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Antibiotic Resistance in Bacteria on Burn Wound Patients: A Review of Current Literature

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ABSTRACT

Burn injuries are commonly complicated by health-associated infections (HAIs), and bacterial infections are one of the major threats to recovery in burn patients. In these patients, early and appropriate antibiotic therapy is critical because delayed treatment can increase mortality. Diagnosis of infection in these patients is also challenging because the symptoms of burn- induced inflammation overlap with those of infection. Empiric antibiotic therapy is often initiated in response to clinical manifestations, but it is important to modify the treatment regimen once microbiological findings are obtained. Commonly used antibiotics for the treatment of infections related to burns include cefotaxime, amikacin, and cefuroxime, which exhibit broad spectrum activity against a wide range of pathogens, including *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*. Despite their activity, an increased incidence of antibiotic resistance, including multidrug resistance, has made the treatment challenging. Resistance mechanisms, such as efflux pumps, inactivation by enzymes, and target-site modifications, have a key role in the development of antibiotic-resistant bacteria. For this reason, susceptibility testing is crucial, and treatment should be altered based on the obtained results. It is of paramount importance to understand bacterial resistance dynamics and the correct use of antibiotics in order to treat burn patients effectively, especially within the hospital setting, where nosocomial infections are common. The increasing apprehension regarding antibiotic resistance underscores the necessity for ongoing monitoring and the innovation of new antimicrobial approaches to address resistant pathogens in the context of burn treatment.

Keywords: burn injuries; bacterial infections; antibiotic resistance.

INTRODUCTION

Burn injuries are a significant global health concern, causing approximately 180,000 deaths annually, as reported by the World Health Organization (WHO). These injuries result from exposure to high temperatures, electrical energy, chemicals, or radiation, with thermal burns being the most common type. Thermal burns arise from flame, blasts, or contact with hot objects, and the severity of skin damage depends on factors such as the temperature of the heat source and insulation. Burn injuries disrupt the skin's protective barrier, increasing susceptibility to infections. In Indonesia, burn injuries rank as the sixth most common unintentional injury, surpassing other injuries like concussions and organ damage.

Infections are the most frequent complication in burn patients, contributing significantly to morbidity and mortality. Studies, including the National Burn Repository Report of 2016, highlight infectious complications like pneumonia, urinary tract infections, and cellulitis as predominant issues. Multidrug-resistant bacteria exacerbate this problem, with studies from Pakistan and Indonesia showing prevalent bacterial strains like *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Burn centers in Indonesia, such as those in Jakarta, Bali, and Bandung, report significant numbers of infected patients, underscoring the need for improved infection control measures.

Antibiotic resistance is a pressing issue in burn care, especially in Indonesia, where antibiotics are often misused due to easy accessibility without prescriptions. Studies from Indonesian hospitals like Ciptomangunkusumo, Soetomo, and Hasan Sadikin reveal widespread bacterial resistance to commonly used antibiotics, including amikacin, cefepime, and ciprofloxacin. This resistance complicates treatment and highlights the need for tailored antibiotic protocols based on sensitivity patterns.

Given the challenges of infection and antibiotic resistance, there is a critical need for research on bacterial patterns and antibiotic sensitivity in burn patients. Addressing the misuse of antibiotics in Indonesia through stricter regulations and education could mitigate the rise of multidrug-resistant bacteria and improve outcomes for burn patients. This literature review aims to help understand the role of antibiotic and the effect of antibiotic resistance on burn wound patient by synthesizing recent study findings. It will explore the pathophysiological link of burn wound to bacterial infection and the correlation between antibiotic abuse and antibiotic resistance.

REVIEW CONTENT

1. Burn Wound

1.1 *Definition and Ethiology of Burn Wound*

The skin, the largest and heaviest organ in the human body, accounts for about 15% of an adult's total body weight and consists of three layers: the epidermis, dermis, and subcutis (Lai-Cheong and McGrath, 2013). It serves multiple functions, including acting as a physical barrier, preventing water loss, supporting immunity, regulating body temperature, enabling sensory perception, and aiding bone formation through vitamin D synthesis (Lai-Cheong and McGrath, 2013). Burn injuries, caused by exposure to high temperatures, chemicals, electrical energy, or radiation, can cause varying degrees of damage depending on the duration and intensity of exposure (Sarabahi and Tiwari, 2012). Thermal burns, the most common type, result from heat sources like flames and hot liquids and account for 86% of all burn injuries (Kara, 2018). Chemical burns, while less frequent, are often more severe due to their ability to alter tissue pH (Hardwicke et al., 2012). Electrical burns typically affect those with occupational exposure, with male patients comprising the majority of cases (Gajbhiye et al., 2013). Radiation burns, caused by ionizing radiation exposure, can lead to acute radiation syndrome depending on the dosage (Cancio et al., 2017). Each type of burn presents unique challenges and necessitates tailored interventions to manage complications and enhance recovery outcomes.

1.2 *Epidemiology of Burn Wound*

Burn injuries are a major global health concern, predominantly affecting low- and middle-income countries. According to the WHO, nearly two-thirds of burn-related deaths occur in the African and South-East Asia regions, contributing to an estimated 180,000 deaths annually. Globally, over 8.3 million new burn injury cases were reported in 2019 (Yakupu et al., 2022), with a significant rise in incidence observed since 2016 (Institute for Health Metrics). In Indonesia, burn injuries ranked as the sixth most common unintentional injury in 2014, with a prevalence of 0.7% (Wardhana et al., 2017). By 2018, the prevalence increased to 1.3%, surpassing other injuries such as concussions, eye injuries, and organ damage, according to the Indonesian Ministry of Health's Basic Health Research (Riskesdas, 2018). This growing burden underscores the need for targeted prevention and treatment strategies.

1.3 *Pathophysiology of Burn Wound*

Burn injuries cause significant physiological changes beginning with the denaturation and coagulation of skin cell proteins, leading to thrombosis in blood vessels. This process increases vascular permeability and intercellular osmotic pressure as substances like serotonin, prostaglandins, kinins, and other vasoactive amines are released from damaged tissues. These changes also trigger leukocyte and platelet adhesion to the endothelium and activate the complement system, resulting in cytotoxic T cell proliferation and transforming the tissue into a site vulnerable to infection. Jackson (1947) described three distinct zones of damage in cutaneous burn injuries: the zone of coagulation, the zone of stasis, and the zone of hyperaemia.

The zone of coagulation, closest to the heat source, represents the area of necrosis with irreversible damage sustained at the time of injury. Surrounding this is the zone of stasis, characterized by reduced tissue perfusion due to vascular transudate, vasoconstriction, and local inflammation. Cells in this zone may recover with proper treatment and wound care; otherwise, ischemia and necrosis can occur within 48 hours. The outermost zone, the zone of hyperaemia, exhibits increased blood flow and arterial vasodilation due to inflammation. This area has a high likelihood of healing within 7–10 days if not compromised by complications such as infection. When a burn injury affects more than 30% of the total body surface area (TBSA), systemic complications such as burn shock can arise. This state involves hypovolemia, the release of inflammatory cytokines, and widespread circulatory and microcirculatory damage, leading to irreversible edema even with prompt treatment and hydration support. Plasma extravasation increases systemic vascular resistance and reduces peripheral blood flow, causing hemodynamic disturbances, decreased cardiac output, and reduced urine excretion due to diminished plasma volume. These pathophysiological changes underscore the complexity and severity of extensive burn injuries.

1.4 *Clinical Manifestation of Burn Wound*

Clinical manifestations of burns include impairment on the skin based on the depth and severity of the burn. On the first-degree burn (superficial), the affected part of the skin is the epidermis with symptoms of numbness, hyperesthesia (hypersensitivity, but the pain disappears if cooled and treated properly. The appearance of scratching wound, becoming white when pressed minimally or without edema. On second degree burn (partial thickness), disrupted layers are the epidermis and part of dermis with symptoms of pain, hyperesthesia, and sensitive to cold air. The appearance of wound is flushing, the base of the wound is red spots, the epidermis is cracked, the surface of the injury is wet, and edema is found. Lastly, grade three burn (full thickness) damaged the epidermis, dermis, and sometimes subcutaneous tissue with no symptoms

of pain, shock, hematuria (blood in the urine) and possibly hemolysis (red blood cells destruction), possible in and out injury (on electrical burn patient). The appearance of wounds are dry, white burns such as skin material or rubbing, skin cracks with visible fatty parts, and edema is found.

2. Bacteria

2.1 *Definition of Bacteria*

Infection is a condition caused by the proliferation of pathogenic microorganisms within or on a host's body. It can result in disease, remain asymptomatic, or even provide benefits to the host. When an infection becomes transmissible to the extent that patient isolation is required, it is classified as an infectious disease. However, while all infectious diseases stem from infections, not all infections lead to infectious diseases. Pathogenic bacteria, which are capable of causing disease, must meet specific criteria for pathogenicity, as outlined by Welsby (1981). The first criterion is that the organism must reach the host through an appropriate transmission method. For smaller organisms like viruses, aerosol or droplet transmission allows for broad environmental dispersal. In contrast, larger organisms, such as most bacteria, rely on direct contact, mechanical transmission, or fomite transmission. Some pathogens that cannot survive outside a host require a vector for transmission, such as insect carriers for typhus. Transplacental transmission is another mechanism, especially for diseases affecting foetus due to their vulnerable immune systems and developing organs. Secondly, pathogens must adhere to specific bodily surfaces, often showing tissue specificity.

Third, infection is established through an intermediate colonization stage where the pathogen's growth is restricted to host surfaces. Finally, the pathogen launches an attack on the host through mechanisms such as localized or systemic spread, production of harmful substances, competition for nutrients, stimulation of inflammatory responses, or interference with host defense mechanisms like phagocytosis. These processes collectively determine the ability of a microorganism to cause disease and highlight the complexity of infection dynamics.

2.2 *Types of Bacteria*

Pseudomonas aeruginosa is a gram-negative, rod-shaped bacterium characterized by a grape-like odor and pearl-crescent appearance. It thrives in diverse environments, including hospitals, and is distinguishable by its ability to grow at 42°C, unlike other Pseudomonas species. This bacterium is both invasive and toxigenic, capable of causing infections in plants, animals, and humans, particularly in immunocompromised patients with cancer, severe burns, or cystic fibrosis. It is a major cause of nosocomial infections. P. aeruginosa utilizes various complex secretion systems—types I, II, III, V, and VI—to transport virulence factors into host cells or the extracellular environment. These systems release toxins and enzymes such as exotoxin A, rhamnolipids, elastases, and phospholipase C, which enhance its pathogenicity (BIOL 230 Lab Manual: Gram Stain of *Pseudomonas aeruginosa*).

Staphylococcus spp. are gram-positive cocci that form grape-like clusters. Among the 32 identified species, *Staphylococcus aureus* and Staphylococcus epidermidis are the most studied and clinically relevant. These bacteria are non-motile, non-spore-forming facultative anaerobes that can grow through aerobic respiration or fermentation. S. aureus is a highly virulent pathogen with significant antibiotic resistance, while S. epidermidis is typically a harmless component of the skin's normal flora. Both species require essential amino acids such as arginine and valine, as well as B vitamins like thiamine and nicotinamide, for growth. Colonies of S. aureus often appear golden due to its unique pigmentation, while S. epidermidis colonies are pale and translucent. The thick protective cell wall of S. aureus contributes to its resilience and virulence (Harris et al., 2002; Kloos and Bannerman, 1994; Foster, 2017).

Streptococcus spp. represent a diverse group of gram-positive cocci within the lactic acid bacteria family. These bacteria serve as commensals, opportunistic pathogens, or primary pathogens in humans and animals. Certain species, such as Streptococcus pyogenes, S. agalactiae, and S. pneumoniae, are highly virulent and cause a range of diseases. S. pyogenes is notable for its ability to cause β-hemolysis on blood agar, producing white colonies surrounded by clear zones of tissue lysis. This bacterium is primarily spread through respiratory droplets and can colonize the nasopharynx or perineal area asymptomatically. Streptococcal infections are generally treated with antibiotics like penicillins and macrolides, though emerging resistance has been observed globally. Resistance genes can spread among streptococci through transposons and integrative elements (Kamel, 2015; Brooks, 2018).

Klebsiella pneumoniae is a gram-negative, rod-shaped bacterium within the Enterobacteriaceae family. Known for its thick capsule, it is an opportunistic pathogen found in the gastrointestinal tract, respiratory system, and medical devices. It primarily affects immunocompromised individuals and is a leading cause of nosocomial infections. The persistence of *K. pneumoniae* in hospital environments is exacerbated by its multidrug resistance, often mediated by extended-spectrum β-lactamases and carbapenems, complicating treatment choices (Li et al., 2014).

Escherichia coli, a facultative anaerobic gram-negative rod, was first identified by Theodor Escherich in 1885. While it is generally a harmless commensal in the human intestine, pathogenic strains can cause diseases such as diarrhea, urinary tract infections, and respiratory illnesses. Pathogenicity arises when E. coli invades tissues where it does not belong or acquires virulent traits.

The bacterium is motile, non-spore-forming, and can survive in both aerobic and anaerobic conditions. Various strains, such as Enterotoxigenic E. coli (ETEC) and Enteropathogenic E. coli (EPEC), exhibit distinct mechanisms of pathogenicity (Kamel, 2015). *Acinetobacter baumannii* is a gram-negative, non-motile coccobacillus and a significant multidrug-resistant pathogen in hospitals worldwide. This opportunistic bacterium is responsible for a wide array of infections, particularly in immunocompromised patients, with mortality rates reaching 35%. It forms smooth, occasionally mucoid colonies and thrives on common laboratory media such as blood agar. Its resistance to antibiotics poses a severe challenge in clinical settings (Antunes et al., 2014).

Lastly, *Enterobacter cloacae* is a gram-negative bacterium from the Enterobacteriaceae family, initially described as "*Bacillus cloacae*" in 1890. Found in diverse environments, it serves as a commensal in human and animal digestive tracts. It is a significant nosocomial pathogen, causing infections such as bacteremia, lower respiratory tract infections, urinary tract infections, and septic arthritis. The species' genetic diversity allows it to thrive in various settings, contributing to its pathogenic potential. The most common points of entry for infections are the skin and gastrointestinal tract (Mezzatesta et al., 2012).

3. Antibiotics

3.1 *Definition of Antibiotics*

Antibiotics are defined as substances produced by microorganisms or their chemically synthesized equivalents that inhibit the growth of other microorganisms at low concentrations (Russell, 2004). The initial definition, limited to naturally produced substances, has evolved due to advancements in synthetic methods. Diagnosing infections in burn patients presents unique challenges because common clinical and biological markers, such as hyperthermia, hyperleukocytosis, and elevated C-reactive protein (CRP) levels, are often unreliable, particularly in those with severe burns. Severe burns can induce a systemic inflammatory response syndrome (SIRS) that mimics the clinical and biochemical signs of infection, complicating accurate diagnosis. As a result, antibiotic therapy decisions based on these general disease characteristics can lead to inappropriate treatments. To address this issue, experts have established specific criteria for diagnosing infections in burn patients, distinguishing between colonization and infection since the mere presence of bacteria on a wound does not confirm an infection.

When a serious infection is identified, initiating antibiotic therapy promptly is crucial, especially for life-threatening infections or those poorly tolerated, as delays can significantly increase mortality rates. In less critical cases, such as infections that are well-tolerated and not associated with organ failure, antibiotic therapy may be deferred until microbiological evidence is obtained. In cases of severe but undocumented infections, bacteriological sampling should be conducted before starting antibiotic treatment, but without delaying therapy. When no microbiological documentation is available, antibiotic therapy is empirical, relying on broad-spectrum agents to maximize effectiveness. The choice of empirical treatment is guided by several factors, including the patient's condition, the ecological characteristics of the healthcare environment, the duration of hospital stay, prior antibiotic use, and the patient's overall state.

CONCLUSION

Burn-related injuries performed are attributed to heat, chemicals, electrical sources, or radiation. Burn injuries injure the skin, which serves as a barrier, regulates heat, and is an important immune system aid. Burns are classified into three categories of burns: first, second, and third. The superficial burn is characterized by injuries to the outer skin. On the other hand, burns that affect all skin layers and deeper tissues are classified as third-degree burns. Severe burns require surgical treatment. Epidemiologically, burns become a global health problem; in particular, those from low-and middle-income countries (LMICs) with the most comprehensive focus on children and the elderly would deem vulnerable. People generally differ in socioeconomic factors and even gender; such issues directly influence the rates of burn injury among different population segments: for example, males in high-income countries fall most to work-related burns, while females in LMICs mostly fall to domestic accidents or self-burns. The infection caused by bacteria may vary between infective and non-infective pathogens. Important hospital-associated species include *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter baumannii*, and *Enterobacter cloacae*. The patient with an altered immune response may present with serious infection from a few of these bacteria, as they are all resistant to antibiotics. While antibiotics are essential in the treatment of burn infections, such treatment is very difficult due to the challenges of differentiating infection from SIRS. Broad-spectrum compounds including cefotaxime, amikacin, and cefuroxime are used for empirical therapy. Yet, antibiotic resistance is the major menace that results from intrinsic resistance, acquired mutations, cross-resistant, and multidrug resistance (MDR). Through misuse of antibiotics, MDR complicates treatment and necessitates a careful choice of antibiotics to ensure effectiveness.

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