Evaluation of Risk Factors for Amputation and Mortality in Patients of Necrotizing Fasciitis

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ABSTRACT

Background: Necrotizing fasciitis (NF) is a serious infection of the skin and soft tissues including subcutaneous tissue and fascia, which rapidly progresses along the deep fascia and becomes a medical and surgical urgency. Delayed treatment is associated with loss of limb and infection in patients with NF.

Materials and methods: All adult patients presented in General Surgery OPD/emergency and plastic surgery OPD of MGUMST with NF were assessed, admitted, and treated with broad-spectrum antibiotics from January 2019 to June 2020. All routine blood parameters were evaluated and were provided proper emergency surgical treatment. The surgical interventions included incision and drainage, debridement, fasciotomy, and amputation. The clinical data and demographic characteristics within the first day of admission and after 48–72 hours were documented. Important data associated with the investigations and treatment of NF, i.e., wound appearance, site of infection, organisms involved, and laboratory data within the first day of admission and after 48–72 hours, surgical intervention and outcome, were documented. Patients were divided into two groups: survival and mortality which were further grouped into two groups: those with amputation and without amputation.

Results: Among 100 patients with diagnosis of NF, 20% died and 10% underwent amputation. From multivariable analysis, the predictors of mortality among patients of NF were patients of age ≥60 years [risk ratio (RR) = 58.57, 95% CI = 3.64–941.85, p = 0.004], having diabetes mellitus (DM) (RR = 28.70, 95% CI = 1.78–461.51, p = 0.017), gangrene (RR = 3.86, 95% CI = 1.91–7.75, p = 0.0002), severe sepsis (RR = 158.14, 95% CI = 9.96–2508.89, p = 0.0003), involvement of multiple sites (RR = 9.06, 95% CI = 4.25–19.31, p = 0.0001), total leukocyte count (RR = 158.14, 95% CI = 9.96–2508.89, p = 0.0003), and serum creatinine (RR = 126.28, 95% CI = 7.92–2013.12, p = 0.0006) on admission and within 48–72 hours of admission and the independent predictors of amputation among patients of NF included having gangrene (RR = 173.73, 95% CI = 10.91–2764.80, p = 0.0003), severe sepsis (RR = 6.00, 95% CI = 1.86–19.26, p = 0.002), total leukocyte count (RR = 6.00, 95% CI = 1.86–19.26, p = 0.002), and serum creatinine (RR = 64.68, 95% CI = 3.92–1064.68, p = 0.003) on admission and within 48–72 hours of admission.

Conclusion: In our study, we concluded that gangrene, severe sepsis, total leukocyte count >25,000, and serum creatinine values >1.6 mg/dL on admission as well as within 48–72 hours, as independent predictors for both amputation and mortality and some other factors like age >60 years, the involvement of multiple sites, DM mainly predicting the mortality rate independently.

Keywords: Amputation, Debridement, Fasciotomy, Gangrene, Necrotizing fasciitis.

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INTRODUCTION

Necrotizing fasciitis (NF) is a rare, sometimes lethal, bacterial infection characterized by widespread skin, superficial fascia, and subcutaneous tissue necrosis.¹ ² The incidence has been reported between 0.4 and 0.53 cases per 100,000 population.³ ⁵ Now, an increasing incidence of NF has been reported, which can be attributed by a better reporting system and an increment in strains which are associated with NF because of unreasonable use of antibiotics. Patients presenting with preexisting factors, trauma, many young individuals may also be affected by this disease. Approximately half of the cases of NF (caused by streptococcal) are found in young and previously healthy patients.⁵ The overlying skin appears normal but it is the necrotic process that works underneath. Later on, the patient becomes extremely toxic and presents with painful, red as well as necrotic skin as blood supply to the skin is gradually hampered. Pathophysiologically, it is caused by septic thrombosis of the vessels that are between skin and the deeper layers.

Necrotizing fasciitis results from either trauma to the skin or from hematogenous spread.¹ Any kind of trauma whether major or minor which breaches skin integrity including needle punctures, bites from insects, burns, lacerations, surgical wound, blunt trauma, etc., may develop this aggressively spreading, insidiously advancing soft-tissue condition.¹ ² Necrotizing fasciitis occurs in any part of the body but primarily it involves the superficial layers of the extremities, abdomen, or perineum.⁷
The various presentations of microbial involvement in these tissues may include simple contamination and self-limited bacterial contamination to an unrelapsing, unpredictable clinical course and projecting to septicemia, multiple organ failure, and death. The purpose of our study is to identify the risk factors which may be used to predict amputation and mortality in patients with NF.

**AIMS AND OBJECTIVES**

To evaluate the risk factors for amputation and mortality in patients with NF.

**MATERIALS AND METHODS**

- **Type of study:** Prospective cohort study.
- **Place of study:** General Surgery OPD, Mahatma Gandhi Medical College and Hospital, Jaipur.
- **Ethical clearance:** Institute Ethics Committee approval was obtained before the start of the study.
- **Written and informed consent was obtained from all participants before enrolment into the study.**

**Sample Size**
The study included 100 adult patients presenting with NF in OPD/emergency of general surgery department/plastic surgery OPD/emergency of Mahatma Gandhi Medical College and Hospital, Jaipur of all surgical units.

**Plan of Study**
Patients presenting to surgical OPD/plastic surgery OPD/emergency with features of NF were evaluated.

**Inclusion Criteria**
All the adult patients presenting with features of NF will be included in the study.

**Exclusion Criteria**
- Unwilling patients.
- Patients with age <18 years.

**Methods**
All adult patients presented in General Surgery OPD/emergency and plastic surgery OPD of MGUMST with NF were assessed, admitted, and treated with broad-spectrum antibiotics. All routine blood parameters including complete blood counts, renal and hepatic function tests, coagulation profile, and random blood sugar were evaluated and were provided proper emergency surgical treatment. The surgical interventions included incision and drainage, debridement, fasciotomy, and amputation. The clinical data and demographic characteristics including sex, age, body mass index, education, occupation, underlying disease, vital signs within the first day of admission and after 48–72 hours were documented. Important data associated with the investigations and treatment of NF, i.e., wound appearance, site of infection, organisms involved, and laboratory data within the first day of admission and after 48–72 hours, surgical intervention and outcome, were documented. Patients were divided into two groups: survival and mortality which were further grouped into two groups: those with amputation and without amputation.

**Statistical Analysis**
The collected data were analyzed with IBM. SPSS statistics software 23.0 Version. For the description of the data, descriptive statistics frequency analysis and percentage analysis were used for categorical variables, and the mean and SD were used for the continuous variables. To find the significant difference between the bivariate samples in independent groups the unpaired sample t-test was used. To find the significance in categorical data, Chi-square test was used similarly if the expected cell frequency is <5 in 2 × 2 tables then the Fisher’s exact was used.

In the above statistical tools, the probability value of 0.05 was considered significant.

**Observations and Results**
A total of 100 patients with NF were enrolled in this study and various factors including predisposing factors, age, wound appearance, laboratory investigations, and wound appearance were taken into account that possibly affect the outcome of NF and its morbidity and mortality.

Among 100 patients in our study, 59 patients were above 60 years of age and 41 patients were below 60 years of age and most of the patients were males (65) as compared to females (35). Regarding the comorbid conditions causing NF, the commonest being diabetes mellitus (DM) in 59% cases, followed by gout, coronary heart disease, renal disease, and cirrhosis. Regarding the clinical presentation, the commonest symptom being swelling and is present in about 95% of cases. Next to swelling is redness and severe pain in 90 and 75%, respectively. Among the 100 patients, we had studied, the most common part to be affected was the lower limb (35%), next to it was upper limbs (22%), and involvement of trunk in 15% of patients. By blood investigations from our study, we noticed that 36% of patients had total leukocyte count >25,000 on admission which decreases to 20% after 48–72 hours of admission and 39% had elevated serum creatinine on admission which reduces to 24% after 48–72 hours.

In about 40% of patients, we performed incision and drainage and in 30% of patients, we performed wound debridement. In about 20%, we had done fasciotomy and amputation in 10% of patients. Seventeen percent of patients developed severe sepsis. Most of the patients discharged after 20 days of hospital stay. And their mortality in our study was 20%. Following are the tables showing a comparison of factors between mortality and survival and another table showing a comparison of factors between amputation and non-amputation (Tables 1 to 4).

**Comparison of Factors between Mortality and Survival Group**
Patient demographic and clinical characteristics including age (>60 years), underlying morbidity like DM, wound appearance such as redness, blebs, gangrene, severe pain, involvement of multiple sites, WBC count (>25,000), serum creatinine level (>1.6) on admission and within 48–72 hours after admission, severe sepsis and length of hospital stay showed statistically significant differences (p value < 0.05) between mortality and survival groups. Other factors did not differ significantly between the two groups.
### Table 1: Comparison of factors between mortality and survival group

|                | Mortality |          |          | $\chi^2$-value | $p$ value |
|----------------|-----------|----------|----------|----------------|-----------|
|                | Alive | Dead | Total |                |           |
| **Comparison of age with mortality** | | | | | |
| Age <60 | Count | 59 | 0 | 59 | 35.976 | 0.0005** |
| | % | 73.8% | 0.0% | 59.0% | | |
| Age >60 | Count | 21 | 20 | 41 | | |
| | % | 26.3% | 100.0% | 41.0% | | |
| **Comparison of gender with mortality** | | | | | |
| Gender Female | Count | 26 | 9 | 35 | 1.099 | 0.295# |
| | % | 32.5% | 45.0% | 35.0% | | |
| Gender Male | Count | 54 | 11 | 65 | | |
| | % | 67.5% | 55.0% | 65.0% | | |
| **Comparison of underlying morbidities with mortality** | | | | | |
| Diabetes mellitus | Count | 39 | 20 | 59 | 17.373 | 0.0005** |
| | % | 48.8% | 100.0% | 59.0% | | |
| Coronary heart disease | Count | 9 | 1 | 10 | 0.694 | 0.405# |
| | % | 11.3% | 5.0% | 10.0% | | |
| Renal disease | Count | 6 | 0 | 6 | 1.596 | 0.597# |
| | % | 7.5% | 0.0% | 6.0% | | |
| Cirrhosis | Count | 5 | 0 | 5 | 1.316 | 0.580# |
| | % | 6.3% | 0.0% | 5.0% | | |
| Gout | Count | 14 | 1 | 15 | 1.961 | 0.292# |
| | % | 17.5% | 5.0% | 15.0% | | |
| **Comparison of wound appearance with mortality** | | | | | |
| Swelling | Count | 75 | 20 | 95 | 1.316 | 0.580# |
| | % | 93.8% | 100.0% | 95.0% | | |
| Redness | Count | 76 | 14 | 90 | 11.111 | 0.004** |
| | % | 95.0% | 70.0% | 90.0% | | |
| Bleb | Count | 40 | 0 | 40 | 16.667 | 0.0005** |
| | % | 50.0% | 0.0% | 40.0% | | |
| Skin necrosis | Count | 23 | 7 | 30 | 0.298 | 0.585# |
| | % | 28.8% | 35.0% | 30.0% | | |
| Gangrene | Count | 4 | 6 | 10 | 11.111 | 0.004** |
| | % | 5.0% | 30.0% | 10.0% | | |
| Severe pain | Count | 55 | 20 | 75 | 8.333 | 0.003** |
| | % | 68.8% | 100.0% | 75.0% | | |
| **Comparison between the site of wound with mortality** | | | | | |
| Head and neck Present | Count | 10 | 0 | 10 | 2.778 | 0.096# |
| | % | 12.5% | 0.0% | 10.0% | | |
| Trunk Present | Count | 14 | 1 | 15 | 1.961 | 0.292# |
| | % | 17.5% | 5.0% | 15.0% | | |
| Upper limb Present | Count | 20 | 2 | 22 | 2.098 | 0.228# |
| | % | 25.0% | 10.0% | 22.0% | | |
| Lower limb Present | Count | 31 | 4 | 35 | 2.473 | 0.189# |
| | % | 38.8% | 20.0% | 35.0% | | |
| Multiple sites Present | Count | 4 | 13 | 17 | 40.822 | 0.0005** |
| | % | 5.0% | 65.0% | 17.0% | | |
| **Comparison of vital sign—temperature (F) with mortality by unpaired $t$-test** | | | | | |
| Mortality | N | Mean | SD | $t$-value | $p$ value |
|-------------|---|------|---|---------|---------|
| On admission | Dead | 20 | 100.75 | 1.16 | 6.346 | 0.0005** |
| | Alive | 80 | 99.14 | 0.98 | | |

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All clinically and statistically significant variables were included in the multivariate analysis model which demonstrated that the predictors of mortality among patients of NF were patients of age >60 years (risk ratio (RR) = 58.57, 95% CI = 3.64–941.85, p = 0.004), having DM (RR = 28.70, 95% CI = 1.78–461.51, p = 0.017), gangrene (RR = 3.86, 95% CI = 1.91–7.75, p = 0.0002), severe sepsis (RR = 158.14, 95% CI = 9.96–2508.89, p = 0.0003), involvement of multiple sites (RR = 9.06, 95% CI = 4.25–19.31, p = 0.0001), total leukocyte count (RR = 158.14, 95% CI = 9.96–2508.89, p = 0.0003), and serum creatinine (RR = 126.28, 95% CI = 7.92–2013.12, p = 0.0006) on admission and within 48 to 72 hours of admission.

**Comparison of Factors between Amputation and Non-amputation Group**

Patient demographic and clinical characteristics including underlying morbidity like gout, wound appearance such as...
**Table 2:** Independent predictors of mortality

| Risk factors                                | RR   | 95% CI         | p value |
|---------------------------------------------|------|----------------|---------|
| Swelling                                    | 2.56 | 0.17–37.42     | 0.491*  |
| Skin necrosis                               | 1.26 | 0.55–2.83      | 0.582*  |
| Gangrene                                    | 3.86 | 1.91–7.75      | 0.0002**|
| Diabetes mellitus                           | 28.70| 1.78–461.51    | 0.017** |
| WBC—after 48–72 hours                       | 158.14| 9.96–2508.89  | 0.0003**|
| Creatinine—after 48–72 hours                | 126.28| 7.92–2013.12  | 0.0006**|
| Age >60 years                                | 58.57| 3.64–941.85    | 0.004** |
| Severe sepsis                               | 158.14| 9.96–2508.89  | 0.0003**|
| Multiple sites                              | 9.06 | 4.25–19.31     | 0.0001**|
| Lower limb                                  | 0.46 | 0.16–1.28      | 0.1387* |

*No statistical significance at p > 0.05
**Highly significant at p < 0.01
*Statistical significant at p < 0.05

**Table 3:** Comparison of factors between amputation and non-amputation group

| Outcome                              | Non-amputation | Amputation | Total | χ²-value | p value |
|--------------------------------------|----------------|------------|-------|----------|---------|
| **Comparison between age with amputation** |                |            |       |          |         |
| Age <60                              | Count 55       | 4          | 59    | 35.976   | 0.310*  |
|                                       | % 61.1%        | 40.0%      | 59.0% |          |         |
| Age >60                              | Count 35       | 6          | 41    |          |         |
|                                       | % 38.9%        | 60.0%      | 41.0% |          |         |
| **Comparison between gender with amputation** |                |            |       |          |         |
| Gender                               |                |            |       |          |         |
| Female                               | Count 29       | 6          | 35    | 3.053    | 0.094*  |
|                                       | % 32.2%        | 60.0%      | 35.0% |          |         |
| Male                                 | Count 61       | 4          | 65    |          |         |
|                                       | % 67.8%        | 40.0%      | 65.0% |          |         |
| **Comparison between underlying morbidities with amputation** |    |            |       |          |         |
| Diabetes mellitus                    | Count 52       | 7          | 59    | 0.556    | 0.520*  |
|                                       | % 57.8%        | 70.0%      | 59.0% |          |         |
| Coronary heart disease               | Count 9        | 1          | 10    | 0.000    | 1.000*  |
|                                       | % 10.0%        | 10.0%      | 10.0% |          |         |
| Renal disease                        | Count 6        | 0          | 6     | 0.709    | 1.000*  |
|                                       | % 6.7%         | 0.0%       | 6.0%  |          |         |
| Cirrhosis                            | Count 4        | 1          | 5     | 0.585    | 0.416*  |
|                                       | % 4.4%         | 10.0%      | 5.0%  |          |         |
| Gout                                 | Count 11       | 4          | 15    | 5.447    | 0.041*  |
|                                       | % 12.2%        | 40.0%      | 15.0% |          |         |
| **Comparison between wound appearance with amputation** |                |            |       |          |         |
| Swelling                             | Count 85       | 10         | 95    | 0.585    | 1.000*  |
|                                       | % 94.4%        | 100.0%     | 95.0% |          |         |
| Redness                              | Count 90       | 0          | 90    | 100.000  | 0.0005**|
|                                       | % 100.0%       | 0.0%       | 90.0% |          |         |
| Bleb                                 | Count 40       | 0          | 40    | 7.407    | 0.005**|
|                                       | % 44.4%        | 0.0%       | 40.0% |          |         |
| Skin necrosis                        | Count 30       | 0          | 30    | 4.762    | 0.030*  |
|                                       | % 33.3%        | 0.0%       | 30.0% |          |         |
| Gangrene                             | Count 0        | 10         | 10    | 100.000  | 0.0005**|
|                                       | % 0.0%         | 100.0%     | 10.0% |          |         |

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### Outcome

| Outcome | Total | Non-amputation | Amputation | $\chi^2$-value | p value |
|---------|-------|----------------|------------|----------------|---------|
| Severe pain | 75 | 10 | 75 | 0.062^2 |         |
| % | 75.0% | 100.0% | 75.0% |       |         |

**Comparison between the site of wound with amputation**

| Head and neck | 10 | 0 | 10 | 1.235 | 0.094^2 |
| % | 0.0% | 0.0% | 100.0% |       |         |

**Trunk**

| Upper limb | 22 | 4 | 22 | 2.098 | 0.220^7 |
| % | 40.0% | 40.0% | 22.0% |       |         |

**Lower limb**

| Multiple sites | 17 | 0 | 17 | 2.276 | 0.204^7 |
| % | 0.0% | 0.0% | 17.0% |       |         |

**Comparison of vital sign—temperature (F) with amputation by unpaired t-test**

| Outcome | N | Mean | SD | t-value | p value |
|---------|---|------|----|---------|---------|
| On admission | Amputation | 10 | 100.20 | 1.62 | 2.088 | 0.039^* |
| Non-amputation | 90 | 99.38 | 1.13 |         |         |
| After 48–72 hours | Amputation | 10 | 99.40 | 1.07 | 3.533 | 0.001** |
| Non-amputation | 90 | 98.18 | 1.03 |         |         |

**Comparison of vital signs pulse with amputation by unpaired t-test**

| Outcome | N | Mean | SD | t-value | p value |
|---------|---|------|----|---------|---------|
| On admission | Amputation | 10 | 95.20 | 2.90 | 0.062 | 0.951^# |
| Non-amputation | 90 | 95.26 | 2.69 |         |         |
| After 48–72 hours | Amputation | 10 | 93.50 | 9.59 | 2.326 | 0.022^* |
| Non-amputation | 90 | 87.32 | 7.78 |         |         |

**Comparison between lab findings—WBC with amputation**

| Outcome | N | Mean | SD | t-value | p value |
|---------|---|------|----|---------|---------|
| On admission | <25,000 | 64 | 0 | 64 | 19.753 | 0.0005** |
| % | 71.1% | 0.0% | 64.0% |       |         |
| >25,000 | Count | 26 | 10 | 36 |         |         |
| % | 28.9% | 100.0% | 36.0% |       |         |
| After 48–72 hours | <25,000 | Count | 76 | 0 | 76 | 11.111 | 0.004** |
| % | 84.4% | 0.0% | 80.0% |       |         |
| >25,000 | Count | 14 | 6 | 20 |         |         |
| % | 15.6% | 60.0% | 20.0% |       |         |

**Comparison between lab findings—creatinine with amputation**

| Outcome | <1.6 | Count | 61 | 0 | 61 | 17.379 | 0.0005** |
| % | 67.8% | 0.0% | 61.0% |       |         |
| >1.6 | Count | 29 | 10 | 39 |         |         |
| % | 32.2% | 100.0% | 39.0% |       |         |

**Comparison between treatment with amputation**

| Incision and drainage | Count | 40 | 0 | 40 | 7.407 | 0.005** |
| % | 44.4% | 0.0% | 40.0% |       |         |

| Debridement | Count | 30 | 0 | 30 | 4.762 | 0.030^1 |
| % | 33.3% | 0.0% | 30.0% |       |         |

| Fasciotomy | Count | 20 | 0 | 20 | 2.778 | 0.205^5 |
| % | 22.2% | 0.0% | 20.0% |       |         |

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Evaluation of Risk Factors for Amputation and Mortality in Patients of Necrotizing Fasciitis

**Highly significant at** 0.01

**No statistical significance at**

Table 4: Independent predictors of amputation

| Risk factors | RR  | 95% CI    | p value |
|--------------|-----|-----------|---------|
| Swelling     | 1.31| 0.08–19.81| 0.844*  |
| Skin necrosis| 0.11| 0.00–1.80  | 0.121*  |
| Gangrene     | 173.73| 10.91–2764.80 | 0.0003**|
| Diabetes mellitus | 1.62| 0.44–5.90  | 0.463*  |
| WBC—after 48–72 hours | 6.00| 1.86–19.26 | 0.002** |
| Creatinine—after 48–72 hours | 64.68| 3.92–1064.68 | 0.003** |
| Age >60 years | 2.15| 0.64–7.17  | 0.209*  |
| Severe sepsis | 6.00| 1.86–19.26 | 0.002** |
| Multiple sites | 0.22| 0.01–3.62  | 0.290*  |
| Lower limb   | 2.78| 0.84–9.21  | 0.093*  |

*No statistical significance at p > 0.05

**Highly significant at p < 0.01

Diagnosing NF early is essential in stopping the progression of this disease and for achieving a better prognosis. Late detection almost leads to a grave prognosis. We diagnose NF, whenever necrosis of subcutaneous tissues occurs extending through the fascial planes. Scarce cutaneous findings early in the course of the disease make it even more difficult to diagnose this condition. Often the disease is masqueraded as cellulitis or abscesses. In these patients, the diagnosis was made when the infection progressed despite treatment with (broad-spectrum) intravenous antibiotics. Many studies that were conducted in the past concluded that recognizing the disease early with early surgical intervention prevents morbidity and mortality in patients with NF. It is difficult to differentiate between NF from other soft tissue infections such as cellulitis due to minimum specific cutaneous signs, making its diagnosis even more difficult.

Our study involved a prospective assessment of various risk factors that serve as independent predictors of amputation and mortality in patients with NF. Our results should indicate the ways and means for early recognition of NF, to preserve limb from amputation and reduce mortality. Necrotizing fasciitis being an emergency surgery condition having a high mortality rate and with sufficient treatment also, the reported rate of mortality could affect the survival and preservation of limbs of patients which could assist the surgeons, to counter these risk factors for achieving a successful outcome of treatment in all patients. Our study identified gangrene, severe sepsis, total leukocyte count >25,000, and serum creatinine values >1.6 mg/dl on admission as well as within 48–72 hours, as independent predictors for both amputation and mortality and some other factors like age >60 years, the involvement of multiple sites, DM mainly predicting the mortality rate independently. Previous studies found that being female, having DM, cutaneous gangrene noted on admission, evidence of an underlying condition, heart disease, serum creatinine >1.6, and shock (systolic blood pressure, 90 mm Hg) at hospital admission were independent predictors for limb loss.

**Highly significant at** 0.0005**

**No statistical significance at**

| Outcome | Non-amputation | Amputation | Total | χ²-value | p value |
|---------|----------------|------------|-------|----------|---------|
| Amputation | Count | 0 | 10 | 10 | 100.000 | 0.0005** |
| %       | 0.0% | 100.0% | 10.0% |          |         |
| Severe sepsis | Count | 14 | 6 | 20 | 11.111 | 0.004** |
| %       | 15.6% | 60.0% | 20.0% |          |         |

Comparison of length of hospital stay with amputation by unpaired t-test

| Outcome | N | Mean | SD | t-value | p value |
|---------|---|------|----|---------|---------|
| Length of hospital stay | Amputation | 10 | 18 | 8.66 | 3.527 | 0.001** |
| Non-amputation | 89 | 10 | 6.55 |     |         |

| No statistical significance at p > 0.05
| Highly significant at p < 0.01
Statistical significant at p < 0.05

redness, blebs, gangrene, skin necrosis, WBC count (>25,000), serum creatinine level (>1.6) on admission and within 48–72 hours after admission, severe sepsis and length of hospital stay showed statistically significant differences (p value < 0.05) between amputation and non-amputation groups. Other factors did not differ significantly between the two groups.

All clinically and statistically significant variables were included in the multivariate analysis model which demonstrated that the independent predictors of amputation among patients of NF included having gangrene (RR = 173.73, 95% CI = 10.91–2764.80, p = 0.0003), severe sepsis (RR = 6.00, 95% CI = 1.86–19.26, p = 0.002), total leukocyte count (RR = 6.00, 95% CI = 1.86–19.26, p = 0.002), and serum creatinine (RR = 64.68, 95% CI = 3.92–1064.68, p = 0.003) on admission and within 48 to 72 hours of admission.

**Discussion**

Necrotizing fasciitis was initially described as gangrene of the subcutaneous tissue which was spreading very, rapidly caused by beta-hemolytic streptococci group I and later being considered as a clinical entity rather than a specific bacterial infection. Necrotizing fasciitis is a surgical emergency. Early recognition and prompt aggressive surgical debridement of all necrotic tissue are critical for survival.9

**Table 4: Independent predictors of amputation**

| Risk ratio of amputation | RR  | 95% CI    | p value |
|-------------------------|-----|-----------|---------|
| Swelling                | 1.31| 0.08–19.81| 0.844*  |
| Skin necrosis           | 0.11| 0.00–1.80  | 0.121*  |
| Gangrene                | 173.73| 10.91–2764.80 | 0.0003**|
| Diabetes mellitus       | 1.62| 0.44–5.90  | 0.463*  |
| WBC—after 48–72 hours   | 6.00| 1.86–19.26 | 0.002** |
| Creatinine—after 48–72 hours | 64.68| 3.92–1064.68 | 0.003** |
| Age >60 years           | 2.15| 0.64–7.17  | 0.209*  |
| Severe sepsis           | 6.00| 1.86–19.26 | 0.002** |
| Multiple sites          | 0.22| 0.01–3.62  | 0.290*  |
| Lower limb              | 2.78| 0.84–9.21  | 0.093*  |
and mortality in patients with NF. In our study, the association of DM related to mortality is consistent with that of a previous study reported by Dworkin et al. Some independent studies concluded that although DM was the most frequently occurring comorbidity in NF patients, significantly it did not increase amputation or mortality rates. Diabetes mellitus was also the most common comorbidity in our patients, as reported by other investigators. The pathophysiology of DM is related to the worst outcomes of NF because hyperglycemia induces bacterial growth and tissue ischemia as a result of peripheral vascular disease, leading to amputation and mortality. Patients with DM often develop severe atherosclerosis. The atherosclerotic changes occurring in the limb vessels were found to be more extensive in small-caliber arteries, resulting in ischemia and gangrene, ultimately leading to amputation or mortality. Nearly 45% of sites of amputation which were involving fingers or toes, distinguishing between wet gangrene of the DM foot from NF, which sometimes occur simultaneously could not be differentiated. Elderly persons with or without underlying diseases, such as chronic heart disease and liver cirrhosis, with the involvement of multiple sites in disease, were considered as having worse prognostic factors, similar to previous studies reporting that advanced age was associated with an increased risk of mortality. This study found that age being >60 years, increased the mortality rate significantly. However, some studies found that advanced age did not affect mortality.

Necrotizing fasciitis presenting with severe sepsis, with total leukocyte count >25,000 on admission as well as within 48–72 hours of admission and gangrene at the time of diagnosis was found to be significantly predictive for mortality (p = 0.0003, p = 0.0003, respectively) and amputation (p = 0.002, p = 0.002, p = 0.003, respectively) in our study. Dworkin et al. also reported that cutaneous gangrene which was present on admission was significantly (p = 0.005) associated with increased risk of loss of limb. In previous studies, the presence of gangrene was observed in late-stage NF and was the leading cause of an adverse outcome. As in other previous studies, we found that soft tissue swelling of the affected area was a common clinical manifestation in most patients with NF. The infection which spreads into lymphatic and vascular systems causes tissue edema and muscle necrosis, and eventually, skin necrosis will occur consequent to thrombosis of microvascular vessels and dysfunction of the nerve supply. Gangrene is tissue necrosis due to lack of blood supply. Whenever gangrene was present, debridement or amputation was needed depending on the extension of necrotic areas.

Our study found that serum creatinine values >1.6 mg/dL posed an increased risk for limb loss and death. An increase in the serum creatinine levels reflects renal dysfunction, which may be associated with septic shock. Anaya et al. reported that shock (systolic blood pressure, 90 mm Hg) at admission was an independent predictor for limb loss, raised creatinine level, and higher mortality similar to many previous studies. However, as reported by Dos Santos et al., serum creatinine levels were not associated with major amputation.

As per literature, prognostic factors to evaluate the severity of NF patient included the LRINEC (laboratory risk indicator for NF) score, composed of six marker variables, including C-reactive protein, total white blood cell count, hemoglobin, serum sodium, serum creatinine, and serum glucose; and acute physiology and chronic health evaluation II (APACHE II) scores were including the patient’s vital signs (temperature, mean arterial pressure, heart rate, and respiratory rate), oxygenation [A-PaO₂ (FiO₂ 0.50%) or PaO₂ (FiO₂ 50%)], metabolic parameters [sodium, potassium, creatinine, bicarbonate concentrations (arterial pH or HCO₃), hematocrit, white blood cell count] were used as a prognostic scoring system for critical care, and Glasgow coma score and calculates a score relating to the severity of the disease of a patient who was admitted to the ICU.

The limitations of our study include that neither of these scoring systems could be applied (LRINEC and APACHE II). Despite the limitations of our study, the results of our study might be useful in clinical practice while caring for NF patients in provincial hospitals and physicians can make use of the risk factors for evaluating the patients despite limited resources that are available at local hospitals.

**CONCLUSION**

In our study, we concluded that gangrene, severe sepsis, total leukocyte count >25,000, and serum creatinine values >1.6 mg/dL on admission as well as within 48–72 hours, as independent predictors for both amputation and mortality and some other factors like age >60 years, the involvement of multiple sites, DM mainly predicting the mortality rate independently. Thus for patients presenting with any of these clinical predictors, the treating surgeon should have direct concern toward the progression of the disease and might be considered for early investigation and close monitoring to prevent morbidity and mortality as well as limb loss as much as possible.

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