# Factors influencing adverse outcomes in non diabetic necrotizing fascitis- a retrospective study

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## Abstract

**Background**: Necrotising fasciitis is a rare severe soft tissue infection with a paucity of early symptoms to diagnose the condition. Early diagnosis and institution of treatment may improve outcome.

**Aim:** To study the factors likely to influence rate of mortality.

**Methods:** We present a retrospective analysis of a cohort of 42 patients of non-diabetic necrotising fasciitis over 10 years. After clinical examination and workup patient underwent early debridement with empirical antibiotic therapy. The features used for analysis included age, gender, concurrent systemic diseases (diabetes mellitus, coronary artery disease, chronic liver disease, chronic kidney disease and cancer), duration between the onset of symptom and wound debridement and laboratory parameters

**Results**: Analysis showed that the duration between onset of first symptom and debridement was the key factor deciding the outcome. Mortality is not affected by the microbiological spectrum.

**Conclusion:** Early adequate source control with debridement gives the best results. Morbidity, mortality and renal risk increase with delay in treatment. Early empirical antibiotic therapy only helps in masking the symptoms.

**Key words**: necrotizing fasciitis; non-diabetic; systemic diseases

## Introduction

Necrotising fasciitis (NF) is a rare disease with high mortality and major disabling consequences. The disease is characterized by rapidly spreading soft issue infection mostly in subcutaneous plane resulting in destruction of overlying skin. NF does not show any age or gender predilection but higher incidences are noted among patients with diabetes mellitus, immunocompromised state, obesity and alcohol abuse[1]. Giuliano A et al described three distinct bacteriological types in NF[2]. In a multicenter study enrolling 1504 patients, mortality rate was found 19.3% and multivariable risk regression analysis showed female gender, concurrent chronic heart disease or cirrhosis, skin necrosis, pulse rate >130/min, systolic blood pressure <90 mmHg and serum creatinine ≥1.6 mg/dL were factors that influenced the outcome of the disease[3]. NF is more common in patients with advanced age and systemic debilitating diseases. Early surgical debridement, appropriate antimicrobial therapy and supporting treatment to improve general health status are the key to a better outcome.[4]

The aim of the present study is to define factors likely to influence the rate of mortality in patients with NF. We felt that the duration between onset of first symptom and debridement is the key factor deciding the outcome. We hypothesized that delay more than 4 days was significantly associated with mortality.

## Materials and Methods

### *Study design:*

A retrospective study was done on patients admitted with confirmed diagnosis of acute necrotising fasciitis during January 2005 to December 2015. All patients admitted with a diagnosis of Necrotising facitis and managed in the General surgery department were included in the study. Patients with a known history of diabetes were not included in the study. The confirmation was done on basis of clinical and operative findings (greyish necrotic fascia, demonstration of a lack of resistance of normally adherent muscular fascia to blunt dissection, lack of bleeding of the

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fascia during dissection, and the presence of foul-smelling pus). Data regarding treatment received from elsewhere prior to admission were reviewed.

After complete clinical examination blood samples were drawn for blood counts, aerobic culture, random blood sugar, serum creatinine, electrolyte profile and liver function. All patients underwent complete debridement as emergency and tissue was sent for aerobic culture. Patients received Cefoperazone Sulbactum combination as empirical antibiotic therapy and were switched over to appropriate drug when the tissue culture was available. Wound care included serial debridement of slough, low pressure dressings and appropriate reconstruction.

The features used for analysis included age, gender, concurrent systemic diseases (diabetes mellitus, coronary artery disease, chronic liver disease, chronic kidney disease and cancer), duration between the onset of symptom and wound debridement and laboratory parameters (White cell count, Hemoglobin, serum sodium, liver function tests and serum creatinine).

Charts of the patient were reviewed and data was collected. The collected data were compiled by using Micro Soft Excel 2010 and were analyzed by using statistical software SPSS 20.0 version.

**Definitions:**

1. Haemodynamic instability: Pulse rate above 120/ minute and or systolic blood pressure below 90 mm of Hg.
2. Uncontrolled Diabetes Mellitus: RBS > 200 mg/dl and HbA1C >7.3%
3. Renal risk- Serum creatinine >1.8 mg /dl[5]
4. Acute Liver Dysfunction (ALD): International Normalized Ratio (INR).1.5, in a patient without pre-existing cirrhosis[6].
5. Severe hyponatraemia: serum sodium < 125mg/dl
6. Multi Drug Resistance (MDR): Non-susceptibility to at least one agent in three or more antimicrobial categories (7)

**Results**

The cohort included 42 patients (52% male: n.22) with a mean age of 57.55 years (SD: 16.087)

Of the group 20 (47.6%) did not have any systemic diseases requiring ongoing treatment.

Pain of the affected site and fever were the first symptoms of all patients. Of the whole group, only 14 (33%) gave a history of trauma with abrasions on the lower limbs few days prior to onset of symptoms. No patient had episode of systemic infection prior to onset of present symptom (Table 1).

**Table-1. Details of concurrent systemic diseases**

| Features | Number | Percentage |
|---|---|---|
| Diabetes Mellitus | 11 | 26% |
| Hypertension | 12 | 28% |
| Coronary Artery Disease | 5 | 12% |
| Chronic Liver Disease | 5 | 12% |
| No associated diseases | 20 | 47.6% |
| Total | 42 | 100% |

Thirteen patients (31%) reported directly to the Institution and 19 received empirical antibiotic therapy from primary care hospitals. Ten patients (24%) had incision and drainage without adequate debridement at local hospital along with antibiotic therapy. The site affected were Right leg- 20 (37.6%), left leg- 14 (33.5%), left upper limb 2 (5%), right upper limb 1 (2.5%) and scrotum 5 (12%). At the time of admission there were 5 (12%) patients with hemodynamic instability, 7 (16.5%) with renal risk and 10 (24%) with acute liver dysfunction and nine patients (21%) with severe hyponatraemia. The mean duration between onset of first symptom and adequate debridement was 8.24 days (median 7)

Laboratory parameters are noted in table 2 and microbiological profile is given in table 3. There were 7 instances of MDR (Klebsiella Pneumoniae 4, Pseudomonas aeruginosa 3) associated with poly-microbial infections.

**Table 2. Laboratory parameters of the group**

| Features | Mean (SD) | Ref range |
|---|---|---|
| Total leucocytic count | 16.06 7.641) | 4.0 - 10.0 (K/uL) |
| Hemoglobin | 11.32 (1.325) | 13.0 - 17.0 (g/dl) |
| Platelet count | 238.214 (160.41) | 150.0-400.0 (K/uL) |
| Serum Creatinine | 1.420 (1.166) | 0.84 - 1.25 (mg/dl) |
| Serum Sodium | 131.76 (5.912) | 136.0 - 146.0 (mmol/L ) |
| Serum bilirubin | 1.96 (2.267) | 0.2 - 1.2 (mg/dl) |
| SGPT | 35.43 (21.479) | 5.0 - 45.0 (IU/L) |
| SGOT | 46.21 (43.168) | 5.0 - 35.0 (IU/L) |
| Total Proteins | 6.34 (0.937) | 6.6 - 8.3 (g/dl) |
| Alkaline Phosphatase | 164.43 (90.082) | 42.0 - 128.0 (IU/L) |
| PT/INR | 1.27 (0.376) | 0.9-1 |

**Table 3. Microbiological profile of the group**

| Organisms | Number | Percentage |
|---|---|---|
| Streptococcus Pyogens -A | 7 | 16.7% |
| Streptococcus Group G | 1 | 2.4% |
| Enterococcus species | 3 | 7.2% |
| Staphylococcus Aureus | 4 | 9.5% |
| Staphylococcus aureus (MRSA) | 2 | 4.8% |
| Staphylococcus Coagulase negative | 4 | 9.5% |
| Escherichia Coli | 1 | 2.4% |
| Pseudomonas Species* | 2 | 4.8% |
| Klebsiella pneumoniae | 2 | 4.8% |
| Polymicrobial | 11 | 28.6% |
| No growth | 5 | 12% |
| Total | 42 | |

**Pseudomonas aeruginosa & Pseudomonas putida*

**Table 4. Factors associated with fatal outcome**

| Features | Mortality | Total | P value | OR | C I |
|---|---|---|---|---|---|
| Co-morbidity | 4 (18%) | 22 | 0.203 | | |
| Male gender | 5(22.7%) | 22 | 0.023 | 1.294 | 1.302-1.623 |
| Hemodynamic instability | 3(60%) | 5 | 0.003 | | |
| Mean age | 54.24(12.478) | 57.55(16.078) | 0.292 | | |
| Duration in days | 12 (8.093) | 7.73(4.834) | 0.096 | | |
| Duration > 4 days | 5 (13.5%) | 37 | 0.512 | | |
| Monomicrobial infection | 3(13.6%) | 22 | 0.716 | | |
| Poly microbial | 2(16.7%) | 12 | 0.547 | | |
| Severe Hyponatreamia | 2 (22.2%) | 9 | 0.281 | | |
| Renal risk | 3(42.9%) | 7 | 0.006 | 7.500 | 1.522-36.947 |
| Acute liver dysfunction | 2(20%) | 10 | .365 | | |

Mean duration of hospitalization was 20.57 (14.367) days. 5 (11.9%) had fatal outcome. The cohort was divided into two to analyze the features related to fatal outcome. The details are given in table 4. The mortality was not influenced by the microbiological profile; there were 3 deaths with mono-microbial and 2 in poly- microbial infections. Renal risk was found in patients whose definite procedure was delayed more than 4 days. Mortality occurred in patients whose procedures were delayed for more than 4 days.

Linear regression analysis with male gender, renal risk and hemodynamic instability was done. Hemodynamic instability retained the significance (Beta.541 t 4.52; p.000) and male gender (Beta -.209; t -1.742 p=.090) and renal risk (Beta.208, t 1.678 p=.101) lost significance.

## Discussion

Overall mortality of NF varies from 15 to 36%[8,9] and the present series noted 11.9% mortality comparable to other series. The delay in debridement was conspicuous but lost statistical significance. Hemodynamic instability as well as renal risk were noted only when delay in debridement exceeded 4 days. Death in NF is directly influenced by severity of sepsis. Key factors likely to influence the outcome of sepsis management are organ system support and effective antimicrobial eradication with antibiotics and source control. Early diagnosis is necessary for optimization of these factors[10]. Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score was proposed by Wong et al (2004)[11,12] is a good diagnostic tool but not validated for risk stratification. LRINEC score will enhance the diagnostic accuracy and thereby reduce the delay in debridement.

A high index of suspicion is mandatory to diagnose and treat the patient early since the disease is associated with a paucity of symptoms defining severity. A retrospective case series observed significant reduction in mortality when early surgical debridement was performed[13-15]. Voros D et al

observed a delay in surgery of just one day correlated with increased mortality ($p < 0.05$; relative risk = 9.4)[14]. International Guidelines for management of Severe Sepsis and Septic Shock recommends that early anatomical diagnosis of infection should be made and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible[15]. Mortality was appreciably low in septic patients who underwent source control[16-18].

We observed that a considerable delay in debridement was associated with mortality but did not attain statistical significance. But the features associated with mortality occurred in patients who had delay in debridement for more than 4 days.

The present series did not have type 3 NF. We did not find significant difference in the outcome between the type 1 and type 2 NF in terms of mortality or duration of hospitalization. Of the group mono-microbial infection was seen in 26 (64%) patients and streptococcal and staphylococcal species were the most common pathogen. Wong and colleagues observed poly-microbial synergistic infection as the common cause of NF. We also observed single gram negative isolates in 5 patients[19].

There was one incidence of group G streptococci (GGS) noted in a patient with type 2 diabetes mellitus. GGS is part of normal flora in the body but increasing incidences of infections by the organism is being reported[20]. The patient of this series was on regular treatment for type 2 diabetes mellitus (HbA1C-7.4). There were 2 instances methicillin-resistant *S.* aureus *(*MRSA) and these patients did not have any concurrent morbidity. These patients did not undergo hospitalization or interventional procedures and so likely to be community acquired infection. All these patients responded to conventional treatment. Mortality was not influenced by the microbiological spectrum. There seems to be a change in the spectrum of bacteriological isolates in recent case series[21].

## Conclusion

Necrotising fasciitis is a rare severe soft tissue infection with a paucity of early symptoms to diagnose the condition. Early adequate source control with debridement gives the best results. Morbidity, mortality and renal risk increase with delay in treatment. Early empirical antibiotic therapy only helps in masking the symptoms.

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