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Incidence of Microbial Infections with Multidrug Resistance (MDR) Microbial Strains

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ABSTRACT

Prolonged use of antimicrobial drugs for the treatment of microbial infections developed several multidrug resistance (MDR) microbial strains. Multidrug resistant organisms showed resistant to given antimicrobial drugs (previously sensitive) contributes to inadequate treatment and persistent spread of MDR in large community and nosocomial infections specifically in the immune-compromised patients. Pathogen identification and antibiotic susceptibility testing were done by using VITEK 2 systems (bioMerieux, Craponne, France). In this cross-sectional study, adult patients (Twenty five), reported as infected with Multidrug resistant bacteria by the Microbiology laboratory (Fortis Hospital Noida, India) were selected to observe the occurrence of multidrug resistant microbes (MDR) and their resistance towards antimicrobial drugs. Most of the strains of Acinetobacter baumannii, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, while all the strains of Providencia rettgeri, Pseudomonas aeruginosa, Staphylococcus aureus showed resistant to antimicrobial drugs such as Amikacin, Amoxicillin clavulanic acid, Ampicillin, Cefuroxime, Ertapenem, Nitrofurantoin, Ciprofloxacin, Gentamicin, Imipenem, Meropenem, Piperacillin tazobactam, Trimethoprim sulfamethoxazole. The incidence of resistance of bacterial isolates to at least three antibiotics indicates the emergence of MDR of Acinetobacter baumannii, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Providencia rettgeri, Pseudomonas aeruginosa, Staphylococcus aureus. Nosocomial or community infections by drug resistant microbial (MDR) strains can increase morbidity, mortality, extended hospitalization of the patients. The extended use of inappropriate antimicrobial drugs for treating microbial infections has evolved the appearance and distribution of multidrug resistance (MDR) microbial strains in large community and may lead to nosocomial infections; enhanced morbidity, mortality and extended hospitalisation of the patients. Therefore, it is concluded that the prolonged and inappropriate use of antimicrobial drugs for the treatment of microbial infections must be stopped by using appropriate antimicrobials to reduce the risk for development of MDR microbial strains.

Introduction

Incidence of microbial infections with Multidrug-resistant bacteria (MDRB) has upraised since the last few decennium and become not only the serious threat in modern medicine but also responsible for many healthcare-related infections (Russell & Martin-Loeches, 2023). Prolonged and ongoing use of antimicrobial drugs for the treatment of microbial infections led to the development of multidrug resistance (MDR) microbial strains (Tanvir *et al*., 2021). Multidrug resistant organisms show resistance to at least three or additional antimicrobial drugs (Wolfensberger *et al*., 2019; Magiorakos *et al*., 2012). Multidrug resistance is the resistance (insensitivity) of microorganisms towards the given antimicrobial drugs, previously sensitive (Tanwar *et al*., 2014; Singh, 2013); contributes to inadequate treatment and persistent spread of MDR in large community

and nosocomial infections (hospital acquired infection) specifically in the immune-compromised patients and patients in intensive care units (Moreau *et al*., 2018; Cerceo *et al*., 2016). Hospital acquired infections by drug resistant gram-negative bacteria (GNB) is a risk to public health universally (Exner *et al*., 2017; Magiorakos *et al*., 2012). Bacteria (<70%) causing hospital acquired infections are resistant to antimicrobial agents (at least one) used to treat them (Kang *et al*., 2005). Most prevalent hospital acquired drug-resistant GNBs are Enterobacteriaceae (*Klebsiella pneumoniae* & *Escherichiacoli*), *Pseudomonas aeruginosa*, *Acinetobacter baumannii* (Cerceo *et al*., 2016; Lockhart *et al*., 2007). MDR microbial strains increase morbidity, mortality, extended hospitalization of the patients (Cerceo *et al*., 2016).

Materials and methods

Methods: Study Design and Settings

This cross-sectional study was conducted at Fortis Hospital Noida, India a period of one year. Approval was taken from the hospital authorities to conduct the study. Medical records were accessed to collect the data. Adult patients (Twenty five) were selected in present study that were consecutively hospitalized and admitted during the study period. Only those patients were included in the study that was reported as infected with Multidrug resistant bacteria by the Microbiology laboratory. All data were obscurity to maintain the privacy of the participants. Information collected from the medical records included age, gender, type of infection (Multidrug resistant: MDR), source of infection, and type of bacteria (Madrazo *et al*., 2021).

Microbiological Procedures

Pathogen identification and antibiotic susceptibility testing were done by using VITEK 2 system (bioMerieux, Craponne, France). The machines displayed the identity of the organism with the percentage of assurance and susceptibility to 15–20 drugs (sensitive, intermediate, or resistant). GeneXpert (Xpert®Carba-R; Cepheid, Sunnyvale, CA, USA) was used to detect and differentiate. The breakpoints and susceptibility interpretive criteria were based on the ones defined by the Clinical and Laboratory Standards Institute (CLSI).

Statistical analysis

The collected data was compiled by using MS-Office Excel- 2007. InStat (version 3) was used for data analysis. Graph Pad Prism 5.0 was used for graph preparation.

Results and Discussion

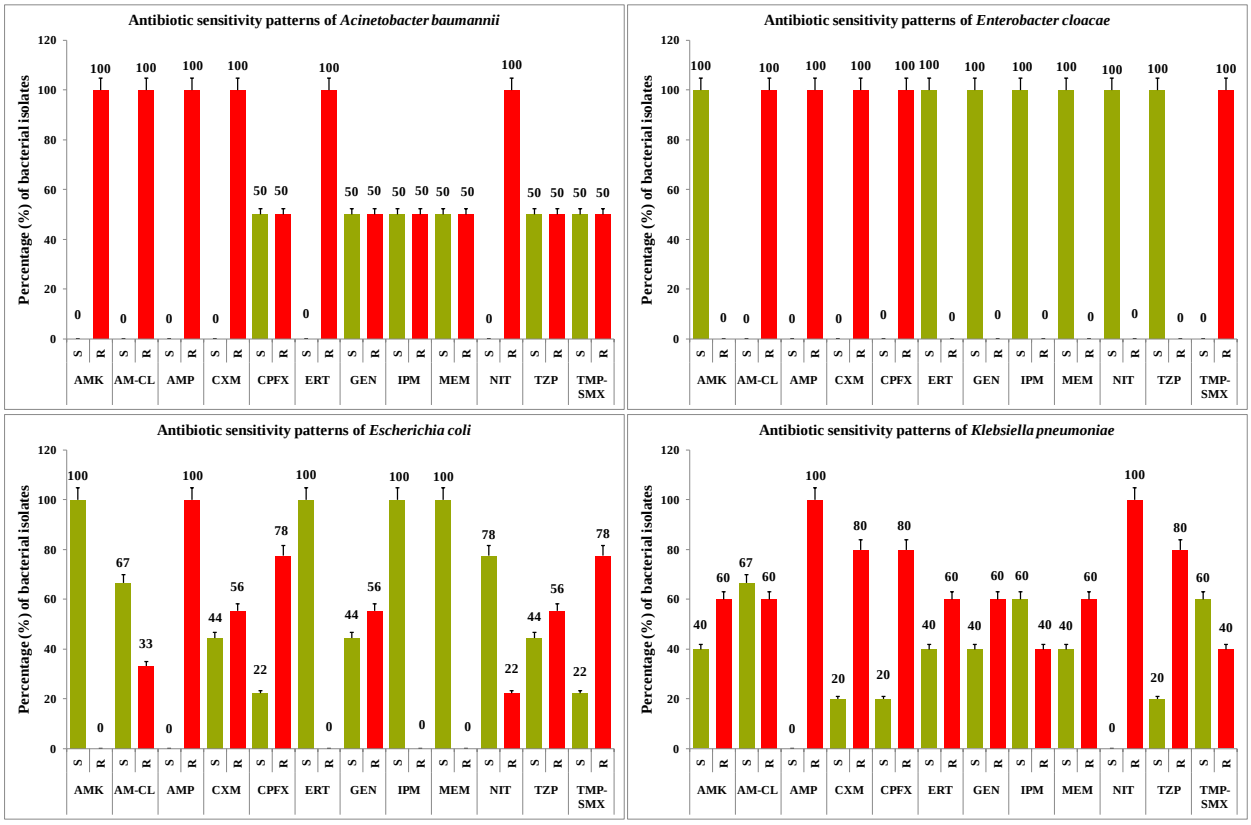

Fig1. Antibiotic sensitivity pattern of bacterial isolates (*Acinetobacter baumannii*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae)* to reference antibiotics. (Amikacin- AMK; Amoxicillin clavulanic acid- AM-CL; Ampicillin- AMP; Cefuroxime- CXM; Ciprofloxacin- CPFX; Ertapenem- ERT; Gentamicin- GEN; Imipenem- IPM; Meropenem- MEM; Nitrofurantoin- NIT; Piperacillin Tazobactam- TZP; Trimethoprim sulfamethoxazole- TMP-SMX).

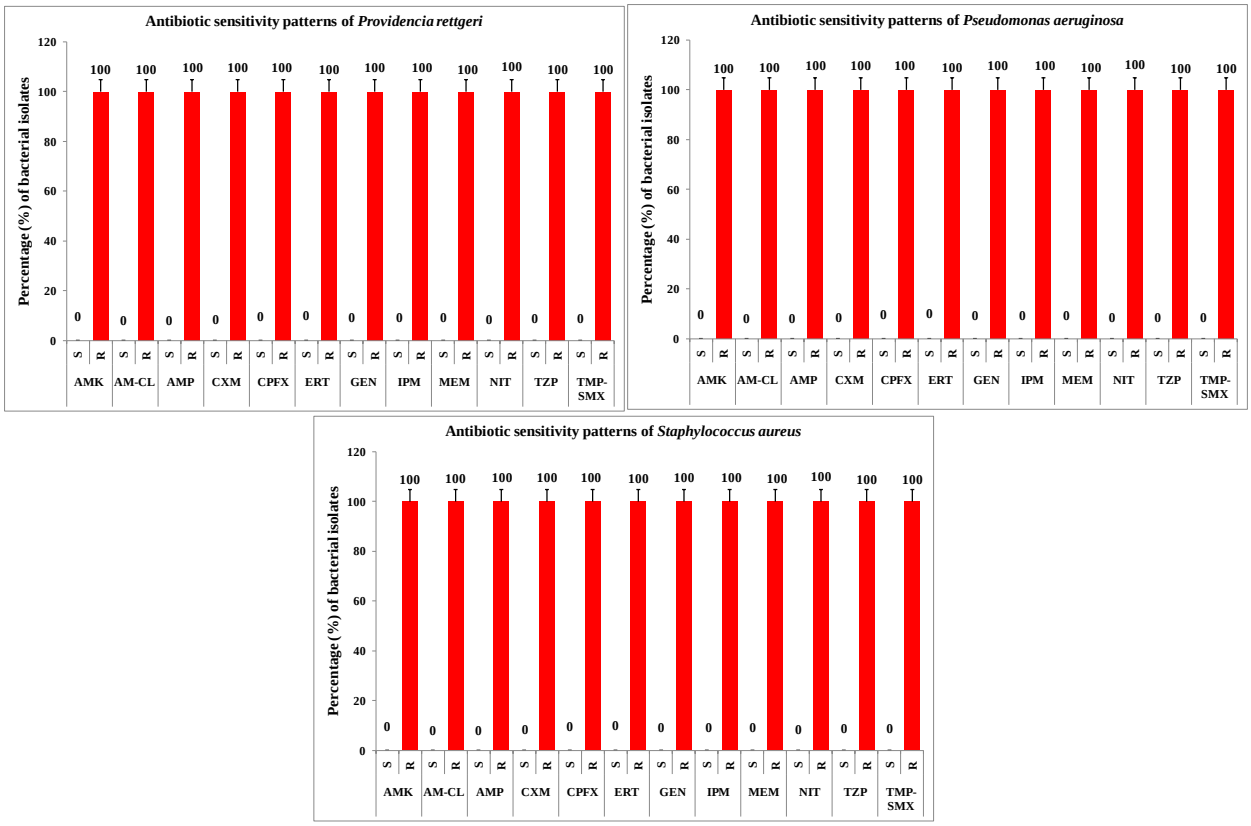

Fig 2. Antibiotic sensitivity pattern of bacterial isolates (*Providencia rettgeri*, *Pseudomonas aeruginosa*, *Staphylococcus aureus)* to reference antibiotics. (Amikacin- AMK; Amoxicillin clavulanic acid- AM-CL; Ampicillin- AMP; Cefuroxime- CXM; Ciprofloxacin- CPFX; Ertapenem- ERT; Gentamicin- GEN; Imipenem- IPM; Meropenem- MEM; Nitrofurantoin- NIT; Piperacillin Tazobactam- TZP; Trimethoprim sulfamethoxazole- TMP-SMX).

Antibiotic sensitivity patterns of *Acinetobacter baumannii* reveal that most of the bacterial isolates of *Acinetobacter baumannii* were resistant to Amikacin, Amoxicillin clavulanic acid, Ampicillin, Cefuroxime, Ertapenem, Nitrofurantoin, Ciprofloxacin, Gentamicin, Imipenem, Meropenem, Piperacillin tazobactam, Trimethoprim sulfamethoxazole; while some of the bacterial isolates of *Acinetobacter baumannii* were susceptible to the Ciprofloxacin, Gentamicin, Imipenem, Meropenem, Piperacillin tazobactam, Trimethoprim sulfamethoxazole (Figure 1). The incidence of resistance of bacterial isolates to at least three antibiotics indicates the emergence of multidrug resistant *Acinetobacter baumannii.* Dent *et al*., (2010) also reported the resistance of *Acinetobacter baumannii* isolates (more than half; 143/247: 58%) to amikacin, imipenem, and ampicillin-sulbactam; 72% of *Acinetobacter baumannii* isolates were and 37 patients were died with *Acinetobacter* colonization/infection. Multidrug resistant *Acinetobacter baumannii*, one of the major causes of nosocomial infection (hospital acquired infection) increased mortality and prolonged stay in hospital (Jamulitrat *et al*., 2009). Occurrence of Multidrug resistant isolates of *Acinetobacter baumannii*and their resistance to amikacin, ampicillin-sulbactam, ceftazidime, gentamicin, piperacillin, piperacillin-tazobactam, netilmicin, cefepime, imipenem, trimethoprim-sulfamethoxazole, meropenem, ciprofloxacin, levofloxacin and tetracycline was reported by Sari *et al*., (2015).

Antibiotic sensitivity patterns of *Enterobacter cloacae* reveal that the bacterial isolates of *Enterobacter cloacae* were resistant to the Amoxicillin clavulanic acid, Ampicillin, Cefuroxime, Ciprofloxacin, Trimethoprim sulfamethoxazole while some of the bacterial isolates of *Enterobacter cloacae* were susceptible to the Amikacin, Ertapenem, Gentamicin,I mipenem, Meropenem, Nitrofurantoin, Piperacillin tazobactam (Figure 1). The incidence of resistance of bacterial isolates of *Enterobacter cloacae* to at least three antibiotics indicates the emergence of MDR *Enterobacter cloacae.* Iwu *et al*., (2020) also reported the resistance of *Enterobacter cloacae* isolates against ampicillin (84.5%), cefuroxime (81.0%), nitrofurantoin (81.0%), amoxicillin/clavulanic acid (77.6%), and tetracycline (60.3%) while some strains of *Enterobacter cloacae* were reported as susceptible to gentamicin (98.3%), and ciprofloxacin (86.2%). Davin-Regli & Pages, (2015) reported the resistance of *Enterobacter cloacae*to Ampicillin, Amoxicillin, Cephalosporins, and Cefoxitin. Enterobacter cloacae being a nosocomial pathogens cause several infections, such as pneumonia, urinary tract infections (UTI), and septicemia (Wisplinghoff *et al*., 2004)

Antibiotic sensitivity patterns of *Escherichia coli* reveal that the bacterial isolates of *Escherichia coli* were resistant to the Amoxicillin clavulanic acid, Ampicillin, Cefuroxime, Ciprofloxacin, Gentamicin, Nitrofurantoin, Piperacillin tazobactam,

Trimethoprim sulfamethoxazole while some of the bacterial isolates of *Escherichia coli* were susceptible to the Amikacin, Amoxicillin clavulanic acid, Cefuroxime, Ciprofloxacin, Ertapenem, Gentamicin, Imipenem, Meropenem, Nitrofurantoin, PiperacillinTazobactam, Trimethoprim sulfamethoxazole (Figure 1). The incidence of resistance of bacterial isolates of *Escherichia coli* to at least three antibiotics indicates the emergence of MDR *Escherichia coli.* Hrbacek *et al*., (2020) reported the high resistance of *Escherichia coli* strains to ampicillin, amoxicillin, piperacillin/tazobactam, cefuroxime and ciprofloxacin. Magyar *et al*., (2017) also reported the resistance of *Escherichia coli* strains for penicillins, cefuroxime, ciprofloxacin and nitrofurantoin. Gangcuangco *et al*., (2015) reported the resistance of *Escherichia coli* to ampicillin (64.2%), TMP–SMX (41.3%), amoxicillin–clavulanic acid (11.7%), fluoroquinolones, gentamicin, cephalosporins and nitrofurantoin was rare (<7%). Ibrahim *et al*., (2012) reported the presence of Multidrug resistant *Escherichia coli* was 92.2%; and *Escherichia coli* strains wereresistance toamoxicillin (97.7%), cefuroxime (92.5%), trimethoprim-sulfamethoxazole (88.3%), nalidixic acid (72%), ceftriaxone (64%), ciprofloxacin (58.4%), amoxicillin-clavulanate (50.4%), gentamicin (35%), nitrofurantoin (22.4%), and amikacin 1.9%.Mutters *et al*., (2018) also reported that majority of *Escherichia coli* strains (54.5%) were MDR.

Antibiotic sensitivity patterns of *Klebsiella pneumoniae* reveal that the bacterial isolates of *Klebsiella pneumoniae*were resistant to the amikacin; amoxicillin clavulanic acid, ampicillin, cefuroxime, ciprofloxacin, ertapenem, gentamicin, imipenem, meropenem, nitrofurantoin, Piperacillin / tazobactam, trimethoprim sulfamethoxazole while some of the bacterial isolates of *Klebsiella pneumoniae* were susceptible to the amikacin; amoxicillin clavulanic acid, cefuroxime, ciprofloxacin, ertapenem, gentamicin, imipenem, meropenem, piperacillin tazobactam, trimethoprim sulfamethoxazole (Figure 1). The incidence of resistance of bacterial isolates of *Klebsiella pneumoniae*to at least three antibiotics indicates the emergence of MDR *Klebsiella pneumoniae.* Fajfr *et al*., (2017) reported that 47% of *Klebsiella* strains were resistant to ciprofloxacin. Iwu *et al*., (2020) reported the resistance of *Klebsiella pneumoniae* strains against amoxicillin/clavulanic acid (80.6%), ampicillin (88.9%), and cefuroxime (61.1%). Some *Klebsiella pneumoniae* strains were susceptible gentamicin (97.2%), meropenem (91.7%), ciprofloxacin (86.1%), imipenem (83.3%), and norfloxacin (86.1%). Effah *et al*., (2020) reported the resistance of *Klebsiella pneumoniae* to imipenem (65.6%), ciprofloxacin (59.8%) and amikacin (40.8%). Andrade *et al*., (2014) reported the resistance of *Klebsiella pneumoniae* to amikacin and gentamicin. Diaz *et al*., (2004) also reported the resistance of *Klebsiella pneumoniae* to gentamicin (65%), amikacin (47%), and ciprofloxacin (29%).

Antibiotic sensitivity patterns of *Providencia rettgeri* reveal that the bacterial isolates of *Providencia rettgeri* were resistant to the amikacin, amoxicillin clavulanic acid, ampicillin, cefuroxime, ciprofloxacin, ertapenem, gentamicin, imipenem, meropenem, nitrofurantoin, piperacillin tazobactam, trimethoprim sulfamethoxazole while none of the bacterial isolates of *Providencia rettgeri* were susceptible to the antibiotics (Figure 2). The incidence of resistance of bacterial isolates of *Providencia rettgeri* to at least three antibiotics indicates the emergence of MDR *Providencia rettgeri.* Barrios *et al*., (2013) reported the resistance of *Providencia rettgeri* strains to amoxicillin-clavulanic acid, ampicillin, piperacillin/tazobactam, and cephalosporins (Barl *et al*., 2012). Some *Providencia rettgeri*strains are susceptible to imipenem, and meropenem (Pitkin *et al*., 1997). Presence of multidrug resistant *Providencia rettgeri* strains, resistant to imipenem, meropenem, ciprofloxacin, cefepime were reported by Barrios *et al*., (2013) & Aibinu *et al*., (2011). *Providencia rettgeri* primarily cause nosocomial urinary tract infection (O'Hara *et al*., 2000). Godebo *et al*., (2013) reported that 75% of Providencia isolates were multi-drug resistant; cause urinary tract infection (Linhares *et al*., 2013).

Antibiotic sensitivity patterns of *Pseudomonas aeruginosa* reveal that the bacterial isolates of *Pseudomonas aeruginosa* were resistant to the amikacin, amoxicillin clavulanic acid, ampicillin, cefuroxime, ciprofloxacin, ertapenem, gentamicin, imipenem, meropenem, nitrofurantoin, piperacillin tazobactam, trimethoprim sulfamethoxazole while none of the bacterial isolates of *Pseudomonas aeruginosa* were susceptible to the antibiotics (Figure 2). The incidence of resistance of bacterial isolates of *Pseudomonas aeruginosa* to at least three antibiotics indicates the emergence of multi-drug resistant *Pseudomonas aeruginosa.* Hrbacek *et al*., (2020) reported the resistance of *Pseudomonas aeruginosa strains* to cefepime, meropenemor piperacillin/tazobactam, amikacin, and gentamicin. George & Pentti, (2001) reported the resistance of *Pseudomonas aeruginosa* to trimethoprim sulfamethoxazole. *Pseudomonas aeruginosa* belong ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter spp.*) Karlowsky *et al*., (2017) that have been associated with serious health care-associated infections worldwide and frequently display a multi-drug-resistant phenotype. It is intrinsically resistant to many antibiotics due to complementary mechanisms, including low outer membrane permeability, AmpC-beta-lactamase production, and the production of several efflux systems. In addition, it can acquire other resistance determinants, such as beta-lactamases and carbapenemases (Lupo *et al*., 2018), and its survival is enhanced by biofilm formation Tolker-Nielsen *et al*., (2000).

Antibiotic sensitivity patterns of *Staphylococcus aureus* reveal that the bacterial isolates of *Staphylococcus aureus* were resistant to the amikacin, amoxicillin clavulanic acid, ampicillin, cefuroxime, ciprofloxacin, ertapenem, gentamicin, imipenem, meropenem, nitrofurantoin, piperacillin tazobactam, trimethoprim sulfamethoxazole while none of the bacterial isolates of *Staphylococcus aureus* were susceptible to the antibiotics (Figure 2). The incidence of resistance of bacterial isolates of *Staphylococcus aureus* to at least three antibiotics indicates the emergence of MDR *Staphylococcus aureus.*

Hammerberg *et al*., (1986) reported the resistance of *Staphylococcus aureus* strains to amikacin and gentamicin. Deyno *et al*., (2017) also reported the resistance of *Staphylococcus aureus* strains to amoxicillin ampicillin, tetracycline, Methicillin, ciprofloxacin.Watanakunakorn, (1991) reported the resistance of *Staphylococcus aureus* strains to imipenem, gentamicin and rifampin. Chaturvedi *et al*., (2014) reported the emergence and the spread of multidrug-resistance *Staphylococcus aureus* strains lead to nosocomial infections, and become a global threat for the therapeutic management of staphylococcal infections.

Conclusion

The Prolonged and inadequate use of antimicrobial drugs for the treatment of microbial infections has developed the emergence and spread of multidrug resistance (MDR) microbial strains. Multidrug resistance microorganisms become resistant towards the given antimicrobial drugs; contributes to spread of MDR microbes in large community and nosocomial infections (hospital acquired infection) specifically in the immune-compromised patients. Infection with MDR microbial strains increase morbidity, mortality, extended hospitalization of the patients (Cerceo *et al*., 2016). So, the prolonged and inappropriate use of antimicrobial drugs for the treatment of microbial infections must be stopped by using appropriate antimicrobials to reduce the risk for development of MDR microbial strains.

Disclosure

The authors declare that they have no conflict of interests regarding this work.

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