

HOSPITAL-ACQUIRED MRSA SEPSIS IN BURN CARE UNIT OF A TERTIARY CARE CENTER IN NORTH INDIA.

Microbiology

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ABSTRACT

INTRODUCTION: Bloodstream infection and the subsequent development of sepsis are among the most common infection complications occurring in burn patients. Hospital-Acquired transmission of microorganisms are associated with the emergence of antimicrobial resistance among a variety of bacterial and fungal burn wound pathogens which limits the therapeutic options for the treatment of infections associated with burns. Over the last several decades, antibiotic resistant organisms have resulted in increased mortality in burns patients. **MATERIAL AND METHODS:** This prospective study was conducted in the Department of Microbiology, Government Medical College, over a period of 1 year The patients admitted to burn care unit with the following criteria were included in the study: No infection at the time of admission and up to 48 hrs (cultures negative); Length of stay in the hospital more than 48 hrs; Signs and symptoms suggestive of infection. Patients referred from other hospitals were excluded. Samples from patients falling under the inclusion criteria of the study and manifesting any symptoms and signs of Hospital-Acquired infection during the management of burns were included in the study. Hospital-Acquired infections were defined based on CDC criteria as described below: Blood samples for culture were collected from patients with burn wounds showing signs of infection as defined by CDC. Positive Isolates were confirmed by conventional biochemical tests. Isolates exhibiting ambiguous taxonomic classification were confirmed by Vitek-2 Compact Automated Identification System following the manufacturer's instructions. Antimicrobial susceptibility testing were performed using the Kirby-Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI). **OBSERVATIONS AND RESULTS:** A total 71 patients developed Hospital-Acquired infections out of these 20 % developed blood stream infection. Most common age group in our study was between 31-40 years (33.80%) Most frequent organisms isolated from blood culture were MRSA (20%) followed by pseudomonas aeruginosa (15%) and Acinetobacter spp (10%). Candida spp was isolated from 10% of cultures. All isolates of staphylococcus aureus were Methicillin resistant however all five isolates were sensitive to vancomycin, clindamycin and linezolid. All isolates of Pseudomonas were sensitive to polymyxin-b, while as 33% were sensitive to Gentamicin. All isolates of Acinetobacter were sensitive to Gentamicin and Tobramycin while as only 50% were sensitive to Ofloxacin. **CONCLUSION:** Further burn units are ideal for outbreaks of MDR pathogens which can affect other patients, so adequate infection control measures need to be in place. Culture and antimicrobial susceptibility testing should be performed routinely, including MRSA and ESBL screening, whenever burn wound and blood stream infections are suspected. Antimicrobial sensitivity test results should be used to guide the choice of antibiotics. Also we need to conduct molecular studies on the isolates to determine their resistance genes and strains typing to determine which strains are implicated in these hospital acquired infections.

KEYWORDS

Hospital-Acquired MRSA, Sepsis in Burn Care Unit, burn wound infections, HAI.

INTRODUCTION

Hospital-Acquired infections (HAI) are defined as infections that are not present or incubating at the time of hospital admission and develop after 48 hours or more of admission, 3 days of discharge or 30 days of an operation (1,2) They affect 1 in 10 patients admitted to hospital. They are associated with prolonged hospital stay, mortality and health care costs. The infections are caused by bacteria, fungi and viruses. The most common types infection in the hospital setting are blood stream infection, urinary tract infections, pneumonias, and skin and soft tissue infections. (2) Burn patients are also at a high risk for infection as a result of the nature of the burn injury itself, the immunocompromising effects of burns, prolonged hospital stays, and intensive diagnostic and therapeutic procedures. If patients survive the initial burn and resuscitative phase, infections are a leading cause of mortality (75% of cases) in these patients. (3) burn patients are at an increased risk of blood stream infections (BSIs) especially those with central venous catheter compared with patients in other intensive care units (ICUs) (4,5) the longer the patient stays in the hospital, the higher the chances for the patient to acquire Hospital-Acquired infections in the wound. —(69).

Primary sites of infections are the blood-stream, lungs, wound, and urinary tract. Bloodstream infection and the subsequent development of sepsis are among the most common infection complications occurring in burn patients. Septic shock and multiple-organ dysfunction syndrome remain important causes of death after burn trauma despite immediate admission to an intensive care unit. Sepsis syndrome is clinically heralded by the onset of hypothermia or hyperthermia, hypotension, decreased urinary output, hyperglycemia, neutropenia or neutrophilia, and thrombocytopenia. (10) Although the incidence of invasive wound infection as the primary source for burn wound sepsis has decreased substantially since the advent of early

excision therapy, sepsis in burn patients was more often secondary to catheter-related infection or pneumonia rather than a result of the burn wound itself. Burn patients are particularly susceptible to the complications associated with insertion of intravenous and intra-arterial catheters and lines, particularly infection. Catheter-associated infections have been reported to affect from 8 to 57% of burn patients. Infected peripheral and central catheters are a significant source of sepsis in the burn patient. (10,11)

Although the initial burn wound is sterile, immediately following thermal injury, these wounds become colonized with microorganisms. (12) Gram positive bacteria that survive the thermal insult such as staphylococci located deep within sweat glands and hair follicles heavily colonize the wound surface within the first 48 hours. (13,14) The presence of devitalized, avascularized tissue provides a favorable niche for microbial growth, and later bacteria from the host's normal gastrointestinal and upper respiratory flora colonize the burn wound. Microorganisms transferred to a patient's skin surface via contact with contaminated external environmental surfaces, water, fomites, air, and the soiled hands of health care workers can further contaminate the wound. (12) Wound colonization by yeasts and fungi usually occurs later due to the use of broad-spectrum antibiotic therapy. (13,14) Immune suppression, intestinal bacterial translocation, extended hospitalization and invasive diagnostic and therapeutic procedures including intubation and catheterization can all contribute to contamination of burn wounds and development of systemic infection. (12,14)

Prior to the antibiotic era, *Streptococcus pyogenes* (group A beta-hemolytic streptococci) was the predominant pathogen implicated in burn wound infections and was a major cause of death in severely burned patients. (15) *Staphylococcus aureus* became the principal

etiological agent of burn wound infections shortly after the introduction of penicillin G in the early 1950s, which resulted in the virtual elimination of *Streptococcus pyogenes* as a cause of infection in thermally injured patients.(16) Although *Staphylococcus aureus* remains a common cause of early burn wound infection, *S. aureus* belonging to methicillin resistant *S. aureus* (MRSA) group, is the most predominant gram positive causing infections, with methicillin resistant *S. epidermidis* (MRSE) following closely.—(1517). MRSA in burn patients is favored by prolonged hospital stay and extended use of antibiotics.(18).

Hospital-Acquired transmission of microorganisms are associated with the emergence of antimicrobial resistance among a variety of bacterial and fungal burn wound pathogens which limits the therapeutic options for the treatment of infections associated with burns. Over the last several decades, antibiotic resistant organisms have resulted in increased mortality in burns patients.

Changes in resistance pattern may be attributed to factors such as, cross infection, inappropriate use of antibiotics, selective pressure and even mutations in bacterial genome.(17,19) Prolonged courses of antibiotics, often in combination result in selection of multidrug resistant Hospital-Acquired strains.(4).The widespread use of broad spectrum antibiotics in the last decade, have led to the emergence of multidrug resistant organisms such as - the extended spectrum beta-lactamase (ESBL) and metallo-beta lactamase (MBL) producing Enterobacteriaceae, MBL producing *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, methicillin resistant *Staphylococcus aureus* and vancomycin resistant *enterococci* (4,12) All these multi-drug-resistant organisms (MDRO) may cause infections which are particularly challenging to treat as there are few antimicrobial agents still effective to combat them. In terms of new antibiotics, the pipeline is virtually dry. Effort should therefore be directed toward preserving the activity of the available antimicrobials, combating antimicrobial resistance, and providing effective infection control measures for prevention of infection with MDRO strains in particular.(4)

This study is therefore aiming to provide data on pattern of bacteria infecting BSI in burn patients, antimicrobial susceptibility patterns and factors predisposing burn patients to infections at Government Medical College and Associated Hospitals Srinagar Kashmir. The information will help clinicians to provide appropriate antibiotics to patients as the empirical drugs will be 'tailor made' based on the predominating microorganism in burn unit and at that particular time, thus improving the overall infection-related morbidity and mortality. This will in turn allow burn centers to establish gains in infection control and control the emergence of multi-drug resistant organisms caused by the irrational and over use of broad spectrum antibiotic.

MATERIAL AND METHODS

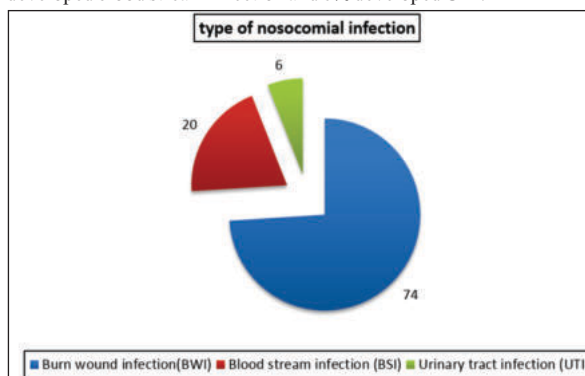
This prospective study was conducted in the Department of Microbiology, Government Medical College, over a period of 1 year .The patients admitted to burn care unit with the following criteria were included in the study: No infection at the time of admission and up to 48 hrs (cultures negative); Length of stay in the hospital more than 48 hrs; Signs and symptoms suggestive of infection. Patients referred from other hospitals were excluded. Samples from patients falling under the inclusion criteria of the study and manifesting any symptoms and signs of Hospital-Acquired infection during the management of burns were included in the study. Hospital-Acquired infections were defined based on CDC criteria as described below:(20) A Structured standard proforma was used to collect socio-demographic data. Blood samples for culture were collected from patients with burn wounds showing signs of infection as defined by CDC. (20)Blood collection was done using aseptic technique.(21) Nurses assisting in blood collection were trained and orientated in the use of BacT/ALERT blood culture vials. Aseptic techniques were ensured to avoid contamination of the sample. Adult patient (50 kg): 10-20 ml, blood. Pediatric patient: 3-10 ml.(21).For conventional blood culture: conventional blood culture bottle was used having capacity of 120 ml and containing 50 ml of liquid broth .For automatic blood culture system (BACTALERT) company provided automatic blood culture bottle was used. incubation conditions were maintained to allow recovery of microorganisms (according to manufacturer's instructions).Cultures were examined daily the bottles were examined daily and subculture on solid media was done whenever there was a visible sign of growth* in the bottle or a positive flag was given by BacT/ALERT system. Smear was also made from positive blood

culture bottles, gram stained and the clinician was informed about the organism, so that empirical treatment could be started .Subcultures were done on solid media based on the Gram stain results. Then follow-up work up of positive blood culture isolates was done. For —"No growth cultures", the length of incubation was indicated.eg :- "No growth after x days of incubation" for both preliminary and, final reports (automated systems – 5 days, manual systems – 5-7 days).Positive Isolates were confirmed by conventional biochemical tests.(22) Isolates exhibiting ambiguous taxonomic classification were confirmed by Vitek-2 Compact Automated Identification System following the manufacturer's instructions. Antimicrobial susceptibility testing were performed using the Kirby-Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI). (23) Diameters of the zone of inhibition around the disk were measured millimeters and interpreted according to CLSI 2015 criteria; sensitive, intermediate, and resistant. *P. aeruginosa* American Type Culture Collection (ATCC) 35218, *S. aureus* ATCC 25923 and *E. coli* ATCC 25922 were used as control organism.

The *Staphylococcus* isolates were tested for methicillin resistance using cefoxitin as outlined by CLSI 2015 (23) Cefoxitin disks (30 µg) (HIMEDIA INDIA) were used following the standard disk diffusion method. Incubation of plates was at 33 to 35°C; ambient air for 16 to 18 hours. For interpretation, zone of inhibition ≤ 21 mm was reported as MRSA and ≥ 22mm was considered as Methicillin susceptible *S.aureus* (MSSA).

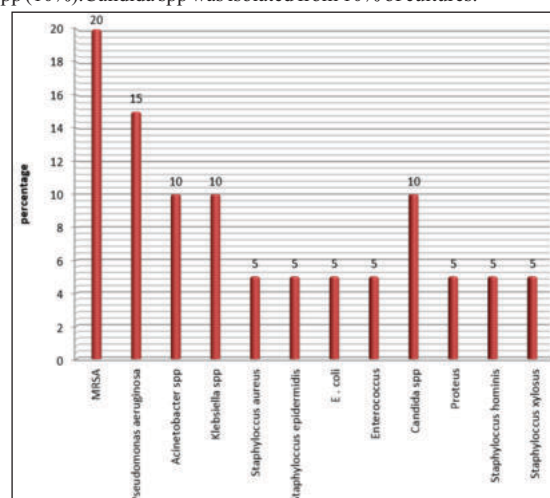
OBSERVATIONS AND RESULTS

A total of 71 percent (71/100) of patients developed Hospital-Acquired infections out of these 74% developed burn wound infection, 20 % developed blood stream infection and 6% developed UTI.



Most common age group in our study was between 31-40 years (33.80%) followed by children in age group of 10-12 years (32.3%). Out of the total (106) blood samples processed 81.13% showed no growth (sterile) and only 18.16% showed growth of organism. All (100%) the blood cultures in this study yielded single isolate.

Most frequent organisms isolated from blood culture were MRSA (20%) followed by pseudomonas aeruginosa (15%) and Acinetobacter spp (10%).Candida spp was isolated from 10% of cultures.



All isolates of staphylococcus aureus were Methicillin resistant

however all five isolates were sensitive to vancomycin, clindamycin and linezolid. All isolates of *Pseudomonas* were sensitive to polymyxin-b, while as 33% were sensitive to Gentamicin. All isolates of *Acinetobacter* were sensitive to Gentamicin and Tobramycin while as only 50% were sensitive to Ofloxacin.

DISCUSSION

Hospital-Acquired infections are a significant problem for health services in all countries, with important effects on the survival of high-risk patients, such as burn patients. Despite numerous epidemiological studies that have been published in burn wound infections in India, inadequate data is available on Hospital-Acquired infection. The most common age groups in our study was between 11-20 years (32.4%) and 31- 40 years (33%). The age distribution seen in our study is in concordance with that seen in other studies. (24,25) however it differs from other series where the peak age incidence is reported to be in adolescence and adulthood (26,27) and might be explained by the lack of coordination and awareness of dangerous substances that play an important role in the occurrence of burns in children. A number of factors have been proposed to lead to sepsis in burn patients. Burn injury causes suppression of immune response and severe catabolism proportional to the extent of injury, dysfunction of immune response, a large cutaneous bacterial load, the possibility of gastrointestinal bacterial translocation, prolonged hospitalization, and invasive diagnostic and therapeutic procedures, all contribute to sepsis. (28) In our study, we observed that 81.3% of blood cultures were sterile whereas 18.86% were positive. All cultures showed growth of single isolate. Multiple isolates were not detected in any of blood cultures. Our observations are in contrast to that of Bang *et al.* (29) Who reported multiple isolates in 13% of the blood cultures. Bang *et al.* (29) reported 54.4% of septicemic episodes due to *S. aureus*.

MRSA was the major cause of Bacteremia (20%) in our study followed by *Pseudomonas* spp (15%). a number of factors are attributed to Bacteremia by these two bacteria such as ; acquisition of *pseudomonas aeruginosa* and MRSA can occur both exogenously and endogenously as both of these are quite hardy bacteria , exogenous acquisition occurs through contaminated hands of health care workers and from environmental reservoirs (sinks ,taps shower handles ,portable water ,cleaning equipment, like mops and buckets, soap dispensers etc) in a health care setting. Also *Pseudomonas* spp and MRSA possess a plethora of different resistance mechanisms, resistance to common disinfection and multi drug resistance is among the highest in these bacteria. Further burn units are ideal for outbreaks of MDR pathogens which can affect other patients, so adequate infection control measures need to be in place. Culture and antimicrobial susceptibility testing should be performed routinely, including MRSA and ESBL screening, whenever burn wound and blood stream infections are suspected. Antimicrobial sensitivity test results should be used to guide the choice of antibiotics. Also we need to conduct molecular studies on the isolates to determine their resistance genes and strains typing to determine which strains are implicated in these hospital acquired infections.

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