Analysis of Antimicrobial Drugs Usage Pattern and it's Cost Analysis in the Pediatric Department of a Tertiary Care Hospital

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ABSTRACT

Background

Antimicrobials agents are the most widely and often imprudently used therapeutic drugs globally. The pediatric population comprises 20-25% of the total world population, and various acute and chronic diseases are prone to this group. It is also estimated that 50% to 85% of children are prescribed with antimicrobials in developed and developing countries. The misuse of antimicrobials not only contributes not only to the development of antimicrobial resistance but also results in economic burden on the health care system.

Objective

To analyze the antimicrobial usage and its cost analysis in the Pediatric department of a tertiary care hospital at sub-urban area.

Method

A hospital based retrospective study was conducted among patient (aged 1 to 18 years) admitted in pediatric ward and intensive care unit for at least 24 hours and dispensed at least one antimicrobial drug from January 2018 to December 2019. Data were collected from electronic medical record using a structured data collection form. The data was entered and analyzed using Microsoft Excel. A descriptive analysis was presented as mean ± (standard deviation) for the continuous variables and frequencies and proportions for categorical variables.

Result

Among the 1,281 patients, the antimicrobials were prescribed mostly in the respiratory tract infection (39.6%), followed by sepsis (19.75%), enteric fever (11.94%), seizure (10.07%), urinary tract infection (4.29%). Penicillins (1238 times) were highly prescribed followed by Cephalosporin (733 times), Nitro-imidazole (292 times), Aminoglycosides (180 times) and Fluoroquinolones (144 times). During study period in the Pediatric Department, approximately NRs. 1,619,121.11 was spent in the antimicrobial drugs and the highest expenditure was found to be in the Cephalosporin group of antimicrobials (NRs. 530,988.6), followed by Penicillin group of drug (NRs. 3,81,842.2).

Conclusion

The study concludes that the Penicillin groups of drugs were the most commonly prescribed drug and the highest cost was found to be in Cephalosporin group drugs followed by Penicillin group of drugs.

KEY WORDS

Antimicrobial drugs, Antimicrobial usage pattern, Cost analysis, Tertiary care hospital

INTRODUCTION

Antimicrobials agents are the most widely and often imprudently used therapeutic drugs globally.[1,2] Although antibiotics are classified as prescription-only drugs, they are widely used as over-the-counter drugs in Nepal. The pediatric population comprises 20-25% of the total world population, and various acute and chronic diseases are prone to this group.[3,4] Moreover, in developing countries like Nepal, infants and children are among the most vulnerable population groups to suffer from diseases. Drug therapy containing antibiotics has become a common practice for the treatment of pediatrics illnesses.[3,5-8] Some of the previous studies have estimated that 150 million ambulatory visits result in an antibiotic prescription annually, which includes 30 million prescriptions for children.[9,10] It was indicated that 50% to 85% of children are prescribed with antibiotics in developed and developing countries.[11]

Over the last decade, it has become clearer that antimicrobial resistance is increasing, and many antibiotics have lost their effectiveness against common bacterial infections.[12] Many of the antibiotics are unnecessarily prescribed for viral infections such as a common cold. A study found that, 60% of patients were prescribed antibiotics for the common cold.[13] The unnecessary use of antibiotics contributes not only to the development of antimicrobial resistance but also presents an economic burden on the health care system.[14,15] The rising incidence of bacterial resistance to common antibiotics, particularly, multidrug-resistant pneumococci, has prompted the need to use antibiotics judiciously in pediatrics practice.[8] Antimicrobial resistance considerably increases already-rising health care costs and increases patient morbidity and mortality.[16]

Pharmacoeconomics is a branch of economics that measures the cost-benefit, cost-effectiveness, cost minimization, cost-of-illness and cost-utility analysis to compare drug therapy and treatment management.[17,18] Medicines form a small but significant amount of total health care costs accounting for up to 70% of overall health spending on medicine in developing and less developed countries, compared to 10-18% in the developed world.[19] Moreover, most of the people from Bangladesh, India and Nepal spend out-of-pocket for these medicines estimated to be 48–69%.[20] Expenditure on medicines imposes a major financial burden on households, especially when it is met from the out-of-pocket expenditure due to lack of health insurance and risk protection.[21] Therefore, many poor people frequently face a choice between buying medicines or buying food or other necessities due to limited resources and high pricing of drugs.[22] With the scenario such as an increase in health care costs, lack of uniformity in drug prescribing and the emergence of antibiotic resistance, the use and monitoring of antibiotics is of growing concern.[23] The current study was conducted to analyze the use of antimicrobials and its cost analysis in the Pediatric Department of a tertiary care hospital.

METHODS

A hospital based retrospective study was conducted in a tertiary care hospital during January 2018 to December 2019. Dhulikhel Hospital, Kathmandu University (DH, KUH), located in Kavrepalanchowk district, is an independent, not for profit, non-governmental institute. The hospital is 425 bedded and covers a population of approximately 1.9 million populations from its neighboring districts.[24] It is a tertiary care center with different departments including medicine, obstetrics and gynecology, surgery, orthopedics, dental, ear, nose and throat, intensive care unit etc. with average admission cases of 50 per day. A pediatric service has been provided through the hospital with 60 beds (42 General, 12 Neonatal Intensive Care Unit and 6 Pediatric Intensive Care Unit). The study was conducted after the prior ethical approval by the Kathmandu University School of Medical Sciences, Institutional Review Committee and the populations included all the patient (aged 1-18 years) admitted in pediatric ward and intensive care unit for at least 24 hours and dispensed at least one antimicrobial drug at DH, KUH.

A self-designed data collection form was developed with the consultation from experts from the Department of Pharmacology, Department of Community and Public Health program and Information Technology department. Trained data collector collected the data which includes demographics data, clinical data (diagnosis, length of stay etc.) and drug therapy and cost (type of antibiotics, dosage, frequency of administration, duration, route of administration and cost.) from electronic medical record. Confidentiality was maintained by replacing personal identifiers with the code and using a password protected electronic database. Data collection was supervised by the principal investigator and study team. The cost of the medicines was calculated in Nepalese Rupee using the hospital rate list.

Data were entered using a KoBo Toolbox, a free and open source online data entry tool developed by Harvard Humanitarian initiative with support from various organizations like Brigham and Women's Hospital, USAID etc. and analyzed by using Microsoft Excel. A descriptive analysis was summarized in mean (standard deviation) for the continuous variables and frequencies and proportions for categorical variables.[25]

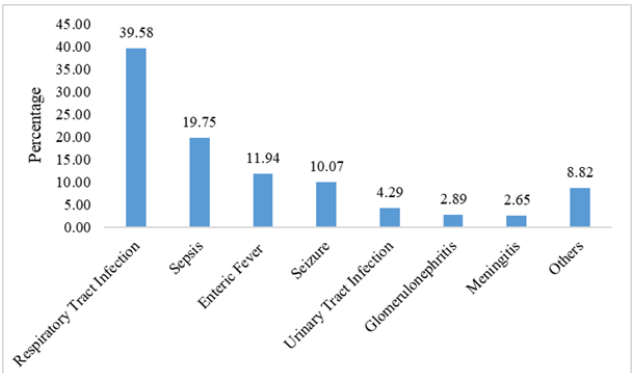
RESULTS

During two years of the admission in the Pediatric Department, the total number of patient admitted in the Pediatric department was found to be 2,583. Among those admitted cases, total 1,281 cases which met the study inclusion criteria (≤ 1 to ≥ 18 years, ≥ 24 hours of

admission and prescribed at-least one antimicrobial agent) were included in this study. The cost analysis was done for those prescribed antimicrobial drugs. Among 1,281 cases, the highest proportion of male patients (60.0%) had received the antimicrobial drugs (Table 1). The mean age of pediatric patients was 5.94 ± 4.59 years whereas, the highest number of patients were from age group 1-5 years (56.5%) followed by 6-10 years (21.9%), 11-15 years (19.7%), and 16-18 years (2%). The study shows that the patients stayed for approximately 5 days on average where most of the patients stayed for 1-5 days (67.0%), followed by 6-10 days (23.4%), 11-15 days (7.3%), and more than 16 days (2.3%). Most of the patients were discharged normally after the treatment in hospital, whereas few of them were referred (Table 1).

Table 1. Demographic Profile of Patients

Characteristics	Number	Percentage (%)
Gender		
Male	775	60.0
Female	506	40.0
Age		
1-5	724	56.5
6-10	280	21.9
11-15	252	19.7
16-18	25	2
Age (Mean ± SD)	5.94±4.59	
Discharged Type		
Normal Discharge	1199	93.6
Left against medical advice	2	0.16
Left on Request	70	5.46
Refer to other hospital	10	0.78
Hospital Stay		
1-5 days	858	67
6-10 days	300	23.4
11-15 days	94	7.3
16 days and above	29	2.3
Total Hospitalization Days (Mean ± SD)	**5.53 ± 4.77**	



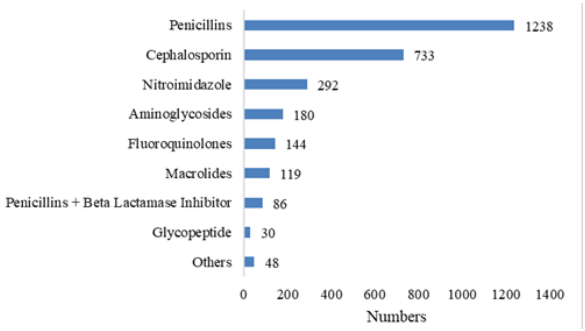
*Others: Dysentery, Hepatitis, Neutropenia, Gastroenteritis, Rheumatic Fever, Pancreatitis, Urticaria, Arthritis, Thyroidism, Osteomyelitis

Figure 1. Disease Pattern in Pediatric Department

The most common disease in pediatric department for which antimicrobials were prescribed were respiratory tract infection (39.6%), followed by sepsis (19.75%), enteric fever (11.94%), seizure (10.07%), urinary tract infection (4.29%; Figure 1).

In the study, the current study showed the most frequently prescribed drug was found to be of Penicillin group (1238 times) which was followed by Cephalosporin (733 times), Nitro-

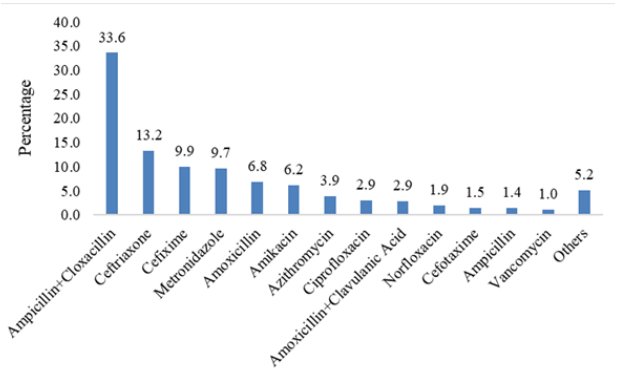
imidazole (292 times), Aminoglycosides (180 times) and Fluoroquinolones (144 times) as shown in the Figure 2.



*Others: Carbapanem, Sulfonamides, Carbapenem + Dehydropeptidase Inhibitor, Lincosamide, Nitrofuran, Tetracycline

Figure 2. Frequency of antimicrobials prescribed in pediatric department

Among the pediatric patients, ampicillin + cloxacillin (n = 963, 33.6%) was the most commonly used antimicrobial drugs followed by ceftriaxone (n = 379, 13.2%), cefixime (n = 285, n = 9.9%), metronidazole (n = 277, 9.7%), amoxicillin (n = 195, 6.8%), amikacin (n = 178, 6.2%), azithromycin (n = 111, 3.9%) and ciprofloxacin (n = 84, 2.9%; Figure 3).



*Others: Cefuroxime, Benzyl Penicillin, Doxycycline, Nitrofurantoin, Clindamycin, Metronidazole + Diloxanide Furoate, Flucloxacillin, Imipenem and Cilastatin, Erythromycin, Benzathine Penicillin, Cloxacillin, Cotrimoxazole, Levofloxacin, Meropenem, Piperacillin + Tazobactam, Secnidazol, Cefazolin, Ceftazidime, Gentamicin, Ofloxacin, Tinidazole, Clarithromycin, Phenoxymethyl Penicillin

Figure 3. Distribution of antimicrobial drugs at pediatric department

Considering the degree of polypharmacy, two antimicrobial agents was administered in 508 (39.7%) patients, one antimicrobial in 374 (29.2%) and three antimicrobials in 225 (17.6%), four antimicrobials in 107 (8.4%) and five or more antimicrobials in 66 (5.2%) among all the cases. The average number of antimicrobials per patient was found to be 2.24 ±1.24 (Figure 4).

In the current study, Oral and Parenteral routes were used for the administration of antimicrobial drugs. There are altogether 36 types of antimicrobials including oral and parenteral were prescribed. Both parenteral (51.46%) and oral (48.54%) routes were used nearly equally as shown in the Figure 5.

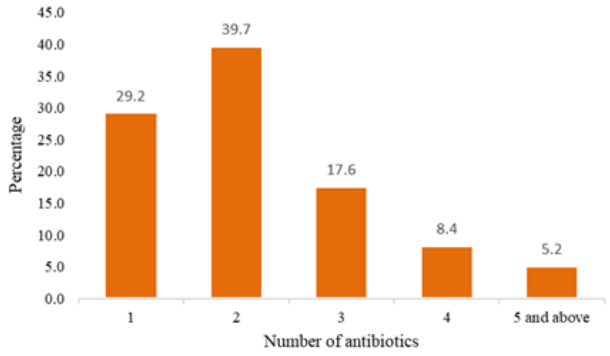


Figure 4. Distribution of number of antibiotics per patient in the pediatric department

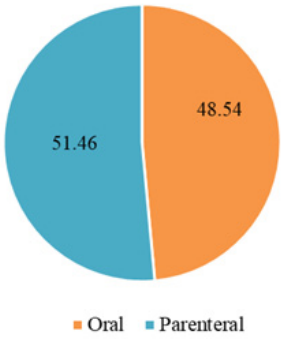


Figure 5. Route of antimicrobial drugs administered in pediatric department

Cost of Antimicrobial agents

While analyzing the price of antimicrobials used among the patients, the minimum price was found to be of Benzathin Pencillin (NRs. 0.95) and the maximum price was found to be of Imipenem + Cilastatin (NRs. 1,276.02). Among oral route group, the cheapest drug prescribed was Doxycycline (NRs. 1.73) and the highest price was found to be of Syrup Levofloxacin (NRs. 219.38). In similar manner, among parenteral route, the lowest cost was Injection Benzathin Pencillin (NRs. 0.95) and the highest cost was found to be of Injection Imipenem+Cilastatin (NRs. 1,236.15). The average price was found to be NRs. 59.5 ± 96.8 when both Oral and Parenteral routes are combined. During the two years' period, total amount of expenditure in the use of antimicrobial drugs in pediatrics department was NRs. 1,619,121.11 (Figure 6). Out of various classes of antimicrobials drugs consumed, the highest amount of money was spent in Cephalosporin (NRs. 530,988.6) followed by Penicillins (NRs. 381,842.2) and Glycopeptide (NRs. 294,478).

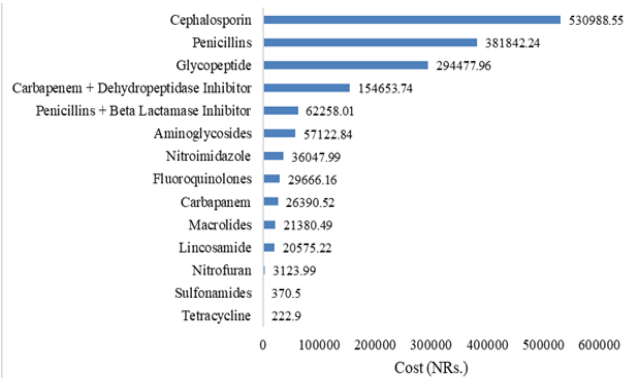
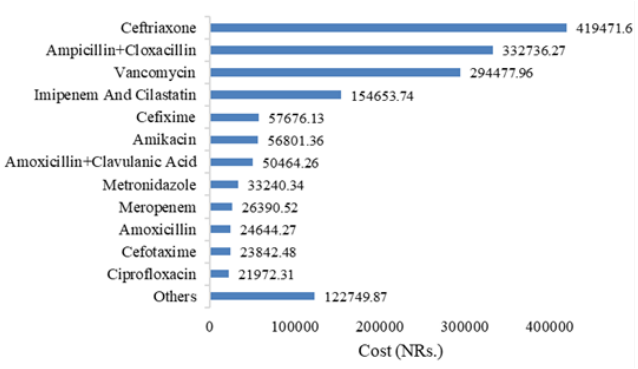


Figure 6. Cost wise distribution of antimicrobial class in pediatric department

Among the antimicrobials drugs used in pediatric department, more expenses was observed in Ceftriaxone (NRs. 419,471.6) followed by Ampicillin + Cloxacillin (NRs. 332,736.3) and Vancomycin (NRs. 294,478). The current study revealed that Injection Benzathin Pencillin was least prescribed drugs which accounted for NRs. 6.7 and Tablet Doxycylcine being the second least prescribed drugs which accounted for NRs. 223 (Figure 7).



*Others: Clindamycin, Cefuroxime, Azithromycin, Piperacillin + Tazobactam, Benzyl Penicillin, Ceftazidime, Ampicillin, Norfloxacin, Cloxacillin, Nitrofurantoin, Flucloxacillin, Levofloxacin, Metronidazole + Diloxanide Furoate, Secnidazol, Clarithromycin, Erythromycin, Phenoxymethyl Penicillin, Cefazolin, Cotrimoxazole, Tinidazole, Gentamicin, Ofloxacin, Doxycycline, Benzathine Penicillin

Figure 7. Cost wise distribution of antimicrobial drugs in pediatric department

DISCUSSION

The current study aimed to analyze the antimicrobial use pattern and it's cost analysis in the patients admitted in pediatrics department. Among 1281 patients, a higher number of patients were observed among age group one to five years (56.5%), resembling other similar studies with higher patients of same age group which might indicate that the age group is more prone to infection.[26,27] The risk

of infection is higher among a child due to the innate and adaptive immune systems.[28] Whereas the occurrence of microbial infection was more common in males compared to females as observed in other studies.[27,29] In a general human being, humoral and cellular immunity of females were found stronger than that of males. The underlying mechanism for this sexual dimorphism is multifactorial, including the endocrine and genetic effects on the immune system.[30] The average hospital stay is around 5.5 days which is much lesser in compared with other study done in several place.[31,32] The average hospital stay was found to be 10.8 days in the study conducted in India whereas, the average 7.3 days was found to be in study done in a pediatric hospital at Kathmandu.[31,32] There could be the various reasons behind this disparity and the degree of case severity. Both previous studies had included the age group lesser than 1 year and it has been suggested that the age group lesser than 2 years will be vulnerable to the infections which could be due to the immature immune system at those age.[33]

Respiratory tract infections including sepsis, enteric fever and seizure were commonly diagnosed among the patients admitted in pediatrics. Respiratory tract infection is the most common indication among patients which is similar to several other studies.[31-36] Respiratory tract infection is one of the top ten illnesses in below 5 years leading to hospital admission in Nepal.[37] It is also observed that respiratory tract infection results in about 95% of the burden in the below 14 age group.[38] Some of the reasons could be improper growth of respiratory organs during the early childhood, less developed immune system and poor air quality.[39,40] Acute respiratory infection is common among children below five regardless of the place they live or economic condition.[41] One of the studies also discussed that the reasons could be poverty and lack of access to healthcare in developing countries.[42] It is because of the particular etiologies and risk factors; the severity is worse in a developing countries leading to higher mortality.[39] Despite the evidence of the dominance of chronic diseases, infectious diseases such as respiratory diseases persist among the top ten causes of mortality and morbidity worldwide.[43]

In this study, Penicillin group of drug being the most commonly prescribed antimicrobials followed by Cephalosporin and Nitroimidazole. The study conducted in another hospital in Nepal showed the cephalosporin was the topmost frequently prescribed antimicrobials followed by the penicillin group which is similar with other studies.[23,32,35,44-46] Further Ampicillin + Cloxacillin (33.6%), Ceftriaxone (13.2%), Cefixime (9.9%), Metronidazole (9.7%) and Amoxicillin (6.8%) were most frequently prescribed antimicrobials drugs. A study conducted by Jangra et al. reported that Amoxcillin + Clavulanic acid, Ceftriaxone, and Cefixime were most prescribed among pediatric patients similar to another study conducted in India.[23,47] Thus, the prescription pattern of antimicrobials is quite different in various studies. The cause of this difference is that every hospital has its infection control committee and antimicrobial use policies.[48]

In our study, most of the patients were prescribed more than two antimicrobials (39.7%) followed by one prescription (29.2%) with a mean of 2.24 antimicrobials per prescription which is similar to other studies and higher than our study.[32,34] A study conducted in Chitwan district, Nepal showed 1.86 an average prescription, 1.41 in a study conducted in India which lower than our study.[23,45] The average number of prescriptions is considered to be an important indicator of the rational use of antibiotics. World Health Organization has considered as 1.6 to 1.8 drugs per prescription is the standard range of prescription of antimicrobials in the pediatric department.[49] To minimize the drug-drug interactions, development of antimicrobial resistance, and burden of the medical cost, there should be rational use of medicines.

In the current study both parenteral and oral routes were used most commonly and nearly equally though, use of parenteral route of drug administration was found to be slightly higher in compare with oral route. Our finding is supported by the previous study as well where the most preferred route of antimicrobial administration in pediatrics was parenteral route of drug administration.[26,36] This is reasonable as the age group between 1-5 years was found to be the highest number of admission in the current study and parenteral route of drug administration will be preferred rather than oral route in the children at those ages because the swallowing of drugs will be difficult.[1] In our study, among the drugs administered orally Ampicillin + Cloxacillin was the most frequently prescribed whereas Ceftriaxone 1 gm was highly prescribed in parenteral form. But in the other study, mostly prescribed drugs in oral form were Ciprofloxacin 250 mg and Azithromycin 500 mg whereas Ampicillin 250 mg and Ceftriaxone 500 mg and 1 gm were highly administered drugs through parenteral route.[50] In another study showed that the Cephalosporin including fluroquinolones, Penicillin group of drugs and Carbapenems were the most commonly prescribed drugs suggesting the most commonly misused and inappropriate prescription.[51]

The total NRs. 1,619,121.11 was spent in antimicrobials during the two-year study period and Cephalosporin drugs accounted for the highest total amount followed by Penicillin group of drugs and glycopeptides which is similar to the previous study.[31] The previous study showed that the Cephalosporin group of drugs being the most prescribed drugs and showing the highest expenditure in this class.[31] Among the parenteral antimicrobials use, Imipenem + Cilastatin had the highest cost per dispensing while Ampicillin + Cloxacillin had the least cost per dispensing. In contrast, another study showed that Amoxiclav (IRs. 133.56) was found to be of high cost whereas the lowest cost was found to be with Sulfamethoxazole

+ trimethoprim (IRs.12.9) for the oral administration indicating that syrup form is the most commonly used as of the pediatric age group.[50] While considering the parenteral route, Meropenem (NRs. 14,074.94) was the drug of the highest cost.[50] In the both cases, as the current study has also showed as the respiratory tract infection as the most common diseases among pediatric age group and the use of Amoxiclav and Cotrimoxazole are the preferable drugs as per the guideline. Further our study showed that third generation cephalosporins were highly prescribed and accounted for the significant cost whereas antimicrobials like Vancomycin, Imipenem+Cilastatin, Meropenem etc also contributed in the significant expenditure of the total antimicrobial use. This might be because our hospital is a tertiary care hospital with specialized care service for the pediatric population. The patient might have encountered lower generation antimicrobials for several times and probably developed resistance to those antimicrobials which results in prescribing higher generation antimicrobials leading to increased cost of therapy. However, in the current study, antimicrobial resistance pattern in relation to the use of higher antimicrobial agents has not been studied. Nevertheless, the current study has analyzed only the direct cost incurred by the use of antimicrobial agents and has not included indirect cost like laboratory test cost, hospital stay cost etc. Therefore, the cost burden due to the antimicrobial resistance and causing the hospital admission could be another cost analysis which can give insight pharmacoeconomic perspective of antimicrobial use.

CONCLUSION

Our study showed that the Respiratory tract infection was the most common indication among the patients admitted in paediatrics. Penicillin group of drugs was the most commonly prescribed antimicrobials followed by Cephalosporin groups and Nitroimidazole with the parenteral route being the most common route of drug administration in pediatric patients. Among the drugs administered orally Ampicillin + Cloxacillin was the most frequently prescribed whereas Ceftriaxone was most commonly prescribed drugs in parenteral form. The highest antimicrobial expenditure was found to be in the Cephalosporin group of drugs followed by Penicillin group of drugs. The current study has analyzed the direct antimicrobials cost however, it is important to study direct and indirect medical cost to explore the cost burden of the patient.

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Conflicts of Interest. All Authors, no reported conflicts.

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