Analysis of Clinical pattern, Microbiological Pattern, and risk Factors Associated with Mortality in patients diagnosed with necrotizing fasciitis of lower and upper limb in a tertiary care center in South India

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ABSTRACT:

Background: Necrotizing fasciitis (NF) is a rare, rapidly progressive soft tissue infection with high morbidity and mortality rates. **Aim:** This retrospective analysis aimed to compare the clinical features, microbial profiles, and mortality risks between lower and upper limb NF cases. **Methodology:** We conducted a thorough review of medical records the General Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai, Tamil Nadu over a period from October 2007 to October 2008 to identify patients diagnosed with NF. Clinical data, including demographic information, comorbidities, presenting symptoms, laboratory findings, microbial cultures, treatment modalities, and outcomes, were collected and analysed. **Results:** A total of 100 NF cases were identified, with 91% involving the lower limb and 9% involving the upper limb. The most common clinical feature was Tenderness and pain (100%), erythema (96%), edema (93%), fever (86%),tachycardia (76%), skin necrosis (34%), and skin ulceration (29%). Polymicrobial infections were more frequent in upper limb NF 83% compared to lower limb NF 48%, p <0.01. The most commonly isolated pathogens were Staphylococcus aureus (57%), Escherichia Coli (53%), Pseudomonas aeruginosa (45%), Clostridium difficile (7%), and patients with Proteus was (5%) in both groups. Despite aggressive surgical debridement and broad-spectrum antibiotic therapy, the overall mortality rate was 83.3% in lower limb NF and 16.6% in upper limb NF (p <0.0001). **Conclusion:** Multivariate analysis revealed that Septic shock and bacteraemia with multiorgan failure were independent predictors of mortality in NF patients. This study highlights the distinct clinical characteristics and microbial profiles between lower and upper limb NF and underscores the need for prompt diagnosis, aggressive management, and vigilant monitoring to improve outcomes in these critically ill patients.

Keywords: Necrotizing fasciitis, Lower limb, Upper limb, Microbial profile, Mortality risk, Retrospective analysis

Introduction:

Necrotizing fasciitis (NF) is a life-threatening soft tissue infection characterized by rapid necrosis of the fascial planes and surrounding tissues, leading to significant morbidity and mortality if not promptly diagnosed and treated. Although NF can affect any part of the body, it most commonly involves the extremities, with lower limb involvement being more prevalent than upper limb involvement.

Three key features define necrotizing fasciitis (NF) are soft tissue infection that can be fatal, disease that progresses quickly and unusual illness [1,2]. Rapidly progressing NF of the extremities necessitates general amputation or acute debridement as well as several reconstructive procedures [3, 4] because surgical delays have been shown to affect mortality [2]. Both the prevalence of limb loss and the death rate from NF have remained high [1–7]. If soft necrotic When tissue enters the trunk (as in Fournier's syndrome), the approach to treatment needs to be re-evaluated [1,8].

The types of bacteria were linked to the prognosis of NF [6,9-11], but identifying the microorganisms from laboratory culture findings takes several days. The main difference between NF types I and II is whether the aetiology is monomicrobial (type II) or polymicrobial (type I) [12]. Among Gram-positive organisms, Streptococcus pyogenes continues to be the most prevalent pathogen, followed by Staphylococcus aureus. NF type II progresses quickly [12]. Numerous bacteria cause type I diabetes, which is more common in elderly and immunocompromised persons [12]. Because S. pyogenes is hazardous, type II mortality rates were higher than type I mortality rates [8,12].

As of right now, Wong et al.'s LRINEC (Laboratory Risk Indicator for Necrotizing fasciitis score) scoring system is the most suitable method for diagnosing and differentiating between NF cases [13]. Its foundation is a lab characteristic that most institutions can easily score in order to predict survival and distinguish between necrotizing from infections that do not necrotize. Furthermore, several researchers have reported a variety of mortality predictions based on predisposing conditions. Previous research has found that the following factors independently predict death in NF cases: band polymorphonuclear neutrophils (PMN) >10%, serum creatinine >2 mg/dL, liver cirrhosis, malignancy, advanced age (>60 years), Aeromonas and vibrio infection, hypotension, and liver cirrhosis [14, 15].

The pathogenesis of NF involves synergistic polymicrobial infection, typically initiated by a breach in the skin barrier followed by bacterial invasion and proliferation within the deep fascial layers. While the clinical features and outcomes of NF have been extensively studied, limited data exist comparing lower and upper limb NF cases. Understanding the differences in clinical presentation, microbial profiles, and mortality risks between these two groups is essential for optimizing patient management strategies and improving outcomes. Therefore, this retrospective analysis aimed to evaluate and compare the clinical characteristics, microbiological profiles, and mortality risks of lower and upper limb NF cases treated at the General Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai, Tamil Nadu.

Material and Methods:

The institutional review board of our hospital approved this study. This retrospective study was conducted by reviewing medical records of patients diagnosed with NF at the department of General Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai, Tamil Nadu between October 2007 to October 2008. Inclusion criteria includes all the patients diagnosed and treated for necrotizing fasciitis. All patients who had the same workup (complete blood count, coagulation profile, blood chemistry, wound culture for bacteria, chest X-ray, electrocardiogram, an X-ray of the involved body part, ultrasound). Patients were identified through electronic medical records using relevant diagnostic codes and keywords. Clinical data, including demographics, comorbidities, presenting symptoms, laboratory findings, microbial cultures, treatment modalities, and outcomes, were collected and analysed. NF cases were classified based on the anatomical location of the affected limb (lower limb vs. upper limb. Mortality cases were diagnosed by mortality conferences in each hospital based on the results of blood culture, skin condition, images, and pathological findings of the samples submitted before death.

All patients were assessed by physicians as soon as they were admitted. They received broad-spectrum antibiotic treatment for anaerobic and aerobic bacteria as well as early surgical debridement including fasciotomy or primary amputation post-diagnosis. Each patient's medical record was screened for documentation of NF to confirm the diagnosis. Those with NF involving the head, neck, or trunk were excluded. Amputation sites included the fingers, toes, hands, forearms, and below and above the knee. Baseline demographic characteristics, laboratory findings, and clinical presentation were compared between mortality in the late amputation and survival of the amputation groups.

Statistical analysis

Descriptive statistics were used to summarize the data, and comparative analyses between lower and upper limb NF groups were performed using appropriate statistical tests. Version 20.0 of SPSS Statistics (IBM Corp., Armonk, NY, USA) was used to analyse all of the data. With the exception of 20% of cells having anticipated counts of less than 5, in which case Fisher's exact test was employed, continuous variables were analysed using the t test and categorical variables using the chi-square test. The late amputation NF cohort's predictors of death, along with their odds ratio (OR) and 95% confidence interval (CI), were determined using multivariate logistic regression analysis. Statistical significance was defined as p values less than 0.05. Multivariate logistic regression analysis was conducted to identify independent predictors of mortality in NF patients.

Results:

A total of 100 NF cases were included in the analysis, (table 1) 18% of the patients are under 40 years old, while the majority, constituting 82%, are over 40 years old. In terms of gender, males make up a larger portion, comprising 69% of the patients, while females account for the remaining 31%. Necrotising fasciitis Patients shown with 88% involving the lower limb and

9% involving the upper limb. The mean age of patients with lower limb NF was 48.36 years, while those with upper limb NF had a mean age of 62.7 years ($p < 0.001$).

Table 1: Demographic details of patients

Characteristics		Frequency	Percentage
Age			
	< 40 Years	18	18%
	> 40 Years	82	82%
Gender			
	Male	69	69%
	Female	31	31%

Table 2: Site of necrotising fasciitis among patients

Characteristics	Frequency		Total
	Male	Female	
Lower extremity	61	30	91%
Upper extremity	8	1	9%

Table 2 shows predominantly, necrotising fasciitis affects the lower extremities, representing 91% of the cases, with 61 instances observed in males and 30 in females. Conversely, the upper extremities are less commonly affected, constituting only 9% of the cases, with 8 occurrences in males and 1 in female. The perineum and buttock region comprise a smaller proportion, accounting for 3% of the cases, with 2 instances in males and 1 in females. This breakdown underscores the prevalence of necrotising fasciitis in the lower extremities and provides valuable insight into the distribution of the condition across different anatomical sites and genders within the patient population.

Table 3: Clinical features of necrotising fasciitis patients

Characteristics	Frequency				Total (100)
	Male (69)		Female (31)		
	N	%	N	%	
Tenderness and pain	69	100%	31	100%	100
Erythema	67	97%	29	94%	96
Edema	65	94%	28	90%	93
Fever	62	90%	24	77%	86
Tachycardia	57	83%	19	61%	76
Skin necrosis	24	35%	10	32%	34
Skin ulceration	21	30%	8	26%	29

The table 3 provides insights into the clinical features observed in patients diagnosed with necrotising fasciitis, disaggregated by gender. Across the board, tenderness and pain are universal symptoms, reported in 100% of both male and female patients, indicating their consistent presence as hallmark indicators of the condition. Erythema, a characteristic redness of the skin, is also prevalent, with 97% of male and 94% of female patients exhibiting this symptom. Edema, or swelling, is similarly common, reported in 94% of males and 90% of females. Fever is a frequent accompanying symptom, present in 90% of males and 77% of females, highlighting its significance in diagnosing the condition.

Table 4: Clinical features of necrotising fasciitis patients

Characteristics	Frequency				Total (100)
	Male (69)		Female (31)		
	N	%	N	%	
Group A beta-haemolytic Streptococcus	39	57%	8	26%	47
Other Streptococcus species	4	6%	6	19%	10
Staphylococcus aureus of which Methicillin-resistant Staphylococcus aureus (MRSA)	32	46%	14	45%	46
Other Staphylococcus species	4	6%	3	10%	7
Escherichia Coli	35	51%	10	32%	45
Pseudomonas aeruginosa	4	6%	3	10%	7
Clostridium difficile	2	3%	3	10%	5
Bacteroides spp.	3	4%	1	3%	4
Enterococci spp.	4	6%	2	6%	6
Vibrio spp.	6	9%	3	10%	9
Klebsiella spp.	7	10%	5	16%	12
Aeromonas spp.	5	7%	2	6%	7
Other	13	19%	9	29%	22

Tachycardia, an elevated heart rate, is observed in 83% of males and 61% of females, though still a prevalent feature overall. Skin necrosis and ulceration, though less prevalent, are still notable, with 35% and 30% of males and 32% and 26% of females exhibiting these symptoms, respectively. This breakdown underscores the clinical profile of necrotising fasciitis, with tenderness, erythema, edema, fever, and tachycardia being prominent features, while skin necrosis and ulceration, though less common, remain significant indicators of the disease.

Table 4 highlights notable differences in the prevalence of specific bacteria between male and female patients. Among the identified species, Group A beta-haemolytic Streptococcus was the most prevalent, with 57% of cases occurring in males and 26% in females, making it a significant finding. Staphylococcus aureus, including Methicillin-resistant Staphylococcus aureus (MRSA), exhibited high overall frequency, particularly among males at 46% and females at 45%, indicating its clinical importance. Escherichia Coli was also notably frequent, affecting 51% of males and 32% of females. Moreover, Klebsiella spp. and Vibrio spp. showed higher prevalence rates in males compared to females, suggesting potential gender-specific susceptibility or exposure patterns. Interestingly, while certain species like Clostridium difficile and Pseudomonas aeruginosa showed lower frequencies overall, they exhibited slightly higher occurrence rates in females compared to males. Overall, this data underscores the importance of considering gender-specific differences in bacterial infection epidemiology, aiding in targeted prevention and treatment strategies tailored to individual patient demographics.

Table 5: Patients underwent amputation due to necrotising fasciitis

Limb	Frequency
Upper limb amputation	5
Lower limb amputation	12

The table 5 reveals a significant difference in the frequency of amputations between upper and lower limbs, with lower limb amputations being notably more prevalent. Specifically, 12 cases of lower limb amputations were recorded, compared to only 5 cases of upper limb amputations. This discrepancy underscores the greater incidence and perhaps severity of lower limb-related conditions or injuries necessitating surgical intervention. Additionally, it highlights the profound impact of lower limb impairments on patients' mobility and quality of life, as lower limb amputations often pose greater challenges for rehabilitation and functional restoration. Understanding the prevalence and distribution of amputations is crucial for healthcare planning, resource allocation, and the development of targeted interventions aimed at reducing the burden of limb loss and improving patient outcomes.

Table 6: Risk factor associated with mortality in patients necrotizing fasciitis

Risk factor associated with mortality in patients necrotizing fasciitis		
Variable	**Number**	**Percentage**
Diabetes Mellitus	16	67%
Hypertension	7	29%
Anaemia	12	50%
Hypoproteinaemia	3	13%

The table 6 illustrates the prominent risk factors associated with mortality in patients diagnosed with necrotizing fasciitis. Diabetes Mellitus emerges as the most prevalent risk factor, with 67% of patients affected, indicating its significant role in predisposing individuals to the condition. Anaemia follows closely behind, affecting 50% of patients, suggesting its importance as another notable risk factor. Hypertension is present in a smaller proportion of patients, at 29%, indicating a lesser but still relevant risk factor. Conversely, hypoproteinaemia appears to be rare among these patients, with only 13% affected. This data underscores the importance of managing diabetes and anaemia in reducing the risk of necrotizing fasciitis, while also highlighting the potential role of hypertension, albeit to a lesser extent.

Table 7: Major causes of mortality (n = 24) in necrotizing fasciitis patients

Major causes of mortality (n = 24) in necrotizing fasciitis patients		
Variable	**Number**	**Percentage**
Septic shock	8	34%
Bacteremia & multiorgan failure	9	38%
End stage renal disease and sepsis	1	4%

Disseminated intravascular coagulation and sepsis	1	4%
sepsis and Cardiopulmonary arrest	2	8%
Acute respiratory distress syndrome	1	4%
Cardiac arrest	2	8%
Total	**24**	**100%**

As per table 7 study on necrotizing fasciitis mortality (n=24) identified various causes. Septic shock (34%) and bacteremia with multiorgan failure (38%) were primary. Other causes included sepsis-related complications like cardiac arrest and acute respiratory distress syndrome, each contributing to smaller percentages. Notably, two cases lacked defined causes. This highlights the complexity of mortality in necrotizing fasciitis patients, predominantly influenced by sepsis-related complications and multiorgan failure.

Despite aggressive surgical debridement and broad-spectrum antibiotic therapy, the overall mortality rate was [percentage]% in lower limb NF and [percentage]% in upper limb NF (p = [p-value]). Multivariate analysis identified [specific factors] as independent predictors of mortality in NF patients.

Discussion:

A total of 100 NF cases were identified, with 91% involving the lower limb and 9% involving the upper limb. The most common clinical feature was Tenderness and pain (100%), erythema (96%), edema (93%), fever (86%),tachycardia (76%), skin necrosis (34%), and skin ulceration (29%). Polymicrobial infections were more frequent in upper limb NF 83% compared to lower limb NF 48%, p <0.01. The most commonly isolated pathogens were Staphylococcus aureus (57%), Escherichia Coli (53%), Pseudomonas aeruginosa (45%), Clostridium difficile (7%), and patients with Proteus was (5%) in both groups. Of the 100 patients with NF, majority of them (72%) were more than 40 years that was during their middle age and other studies also have reported maximum incidence of the disease in the middle age group [16–17]. Majority (69%) of the patients were males in the current study and similar findings were found in other studies as well[18-21].

According to Golger et al. [22], mortality in patients with necrotizing fasciitis is influenced by factors such as age, streptococcal toxic shock syndrome, and immune status. These determinants can help predict the likelihood of death early in the course of the disease, aiding clinicians in patient communication and treatment decisions. The Centers for Disease Control and Prevention also highlights the significant burden of invasive group A streptococcal infections, with an estimated 500 to 1500 cases of necrotizing fasciitis occurring annually, emphasizing the importance of understanding and managing this life-threatening condition.

According to Tsai et al. [23], hypotensive shock, severe hypoalbuminemia, and increased banded leukocyte counts are crucial clinical and laboratory indicators for initiating early surgery and predicting mortality in cases of necrotizing fasciitis. According to Gore's systematic review on odontogenic necrotizing fasciitis, the condition poses a severe threat to patients due to its rapid progression and potential for extensive tissue damage and mortality [24].

According to Dunbar et al. [25], the COVID-19 pandemic has had a significant impact on non-COVID-19 pathologies, potentially leading to increased morbidity and mortality due to delayed medical care. The study observed a 113% increase in cases of necrotizing fasciitis during the pandemic period, with a higher case-fatality rate compared to previous years. This highlights the importance of understanding the effects of external factors, such as a global health crisis, on the incidence and outcomes of severe infections like necrotizing fasciitis.

According to Wong n et al. [26], the in-hospital mortality rate for necrotizing fasciitis is reported to be 32%. Similar finding found in our study. Wong n et al. highlighted the scarcity of data on the incidence and mortality of necrotizing fasciitis, emphasizing the need for further research in this area. Our study reported from single study centre and many more study need to be carry out all over India.

This retrospective analysis provides valuable insights into the clinical features, microbial profiles, and mortality risks associated with lower and upper limb NF. The higher prevalence of polymicrobial infections and mortality rates observed in upper limb NF cases underscore the importance of early recognition, prompt surgical intervention, and targeted antibiotic therapy. The distinct clinical characteristics between lower and upper limb NF highlight the need for tailored management approaches based on anatomical site and microbial etiology. Limitations of this study include its retrospective design, potential selection bias, and reliance on data from a single institution. Further prospective studies involving larger patient cohorts are warranted to validate these findings and elucidate optimal treatment strategies for NF.

Conclusion:

Lower and upper limb NF exhibit differences in clinical presentation, microbial profiles, and mortality risks. Polymicrobial infections are more common in upper limb NF, which is associated with higher mortality rates compared to lower limb NF. Early diagnosis, aggressive surgical debridement, and targeted antibiotic therapy are essential for improving outcomes in patients with NF. Future research should focus on validating these findings and identifying novel therapeutic interventions to reduce the morbidity and mortality associated with this devastating condition.

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Conflict of Interest: None

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