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Prevalence of Beta-Lactamase Producers in ICUs of a Tertiary Care Teaching Hospital of North India

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Methods: Clinical samples obtained over a period of 12months from January 2014 to December 2014 from six ICUs of a tertiary care hospital were analyzed. Identification of micro organisms to species level and their antimicrobial susceptibility testing was performed as per CLSI guidelines. For control, 500 samples each from the environment & staff of ICU were collected & processed in the same way.

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Prevalence of Beta-Lactamase Producers in ICUs of a Tertiary Care Teaching Hospital of North India

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Methods: Clinical samples obtained over a period of 12months from January 2014 to December 2014 from six ICUs of a tertiary care hospital were analyzed. Identification of micro organisms to species level and their antimicrobial susceptibility testing was performed as per CLSI guidelines. For control, 500 samples each from the environment & staff of ICU were collected & processed in the same way.

Results: Of the total 1545 clinical samples collected during the study period, 522 were culture positive. The percentage of Gram negative and gram positive organisms isolated from them was 79.88% (417/522) and 19.37% (101/522) respectively and that of Candida was only 0.76% (4/522). Further, 50.8% (212/417) of Gram negative and 56.4% (57/101) of Gram positive isolates from clinical samples were beta-lactamase producers. The latter were maximum in clinical samples followed by environmental and staff samples.

Conclusion: Prevalence of beta-lactamase producing isolates in environmental and staff samples in addition to clinical samples indicates towards the possibility of cross infection by these organisms from the environment and staff to the patients. Therefore infection control strategies such as hand hygiene, rational antibiotic use, training and performance feedback can lead to significant reduction in the cross infection rates.

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I. Introduction

Intensive care units (ICUs) are of great value in the control and treatment of the severe illnesses that affect the human body. In spite of their invaluable and well-established role, ICUs lead to some degree of morbidity to patients, and nosocomial infection is clearly related to that.

Exposure to life-saving invasive procedures, serious underlying disease of patients and increased patient contact with healthcare personnel put patients admitted to the ICU at higher risk of acquiring nosocomial infections. ICU staff and the equipment used for patient care during the hospitalisation are the primary sources of cross-transmission of nosocomial pathogens.

Nosocomial infections increase patient morbidity, length of hospital stay, hospital costs, and may also increase mortality rates. When serious infections are suspected, treatment must be commenced immediately to increase the likelihood of a satisfactory outcome for the patient. Empirical knowledge, to select appropriate antibiotics, must be used so that the most likely infecting organisms are treated.

The prevalence of ICU-acquired infections varies between 4.4% and 88.9% being significantly higher in developing countries than in developed countries (1). Furthermore, device-associated infection rates in developing countries, especially ventilator-associated pneumonia (VAP) followed by central venous catheter-related bloodstream infections (CRBSIs), occur at a higher frequency than in European countries and USA (2,3).

The aim of this study was to identify the prevalence rates, sites and types of infection, the most prevalent microorganisms, and the antimicrobial resistance patterns especially the beta-lactamase producers present in ICUs of a tertiary care hospital.

II. Materials and Methods

The present study was conducted in 6 intensive care units of a tertiary care teaching hospital .We retrospectively analyzed consecutive culture-positive isolates and studied the antimicrobial susceptibility patterns of micro- organisms during the period from January 2014 to December 2014. The BacT/Alert (bioMerieux) was used for blood culture. Identification of micro organisms to species level and antimicrobial susceptibility testing was performed by the Vitek method. The interpretation of antimicrobial susceptibility results was done as per Clinical and Laboratory Standard Institute (CLSI) guidelines (4). For control, 500 samples each from the environment & staff of ICU were collected & processed in the same way. Informed consent was taken from staff before collecting samples. This study was conducted on hospitalised patients from

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whom samples were received in microbiology department so the article didn't need an approval from ethical committee.

a) Statistical Analysis

Statistical analysis was conducted. The chi-square test and odds ratio was applied for the comparison of categorical variables. *P* values less than 0.05 were considered as statistically significant.

III. Results

Total number of clinical samples collected during one year period were 1545. Out of which, 522 were culture positive as shown in Table1.

Table 1: Distribution of various clinical samples obtained from ICUs

S.no.	Samples	Total no.	Positive
1	Blood	704	158 (22.4%)
2	Urine	498	118 (23.7%)
3	Pus	160	124 (77.5%)
4	Suction tip	100	83 (83%)
5	Respiratory	47	33 (70.2%)
6	Body fluids	27	02 (7.4%)
7	Central lines	09	04 (44.4%)
		1545	522 (33.8%)

The percentage of Gram negative organisms isolated from clinical samples was79.88% (417/522), the percentage of gram positive organisms was 19.37% (101/522) & that of Candida was 0.76% (4/522) as shown in Table 2.

Table 2 : Distribution of various organisms in clinical samples

S.No.	ORGANISM	TOTAL No.
1	ACINETOBACTER	151
2	E.COLI	105
3	S. AUREUS	93
4	ENTEROBACTER	89
5	PSEUDOMONAS	29
6	KLEBSIELLA	21
7	CITROBACTER	16
8	ENTEROCOCCUS	06
9	PROTEUS	06
10	CANDIDA	04
11	CONS*	02
	Total	522

**Coagulase Negative Staphylococcus*

The prevalence of Gram positive and Gram negative isolates in environmental & staff samples is shown in Table 3. The prevalence of β-lactamase producing Gram negative and Gram positive isolates in clinical, environmental & staff samples is shown in Table 4 & 5 respectively.

Table 3 : Prevalence of various organisms in ICU, staff & environment.

S.No.	ISOLATES	Environment	Staff
1	Gram positive	50(10%)	34 (6.8%)
2	Gram negative	78(15.6%)	208 (41.6%)
3	Positive samples	128 (25.6%)	242 (48.4%)
4	Sterile samples	372 (74.4%)	258 (51.6%)
	Total samples	500	500

Table 4 : Prevalence of Beta-lactamase producing Gram negative isolates in clinical, environmental & staff samples

SNo.	ORGANISMS	CLINICAL ISOLATES		ENVIRONMENTAL ISOLATES		ISOLATES FROM STAFF	
		TOTAL	BETA LACTAMASES PRODUCING	TOTAL	BETA LACTAMASES PRODUCING	TOTAL	BETA LACTAMASES PRODUCING
1	ACINETOBACTER	151	88 (58.3%)	12	0	20	2 (10%)
2	E.COLI	105	56 (53.3%)	22	08 (36.3%)	52	10 (19.2%)
3	ENTEROBACTER	89	31 (34.8%)	14	02 (14.3%)	10	0
4	PSEUDOMONAS	29	15 (51.7%)	10	02 (20%)	46	10(21.7%)
5	KLEBSIELLA	21	13 (61.9%)	20	10 (50%)	70	22 (31.4%)
6	CITROBACTER	16	09 (56.3%)	0	0	06	0
7	PROTEUS	06	0 (0%)	0	0	04	0
	Total	417	212 (50.8%)	78	22 (28.2%)	208	44 (21.2%)

Table 5 : Prevalence of Beta-lactamase producing Gram positive isolates in clinical, environmental & staff samples

S.No.	ORGANISMS	CLINICAL ISOLATES		ENVIRONMENTAL ISOLATES		ISOLATES FROM STAFF	
		TOTAL	BETA LACTAMASES PRODUCING	TOTAL	BETA LACTAMASES PRODUCING	TOTAL	BETA LACTAMASES PRODUCING
1	MSSA	36	17(47%)	18	08 (44.4%)	14	04 (28.6%)
2	MRSA	57	40 (70%)	06	04 (66.7%)	08	04 (50%)
3	CONS	02	0	26	0	12	00
4	ENTEROCOCCI	06	01 (16.7%)	0	0	0	0
	Total	101	57 (56.4%)	50	12 (24%)	34	08 (23.5%)

IV. Observations

1. Maximum number of infections in ICU were Blood stream infections followed by Urinary tract, wound and respiratory tract infections.
2. Among the clinical isolates, the most prevalent bacterial agent was Acinetobacter 28.9% (151/522), followed by organisms of family Enterobacteriaceae and *Staphylococcus aureus,*
3. Concerning resistance patterns for *S. aureus*, 61.3% were resistant to methicillin and 100% had sensitivity to vancomycin.
4. Isolates obtained from staff samples were more than the ones obtained from clinical samples. More than 50% *S.aureus* obtained from staff & environmental samples were Methicillin resistant (MRSA) however all were sensitive to Vancomycin.
5. Among the clinical isolates, 50.8 %(212/417) of Gram negative isolates and 56.4 %(57/101) of Gram positive isolates were beta latamase producers.
6. The most frequently used antimicrobials in ICUs were cephalosporins, imipenem, levofloxacin, piperacillin-tazobactum and metronidazole. Actually, empirical treatment schemes are based on knowledge of local microbiota
7. *E.coli* & Klebsiella sp were the most common isolates recovered from environment & staff of ICU. Acinetobacter followed by *E. coli* were the more prevalent isolates from clinical samples
8. Prevalence of Gram negative organisms was more than gram positive in all the 3 groups as shown in Table 6.

Table 6 : Comparison of various isolates in the 3 groups

ISOLATES	TOTAL PERCENTAGE	GRAM POSITIVE%	GRAM NEGATIVE %	BETA LACTAMASES PRODUCERS
CLINICAL	33.8	19.4	79.8	51.9
ENVIRONMENTAL	25.6	10	15.6	26.56
STAFF	48.4	6.8	41.6	21.48

9. Beta lactamase producers were maximum in clinical samples followed by environmental and staff samples as shown in Table 6.
10. By calculating the odds ratio, isolates from clinical samples were twice more likely to be beta lactamase producers than the ones from environmental samples (odds ratio=2.98) and isolates from clinical samples were four times (odds ratio=3.94) more likely to be betalactamase producers than from staff samples.
11. By using chi-square test no significant (p=0.2) association was found between isolates from environmental and staff samples.

V. Discussion

In this study, Gram-negative bacteria were more common than Gram-positive bacteria, which is in accordance with the other studies (5,6,7). Treatment becomes challenging in gram-negative organisms causing serious infections in ICUs including pneumonia, bloodstream infections, wound or surgical site infections and meningitis. These organisms also exhibit multidrug resistance, and therapeutic alternatives have declined due to stagnation in novel antimicrobial agents (7,8).

In the present study, blood stream infections were most common, followed by urinary tract, wound and respiratory infections. However in the study by Boyles S (9) respiratory infections were more common in ICU followed by wound, blood stream and urinary tract infections. The probable reason could be that the sample size in their study was much larger (14000 patients) than ours.

Acinetobacter species was the most common pathogen isolated which is in accordance with the study by Datta P et al (6, 7). The prevalence of MRSA among clinical, environmental and staff samples was more than 50% which shows that more stress should be laid on hand hygiene in our ICUs as improved hand hygiene can reduce acquisition of antimicrobial resistant bacteria, particularly MRSA (10).

There has been increase in incidence of beta lactam resistant organisms in ICUs of our hospital which is in accordance with a study conducted by Shaikh S et al (11). Among the clinical isolates, 50.8% of Gram negative isolates and 56.4% of Gram positive isolates were beta lactamase producers. This data confirms that in the intensive care medical environment, the most virulent in general are the most resistant and are the most frequently found organisms (12,13).

Prevalence of beta-lactamase producers in environmental and staff samples apart from clinical samples indicates towards the possibility of cross infection by these organisms from the environment and staff to the patients. Infection control strategies such as hand hygiene, rational antibiotic use, training and performance feedback can lead to significant reduction in the cross infection rates. In addition patients colonized or infected with beta lactamase-producing organism should be placed under contact precautions to avoid hospital transmission (14).

Hand hygiene is the most important way of decreasing the spread of infections in ICUs especially in developing countries like ours. Initial empirical therapy with broad-spectrum antibiotics is a life-saving strategy, which improves clinical outcome and reduces selection of resistant organisms. However, it is imperative to de-escalate these antibiotics according to culture and antibiotic susceptibility results. Antibiotic cycling can be used as an effective approach to control antibiotic resistance. Strict antibiotic policies in ICUs can prevent the use of long term antibiotics and shorten the duration of the antimicrobial therapy (15).

Conducting infection surveillance and control activities in ICUs and rational antibiotic utilisation policies are valuable measures for infection control. These measures provide current knowledge about antibiotic resistance patterns, early recognition and management of outbreaks, which is essential for infection control (16).

Increasing drug resistance and spreading of multidrug-resistant (MDR) pathogens in the ICU environment results in limited therapeutic options and prolonged hospitalisations. Consequently, the prevalence of ICU-acquired infection, healthcare costs and mortality rates are higher in developing countries due to limited resources associated with the quality of care (17).

In conclusion, our study shows that multidrug resistant bacteria are on rise in our hospital. The rise in beta-lactamase producers emphasizes the importance of stringent infection control practices, rational prescribing policies and need for development of new drugs and vaccines. Also, there is a need for the continuous evaluation of the local antibiotic resistance patterns for the formulation of a rational antibiotic policy. Limiting use of antibiotics to patients with clear evidence of infection rather than colonization is essential & discontinuation of antibiotics when their possible benefits have been obtained is also critical. Further, new drugs are required to replace the increasingly obsolete classes of antibiotics that currently exist and there is need for strict compliance with infection control practices.

Conflict of Interest Statement

We declare that we have no conflict of interest.

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