Research article

Prevalence of nosocomial infections by multidrug resistant organisms in patients admitted to the critical care area of the Regional Cancer Center, Gujarat, India

FM Patel[1], MM Vegad[2]

Sri Lankan Journal of Infectious Diseases 2019 Vol.9 (2):129-140

DOI: http://doi.org/10.4038/sljid.v9i2.8261

Abstract

Introduction: Nosocomial infection is a main cause of mortality and morbidity among patients admitted in different critical areas [post-operative, Intensive Care Units (ICU), and for bone marrow transplantation (BMT)] in a hospital. Availability of a clinical microbiology service for patients admitted to critical areas can significantly improve clinical outcome.

Methods: During the study period (January 2014 to March 2014) 330 patients from different oncology departments were admitted to critical areas of the hospital. Conventional and molecular methods were used to determine resistance mechanisms [methicillin resistance (MRSA), extended spectrum β-lactamase (ESBL), carbapenemases and Amp C) of clinically significant isolates.

Results: Of 330 patients admitted to critical care areas during the study period, 84 (25.4%) were identified as having acquired infection during their stay in the critical areas. Of these 84 patients 16 had dual infections. The mean age of patients was 44.5 yrs. The most common infection in the ICU was wound infection (49%) followed by respiratory infection (19%). The most common isolated organisms from wound infection were *Escherichia coli* (42.8%) followed by *Pseudomonas aeruginosa* (14.2%). The majority of bacterial isolates were multidrug resistant (MDR). Using both conventional and molecular methods of 88 isolated Gram negative bacilli (GNB), 45.9% were found to be ESBL producers, 16 % Amp C producers and 4.5% carbapenemase producers. The prevalence of MRSA was 30.7% (4/13) by a conventional method and 23% (3/13) using a molecular method.

Conclusion: From this study, we concluded that cancer patients admitted to critical areas are at a greater risk of acquiring nosocomial infection. However, the increasing prevalence of MDR-GNBs, especially those resistant to cephalosporins and carbapenems, could contribute to both

[1]*Ph.D Scholar, Gujarat University; Department of Microbiology, The Gujarat Cancer & Research Institute, Asarwa, Ahmedabad, Gujarat, India*
[2]*Department of Microbiology, B. J. Medical College, Asarwa, Ahmedabad, Gujarat, India*

Address for correspondence: Dr Foram Patel, Department of Microbiology, The Gujarat Cancer & Research Institute, Asarwa, Ahmedabad, Gujarat, India Telephone: +9898070240 Email: drforam9@gmail.com

https://orcid.org/0000-0002-6692-2724

Received 8August 2019 and revised version accepted 20 October 2019

increased morbidity and mortality due to non-response to routinely used first line antibiotics and resultant recourse to colistin.

Keywords: MDR, Critical care area, Cancer patients

Introduction

Nosocomial infection is a main cause of mortality and morbidity among patients admitted to the different critical areas (post-operative, ICU, and BMT) in hospital. Knowledge with regard to clinical microbiology of patients admitted in these critical areas can significantly improve clinical outcome.[1]

The critical care support offered in hospitals is classified as general ICU, post-operative ICU, cardiothoracic ICU, neuro-ICU, neonatal/paediatric ICU and bone marrow transplant unit.

Infection is a major problem in patients with cancer. Recent advances in technology, such as bone marrow and hematopoietic stem cell transplantation and the use of chemotherapeutic regimens have added to the number of patients who are able to survive malignancy but with seriously impaired host defense mechanisms that compromise their ability to resist or contain infections.[2]

Common infections in critical care unit patients[3] include ventilator associated pneumonia, skin and soft tissue infection, blood stream infections (BSIs) including catheter related and urinary tract infection.

Burden of Infection in critical areas:

Infection rate in indoor patients range from 5% to 17%.[4] In critical areas, where frequent use of invasive procedures and multiple therapies expose patients to an increased risk, prevalence rates are even higher.[5] Patients in critical areas account for about 25% of all hospital infections. The prevalence of infections acquired in critical care areas is significantly higher in developing countries than in developed countries, varying between 4.4% and 88.9%.[6] A recently published World Health Organization (WHO) review showed that "in low- and middle-income countries, the frequency of ICU-acquired infection is at least 2–3 times higher than in high-income countries; device-associated infection densities are up to 13 times higher than in the USA".[7] Critically ill patients with severe sepsis in intensive care units (ICUs) require lengthy and expensive management, with an associated high mortality, with rates ranging from 30% to 50%.[7] Graft versus host disease (GVHD) occurs in 20% to 70% of bone marrow transplant(BMT) recipients receiving grafts from different donor sources and are associated with bacteremia.[8]

This study includes discussions on a variety of common clinical-microbiological problems faced in the critical areas and detection of their etiological agents and resistance patterns by conventional and molecular methods.

Materials and methods

This prospective study was carried out from January to March 2014 at the Department of Microbiology, Gujarat Cancer & Research Institute (GCRI), which is a tertiary care cancer hospital.

All patients who were admitted to the critical care areas with different complaints and presentations and who developed clinical features of infection were included in this study.

Different types of clinical samples were collected from these patients depending on the system involved. All samples were transferred to the microbiology laboratory according to standard microbiology protocols.

In the laboratory, all samples were processed according to standard guidelines for isolation of the causative microorganism(s). All isolates were identified on an automated bacterial identification and sensitivity system (Vitek 2 compact, Biomerieux) using Gram negative and Gram positive identification cards. Antibiotic sensitivity testing (AST) was performed using different AST cards on the same system and the minimum inhibitory concentration (MIC) of antibiotics for each isolate recorded.

Presence of MRSA, ESBL, carbapenemases and Amp C in all isolates was investigated using conventional and molecular methods (Table 1).

Table 1: Conventional and molecular methods for identification of antimicrobial resistance (AMR)

AMR	Conventional Method	Molecular method	Target gene
MRSA	Cefoxitin screening test	PCR + Reverse hybridization	mec –A, ileS, lukS – lukF
ESBLs	Double disc potentiating test	PCR + Reverse hybridization	bla_{TEM}, bla_{SHV}, bla_{CTX-M}
Carbapenemases	Modified Hodge test	PCR + Reverse hybridization	OXA-51, OXA-23, OXA-40, OXA-58
Amp C	Cefoxitin inhibition test	--	--

Results

During the study period 330 patients from different oncology departments (medical, surgical, gynecology, neurology, pediatric, and emergency) were admitted to critical areas. Of these patients, 84 (25.4%) developed clinical signs and symptoms of infection during their stay in the critical areas. Of these 84 patients, 16 had mixed infections (two or more pathogens being isolated).

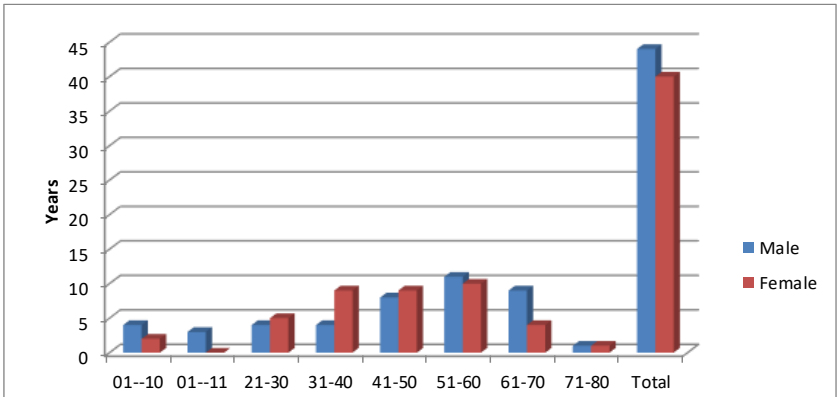

Fig. 1: Demographic data of patients. (n=84)

Fig.1 shows the age distribution of the 84 patients. Mean age of these patients was 44.5 yrs. Fig. 2 shows the unit source of patients in the study. Fig. 3 shows the sites of infections.

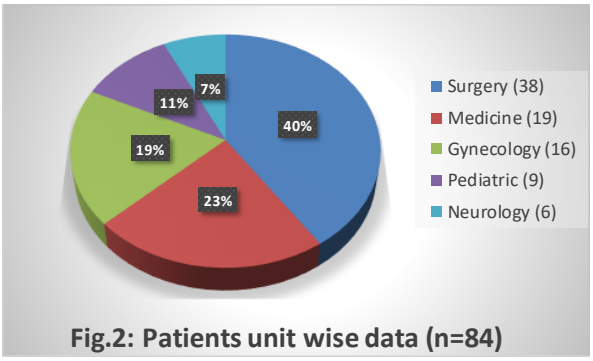

Fig.2: Patients unit wise data (n=84)

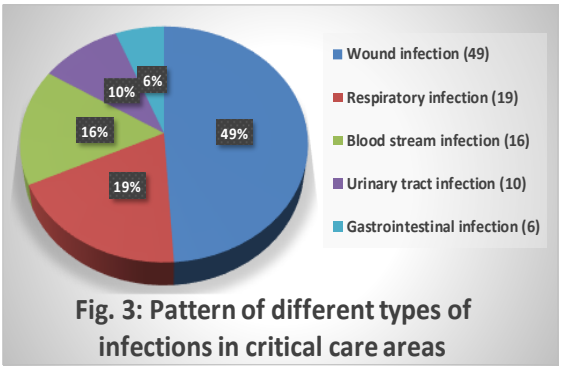

Fig. 3: Pattern of different types of infections in critical care areas

Fig. 4 demonstrates the bacterial isolates from the study patients.

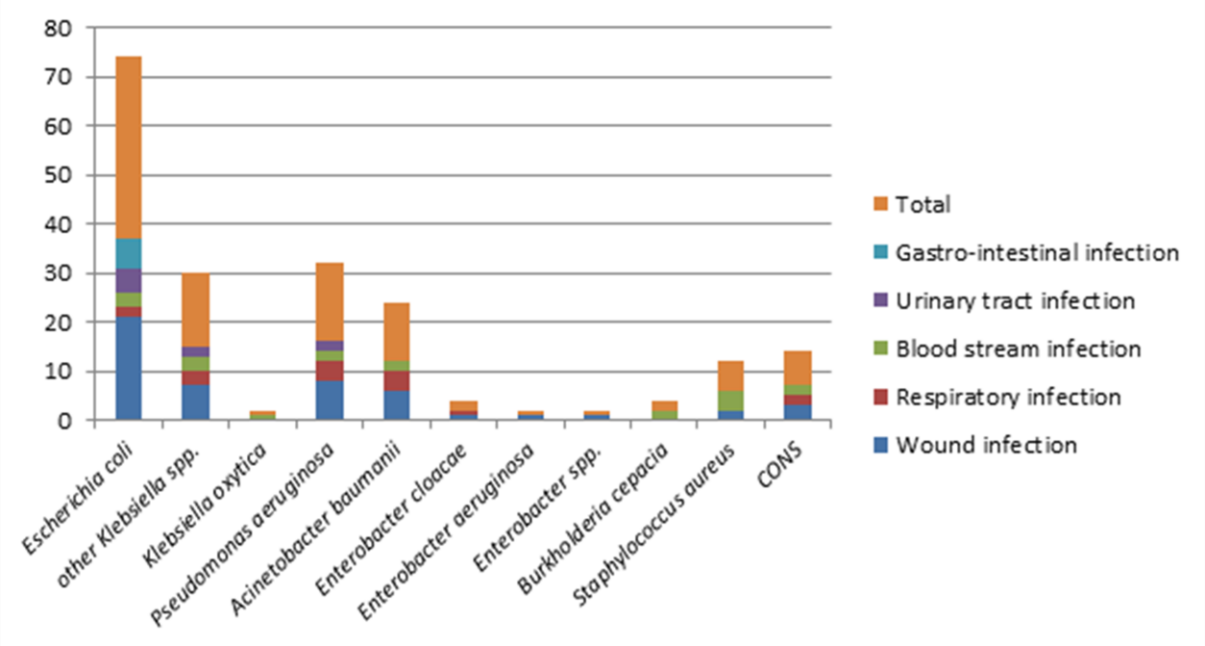

Fig. 4: Infection caused by different pathogens (n=100)

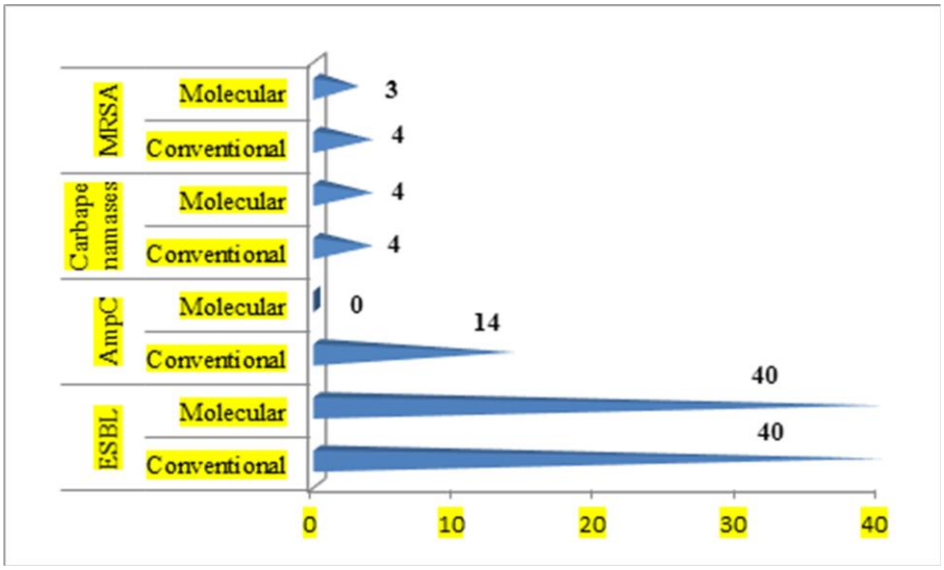

Fig. 5: Comparison of molecular and conventional testing of resistance mechanisms in Gram negative and Gram positive organisms (n=100)

Table 2: Multi resistance mechanisms in isolated organisms (n=17)

Organism	ESBL + Amp C + Carbapenemase	ESBL + Amp C	Amp C + Carbapenemase	ESBL + Carbapenemase
Escherichia coli	1 Pus swab	7 Pus swabs-6 Peripheral blood-1	1 Pus swab	2 Pus swabs-2
Klebsiella pneumoniae	-	2 ET secretion-1 pus swab-1	-	1 Urine
Pseudomonas aeruginosa	-	2 Peripheral blood- 2	-	-
Burkholderia cepacia	-	-	-	1 Peripheral blood-1
Total	1	11	1	4

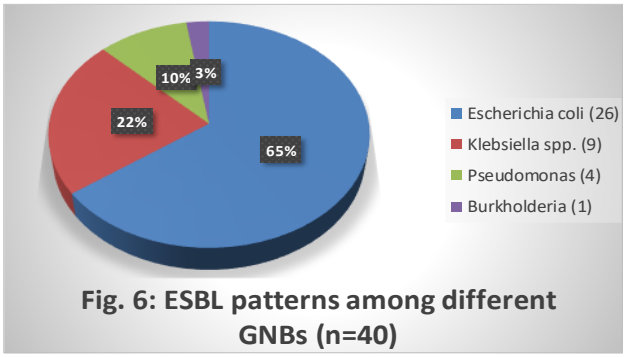

Fig. 6: ESBL patterns among different GNBs (n=40)

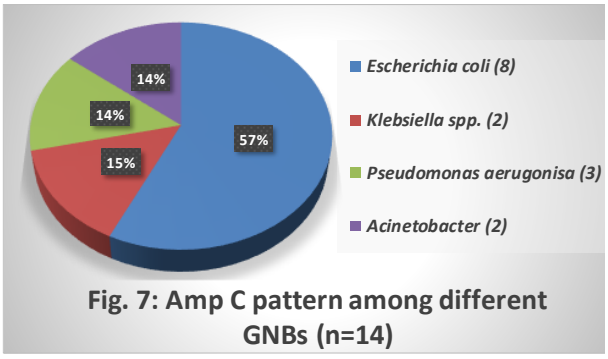

Fig. 7: Amp C pattern among different GNBs (n=14)

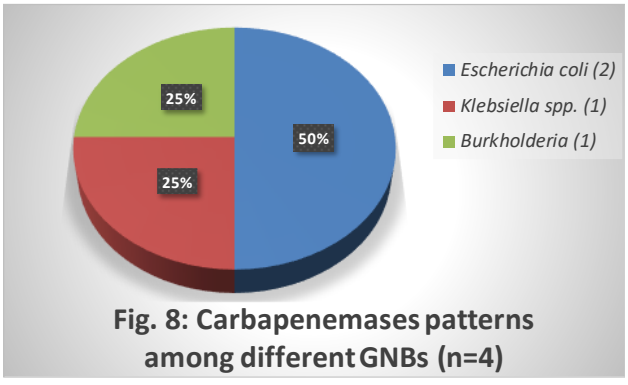

Fig. 8: Carbapenemases patterns among different GNBs (n=4)

Table 3: Prevalence of antibiotic resistance in Gram negative bacilli (n=87)

	E. coli n=37	*Klebsiella n=16*	*P. aeruginosa n=16*	*Acinetobacter n=12*	*Enterobacter n=4*	*Burkholderia n=2 (as per CLSI)*
Antibiotics	n (%)					
β-lactam						
Ampicillin	20 (54)	11(68)	NT	NT	2 (50)	1 (50)
Amoxicillin/ Clavulanic Acid	14 (37)	10 (62)	NT	NT	2 (50)	1 (50)
Piperacillin/ Tazobactum	12 (32)	9 (56)	4 (25)	2(12)	2 (50)	1 (50)
Cefuroxime	22 (59)	11(68)	NT	NT	1(25)	1 (50)
Ceftriaxone	22 (59)	11(68)	NT	NT	1(25)	1 (50)
Cefoperazone/ Sulbactam (manufacturer's defined criteria - Biomerieux)	10 (27)	9 (56)	5 (31)	3 (25)	2 (50)	1 (50)
Cefepime	27 (72)	11(68)	5 (31)	6 (50)	2 (50)	1 (50)
Aminoglycosides						
Amikacin	4 (10)	9 (56)	4 (25)	3 (25)	2 (50)	1 (50)
Gentamicin	14 (37)	8 (50)	3 (18)	7 (58)	2 (50)	1 (50)
Quinolones						
Ciprofloxacin	24 (64)	12 (75)	4 (25)	7 (58)	1(25)	0
Levofloxacin	2 (5)	3(18)	5 (31)	6 (50)	2 (50)	2 (100)
Carbapenems						
Imipenem	5 (13)	9 (56)	4 (25)	6 (50)	2 (50)	1 (50)
Meropenem	5 (13)	9 (56)	3 (18)	2(12)	2 (50)	1 (50)
Ertapenem	3 (8)	7 (43)	NT	NT	1(25)	NT
Others						
Aztreonam	NT	NT	NT	4 (33)	1(25)	NT
Minocycline	NT	NT	8 (50)	2(12)	NT	NT
Tigecycline	0	4 (25)	NT	NT	1(25)	NT

Table 4: Prevalence of antibiotic resistance in Gram positive cocci (n=13)

	S. aureus (n=6)	*CONS (n=7)*
Antibiotics	**n (%)**	
β lactam		
Penicillin	6 (100)	7 (100)
Aminoglycosides		
Gentamicin	3 (50)	2 (28)
Quinolones		
Ciprofloxacin	3 (50)	4 (57)
Levofloxacin	2 (33)	3 (42)
Others		
Tigecycline	2 (33)	0
Co-trimoxazole	3 (50)	5 (71)
Clindamycin	3 (50)	1(14)
Erythromycin	3 (50)	3 (42)
Linezolid	1(16)	0
Tetracycline	2 (33)	1(14)
Vancomycin	0	0
Teicoplanin	2 (33)	0

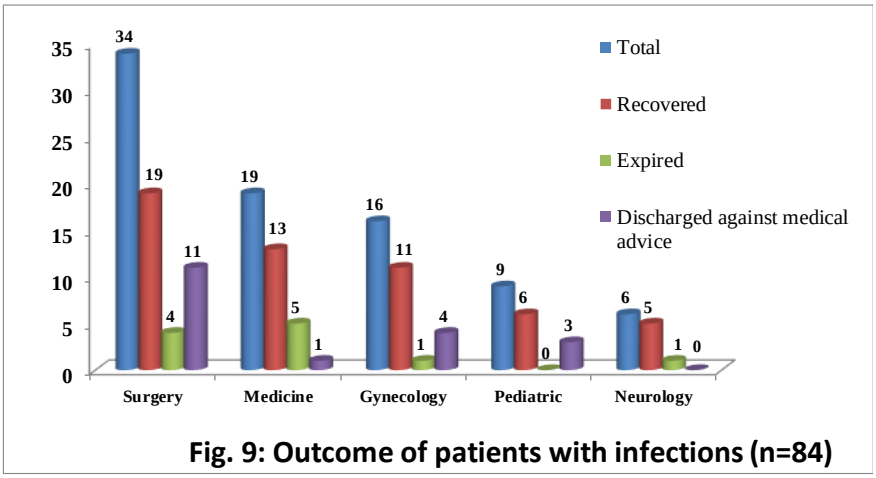

Fig. 9: Outcome of patients with infections (n=84)

Discussion

Cancer patients having treatment in all the critical areas like the ICU and BMT unit are at a higher risk of nosocomial infections due to different causes such as disruption of barriers to infection by endotracheal intubation and tracheostomy, urinary bladder catheterization and central venous catheterization, and also by immuno-suppression and bone marrow transplantation.
The percentage of nosocomial infection in our study was 25.4%. In a study done by Shaikh JM1*et al*, the frequency of nosocomial infection in general patients in the ICU was 29.13%.[9] A similar study by Moolchandani *et al* from southern India showed an infection rate of 22.2% in the ICUs.[10] In another recent study from eastern India by Sugata *et al*, the nosocomial infection rate in the ICU settings was 11.98%.[11] The higher rate of infection in the current study compared to the study of Dasgupta S *et al* was attributed to the fact that patients in the current study were immunocompromised.

Amongst 84 patients admitted into critical areas, the largest group of patients were from the surgery department (40.4%) followed by the medicine department (22.6%).

Common infections observed in ICUs are wound infection, respiratory infection including VAP, bloodstream, urinary tract and gastrointestinal infections. The most common infections in ICUs in the current study were wound infection (49%) followed by respiratory infection (19%). In a study by Shaikh JM1 *et al*, the commonest infection in the ICU was urinary tract infection (39.2%) followed by respiratory (30%) and wound (22.7%) infections.[9] A higher incidence of wound infection in our study was possibly because we had more surgical patients from both the gynecology and surgery departments as compared to the latter study.

Wound infections were the most common nosocomial infection as the highest number of admissions to critical care areas were surgical patients (49%). The most commonly isolated organisms from wound infection were *E. coli* (42.8%) followed by *P. aeruginosa* (14.2%).

Respiratory tract infections were the second commonest nosocomial infection in patients in the critical care setting. The frequency of respiratory tract infection in ICUs reported in different studies were 29% (Moolchandani *et al*[10]) and 27% (by Dasgupta *et al*[11]). In the current study, 19% of the patients in critical care areas acquired respiratory infection. The predominant pathogens causing respiratory infections were *P. aeruginosa* (21%), *A. baumannii* (21%) followed by *K. pneumonia* (15.7%). Similar findings were noted by Shaikh JM1 *et al* who found *P. aeruginosa* as the predominant organism causing respiratory tract infection.[9]

Blood stream infection was also a common infection observed in critically ill patients. Frequency of blood stream infection in our study was 16%. The common pathogens isolated from these patients were *S. aureus* (25%) followed by *K. pneumoniae* (18.7%) and *E. coli* (18.7%). Blood stream infections in the study by Shaikh *et al* was 22.7% with *S. aureus* being the predominant pathogen.[9]

In our study, urinary tract infection was found in 10 patients and was mainly caused by *E. coli* (50%) followed by *P. aeruginosa* and *Klebsiella*. Gastrointestinal infection caused by *E. coli* in six patients was also observed in the current study.

Prevalence of antibiotic resistance in nosocomial infection

Antibiotic sensitivity testing showed that the majority of bacterial isolates were resistant to multiple antibiotics (MDR). More than 50% of *E. coli* was resistant to all β-lactams. Quinolones, carbapenems, amikacin and levofloxacin showed relatively good sensitivity against *E. coli.* Approximately 60% of *Klebsiella* showed resistance to β-lactams and β-lactam inhibitors, quinolones and to aminoglycosides. *Klebsiella* showed better sensitivity against levofloxacin and tigecycline. *P. aeruginosa* showed less resistance to commonly used antibiotics as compared to *E. coli* and *Klebsiella*. *Acinetobacter* showed resistance of around 50% to gentamicin, quinolones and imipenem. *A. baumannii* showed good response to piperacillin/tazobactam, meropenem and to minocycline.

Resistance to antibiotics in Gram positive bacteria was less as compared to Gram negative pathogens. Tigecycline, linezolid, tetracycline and teicoplanin were active against the isolated Gram positive cocci. No strain was resistant to vancomycin.

A study by Moolchandani *et al*[10]observed that Gram negative bacilli isolated in their study were multidrug resistant (MDR) and were resistant to cephalosporins, carbapenems, aminoglycosides, tetracycline and fluoroquinolones.

Antibiotic resistance mechanism in isolated pathogens

Amongst 88 isolated Gram negative pathogens, 45.9% were ESBL producers, 16% were Amp C producers and 4.5% were carbapenemase producers when tested by both conventional and molecular methods. The prevalence of MRSA showed a discrepancy between the conventional method (4/13:30.7%) and the molecular method (3/13:23%). No vancomycin resistant strains were isolated in the current study. Similar results were noted in an ICU based study by Chiranjay *et al*.[4]

Multi drug resistance mechanisms were observed in 17 strains in the current study. Similar findings were observed in a study by Moolchandani *et al*.[10]

Of the ESBL producers*, E. coli* from pus swabs (17/40) was the commonest followed by *Klebsiella spp.* (3/40). Of the 40 ESBL positive strains, Amp C expression was observed in 14 strains, of which the commonest strains were *E. coli* from pus swabs (7/14). Similarly, 2 of the 4 carbapenemase producing strains were *E. coli* isolated from pus swabs.

Of the 84 patients, 11 discharged themselves from surgical units. The highest mortality was observed in the medicine department (5/84) followed by 4 patients from the surgery department. This could be due to MDR *E. coli* which was more prevalent in these units. In the study by Shaikh JM1 *et al*, the highest mortality was observed in surgical (11/97) and medicine (3/97) departments.[9]

Conclusion

From this study, we conclude that cancer patients admitted to critical areas are at a greater risk of acquiring nosocomial infection. Infection is not always the single contributory factor for mortality and morbidity for patients in critical areas. However, the increasing prevalence of MDR-GNBs, especially those resistant to cephalosporins and carbapenems, could contribute to both increased morbidity and mortality due to non-response to routinely used first line antibiotics and recourse to colistin.

We recommend that education and awareness among healthcare workers and professionals as well as adherence to standard guidelines for prevention of nosocomial infection should be used to reduce frequency of nosocomial infection in critical care areas. A multidimensional approach including Care Bundle, education, surveillance, performance feedback of infection control practices should be implemented to reduce hospital acquired infections. Of all the strategies, hand hygiene remains the corner stone in healthcare associated infection prevention.

Ethics: Approval of the Institutional Review Board and Ethics committee was taken for the study.

References

1. Bhattacharya S, Mondal A. Clinical microbiology in the intensive care unit: Strategic and operational characteristics. *Indian J Med Microbiol*. 2010;28(1):5. *doi:10.4103/0255-0857.58720*
2. Patel Foram M, Lunagariya Rahul C, Varun GPN. Infections in Patients with Cancer - GCRI (Gujarat Cancer and Research Institute) Experience. *Gujarat Cancer Society Research Journal* 2013;15(2):22-28.*No doi*
3. Weinstein RA. Nosocomial infection update. Emerg Infect Dis. 1998;4(3):416-420. *doi: 10.3201/eid0403.980320*
4. Mukhopadhyay C. Infection control in intensive care units. *Indian Journal of Respiratory care* 2018; 7(1):14-21. *doi: 10.4103/ijrc.ijrc_9_17*
5. Toufen Junior C, Hovnanian ALD, Franca SA, Carvalho CRR. Prevalence rates of infection in intensive care units of a tertiary teaching hospital. *Rev Hosp Clin Fac Med Sao Paulo*. 2005;58(5):254-259. *doi:10.1590/s0041-87812003000500004*
6. Ulu-Kilic A, Ahmed S, Alp E, Doğanay M. Challenge of intensive care unit-acquired infections and *Acinetobacter baumannii* in developing countries. *OA Crit Care*. 2013;1(1):1-5. *doi:10.13172/2052-9309-1-1-382*
7. Iwuafor AA, Ogunsola FT, Oladele RO, et al. Incidence, clinical outcome and risk factors of intensive care unit infections in the lagos university teaching hospital (LUTH), Lagos, Nigeria. *PLoS One*. 2016;11(10):1-15. *doi:10.1371/journal.pone.0165242*
8. Bock AM, Cao Q, Ferrieri P, et al. Bacteremia in blood or marrow transplantation patients : Clinical risk factors for infection and emerging antibiotic resistance. *Biol Blood Marrow Transplant*. 2013;19(1):102-108. *doi:10.1016/j.bbmt.2012.08.016*
9. Shaikh JM1, Devrajani BR, Shah SZ, et al. Frequency, pattern and etiology of nosocomial infection in intensive care unit : an experience at a tertiary care hospital *J Ayub Med Coll Abbottabad*. 2008;20(4):37-40. *PMID: 19999200*

10. Moolchandani K, Sastry AS, Deepashree R, et al. Antimicrobial resistance surveillance among intensive care units of a tertiary care hospital in South India. *J Clin Diagnostic Res*. 2017;11(2):DC01-DC07. *doi:10.7860/JCDR/2017/23717.9247*
11. Dasgupta S, Das S, Chawan NS, Hazra A. Nosocomial infections in the intensive care unit: Incidence, risk factors, outcome and associated pathogens in a public tertiary teaching hospital of Eastern India. *Indian J Crit Care Med*. 2015; 19(1):14-20. *doi:10.4103/0972-5229.148633*