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Emergence of Multidrug Resistant Microbial Species in the Bacterial Profile of Burn Wounds: A Cohort Study from Pak Italian Modern Burn Center, Multan

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ABSTRACT

Objective: To document the prevalence of microflora causing burn wound infections in our setup, track any trends of change in the flora after a 7-day treatment period, and document any rise in the incidence of multidrug-resistant microbes.

Methods: This cohort study was conducted at the Pak Italian Modern Burn Centre (PIBC), Multan, over a one-year period from January 2022 to December 2022. Surface wound swabs were collected from 150 patients admitted to the Burn unit on day 3, day 10, and day 17 after sustaining burns. Standard procedures for isolation and identification of microorganisms were followed, and the growth of microflora obtained was subjected to antibiotic sensitivity testing following the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: Gram-negative isolates included Pseudomonas aeruginosa, Escherichia coli, Klebsiella spp., Citrobacter spp., Proteus vulgaris, and Providencia mirabilis. Gram-positive isolates included Staphylococcus aureus and methicillin-resistant Staphylococcus aureus (MRSA). Pseudomonas aeruginosa caused 39.3% of wound infections within 72 hours of admission and 56.9% of wound infections by the first week post-burn. Proteus vulgaris (36%) was the most frequently isolated microorganism in the second week post-burn. All these isolates exhibited an alarming level of resistance to routinely used antibiotics, necessitating the use of older, less safe antibiotics like colistin for gram-negative infections.

Conclusions: The rising incidence of antimicrobial resistance can be attributed to the emergence of multidrug-resistant bacterial species found in burn patients. Overcrowding in burn treatment facilities further exacerbates the risk of cross-contamination.

Keywords:, Antimicrobial resistance, Bacteriological profile, Drug Resistance, Microbial, Pseudomonas Infections

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Introduction

Burns remain one of the most devastating forms of trauma, inflicting both physical and mental harm on sufferers worldwide. Effective measures for infection prevention and control are crucial for the survival of patients with significant burns. Numerous studies have highlighted a strong correlation between infection and mortality rates. Research indicates that up to 73% of all deaths occurring within the first five days following burns are directly or indirectly attributed to infectious processes.[1]

Despite significant improvements in the critical care and surgical approach in burn management, the burn victims continue to run the high risk of infection. In patients with

less severe burns, infections may result in prolonging the hospital stay and the associated morbidity.[1, 2]

Burn wounds are prone to all forms of opportunistic infections. Antibiotic-resistant organisms such as MRSA, Vancomycin-resistant Enterococci, and multiply-resistant gram negative rods, including P. Aeruginosa, Acinetobacter spp., and various members of the family Enterobacteriaceae, have been associated with infections of the burn wounds and other sites among patients with major burns. The same causes the occasional outbreaks of nosocomial infections in burns units. [2-4]

Clinical diagnosis of burn wound infection relies on regular monitoring of vital signs and inspection of the entire burn wound surface, preferably during each dressing change. Local signs of burn wound infection with invasion include conversion of a partial-thickness injury to a full-thickness wound, rapidly extending cellulitis of healthy tissue surrounding the injury, rapid eschar separation, and tissue necrosis. [4]

Alongside the inevitability of infections, emergence of multidrug-resistant bacterial species [5] is a further added challenge for clinicians in selection of appropriate antibiotics for treatment as it limits the choices in terms of availability and efficacy.

Regrettably, pharmaceutical companies have not achieved much in the recent decade to tackle this issue. Non-availability of new and effective antibiotics against these MDR bacterial species or "Superbugs" has led to renewed interest in revival of older antibiotics that were discontinued from clinical use due to their reported Nephrotoxicity and Neurotoxicity, in particular, the "Polymyxins" notably Colistin and Polymyxin B. [6,7]

Methodology

This cohort study was conducted at the Pak Italian Modern Burn Centre in Multan over a one-year period, spanning from January 2022 to December 2022. During this time frame, a total of 2,197 patients were admitted to the Department of Plastic Surgery and Burn. Out of these, 835 patients presented with various burn injuries. For the study, patients of all genders aged between 15 and 45 years, with acute burn injuries involving a Total Body Surface Area (TBSA) of 15-40%, were included. Patients with associated co-morbidities were excluded, resulting in 150 patients meeting the inclusion criteria. The mode of burn injury, time taken to reach the hospital, and mean period of hospital stay were documented, along with all relevant investigations.

These patients were initially assessed and managed in the surgical emergency of Nishtar Medical University and Hospital where burn TBSA was calculated and initial resuscitation was performed using the Modified Parkland's Formula. Patients were then shifted to Pak Italian Modern Burn Centre where the remaining resuscitation and further management was completed.

Surface wound swabs were collected on days 3, 10, and 17 post-burns, adhering to standard aseptic protocols. A minimum interval of 7 days was maintained between consecutive samples from the same patient. Throughout this interval, antibiotic therapy was administered either empirically or based on Culture and Sensitivity reports obtained from previous samples. The specimens underwent aerobic culture, and sensitivity was assessed using conventional methods. Cultures were performed on Nutrient agar, MacConkey agar, and Blood agar at 37°C for 24 hours. Subsequently, isolates were identified through culture staining and biochemical testing, including oxidase, catalase, and fermentation of lactose and maltose. Antibiotic sensitivity was determined using the Kirby Bauer disc diffusion technique. All specimens were processed under the supervision of a Pathologist. Data analysis was conducted using SPSS version 20, and frequency and percentage tables were generated.

Results

Out of the 150 included patients, there were 89(59.33) males and 61(40.66%) females. The underlying types of burns included: Flame burns (n=125; 83.33%), scalds (16; 10.66%) and electric burns (9; 6%). Day 3 culture showed 66.7% isolated bacterial cultures and 33.3% sterile growths. Most common gram negative isolates included P.Aeruginosa, Klebsiella, E.coli, Citrobacter, Acinetobacter, P.Vulgaris, P.Mirabelis whereas gram positive isolates included S.Aureus and MRSA. In the present study no isolate of β-haemolytic Strepto-cocci was seen. (Table 1)

Most prevalent isolate was found to be P.Aeruginosa causing 39.3% of the infections within 72hrs of acute burn injuries, followed by S.Aureus 10.7%. P.Aeruginosa appearing as the most prevalent bacterial isolate from day 10 samples (56.6%) followed by MRSA 16.6% and P.vulgaris 13.4%. (Table I) This trend seemed to shift in day 17 isolates where P.Vulgaris was 36%, followed by P.Aeruginosa 32%. (Table I)

Frequency of sterile cultures was noted as 33.3% by day 3, 13.4% by day 10 and zero % by day 17 post burn.

Summarize the antibiotic sensitivity pattern of the various bacteria cultured was mention in Table II.

Table I: Results of bacterial cultures in different days. (n=150)

Day 3			Day 10			Day 17		
Bacteria isolated	No. of isolates	%	Bacteria isolated	No. of isolates	%	Bacteria isolated	No. of isolates	%
Aeruginosa	59	39.3%	P.Aeruginosa	85	56.6%	P.Aeruginosa	48	32.0
Klebsiella	9	6.0%	P.Vulgaris	20	13.4%	Klebsiella	48	32.0
Enterobacter	8	5.3%	MRSA	25	16.6%	P.Vulgaris	54	36.0
Citrobacter	8	5.3%	No Pathogen	20	13.4%	-	-	-
S.aureus	16	10.7%	-	-	-	-	-	-
No Pathogen	50	33.3%	-	-	-	-	-	-
Total	**150**	**100%**	**-**	**150**	**100%**	**Total**	**150**	**100.0**

Table II: Antibiotic sensitivity pattern in specified isolates days. (n=150)

	P.aeruginosa		*S.aureus*		*Klebsiella*		*P.aeruginosa*		*S.aureus*		*Klebsiella*	
	Day 3						Day 10					
Antibiotic	S	R	S	R	S	R	S	R	S	R	S	R
Amikacin	-	100	-	-	-	100	-	100	-	-	47.1	52.9
Azithromycin	-	-	50	50	-	-	-	-	-	100	-	-
Ceftriaxone	-	-	50	50	-	100	-	-	-	100	-	100
Ciprofloxacin	20	61	-	-	-	100	20	61	-	-	-	100
Levofloxacin	6	54	-	-	-	100	6	54	-	-	-	52.9
Gentamycin	-	73	50	50	-	100	-	73	-	-	-	100
Imipenem	5	95	-	-	-	47	7	93	-	-	-	52.9
Meropenem	18	82	50	50	-	100	21	79	-	100	47.1	52.9
Cefipime	6	94	-	-	-	100	6	94	-	-	-	47.1
Linezolid	-	-	50	50	-	-	-	-	100	-	-	-
Ampicillin	-	14	-	-	-	52.9	-	14	-	-	-	-
Piperacillin/Tazobactam	7	86	-	-	-	100	7	86	-	100	100	-
Colistin	73	-	-	-	52.9	-	73	-	-	-	-	-

S = sensitive, R = resistant

- no comments were made in antibiogram

Discussion

A review of the Antibiotic sensitivity patterns revealed alarming level of resistance in these bacterial isolates to commonly used antibiotics like Ampicillin, Erythromycin, Ciprofloxacin, Gentamycin etc. which are being indiscriminately used on empirical basis for prolonged duration of time. Resistance to various routinely antibiotics has been reported in several studies.[8,9]

In the context of multidrug-resistant gram-negative pathogens, the use of Colistin has re-emerged as an effective therapeutic option.

Various studies worldwide report the emerging incidences of multidrug resistant microbes in the setting of infections of various sorts, from common skin and blood stream infections to infections acquired in major burns. [10,11] The common bacteria that keep continues appearing in most of these studies is P. Aeruginosa.

There are several major reasons why the emergence and dissemination of multidrug-resistant (MDR) and extensively drug-resistant (XDR) Pseudomonas Aeruginosa strains have recently become an issue of public health concern. P. Aeruginosa not only causes severe infections, particularly in health care settings and in immunocompromised patients, it has an outstanding capacity for being selected and for spreading antimicrobial resistance in vivo. The successful worldwide spread of these "high-risk" clones of P. Aeruginosa is a threat to global public health that needs to be studied in depth and managed with urgency and determination. [12]

A corner stone in treatment of Beta-lactam and Carbapenem resistant gram negative microbes specially P.aeruginosa is the use of Polymyxins namely Colistin. Usage of Colistin is frequently associated with Nephrotoxicity and incidence of CRRT during or after completion of the therapeutic course however there are several studies that support the safety of Colistin Therapy.[13]

Moreover, combination therapy e.g., Carbapenem with Colistin or Amikacin is routinely used in clinical practice

to broaden the antimicrobial spectrum and reduce the risk of initial inappropriate therapy, although its potential for antimicrobial synergy and delaying or preventing antimicrobial resistance remains a subject of constant scrutiny and progressive research.[14]

In our clinical setting, the problem of MRD and XDR is a nuisance in treatment of major burns which overlaps with overcrowding of patients and extended hospital stay. Combination therapy is frequently used and Colistin is the last resort of effective antimicrobial agent as suggested by the Antibiogram. These issues prompted our current year long careful analysis of patient data in culture and sensitivity in a hope to outline the specific microbes prevalent in our burn center, the sensitivity pattern and the choices of antibiotics available and to have a comparative insight of this same problem worldwide.

Conclusion

Pseudomonas aeruginosa has emerged as the main culprit in burn wound infections, followed by and Proteus vulgaris and Klebsiella pneumonia among gram negative species and MRSA and Staphylococcus aureus from the gram positive species. Antibiogram analysis of the microbes reveals resistance to most of the routinely used antibiotics.

Emergence of multidrug resistant antimicrobial species is a rising threat as the emergence of the “superbugs” imply the limited choices of safe antibiotics for routine use in patients and a challenge for the clinicians providing care for the burn victims. The solution to this crisis lies in allocating more resources towards basic and clinical research and antibiotic stewardship policies for infection prevention, to develop new antimicrobials, and to optimize the use of the ones that are currently available.

References

1. Tancheva D, Hadjiiski O. Effect of early nutritional support on clinical course and septic complications in patients with severe burns. Annals of burns and fire disasters. 2005 Jun 6;18(2):74.
2. Cochran, A., Morris, S. E., Edelman, L. S., & Saffle, J. R. (2002). Systemic Candida infection in burn patients: a case-control study of management patterns and outcomes. Surgical infections, 3(4), 367-374. https://doi.org/10.1089/109629602762539580
3. Capoor MR, Sarabahi S, Tiwari VK, Narayanan RP. Fungal infections in burns: Diagnosis and management. Indian Journal of Plastic Surgery. 2010 Sep;43(S 01):S37-42. https://doi.org/10.1055/s-0039-1699460
4. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. Clinical microbiology reviews. 2006 Apr;19(2):403-34. https://doi.org/10.1128/CMR.19.2.403-434.2006
5. Nikokar I, Tishayar A, Flakiyan Z, Alijani K, Rehana-Banisaeed S, Hossinpour M, Amir-Alvaei S, Araghian A. Antibiotic resistance and frequency of class 1 integrons among Pseudomonas aeruginosa, isolated from burn patients in Guilan, Iran. Iranian journal of microbiology. 2013 Mar;5(1):36.
6. Lim LM, Ly N, Anderson D, Yang JC, Macander L, Jarkowski III A, Forrest A, Bulitta JB, Tsuji BT. Resurgence of colistin: a review of resistance, toxicity, pharmacodynamics, and dosing. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2010 Dec;30(12):1279-91. https://doi.org/10.1592/phco.30.12.1279
7. Bialvaei AZ, Samadi Kafil H. Colistin, mechanisms and prevalence of resistance. Current medical research and opinion. 2015 Apr 3;31(4):707-21. https://doi.org/10.1185/03007995.2015.1018989
8. Vinaik R, Barayan D, Shahrokhi S, Jeschke MG. Management and prevention of drug resistant infections in burn patients. Expert review of anti-infective therapy. 2019 Aug 3;17(8):607-19. https://doi.org/10.1080/14787210.2019.1648208
9. Lachiewicz AM, Hauck CG, Weber DJ, Cairns BA, Van Duin D. Bacterial infections after burn injuries: impact of multidrug resistance. Clinical Infectious Diseases. 2017 Nov 29;65(12):2130-6. https://doi.org/10.1093/cid/cix682
10. Sader HS, Castanheira M, Duncan LR, Flamm RK. Antimicrobial susceptibility of Enterobacteriaceae and Pseudomonas aeruginosa isolates from United States medical centers stratified by infection type: results from the International Network for Optimal Resistance Monitoring (INFORM) surveillance program, 2015-2016. Diagnostic microbiology and infectious disease. 2018 Sep 1;92(1):69-74. https://doi.org/10.1016/j.diagmicrobio.2018.04.012
11. Walkty A, Lagace-Wiens P, Adam H, Baxter M, Karlowsky J, Mulvey MR, McCracken M, Zhanel GG. Antimicrobial susceptibility of 2906 Pseudomonas aeruginosa clinical isolates obtained from patients in Canadian hospitals over a period of 8 years: results of the Canadian Ward surveillance study (CANWARD), 2008-2015. Diagnostic microbiology and infectious disease. 2017 Jan 1;87(1):60-3. https://doi.org/10.1016/j.diagmicrobio.2016.10.003
12. Horcajada JP, Montero M, Oliver A, Sorlí L, Luque S, Gómez-Zorrilla S, Benito N, Grau S. Epidemiology and

treatment of multidrug-resistant and extensively drug-resistant Pseudomonas aeruginosa infections. Clinical microbiology reviews. 2019 Sep 18;32(4):10-128. https://doi.org/10.1128/CMR.00031-19

13. Mariano F, Malvasio V, Risso D, Depetris N, Pensa A, Fucale G, Gennari F, Biancone L, Stella M. Colistin therapy, survival and renal replacement therapy in burn patients: a 10-year single-Center cohort study. International Journal of General Medicine. 2022 May 25:5211-21. https://doi.org/10.2147/IJGM.S357427
14. Asempa TE, Nicolau DP, Kuti JL. In vitro activity of imipenem-relebactam alone or in combination with amikacin or colistin against Pseudomonas aeruginosa. Antimicrobial Agents and Chemotherapy. 2019 Sep;63(9):10-128. https://doi.org/10.1128/AAC.00997-19