MANAGEMENT OF β-LACTAMASE PRODUCERS THROUGH INFECTION CONTROL MEASURES IN BURN ICU

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ABSTRACT

BACKGROUND AND OBJECTIVES

Multi-Drug Resistant (MDR) pathogens due to various β-lactamases are major contributors in increasing morbidity and mortality rates in Burn Intensive Care Units, ICU. This study is aimed to apply the various infection control measures and to compare the results of two halves of study and to establish a relation between environment, Health Care Workers (HCWs) and patients regarding manifestation of nosocomial infection.

DESIGN AND SETTING

Over a period of three years (June 2010 to June 2013), Clinical, Environment and Health care providers samples from Burn ICU were processed in the Department of Microbiology, Sri Guru Ramdas Institute of Medical Sciences and Research, Amritsar. Organisms were identified by standard microbiological techniques and their antibiotic susceptibility was determined by Kirby Bauer disc diffusion method. The MDR were further tested for various β-lactamases by Clinical Laboratory Standard Institute (CLSI) disc diffusion method using Ceftazidime and Ceftazidime + clavulanate and Cefotaxime and Cefotaxime clavulanate for Extended Spectrum Beta Lactamases (ESBL), Meropenem and meropenem + EDTA for Metallo Beta Lactamases (MBLs) and 3-Dimensional test for AmpC beta lactamases.

MATERIAL AND METHODS

307 clinical, 210 environmental and 117 HCWs samples in 1st and 192 clinical, 62 environmental and 92 HCWs samples in 2nd half of study were processed by standard microbiological techniques. After identification all MDR isolates were first screened for ESBL, AmpC and MBL then confirmed by the respective confirmatory tests. Results of two halves were statistically analyzed.

RESULTS

Infection rate was reduced from 50.16% to 40.10% in Burn patients. Culture positivity was reduced from 38.0% to 27.41% in environmental and 27.35% to 7.60% in HCWs samples. β-lactamases prevalence in Gram positive was 54.23% and Gram negative was 60.86% before and 37.03% and 54.05% after interventions.

CONCLUSION

In addition to the economic burden for antibiotic treatment, it is important to monitor the bacteriology, resistance pattern, antibiotic susceptibility and β-lactamases production in burn ICU. The development of new agents, strict antibiotic policy and effective infection control measures are paramount in the ongoing battle against multi-resistant organisms.

KEYWORDS

BICU, MDR, ESBL, MBL, AmpC.

INTRODUCTION

Burn patients are at higher risk for local and systemic infections and continue to be the leading cause of death despite of broader spectrum antibiotics.[1] Centers for Disease Control and Prevention (CDC) demonstrated that burn Intensive Care Units (ICUs) have the highest rates of primary blood stream infection in patients with central venous catheters among all ICUs.[2] In developing country like India, delay in arrival in a burn facility from remote villages, lack of early coverage of the wound and sepsis are the most important factors dictating the patient outcome.

Disruption of the skin barrier, large cutaneous bacterial load, the possibility of the normal bacterial flora becoming opportunistic pathogens and severe depression of the immune system causes sepsis in burn patient.[3] results 73% of deaths.[4] Emerging Multi-Drug Resistant (MDR) pathogens have caused an unexpected rise in burn wound infections, sepsis and associated death worldwide.[5] and have been reported as the cause of nosocomial outbreaks of infection in burn unit.[6,7] Gram-negative organisms cause serious infection in burn patients.[8] extended spectrum beta-lactamases (ESBL), AmpC (Ampicillin resistant) and Metallo beta lactamases (MBL) β-lactamases producing organisms pose a major problem for treating burn victims.[9,10]

The routine susceptibility tests done by clinical laboratories fail to detect β-lactamases production.[11,12,13] Hence, it is necessary to know the prevalence of β-lactamases producers in a burn ICU where infections due to resistant organisms are much higher. Information regarding prevalence of organisms in environment and Health Care Workers (HCWs) is also very important.

There is not enough information from the Indian subcontinent regarding the prevalence of β-lactamases mediated resistance, environmental sources of pathogens and infection control management in burn ICU. The aim of the present study is to find the prevalence of MDR pathogens in patients and environment and HCWs and to analyze the effect of infection control measures in burn ICU. Infection with β-lactamases producing pathogens is a cause of concern in burn ICU for many hospitals worldwide. These infections are associated with increased morbidity, mortality and hospital costs. Our aim was to control the infections with multi-drug resistant organism by various control measures and to understand the exact route in which infection travels.

The few studies documented a direct relationship between nosocomial infections and its potential route, which includes environment and health care workers as carriers. Our aim was also in recommending an intervention to decrease the nosocomial infections in ICUs and to check statistically whether the interventions have positive impact in reducing the nosocomial infections with multidrug resistant organisms and antibiotic resistance due to β-lactamases.

MATERIAL AND METHODS
A prospective study was conducted over a period of three years (June 2010 to June 2013) and was divided in Pre-intervention period (1st half) and post intervention period (2nd half) in the Department of Microbiology, Sri Guru Ram Das Institute of Medical Sciences and Research Vallah, Amritsar. Clinical, environmental and HCWs samples were collected from Burn ICU of Sri Guru Ram Das Charitable Hospital Valla, Amritsar. All the specimens were processed by standard techniques for isolation and identification.[14] Antimicrobial susceptibilities of the isolates were detected by Kirby-Bauer Standard Disk Diffusion (SDD) method using various antimicrobial agents as per Clinical and Laboratory Standards Institute (CLSI) guidelines. Quality control was achieved by using standard strain of Escherichia coli ATCC 25922.[15]

Gram-negative isolates resistant to third-generation cephalosporin were further tested for ESBL, MBL and AmpC phenotype. ESBLs were detected by the (disc diffusion methods using Ceftazidime and Ceftazidime+clavulanate and Cefotaxime and Cefotaxime+clavulanate discs) for ESBLs and (Meropenem and meropenem+EDTA disc) for MBLs confirmatory method of Clinical and Laboratory Standards Institute (CLSI). Inducible AmpC β-lactamase was detected by 3D test.[16] Quality control was achieved by using known AmpC positive isolate of K. Pneumoniae ATCC 700603. Metallo β-lactamase production was detected by Meropenem- EDTA disk test by disc potentiation method. Lactamases in Gram positive isolates were detected by Nitrocefin method. Environment samples were taken by standard swab culturing technique from various sites like wall, floor, bed trolley, monitor, IV stand, etc. Swab from hand, nose, uniform etc. were taken from healthcare providers in Burn ICU. Chi-square test was employed to compare results regarding positive samples before and after intervention. The various infection control measures taken in Burn ICU were:
1. Training of healthcare workers in ICUs for enforcing hand hygiene and sample collection by aseptic techniques.
2. Circulation of MDR data to treating doctors in ICUs.
3. Formulation of Antibiotic policy and circulation of Antibiogram for antibiotic use accordingly.
4. Formulation of disinfection policy.
5. Awareness of ICUs staff to adopt standard precautions and proper hygienic measures to reduce nosocomial infections.
6. Monitoring of microbial load after fumigation in ICUs by strict control over the movement of people and material in ICUs.

RESULTS
Bacterial isolation was 50.16% clinical, 38.0% environmental and 27.35% in staff before interventions, while it was reduced to 40.10% in clinical, 27.41% in environmental and 7.60% in HCWs after interventions. Level of significant was 0.001. Similarly, β-lactamases prevalence was reduced to 46.67% from 66.67% in Gram +ve and 58.06% from 65.49 in Gram –ve isolates as shown in Table 1.

Prevalence of Gram +ve has increased in 2nd half from 3.90% to 7.81% in patients, while it decreases from 13.80% to 11.29% in environment and from 15.38 to 5.43% in HCWs. Prevalence of Gram negative isolates was reduced from 65.49% to 58.06% in patients, 52.94% to 40.0% in environment and 42.85% to nil in HCWs samples. Methicillin resistant S aureus prevalence was decreased from 58.33% to 53.33% in patient, 27.58% to 14.28% in environment and 22.23% to 20.0% in staff as shown in Table 2.

Prevalence of Gram -ve isolates decreased from 62.54% to 32.29% in patients, 24.28% to 16.12% in environment and 11.96% to 2.1% in staff in 2nd half after interventions. Pseudomonas was maximum prevailed isolates in patient, environment and staff as shown in Table 3. Among 93 β-lactamases in patient, maximum phenotype detected in 1st and 2nd half was ESBL 32.25% and 33.34% respectively followed by others as shown in Table 4.

DISCUSSION
The infection of burn wounds with multiple organisms with the super added problem of drug resistance due to presence of β-lactamases.[17] This necessitates a drug policy by the hospitals for burn patients. Burn wound monitoring requires the study of changing bacterial flora and the antibiotic sensitivity reports. Repeated swab cultures and Antibiogram are advised for proper selection of antibiotics to control sepsis.[18] In present study, we observed that maximum cases of burn infection was with pseudomonas 35.1%, which is similar like other studies.[19] Our study is in contrast to some other studies, especially from developed countries which report S. aureus as predominant organism.

In present study, one of the most striking differences was the prevalence of Klebsiella spp. which is contrary to study conducted in Nigeria.[20,21] where Klebsiella spp. was the most frequent pathogen isolated. No isolate of β-hemolytic Streptococci was seen, which is in agreement with the previous studies.[22] but contrary to findings in other study.[23]

In our study, pseudomonas aeruginosa was predominant pathogen in patient and environment sample which was the most common cause of burn wound infections in many centers.[24] Many centers from India have also reported the same.[25,26] As similar organism in patient, environment and HCWs were found in our study, an effective infection control policy is required to reduce or eliminate endemic pathogenic and antibiotic resistant organisms. Effective policy helps to prevent the establishment of antibiotic-resistant organisms as the predominant nosocomial flora of the burn unit and prevent cross-contamination.[27]

High prevalence 55.31% of β-lactamases was seen in our study. This may be due to the treatment of patients empirically by clinicians. Thus study suggests the empirical therapy policy in hospital, which should be based not only on the sensitivity pattern of organisms, but also on the basis of presence of various β-lactamases.

CONCLUSIONS
Overcrowding, inadequate sterilization and disinfection practices, cross contamination of the environment, lack of isolation facilities, inadequate hand washing and barrier nursing are some of the reasons for high cross infection and sepsis rates in burn ICU in many developing countries.[28]

The infection control programme in burn ICU requires strict compliance with a number of environmental control measures that include strictly enforced hand hygiene and the universal precautions. Health care workers must be gowned (Including use of disposable or reusable gowns and disposable plastic aprons to prevent soiling of health care workers' clothing during wound care procedures) and gloved at each entry to the burn ICU. During the study, it was also observed that large number of Gram-negative bacteria and emerging pathogens such as Pseudomonas, Klebsiella spp. and Citrobacter species showed resistance to some disinfectants and antiseptic solutions. Hence, study also suggests the disinfection and sterilization and monitoring practices in burn ICU.

Same strains of microbes were isolated from patients, environment and HCWs. This concludes that microbes are transferring from one source to other, i.e. from environment to HCWs and to patients and vice versa. Awareness and knowledge of the extent of the nosocomial infection, its causes, modes of transmission, and types of isolates help the health care providers to make effective infection control policy. During study it was observed that the infection control policy applied to control the sources of infection, preventing cross transmission with proper hand hygiene and implementation of antibiotic policy was effective in decreasing the nosocomial infections and antibiotic resistance in burn ICU. In some countries, there is antibiotic restriction policy that means Infectious Disease physician should give justification for prescription of antimicrobials (Restrictive education antibiotic stewardship programme). Such like antimicrobial restriction policy should be implemented in our country also.

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	Patients		Environment		HCWs	
	1st half	2nd half	1st half	2nd half	1st half	2nd half
Bacterial isolation	50.16	40.10	38.09	27.41	27.35	7.60
Gram +ve	3.90	7.81	13.80	11.29	15.38	5.43
Gram -ve	62.54	32.29	24.28	16.12	11.96	2.1
β-lactamases prevalence	65.58	54.54	52.5	35.29	46.87	14.28
Gram +ve	66.67	46.67	51.72	28.57	50.0	20.0
Gram -ve	65.49	58.06	52.94	40.0	42.85	0.0

Table 1: Prevalence (%) of Various Organisms in Patient, Environment and HCWs Before and After Interventions

	Patients		Environment		HCWs	
	1st half	2nd half	1st half	2nd half	1st half	2nd half
MS S aureus	41.66	46.67	48.27	28.57	44.45	40.0
MR S aureus	58.33	53.33	27.58	14.28	22.23	20.0
CONS	--	--	24.13	57.14	33.34	40.0
Total Gram +ve Isolates	**3.90**	**7.81**	**13.80**	**11.29**	**15.38**	**5.43**

Table 2: Prevalence (%) of Gram +ve Bacterial Isolates in Patient, Environment and HCWs Before and After Interventions

	Patients		Environment		Staff	
	1st half	2nd half	1st half	2nd half	1st half	2nd half
E coli	25.35	24.19	19.90	20.0	21.42	50.0
Klebsiella	10.47	11.29	31.37	30.0	28.57	00
Pseudomonas	38.73	37.09	49.01	50.0	35.71	50.0
Citrobacter	9.15	11.29	Nil	Nil	14.28	Nil
Acinetobacter	7.04	8.06	Nil	Nil	Nil	Nil
Enterobacter	4.22	6.45	Nil	Nil	Nil	Nil
Proteus	3.52	1.61	Nil	Nil	Nil	Nil
Total Gram -ve Isolates	**62.54**	**32.29**	**24.28**	**16.12**	**11.96**	**2.1**

Table 3: Prevalence (%) of Gram -ve Bacterial Isolates in Patient, Environment and HCWs Before and After Interventions

Sl. No.	Phenotype	1st half (Before Interventions)		2nd half (After Interventions)	
		No.	% age	No.	% age
1	ESBL	30	32.25	12	33.34
2	MBL	26	27.95	10	27.77
3	AmpC	10	10.75	4	11.12
4	Carbapenemase	13	13.97	4	11.12
5	MBL+AmpC	5	5.37	4	11.12
6	ESBL+MBL	9	9.67	2	5.56
	Total	**93**		**36**	

Table 4: Prevalence (%) of Various Phenotypes of β-lactamases in Gram Negative Isolates Before and After Interventions