

Study of Nosocomial Infections and Molecular Diagnosis of Bacterial Resistance in Patients Admitted in Intensive Care Units of Regional Cancer Center

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Abstract

Background: Nosocomial infection (NI) or health care associated infection is defined as an infection developing in hospitalized patients after 48 hours, neither present nor in incubation at the time of their admission. The objectives of this study were to determine the frequency and pattern of nosocomial infection in patients admitted in ICU of tertiary cancer hospital and to detect the etiological agent with their antimicrobial resistance by molecular methods and potential source of infection.

Methods: This was an observational study conducted from January 2014 to March 2014. Total 100 different types of samples were collected from 330 admitted patients who developed clinical evidence of infection after 48 hrs. of admission in ICUs. Organisms causing infections were identified and they were further subjected for Antibiotic susceptibility testing by MIC and molecular diagnosis of bacterial resistance using reverse hybridization technique.

Results: During the study periods, 100 (30.3%) out of 330 patients acquired nosocomial infection. Wound infection was seen in 49%, followed by respiratory tract infection in 19% and blood stream infection in 16%, other infections were urinary tract and gastrointestinal infections. Antibiotic resistance profile revealed that majority of bacterial isolates were resistance to multiple antibiotics. Different types of resistance mechanisms were observed in isolated organisms by molecular methods (reverse hybridization). Amongst Gram negative pathogens, 40.90% were ESBL producers, 6.81% were positive for Carbapenamases production. 25% of Gram positive cocci were MRSA positive.

Conclusion: Patients admitted in ICUs are at higher risk of acquiring nosocomial infection. Isolated pathogens are multidrug resistant. Standard guidelines for infection prevention should be followed in ICU to reduce the nosocomial infection.

Keywords: Imidazole; Heterocyclic; Aromatic; Anti-convulsant; Antiulcer; Antiallergic; Antiviral

Introduction

Infection is a major factor determining clinical outcome among patients requiring intensive care unit (ICU) support. The causes of infection within ICU are multi-factorial, and consequences depend on source involved, organisms associated, underlying morbidity, timeliness and appropriateness of the treatment/interventions received [1,2]. It is associated with increased morbidity and mortality. Nosocomial infection (NI) or health care associated infection is defined as an infection developing in hospitalized patients after 48 hrs., neither present nor in incubation at the time of their admission [3]. NI is amongst the most difficult problems confronting clinicians who deal with severally ill patients. The incidence of NI is estimated at 9% to 37% in tertiary care hospitals reaching up to 28% in ICU of different population and different definitions [4].

Clinical profile of patients requiring intensive care support

Any clinical event, which compromises the airway, breathing, circulation (ABC) of a patient or breaches significantly the integrity and functioning of tissues and organs (post-surgery, post trauma) may results in the requirement of ICU or high dependency unit (HDU) support [1].

Sources of hospital infections

Predisposing factors for infection in the hospital are: A susceptible host, a microbe capable of producing an infection, an environment that is congenial for the multiplication of the microbe. The source of the

infecting organism may be exogenous – either from another patient or a member of the hospital staff, or from the inanimate environment in the hospital; or it may be endogenous from the patient's own flora at the time of infection may include organisms brought into the hospital at admission. Infecting organisms may spontaneously invade the tissues of the patient or may be introduced into them by surgical procedures, instrumental manipulation or nursing procedures. The inanimate environment of the hospital that acts as an important source comprises of: Contaminated air, water, food and medicaments, used equipment and instruments, soiled linen and hospital waste (Biomedical waste) [5].

Infections among patients in the intensive care unit

Infection among ICU patients might be community acquired (viral encephalitis, bacterial meningitis, pneumonia, endocarditis, intra-visceral abscesses, and urinary tract infections-UTIs) or hospital and health care associated infections (surgical site infections-SSIs, hospital acquired pneumonia-HAP, catheter related blood stream infections-

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CRBSI, and catheter associated UTI) [6].

Common Health Care Associated Infections in Intensive Care Unit Patients are as follows [1]:

1. Ventilator associated pneumonia.
2. Skin and soft tissue infection.
3. Blood stream infections (BSIs) including catheter related.
4. Urinary tract infection.

In the past, *staphylococci*, *pseudomonas*, and *Escherichia coli* have been the main cause of nosocomial infection. Nosocomial pneumonia, surgical wound infections, and vascular access-related bacteremia have caused the most illness and death in hospitalized patients; and intensive care units have been the epicenters of antibiotic resistance. In addition to their association with increased morbidity and mortality, nosocomial infections are frequently associated with drug-resistant micro-organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended spectrum - lactamase (ESBL)-producing gram-negative bacteria, Carbapenamases producers and multi drug resistance *Acinetobacter* which can pose considerable therapeutic problems [6,7].

This study is to determine the frequency and pattern of nosocomial infection in cancer patients admitted in ICU of tertiary cancer hospital and to detect the etiological agent with their antimicrobial resistance by molecular methods and potential source of infection.

Materials and Methods

This hospital-based study was conducted at Intensive care units of The Gujarat Cancer and Research Institute (GCRI), a tertiary cancer care hospital. All patients who are admitted in the ICUs for more than 48 hours with different complaints and presentations and develop clinical evidence of infection that is not originate from patient's original admitting diagnosis, was included in this study.

Critical patients from different oncology departments like: medical, surgical, gynecology, neurology, pediatric, nephrology, urology and emergency which referred for monitoring, observation and management were included. A Performa was designed and used for data collection. This study was approved by Ethics and Scientific board of hospital.

From study periods of January 2014 to March 2014, total 100 different types of samples were collected from patients who are having history of fever after 48 hours of admission, like urine from urinary catheter, stool, peripheral blood, catheter blood, tracheal tube aspirate, wound secretion from surgical wound or bedsore. All samples were transferred to a microbiology laboratory by trained technicians according to standard microbiology protocol. After receiving samples in laboratory all samples were followed according to standard CLSI

S.no	Age group (yrs.)	No. of males	No. of females
1	1-10	4	3
2	11 - 20	3	0
3	21 - 30	6	6
4	31 - 40	5	7
5	51-60	10	11
6	61-70	11	19
7	71-80	9	4
8	81-90	1	1
Total		49	51

Table 1: Demographic data of patients, n=100.

guidelines for identification of etiological agent using automated bacteriological system (Vitek 2 compact, Biomerieux). Antibiotic sensitivity testing was done by MIC technique using same system.

Resistance mechanism detected by molecular methods. Then organisms are subjected to DNA extraction by Nucleo pore fungus/bacteria kit (Genetix Biotech Asia Pvt. Ltd.) and then they were subjected for detection of different resistance gene by PCR and reverse hybridization method like mec A gene for MRSA, OXA family for Carbapenamases, TEM and SHV gene detection for ESBL producers using Multiplex PCR module and Multiplex Hybridization module (Krishgen biosystem).

Result

During the study periods of January 2014 to March 2014, total of 100 patients were identified who acquired infection during their stay in all ICUs, like medical ICU, post-operative ICU, surgical ICU, bone marrow transplant unit from total 330 admitted patients. Demographic data of patients who acquire infection are summarized in Table 1. Out of 100 patients 48 were from urban area and 52 from rural area. Patient's Unit wise data is mentioned in Table 2. Common infections observed in such patients is given in Table 3. Nosocomial infections caused by different pathogens like *E. coli*, *Klebsiella*, and *Pseudomonas* etc. details are given in Table 4. Prevalence of antibiotic resistance in Nosocomial infection given in Table 5. Antibiotic resistance profile revealed that majority of bacterial isolates was resistance to multiple antibiotics. Different types of resistance mechanisms were observed in isolated organisms by molecular methods. Data are given in Table 6.

Discussion

Cancer patients having treatment in intensive care units are at a higher risk of nosocomial infection due to different causes like disruption of barriers to infection by endotracheal intubation and tracheostomy, urinary bladder catheterization and central venous catheterization.

Nosocomial infection in critical areas

The percentages of nosocomial infection in our study were 30.30%. In recent study by Muhammad et al., the frequency of nosocomial

S.no	Unit of referral	No. of patients
1	Surgery	45
2	Medicine	21
3	Gynecology	16
4	Pediatric	10
5	Neurology	8

Table 2: Patient's unit wise data, n=100.

S.no	Type of Infection	Type of samples received	No. of Patients
1	wound infection	Pus, Pus swab	49
2	respiratory infection	Sputum, BAL, ET secretion, Tracheostomy, ET tip etc	19
3	Blood stream infection	Peripheral and Catheter blood	16
4	Urinary tract infection	Urine	10
5	Gastrointestinal infection	Stool	6

Table 3: Pattern of nosocomial infection in critical care areas, n=100.

S. no	Organism	Wound Infection	Respiratory Infection	Blood Stream Infection	Urinary tract Infection	Gastrointestinal Infection	Total
1	<i>E. coli</i>	21	2	3	6	6	38
2	<i>Klebsiella</i>	7	4	4	2	0	17
3	<i>Pseudomonas aeruginosa</i>	8	4	2	2	0	16
4	<i>Acinetobacter</i>	6	4	1	0	0	11
5	<i>Enterobacter</i>	2	2	0	0	0	4
6	<i>Burkholderia</i>	0	0	2	0	0	2
7	<i>S. aureus</i>	2	0	2	0	0	4
8	CONS	3	3	2	0	0	8
Total		49	19	16	10	6	100

Table 4: Nosocomial infection cause by different pathogens, n=100.

Antibiotics	<i>E. coli</i> (n=38)	<i>Klebsiella</i> (n=17)	<i>Pseudomonas aeruginosa</i> (n=16)	<i>Acinetobacter</i> (n=11)	<i>Enterobacter</i> (n=4)	<i>Burkholderia</i> (n=2)	<i>S. aureus</i> (n=4)	CONS (n=8)
B- lactam								
N=100								
Ampicillin	20	11	0	0	2	1	4	4
Amoxicillin/ Clavulanic Acid	14	10	0	0	2	1	0	0
Piperacillin/tazobactam	12	9	4	2	2	1	0	0
Cefuroxime	22	11	0	0	1	1	0	0
Ceftriaxone	22	11	0	0	1	1	0	0
Cefoperazone/Sulbactam	10	9	5	3	2	1	0	0
Cefepime	27	11	5	6	2	1	0	0
Amino Glycosides								
Amikacin	4	9	4	3	2	1	0	0
Gentamycin	14	8	3	7	2	1	3	5
Quinolone								
Ciprofloxacin	24	12	4	7	1	0	3	4
Levofloxacin	2	3	5	6	2	2	2	3
Carbapenems								
Imipenem	5	9	4	6	2	1	3	5
Meropenem	5	9	3	2	2	1	2	4
Ertapenem	3	7	0	0	0	0	0	0
Others								
Aztreonam	0	0	0	4	1	0	0	0
Minocycline	0	0	8	2	0	0	0	0
Tigecycline	0	4	8	2	1	0	0	0

Table 5: Prevalence of antibiotic resistance in nosocomial infection.

S.no	Organism group	Resistance pattern	Number	Percentage
1	GNB (n=88)	ESBL	36	40.9
2		Carbapenemases	6	6.81
3	GPC (n=12)	MRSA	2	16.6
4		VRSA	0	0

Table 6: Resistance mechanism in isolated organisms by molecular methods.

infection in Immuno-compromised patients in ICU was 39.7% [8]. Common infections observed in ICUs are wound infection, respiratory infection including VAP, bloodstream infection, urinary tract and gastrointestinal infections. The most common infection in ICU was wound infection (49%) followed by respiratory infection (19%).

Wound infection is the most common because surgical patients are highest admitted in ICU (49/100). Most common isolated organism from wound infection is *E. coli* followed by *Pseudomonas*.

Nosocomial pneumonia is the second most common nosocomial infection in critical patients. Frequencies of VAP reported in different studies are 9%, 18% and 21%. In current study, 19% patients acquired VAP in ICU. The predominant pathogens causing VAP are *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella*, coagulase negative *staphylococcus*.

Blood stream infection is also a common infection observed in ICU patients. Frequency of blood stream infection in our study was 16%, while in the study by Muhammad et al., it was 27% [9]. It was high in their study because study was conducted amongst nephrology patients. The pathogens isolated from these patients are *Klebsiella*, *E. coli*, *Pseudomonas aeruginosa*, *Burkholderia*, *Staphylococcus aureus*.

In our study, urinary tract infection found in 10 patients, was caused by *E. coli*, *Pseudomonas* and *Klebsiella* and gastrointestinal infection in six patients was caused by *E. coli*.

Prevalence of antibiotic resistance in nosocomial infection

Antibiotic resistance profile revealed that majority of bacterial isolates were resistance to multiple antibiotics (Table 5). More than 50% of *E. coli* was resistant to all B-lactams and B-lactams inhibitors, Quinolones. *Klebsiella* shows 70% resistance to B-lactams and B-lactams

inhibitors, Quinolones and to amino glycosides. *Acinetobacter* shows 50% resistance to amino glycosides, Quinolones and to Imipenem. Resistance to antibiotics in Gram positive bacteria was less as compared to Gram negative pathogens. In the study conducted by Kailash Mulchandani et al., from south India shows similar resistance pattern in ICU [10]. In their study *E. coli* shows 60-90% of resistance to B-lactams and B-lactams inhibitors, Quinolones and to amino glycosides. *Klebsiella* and *Acinetobacter* show 44% to 83% and 45% to 90% of resistance to same class of antibiotics respectively.

Antibiotic resistance mechanism in isolated pathogens

Amongst Gram negative pathogens, 40.90% were ESBL producers, 15.90% were Amp C producer and 4.54 to 6.81% were positive for Carbapenamases production. 25% of Gram positive cocci were MRSA positive.

Conclusion

Infections that develop in people who have cancer or who are getting cancer treatment can be more serious than those in people who are otherwise healthy. They can also be harder to treat. Joint efforts of microbiologist and clinicians can save more lives.

Key action plan of clinical microbiology for infection control in ICUs [1]:

1. Regular Rounds in ICU by microbiologist [11].
2. Prompt information about critical microbiology results.
3. Change, stoppage and optimization of antibiotic therapy as per local antibiotic policy.
4. Use of 'Care bundles' in ICU for management of ICU infection [12-14].
5. Antibiotic resistance, audit and policy implantation [15].

We concluded as follows:

- a. Critically ill cancer patients admitted to ICU are at a greater risk of acquiring nosocomial infection.
- b. The common infections observed in our study were wound infection, nosocomial pneumonia including VAP, blood stream infection.
- c. *E. coli*, *Klebsiella* and *Pseudomonas* were most common pathogens in ICU, and they were multidrug resistant.
- d. Production of ESBL and Carbapenamases were high in ICU pathogens.

It is suggested that proper nursing care, sterilization and disinfection of equipment and proper handling of invasive devise are

the best guidelines to control ICU infection. Education and awareness among health care workers as well as adherence to standard guidelines for prevention of nosocomial infection should be followed to reduce frequency of nosocomial infection in intensive care unit. Further studies regarding surveillance of nosocomial infection are required and it will play an important role in the monitoring of infection and assessment of action plans to prevent ICU infection.

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