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Infections in burn patients: Literature review

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Abstract

Burns are one of the most common and devastating types of trauma. Patients suffering from severe thermal injury require immediate specialized care to reduce morbidity and mortality. Significant thermal injuries cause immunosuppression, which predisposes burn patients to infectious complications. Several etiological factors mainly Staphylococcus aureus continues to be the leading cause of burn wound infection by producing toxic products that allow it to invade local tissues and spread hematogenously, causing generalized systemic infection and sepsis. This review aims to emphasize the significance of burn wounds and their complications, particularly sepsis, which is associated with high morbidity and mortality rates. Sepsis and septic complications are responsible not only for poor outcomes in burn patients but also for lengthy hospital stays. Integrated management, which includes but is not limited to fluid resuscitation, nutritional support, antimicrobial therapy, and vasoactive medications, is beneficial for the prevention and prognosis of sepsis by focusing on the events that lead to sepsis after burn injury.

Introduction

Infection is the leading cause of death and morbidity following burn injury; it is a surgical emergency due to the high concentrations of bacteria (>10^5 CFU) in the wound and surrounding area [1,2]. It is caused by an infection of the otherwise healthy tissues surrounding the wound and is frequently accompanied by increased warmth in the area, pain or tenderness, advancing swelling, or induration. Although Staphylococcus aureus is the most common infective bacterium in burn wounds, Pseudomonas, Enterobacteriaceae (*Escherichia coli, Klebsiella, Enterobacter, Serratia, Proteus*), and, in rare cases, viral infections also play important roles in etiology. The natural pathophysiology of burns infection interferes with the activation of the inflammatory cascade, which is mediated by macrophage production of inflammatory mediators, resulting in the formation of suppressed cell-mediated and humoral immune activities. The severity of the immunosuppression is inversely proportional to the severity of the burn damage [3,4]. Burn patients may experience severe local and systemic complications affecting nearly every organ system [5]. Sepsis, on the other hand, is the most severe. Sepsis is a change in a burn patient that causes concern about infection. Sepsis is a potentially fatal disease characterized by acute circulatory collapse and prolonged hypotension resistant to intravenous fluid therapy. Patients who have been severely burned frequently experience varying degrees of organ failure, and when multiple major organs are affected, mortality becomes extremely high [3]. Sepsis caused by a severe,

injury-induced immunoinflammatory response remains a common complication and one of the leading causes of multi-organ failure and death in patients with significant wounds [6]. Sepsis is a presumptive diagnosis that requires the administration of antibiotics as well as the investigation of the source of the infection. Whereas clinical interpretation is required, the diagnosis must be linked to the discovery of an infection. However, strategies for preventing and managing drug resistance must be implemented, such as infection control programs that include hand hygiene, monitoring agreements with local antimicrobial agent guidelines, and the development of antimicrobial stewardship programs in burn centers [7]. Nonetheless, strict infection control measures, continuous wound surveillance with regular tissue sampling for quantitative culture, and early excision and wound closure remain the primary adjuncts for controlling invasive infection in burn patients.

Discussion

Following a burn injury, infection is the leading cause of death and morbidity, accounting for 51% of all deaths. It is defined as the presence of high concentrations of bacteria in the burn wound and scab (>10^5 organisms/g tissue) [1]. Color change, exudative drainage, lesion odor, and systemic sepsis differentiate an invasive infection from others [1,8]. Infections are classified as bacterial or viral, entering the body directly or indirectly through the bloodstream [1,8,9].

Friction, cold, heat, radiation, chemical, or electric sources can all cause burn injuries, but the heat from hot liquids, solids, or fire is the most common. As a result, burns are classified as thermal, electrical, or chemical. Another classification is the depth of the burn. Four factors must be considered when determining the depth of a burn: look, blanching to pressure, pain, and feeling [10]. A burn's depth is classified into three types based on how deep it penetrates the epidermis or dermis. Superficial burns, also known as first-degree burns, are hot, painful, red, soft, and blanch when touched. Normal blistering does not occur. Second-degree partial-thickness burns penetrate the epidermis and into the dermis. Depending on whether the penetration is superficial or deep, the depth of penetration into the dermis may vary. When touched, these burns are often painful, red, blistering, wet, squishy, and blanch. Full-thickness or third-degree burns reach the epidermis, dermis, subcutaneous fat, and deeper layers of skin. These burns are not painful, and they can be white, brown, or charred. They have a stiff and leathery feel to the touch and no blanching [11].

The etiology of the burn influences its location [12]. Legs are the most commonly burned areas in general, with the upper limb being more burned than the lower limb. There is some variation in burn pathogenesis. The most commonly scalded body part in scald-induced burns is the limb, followed by the trunk. Electrical burns are most common on limbs, then on hands. The most frequently burned areas for explosions are the head, face, and neck, followed by the extremities [12,13].

Bloodstream Infections (BSIs) are very common in critically ill patients and are associated with an increased risk of mortality, longer hospital stays, and higher healthcare costs. Because of impaired skin barriers, immunocompromised status, the use of invasive devices, the occurrence of multiple wound manipulations, and their prolonged hospitalization, burn patients are especially vulnerable to BSIs [9]. Bacteremia in burn patients has been reported to be caused by more resistant and fatally invasive pathogens such as Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, and the Acinetobacter baumannii -calcoaceticus complex [14]. Methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa (PA) are the most common multidrug-resistant (MDR) bacteria found in burn wound infections [15-19]. Due to resistance, such infections are frequently fatal and difficult to treat, making them a major concern. Though MRSA and P. aeruginosa are common causes of nosocomial infections, burn patients who stay in the hospital for an extended period of time are at a higher risk of infection [20], in addition to Healthcare-associated infections, also known as nosocomial infections, are among the most lethal sequelae of burn injuries [21]. In contrast, viral infections in burn patients are less common and less accurately described by healthcare professionals than fungal and bacterial infections [22].

Many factors have been identified as risk factors for increased mortality and morbidity in burn victims. To begin, gender is a predictor of both mortality and morbidity in burn patients, with males being more likely than females to develop burn injuries [23]. Second, the percentage of total body surface burned is linked to infections in burn victims, with 70% of patients with more than 20% total body surface area burns requiring surgical intervention [24,25]. Third, inhalation injuries frequently result in pulmonary and systemic complications, increasing the risk of death after burns [25]. Inhalation injury occurs when fumes or poisonous gases enter the body. This type of injury can occur in a variety of settings, including fires, industrial accidents, and chemical spills. Breathing hot air damages the bronchus and can cause laryngopharyngeal edema, which obstructs the upper airway and necessitates immediate intubation. Edema caused by neurogenic inflammation can narrow the airway lumina, resulting in clinical problems such as airway mucosal hyperemia, the formation of obstructive casts in the airway, and bronchospasm [26]. As a result, following an inhalation injury, respiratory complications contribute to pulmonary oedema and pneumonia, and Acute Respiratory Distress Syndrome (ARDS) can develop rapidly [26-28]. Furthermore, delays in sepsis diagnosis and antibiotic administration, as well as the early start of critical medications, such as appropriate antibiotics, have been linked to increased mortality in critically ill patients [29].

Furthermore, studies have shown that blood alcohol level predicts infectious complications in burn patients, and diabetes and hypertension are linked to an increased risk of death in older adults [23,30]. Diabetes mellitus has consistently been identified as one of the top ten leading causes of death. Burns patients with diabetes mellitus may have poorer clinical outcomes and increased complications due to the numerous pathological changes and associated disease processes seen in these patients [31]. The triad of vasculopathy, monopathy, and neuropathy is the primary explanation. Poor blood supply as a result of mechanisms such as increased hyperviscosity caused by hyperglycemia slows the ingress of oxygen and already defunct inflammatory cells into injured areas, compromising healing and creating an anaerobic environment conducive to the growth of opportunistic bacteria. Diabetes also has a negative impact on the immune system by impairing the function of polymorpho-

nuclear leukocytes, macrophages, and lymphocytes. As a result, diabetic patients are more likely to develop infections, have poor wound healing, and eventually require amputation [31]. Diabetics had significantly lower limb burns [31,32]. Diabetes was also linked to an increased risk of bacteremia and sepsis [33].

Septic shock, also known as sepsis, is a potentially fatal disease process characterized by acute circulatory collapse and persistent hypotension that does not respond to intravenous fluid therapy [34-36]. Many studies have found that being over the age of 50, having a total body surface area burn, an inhalation injury, and being male are all risk factors for sepsis and Multiple Organ Dysfunction Syndrome (MODS). Individuals with weakened immune systems, such as those with diabetes, renal failure, liver failure, or cancer, are also at risk [36]. Conventional diagnostic markers used to determine an inflammatory response to infection are neither specific nor sensitive in burn patients; thus, a fast sequential organ failure assessment QSOFA score based on three parameters was developed to diagnose sepsis: altered mental status, tachypnea, and hypotension [37]. Furthermore, biomarkers can aid in the detection of sepsis in burn patients [38,39]. Among a wide range of laboratory tests, Procalcitonin (PCT) has emerged as the leading biomarker for accurately and quickly indicating the presence of systemic infection. PCT blood levels in healthy people are barely detectable. However, in the presence of systemic bacterial infection, its levels rise dramatically during the infection course and then rapidly fall after the septic process is controlled [40]. It has the potential to be regarded as a biomarker with a strong diagnostic ability to differentiate between septic and non-septic burn patients [41]. Another useful biomarker is Mid-Regional pro-Adrenomedullin (MR-proADM). Increased MRproADM levels have been linked to burning injuries.

When compared to other critically ill patients, those who have suffered severe burns are more likely to develop infections, systemic inflammatory responses, and sepsis. Infections are frequently linked to both the burn wound and the devices. When a patient is critically ill, hygiene precautions and targeted digestive decontamination are used as preventative measures because most infections begin with the colonization of the digestive tract [42]. Sepsis caused by bacterial translocation from the gastrointestinal tract is a well-known cause of morbidity and mortality in people with severe burns (GIT). This translocation is dependent on the GIT flora. Consumption of Lactobacillus bacteria has been shown to reduce translocation [43]. Probiotics have been shown to benefit burn patients by regulating the intestinal barrier and reducing inflammation. In contrast to interleukin 6, which is a pro-inflammatory mediator and is frequently produced in burns, Immunoglobulin A (IgA) is an anti-inflammatory antibody [44]. When the intestinal barrier fails and inflammatory mediators enter the systemic circulation via mesenteric lymph channels, they contribute to the development of Multiple Organ Dysfunction Syndrome (MODS) [45]. The postburn acute-phase response, on the other hand, is characterized by multiorgan dysfunction [46]. Patients who have been severely burned frequently experience varying degrees of organ failure, and when multiple major organs are affected, mortality becomes extremely high [47]. Sepsis due to a severe, injury-induced immunoinflammatory response remains a common complication and one of the leading causes of multi-organ failure and mortality in patients with significant wounds [47]. In the early post-burn phase, numerous mediators are released, including cytokines (TNF, IL-1, etc.), eicosanoids (Prostaglandins [PGs], thromboxane, leukotrienes), and Platelet Aggregating (Activating) Factor (PAF). They promote vascular permeability and tissue injury in a variety of ways.

Burn injuries can result in a variety of complications, which can be classified as local or systemic. Skin contracture, hypertrophic scar and keloid, alopecia, wound infections, and ophthalmic complications are examples of local ones, whereas systemic ones affect nearly every organ system [48,49]. Local complications include skin contractures, which are known to be serious complications following burn injury. Burn scar contracture is a condition in which the skin is replaced by pathologic scar tissue that is too short and extensible, impairing mobility or tissue alignment of an associated joint or anatomical structure [50]. Another local complication is wound infection, which, if left untreated, can lead to systemic infection and death. Staphylococcus and Pseudomonas species are the most common pathogens. In the diagnosis and treatment of infections in burn patients, physical examination, cultures, and wound pathology all play roles. Organisms should be treated appropriately based on their temporal relationships to the time of admission, and those prevalent in the burn unit should be treated specifically based on their antibiograms [51]. Ocular burns can cause peri-orbital tissue edema as a result of aggressive fluid resuscitation, eyelid retraction leading to ocular exposure, direct injury to the globe, blunted Bell's and blink response secondary to sedation, and direct injury to the eye. All of these factors, individually or collectively, can result in exposure keratopathy, corneal infection, ulceration, and, finally, corneal scarring or perforation [52].

Local complications include alopecia, hypertrophic scar, keloid formation, and Margolin ulcer, a cutaneous ulcer that develops in the presence of previously burned skin, longstanding scars, and chronic wounds [53,54].

Systemic complications from burns, on the other hand, can result in organ failure and death. One of the most serious burn-related complications, with a high mortality rate [55], is acute renal failure. The majority of renal failures occur immediately after an injury or later, when sepsis develops. Despite adequate fluid therapy, decreased urine production is usually the first sign of acute renal failure. If renal failure in burn victims is adequately predicted and treated promptly, morbidity and overall mortality will be significantly reduced, particularly in severe burn injuries [56]. Cellular hypoxia, on the other hand, causes cerebral edema and an increase in intracranial pressure in cases of severe burns. Agitation, disorientation, ataxia, abnormal posture, brief loss of consciousness, seizures, and even shock are other symptoms of central nervous dysfunction [49]. One of the most common complications in people who have had severe burns is intestinal infection. It has the potential to cause sepsis and multiple organ dysfunction syndrome (MODS), both of which are leading causes of death in these patients. Most gut-derived infections are caused by abnormal translocation of intestinal bacteria or endotoxins caused by a faulty gut barrier [57]. Furthermore, burn patients may experience intraabdominal hypertension (IAH) and secondary abdominal compartment syndrome (ACS), which are two potential side effects of systemic burn injuries, particularly in those with burns covering more than 60% of the body surface area [49,58].

In people who have had systemic burns, smoke inhalation injuries are common. Thermal damage and irritant adhesion to the upper respiratory tract cause the release of inflammatory mediators and reactive oxygen species, as well as increased vascular permeability and edema [59]. Finally, tachycardia, in-

creased cardiac output, and increased myocardial oxygen demand are signs of severe burn-related cardiac dysfunction [58]. These complications, however, are regarded as difficult, particularly in children. Children require more fluid resuscitation than adults for burns of any size because their body surface area to mass ratio is greater, making them more susceptible to hypothermia. They also have smaller and narrower tracheas than adults, making them more prone to airway obstruction and necessitating intubation by a medical professional who is familiar with dealing with difficult juvenile airways [60].

The first step in burn therapy is wound cleaning and debridement to remove necrotic tissue, which significantly reduces blood flow and immune system access [61]. The implementation of a universal decolonization protocol in an adult and pediatric burn center resulted in a significant reduction in all hospital-acquired infections. This is explained by the lack of a treatment delay because it does not require evidence of positive MRSA culture to be applied. Furthermore, daily chlorhexidine bathing has been shown to reduce both skin colonization and the overall environmental microbial burden. These precautions help to reduce the possibility of secondary infections and the risk of patient-to-patient transmission [62]. If topical antibiotics and dressings do not work, or if the patient rapidly develops a high level of resistance to multiple antibiotics, IV antibiotics are administered. However, drug resistance in burn patients can be caused by several factors, which is a major concern due to limited therapeutic options and decreased treatment efficacy [63]. Long-term antibiotic use, prophylactic antibiotics in unnecessary situations (first 3 days of new burn cases), antibiotic misuse or inadequate dosing, and overuse of broad-spectrum antibiotics due to their low cost are among these factors [64]. As a result, it is critical to determine the pathogen spectrum and drug sensitivity of pathogens associated with nosocomial infection in burn patients [65]. As a result, drug resistance prevention and management strategies such as infection control programs that include hand hygiene, monitoring of agreements with local antimicrobial agent guidelines, and the development of antimicrobial stewardship programs in burn centers are critical. As a result, drug resistance prevention and management strategies such as infection control programs that include hand hygiene, monitoring of agreements with local antimicrobial agent guidelines, and the development of antimicrobial stewardship programs in burn centers are critical.

In severe inhalation injury due to severe respiratory distress or because the patient's airway is compromised by laryngeal edema, however, airway management, including endotracheal intubation and mechanical ventilation, may be required [66]. Immediate assessment includes conscious level and vital signs assessment, airway evaluation with cervical spine stabilization, breathing, circulation, and coexisting whole body burns and trauma [67].

Conclusion

The burn wound is a vulnerable site for opportunistic colonization by organisms of endogenous and exogenous origin. The likelihood of invasive burn wound infection is determined by patient factors such as age, the extent of injury, and depth of burn combined with microbial factors such as type and several organisms, enzyme and toxin production, and motility. Burn wound infections are classified based on the causative organism, the depth of invasion, and the tissue response. Although the survival rate after devastating burn injuries has increased in recent decades due to medical advances in burn wound care, nutritional and fluid resuscitation, and improved infection control practices, there are still a large number of patients at a high risk of death. Sepsis is a common burn complication that is defined as "severe organ dysfunction attributed to the host's disordered response to infection" and is the leading cause of death in burn patients. Indeed, burn injuries are associated with a cascade of events that can lead to sepsis and multiple organ dysfunction syndrome, such as hypovolaemic shock, immune and inflammatory responses, and metabolic changes. As a result, critical care is a critical step in preventing mortality in burn patients.

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References

1. Norbury W, Herndon DN, Tanksley J, Jeschke MG, Finnerty CC. Infection in Burns. Surgical infections. 2016; 1: 250-255.

2. Barret JP, Herndon DN. Effects of burn wound excision on bacterial colonization and invasion. Plastic and reconstructive surgery. 2003; 111: 744-752.

3. Greenhalgh DG, Saffle JR, Holmes JH, 4th Gamelli RL, Palmieri TL, et al. American Burn Association Consensus Conference on Burn Sepsis and Infection Group. American Burn Association consensus conference to define sepsis and infection in burns. Journal of burn care & Research: official publication of the American Burn Association. 2007; 28: 776-790.

4. Dvorak JE, Ladhani HA, Claridge JA. Review of Sepsis in Burn Patients in 2020. Surgical infections. 2021; 22: 37-43.

5. Belba MK, Petrela EY, Belba AG. Epidemiology and outcome analysis of sepsis and organ dysfunction/failure after burns. Burns: journal of the International Society for Burn Injuries. 2017; 43: 1335-1347.

6. de Macedo JL, Rosa SC, Castro C. Sepsis in burned patients. Revista da Sociedade Brasileira de Medicina Tropical. 2003; 36: 647-652.

7. Javanmardi F, Emami A, Pirbonyeh N, Rajaee M, Hatam G, et al. Study of multidrug resistance in prevalent Gram-negative bacteria in burn patients in Iran: A systematic review and meta-analysis. Journal of Global Antimicrobial Resistance. 2019; 19: 64-72.

8. Ladhani HA, Yowler CJ, Claridge JA. Burn Wound Colonization, Infection, and Sepsis. Surgical infections. 2021; 22: 44-48.

9. Tang CQ, Li JQ, Shou BM, Pan BH, Chen TS, et al. Epidemiology and outcomes of bloodstream infections in 177 severe burn patients from an industrial disaster: A multicentre retrospective study. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2018; 24: 199.e1-199.e7.

10. Warby R, Maani CV. Burn Classification. In StatPearls. StatPearls Publishing. 2022.

11. Schaefer TJ, Szymanski KD. Burn Evaluation And Management. In StatPearls. StatPearls Publishing. 2022.

12. Li H, Yao Z, Tan J, Zhou J, Li Y, et al. Epidemiology and outcome analysis of 6325 burn patients: A five-year retrospective study in a major burn center in Southwest China. Scientific reports. 2017; 7: 46066.

13. Mulugeta T, Alemayehu H, Gerema U. Clinical Profiles and the Outcomes of Burn Patients Admitted to the Burn Unit of Jimma Medical Center. Clinical, cosmetic and investigational dermatology. 2021; 14: 859-866.

14. Ressner RA, Murray CK, Griffith ME, Rasnake MS, Hospenthal DR, et al. Outcomes of bacteremia in burn patients involved in combat operations overseas. Journal of the American College of Surgeon. 208; 206: 439-444.

15. Mir MA, Khurram MF, Khan AH. What should be the antibiotic prescription protocol for burn patients admitted t the department of burns, plastic and reconstructive surgery. International wound journal. 2017; 14: 194-197.

16. Mater ME, Yamani AE, Aljuffri AA, Binladen SA. Epidemiology of burn-related infections in the largest burn unit in Saudi Arabia. Saudi medical journal. 2020; 41: 726-732.

17. Murphy RA, Nisenbaum L, Laba AS, Sheridan RL, Ronat JB, et al. Invasive Infection and Outcomes in a Humanitarian Surgical Burn Program in Haiti. World journal of surgery. 2016; 40: 1550-1557.

18. Escandón-Vargas K, Tangua AR, Medina P, Zorrilla-Vaca A, Briceño E, et al. Healthcare-associated infections in burn patients: Timeline and risk factors. Burns: Journal of the International Society for Burn Injuries. 2020; 46: 1775-1786.

19. Bourgi J, Said JM, Yaakoub C, Atallah B, Al Akkary N, et al. Bacterial infection profile and predictors among patients admitted to a burn care center: A retrospective study. Burns: Journal of the International Society for Burn Injuries. 2020; 46: 1968-1976.

20. Griffiths R, Fernandez R, Halcomb E. Reservoirs of MRSA in the acute hospital setting: A systematic review. Contemporary nurse. 2002; 13: 38-49.

21. Escandón-Vargas K, Tangua AR, Medina P, Zorrilla-Vaca A, Briceño E, et al. Healthcare-associated infections in burn patients: Timeline and risk factors. Burns: Journal of the International Society for Burn Injuries. 2020; 46: 1775-1786.

22. Zajíček R, Hrbáčková H, Šuca H, Pafčuga I, Labská K, et al. A combination of herpes virus infection (hsv-1, hhv-6) and multi-resistant bacterial infection in a severely burned pediatric patient - a case report. A combination of herpes virus infection (hsv-1, hhv-6) and multi-resistant bacterial infection in a severely burned pediatric patient - a case report. Acta chirurgiae plasticae. 2020; 60: 62-67.

23. Griffin R, Poe AM, Cross JM, Rue LW, McGwin G. The Association between Blood Alcohol Level and Infectious Complications among Burn Patients. Journal of Burn Care & Research. 2009; 30: 395-399.

24. Renau Escrig AI, Salavert M, Vivó C, Cantón E, Pérez del Caz MD, et al. Candidemia in major burns patients. Mycoses. 2016; 59: 391-398.

25. Guo HL, Zhao GJ, Ling XW, Xu JJ, Lu CJ, et al. Using competing risk and multistate model to estimate the impact of nosocomial infection on length of stay and mortality in burn patients in Southeast China. BMJ open. 2019; 8: e020527.

26. Kubo T, Osuka A, Kabata D, Kimura M, Tabira K, et al. Chest physical therapy reduces pneumonia following inhalation injury. Burns. 2021; 47: 198-205.

27. Yamamura H, Morioka T, Hagawa N, Yamamoto T, Mizobata Y. Computed tomographic assessment of airflow obstruction in smoke inhalation injury: Relationship with the development of pneumonia and injury severity. Burns. 2015; 41: 1428-1434.

28. Azzena B, Perozzo FAG, De Lazzari A, Valotto G, Pontini A. Burn Unit admission and management protocol during COVID-19 pandemic. Burns. 2020.

29. Lavrentieva A, Voutsas V, Konoglou M, et al. Determinants of Outcome in Burn ICU Patients with Septic Shock. Journal of Burn Care & Research. 2017; 38: e172-e179.

30. Secanho MS, Rajesh A, Menezes Neto BF, et al. Epidemiology of Burn-Related Morbidity and Mortality in Patients Over 80 Years of Age. Journal of Burn Care & Research. 2021; 43: 10421047.

31. Low ZK, Ng WY, Fook-Chong S, Tan BK, Chong SJ, Hwee J, et al. Comparison of clinical outcomes in diabetic and non-diabetic burns patients in a national burns referral centre in southeast Asia: A 3-year retrospective review. Burns: Journal of the International Society for Burn Injuries. 2017; 43: 436-444.

32. Sayampanathan AA. Systematic review of complications and outcomes of diabetic patients with burn trauma. Burns: Journal of the International Society for Burn Injuries. 2016; 42: 1644-1651.

33. Yang B, Cai YQ, Wang XD. The impact of diabetes mellitus on mortality and infection outcomes in burn patients: a meta-analysis. European review for medical and pharmacological sciences. 2021; 25: 2481-2492.

34. Belba MK, Petrela EY, Belba AG. Epidemiology and outcome analysis of sepsis and organ dysfunction/failure after burns. Burns. 2017; 43: 1335-1347.

35. Gille J, Ostermann H, Dragu A, Sablotzki A. MR-proADM. Journal of Burn Care & Research. 2017; 38: 290-298.

36. Dvorak JE, Khandelwal A, Ladhani HA, Claridge JA. Review of Sepsis in Burn Patients in 2020. Surgical Infections. 2021; 22: 37-43.

37. Lavrentieva A, Voutsas V, Konoglou M, et al. Determinants of Outcome in Burn ICU Patients with Septic Shock. Journal of Burn Care & Research. 2017; 38: e172-e179.

38. Cabral L, Afreixo V, Almeida L, Paiva JA. The Use of Procalcitonin (PCT) for Diagnosis of Sepsis in Burn Patients: A Meta-Analysis. PloS one. 2016; 11: e0168475.

39. Mehanic S, Baljic R. The importance of serum procalcitonin in diagnosis and treatment of serious bacterial infections and sepsis. Materia socio-medica. 2013; 25: 277-281.

40. Cabral L, Afreixo V, Santos F, Almeida L, Paiva, JA. Procalcitonin for the early diagnosis of sepsis in burn patients: A retrospective study. Burns: journal of the International Society for Burn Injuries. 2017; 43: 1427-1434.

41. Gille J, Ostermann H, Dragu A, Sablotzki A. MR-proADM: A New Biomarker for Early Diagnosis of Sepsis in Burned Patients. Journal of burn care & research: Official publication of the American Burn Association. 2017; 38: 290-298.

42. Hidalgo F, Mas D, Rubio M, Garcia-Hierro P. Infections in critically ill burn patients. Medicina intensive. 2016; 40: 179-185.

43. Koren L, Gurfinkel R, Glezinger R, Perry ZH, Lev-Ari S, et al. The effect of Lactobacillus bacteria supplement on sepsis and its complications in patients with acute burns. Burns. 2007; 33: 594-598.

44. Saputro ID, Putra ON, Pebrianton H, Suharjono. Effects of probiotic administration on IGA and IL-6 level in severe burn patients: a randomized trial. Annals of burns and fire disasters. 2019; 32: 70-76.

45. Shimizu K, Ogura H, Asahara T, et al. Gut microbiota and environment in patients with major burns-a preliminary report. Burns. 2015; 41: e28-e33.

46. Jeschke MG, Chinkes DL, Finnerty CC, Kulp G, Suman OE, et al. Pathophysiologic response to severe burn injury. Annals of surgery. 2008; 248: 387-401.

47. Aikawa N, Shinozawa Y, Ishibiki K, Abe O, Yamamoto S, Motegi M, Yoshii H, et al. Clinical analysis of multiple organ failure in burned patients. Burns, including thermal injury. 1987; 13: 103-109.

48. Ogawa R. Keloid and Hypertrophic Scars Are the Result of Chronic Inflammation in the Reticular Dermis. International journal of molecular sciences. 2017; 18: 606.

49. Nielson CB, Duethman NC, Howard JM, Moncure M, Wood JG. Burns: Pathophysiology of Systemic Complications and Current Management. Journal of burn care & research: Official publication of the American Burn Association. 2017; 38: e469-e481.

50. Parry I, Walker K, Niszczak J, Palmieri T, Greenhalgh D. Methods and tools used for the measurement of burn scar contracture. Journal of burn care & research: fficial publication of the American Burn Association. 2010; 31: 888-903.

51. D'Abbondanza JA, Shahrokhi S. Burn Infection and Burn Sepsis. Surgical infections. 2021; 22: 58-64.

52. Cabalag MS, Wasiak J, Syed Q, Paul E, Hall AJ, et al. Early and late complications of ocular burn injuries. Journal of plastic, reconstructive & aesthetic surgery: JPRAS. 2015; 68: 356-361.

53. Agaoglu G, Özer F, Karademir S, Agaoglu E, Erol O. Hair Transplantation in Burn Scar Alopecia After Combined Non-Ablative Fractional Laser and Microfat Graft Treatment. Aesthetic surgery journal. 2021; 41: NP1382-NP1390.

54. Shah M, Crane JS. Marjolin Ulcer. In: StatPearls. Treasure Island (FL): StatPearls Publishing. 2023.

55. Folkestad T, Brurberg KG, Nordhuus KM, Tveiten CK, Guttormsen AB, et al. Acute kidney injury in burn patients admitted to the intensive care unit: a systematic review and meta-analysis. Critical care (London, England). 2020; 24: 2.

56. Emara SS, Alzaylai AA. Renal failure in burn patients: a review. Annals of burns and fire disasters. 2013; 26: 12-15.

57. Wang C, Li Q, Ren J. Microbiota-Immune Interaction in the Pathogenesis of GutDerived Infection. Frontiers in immunology. 2019; 10: 1873.

58. Lightfoot E, Horton JW, Maass DL, White DJ, McFarland RD, et al. Major burn trauma in rats promotes cardiac and gastrointestinal apoptosis. Shock (Augusta, Ga.). 1999; 11: 29-34.

59. Foncerrada G, Culnan DM, Capek KD, González-Trejo S, Cambiaso-Daniel J, et al. Inhalation Injury in the Burned Patient. Annals of plastic surgery. 2018; 80: S98-S105.

60. Palmieri TL. Pediatric Burn Resuscitation. Critical care clinics. 2016; 32: 547-559.

61. Thomas RE, Thomas BC. Reducing Biofilm Infections in Burn Patients' Wounds and Biofilms on Surfaces in Hospitals, Medical Facilities and Medical Equipment to Improve Burn Care: A Systematic Review. International journal of environmental research and public health. 2021; 18: 13195.

62. Johnson AT, Nygaard RM, Cohen EM, Fey RM, Wagner AL. The Impact of a Universal Decolonization Protocol on Hospital-Acquired Methicillin-Resistant Staphylococcus aureus in a Burn Population. Journal of burn care & research: Official publication of the American Burn Association. 2016; 37: e525-e530.

63. Ackerman BH, Guilday RE, Reigart CL, Patton ML, Haith LR. Evaluation of the relationship between elevated vancomycin trough concentrations and increased efficacy and/or toxicity. Journal of burn care & research: official publication of the American Burn Association. 2013; 34: e1-e9.

64. Javanmardi F, Emami A, Pirbonyeh N, Rajaee M, Hatam G, et al. Study of multidrug resistance in prevalent Gram-negative bacteria in burn patients in Iran: A systematic review and meta-analysis. Journal of global antimicrobial resistance. 2019; 19: 64-72.

65. Sun FJ, Zhang XB, Fang Y, et al. Spectrum and drug resistance of pathogens from patients with burns. Burns: Journal of the International Society for Burn Injuries. 2012; 38: 1124-1130.

66. Brusselaers N, Logie D, Vogelaers D, Monstrey S, Blot S. Burns, inhalation injury and ventilatorassociated pneumonia: Value of routine surveillance cultures. Burns. 2012; 38: 364-370.

67. Desai S, Zeng D, Chong S. Airway management in inhalation injury: A case series. Singapore Medical Journal. 2020; 61: 46-53.