the National Research Council based on the degree of expected microbial contamination during surgery[2]. It stratifies wounds as clean, clean-contaminated, contaminated, or dirty.

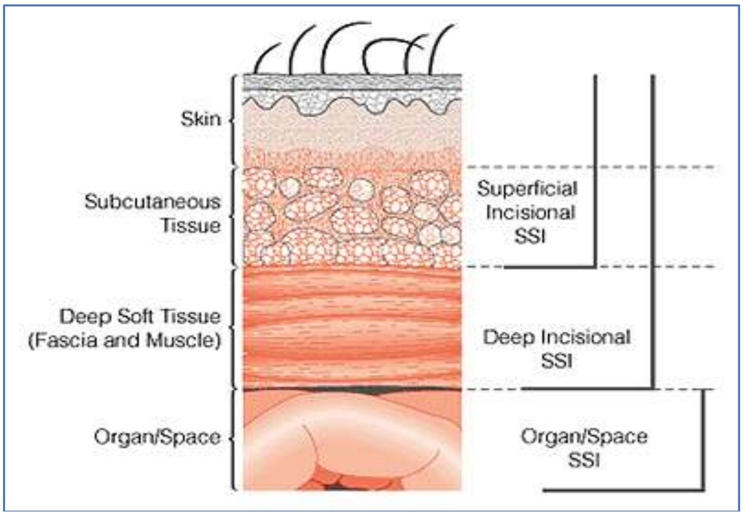


Figure-1: SSI of different types.

In India, Healthcare-associated infections (HAIs) present a significant source of preventable morbidity and mortality. More than 30% of all HAIs are represented by Surgical Site Infections (SSIs), making them the most common subtype [3]. Current estimates place the incidence of SSI between 2% and 3%[4], but it is evident that SSI is underreported and, on the rise, not only as a result of improved reporting but also because people are living longer and more antibiotic-resistant bacteria are emerging. Studies suggest that 40% to 60% of these infections are preventable[5]. Despite this, many hospitals have yet to implement evidence-based best practices[6].

Antibiotics play a particularly important role in the post-operative care of patients undergoing elective surgery because of the high incidence of SSI. It has been reported that 30-40% of patients experience post-operative SSI when a prophylactic antibiotic is not administered[7,8]. Appropriately selected antibiotic prophylaxis can protect patients from postoperative infection by reducing the bacterial load present within the surgical site at the time of operation[9].

In the treatment of Superficial Incisional SSI, Management may involve outpatient visits, visits from home health nurses, or both. The treatment of these infections is relatively inexpensive. In Deep incisional SSI, a prolonged hospital stay is common, and patients are frequently readmitted after being discharged. Possibly additional procedures are required. Infections that affect an organ or space are the most dangerous[10]. Expect prolonged initial hospitalization, hospital readmissions, and additional procedures. Morbidity and mortality risk are both elevated compared to patients with less severe SSIs. The total expense is high to extremely high[11].

The different types of costs to be undertaken include Direct cost (medication cost, investigation charge, procedure charge), Indirect cost (loss of wages, loss of productivity), Intangible Cost (associated with pain, worry, distress, or suffering), opportunity cost (benefit lost when choosing one therapy over next best alternative), marginal cost(additional cost incurred to increase the benefit within available resources). It is very important to carry out a cost analysis of antibiotic prophylaxis used in Surgical Site Infections (SSI)to reduce the disease burden of the community, to choose the least costly antibiotic for reducing the economic burden of the patient, and to minimize the cost for the government as well. By analyzing both the costs and clinical benefits associated with prophylactic antibiotics, this research aims to offer a comprehensive assessment of their economic viability within the context of surgical procedures performed at GSVM Medical College. This evaluation will help determine whether the financial investment in prophylactic antibiotics translates into significant reductions in SSI rates and overall healthcare costs, thereby informing evidence-based practices and policy decisions.

The need for such an analysis is underscored by the growing emphasis on cost-effective healthcare delivery and the ongoing challenge of balancing clinical efficacy with economic constraints. Through a rigorous examination of cost data, clinical outcomes, and relevant economic metrics, this study seeks to contribute to the broader understanding of how prophylactic antibiotic impacts both patient safety and healthcare expenditures, ultimately supporting efforts to enhance surgical care quality and efficiency.[12,13]

Prophylactic antibiotic use is a widely accepted strategy to mitigate the risk of SSIs, but the economic implications of such interventions are a critical area of inquiry. At GSVM Medical College Kanpur, a premier institution in medical research and education, evaluating the cost-effectiveness of prophylactic antibiotic protocols can provide valuable insights into optimizing resource allocation and improving patient outcomes. With this background, this study was conducted to analyze the frequency of different antibiotics used for the prevention of SSIs in study subjects, to assess the total cost of illness associated and to assess the cost minimization analysis associated with Prophylactic antibiotics used for the prevention of SSI.

MATERIAL AND METHODS:

An observational prospective study was conducted by the Department of Pharmacology in collaboration with the Department of Surgery, G.S.V.M Medical College, Kanpur from February 2023 to June2024.

All patients of either Sex and above 18 years of age who were admitted for elective Surgery in the Department of Surgery, GSVM Medical College, Kanpur (U.P) were included after taking written informed consent. However, patients below 18 years of age or admitted for emergency surgeries or Patients undergoing antibiotic prophylaxis for any other cause were excluded from the study.

According to the prevalence of SSIs in India [3], Sample size was calculated using Cochran's Formula, $n=Z^2 PQ/d^2$ considering non-responsive rate of 10% and at 5% level of significance, minimum sample size was 120. Their prescription was collected and further studied. All their basic personal details and prescribed antibiotics for SSIs were collected and entered in predesigned proforma having the following sections as follows

Section A includes the Patient's socio-demographic details accompanied by attendant details, diagnosis, procedure, medication from private or government, etc.

Section B includes details of prescribed antibiotics whereas various indirect cost expenses were considered in **Section C** like Travelling cost, food cost/day, cost for food & travel of attender, income per day of attender which loss due to illness & laboratory investigation charges.

Cost of illness: We have considered the total cost of illness by summation of indirect cost (income of patient + income of attendant) and direct cost (medication cost + investigation cost + cost of food + traveling cost+ cost of stay+ cost of attendee stay (if any) + cost of traveling for attender and food.

Cost minimization analysis was also calculated;

For cost minimization analysis- The different groups of therapeutic regimens are compared for the lowest cost. It was calculated in the form of percentage cost variation in the respective group. **Percentage of cost variation = ({maximum cost-minimum cost}/minimum cost) X 100.**

Statistical Package for the Social Sciences (SPSS) software version 23.0 (SPSS1 Inc., Chicago, IL, USA) was used for statistical analysis of data. Chi-square test was used to determine the association among categorical variables and P value < 0.05 was considered statistically significant.

RESULTS

Most of the study patients who were prescribed antibiotics for prevention of Surgical site infections were middle age group and above with males predominance over females. The most common occupation was business or shop owner and private job mainly belonged to the upper lower class (IV) (34.78%) and lower middle class(III) (26.81%).

In our study elective surgery was considered for most common gastrointestinal problem (74.64%) followed by urinary system involvement and Multisystem or generalized anomalies or diseases (15.94%).

The most common antibiotics were third-generation cephalosporin antibiotics (32.61%) and third-generation cephalosporin antibiotics+ beta-lactamase inhibitor which was given in 16.39%. Common prescribed prophylactic antibiotics are Ceftriaxone (24.64%), Piperacillin+ Tazobactam (21.02%), and Ceftriaxone+ Sulbactam (12.32%).

COST OF ILLNESS IN PROPHYLACTIC ANTIBIOTICS USED FOR THE PREVENTION OF SSI:

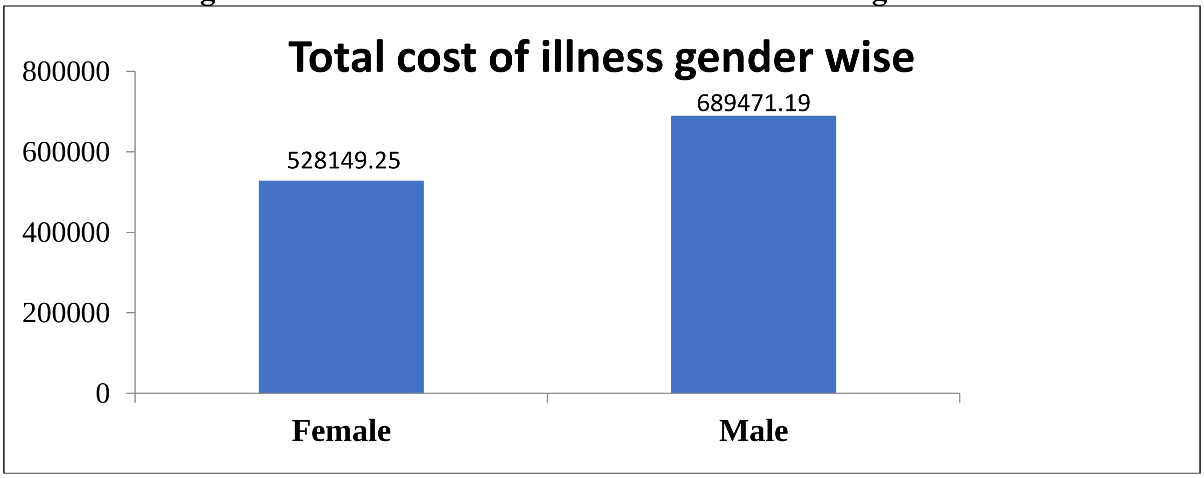
In the present study, the overall total cost of illness among elective surgery patients was Rs. 1217620.44 and the average cost of illness was Rs. 8823.34. Maximum total cost of illness was found in the middle age group (Rs. 617485.84) and minimum total cost of illness was Rs. 92404.19 with age less than 24 years.

Table 1: Distribution of the cost of illness according to age

Age Interval (Years)	Total cost of illness	Average cost
Up to 24 Years	92404.19	9337.603333
25-40 Year	617485.84	8879.69185
41-60 Year	356209.75	8795.539655
Above 60 Years	151520.65	8774.492213

Total cost of illness was found higher among male elective surgery patients (Rs. 689471.19) and which was higher than total cost of illness in female patients (Rs. 528149.25).

Figure 2: Distribution of the cost of illness according to Gender



On observing the prescribed antibiotics by classes, the maximum cost of illness was found with Penicillin beta-lactam plus beta-lactamase inhibitor with Rs.422960.86.and followed by 3rd Generation Cephalosporin with Rs.323525.41. The minimum cost of illness was found with Beta-lactam (Carbapenem) and Rs. 55565. Similarly on observing the average cost of illness of prescribed class of antibiotic to the patients. The maximum average cost of illness was found with

Aminoglycosides Rs. 10142.24 and, minimum average cost of illness was found with by 3rd generation cephalosporin and was Rs. 7189.45. [Table 2]

Table 2: Distribution of Cost of illness by classes of antibiotics

Categories of Prescribed Medications classes	Total Cost of illness	Average Cost of illness
3rd Generation Cephalosporin	323525.41	7189.45
3rd Generation Cephalosporin + beta lactamase inhibitor	195614.75	9708.70
Aminoglycoside	182560.4	10142.24
Beta lactam (Carbapenem)	55565	9260.83
Penicillin beta lactam plus beta lactamase inhibitor	422960.86	9198.59

Figure.3: Distribution of cost of illness of study patients by occupation

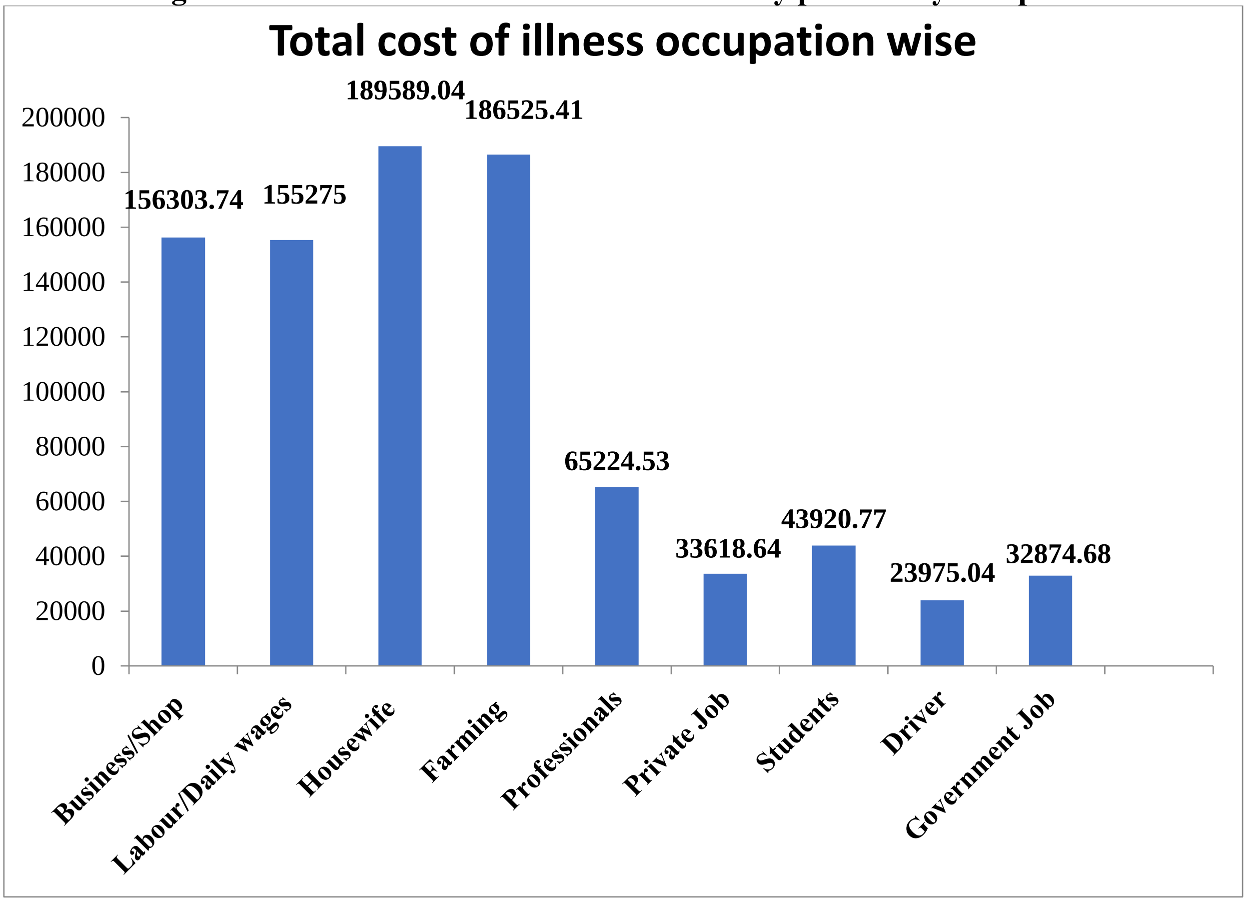


Figure 4: Distribution of Cost of illness by Diagnosis and System : Gastrointestinal System

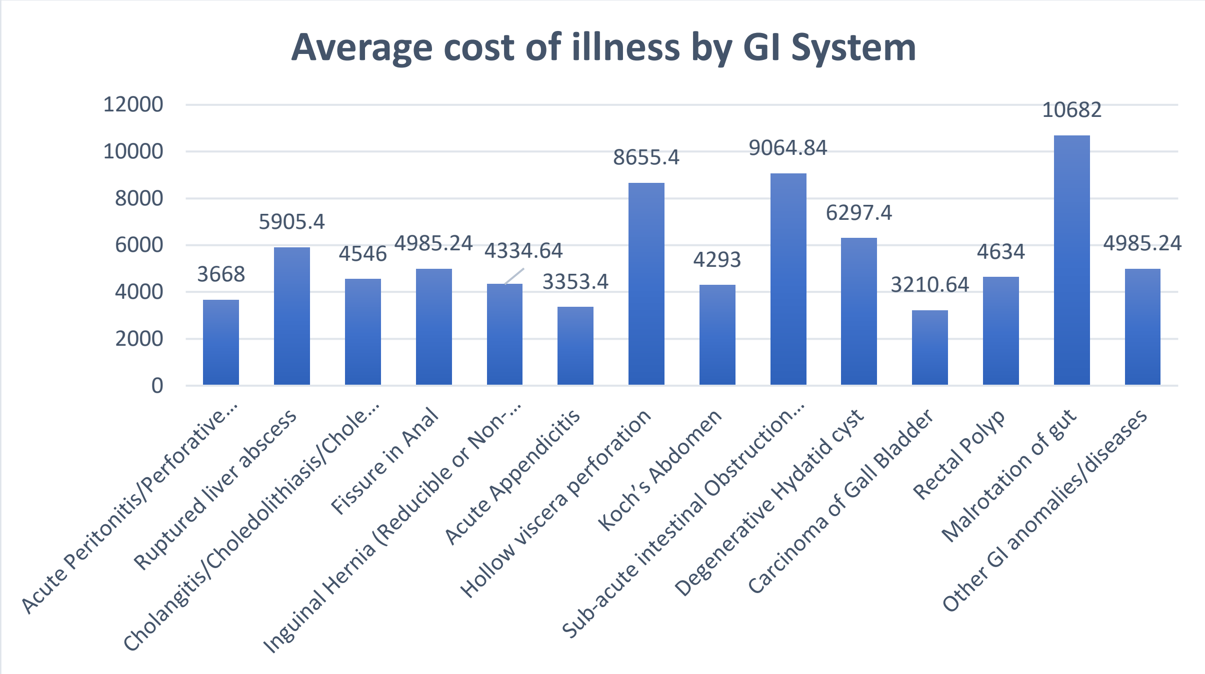


Table 3: Distribution of Cost of illness by Urinary System

Diagnosis and System involved	Minimum Cost of Illness	Average Cost of Illness	Maximum Cost of Illness
Urinary System			
Hydro Ureteronephrosis	12549.72	6819.2	21303
Renal Calculi	11241.23	6391.64	15415.64
Urinary Bladder calculi	5892.777	4435.205	7731.12
Benign Prostatic Hyperplasia	3886.92	2380.84	5393
Urethral stricture	7511.24	7086.24	7936.24
Other Urinary anomalies/diseases	4877	3895	5859

The different categories of antibiotics were compared for the maximum and the minimum cost and calculated in the form of cost variation in the respective group. On considering cost minimisation analysis the prophylaxis by various prescribed categories of antibiotics, the cefoperazone showed a maximum percentage of variation with Rs. 11048 (464%) followed by amikacin Rs 16757 (369%) while the minimum percentage of variation was seen in prophylaxis with Cefoperazone+ Sulbactam, 5550 (88%). [Table 3]

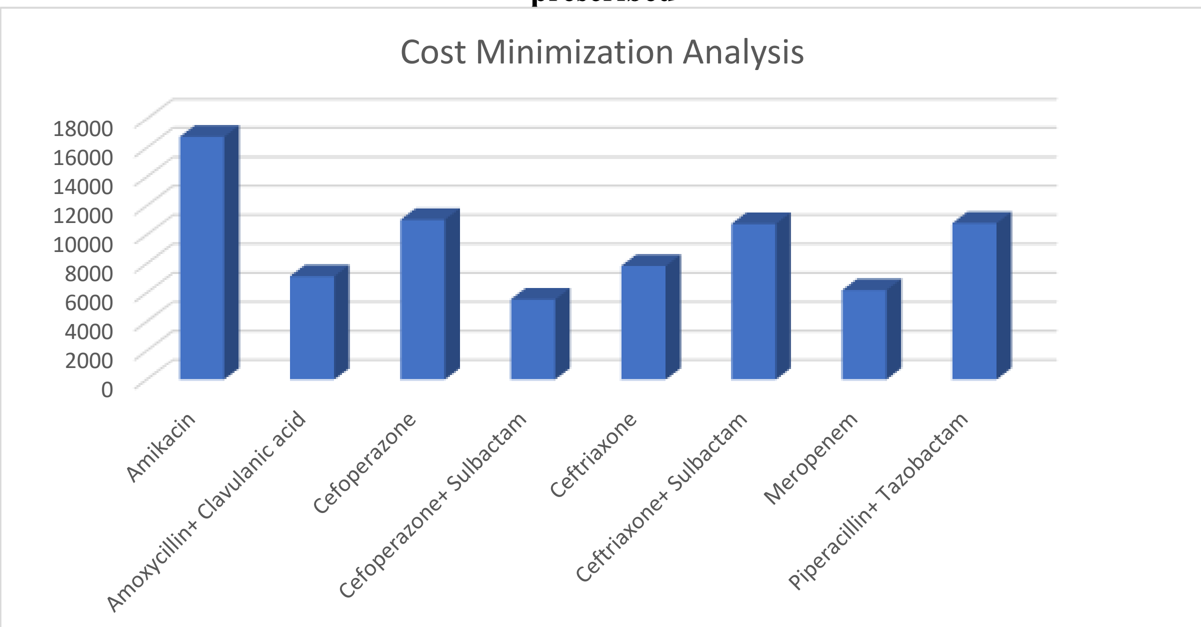
Table 4: Distribution of Cost of illness by Diagnosis and System: Generalised System

Diagnosis and System involved	Minimum cost of illness	Average Cost of illness	Maximum Cost of illness
Generalized System			
Cellulitis (Hand/foot/other organs)	7707.64	4615.64	10799.64
Rodent Ulcer	10785.4	10110.4	11460.4
Lower limb Varicose Vein	3683.4	3483.4	3883.4
Other generalized Anomalies/diseases	8865.43	5436.97	10787.4

Table 5: Cost minimization analysis by prescribed antibiotics

Various Antibiotics	Minimum Cost	Maximum Cost	Cost Minimization Analysis	
Amikacin	4546	21303	16757	369%
Amoxycillin+ Clavulanic acid	5972.2	13107.2	7135	119%
Cefoperazone	2380.84	13428.84	11048	464%
Cefoperazone+ Sulbactam	6325.4	11875.4	5550	88%
Ceftriaxone	3772.64	11615.24	7842.6	206%
Ceftriaxone+ Sulbactam	4785.11	15541	10755.9	226%
Meropenem	4940	11123	6183	112%
Piperacillin+ Tazobactam	4615.64	15415.64	10800	234%

Figure. 5: Distribution of cost minimization of study patients by different types of antibiotics prescribed



In the present study, the maximum cost incurred by the subjects was investigations of Rs. 5510.97±2441.61 per subject and the minimum cost of staying per day was Rs. 90.72±32.83 per subject. The average medication cost incurred per day was Rs. 536.40±247.80. Maximum therapeutic cost was found with Meropenem (Rs. 987) while minimum therapeutic cost was noted with Ceftriaxone (Rs. 161.24).
Ceftriaxone is a cost-effective alternative to all prescribed antibiotics for SSI prevention in the present study. Piperacillin + Tazobactam is more expensive and provides broader coverage and PA administered 30 minutes before the start of surgery is effective in preventing SSIs.

Overall, this analysis concluded that antibiotic prophylaxis decreased the incidence of SSIs after elective surgery in most patients while noting a high infection rate in gastrointestinal surgery like appendectomy, gastric, small, and large surgeries. The study concluded that antibiotic prophylaxis with a longer duration and broader spectrum significantly reduces the incidence of SSI in high-risk patients, resulting in a substantial reduction in antibiotic costs as well as hospitalization expenses.

DISCUSSION

Out of the total 138 patients, most of elective surgery patients were middle age group of 25-40 years (50%) followed by 41-60 years (31.16%) with mean age± S.D. was 41±14 years and there was male predominance (59.4%) than female (40.6%) patients. Bangaru et al. [14] study there was no significant difference in age (p-value- 0.8103) and gender (p-value- 0.8591).

Various guidelines have been given to promote appropriate use of antimicrobials for Surgical Antibiotics Prophylaxis (SAP) including international guideline by the WHO and several national guidelines such as NCDC, American Society of Healthcare Pharmacists (ASHP), National Institute for Health and Care Excellence, and Scottish Intercollegiate Guidelines Network. [15--17]

In present study, the therapeutic regimen and prescriptions for the prevention of Surgical site infections in study subjects were observed and analyzed for various indicators of drug pattern prescription as per WHO and observed that total number of prescribed antibiotics in 138 elective surgery subjects were 708 and an average number of antibiotics per prescription was found 2.56. In Initial phase, mostly prescribed antibiotics were injectables with an average of 1.56 intravenous antibiotics per prescription encountered. In later phase, 63.8% patients were prescribed with oral antibiotics and an average of one oral antibiotics per prescription encountered (138). National guideline, given by NCDC, recommends single preoperative dose of IV cefazolin 2 g or cefuroxime 1.5 g to be given within 60 min before surgical incision and thereafter twice a day up to 24 h of surgery. [18]

In our study, the maximum total cost of illness was found with Piperacillin + Tazobactam, Rs. 286890.06 and minimum total cost of illness was Rs. 55565 with Meropenem. Although on assessing average cost of illness by medication wise, it was found that maximum average cost of illness by medication was Rs. 10142.24 with Amikacin and Ceftriaxone has minimum average cost of illness of Rs. 6858.006.

Similarly on observing the average cost of illness of prescribed class of antibiotic to the patients. The maximum average cost of illness was found with Aminoglycosides the Rs. 10142.24 and minimum average cost of illness was by 3rd generation cephalosporin and was Rs. 7189.45. Most common antibiotics were Third-generation cephalosporin antibiotics (32.61%) and third generation cephalosporin antibiotics+ beta-lactamase inhibitor which was given in 16.39%. Penicillin beta-lactam+ beta-lactamase inhibitor was given in 32.60% patients respectively. Heit et al.[19]compared the costs of 1-day therapy with Ceftriaxone and penicillin G that were used for the prophylaxis of surgical treatment of mandibular fractures and found Ceftriaxone better. While study by Shinagawa N et al, Cefotiam has been considered to have strongest activity as prophylactic antibiotics for abdominal surgery, followed by Cefmetazole and Cefazolin in this order.[20]

In present study, on considering cost minimisation analysis the prophylaxis by various prescribed categories of antibiotics, the cefoperazone showed a maximum percentage of variation with Rs. 11048 (464%) followed by amikacin Rs. 16757 (369%) while the minimum percentage of variation was seen in prophylaxis with Cefoperazone + Sulbactam, 5550 (88%). Study of the antibiogram revealed that an exceptionally high incidence of resistance to Fluoroquinolones followed by 2nd and 3rd generation Cephalosporins and Aminoglycosides. One of the important reasons for high resistance to Cephalosporins and Aminoglycosides may be the rampant use of these antibiotics in hospitals. Data from earlier studies suggests that prophylactic antibiotics should be chosen from among those to which bacteria from the Intra-abdominal contamination are highly sensitive, and therapeutic antibiotics should be chosen from among those to which bacteria isolated from the SSI are highly sensitive[21,22].

In the present study, for the pharmaco-economic assessment of these prophylactic antibiotics, various direct and indirect costs were observed and cost indicators were analysed. For this, the incidence of superficial SSI as well as the cost of the hospital stay, treatment of SSI, and adverse events among

study participants compared among patients who received antibiotics in complete accordance with the NCDC guidelines. The overall total cost of illness among elective surgery patients was Rs. 1217620.44 and average cost of illness was Rs. 8823.34.
Maximum total cost of illness was found in the middle age group of 25-40 years (Rs. 617485.84) followed by 41-60 years (Rs.356209.75). Minimum total cost of illness was Rs. 92404.19 with age less than 24 years.

In present study the average medication cost per day per patient was Rs.536.40±247.80 and investigation cost including laboratory test and various radiological investigations were Rs. 5510.97±2441.61. The maximum cost incurred by the subjects was of investigations of Rs. 5510.97±2441.61 per subject and the minimum cost of staying per day was Rs. 90.72±32.83 per subject. The average medication cost incurred per day was Rs. 536.40±247.80. This difference in treatment cost however did not translate into better protection from SSI, as there was no relationship found between cost of treatment and rate of SSI. This breaks the myth that the costlier brand of antibiotics would be more efficacious. A number of studies have found low rate of prescription by generic names and high cost. However, to the best of our knowledge, studies comparing the outcome of different brands of the same antibiotic given to surgical patients have not been conducted earlier. An interesting observation is that only a single brand of Metronidazole was prescribed by all the surgeons.[23-24]

In the present study only 6 (4.16%) were developed Superficial site infections. These findings shows that antibiotic prophylaxis decreased the incidence of SSIs after elective surgery in most of patients (95.83%). The incidence of postoperative surgical site infections in this study is low (4.16%) in an international perspective. which can be compared to 7% and 8.5% respectively in the Kanji S, et al. [25]

Although findings of this study indicates that Ceftriaxone is a cost-effective alternative than all prescribed antibiotics for SSI prevention. These antibiotics will use judiciously in pregnant women as it is known that the first generation of cephalosporin is transferred to the foetus [26], and hence some authors have argued that antibiotic prophylaxis should be administered after the umbilical cord has been clamped, in order to avoid unnecessary fetal exposure to prophylactic antibiotics [27]. However, a meta-analysis by Hessen et al. [28] showed no difference in neonatal outcome when administering antibiotic prophylaxis preoperatively compared to administering antibiotics after clamping the umbilical cord, whereas the risk of endometritis was significantly decreased.

Recommendations

1. **Standardize Prophylactic Protocols**: Develop and implement standardized protocols for prophylactic antibiotic use across various surgical procedures. Ensuring consistent application of these protocols can help in reducing the incidence of SSIs and improving cost-effectiveness.
2. **Tailor Antibiotic Choices**: Customize prophylactic antibiotic regimens based on the type of surgery, local infection rates, and patient-specific factors. This approach can optimize antibiotic use and minimize the risk of resistance development.
3. **Enhance Data Collection and Monitoring**: Invest in robust data collection systems to accurately track infection rates, antibiotic use, and patient outcomes. Comprehensive data will facilitate more precise cost-effectiveness analyses and help in refining prophylactic strategies.
4. **Evaluate Long-Term Outcomes**: Conduct longitudinal studies to assess the long-term economic and clinical impacts of prophylactic antibiotic use. This should include monitoring for potential antibiotic resistance and evaluating the overall cost-benefit ratio over extended periods.
5. **Address Antibiotic Resistance**: Incorporate strategies to monitor and mitigate the risk of antibiotic resistance, such as antimicrobial stewardship programs. Educate healthcare providers and patients about the prudent use of antibiotics to maintain their effectiveness.

6. **Expand Research Scope**: Extend the research to include diverse healthcare settings and patient populations. This broader scope can enhance the generalizability of findings and provide a more comprehensive understanding of the economic implications of prophylactic antibiotic use.

By following these recommendations, healthcare institutions can enhance the efficacy and cost-effectiveness of prophylactic antibiotic use, ultimately leading to improved patient outcomes and more efficient use of healthcare resources

Limitations

- **Sample Size and Generalizability**: The study's findings may be limited by the sample size used. If the sample is relatively small or specific to a particular demographic or surgical practice at GSVM Medical College, the results may not be generalizable to other settings or populations.
- **Study Duration**: The time frame of the study might affect its results. Short-term studies may not capture long-term outcomes and costs associated with prophylactic antibiotic use, including potential resistance patterns and late-onset infections.
- **Variation in Surgical Procedures**: Different types of surgical procedures may have varying risks of infection and might not be equally represented in the study. The economic evaluation may not fully account for these variations, potentially skewing the results.
- **Cost Analysis Assumptions**: The cost estimates used in the evaluation may rely on assumptions that do not reflect real-world variations. Factors such as regional drug costs, hospital resource utilization, and changes in antibiotic pricing can influence the accuracy of cost predictions.
- **Antibiotic Resistance**: The study may not fully address the impact of antibiotic resistance on long-term outcomes. Prophylactic use of antibiotics could contribute to resistance, which might alter the cost-effectiveness analysis over time.
- **Outcome Measurement**: The metrics used to measure the effectiveness of prophylactic antibiotics, such as infection rates or patient recovery times, may not capture all relevant outcomes. For instance, quality of life impacts or patient-reported outcomes might be overlooked

CONCLUSION

The pharmaco-economic evaluation of prophylactic antibiotic use for surgical site infection (SSI) prevention conducted at GSVM Medical College Kanpur offers valuable insights into the cost-effectiveness and clinical benefits of this practice. The study demonstrates that prophylactic antibiotics can significantly reduce the incidence of SSIs, which aligns with existing literature supporting their use in surgical settings. However, while the economic analysis indicates that prophylactic antibiotics are generally cost-effective, the findings also underscore the complexity of balancing clinical benefits with long-term costs. The reduction in infection rates can lead to decreased postoperative complications, shorter hospital stays, and overall better patient outcomes, which contribute positively to the economic evaluation.

In conclusion, prophylactic antibiotics, when used judiciously, can be a cost-effective strategy for preventing SSIs in surgical patients. The insights gained from this evaluation at GSVM Medical College Kanpur can inform local and broader healthcare practices, helping to optimize antibiotic use and improve patient care. Future studies should aim to address the identified limitations and explore the long-term implications of prophylactic antibiotic use to enhance both clinical and economic outcomes in surgical settings.

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Nil

Conflicts of Interest

There are no conflicts of interest

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