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Burden of Antibiotic Resistance in Common Infectious Diseases: Role of Antibiotic Combination Therapy

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ABSTRACT

Background: Antimicrobial resistance is growing concern particularly for respiratory tract infections, enteric fever, and infections associated with gram-negative bacilli. The present study was conducted to assess antibacterial resistance against pathogenic bacteria. **Methods:** 280 specimens obtained from various department were detected using a BACTEC 9120 blood culture. Antibiotic resistance was determined using Kirby–Bauer disk diffusion and broth microdilution methods. **Results:** Specimens obtained were from emergency in 80, hematology in 26, neurology in 13, nephrology in 24, renal unit in 22, NICU unit in 10, surgery in 75, urology in 18 and Oncology in 12 cases. Ampicillin (AMP) showed maximum resistance against Enterococcus sp. (84%), amoxicillin-clavulanic acid (AUG) showed against staphylococcus aureus(82%), oxicillin (OX) against ConS (65%), Pencilin (PEN) against Enterococcus sp. (83%), piperacillin/tazobactam against staphylococcus aureus (90%) and Ampicillin-Sulbactam (SAM) against staphylococcus aureus (46%). **Conclusion:** Drug resistant and multidrug resistant bacteria are major concern in the effective management of infection. It is essential to select the appropriate empiric therapy which can completely eradicate target microorganisms.

Keywords: Antibiotics, Amoxicillin-clavulanic acid, Microorganisms.

INTRODUCTION

Antimicrobial resistance is growing concern particularly for respiratory tract infections, enteric fever, and infections associated with gram-negative bacilli (GNB).[1] The important factors responsible for this are misuse of antibiotics and paucity of new and effective antimicrobial agents. Centers for Disease Control and Prevention (CDC) stated that antibiotic resistance is responsible for around 2 million infections, more than twenty thousand deaths and, costs $55 billion each year in the United States. The national pharmaceutical sales data on global antibiotic consumption reveals that total antibiotic consumption grew by more than 30%. The greatest increase in antibiotics use was recorded in Low and Middle Income Countries.[2]

Antimicrobials includes a wide variety of drugs and there is continuous investment in the research for new drugs, however, bacteria are rapidly developing resistance to clinically useful antimicrobials and making them ineffective.[3] In India, antimicrobial resistance is far greater problem since many nonqualified persons/ practitioners prescribe antibiotics and many times in inadequate dosage/duration, sometime for unindicted therapy. Self medication is also noted. This has resulted in high incidence of antibiotic resistance.[4]

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There is high possibility of adequate antibacterial coverage by combining two antibacterial agents than single agent. In cohort of culture-positive bacterial septic shock ICU patients, combination therapy of β-lactam with other antibiotic (aminoglycosides, fluoroquinolones, or macrolides/ clindamycin) reported significant decrease in 28-day mortality (36% versus 29%; p=0.0002), mechanical ventilation-free days and pressor free days compared to β-lactam monotherapy. This is attributed to agents having broad spectrum of activity against Gram-negative organisms causing septic shock.5 The present study was conducted to assess antibacterial resistance against pathogenic bacteria.

MATERIALS AND METHODS

The present study was conducted among 280 specimens obtained from various department. The presence of infection-causing agents was detected using a BACTEC 9120 blood culture. Isolation and identification of bacterial strains were performed using conventional biochemical tests. Antibiotic resistance was determined using Kirby–Bauer disk diffusion and broth microdilution methods. Results were interpreted according to CLSI and EUCAST. Results thus obtained was entered in MS excel sheet for statistical inferences using Mann Whitney U test and chi- square test. P value less than 0.05 was considered significant.

RESULTS

[Table 1, Figure 1] shows that specimens obtained were from emergency in 80, hematology in 26, neurology in 13, nephrology in 24, renal unit in 22,

NICU unit in 10, surgery in 75, urology in 18 and Oncology in 12 cases. The difference was significant (P< 0.05).

Table 1: Distribution of specimens

Specimens	Number	P value
Emergency	80	0.02
Hematology	26	
Neurology	13	
Nephrology	24	
Renal unit	22	
NICU unit	10	
Surgery	75	
Urology	18	
Oncology	12	

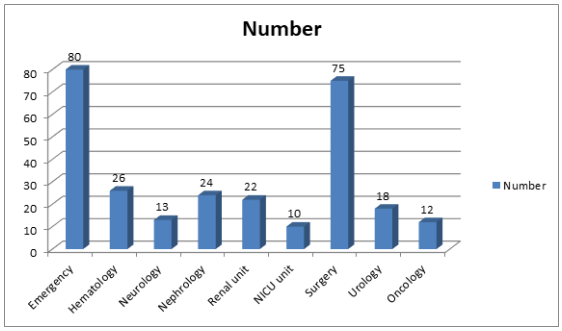

Figure 1: Distribution of specimens

Table 2: Antimicrobial resistance against pathogens

Antibiotics	Staphylococcus Aureus	ConS	Enterococcus Sps	P value
AMP	55%	82%	84%	0.01
AUG	78%	14%	6%	0.04
OX	25%	65%	14%	0.02
PEN	27%	70%	83%	0.03
PTZ	90%	56%	62%	0.05
SAM	46%	12%	40%	0.02

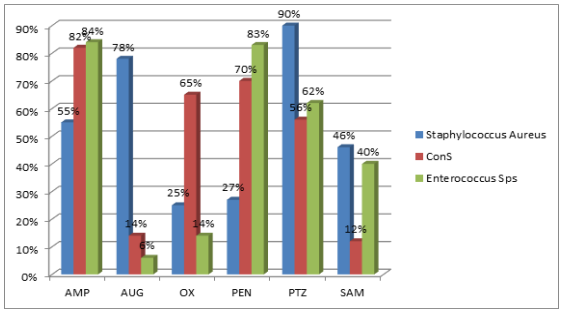

Figure 2: Antimicrobial resistance against pathogens

[Table 2, Figure 2] shows that ampicillin (AMP) showed maximum resistance against Enterococcus sp. (84%), amoxicillin-clavulanic acid (AUG) showed against staphylococcus aureus, oxicillin (OX) against ConS (65%), Pencilin (PEN) against Enterococcus sp. (83%), piperacillin/tazobactam against staphylococcus aureus (90%) and Ampicillin-Sulbactam (SAM) against staphylococcus aureus (46%). The difference was significant (P< 0.05).

DISCUSSION

Human beings have been living unfriendly with a lot of microorganisms that can be a potential cause of infections and diseases.[6] In the case of bacterial infections, due to the introduction of Penicillin for treatment in the early 1940s, there was an improvement. Majority of naturally derived antibiotics are produced from Actinomycetes.[7] In this day, even though the struggle to defeat bacterial pathogens continues, bacteria are evolving ever more clever by manifesting different forms of resistance. In India, antimicrobial resistance is far greater problem since many nonqualified persons/ practitioners prescribe antibiotics and many times in inadequate dosage/duration, sometime for unindicted therapy. Self medication is also noted. This has resulted in high incidence of antibiotic resistance.[8] The present study was conducted to assess antibacterial resistance against pathogenic bacteria.

In present study, specimens obtained were from emergency in 80, hematology in 26, neurology in 13, nephrology in 24, renal unit in 22, NICU unit in 10, surgery in 75, urology in 18 and Oncology in 12 cases. Azimi et al,[9] in their study a total of 1130 different pathogenic bacteria were detected from 14,690 different clinical specimens and the overall detection rate was 7.7% (1130/14,690). Among bacterial pathogen isolated from clinical specimens, 55% (n=622) were GNB and 45% (n=508) were GPB. The predominant GNB isolates were Pseudomonas aeruginosa, Klebsiella spp., Acinetobacter baumannii, Escherichia coli, Enterobacter spp., Citrobacter spp., respectively. Among GPB, CoNS was the most frequent and Enterococcus spp. was found to have low levels of resistance to linezolid. In GNB, most A. baumannii and P. aeruginosa were ceftriaxone resistant. P. aeruginosa was found to have low levels of resistance to levofloxacin and ciprofloxacin.

We found that ampicillin (AMP) showed maximum resistance against Enterococcus sp. (84%), amoxicillin-clavulanic acid (AUG) showed against staphylococcus aureus, oxicillin (OX) against ConS (65%), Pencilin (PEN) against Enterococcus sp. (83%), piperacillin/tazobactam against staphylococcus aureus (90%) and Ampicillin-Sulbactam (SAM) against staphylococcus aureus (46%). Notably seen in treatment of microorganism like Enterobacter, Serratia, or Pseudomonas with combination therapy where induction of β-lactamase by one agent, renders the second agent ineffective. This is more prominent in immunocompromised patients or in infections where localized host defenses may be inadequate such as meningitis and endocarditis. Antagonism may lead to conversion of bactericidal agent to bacteriostatic.[10]

Antibiotic combination therapy permits to explore different molecular targets of individual agents and thereby broaden the spectrum of action.

Antibacterial agents with their broad spectra of activity and multimodal action may prevent emergence of drug resistance. Reduced rate of resistance to rifampin and other anti-tubercular agents is noted due to combination treatment.

Naik et al,[11] in their non-comparative evaluation study reported that fixed dose combination (FDC) of cefixime and oflaxacin provided rapid clinical cure of enteric fever as assessed by the clinical parameters of fever, hepatosplenomegaly and symptoms. Significant improvement was reported in all parameters from baseline with mean fever defervescence time of 4.9 days which showed clinical improvement in short course of 5 days. Faruqui AA,[12] assessed the clinical parameters of fever, sleep interference and respiratory rate in typhoid fever patient. They reported that significant improvement in fever reduction, respiratory rate normalization from baseline to day 3 and day 7 of treatment respectively. Study also reported significant reduction in nocturnal awakening (no sleep interference).

CONCLUSION

Authors found that drug resistant and multidrug resistant bacteria are major concern in the effective management of infection. It is essential to select the appropriate empiric therapy which can completely eradicate target microorganisms.

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