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A study on Clinico-Epidemiological Profile of Bacterial infections in Intensive care unit and its implications on empiric therapy

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Abstract

Background: To study the bacteriological profile of infections in patients admitted to ICU and to determine the antibiotic susceptibility patterns of the bacterial isolates. This study was done as Prospective study of 2 months period with a study population of patients admitted to Intensive care unit of a tertiary care hospital.

Materials and Methods: Selection criteria for this study was with an inclusion criteria of patients admitted to ICU for various reasons and developing infection within 48 hours of admission and the exclusion criteria was patients admitted to ICU and not developing infection and patients admitted to ICU with an already existing infection. All the samples were processed as per standard microbiology guidelines.

Results: Gram negative bacilli were predominant with 73.35% as compared to Gram positive cocci of 9.97% of the total aerobic bacteria grown from various samples of patients admitted in Intensive care unit. *Escherichia coli* were more common with 26.67% of the total bacteria isolated. This was followed by *Acinetobacter* species 16.67%, *Pseudomonas aeruginosa* 16.67%, *Klebsiella pneumoniae* 6.67% and *Enterobacter* species6.67%. Among the Gram positive cocci, *Staphylococcus aureus* was more commonly isolated with 16.67% followed by *Enterococcus* species 6.67% and *Streptococcus* species 3.30%. Antibiotic resistance was observed by most bacteria to Penicillins, third generation Cephalosporins, Fluoroquinolones like Ciprofloxacin, Cotrimoxazole.

Conclusion: Multi-drug resistance is a major hurdle in treating patients admitted to ICU setting in a hospital. Regular surveillance of antibiotic susceptibility patterns is very important for setting orders to guide the clinician in choosing empirical or directed therapy of infected patients.

Keywords: Intensive care unit, Multi-drug resistance, Gram negative bacilli, Nosocomial infections, *Escherichia coli.*

Introduction

Nosocomial infection is infection acquired in hospital due to hospitalisation for various health reasons and is one of the most important worldwide health-care problems. Each nosocomial infection adds 5-10 days to the affected patient's time in the hospital. Nosocomial infections have increased the morbidity and mortality of hospitalised patients and especially the ones admitted in an intensive care setup. The Centre for Disease Control and Prevention (CDC) defines the intensive care unit associated infections as those that occur after 48 hours of ICU admissions or within 48 hours after the transfer of the patients from the ICU.[1,2]

The intensive care unit (ICU) often is called the epicenter of infections, due to its extremely vulnerable population (reduced host defences deregulating the immune responses) and increased risk of becoming infected through multiple procedures and use of invasive devices distorting the anatomical integrity-protective barriers of patients (intubation, mechanical ventilation, vascular access, etc.). In addition, several drugs may be administered, which also predispose for infections, such as pneumonia, e.g., by reducing the cough and swallow reflexes (sedatives, muscle relaxants) or by distorting the normal nonpathogenic bacterial flora (e.g., stress ulcer prophylaxis).[3]

The rate of nosocomial infections in the ICU is rising, mainly because of the increasing use of invasive procedures which are performed in patients admitted to ICU. Intensive care units (ICUs) worldwide are encountering the highest density of nosocomial infections and the spread of antibiotic-resistant pathogens responsible for emerging infection problems in the hospital. Use of different kinds of catheters, endotracheal tubes, oxygen supplying apparatuses and surgeries are the most common pathway of nosocomial infections transmission.[4] The therapeutic interventions which are associated with infectious complications include indwelling catheters, sophisticated life support, intravenous fluid therapy, prosthetic devices, immunosuppressive therapy and the use of long-term broad spectrum antibiotics leading to a spectrum of multidrug resistant pathogens.

Along with the problem of nosocomial infection goes the burden of "multidrug" antimicrobial resistance (MDR). The ongoing emergence of resistance in the community and hospital is considered a major threat for public health. Due to the specific risk profile of its residents, the ICU also is deemed the epicenter of resistance development. The ICU has even been described as a factory for creating, disseminating, and amplifying antimicrobial resistance.[5] Incidence of multi-drug resistant bacterial infections is increasing

especially in patients in Intensive care units. It is of utmost importance to restrict the administration of antibiotics to effectively control the increase of antibiotic resistance among bacteria. As such, the presence of MDR boosts the deleterious impact of nosocomial infection.

Multidrug-resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-resistant *Acinetobacter baumannii*, Enterobacteriaceae that produce extended-spectrum beta-lactamases and/or carbapenemases (ESBL producers), and carbapenem-resistant *Pseudomonas aeruginosa*, are all being isolated with increasing frequency in ICUs.[6] They are of significant concern because they restrict the therapeutic options, cause treatment failures and are increasing in occurrence worldwide.

In a study done by Dasgupta S et al[7] on nosocomial infections in the intensive care unit, they found that pneumonia was the most frequently detected infection (62.07%), followed by urinary tract infections and central venous catheter associated bloodstream infections. In their study, Gram negative Enterobacteriaceae were the most frequently isolated pathogens (n=15; 37.5%) closely followed by *Pseudomonas* species (n= 14; 35%, *Pseudomonas aeruginosa*= 13, *Burkholderia cepacia*= 1).

Materials and Methods

This study was done as Prospective study with a study population of patients admitted to Intensive care unit of a tertiary care hospital for a 2 month study period.

Selection criteria for the study was with an inclusion criteria of patients admitted to ICU for various reasons and developing infection within 48 hours of admission and the exclusion criteria was patients admitted to ICU and not developing infection and patients admitted to ICU with an already existing infection.

The infections were considered to be intensive care unit associated, if they occurred within 48 hours of admission to the ICU. The following signs and symptoms will be considered:

1. Fever > 38^0C, leukocytes >10,000/cu.mm
2. Any symptom suggestive of infection in the body

The known risk factors like the duration of ICU stay, mechanical ventilation and catheterization, the use of broad spectrum antibiotics and immunosuppressive drugs and the extremes of age and preexisting diseases were looked for.

The specific site related investigations included blood cultures and the cultures of intravenous catheter tips, urine and indwelling catheter tips, suction catheter tips, endotracheal secretions, sputum etc. All the samples were processed as per standard microbiology guidelines.[8]

Initial Gram's staining and microscopic examination of the samples was done. All samples were inoculated in 5% sheep blood agar plate and MacConkey agar plate and incubated at 37^0 C for 24 hours. The bacterial isolates grown were identified by microscopic examination and various biochemical reactions as per standard protocol.[9]

Antibiotic susceptibility testing was done for the isolates on Mueller Hinton agar plates by Kirby-Bauer disc diffusion method according to CLSI guidelines. The various antibiotics that were tested against are:

For Gram positive isolates: Penicillin (10 units), Ampicillin (10 µg), Amoxyclav (20/10 µg), Cefoxitin (30µg), Gentamicin (10µg), Amikacin (30µg), Ciprofloxacin (5µg), Erythromycin (15µg), Clindamycin (2µg), Co-trimoxazole (1.25/23.75 µg), Vancomycin, Linezolid (30µg).

For Gram negative isolates: Ampicillin (10µg), Amoxyclav (20/10 µg), Cefotaxime (30 µg), Ceftazidime (30µg), Cefipime (30µg), Gentamicin (10µg), Amikacin (30µg), Ciprofloxacin (5 µg), Co-trimoxazole (1.25/23.75 µg), Piperacillin (100 µg), Piperacillin-tazobactum (100/10 µg), Imipenem (10µg).

The susceptibility was determined by measuring the zone diameter around each antibiotic disc and compared with the recommended zone size for reporting as susceptible or resistance as per CLSI guidelines. The antibiogram pattern of the isolates was evaluated and was used to suggest the antibiotic that can be used for empiric therapy.

Statistical analysis: The data was analysed using SPSS version 16 for descriptive statistics.

Results

Sputum and suction tip are specimen from respiratory tract and they together formed 36.66% of the total specimen followed by urine culture of 26.66%, Blood culture with growth formed 23.33% and pus culture of 13.3%. Thus, Pneumonia was predominant followed by Urinary tract infection, Bloodstream infection from the Intensive care unit during our study period.

Gram negative bacilli were predominant which formed 73.35% as compared to Gram positive cocci of 9.97% of the total aerobic bacteria grown from various samples of patients admitted in Intensive care unit. Among the Gram negative bacilli, *Escherichia coli* were more common with 26.67% of the total bacteria isolated. This was followed by *Acinetobacter* species 16.67%, *Pseudomonas aeruginosa* 16.67%, *Klebsiella pneumoniae* 6.67% and *Enterobacter* species 6.67%. Among the Gram positive cocci, *Staphylococcus aureus* was more commonly isolated with 16.67% followed by *Enterococcus* species 6.67% and *Streptococcus* species 3.30%.

Antibiotic Susceptibility results: All the strains of *Escherichia coli* were resistant to Ampicillin. Among the 8 strains 6 were resistant to cefepime, cefuroxime, ceftazidine and cefotaxime. 1 was an ESBL producer. 5 were resistant to cotrimoxazole. 4 were resistant to

gentamicin. Only 1 strain was susceptible to ciprofloxacin. Two strains from urine were sensitive to nitrofurantoin. 6 strains were sensitive to Piperacillin-tazobactum combination and 2 strains were resistant to it. 7 strains were sensitive to Amikacin and 1 strain was resistant to it. All strains were sensitive to Imipenem. There was one strain that was resistant to all other antibiotics and was sensitive to Imipenem only.

Acinetobacter species was isolated from 5 samples (2 blood cultures, 1pus, 1 suction tip and 1sputum). All strains were resistant to Ampicillin, Cefuroxime, Ceftazidine, Cotrimoxazole. 4 were resistant to Ciprofloxacin and 1 was sensitive to it. 3 were resistant to Gentamicin and Piperacillin- tazobactum combination. 2 strains showed resistance to Amikacin and 3 strains showed resistance to Imipenem. There was one strain which was sensitive only to Amikacin and Chloramphenicol and resistant to other antibiotics including Piperacillin-tazobactum. 2 strains were resistant to all the antibiotics tested.

Pseudomonas was isolated from 3 urine, 1 suction tip, 1 pus sample. All strains were resistant to Piperacillin, 4 were sensitive to Piperacillin-tazobactum and 1 was resistant to Piperacillin-tazobactum. All were resistant to Cefuroxime, 3 were resistant to Ceftazidine, Cefotaxime and Cefipime, 2 were sensitive to Ceftazidine, Cefotaxime and Cefipime. 4 strains were sensitive to Imipenem and 1 was resistant to Imipenem. All were sensitive to Amikacin.

Klebsiella pneumoniae was isolated from suction tip and sputum. Both the strains were resistant to Ampicillin, Cefuroxime, Ceftazidine, Cefotaxime, Cefepime, Cotrimoxazole. One strain was resistant to Piperacillin- tazobactum. Both strains were sensitive to Amikacin, Gentamicin and Imipenem, Chloramphenicol.

Enterobacter species was isolated from blood cultures.[2] Both were resistant to Ampicillin, Cephalosporins. One strain was resistant to Amikacin, Gentamicin and Piperacillin-tazobactum. Both strains were sensitive to Imipenem and Chloramphenicol.

Staphylococcus aureus was isolated from 5 samples (2 pus, 2 blood, 1 suction tip). All 5 isolates were sensitive to Methicillin, Amikacin, Gentamicin, Vancomycin. Three isolates were resistant to Clindamycin and Erythromycin, Ciprofloxacin. All were resistant to Cotrimoxazole. None of the isolates were MRSA.

Enterococcus species was isolated from 2 samples of urine. Both were resistant to Ampicillin, Ciprofloxacin and Erythromycin. They were sensitive to Gentamicin, Amikacin, Vancomycin.

Streptococcus pyogenes was isolated from 1 sputum sample which was sensitive to Penicillins, Aminoglycosides.

Table 1: Specimen wise distribution of bacteria grown in aerobic culture

Aerobic Bacteria	Total no	Blood culture	Urine culture	Sputum culture	Suction tip	Pus culture
GNBs						
Escherichia coli	8	1	3	2	2	0
Acinetobacter sp	5	2	0	1	1	1
Pseudomonas aeruginosa	5	0	3	0	1	1
Klebsiella pneumoniae	2	0	0	1	1	0
Enterobacter sp	2	2	0	0	0	0
GPCs						
Staphylococcus aureus	5	2	0	0	1	2
Enterococcus sp	2	0	2	0	0	0
Streptococcus sp	1	0	0	1	0	0
Total	30	7	8	5	6	4

Discussion

In our study, infected specimen from respiratory tract formed 36.66% of the total specimen followed by urine culture of 26.66%, blood culture with growth formed 23.33% and pus culture of 13.3%. Thus infection of the respiratory tract was predominant followed by urinary tract infection, bloodstream infection in patients admitted to the Intensive care unit during our study period. This correlates with other similar studies.

In the Extended Prevalence of Infection in Intensive Care II study,[10] the most frequently reported sites for ICU acquired infections were the lungs (64%), abdominal (19%), and blood stream (15%). Data from the United States National Nosocomial infections surveillance system showed that the nosocomial pneumonia accounted for 31% of all nosocomial infections followed by urinary tract infections and blood stream infections.[11]

Although recent years have seen swings in the pathogen pattern toward Gram-positive bacterial infections,[12,13] still, most studies report that more than half of the nosocomial infections occurring in the ICU are due to Gram-

negative bacteria.[10,11] In the study of Dasgupta et al[7] too, the most commonly isolated organisms were Gram-negative Enterobacteriacea followed closely by Pseudomonas species.

Our study also revealed that Gram negative bacilli were predominant compared to Gram positive cocci of the total aerobic bacteria grown from various samples of patients admitted in Intensive care unit. This finding is also observed in many studies done in other hospital settings.[14,15]

Again in a study done by Hassanzadeh P et al[16] Gram-negative bacteria were significantly more involved in infections than were Gram-positive bacteria ($P<0.05$). The most frequently reported infections were urinary tract infections. The most frequently isolated bacteria were Pseudomonas (39.1%), which was mainly sensitive to amikacin and ceftazidime.

In our study among the Gram negative bacilli isolated, *Escherichia coli* was predominant followed by *Acinetobacter* species, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Enterobacter* species. *Escherichia coli* showed resistance to Penicillins, third generation Cephalosporin group of antibiotics, Cotrimoxazole, Aminoglycosides like Gentamicin and Fluoroquinolones like Ciprofloxacin. Resistance was also noted to beta lactam/beta lactamase inhibitor drug like Piperacillin-tazobactum yet few were sensitive to it. Amikacin proved to be a good antibiotic against many drug resistant strains except one strain each of *E.coli* and *Enterobacter* species and 2 strains of *Acinetobacter* species. Most of the bacteria were sensitive to Imipenem thus making treatment of the particular infections possible to the clinicians. *Acinetobacter* species proved to be a multi-drug resistant bacteria and Colistin was the only choice left to treat. Most often multi-drug resistant *Acinetobacter* species is a hospital pathogen and is acquired by the patient during stay in ICU setting with an invasive device. The multi-drug resistant *Acinetobacter* species is a major hurdle in treating patients in the ICU setting. This is also observed in a study done by Goel et al.[17] *Acinetobacter* spp. are inheritably resistant to cephalosporins, penicillin's, and aminoglycosides, and especially cause opportunistic infections in critically ill patients.[18] Some strains *of A. baumannii* have been detected that are resistant to all antibiotics.[18,19]

Amikacin, Imipenem and Colistin were found useful to handle the multi-drug resistant Gram negative bacilli in our study.

Antibiotic use contributes to the emergence of antimicrobial resistance in Gram positive as well as Gram negative bacteria. In developing countries, antibiotics are prescribed for most of patients after hospitalization, often inappropriately. The prescribing of antibiotics in the ICU is usually empiric. Most bacteria isolated from Intensive care units are multi-drug resistant.[20,21]

Therefore, the ongoing surveillance of antibiotic susceptibility patterns of predominant bacteria is a fundamental effort to monitor changes in susceptibility patterns and to guide the clinician in choosing empirical or directed therapy appropriately, especially in ICU setting. Appropriate antibiotic utilization in Intensive care units is crucial not only in ensuring an optimal outcome, but also in preventing the emergence of multi drug resistance bacteria.

Regular surveillance of antibiotic susceptibility patterns is very important for setting orders to guide the clinician in choosing empirical or directed therapy of infected patients. Thus there is a need of a hospital infection prevention protocol in every hospital with a working hospital infection control team to ensure that hospital acquired infection by these multi-drug resistant bacteria in critical care patients can be prevented.

Joined efforts of healthcare providers, hospital administrators, policy makers, and patients will certainly be necessary to reduce and optimize the overall antibiotic consumption. "Antibiotic stewardship," or the optimization of antibiotic usage for therapy and prophylaxis, is certainly a keystone to tackle this problem. Restriction of antibiotic consumption by a sensible hospital drug policy and promotion of a more rational use of antibiotics should halt the rising of MDR.[22] Therefore, additional efforts are needed to improve education and training, for example, by implementing guidelines in infection control and antibiotic prescription. Yet, surveillance and monitoring of trends in MDR, with timely updates of local susceptibility data should be implemented as well.[22,23]

Conclusion

Prevention programs should be tailored to the local epidemiology and organized hospital-wide and not only localized to the ICU. A team approach should be preferred, including ICU physicians and nurses, but also the infection control team, and the team especially needs a strong cooperation with infectious disease specialists and clinical microbiology teams.

Infections due to multi-drug resistant microorganisms are a rising problem, especially in the ICU where even sensitive pathogens already cause additional morbidity, mortality, and hospital costs. Therefore, additional efforts are needed in the future to win this battle.

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