ORIGINAL ARTICLE

A Study on Antibiotic Susceptibility and OPD Prescription Pattern Analysis of Antibacterial in a Teaching Hospital

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ABSTRACT

Introduction: India is the largest consumer of antibiotics in the world. Antimicrobial agents (AMA) are also the most misused and excessively prescribed therapeutic agents. A survey of OPD prescription chits of a tertiary care government hospital was carried out to describe the current treatment practices in management of infections.

Methods: 1500 OPD prescriptions were analysed for the prevalence of antimicrobials prescribed by each specialist OPD and the systemic infections which were treated by using these AMA. The data of antibiotic susceptibility tests for the year 2018 was obtained for the analysis on current treatment practices of hospital infections.

Results: 24.4% of all 1500 OPD prescriptions encountered from the seven departments of the hospital contained an antibacterial. Highest proportion of AMA was seen in the dental OPD (66.6%) followed by ENT and surgical OPD (36.8% & 36% respectively) and least AMA were prescribed in gynaecology and obstetrical OPD (11%). Out of the 367 AMA prescriptions, 92 prescriptions had 2 or more anti-bacterials. 54.7% of these AMA prescribed were generic oral drugs and only two prescription counts were of injectable AMA. 62% of the AMA prescriptions were for the duration of use between 5 to 10 days. 53.4% of the AMA prescription counts belonged to the ACCESS group of antibiotics, 44.1% to WATCH group and 2.5% to the RESERVE group as classified by WHO. The present study emphasizes the need to re-formulate local guidelines of antimicrobial use in OPD patients based on hospital antibiotic susceptibility tests.

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INTRODUCTION

Almost 50% of antimicrobial agents (AMA) used even in developed nations like the US are felt to be unnecessary [1]. Non-infectious diseases or infections of viral etiology are often prescribed AMA inappropriately [2]. In 2015, an English surveillance program for antimicrobial utilization and resistance (ESPAUR) reported an increase of 8.5% prescriptions of antimicrobials in outpatient departments of health care settings from 2010 to 2014 [3]. The situation in developing nations is even worse where antibiotics are available freely and to some extent unregulated. No wonder, India is the largest consumer of antibiotics in the world [4]. An effective antimicrobial stewardship program (AMSP) would improve the use of AMA in a health care setup and reduce the burden of infections. All clinicians need to obtain cultures of pathogenic microbes before starting an antibiotic, review it after 48-72 hours and then optimize the dose and duration of antibiotic therapy [3]. A questionnaire-based survey among clinicians of teaching hospitals in eastern India revealed that more than 55% of respondents acknowledged misuse of antibiotics mainly due to deficient training in the rational use of medicines and the absence of antibiotic policy [5]. A survey on AMSP in India reported that AMA usage data was utilized in only 25% health care institutions and AMA prescription audit by only 30% [6]. The world health organization has recently categorized anti-infective agents in the essential medicines list into ACCESS, WATCH and RESERVE groups to restrict widespread use of high-end AMA [7]. Hence, a need was felt to estimate the antibacterial use and pattern in our hospital outpatient department (OPD) based on antibiotic susceptibility tests obtained.

RESEARCH METHODOLOGY

Observational descriptive research was carried out to describe the current treatment practices in the management of infections. The study involved analysis of prescriptions of anti-bacterials and laboratory reports of infectious clinical samples. The departments selected for the study were medicine, surgery, obstetrics & gynecology (OBG), pediatrics, dental, ENT and general OPD. The OPD prescriptions were collected prospectively over a week from the hospital dispensary to cover OPD days of each of the departments mentioned. The prescription chits were analyzed for the prevalence of antimicrobials being prescribed as per the prescribing indicators mandated by WHO [8]. WHO manual on selected drug use indicators recommend at least 600 encounters to be included in a cross-sectional survey to describe the prescribing practices at any health center. We planned to include 1500 OPD prescriptions at an average of 250 prescriptions daily on OPD days. This was estimated to be obtained in a week of six OPD days. Our hospital provides free treatment to entitled patients wherein all drugs prescribed by the clinicians are dispensed from the hospital pharmacy. Prescription chits retained at the dispensary were utilized for the above analysis. The data of antibiotic susceptibility tests for the year 2018 was obtained for the analysis of current treatment practices of hospital infections. Clinical specimens sent to the microbiology lab consisted of urine, blood, pus and sputum specimens. The antibiotic susceptibility tests were carried out by Kirby Bauer disc diffusion method and Vitek® at the accredited laboratory. The data were analyzed using Excel Worksheet of Microsoft Office. The study protocol was approved by the Institutional Ethics committee.

RESULTS

1500 consecutive OPD prescriptions in the first week of June 2018 were included for the survey. Amongst the seven OPD clinics surveyed, the prescription counts encountered from medicine OPD were 466 (31%), followed by OBG with 398 (26.5%), and pediatric and general OPDs with 160 prescriptions each (10.6% each). In our study, 24.4% of all 1500 OPD prescriptions encountered from the seven departments of the tertiary care government hospital contained an antibacterial. The proportion of OPD prescriptions being prescribed anti-bacterials was seen highest in the dental OPD of the hospital (66.6%) followed by

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ENT and surgical OPD (36.8% & 36% respectively). 20% of pediatric OPD prescriptions contained an antibiotic and only 11% of patients attending gynecology & obstetrical OPD were prescribed antibiotics. Out of the 367 AMA prescriptions, 92 prescriptions had 2 or more anti-bacterials. 54.7% of these AMA prescribed were generic oral drugs and only two prescription counts were of injectable AMA (0.1%). The AMA prescriptions were dispensed to 235 male and 132 female patients in this analysis. Most AMA prescriptions were for patients between 30-60 years of age (48%) followed by <30 years (3%). In most prescriptions, the duration of use was between 5 to 10 days (228 counts i.e., 62%). The OPD wise distribution of AMA prescriptions has been depicted as Figure 1.

Figure 2 depicts the system wise distribution of prescriptions with antibiotics. In our study, the largest proportions of AMA prescription counts are for respiratory infections (including ENT infections). Among the 367 prescription counts of AMA, 196 (53.4%) belonged to the ACCESS group of antibiotics, 162 (44.1%) to the WATCH group and 9 (2.5%) to the RESERVE group of AMA as classified by WHO. All the nine prescription counts of RESERVE group of AMA were of linezolid.

Table 1 summarizes the isolated pathogen sensitivity of the ACCESS group of AMA from clinical specimens of patients being treated at our hospital. Tables 2 and 3 depict the isolated pathogen sensitivity of the WATCH group of AMA from clinical specimens. Table 4 depicts the pathogen sensitivity of the RESERVE group of AMA in our study.

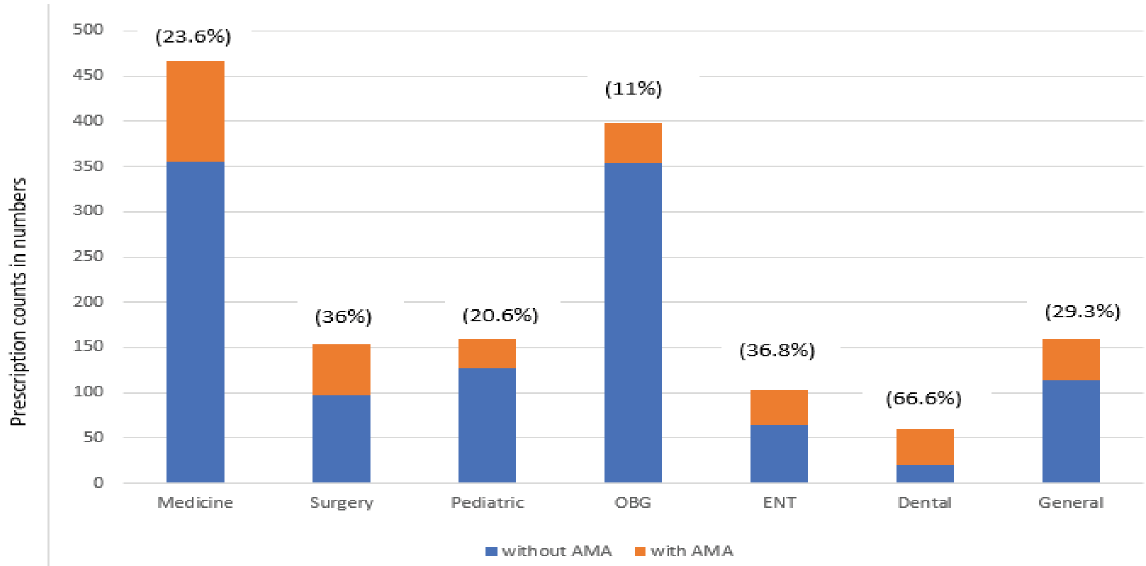

Figure 1: Antimicrobial prescribing pattern of selected OPD clinics (n=1500). Percentage of prescription counts with AMA mentioned in brackets.

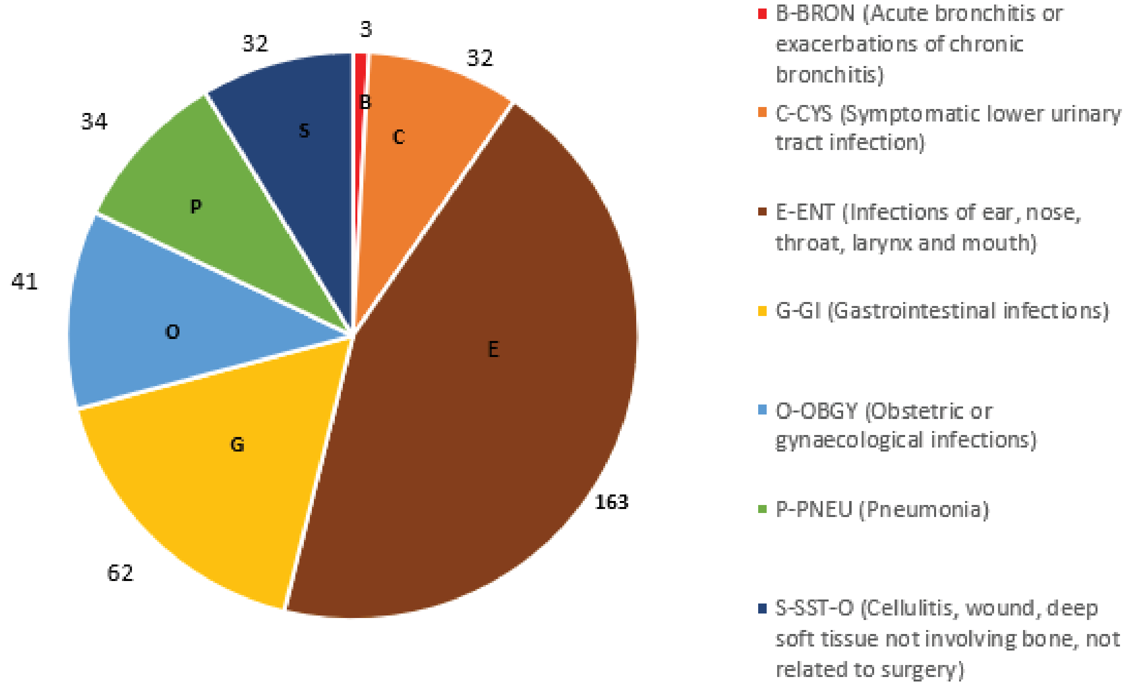

Figure 2: System wise distribution of OPD prescription with antibiotics (n=367) (Number of prescription counts with AMA).

Table 1: Pathogen sensitivity of ACCESS category of AMAs amongst OPD patients.

Antibiotics	Specimen	Sensitive (≥ 70%)	Intermediate (35-70%)	Resistant (≤ 35%)
Ampidllin	Urine	*Enterococci*		-
Amikacin	Urine	*E. coli, Klebsiella, Citrobacter*	*Pseudomonas proteus*	-
Cefazolin	Urine		*Klebsiella, E. coli*	*proteus*
Nitrofurantoin	Urine	*E. coli, Enterobacter*	*Citrobacter, Klebsiella proteus*	-
Cotrimoxazole	Urine	*Citrobacter*	*E. coli, Klebsiella*	*proteus*
Penicillin	Blood	-	-	*Staph. aureus Staph. epidermidis*
Cefoxitin	Blood	-	-	*Staph. aureus Staph. epidermidis*
Clindamycin	Blood	-	*Staph. aureus Staph. epidermidis*	
Amikacin	Blood	*E. coli*	*Klebsiella pneumoniae*	-
Cotrimoxazole	Blood	-	*Staph. aureus Staph. epidermidis*	-
Tetracycline	Blood	*Staph. aureus Staph. epidermidis*	-	-
Amikacin	Pus	*E. coli, Citrobacter, Klebsiella*	-	-
Cefoxitin	Pus	-	*Staph. aureus*	
Clindamycin	Pus	*Staph. aureus*		-
Cotrimoxazole	Pus	*Staph. aureus*	-	-
Tetracycline	Pus	*Staph. aureus*	-	-
Amikacin	Sputum		*Enterobacteriaceae*	-

Table 2: Pathogen sensitivity of WATCH category of AMAs amongst OPD patients (Urine and sputum specimens).

Antibiotics	Specimens	Sensitive (≥70%)	Intermediate (35-70%)	Resistant (≤35%)
Cefotaxime	Urine	-	*proteus, Citrobacter*	*Klebsiella, E. coli*
Ceftazidime	Urine	-	*Pseudomonas*	-
Ciprofloxacin	Urine	-	*Citrobacter Klebsiella Pseudomonas proteus*	ES. Qii Enterococci
Piperacillin+ Tazobactam	Urine	*Proteus*	*Loll Pseudomonas Citrobacter Klebsiella*	-
Vancomycin	Urine	*Enterococci*	-	-
Imipenem	Urine	*La proteus, Klebsiella, Citrobacter, Pseudomonas*	-	-
Levofloxacin	Urine	-	*Citrobacter, proteus, Klebsiella, Pseudomonas F coil*	-
Ertapenem	Urine	-	*La Citrobacter, Klebsiella*	-
Cefotaxime	Urine	-	*proteus, Citrobacter*	*Klebsiella, E. coli*
Teicoplanin	Urine	*Enterococci*	-	-
Cefotaxime	Sputum	-	-	Enterobacteriaceae
Ceftazidime	Sputum	-	-	Enterobacteriaceae
Ciprofloxacin	Sputum	-	*Enterobacteriaceae*	
Ertapenem	Sputum		*Enterobacteriaceae*	-
Imipenem	Sputum	-	-	*Enterobacteriaceae*
Levofloxacin	Sputum	-	*Enterobacteriaceae*	
Meropenem	Sputum	-	*Enterobacteriaceae*	-
Piperacillin+ tazobactam	Sputum	-	*Enterobacteriaceae*	-

DISCUSSION

Antimicrobial agents as a group have proved to be the most effective medicines in reducing the morbidity and mortality of living beings and thereby increasing the life expectancy to the present-day levels. However, these are also the most misused and excessively prescribed therapeutic agents [9]. In developing nations, empirical treatment of infections is high due to the following reasons:-

1. Bacterial culture is not routinely sent before starting AMA,
2. Infection control is poor in the health care institution and the community,
3. Self-medication is common even for suspected infections and
4. Pressure exists from the pharmaceutical industry and corporate hospitals to unethically inflate bills of medical treatment.

That is, therefore, an urgent and regulated need to curb the unnecessary consumption of anti-bacterials at all levels. The regulatory and controlling authorities at global, national and regional levels have tried to join hands to curb the menace of the rising use of antibiotics. Obtaining periodic scientific data on the pattern of consumption of antibiotics in a hospital setting is an important step towards rational therapy of infections [10]. The existing practice of prescribing antibiotics in the OPDs of a large hospital can only be amended if epidemiological

Table 3: Pathogen sensitivity of WATCH category of AMAs amongst OPD patients (Blood and pus specimens).

Antibiotics	Specimen	Sensitive (≥70%)	Intermediate (35-70%)	Resistant (≤35%)
Cefotaxime	Blood	-	-	*E. coli Klebsiella*
Ceftazidime	Blood	-	-	*E. coli Klebsiella*
Ciprofloxacin	Blood	-	*E. coli, Staph. epidermidis*	*Klebsiella Staph. aureus*
Erythromycin	Blood	-	-	*Staph. aureus Staph. epidermidis*
Levofloxacin	Blood	-	-	*E. coli Klebsiella*
Meropenem	Blood	-	*E. coli*	*Klebsiella*
Piperacillin+ Tazobactam	Blood	-	*E. coli*	*Klebsiella*
Imipenem	Blood	-	*E. coli*	*Klebsiella*
Vancomycin	Blood	Staph. aureus Staph. epidermidis	-	-
Cefotaxime	Pus	-	-	*E. coli Klebsiella*
Ceftazidime	Pus	-	*Klebsiella*	*E. coli*
Ciprofloxacin	Pus	-	*Staph. aureus Klebsiella*	-
Levofloxacin	Pus	Citrobacter	*Klebsiella*	*E. coli*
Meropenem	Pus	-	*E. coli Klebsiella*	-
Piperacillin+ tazobactam	Pus	Citrobacter	*E. coli Klebsiella*	-
TeicoDlanin	Pus	Staph. aureus	-	-

Table 4: Pathogen sensitivity of RESERVE category of AMAs amongst OPD patients.

Antibiotics	Specimen	Sensitive (≥70%)	Intermediate (35-70%)	Resistant (≤35%)
Linezolid	Urine	*Enterococci*	-	-
Colistin	Urine	*E. coli*	-	-
Linezolid	Blood	*Staph. aureus Staph. epidermidis*	-	-
Linezolid	Pus	*Staph. aureus*	-	-

studies are carried out to estimate the burden and type of anti-bacterials being prescribed along with the antibiotic susceptibility patterns of the pathogens isolated from clinical specimens of the hospital patients. The hospital antibiotic policy should be formulated based on the antibiotic susceptibility tests carried out in the regional laboratory and the clinical response to the prescribed antibiotics.

The proportion of AMA prescriptions in our study was 24.4%, which is less compared to a study in another teaching hospital in the same region [11]. and within the WHO stipulated range of 15-25% for regions where infectious diseases are prevalent [8]. The proportion of OPD prescriptions being prescribed anti-bacterials was seen highest in the dental OPD of the hospital (66.6%) followed by ENT and surgical OPD (36.8% & 36% respectively). Our survey revealed that two or more antibiotics were prescribed in only 25% of OPD prescriptions, which is reasonable [12]. The percentage of injectables prescribed to the OPD patients in our study is less compared to other studies in India [13,14].

It is well established that antimicrobial resistance (AMR) is likely to increase with heavy consumption of anti-bacterials. Further, surgical procedures should be carried out with due asepsis and adequate drainage or debridement that the need for antimicrobials is minimal. Time and again, it has been brought out that the OPD consumption of antibiotics in dental prescriptions is high and needs introspection and drug audit for rational pharmacotherapy. Drug utilization pattern in surgery OPD of a tertiary hospital in north-eastern India revealed that 18.25% of the prescriptions contained AMA, commonest being amoxicillin+clavulanic acid and cefixime [15]. The fact that only 11% of patients attending gynecology & obstetrical OPD were prescribed antibiotics proves the point that it is possible to reduce antibiotic usage by adequate precautions, patient education, and training of health care professionals to prescribe anti-bacterial only when unavoidable. It was also heartening to observe that only around 20% of pediatric OPD prescriptions contained an antibiotic. Diarrhoeal and respiratory diseases are the common types of infections seen in the pediatric population, and most are believed to be of viral origin. Our survey is in marked variation from an analysis of prescriptions from gynecology OPD of a teaching hospital in southern India where 72% of the OPD prescriptions contained AMA, commonest being metronidazole (39.8%), doxycycline (33%) and fluconazole (2.4%) [16].

The highest systemic consumption of OPD anti-bacterials consisted of respiratory infections including those of ear, nose, and throat followed by gastrointestinal infections. 62% of the AMA prescriptions in our survey were for the duration of use between 5 -10 days, which is as per the recommendations of treatment for common infections [17,18]. The common OPD infections namely simple UTI or URTI require anti-bacterials for 3 or 5-10 days only.

It was heartening to observe that the OPD consumption of the RESERVE group of anti-bacterials was minimal in our survey. However, the proportion of prescription counts containing the WATCH group of anti-bacterials in OPD patients was high and of concern to re-formulate a stringent antibiotic policy in the hospital. The low consumption of RESERVE antibiotics could also be due to the liberal practice in our institution for early hospital admissions and restricted availability of such medicines for free distribution to OPD patients.

In urine samples, *Proteus* spp. has been cultured in our laboratory which was resistant to cefazolin and co-trimoxazole and intermediate to amikacin and nitrofurantoin. Hence, such resistant strains causing UTI would need higher-end antibiotics. *E. coli*, *Klebsiella* spp. and *Citrobacter* spp. isolated from clinical specimens of our hospital patients were found to be sensitive to the ACCESS AMA nitrofurantoin, co-trimoxazole, and amikacin. Enterococci from urine samples were sensitive to ampicillin. Similarly, many blood-borne strains of *Staphylococcus aureus*, Staphylococcus epidermidis have been found to be intermediate in sensitivity to oral ACCESS group of antibiotics. Wounds harboring *Staphylococcus aureus* or epidermidis have however been found to be sensitive to tetracyclines, clindamycin or co-trimoxazole in the ACCESS group. *Enterobacteriaceae* spp. obtained from sputum has been found to be of intermediate sensitivity to amikacin in the ACCESS group.

The antibiotic sensitivity tests of pathogens for the 'WATCH' group of antimicrobials, is even more disturbing. *E. coli, Klebsiella* spp. strains were resistant to cefotaxime from urine, blood and pus samples. Pseudomonas strains from urine and sputum were not sensitive to ceftazidime, piperacillin + tazobactam, and carbapenems. The Enterobacteriaceae strains of pathogens obtained from the sputum of serious cases were not sensitive to third-generation cephalosporins, carbapenems or newer fluoroquinolones, raising the red flag for the alarming spread of AMR in hospital isolates. Luckily, strains of *S aureus*, *S. epidermidis* and enterococci obtained from blood or urine were found sensitive to vancomycin and teicoplanin. *Citrobacter* sp. from pus was sensitive to the combination of piperacillin and tazobactam or newer FQ but those obtained from urine samples showed intermediate sensitivity. In such a situation of widespread prevalence of AMR in the hospital isolates, the high consumption of the WATCH group of AMA seems irrational and could be best used in conformity to the antibiotic sensitivity tests of the laboratory. Perhaps, there is a need to carry out the culture of bacteria in all suspected patients of infection and determine its *in vitro* susceptibility test to the available AMA. The expenditure on bacterial culture and antibiotic sensitivity tests would definitely prove to be cost-effective and help in the containment of AMR.

Presently, ten laboratories in India have been tasked to establish an AMR surveillance system under the aegis of the National Centre for Disease Control [19]. To begin with, the pathogens under surveillance are *Klebsiella* spp., *E. coli, Staphylococcus aureus* and *Enterococcus* spp. *Pseudomonas aeruginosa* and *Acinetobacter* spp. are also contemplated to be included for AMR testing. Initial reports have shown high resistance to fluoroquinolones, third-generation cephalosporins, and carbapenems but sensitivity to reserve drugs like vancomycin and colistin are still maintained [20].

CONCLUSION

As a ray of hope in the present-day epidemic of AMR in the health care setting, all bacteria isolated were found sensitive to the RESERVE category of AMA in our study. This could be attributed to a reasonably satisfactory hospital infection control practices and the protocol of limiting the use of high-end AMA to rare and life-threatening infections only. Restricting the use of RESERVE AMA is perhaps the only way to preserve its sensitivity to difficult bugs encountered in infections.

The high use of empirical AMA especially from the WATCH category is a disturbing trend as observed in our study. It cannot be more emphasized that there is an urgent need to identify and isolate pathogenic bacteria from body fluids before starting with anti-bacterials. Microscopic examination of stained bacteria, antigen testing, polymerase chain reaction, serology and culture with antibiotic sensitivity tests in the microbiological laboratory is a stringent requirement and needs to be incorporated in all hospital audit procedures. AMA especially the restricted group perhaps needs to be prescribed and dispensed after getting clearance from a duly constituted independent authorization team in order to reduce the use of WATCH/RESERVE category anti-bacterials.

The National Action Plan on containment of antimicrobial resistance has envisaged the need to focus on antibiotic consumption patterns and their rational use to treat infections. The present study is an effort in this direction to describe the current treatment practices which would help streamline the management of clinical infections in medical institutions.

The study once again emphasizes the need to re-formulate local guidelines of antimicrobial use based on regional antibiotic susceptibility patterns and using national treatment guidelines as a reference only. Conducting such studies and analysis periodically, would pave way for promotion of rational use of antimicrobials and help restrict the emergence of resistant strains of bacteria.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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