EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 12
Issue: 10
Year: 2025

NECROTIZING FASCIITIS: - A NARRATIVE REVIEW OF EPIDEMIOLOGY, PATHOGENESIS, AND EMERGING THERAPIES IN WESTERN UGANDA

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DOI: https://doi.org/10.5281/zenodo.17221568

Article Received on 02/08/2025 **Article Revised on 22/08/2025** **Article Accepted on 11/09/2025**

ABSTRACT
Necrotizing fasciitis (NF) is a rapidly progressing soft tissue infection with high mortality, characterized by fascial necrosis and systemic toxicity. Despite advances in surgical and antimicrobial therapies, NF remains a clinical challenge. This narrative review examines its epidemiology, pathogenesis, and emerging treatments. NF is primarily polymicrobial, with Group A Streptococcus (GAS) and mixed anaerobic-aerobic infections being most common. Pathogenesis involves bacterial virulence, immune evasion, and host susceptibility (e.g., diabetes, immunosuppression). Early surgical debridement and broad-spectrum antibiotics remain the cornerstone of treatment, while emerging therapies—such as immunomodulation (IVIG, hyperbaric oxygen), novel antimicrobials, and bacteriophage therapy—show promise. A multidisciplinary approach is essential, and further trials are needed to validate new treatments.

KEYWORDS: Necrotizing fasciitis, infection, epidemiology, pathogenesis, immunomodulation, bacteriophage therapy.

INTRODUCTION
Necrotizing fasciitis (NF) is a life-threatening soft tissue infection characterized by rapid fascial destruction, systemic toxicity, and mortality rates exceeding 20-40% in resource-limited settings (Stevens & Bryant, 2017; Miller et al., 2021).

The disease is notoriously challenging to manage due to its polymicrobial etiology, which often involves a synergistic combination of aerobic and anaerobic bacteria, including Streptococcus pyogenes, Staphylococcus aureus, and Clostridium species (Hakkarainen et al., 2014).

The pathogenesis of NF involves bacterial virulence factors, host immune responses, and ischemic tissue damage, culminating in fascial necrosis and sepsis (Sarani et al., 2009).

Early diagnosis remains difficult due to nonspecific initial symptoms, often leading to delays in surgical intervention, which is critical for survival (Goh et al., 2014).

This narrative review explores the latest epidemiological trends, including rising incidence rates associated with comorbidities such as diabetes and obesity (Misiakos et al., 2014). Additionally, it examines advances in diagnostic tools (e.g., imaging and biomarkers) and emerging therapies, including hyperbaric oxygen, immunomodulatory treatments, and novel antibiotics (Hua et al., 2020). By synthesizing current evidence, this review aims to provide a comprehensive understanding of NF management and future directions in research. Epidemiology of Necrotizing Fasciitis.

Necrotizing fasciitis is a rare but life-threatening condition with significant regional variations in its incidence and outcomes. Global studies have provided valuable insights into the epidemiology of the disease, showing differing mortality rates, pathogen distributions, and clinical outcomes based on geographic region, healthcare access, and patient characteristics.

Global Incidence and Mortality Rates
In the United States, studies report the incidence of necrotizing fasciitis as 0.3 to 0.4 cases per 100,000 person-years (Huang et al., 2020). Mortality rates are

high, with figures ranging from 6.9% in Japan (Suzuki et al., 2021) to 31.7% in the Netherlands (van Stigt et al., 2022). Variations in mortality rates can be attributed to factors such as healthcare infrastructure, early detection, and the timeliness of surgical intervention.

In developing countries, delayed diagnosis and limited access to advanced medical care contribute to poorer outcomes and higher fatality rates, with mortality often exceeding 40% in regions with inadequate resources (Miller et al., 2021).

Risk factors for necrotizing fasciitis include

Chronic Conditions: Diabetes mellitus, immunocompromised states (such as HIV), and malignancy are major predisposing factors (van Stigt et al., 2022; Miller et al., 2021).

Trauma and Surgery: The disease often follows trauma, surgical procedures, or the introduction of foreign bodies (e.g., intravenous drug use, penetrating injuries).

Skin Infections: Skin and soft tissue infections, including cellulitis, increase the risk of developing necrotizing fasciitis.

Vibrio vulnificus Infections: In coastal areas, infections due to Vibrio vulnificus following exposure to contaminated seawater or raw shellfish ingestion are notable contributors to necrotizing fasciitis (Wang & Lim, 2014).

Key Risk Factors

Category	Examples
1. Medical	Diabetes, HIV, malignancy
2. Trauma	Surgery, IV drug use, burns
3. Environmental	*Vibrio vulnificus* exposure (Wang & Lim, 2014)

PATHOGENESIS OF NECROTIZING FASCIITIS

The pathogenesis of necrotizing fasciitis involves complex interactions between the host's immune system and the infecting microorganisms. The disease can be triggered by both aerobic and anaerobic bacteria, and the rapid spread of infection is exacerbated by factors such as the ability of pathogens to produce toxins and enzymes that degrade tissue and evade immune defences.

MICROBIAL ETIOLOGY

Necrotizing fasciitis is most commonly polymicrobial, involving both Gram-positive and Gram-negative bacteria, as well as anaerobes.

Key pathogens include: Gram-positive bacteria: Streptococcus pyogenes (Group A Streptococcus, GAS) and Staphylococcus aureus, including methicillin-resistant S. aureus (MRSA), are frequently implicated (Halbhavi et al., 2018).

Gram-negative bacteria: Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa have been identified as important contributors to the infection, particularly in patients with comorbidities (Li et al., 2022).

Anaerobic bacteria: Clostridium species, Bacteroides fragilis, and Peptostreptococcus are involved in the pathogenesis, as they produce potent toxins that contribute to tissue necrosis (Horn et al., 2017).

Pathogenesis for Microbial Etiology

Gram-positive (60–70%):	• *S. pyogenes (GAS)* • *MRSA (Halbhavi et al., 2018)*
Gram-negative (20–30%):	• *E. coli, K. pneumoniae* (Li et al., 2022)
Anaerobes (10–20%):	• *Clostridium spp. (Horn et al., 2017)*

PATHOPHYSIOLOGY

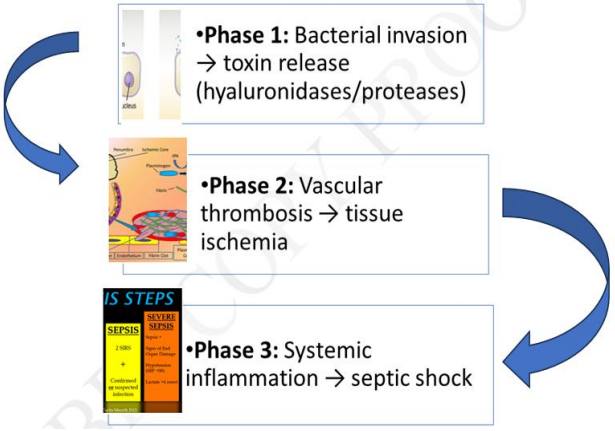
The progression of necrotizing fasciitis begins with bacterial invasion and colonization of the subcutaneous tissue and fascia, leading to the production of a variety of virulence factors:

Toxins and Enzymes: Bacteria produce exotoxins, proteases, and hyaluronidases that break down host tissue, facilitate bacterial spread, and damage blood vessels, leading to ischemia and necrosis (Miller et al., 2021).

Immune Evasion: The pathogens involved in NF have evolved mechanisms to evade the host immune response, including the production of biofilms, which make bacterial colonies more resistant to antibiotics and phagocytosis (Miller et al., 2021).

Systemic Inflammation and Shock: As the infection progresses, it can lead to sepsis and systemic inflammatory response syndrome (SIRS). The release of pro-inflammatory cytokines, such as TNF-alpha and interleukins, contributes to widespread tissue damage and organ failure (Halbhavi et al., 2018).

Pathophysiological Mechanisms



EMERGING THERAPIES AND TREATMENT STRATEGIES

The treatment of necrotizing fasciitis requires a multi-faceted approach, including early diagnosis, surgical intervention, broad-spectrum antibiotic therapy, and supportive care. In recent years, emerging therapies and advancements in the management of necrotizing fasciitis have shown promise in improving outcomes and reducing mortality.

Surgical Debridement

Surgical intervention is the cornerstone of treatment for necrotizing fasciitis. The primary goal is to remove necrotic tissue and halt the spread of infection. Early and aggressive debridement is associated with improved survival rates. Multiple surgical interventions may be necessary, as the infection can spread rapidly through the fascial plane (Miller et al., 2021).

ANTIBIOTIC THERAPY

Empiric antibiotic therapy is initiated immediately upon suspicion of necrotizing fasciitis and is tailored based on microbial culture results. The following antibiotic regimens are commonly used:

Broad-spectrum Coverage: Empiric therapy typically includes antibiotics that cover Gram-positive, Gram-negative, and anaerobic organisms, such as piperacillin-tazobactam, meropenem, and vancomycin.

MRSA and Streptococcus pyogenes: In areas with a high prevalence of MRSA or Group A Streptococcus (GAS), vancomycin or clindamycin is added for better coverage (Wang & Lim, 2014).

Vibrio vulnificus: For infections related to Vibrio vulnificus, a combination of third-generation cephalosporins and doxycycline is recommended (Wang & Lim, 2014).

Hyperbaric Oxygen Therapy (HBOT)

Hyperbaric oxygen therapy (HBOT) has been investigated as an adjunctive treatment for necrotizing fasciitis. HBOT is thought to promote tissue healing by enhancing oxygen delivery to hypoxic tissues, inhibiting bacterial growth, and improving the effectiveness of white blood cells in killing bacteria. However, its role remains controversial, and more research is needed to establish definitive clinical guidelines (Miller et al., 2021).

IMMUNOMODULATORY THERAPY

Recent studies suggest that immunomodulatory therapies, such as intravenous immunoglobulin (IVIG), may help in controlling the excessive immune response in necrotizing fasciitis, particularly in cases caused by Streptococcus pyogenes or Staphylococcus aureus. IVIG has been shown to reduce the severity of toxic shock and improve outcomes in some cases (Horn et al., 2017).

NOVEL ANTIMICROBIAL AGENTS

With the increasing prevalence of antimicrobial resistance, the development of new antibiotics and adjuvants is crucial in treating necrotizing fasciitis. Research into novel antimicrobial peptides, bacteriophage therapy, and drug delivery systems holds promise for more effective treatments in the future (Li et al., 2022).

Necrotizing Fasciitis Management Algorithm

START

↓

Patient with Suspected NF

↓

Immediate Actions (0-1h):

Call surgical team STAT

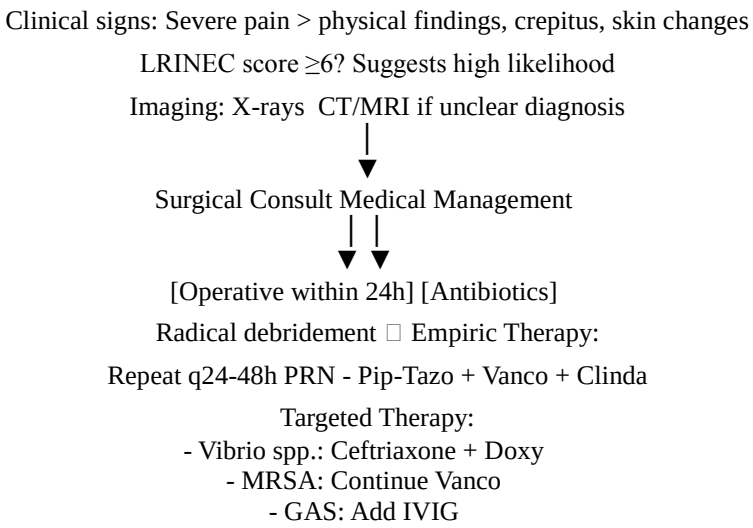
IV access + resuscitation (fluids, vasopressors if needed)

 Labs: CBC, lactate, blood cultures

Start broad-spectrum antibiotics: Pip-Tazo + Vanco + Clinda

↓

Diagnostic Confirmation:



Critical Analysis & Future Directions

Diagnostic challenges: LRINEC score has 60–80% sensitivity

Research gaps: Need for RCTs on HBOT/IVIG

Equity concerns: 80% of deaths occur in low-income regions

CONCLUSION

Necrotizing fasciitis remains a challenging and life-threatening infection, requiring rapid diagnosis and aggressive management. While surgical debridement and broad-spectrum antibiotics remain the standard of care, emerging therapies such as hyperbaric oxygen therapy, immunomodulatory treatments, and novel antimicrobial agents may offer additional benefits in improving patient outcomes. Continued research into the microbiology, pathogenesis, and innovative therapies for necrotizing fasciitis is essential to reduce mortality and improve survival rates.

Additional Information

Authors contribution: All authors have Comprehensive reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Abdifatah Abdi Ali

Critical review of the manuscript for important intellectual content = Mai Abdulla Ali

Funding: This study has no funds

Ethical approval and consent: Not applicable

Availability of data: Data will be available as supplementary materials

ACKNOWLEDGEMENTS

I sincerely thank my academic mentors and advisors for their invaluable guidance and support throughout this review on Necrotizing Fasciitis. Their expertise in infectious diseases has been essential to this work.

I also acknowledge the healthcare professionals, clinicians, and researchers whose contributions in the areas of epidemiology, pathogenesis, and emerging therapies have shaped this review. Their work has been vital in advancing our understanding of this severe condition.

Gratitude is also extended to the institutions and organizations that provided access to the latest research and data, enriching this review.

Additionally, I appreciate the editorial team and peer reviewers for their constructive feedback that improved the manuscript's quality.

Lastly, I am deeply grateful to my family and friends for their unwavering support and encouragement throughout this research process.

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