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Antimicrobial Profile of Clinical Isolates in Intensive Care Unit at a Tertiary Care Hospital

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ABSTRACT

Introduction: *Intensive Care Units (ICU's) provides a suitable environment for the proliferation and persistence of multidrug resistant organisms. The burden of nosocomial infections among critically ill patients is much higher in developing countries.* ***Aims and Objectives:*** *The present study was conducted to know the prevalence of bacterial pathogens from various ICU's of a tertiary care hospital and to determine their resistance profile.* ***Materials and methods:*** *A retrospective study was done on 188 isolates collected over a period of 10 months from January 2018 to October 2018. The isolates were identified by the conventional biochemical method and antimicrobial susceptibility testing was performed by Kirby bauer disc diffusion method.* ***Results:*** *The most common gram negative isolate obtained in this study was Klebsiella spp. 90/188 (47.87%), followed by Pseudomonas aeruginosa 22/188 (11.70%), Acinetobacter spp. 21/188 (11.17%), and E. coli 20/188 (10.64%). The predominant gram positive cocci isolated were Enterococcus spp. 9/188 (4.79%). All gram negative bacilli were sensitive to Imipenem. About 23.33% of Klebsiella isolates were resistant to Piperacillin tazobactam and 18.89% to Cefoperazone sulbactam. The most effective drugs against gram negative bacilli were Imipenem, Piperacillin tazobactam, and Cefoperazone sulbactam.* ***Conclusion:*** *This study showed the prevalence of multidrug resistant Klebsiella spp. from various ICU's. These isolates were resistant to third generation cephalosporins, quinolones, and aminoglycosides and were sensitive to carbapenems. Among the non-fermenting gram negative bacilli, the resistance rates were higher for Acinetobacter isolates compared to Pseudomonas aeruginosa.*

Keywords: Intensive care unit, Multidrug resistant, *Klebsiella*, Third generation cephalosporin resistance, Carbapenem sensitive

INTRODUCTION

Intensive Care Units (ICU's) harbour up to 30% of the nosocomial infection in the hospital due to extremely debilitated population group with reduced host defence, multiple procedures and use of invasive devices such as endotracheal intubation, central venous cannulations, mechanical ventilation, and urinary catheterization. The most important hospital acquired the infection in the ICU are catheter related blood stream infections, ventilator associated pneumonia, and catheter associated urinary tract infections [1,2]. The prevalence of infections due to gram negative bacteria such as *Acinetobacter baumannii*, Extended Spectrum Beta lactamases (ESBL's) and Metallo Beta lactamase (MBL) producing *E. coli* and *Klebsiella* and drug resistant gram positive organisms are high in Indian ICU's [3].

Multi Drug resistance (MDR) in *E. coli, Klebsiella* spp. and Proteus are consequently emerging in hospital settings and decreasing efficacy among gram negative isolates to cephalosporins, carbapenems, and fluoroquinolones have been reported from various parts of the world. The emergence of MDR is often dedicated to the excessive use of

broad spectrum antibiotics which may select and favor overgrowth of pre-existing resistant flora or by transfer of resistance to susceptible bacteria by mutation [3,4]. Health care workers are carriers of multidrug resistant organisms and suboptimal infection control measures may facilitate the spread of these strains.

Hospital acquired strains of *Pseudomonas* and *Acinetobacter* spp. are resistant to a broad range of antibiotics due to intrinsic resistance to antimicrobial agents. *Pseudomonas* develops resistance rapidly under selection pressure and hyper production of enzymes such as beta lactamases and DNA gyrases, active efflux pumps and permeability changes. *Acinetobacter* spp. can cause opportunistic infection in critically ill patients. These organisms are inherently resistant to cephalosporins, penicillin's and aminoglycosides [5,6].

The risk of acquiring infection with the resistant organism is positively correlated with severity of illness and debility, age, prolonged stay in ICU, prior use of antibiotics and exposure to indwelling prosthetic devices [1,7]. Infection with antibiotic resistant organisms can be associated with the poor outcome if the initial selection of antibiotic does not provide coverage. Strict infection control measures, regular surveillance of local antimicrobial flora and resistance pattern and optimum antimicrobial utilization in ICUs is important for better patient outcome and to prevent the emergence of multidrug resistance [7]. The present study was done to identify the prevalence of bacterial pathogens and their antimicrobial resistance pattern from different ICU's of a tertiary care hospital.

PATIENTS AND METHODS

A retrospective analytical study was conducted over a period of 10 months from January 2018 to October 2018. A total of 188 clinical isolates obtained from various clinical samples from different ICU's [Medical ICU, Surgical ICU, Neonatal ICU, and Cardiothoracic ICU] were included. The specimens were inoculated on Blood agar, Chocolate agar, and Mac Conkey's agar and incubated overnight at 37°C. Bacterial isolates were identified by standard biochemical methods [8].

Antimicrobial susceptibility testing was done on these isolates by Kirby Bauer disk diffusion method using the following antibiotics [9]:

- For gram negative organisms, Piperacillin/Tazobactam (100/10 µg), Ceftriaxone (30 µg), Ceftazidime (30 µg), Cefepime (30 µg), Cefotaxime (30 µg), Imipenem (10 µg), Cefoperazone/sulbactam (75/30 µg), Gentamicin (10 µg), Amikacin (30 µg) and Ciprofloxacin (5 µg), Levofloxacin (5 µg) and Tigecycline (15 µg) were used
- For gram positive cocci, Erythromycin (15 µg), Penicillin (10 U), Ampicillin (30 µg), Clindamycin (2 µg), Cotrimoxazole (25 µg), Cefoxitin (30 µg), Linezolid (30 µg), Teicoplanin (30 µg) and Vancomycin (30 µg) were tested. *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853 were used as quality control strains

RESULTS

The most predominant isolate obtained in this study was *Klebsiella* spp. About 90/188 (47.87%), followed by *Pseudomonas aeruginosa* 22/188 (11.70%), *Acinetobacter* spp. 21/188 (11.17%) and *E. coli* 20/188 (10.64%). Among the gram positive isolates, *Enterococcus* spp. 9/188 (4.79%) was the common isolate obtained followed by *Staphylococcus aureus* 7/188 (3.72%) (Figure 1).

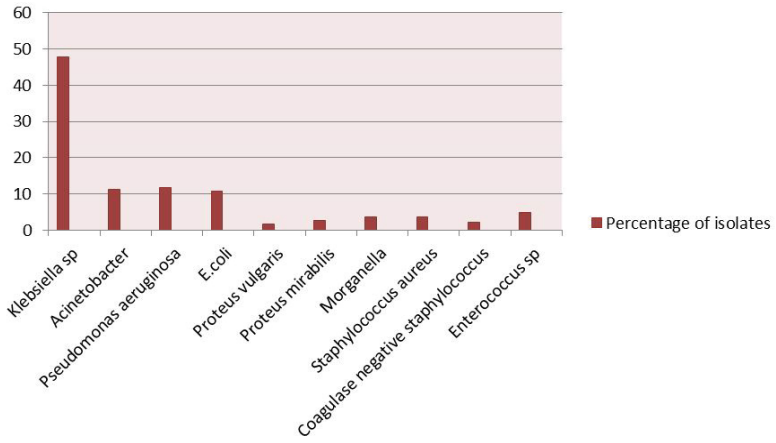

Figure 1 Percentage distribution of isolates from clinical samples

Out of 188 isolates studied, 100 were from patients of MICU (Figure 2). The most common isolate from MICU was *Klebsiella* spp. (49%) followed by *Acinetobacter* spp. (15%) and *E. coli* (13%). Out of 24 bacterial isolates from SICU, *Klebsiella* spp. (50%) was the predominant organism followed by *Pseudomonas aeruginosa* (8.33%) and *E. coli* (8.33%).

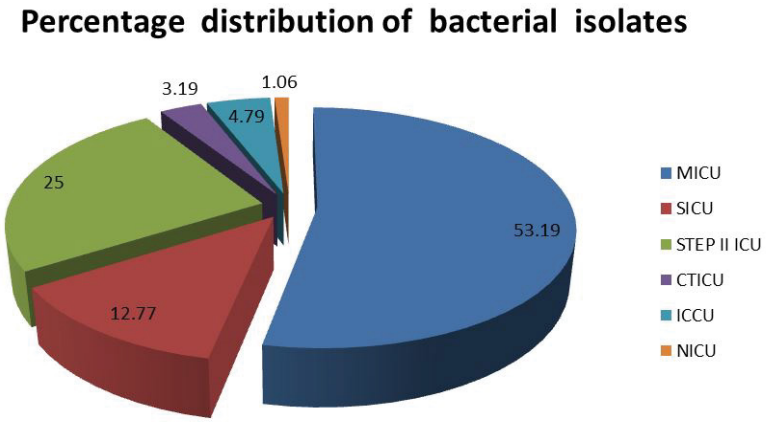

Figure 2 Distribution of bacterial isolates from various ICU's

Out of 168 Gram negative isolates, 24 (14.29%) showed resistance to Piperacillin/Tazobactam and 21 (12.5%) to Cefoperazone/sulbactam. Of the cephalosporins tested, 116 (69.05%) gram negative bacilli were resistant to Ceftazidime, 124 (73.81%) to Ceftrioxone and 98 (58.33%) showed resistance to Cefepime. Among the fluoroquinolones, 61 (36.31%) were resistant to Ciprofloxacin, 68 (40.48%) to ofloxacin and 72 (42.86%) were resistant to Levofloxacin. Among the aminoglycosides studied, 78 (46.43%) were resistant to Amikacin and 76 (45.24%) to Gentamicin. All gram negative bacilli showed 100% sensitivity to Imepenem.

A total of 20 gram positive cocci were studied. About 45% isolates were resistant to Ampicillin, 30% to Gentamicin and levofloxacin respectively, About 25% isolates were resistant to Ciprofloxacin and 20% isolates showed resistance to Amikacin and Clindamycin. About 27.27% (3/11) of *Staphylococcus* isolates were resistant to Cefoxitin.

Among the *Klebsiella* isolates studied,71.11% showed resistance to cefepime, 48.89% to Amikacin and 35.56% to Ciprofloxacin. All isolates were sensitive to Imipenem. About 23.33% of *Klebsiella* isolates were resistant to Piperacillin tazobactam and 18.89% to Cefoperazone sulbactam (Figure 3).

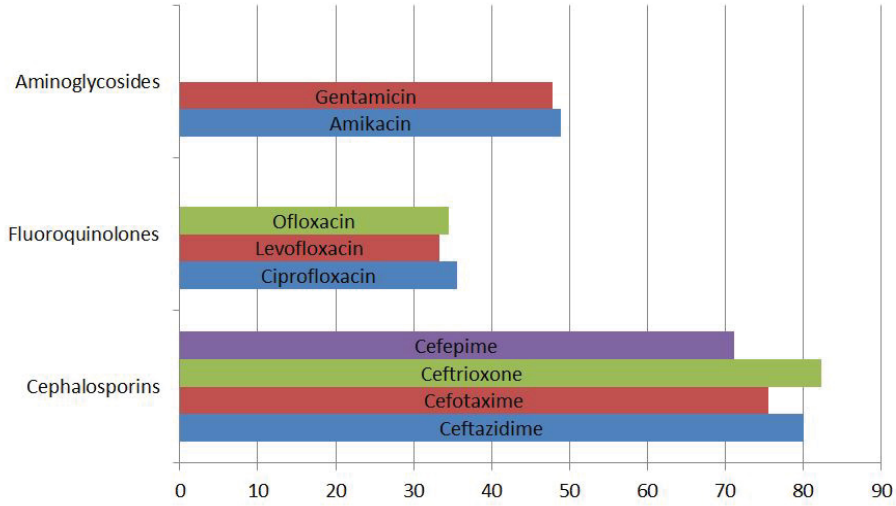

Figure 3 Antimicrobial resistance pattern of *Klebsiella* spp

Out of 21 *Acinetobacter* isolates in our study, 38.09% were resistant to cefepime, 57.14% to Gentamicin and 52.38% showed resistance to Ciprofloxacin. All isolates showed 100% sensitivity to Imipenem, Piperacillin tazobactam and Cefoperazone sulbactam (Figure 4).

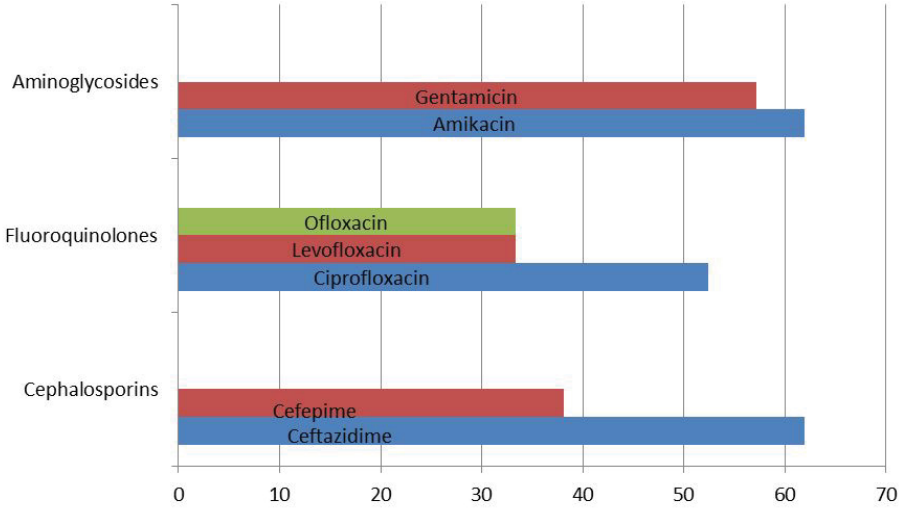

Figure 4 Antimicrobial resistance pattern of *Acinetobacter* spp.

Among the *Pseudomonas aeruginosa* isolates, 72.73% were resistant to Levofloxacin and 18.18% to Ciprofloxacin, 40.91% isolates showed resistance to Amikacin and 36.36% to Gentamicin. All isolates were sensitive to Imipenem, Piperacillin tazobactam and Cefoperazome sulbactam (Figure 5).

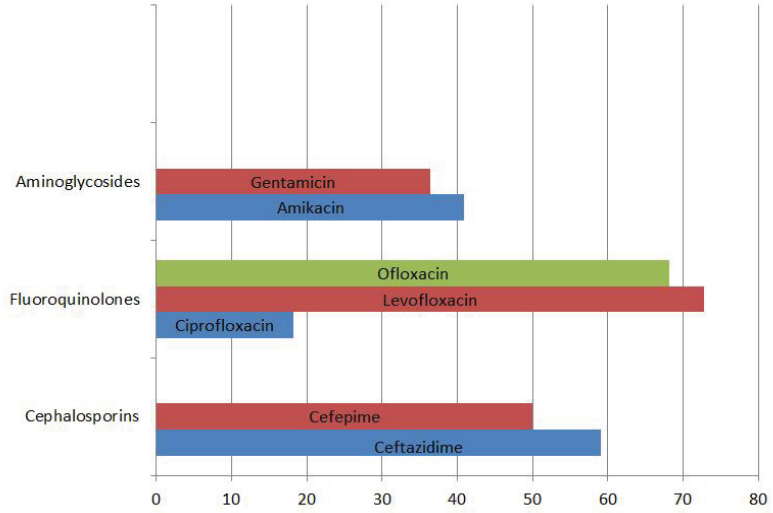

Figure 5 Antimicrobial resistance pattern of *Pseudomonas aeruginosa*

Out of 20 *E. coli* isolates, 45% showed resistance to Ciprofloxacin, 35% to cefepime and 20% isolates were resistant to Amikacin. All isolates were 100% sensitive to Imipenem, Piperacillin tazobactam and Cefoperazome sulbactam (Figure 6).

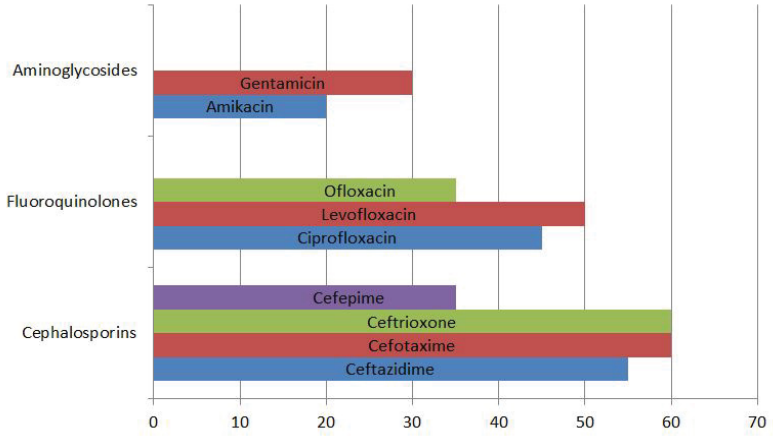

Figure 6 Resistance pattern of *E.coli* isolates

One out of 3 isolates of *Proteus vulgaris* were resistant to Piperacillin tazobactam and Cefoperazone sulbactam. Six out of 7 isolates of Morganella were resistant to Cefepime and Amikacin, 3 isolates showed resistance to Cefoperazone sulbactam and 2 isolates to Piperacillin tazobactam.

Among the gram positive cocci, 44.44% Enterococci showed resistance to aminoglycosides and Penicillin respectively. About 22.22% of isolates were resistant to Ciprofloxacin. Among the *Staphylococcus aureus* isolates, 42.86% showed resistance to Cefoxitin.

DISCUSSION

The incidence of nosocomial infection is 5 to 10 times more among patients admitted in ICU's than in general wards. In developing countries, overcrowding in hospitals, counter antibiotic use, excessive use of invasive devices and suboptimal infection control practices contribute to the development of drug resistance [1,4].

In the present study, 89.36% isolates from ICU's were gram negative bacilli. Various Indian studies have reported gram negative isolates as a major cause of infection in ICU [10-13]. The predominant gram negative isolate obtained in our study was *Klebsiella* spp. (47.87%), followed by *Pseudomonas aeruginosa* (11.70%), *Acinetobacter* spp. (11.17%), and *E. coli* (10.64%). Among the gram positive isolates, *Enterococcus* (4.79%), was the common isolate obtained followed by *Staphylococcus aureus* (3.72%). A similar study from Western India reported that major

infections in ICU were due to *Acinetobacter, E. coli, Klebsiella*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Streptococcus* spp. [14,15].

In our study, *Klebsiella* spp. was the most common isolate from MICU and SICU. In a North Indian study by Javeri, et al., *E. coli* was the predominant isolate from MICU and SICU [16]. In a similar study from North India by Pawar, et al., *Klebsiella* and *Acinetobacter* were the most frequent isolates from Intensive Care Units, with 48.66% *Klebsiella* isolates susceptible to Imipenem [17]. In the present study, all isolates of *Klebsiella* spp. were sensitive to Imipenem. In a North Indian study, Sheth, et al., have reported *Klebsiella* and *Pseudomonas* as predominant gram negative bacilli with 100% sensitivity to Imipenem [18]. In a similar study among urinary pathogens of ICU, Garg, et al., have reported 81.2% isolates sensitive to Imipenem [19].

Among gram negative isolates of Enterobacteriaceae family, *Klebsiella* spp. was found to be more resistant as compared to isolates of *E. coli*. About 79.26% Klebsiella isolates were resistant to third generation cephalosporins, 34.44% to quinolones and 48.34% showed resistance to aminoglycosides, whereas 58.33% *E. coli* isolates were resistant to third generation cephalosporins, 43.33% to quinolones and 30% showed resistance to aminoglycosides tested. This is in accordance with another South Indian study where a high degree of resistance to cephalosporins (67.6%-89.9%) and quinolones (74.1%-90.1%) and aminoglycosides (48.2%-76.2%) was reported [20]. Another North Indian study has reported 44% *E. coli* isolates resistant to third generation cephalosporins [21]. In our study, resistance was significantly lower with Betalactamase inhibitor, where 18.89% of *Klebsiella* isolates were resistant to Cefoperazone sulbactam. One out of 3 isolates of *Proteus vulgaris* and 3 out of 7 sulbactam. All isolates of *E. coli* were sensitive to Cefoperazone sulbactam. isolates of Morganella showed resistance to Cefoperazone

Among the non-fermenting gram negative bacilli, the resistance rate was higher among *Acinetobacter* spp. compared to *Pseudomonas* isolates. About 61.90% *Acinetobacter* spp. were resistant to Ceftazidime, 52.38% to Ciprofloxacin and 61.90% to Amikacin. Among the *Pseudomonas* isolates 59.09% were resistant to Ceftazidime, 18.18% to Ciprofloxacin and 40.91% to Amikacin. All isolates were sensitive to Imipenem and Cefoperazone sulbactam. A North Indian study has reported 100% isolates of *Pseudomonas aeruginosa* resistant to Ceftazidime [18]. A similar study by Gupta, et al., have reported 40% isolates of *Acinetobacter* and *Pseudomonas* resistant to Imipenem [22]. Multidrug resistant *Acinetobacter* spp. have been reported as predominant pathogen from nosocomial bacteremia and Ventilator associated pneumonia [13]. A study by Mythiri, et al., have reported that the incidence of infections increases with the use of invasive devices and higher resistance rate among *A. baumannii* isolates compared to other nosocomial pathogens from ICU [12].

The most effective drugs against gram negative bacilli were found to be Imipenem, Piperacillin tazobactam, and Cefoperazone sulbactam. Enterococci were the predominant gram positive cocci isolated from our study. About 44.44% of isolates showed resistance to aminoglycosides and Ampicillin. 42.86% *Staphylococcus aureus* showed resistance to Cefoxitin. A South Indian study reported 40.6% of *S. aureus* isolates resistant to cefoxitin [20].

There is a need for continuous surveillance in ICU's for multidrug resistant strains to prescribe appropriate empirical treatment and to assess the effectiveness of infection control practices.

CONCLUSION

The present study showed a prevalence of multiple drug resistant strains of *Klebsiella* spp. from ICU's. These isolates showed resistance to third generation cephalosporins, quinolones, aminoglycosides and 100% sensitivity to carbapenems. The resistance rate of *Klebsiella* isolates was higher as compared to *E. coli* studied. Among non-fermenting gram negative bacilli, resistance to cephalosporins, quinolones, and aminoglycosides was higher among *Acinetobacter* spp. compared to *Pseudomonas aeruginosa*.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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