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Original Research Article

Multidrug-Resistant Pathogens in Medical ICU Patients

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Abstract:

Introduction: The risk of infections increases in ICU patients and even the drug resistance of pathogens is more common in ICU patients than other hospital ward patients. This study which is high lightening the MDR pathogens and their antibiotic susceptibility pattern among intensive care unit patients in this community will help to draft an empirical antibiotic therapy.

Materials And Methods: In this prospective study a total number of 302 clinical isolates were identified after receiving samples under aseptic precautions including sputum, ET aspirates, urine, blood, BAL, pus and other fluids were collected from the patients and processed according to CLSI guidelines.

Results: Out of 226 isolates predominant pathogens were Klebsiella species (30.08%), Acinetobacter species (28.7%), and Pseudomonas aeruginosa (17.69%). Ps.aeruginosa, Klebsiella, Acinetobacter pathogens isolation was high from endotracheal aspirates, sputum and bronchoalveolar lavage samples. Around 60% of Gram negative isolates were sensitive to piperacillin+tazobactum, ceftazidime+clavulanic acid and around 70% of isolates showed sensitivity to ertapenem, meropenem, ciprofloxacin, amikacin. Out of 16 isolates of Staphylococcus aureus, 10 (62.5%) were MRSA.

Conclusion: Research works focusing on antimicrobial resistance especially gram negative bacilli is utmost important in India as they can cause outbreaks in ICU settings which is going to be add on morbidity and mortality of critically ill patients.

Keywords: Drug Resistant Pathogens, Intensive care unit patients, Antibiotic sensitivity testing.

Introduction

The Infectious Diseases Society of America (IDSA) recognizes antimicrobial resistance as "one of the greatest threats to human health worldwide [1]". Multidrug resistant organisms (MDRO) are bacteria that have become resistant to certain antibiotics, and these antibiotics can no longer be used to control or kill the bacteria.

MDRO could be MRSA (Methicillin resistant Staphylococcus aureus), VRE (Vancomycin resistant Enterococci), CRAB (Carbapenem resistant Acientobacter Baumannii), Pseudomonas aeruginosa resistant to ceftazidime or carbapenems, Extended Spectrum Beta Lactamases (ESBL) producing Enterobacteriaceae. Other organisms were considered MDR if they were found to be resistant to at least three of the following antibiotic classes: antipseudomonal cephalosporins /penicillins, macrolides, carbapenems, fluoroquinolones, aminoglycosides, colistin, and tigecycline. Infections of multidrug resistant pathogens are becoming a major public health problem. Patients affected with multi drug resistant (MDR) pathogens pose more serious consequences when compared to patients affected with non MDR infections [2]. MDR pathogens causing various infections in ICU patients which could be either community acquired or hospital acquired. They can cause pneumonia, urinary tract infections, septicaemia, and wound infections.

ICU patients are critically ill patients due to the seriousness of the problem, low immunity, on steroids or broad spectrum antimicrobials, and ventilation; all these factors increase the incidence of infections among these patients. Even colonizers or opportunistic infections enhance their pathogenicity if the host lowers their immunity. The risk of infections increases in ICU patients and even the drug resistance of pathogens is more common in ICU patients than other hospital ward patients [3, 4].

The correct choice of empirical treatment is necessary to prevent severity and to improve mortality among ICU patients [5]. Inappropriate antimicrobial empiric therapy may cause delay in treatment and serious health consequences to patient; more vulnerable threat is increase in the drug resistant among pathogens [6]. So this study which is high lightening the MDR pathogens and their antibiotic susceptibility pattern among intensive care unit patients in this community will help to draft an empirical antibiotic therapy.

The aim of the present study is to know the various MDR pathogens in intensive care unit patients, their isolation in different clinical samples and its antibiotic sensitivity pattern in this community.

Materials and Methods

In this prospective study a total number of 302 clinical isolates were identified from patients under admission in medical ICU at Siddhartha Medical College, Vijayawada, from January 2022 to August 2023. All the samples were processed according to central laboratory standard institute, among them 226 MDR pathogenic isolates were obtained and included them in study. Study population included individuals of both sexes and all age groups. The present prospective study was taken up after the review and approval by the IEC (Institutional Ethical Committee). An informed consent was taken from the patients or guardians or attendee's. The study was conducted at the department of microbiology, Siddhartha Medical College in association with critical care medicine department.

Inclusion criteria:

1. Samples which are taken prior to start the antimicrobial therapy.

2. All clinical samples including urine, blood, pus, sputum, BAL, ET secretions, and other body fluids.

Exclusion criteria:

Mixed growth of 3 or more types (probably contaminated sample).

Sample Collection: Under aseptic precautions, samples including sputum, ET aspirates, urine, blood, BAL, pus and other fluids were collected from the patients and transported immediately to the laboratory.

Sample Processing: All samples were processed for microscopic examination, culture and antibiotic susceptibility testing according to CLSI protocols. Specimens were inoculated on to nutrient agar, 5% sheep blood agar, Macconkey agar and chocolate agar. After incubation at 37^0C for 24-48 hours colony count was done and expressed as number of colony forming units per ml for BAL, ET aspirates and urine samples. Pathogen identification up to species was performed by colony characterization, biochemical reactions and inoculation on special media. Bacterial growth with a colony count $\geq 10^5$ cfu/ml (for urine), $\geq 10^5$ cfu/ml (for ET aspirates), $\geq 10^5$ cfu/ml (for BAL) were considered as pathogens.

Antibiotic susceptibility testing (AST):

AST is done by modified Kirby bauer disc diffusion method on Mueller Hinton agar based on CLSI guidelines [7,8]. The quality check done with the quality control strains. – Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853 and S.aureus ATCC 25923.

Antibiotic disks used for Gram positive organisms testing were penicillin (10U), gentamicin (10µg), amoxyclav (30 µg), amikacin (30 µg), ciprofloxacin (5 µg), erythromycin (5µg), clindamycin (2µg), cotrimoxazole (1.25 µg/23.75 µg), cefoxitin (30 µg), linezolid (30 µg), vancomycin (30µg) and teicoplanin (30µg).

Gram negative isolates antibiotics were: amoxyclav (30 µg), piperacillin+tazobactum (100/10 µg), ceftazidime (30 µg), ceftriaxone (30 µg), cefipime (30 µg), Ceftazidime+clavulanic acid (30/10 µg), piperacillin+tazobactum (30/6 µg), levofloxacin (5 µg), meropenem (10 µg), amikacin (30 µg), tigecycline (15 µg) and colistin (50 µg). Standard Quality Control strains were used as a part of testing. Multi Drug testing was done for all strains isolated according to CLSI guidelines.

Data Collection: All details pertaining to patients including age, sex, type of specimen, ICU admission number, socioeconomic status, previous history of hospitalization, antibiotic intake, organism isolated, sensitivity pattern of antibiotics was collected and entered into Microsoft excel sheet. All descriptive quantitative variables were expressed as numbers and percentages.

Results

Among 302 isolates, 226 were detected and categorized as Multidrug resistant bacteria ie., 74.8%. Out of 226 isolates predominant pathogens were Klebsiella species (30.08%), Acinetobacter species (28.7%), and Pseudomonas aeruginosa (17.69%). Other organisms detected were Escherichia coli (10.17%), Staphylococcus aureus (7.07%), Enterobacter species (3.53%), and Citrobacter species (2.65%) (Table 1).

Table 1: Percentage of Multidrug resistant isolates in ICU patients

Organism	No. of isolates	Percentage (%)
Klebisella species	68	30.08
Acinetobacter species	65	28.7
Pseudomonas aeruginosa	40	17.69
Escherichia coli	23	10.17
Staphylococcus aureus	16	7.07
Enterobacter species	8	3.53
Citrobacter species	6	2.65
Total	226	100

The pathogen detection rate from different clinical specimens were as follows pus 30.9%, urine 19%, endotracheal aspirates (ET aspirates) 16.6%, sputum 11.9%, blood 9.5%, catheter tips 7% and body fluids 4.7%. Ps.aeruginosa, Klebsiella, Acinetobacter pathogens isolation was high from endotracheal aspirates, sputum and bronchoalveolar lavage samples (Table 2).

Table 2: Sample wise distribution of various pathogens isolated from critically ill patients

Specimen	Klebsiella spp	Acinetobacter spp	Ps.aeruginosa	Esch.coli	S.aureus	Enterobacter spp	Citrobacter spp	Total (%)
Sputum	18	10	8	0	6	4	2	48 (21.2)
ET aspirates	25	36	16	0	2	0	0	79 (34.9)
BAL	8	14	6	0	2	0	0	30 (13.2)
Urine	10	0	5	16	3	1	2	37 (16.3)
Blood	4	5	3	5	1	0	0	18 (7.9)
Pus	0	0	0	0	2	1	2	5 (2.2)
Body fluids	2	0	0	2	0	2	0	6 (2.6)
Catheter tips	1	0	2	0	0	0	0	3 (1.3)
Total	68	65	40	23	16	8	6	226 (100)

Overall gram negative isolates antibiotic susceptibility testing was tabulated in Table 3. Around 60% of Gram negative isolates were sensitive to piperacillin+tazobactum, ceftazidime+clavulanic acid and around 70% of isolates showed sensitivity to ertapenem, meropenem, ciprofloxacin, amikacin (Table 3). We didn't get colistin resistant isolate at our hospital.

Table 3: Antibiotic susceptibility pattern of gram negative isolates (n=210)

Antibiotics	Sensitive	%	Intermediate	%	Resistant	%
Amoxycillin	32	15.2	5	2.3	173	82.4
Amoxyclav	116	55.2	14	6.6	80	38.1
Ceftazidime	86	40.9	14	6.6	110	52.3
Ceftriaxone	72	34.2	5	2.3	133	63.3
Cefipime	99	47.2	8	3.8	103	49
Ceftazidime-clavulanic acid	124	59	22	10.4	64	30.4
Piperacillin-tazobactum	128	60.9	15	7.1	67	31.9
Levofloxacin	163	77.6	5	2.3	42	20
Amikacin	185	88.1	8	3.8	17	8.1
Meropenem	160	76.1	8	3.8	42	20
Ertapenem	156	74.2	6	2.8	48	22.8
Tigecycline	198	94.2	0	0	12	5.7
Colistin	210	100	0	0	0	0

Gram positive isolates of MDR pathogens isolated in critically ill patients were Staphylococcus aureus only. Out of 16 isolates of Staphylococcus aureus, 10 (62.5%) were Methicillin Resistant Staphylococcus aureus (MRSA). 80-90% of Staphylococcus aureus isolates were sensitive to cotrimoxazole, ciprofloxacin, amikacin, clindamycin, meropenem, linezolid, teicoplanin and vancomycin (Table 4).

Table 4: Antibiotic susceptibility pattern of gram positive isolates (n=16)

Antibiotics	Sensitive	%	Intermediate	%	Resistant	%
Pencillin	4	25	0	0	12	75
Amoxyclav	11	68.7	1	6.2	3	18.7
Cefoxitin	10	62.5	0	0	6	37.5
Erythromycin	10	62.5	0	0	6	37.5
Cotrimoxazole	13	81.2	0	0	3	18.7
Ciprofloxacin	14	87.5	0	0	2	12.5
Amikacin	15	93.7	0	0	1	6.25
Clindamycin	14	87.5	1	6.2	1	6.2
Meropenem	13	81.2	0	0	3	18.7
Linezolid	16	100	0	0	0	0
Teicoplanin	16	100	0	0	0	0
Vancomycin	16	100	0	0	0	0

Discussion

In this study Out of 226 isolates predominant pathogens were Klebsiella species (30.08%), Acinetobacter species (28.7%), and Pseudomonas aeruginosa (17.69%) were predominant MDR pathogens in ICU patients. In similar to this study Han Y et [9] al did a study on multidrug resistant pathogen in ICU patients revealed that gram negative bacteria were predominant isolates accounting for 91.91% and the remaining 8.09% were Staphylococcus aureus strains, among which Acinetobacter baumannii was the most common isolate with the percentage of 35.97 followed by Ps.aeruginosa (24.74%), Esch.coli (21.79%) and Klebsiella pneumoniae (99.42%).

Many of the studies observations was gram negative bacteria were predominant pathogens in India [10,11]. Gram negative microorganisms are usually commonest multidrug resistant pathogens and they cause severe complications in a short time for instance septic shock due to high pathogenicity expressed by lipid A component producing endotoxin and multiple antibiotic resistance properties like porins, enzymes, biofilm formation. Even mortality rate was highest among patients affected by MDR gram negative bacteria (17.7%) when compared with patients affected by gram positive bacteria (10.8%) especially in ICU patients [12]. 26.9% of patients were died due to MDR gram negative microorganisms and 16.0% of patients were died due to gram positive bacteria [12].

The pathogen detection rate from different clinical specimens were as follows pus 30.9%, urine 19%, endotracheal aspirates (ET aspirates) 16.6%, sputum 11.9%, blood 9.5%, catheter tips 7% and body fluids 4.7% in the present study and most the isolates were detected from respiratory samples such as BAL, sputum and ET aspirates. Han Y et al [9] noted most number of isolates in sputum i.e., 55.02% followed by blood (25.17%) and drain fluid (5.65%), urine (4.98%). Adel El Mekes et al [13] did a study on MDR pathogens in adult ICU documented the mortality rate due to MDR pathogens was 12%, the MDR bacteria isolated was 41% among which A.baumannii was predominant pathogen. Among various infections 39% were respiratory tract infections, 7% of post-operative infections, 4% of nosocomial meningitis and 3% urinary tract infection.

Around 60% of Gram negative isolates were sensitive to piperacillin+tazobactum, ceftazidime+clavulanic acid and around 70% of isolates showed sensitivity to ertapenem, meropenem, ciprofloxacin, amikacin. Out of 16 isolates of Staphylococcus aureus, 10 (62.5%) were Methicillin Resistant Staphylococcus aureus (MRSA) in this study. Han Y et al [9] study showed 15.28% of E.coli isolates were resistant to imipenem, 20.38% and 26.3% of Pseudomonas aeruginosa isolates resistant to meropenem and imipenem respectively, 20.2% and 19.9% of Pseudomonas aeruginosa isolates resistant to meropenem and imipenem respectively, and MRSA isolates were 64.71%. Adel El Mekes et al [13] reported *A. baumannii* resistant to imipenem (ABRI) 70%, followed by multi-resistant Enterobactereacae species (18%), *P. aeruginosa* resistant to ceftazidime 7%, and S. aureus resistant to methicillin 5%. In similar to this study Klebsiella and E.coli were predominant multidrug pathogens in intensive care patients as reported by India and Nepal studies [14,15].

Few research studies on MDR pathogens revealed that MDR bacteria increase the mortality and extended stay at hospital. Gandra S et al [12] noted raise in mortality rate up to 32-50% among XDR K.pneumoniae bacteremia patients. Patients infected with A.baumannii MDR pathogen were associated with 2.81 times higher odds of mortality than similar susceptible infections. However MDR Pseudomonas aeruginosa affected cases mortality is not significantly associated with Non MDR Pseudomonas aeruginosa patients. Cosgrove SE et al [16] reported MRSA infected patients linked to higher mortality rates among S.aureus infections; they also observed that there is an association

between drug resistant infections and increase in morbidity and hospital costs.

Acinetobacter and Pseudomonas aeruginosa are most commonly interlinked to device related infections; they are also commonly isolated in ICU settings [17,18]. Acinetobacter and Pseudomonas infections resistant to multiple drug classes including beta lactam/beta lactamase inhibitors might be due to enzymatic activation, alteration of target, acquiring resistance genes from other organisms, porins, and biofilm formation.

Conclusion

Research works focusing on antimicrobial resistance especially gram negative bacilli is utmost important in India as they can cause outbreaks in ICU settings which is going to be add on morbidity and mortality of critically ill patients. Health authorities should strengthen the policies of infection control and antimicrobial stewardship monitoring help us to control the MDR pathogens emergence.

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