

FIGHT AGAINST SUPERBUGS IN A BURN CENTRE: ARE WE DOING ENOUGH

Muhammad Rizwan Aslam, Taokeer Ahmed Rizvi, Muhammad Tariq Munawar, Muhamad Ashraf Hussain, Tabish Samuel*

Combined Military Hospital Kharian/National University of Medical Sciences (NUMS) Pakistan, *Combined Military Hospital /National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine the superbug infection in a burn centre, its impact on mortality/morbidity and to review all preventive/therapeutic steps taken to fight this menace.

Study Design: Retrospective cross sectional study.

Place and Duration of Study: Department of Burns & Plastic Surgery, Army Burn Centre, Combined Military Hospital Kharian, from Oct 2018 to Sep 2019.

Methodology: A detailed retrospective audit of departmental data was carried out. Parameters like direct admission vs transferred patient, percentage of burns (Total Burn Surface Area-TBSA%), records of all burns related deaths and all culture /sensitivity reports were analysed using SPSS-20.

As a standard practice in our unit blood, tracheal secretions and pus culture specimens of all patients are collected at the time of admission and then periodically fresh samples are taken every week or earlier when-ever required.

Results: Out of 515 patients, 283 (54.95%) were children under the age of 12 years. The overall survival rate improved by 13.43% as compared to last year. Out of 584 bacteriology reports 396 (67.81%) were positive and 188 (32.19%) were negative. On culture 508 organisms were isolated, majority of which were Carbapenem Resistant Pseudomonas, Acinetobacter, Enterobacteriaceae and Methicillin resistant staphylococcus aureus.

Conclusion: Multi drug resistant superbug infection is a worldwide menace. The best clinical practices, strict contact isolation, enhanced environmental cleaning and judicious use of appropriate antibiotics are the main strategies in this war. Need for newer more effective antibiotics cannot be overemphasized.

Keywords: Burn, Carbapenem resistant, Mortality, Multi drug resistant, Sepsis, Superbug.

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INTRODUCTION

The first true antibiotic, was discovered by Alexander Fleming, Professor of Bacteriology at St. Mary's Hospital in London in 1928. No new classes of antibiotics have been discovered since the 1980s¹. The antibiotics that have been brought to market in the past three decades are variations of drugs that have been discovered before². Bacteria are highly adaptable organisms which have an extraordinary ability to mutate in response to their environmental conditions. Number of bacterial organisms decipher how to resist the drug's bactericidal effects. These bacteria develop genome mutations or resistance genes. These bacteria multiply to produce a population of antibiotic-resistant organisms. These resistant bacteria transfer their newly acquired resistance genes to other species of bacteria through the process of conjugation (a reproductive interaction)^{3,4}. This transfer of resistance to other bacterial species give rise to new strains that have been termed superbugs which resist the effects of existing antibiotics. Decades of overuse and misuse of antibiotics have caused this crisis. The next major global pandemic may

involve an antibiotic-resistant superbug⁵.

Burn centres worldwide are also facing this challenge because significant thermal injury induces a state of immunosuppression⁶, that predisposes burn patient to overwhelming sepsis and high mortality, this is further compounded by loss of skin barrier the biggest protection against these bugs. As per CDC data they have identified 6 strains of superbugs that are causing life threatening sepsis in ICU's worldwide, table-I.

To prevent spreading MDR superbugs, the CDC recommends use of, contact isolation precautions, enhanced environmental cleaning, dedicated patient care equipment and prudent use of antibiotics⁷. We are following strict contact isolation protocols. All staff is regularly monitored and trained in hand hygiene and barrier nursing techniques. Enhanced environmental cleaning is being ensured by strictly following the protocols of our centre. Acute ICU area has digital lock and limited access to authorized personnel only. Acute ICU area has HVAC system with HEPA filters installed. Rooms are fumigated with formalin/H₂O₂ & Silver vapour. Room is sealed for 12 to 24 hrs, after every patient moving out. Bedding is changed daily before 8 am. Every room has two lidded bins separate color-

Correspondence: Dr Muhammad Rizwan Aslam, Consultant Burn & Plastic Surgeon, CMH Kharian Pakistan

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coded for biohazardous and routine waste. Thrice daily dustbins are emptied in each room. With every new patient complete bed including mattress is changed (previous bed is sent to sanitization bay for washing, spraying and sunlight treatment). Only one attendant is allowed who wears mask and cap with gloves all the time. Only patient is fed inside room, no fruit or food item is allowed to be kept in patient room.

All ventilator disposables are discarded, machine and filters are regularly changed and cleaned with every patient. Every room has mask, gloves and alcohol-based hand sanitizer installed outside the door. Previously 2 but now we have 4 x Operation theatres, One OT is daily closed after fumigation for 24 hrs and three remain functional. Laminar flow air with HVAC system & HEPA filters are installed. Every operation table has a foot end water trap draining into floor trap/receptacle. Every patient is bathed inside operation theatres with 5-20 gallons of Zero tedious RO water. Sterilized Macintosh sheet is changed with each patient. Zero tedious water is used for patient bathing and all staff washing/CSSD. Strict CSSD protocols are followed in our own dedicated CSSD. Hand and nasal swabs of staff are taken after every 3 months. Surface swabbing of critical areas is also done periodically.

We use Filgrastim (Colony stimulating factor) for all cases with neutropenia. All major burns are given Propranolol (Inderal) 1-2 mg/Kg body weight. The Albumin of patient is kept above 30gm, all patients are given Human Albumin as & when required. Immunoglobins (IVIG, BISEKO & Pentaglobin) are used judiciously where required.

METHODOLOGY

This retrospective cross sectional study was conducted at department of Burns & Plastic surgery, Army Burn Centre, Combined Military Hospital Kharian, from October 2018 to September 2019.

All acute burn cases irrespective of age/gender or severity were included in the study whereas all old burns and burn cases requiring secondary surgeries for previously treated burns were excluded from the study. Written permission was obtained from hospital research ethics committee ensuring patient's confidentiality vide (IRB/13/Khn/2019). Burns were tabulated into TBSA% groups and mortality compared in each group.

Bacteriology was not done in non-infected patients with superficial burns that showed intent to heal uneventfully without any major surgical interventions.

Blood, tissue/surface, CVP tips, Foley catheter tips, tracheal secretions/sputum and urine/stool samples were sent for bacteriological examination. Our standard policy is taking blood, tracheal secretions and pus culture specimens of all patients at the time of admission and then periodically take fresh samples every week or earlier when-ever required.

At admission, all patients were given two antibiotics with standard recommended dosage as per age and creatinine clearance. The dosage and type of antibiotics were changed/adjusted after evaluating patient's response, general condition, presence of fever and other signs of infection. Data was analysed using Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics were applied to find frequencies, percentages, means, and standard deviations. Quantitative variables, such as age and TBSA%, were expressed as means and standard deviations. Qualitative variable, such as type of microorganism, was expressed as frequencies and percentages.

RESULTS

A total of 515 patients fulfilling the inclusion and exclusion criteria were included in our study. Their age ranged from 25 days to 73 years (mean 23 ± 12.2 years). There were 295 (57.28%) male and 220 (42.78%) females, male to female ratio was 1.3:1. Children under 12 years of age were 283 (54.95%) and adults 232 (45.05%). There were 294 (57.09%) direct admissions and 221 (42.91%) indirect admissions, who were initially treated at home, by quacks or other hospitals and most of the time brought due to complications/sepsis.

Table-I: Superbug strains in present day intensive care unit's.

Carbapenem-resistant Enterobacteriaceae (CRE) (<i>E. coli</i> , <i>Klebsiella pneumoniae</i> , <i>Providencia</i> , <i>proteus</i>)
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)
ESBL-producing Enterobacteriaceae (extended-spectrum β -lactamases)
Vancomycin-resistant <i>Enterococcus</i> (VRE)
Carbapenem-resistant <i>Pseudomonas aeruginosa</i> (CRPA)
Carbapenem-resistant <i>Acinetobacter Baumannii</i> (CRAB)

*Source CDC official website

TBSA% (Total body surface area percent) of burns ranged from 8% (full thickness) to 95% mixed thickness burns. All the burns were tabulated in to TBSA% groups and mortality compared in each group, table-II.

Comparison of data between Oct 2017-Sept 2018 and October 2018-Sept 2019 reveals that there was an overall improvement in survival rate by 13.43% in year

2018-2019 due to our improved protocols and procedures as explained in introduction.

Bacteriology was not required in 60 (11.65%) non-infected patients with superficial burns that healed uneventfully without any major surgical interventions, whereas in 455 (88.35%) patients one or more bacteriology samples were sent.

teriacae group) were 113 (22.24%), MRSA (methicillin resistant staphylococcus aureus) 86 (16.93%) and CRAB (carbapenem resistant Acinetobacter Baumannii) were 63 (12.40%) besides other lesser virulent strains, table-III.

The most worrisome and serious condition was a synergistic infection with two or more organisms. We

Table-II: Mortality comparison with previous year.

Total Body Surface Area Burn Percentage TBSA %	Mortality						Mortality Ratio Percentage
	Oct 2017-Sept 2018			Oct 2018 - Sept 2019			
	Total	Death	%	Total	Death	%	
1-24	170	5	3.25	245	8	3.27	+ 0.02
25-34	68	13	19.12	99	15	15.15	- 3.97
35-44	82	29	35.37	69	24	34.78	- 0.59
45-54	41	28	68.29	33	18	54.55	- 13.74
55-64	24	22	91.67	19	15	78.95	- 12.72
65-74	33	28	84.85	12	11	99.67	+ 14.82
75-90	36	34	96.80	20	19	95.00	- 1.80
Total	457	159	34.79	515	110	21.36	+ 13.34

Total 584 samples were sent for bacteriological examination, which included 208 (35.62%) Blood, 251 (42.98%) tissue/surface, 56 (9.59%) CVP tips, 29 (4.97%) Foley catheter tips, 22 (3.77%) tracheal secretions/sputum and 18 (3.08%) urine/stool samples, 188 (32.19%) samples yielded no growth and were marked negative whereas 396 (67.81%) reports were positive. Total 508 microorganisms were grown and their sensitivity checked.

Majority of isolates were superbugs; CRPA (carbapenem resistant pseudomonas aeruginosa) were 166 (32.68%), MDR (Multidrug resistant)/XDR (extensively drug resistant) CRE (carbapenem resistant Enterobac-

teriacae group) were 113 (22.24%), MRSA as being the most lethal combinations. In 29 (6.37%) patients there were two concomitant serious isolates (CRPA + CRAB) and in 18 (3.96%) patients three superbugs (CRPA+CRAB+MRSA) were isolated. 65% of these cases did not survive. It was also noted that 85% of these cases were indirect admissions transferred from other hospitals with established sepsis at the time of admission. The drug resistance rate of different organisms is given in table-IV.

It is clearly evident that both Pseudomonas and Acinetobacter are 86% and 92% resistant to carbapenems and 88-98% resistant to quinolones, aminoglycosides and piperacillin/Tazobactam respectively. Staph Aureus showed 34% resistance to fusidic acid and 22% resistance to Clindamycin, but was 100% sensitive to Vancomycin and 94% to Linezolid. The carbapenem resistant Enterobacteriaceae group in our study only showed intermediate resistance to carbapenems about 34-60%²⁵.

There were three outbreaks of these polymicrobial infections during this period of study. In all three episodes we traced back the infection to have come from other burn units/ICU of tertiary care hospitals. Each episode lasted from 1-2 weeks. These bugs are brought by one patient and they end up infecting 3-7 patients admitted at that time, all serious immunocompromised major burns cases. Each time partial closure of burn centre and other extensive measures were taken to eradicate these infections.

Table-III: Microorganisms isolated.

Organism	Positive Tests (%)
MDR Pseudomonas Aeruginosa (CRPA)	166 (32.67)
MDR Acinetobacter Baumannii (CRAB)	63 (12.4)
MDR Staphylococcus Aureus (MRSA)	86 (16.92)
Klebsiella Pneumoniae (CRE)	65 (12.79)
Enterococcus species	21 (4.13)
Citrobacter Freundii	6 (1.18)
Streptophomonas Maltophilia	11 (2.17)
Providentia Stuarti (CRE)	15 (2.95)
Serratia Marcescens	9 (1.77)
E. Coli (CRE)	18 (3.55)
Enterobacter Cloacae	6 (0.12)
Coagulase negative staph species (CONS)	27 (5.31)
Proteus Mirabilis (CRE)	15 (2.95)
Total organisms isolated	508 (100)

Table-IV: Drug resistance pattern among different MDR/XDR organisms.

Drug	% Age Resistance				
	P. Aeruginosa	S. Aureus	A. Baumannii	K. Pneumoniae	E. Coli
Meropenem	88	-	92	70	40
Imipenem	86	-	92	70	40
Ciprofloxacin	94	86	98	92	82
Levofloxacin	94	-	98	84	82
Cetazidime	94	-	96	96	60
Cefepime	84	-	96	92	60
Amikacin	78	14	84	46	20
Clindamycin	-	22	-	-	-
Tazobactm/piperacillin	88	-	94	84	84
Tigecycline	NT	-	46	24	24
Polymyxin B	02	00	00	00	00
Colistin	02	00	00	00	00
Linezolid	-	06	-	-	-
Fusidic acid	-	34	-	-	-
Vancomycin	-	00	-	-	-

DISCUSSION

Multiple drug resistant and carbapenem resistant strains of bacteria are becoming a true menace and challenge for every intensive care setting in health care systems⁸. More and more of these, hospital acquired superbug infections are causing ever increasing rate of mortality. Millions of people are infected with these super bugs worldwide and almost 20-30% of them die in spite of best possible care⁹. Prevention and timely treatment of these MDR infections is a challenge. The fight against these superbugs is multifaceted and complex.

Fight against superbug (MDR strain) infections is a daunting task, faced by all major ICU's and burn centre worldwide^{10,11}. The findings of our study were more or less similar to national and international literature. In our centre majority of fatal/serious infections were due to CRPA, CRAB, CRE and MRSA as is evident from WHO and CDC listing. A similar study in a burn centre in a neighbouring city by Chaudhary *et al*¹¹, also showed a very similar prevalence of MDR superbugs with CRPA/MRSA/CRAB/CRE to be in the same order of prevalence. Although their sample size was much smaller than ours 109 vs 515 patients and 158 vs 508 isolated organisms. CRE are nightmare bacteria, they pose a triple threat¹⁹. First, they are resistant to all or nearly all antibiotics, even some of our last-resort drugs. Second, they have high mortality rates and kill up to half of people who get serious infections with them. Third, they can spread their resistance to other bacteria^{5,6,12}.

A comprehensive literature review presented by Khan *et al*¹³, from Malaysia studied the incidence and

risk of MRSA infection in burn centres. He concluded that there was a 55% risk of MRSA infection in a burn ICU, which is much more than our observation. Prevalence in our centre of MRSA is 17% rather the most common is MDR strain of pseudomonas. So far like their observation the strain prevalent is also sensitive to vancomycin and teicoplanin. Our observation of >85-98% resistance of Pseudomonas, Acinetobacter and Klebsiella to carbapenems, quinolones and aminoglycosides is also proven by a recent research of Gupta *et al*, from India¹¹.

One of the main cause of this worldwide MDR superbug menace is injudicious use of antibiotics^{9,14,15}. But fact of the matter is that the main armamentarium against this menace, besides adhering to all protocols relating to patient/environment and medical management is antibiotics.

We have our own institutional antibiogram¹⁶⁻¹⁸, we strive for scientifically judicious usage of appropriate antibiotics as per our community/hospital bug prevalence. The 13.43% improvement in overall survival rate as compared to last year is a testament to all the policies and procedures that we are strictly adhering to, in the light of CDC guidelines. The main impact on improvement in survival is seen in group from 45-65% serious burns. It was observed that there were more paediatric burns admitted this year (54.95%). The cause of this is that we receive lot of referral/transfers from other hospitals. There is no dedicated paediatric burn care facility in whole country, besides poverty/crammed up living and social distractions are causing more and more careless paediatric accidents mostly scalds and immersions.

The last line of defense against these superbugs are polymyxins/Colistin (table-IV)^{1,2}. Carbapenem-resistant *Acinetobacter baumannii* (CRAB)^{4,16,19,20}, is a perilous nosocomial pathogen causing substantial morbidity and mortality worldwide. Current treatment options for CRAB are limited and suffer from pharmacokinetic limitations, such as high toxicity and low plasma levels²¹⁻²³. There is alarming rise of carbapenem resistance. Management of Carbapenem resistant organism infections is a challenge.

Two groups of polymyxins are currently being used in clinical practice; polymyxin B and polymyxin E (otherwise called as colistin). Polymyxin B is not marketed in Pakistan. The therapeutic challenge includes high nephrotoxicity and neurotoxicity, difficulty in Optimizing dosage, promotion of resistance during sub-optimal dosage, lack of universal harmonization of dosing units with respect to critically ill individuals and narrow therapeutic window and low mutant prevention concentration. The only drug of this group available in Pakistan is Polymyxin E (brand name Colistim 2M units/vial). Therapeutic dose is 2 Million units I/V x 8 hourly. It is fairly ineffective as monotherapy now. Combination therapy with Minocycline, Tigecycline, Chloramphenicol and Fosfomycin are being suggested by extended range sensitivity screening^{24,25}. Novel drugs like Cefiderocol, Eravacycline, Plazomicin are under trials but not freely available for clinical use¹⁸.

We will have to keep on changing our tactics and strictly adhere to prevention protocols to save our patients from these superbugs which are becoming so widely spread in our communities.

CONCLUSION

MDR superbug infection is a worldwide menace. The best clinical practices, strict contact isolation, enhanced environmental cleaning and judicious use of appropriate antibiotics are the main strategies in this war. Need for newer more effective antibiotics cannot be overemphasized.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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