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An outcome analysis of 44 necrotizing fasciitis patients in a single center

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ABSTRACT

Objective: Necrotizing fasciitis (NF) is a life-threatening soft tissue infection with high mortality, requiring prompt diagnosis and surgical intervention. We have investigated the outcomes of NF patients in our center.

Patients and Methods: This retrospective study analyzed 44 patients diagnosed with NF. The study aimed to explore the microbial etiology, predisposing factors, management strategies, The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) scores and their relationship to mortality. Radiological studies, including CT, MRI, and ultrasound, were used to confirm the diagnosis, followed by surgical debridement and appropriate antibiotic therapy.

Results: The most common pathogen was Escherichia coli (26.9%), with diabetes mellitus (DM) being the most frequent comorbidity (75%). The mean age of patients was 54.6 years, and the overall mortality rate was 27.3%. Elevated HbA1c levels and delayed surgical intervention were associated with higher mortality. However, neither LRINEC score nor the location of the infection had a significant impact on outcomes. Early debridement and control of infection were crucial for survival, particularly in patients with DM and high HbA1c.

Conclusion: Our findings support the importance of early intervention and management in reducing mortality from NF. The study highlights the need for timely surgical debridement and careful management of comorbid conditions, particularly diabetes, in improving patient outcomes.

Keywords: Necrotizing fasciitis, LRINEC, Surgical debridement, Fournier's gangrene

1. INTRODUCTION

Necrotizing fasciitis (NF) is a life-threatening soft tissue infection characterized by rapidly progressing fascia necrosis and destruction of surrounding soft tissues along with systemic effects [1]. NF may be caused by a single bacteria species or a polymicrobial infection [2]. A characteristic finding in NF is the easy separation of fascia from surrounding tissues. Because the infection starts in the deep tissues and spreads to the skin only in the late phase, high suspicion of the condition is crucial for early action, such as surgical debridement and initiation of broad-spectrum antibiotics [3]. NF is a devastating infection starting from the deep fascia and involving other structures such as fat, muscle, subcutaneous tissue, and finally skin as it progresses [4]. Fibrous attachment between the fascia and subcutaneous tissues may limit the spread of infection to the hands and feet, unlike the trunk and limbs, where the infection may rapidly spread. Diagnosis is primarily clinical, aided by the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score and inaging such as magnetic resonance imaging (MRI) and computed tomography (CT). Parameters that are calculated in the LRINEC are C-reactive protein (CRP), white blood cell count, glucose, hemoglobin, creatinine and sodium levels. A score of 7 or higher on the LRINEC indicates a high risk of NF [5]. Serial debridement should follow early surgical intervention until disease progression stops and necrotic tissues are totally debrided.

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Although, the incidence is as low as 0.4 to 0.5 cases per 1000,000 population, the mortality rate is very high, approximately 30%, making the condition a surgical emergency [6]. Predisposing factors for NF include diabetes mellitus (DM) (the majority), old age, immunodeficiency, malnutrition and obesity. However, NF has also been reported in otherwise healthy individuals [7]. NF infections are divided into two types: type 1, which is polymicrobial and often associated with chronic wounds such as diabetic wounds, and type 2, which is monomicrobial and may be due to surgical wounds, staph infections, insect bites [8].

This study aimed to retrospectively analyze patients diagnosed with NF, focusing on microbial etiology, predisposing factors, management of NF and their relationship with mortality rates.

2. PATIENTS and METHODS

A retrospective review of consecutive 44 patients treated for NF at Prof. Dr. Cemil Tascioglu City Hospital between January 2010 and December 2020 was performed using the hospital's computer database. The study was approved by Prof. Dr. Cemil Tascioglu City Hospital Ethical Committee on 21.06.2021 with Ethical Approval Number of 244. Inclusion criteria included confirmation of necrotizing fasciitis diagnosis intraoperatively. Data were collected from patient files, including demographics, site of infection, comorbidities, LRINEC scores on admission, wound cultures and antibiograms, HbA1c levels, length of hospitalization, prognosis, time of admission to surgery, imaging methods, and long-term reconstruction methods. Parameters that are calculated in the LRINEC are C – reactive protein (CRP), white blood cell count, glucose, hemoglobin, creatinine and sodium levels. The pre-operative suspicion and probable diagnosis for NF was firstly presented by either ultrasound, CT or MRI scans and then wound cultures were taken from most patients suspected of NF before administering empiric broad-spectrum antibiotics. During administration of antibiotic treatment, appropriate surgical debridement to the necrotic tissue was performed when needed and the decision-making had been done by daily follow up of clinical and laboratory evaluation by the surgical team (Figure 1 – 4).



Figure 1. *A preoperative photo of lower extremity necrotizing fasciitis with skin involvement*



Figure 2. *A peroperative photo of thigh and inguinal region necrotizing fasciitis before the second debridement surgery, demonstrating disease progression*



Figure 3. *A peroperative photo of thigh necrotizing fasciitis showing the necrosis of the fascia without skin involvement*



Figure 4. *A necrotizing fasciitis case with bilateral involvement of the lower extremity, inguinal region and lower abdomen. Staged skin grafting of the wound after serial debridement of the non-viable tissue and vacuum assisted closure application*

Statistical Analysis

Statistical analysis was performed using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 23.0, IBM Corp., Armonk, New York, USA). Data was expressed as "n (%)" for categorical variables. Pearson

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chi-square and Fisher exact tests were performed for categorical variables. After the Kolmogorov-Simirnov test performed for the detection of distribution, data was expressed as "median (25th and 75th percentiles)" for variables without a normal distribution and mean +/ – standard deviation for variables with normal distribution. While, Student-t test was used for comparing quantitative variables with normal distribution, Mann-Whitney U test was used for comparing quantitative variables without normal distribution. The relationship between mortality and other variables was examined. Cross-tabulations were created for categorical variables, and Chi-square tests were applied. Values of $p<0.05$ were considered statistically significant.

3. RESULTS

The study included a total of 44 patients. Radiological studies were performed in 27 patients. Forty-four point four percent of the patients underwent CT, 37% MRI, and 18.5% ultrasound scanning. There were 32 male and 12 female patients. The mean age was 54.6 years. The mean length of stay was 36 days. The most common comorbidity was DM. Other predisposing conditions included hypertension, lymphoma, nasopharyngeal cancer, chronic kidney disease, cirrhosis, chronic heart failure, hyperthyroidism, acute renal failure, and pancreas cancer. The most common site of infection was cruris (43.2%), followed by perineum (36.4%), inguinal (9.1%), sacrum (4.5%), and other sites (6.8%). The mean LRINEC score was 8, and the mean HbA1c value was 10.42. In terms of microbial etiology, Escherichia coli was the most common pathogen (26.9%). Group A beta-hemolytic Streptococcus (23.1%), skin flora (23.1%), Pseudomonas aeruginosa (7.7%), methicillin-resistant Staphylococcus aereus (7.7 %), Escherichia feacalis (3.8%), Citrobacter farmeri (3.8%) and group F beta-hemolytic Streptococcus (3.8%) were also identified. All of the patients were operated for necrotic debridement of the tissues. The debrided anatomic areas were then surgically operated after the control of the infection, to maintain a sterile surgical site. Skin grafts were used in 28 patients (63.6%), flaps in 3 patients (6.8%), one patient required amputation (2.3%), primary closure in one patient (2.3%), and healing with secondary intention in the remaining patients (25%) (Table I). Regarding prognosis, the mortality rate was 27.3%. The disease was more prone to a fatal outcome in patients aged 41-60 years. Although, 75% of patients had preexisting medical conditions, only diabetic patients had a more fatal prognosis. LRINEC scores and the initial site of the disease did not affect prognosis ($p>0.05$). Early surgical intervention and lower HbA1c levels were associated with lower mortality rates ($p<0.05$) (Table II).

Table I. *Patients demographics*

		P Value
Age (years)	54.6	
Gender (M/F%)	2.7 : 1	0.243
Co-morbidities (%)		
Diabetes Mellitus	70.5	
Hypertension	27.2	
Kidney Disease	11.4	
Heart Failure	6.8	
Thyroid Disease	4.5	
Pancreatic Cancer	4.5	
Others	13.6	
Site of Primary Lesion (%)		0.625
Cruris	43.2	
Perineum	36.4	
Inguinal	9.1	
Sacrum	4.5	
Sternum	2.3	
Thorax	2.3	
Hand	2.3	
Wound Culture (%)		
E. Coli	26.9	
GAS	23.1	
Skin flora	23.1	
P. Aerigunosa	7.7	
MRSA	7.7	
E. Feacalis	3.8	
C. Farmeri	3.8	
GFS	3.8	
Reconstruction Method (%)		0.151
Secondary Healing	27.3	
Primary Closure	2.3	
Flap Operation	6.8	
Graft Operation	63.6	
Mean LRINEC Score	8	
Mean HbA1c	10.42	
Admission to Surgery		0.7
Same day	24	
Following day	6	
>1 day	14	
Mean Length of Stay (days)	36	
Prognosis (%)		0.02
Discharge	68.2	
Exitus	27.3	
Other	4.5	

GAS; Group A Beta Hemolytic Streptococcus, MRSA; Methicillin resistant Staphylococcus Aureus, GFS; Group F Beta Hemolytic Streptococcus
P<0.05 is considered as significant

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Table II. *Patient data and their relationship with mortality*

Variables	Mortality (n or %)	P value
Age		>0.05
20 - 40 41 - 60 61 - 80 >80	0 7 4 1	
Gender		>0.05
Female Male	8 4	
Site of Primary Lesion		>0.05
Cruris Inguinal Sacral Perineal	58.3% 16.3% 16.7% 16.7%	
Time to Surgery		>0.05
Same day Following Day >1 day	8 3 1	
Co-morbidities		>0.05
Diabetes Mellitus Hypertension	9 5	
Length of Stay		>0.05
LRINEC		>0.05
HbA1c		>0.05

4. DISCUSSION

Our study highlights several critical factors influencing the prognosis of NF: These include early diagnosis of the disease, timely intervention to lesion and presence of DM with elevated levels of HBA1c. Delayed diagnosis, late intervention, and higher levels of HBA1c were all found to be associated with poor prognosis and increased mortality. The overall mortality rate in our cohort was 27.3%, with notably higher mortality observed in patients aged between 41 to 60 years. Notably, our study is unique in that NF lesions were not confined to a specific anatomical region, but rather were found to affect various sites throughout the body. Additionally, neither the location of the lesions of NF nor the LRINEC score demonstrated a significant association with patient outcomes.

Necrotizing fasciitis is a devastating infection of the deep fascia, characterized by dishwater-gray exudate and rapid widespread tissue destruction. Clinical manifestations include pain, erythema, tenderness, and skin bullae. Histologically, group A beta-hemolytic Streptococcus was once the primary identified monobacterial cause of NF. However, recent studies suggest a more common polymicrobial pathogenesis [9]. The relative incidence of type 1 (polymicrobial) and 2 (monomicrobial) varies by the region [10]. Unlike the recent studies in the literature, the microbiological findings in our study, with Escherichia coli as the most common pathogen, are consistent with type 1 NF due to the high prevalence of immunosuppressed patients (diabetics), followed by streptococcus and skin flora which were mostly staphylococcus. Other unusual pathogens include pseudomonas, MRSA, Enterococcus faecalis, Citrobacter farmeri, group F beta – hemolytic streptococcus, which are also not so common in studies reporting NF [11].

The prompt diagnosis and early suspicion for NF is the key point for initiating appropriate treatment. Delayed intervention is associated with increased mortality, whereas early administration of medical treatment combined with surgical debridement has been shown to significantly reduce mortality rates [12]. The literature predominantly states that early and aggressive debridement of the affected skin, subcutaneous fat tissue and fascia is essential for achieving optimal outcomes [13]. In our study, early surgical intervention was found associated with lower mortality rates consistent with previous studies in literature. In terms of mortality, our studies mortality rate was 27.3% and consistent with literature that the mortality rates ranged between 8.3% to 35% in the previous studies [14-16].

Early surgical intervention is crucial for improving survival rates. Survival rates are significantly increased among the patients who underwent surgical debridement within 24 hours after admission. Our study showed that mortality decreased statistically significantly with early intervention. The recommended treatment for NF includes clindamycin combined with penicillin for infections caused by group A streptococcus for 14 days, and appropriate antibiotics based on wound culture antibiogram results for polymicrobial infections. The Infectious Diseases Society of America (IDSA) currently recommends vancomycin or linezolid plus piperacillin-tazobactam or carbapenem or ceftriaxone-metronidazole for skin and soft tissue infections [16].

Serial debridement should be continued every 2-3 days after initiating antibiotic treatment to remove all devitalized tissue and promote granulation tissue [17]. Intravenous fluid replacement, albumin reinforcement, and additional therapies such as hyperbaric oxygen should be as needed. Sex and length of hospital stay did not affect mortality rates in our study, contrary to the review of Wang et. al., age, however, was found to be statistically insignificant on mortality in both studies [18].

Diabetes was found as the leading predisposing factor, consistent with existing literature [19]. To the best of our knowledge, there is only one study from 2008, which investigated the effect of HbA1c levels on mortality. We found that HbA1c levels were statistically significantly related to mortality. The presence of DM is one of the most common comorbidity in patients with NF [20,21]. Patients with DM has higher risk of NF in patients who had surgical intervention and HBA1c levels >8% is predictor for post-operative adverse events. However, there is limited study evaluating the HBA1c levels and outcome of NF. Oncul et al., presented in a cohort with limited number of patients (<25 patients) that NF patients with DM had longer hospital stay and higher rate of mortality and higher levels of HBA1c were also detected in patients who could not survive with the diagnosis of NF [22]. Our study has nearly twice more patients when compared to their study and showed that older age and presence of DM with elevated HBA1c levels were associated with worse outcome. Our findings were consistent with previous studies. Taviloglu et al., determined that presence of DM was associated with increased mortality, and additionally, older age

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was also associated with idiopathic NF [23]. Vayvada et al., also demonstrated that all non-survivors in their study group had risk factors such as immunosuppression, chronic cardiac disease and diabetes mellitus with high glucose levels [24]. Moreover, additional to DM, older age, increased number of comorbidities and delay for surgical debridement adversely affected the outcome.

Laboratory Risk Indicator for Necrotizing Fasciitis Score has been shown to be associated with decreased prognosis and increased severity of the infection. The findings of the study of Kumar et al., were consistent in terms of presence of DM and outcome of NF, even though, they also showed that patients who had higher LRINEC scores were associated with increased mortality and amputation [25]. However, our findings were contrary regarding LRINEC score. Our study showed that LRINEC score was not associated with the outcomes of NF. This difference might be related to the location of NF. Kumar's study did not state the location of the lesions, however, the rate of amputation was 20% which was ten times more than our study. This difference indicated that their study most probably included patients who had NF in extremities and the distribution of localization of NF might lead to different significance in terms of LRINEC scores. Additionally, one of the largest review and analysis were performed by Abdullah et al., and included eighteen studies about NF. They commented that LRINEC score might be a reliable tool in terms of diagnosis of NF, however, stratification of high risk patients should be evaluated with LRINEC scores together with radiologic modalities and clinical assessment [26]. Moreover, consistent with our study, Breidung et al., determined that LRINEC score, as a diagnostic tool, was not fully reliable and was not a recommended prognostic tool neither [27].

In literature, NF in extremities commonly resulted with amputation. The rate for amputation ranged between 6% to 41% in patients who had NF in the extremities [12,28]. In our study, the rate of amputation was 2.3% as NF was mostly located in the body and not in the extremities.

Limitations

Our study has several limitations. Firstly, our study is conducted in a retrospective design, which inherently carries limitations associated with this type of studies, including potential biases in data collection and the inability to establish causality. Second, the sample size is relatively small, and a larger cohort would likely enhance the statistical power and generalizability of the findings. Third, our study includes patients with NF located throughout the body, rather than being confined to a specific anatomical region. The variability in lesion localization may introduce confounding factors that could influence the outcomes of the study.

Conclusion

In conclusion, this study underscores the significant impact of early diagnosis, timely intervention, and the presence of comorbidities, particularly DM with elevated HbA1c levels, on the prognosis of NF. Our finding confirms that early surgical debridement, in combination with appropriate medical management, is associated with improved survival outcomes, consistent with existing literature. While, the LRINEC scores do not demonstrate a significant correlation with patient outcomes in our cohort, the presence of DM and advanced age are identified as critical factors influencing mortality.

Compliance with Ethical Standards

Ethical approval: The study was approved by Prof. Dr. Cemil Tascioglu City Hospital Ethical Committee in 21.06.2021 with Ethical Approval Number of 244. This study was performed in line with the principles of the Declaration of Helsinki.

Conflict of interest: The authors declare that there is no conflict of interest.

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