

Evaluation of prognostic indicators for necrotizing fasciitis

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Keywords: Necrotizing fasciitis; diabetes; surgical debridement; multidisciplinary

Abstract

Necrotizing Fasciitis (NF) is a rapid spreading lethal infection of the skin, muscles and soft tissues, with progressive inflammation along tissue planes and local destruction. The varied clinical presentation often leads to misdiagnosis. Various co-morbidities can influence the clinical course of the disease. Considering the life-threatening nature of the condition, this study is undertaken to identify significant prognostic factors, which will facilitate early diagnosis and intervention for an optimal outcome. This is a prospective study of 40 cases of Necrotizing Fasciitis, for 2 years. Maximum patients were in the age group of 51 to 70 years. 55% of patients had necrotizing fasciitis of the lower limb. Pain and fever were the commonest presenting features. 58% of patients presented with clinical features of less than 7 days duration. Trauma was the aetiological factor in 28% of patients. Diabetes Mellitus was the commonest co-morbidity (65%). *E. coli* was the commonest isolate in culture reports. The LRINEC Score was more than 8 in 25% of patients and less than 5 in 60% cases. Two patients required amputation, 30 underwent surgical debridement and 8 were subjected to fasciotomy. Out of the 38 cases, another 3 patients required amputation subsequently. Length of hospital stay was more than 3 weeks in 63% of cases. Mortality was noted in 12.5% of patients. The hemodynamic status of the individual at the time of presentation and during the post-operative period has a significant prognostic value. Diabetes Mellitus is a common co-morbidity existing in patients with Necrotizing Fasciitis. Other co-morbidities like hepatic and renal dysfunction, hypertension, Peripheral Vascular Disease, immune-deficient states, also affect the treatment outcome. Initial surgical debridement is of extreme importance and should be a thorough one. Early diagnosis, aggressive surgical debridement, with balanced fluid resuscitation and adequate nutritional support and a multidisciplinary approach is the key to a successful outcome.

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Received: 26-08-2020 Accepted: 20-07-2021

DOI: <http://doi.org/10.4038/sljs.v39i2.8870>



Introduction

Necrotizing Fasciitis (NF) is a rapid spreading lethal infection of the skin, muscles and soft tissues, with progressive inflammation along tissue planes and local destruction [1]. The quick changes seen in the clinical course of the disease are attributed to the polymicrobial nature of infection and synergistic action of aerobes and anaerobes [2]. The incidence of NF is estimated at 500 -1000 cases annually with a global prevalence of 0.40 cases per 10,000 populations. The varied clinical presentation often leads to misdiagnosis. Pain, which is disproportionate to the local swelling or erythematous reaction, is a reliable sign of early NF [3]. Various conditions which can influence the clinical course of the disease include Diabetes Mellitus, immunosuppression, liver dysfunction and renal dysfunction [4]. NF is a surgical emergency, with mortality rates ranging from 9% to 29 % [5]. Various scores have been formulated for predicting mortality in Necrotizing Soft Tissue Infections. None have been sufficiently sensitive or specific to risk application in this condition [6]. Considering the life-threatening nature of the condition, this study is undertaken to identify significant prognostic factors, which will facilitate early diagnosis and intervention for an optimal outcome.

Objective

To evaluate the prognostic factors for necrotizing fasciitis concerning: Presence of co-morbidities: Diabetes Mellitus, Liver dysfunction, Hypertension, Immunodeficiency, Renal Dysfunction and Peripheral Vascular Disease; Advanced age; period between onset of disease and surgical debridement; Extent and variability of infection; Culture reports (Gram-positive vs Gram-negative infections); Intensive Care Unit (ICU) stay.

Materials and Methods

This is a prospective study of 40 patients with necrotizing fasciitis, carried out at MGM Medical College and Hospital, Navi Mumbai, India, from April 2017 to October 2018. The study was approved by the Institute Ethics Committee of the said Institution and written and informed consent was obtained from all enrolled patients. Criteria included for defining necrotizing fasciitis were: evidence of mottled skin appearance, necrotic skin and subcutaneous tissue, digital blunt dissection of adherent fascia with no evidence of any

resistance; a purulent or seropurulent discharge with a fishy odour. Following laboratory investigations were done: White Blood Cell count and Platelet Count; Blood Urea Level; Serum Creatinine level; Serum Creatinine Kinase; C-Reactive Protein; Serum electrolytes; Serum proteins; Blood Glucose Levels; Liver Function Tests. Based on these investigations, the Laboratory Risk Indicators for Necrotizing Fasciitis (LRINEC) score [7] was calculated for each patient. Plain X-ray, USG, CT SCAN/MRI were done in equivocal cases. Limb arterial Doppler studies were done in 4 patients as indicated by clinical examination.

Patients presenting with shock were aggressively resuscitated. Intravenous antibiotics including Inj. Metronidazole were administered. All patients underwent emergency surgical debridement. All wounds were left open. Tissue was obtained for histopathological diagnosis and discharge was sent for culture sensitivity examination. In the postoperative period, dressings were changed twice daily and wounds were inspected for any residual collections / progressive necrosis/septic focus. Serial debridements were done as required. Antibiotics were changed depending upon culture sensitivity reports. Skin grafting was done in cases with healthy granulation tissue, wherever possible.

Factors evaluated included, presence of comorbidities like Diabetes Mellitus (Fasting Blood sugar levels), Liver dysfunction (Serum Bilirubin and Liver enzymes), Hypertension, Immunodeficiency (HIV status, patients on chemotherapy/radiotherapy / immunosuppressive drugs), Renal Dysfunction (Serum Creatinine and Blood Urea levels), Peripheral Vascular Disease (Clinical signs and Arterial Doppler findings); Age > 50 years; the period between onset of disease and surgical debridement; Extent and variability of infection; Culture reports (Gram-positive vs Gram-negative infections); ICU stay.

Statistical analysis was done using the Chi-Square test, Student t-test and SPSS (Version 25.0)

Results

The study included 32(80%) males and 8 (20%) females. Maximum patients were in the age group of 51 to 70 years, with the mean age being 53.67 years. 22 patients (55%) had necrotizing fasciitis of the lower limb. 4 cases (10%) presented with Fournier's Gangrene. Pain and fever were the commonest presenting features, seen in 34 (85 %) and 29 (72.5 %) cases respectively. Local blisters were observed in 20 (50%) cases. 23 (58%) patients presented with clinical features of less than 7 days duration. 11 (28%) of cases were traumatic in origin. Diabetes Mellitus was the commonest co-morbidity seen in 26 cases (65%), followed by Anaemia in 15

patients (38%) and Renal dysfunction in 11 cases (28%) (Table 1). E. coli was the commonest wound isolate, seen in 19 (48%) cases. Table 2 shows the investigation findings. 24 (60%) of patients had an LRINEC score of less than 5 (Graph 1). 30 (75%) patients underwent debridement. 8 (20%) required fasciotomies and 2 (5%) had to undergo amputation. Re-debridement was required in 14 out of 38 cases and another 3 patients required amputation subsequently. 25 (63%) patients stayed for more than 3 weeks in the hospital (Graph 2). Mortality was noted in 5 (12.5%) cases in our study. 4 (80%) patients who succumbed to death were more than 50 yrs of age. Surgical intervention was done after 12 hours of presentation in 4 cases of mortality.

The culture reports showed polymicrobial infection in 1 (20%) and Gram-negative infection in 4 (80%) patients who died, which was not of statistical significance. Diabetes mellitus was present in 4 (80%) patients and renal dysfunction and immunodeficiency 2 (40%) cases. All these patients required intensive unit monitoring. The minimum LRINEC Score was 2 and the maximum was 11. The median score of the data was 5. The association between mortality and morbidity about LRINEC Scoring was not statistically significant. 4 cases (80%) out of those who succumbed, had an LRINEC Score of >8. Morbidity was noted in 2 cases with an LRINEC Score of 7 and in one case with an LRINEC Score of 8. The presence of shock, leukocytosis, renal dysfunction, Peripheral Vascular Disease, Hypertension and ICU requirements, were the significant variables in the study (Table 3).

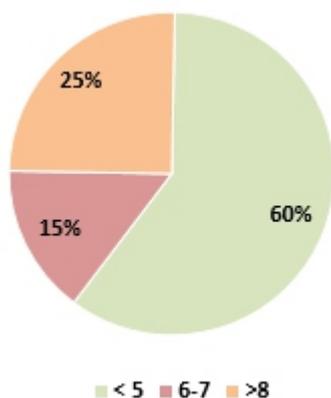
P-value for Age, Males, diabetes mellitus and site of infection was greater than that of 0.05, indicating no significant difference in the observed proportion when compared between < 6 and >= 6 LRINEC scoring. P-value for Hospital stay, was less than that of 0.05; indicating a significant difference in the observed proportion when compared between < 6 and >= 6 LRINEC scoring (Table 4).

Table 1. Co-Morbidities

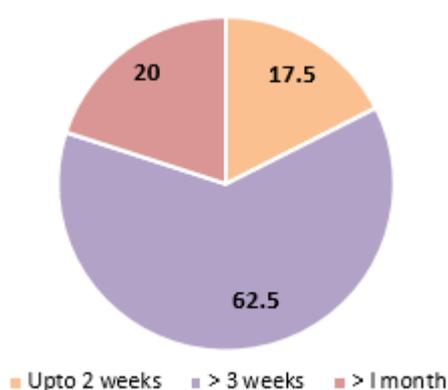
Co-morbid conditions	Number of patients	%
Diabetes mellitus	26	65
Smoking	6	15
Renal dysfunction	11	27.5
Cirrhosis	2	5
HIV	2	5
Tuberculosis	4	10
Anaemia	15	37.5
Skin Disorder	6	15
COPD	4	10

Table 2. Investigation findings

Investigations	Number of patients	%
WBC (/ mm ³)		
a. 15000-25000	20	50
b. >25000	3	7.5
Haemoglobin (gm %)		
a. 11- 13.5	13	32.5
b. <11	27	67.5
Sodium levels (mmol/litre)		
a. >135	15	37.5
b. <135	25	62.5
Serum creatinine (umol/L)		
a. <1.5	29	72.5
b. >1.5	11	27.5
Blood sugar levels (mgm%)		
a. <180	28	70
b. >180	12	30



Graph 1. LRINEC Scoring



Graph 2. Hospital Stay

Table 3. Statistical significance of all variables

Variable	Total (n=40)	Survivors (n=35)	Non-Survivors (n= 5)	p value
Shock	3	0	3 (60)	0.000
Tachycardia	18	16 (45.7)	2 (40)	0.812
Fever	29	26 (74.2)	3 (60)	0.503
Leukocytosis	23	18 (51.4)	5 (100)	0.040
Anaemia	27	23 (65.7)	4 (80)	0.523
Renal Dysfunction	11	7 (20)	4 (80)	0.005
Hyponatremia	25	21 (60)	4 (80)	0.388
Liver Dysfunction	9	8 (22.8)	1 (20)	0.886
Age > 50 years	27	23 (65.7)	4 (80)	0.523
Surgical intervention >24hrs	0	0	0	No difference
Diabetes Mellitus	26	22 (62.8)	4 (80)	0.452
Immunodeficiency	2	1 (2.8)	1 (20)	0.100
PVD	4	2 (5.7)	2 (40)	0.017
Hypertension	7	4 (11.4)	3 (60)	0.008
Gram Negative Infection	28	24 (68.5)	4 (80)	0.602
ICU requirement	5	0	5 (100)	0.000

(Figures in parenthesis indicate percentages) Chi Square test

Table 4. Statistical significance of all variables compared with LRINEC Score

Parameter	< 6 (n=24)	>6 (n=16)	p value
Age (years)			
< 50	8 (33.3 %)	5 (31.2%)	0.890*
> 50	16 (66.6%)	11 (68.7%)	0.41**
(Mean ± SD) (Age)	(52.25±14.61)	(55.81±11.26)	
Males	21 (87.5%)	11 (68.7%)	0.146*
Diabetes mellitus	13 (54.1%)	12 (75%)	0.773*
Site of infection			
Lower Limb	11 (45.8%)	11 (68.7%)	0.102*
Perineum	3 (12.5%)	0	
Hospital stay (days)			
< 7	0	5 (31.2%)	0.003*
> 7	24 (100%)	11 (68.7%)	0.01**
(Mean ± SD) (Hospital Stay)	(25.46±7.07)	(18.75±8.68)	

**Student t test

*Chi Square test

Discussion

In our study, 80% were males and 70% were more than 50 years of age. El-Menyar et al[8] reported a mean age of 48 years, with 74% males in their study. Martinschek et al[9] mentioned a median age of 48 years in their study, with 62% males and 38% females. The lower extremities were the most commonly affected in 63.2% cases in the study by Martinschek et al[9], followed by abdomen in 30.9% and perineum in 14.5%. Another study[10] reported necrotizing fasciitis in lower limbs in 56.6% cases and the perineum in 25%. Trauma was the commonest aetiological factor in our study and Diabetes Mellitus was the commonest co-morbidity (65%). A study[9] reported Diabetes Mellitus in 27.35 and Hypertension in 25.4% of cases. Another study[10] found Diabetes in 53.3%, alcohol and smoking in 18.3% of cases. Local erythema and swelling were reported in 100% of cases by Martinschek et al[9] Typical crepitation were seen in 73.6% of patients. Another study[10] mentioned pain and tenderness as the presenting features for 100% of cases, the duration ranging from 5 days to 2 years, and fever in 35%. Pain and fever were the commonest features in our study, with blister formation being evident in 50% of cases. We did not have any anaerobic infection in our study. This might be due to failure to obtain anaerobic cultures at times. The culture profile for aerobic infection is comparable with other studies[11]. The LRINEC Score was <6 in 60% and > 6 in 40% cases in our study. El-Menyar et al[8] reported a LRINEC Score of < 6 in 45% and > 6 in 55% cases. Corbin et al[12] mentioned that complications are higher in patients with an LRINEC Score of >6. Colaket al[13] observed that LRINEC Score was higher in the non-survivor group. Su et al[14], in their study of 209 patients, also observed that patients with LRINEC Score >6 have a higher rate of mortality. The median LRINEC Score in all deaths was 9 (range: 6 to 12), in a study by Swain et al[15]. A study[16] mentioned that patients with higher LRINEC Score were more likely to need mechanical ventilation and longer hospital stay.

There is no substitute for aggressive early surgical debridement for necrotizing fasciitis. Kalaivani et al[10] mentioned the need for multiple debridements in 35% of patients and amputations in 8.35 cases. Another study[17] reports immediate debridement, broad-spectrum parenteral antibiotics and repeated debridements as a treatment protocol.

Our study had a mortality of 12.5%. El- Menyar et al [8] reported a mortality rate of 15% with LRINEC <6 and 28% with LRINEC >6. Lee et al [18] mentioned 15.2 % mortality. Other studies [9,10,17] have reported a mortality rate of 16.6 %, 25 % and 29 % respectively.

Several studies have studied the significance of multiple variables affecting the clinical outcomes in their series of patients with necrotizing fasciitis. McHenry et al [17] mentioned an average time for surgical intervention as 90 hours in non-survivors versus 25 hours in survivors. Wong et al[19] concluded that advanced age, two or more associated co-morbidities and a delay of more than 24 hours for surgical intervention, had a negative impact on survival. Diabetes mellitus was an associated co-morbidity in 70.8% of their patients. Yanar et al [20] mentioned that raised serum creatinine, age more than 50 years and debridement after 24 hours were associated with a negative outcome. Diabetes has been an important factor in adverse outcomes. Kalaivani et al [10] report a death rate of 31% among diabetics and 17.9% among non-diabetics. The presence of Peripheral Vascular Disease was stated to be an important factor by McHenry et al[17] Advanced age has been mentioned as a significant factor in several studies[9,17,21].

Conclusions

Necrotizing Fasciitis is a life-threatening surgical emergency. The hemodynamic status of the individual at the time of presentation and during the post-operative period has a significant prognostic value. Diabetes Mellitus is a common co-morbidity existing in patients with Necrotizing Fasciitis. Other co-morbidities like hepatic and renal dysfunction, hypertension, Peripheral Vascular Disease, immune-deficient states, also affect the treatment outcome. Advanced age though a contributing adverse factor, cannot be taken as an individual prognostic indicator. The duration between the onset of disease and surgical intervention is extremely crucial. Less the duration, more favourable the outcome. The initial surgical debridement is of extreme importance and should be a thorough one. Proper efforts at procuring adequate and appropriate culture samples can aid in instituting evidence-based antibiotic protocols. The requirement of an intensive care unit is a part of the treatment protocol for fulminant infections. However, prolonged stay in the intensive care unit has adverse effects. Early diagnosis, aggressive surgical debridement, with balanced fluid resuscitation and adequate nutritional support and a multidisciplinary approach is the key to a successful outcome in Necrotizing Fasciitis.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

References

1. Misiakos EP, Bagias G, Patapis P, Sotiropoulos D, Kanavidis P, Machiaras A. Current concepts in the management of necrotizing fasciitis. *Frontiers in Surgery* 2014;1(36):1-10. <https://doi.org/10.3389/fsurg.2014.00036>

2. Levine EG, Monders SM. Life-threatening necrotizing fasciitis. *Clin Dermatol* 2005; 23: 144-147.
<https://doi.org/10.1016/j.clindermatol.2004.06.014>
3. Dworkin M, Westercamp M, Park L, McIntyre A. The epidemiology of necrotizing fasciitis including factors associated with death and amputation. *Epidemiol Infect* 2009; 137:1609-1614. <https://doi.org/10.1017/S0950268809002532>
4. Lee CY, Kuo LT, Peng KT, Hsu WH, Huang TW, Chou YC. Prognostic factors and monomicrobial necrotizing fasciitis: Gram positive versus Gram negative pathogens. *BMC Infectious Diseases* 2011;11(5).
<https://doi.org/10.1186/1471-2334-11-5>
5. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of morbidity for necrotizing soft tissue infections. *Ann Surg* 1995; 221(5): 558-563.
<https://doi.org/10.1097/0000658-199505000-00013>
6. Henry SM, Davis KA, Morrison JJ, Scalea TM. Can Necrotizing Soft Tissue Infection be reliably diagnosed in the emergency department? *Trauma Surg Acute Care Open* 2018;3:1-3.
<https://doi.org/10.1136/tsaco-2017-000157>
7. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC Score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med* 2004; 32:1535-1341.
<https://doi.org/10.1097/01.CCM.0000129486.35458.7D>
8. El-Menyar, Asim M, Mudali IN, Mekkodathil A, Latifi R, Al-Thani H. The laboratory risk indicator for necrotizing fasciitis (LRINEC) scoring: the diagnostic and potential prognostic role. *Scandinavian Journal of trauma, Resuscitation and Emergency Medicine* 2017;25:28.
<https://doi.org/10.1186/s13049-017-0359-z>
9. Martinschek A, Evers B, Lampl L, Gerngross H, Schnidt R, Sparwasser C. Prognostic aspects, survival rates and predisposing factors in patients with Fournier's Gangrene and Necrotizing Soft Tissue Infections: Evaluation of clinical outcome of 55 patients. *Urol Int* 2012;89:173-179.
<https://doi.org/10.1159/000339161>
10. Kalaivani R, Hiremath BV, Indumathi VA. Necrotizing soft tissue infection-risk factors for mortality. *J Clin Diagn Res* 2013;7(8):1662-1665.
11. Bosshardt TL, Henderson VJ, Organ CH. Necrotizing Soft Tissue Infections. *Arch Surg* 1996;131(8):846-852.
<https://doi.org/10.1001/archsurg.1996.01430200056011>
12. Corbin V, Vidal M, Beytout J, et al. Prognostic value of the LRINEC score (Laboratory Risk Indicator for Necrotizing Fasciitis) in soft tissue infections: a prospective study at Clermont-Ferrand University hospital. *Ann Dermatol Venereol.* 2010;137:5-11.
<https://doi.org/10.1016/j.annder.2009.12.002>
13. Colak E, Ozlem N, Kucuk GO, et al. Laboratory Risk Indicators for Necrotizing Fasciitis and associations with mortality. *Turk J Emerg Med.* 2014;14:15-19.
<https://doi.org/10.5505/1304.7361.2014.55476>
14. Su YC, Chen HW, Hong YC, et al. Laboratory risk indicator for necrotizing fasciitis score and the outcomes. *ANZ J Surg.* 2008;78:968-972.
<https://doi.org/10.1111/j.1445-2197.2008.04713.x>
15. Swain RA, Hatcher JC, Azadian BS, et al. A five-year review of necrotizing fasciitis in a tertiary referral unit. *Ann R Coll Surg Engl.* 2013;95:57-60.
<https://doi.org/10.1308/003588413X13511609956093>
16. Bozkurt O, Sen V, Demir O, et al. Evaluation of the utility of different scoring systems (FGSI, LRINEC and NLR) in the management of Fournier's gangrene. *Int Urol Nephrol.* 2015;47:243-248. <https://doi.org/10.1007/s11255-014-0897-5>
17. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for Necrotizing Soft-Tissue Infections. *Ann Surg* 1995;221(5):558-565.
<https://doi.org/10.1097/0000658-199505000-00013>
18. Ching-Yu Lee, Liang-Tseng Kuo, Kuo-Ti Peng, Wei-Hsiu Hsu, Tsan-Wan Huang, Ying-Chao Chou. Prognostic factors and monomicrobial necrotizing fasciitis: gram positive versus gram-negative pathogens. *BMC Infect Dis* 2011;11;5.
<https://doi.org/10.1186/1471-2334-11-5>
19. Wong CH, Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. *J Bone Joint Surg Am* 2003;85:1454-1460. <https://doi.org/10.2106/00004623-200308000-00005>
20. Yanar H, Taviloglu K, Ertekin C, et al. Fournier's Gangrene: Risk factors and strategies for management. *World J Surg* 2006;30:1750-1754. <https://doi.org/10.1007/s00268-005-0777-3>
21. Eke N: Fournier's gangrene: a review of 1726 cases. *Br J Surg* 2000;87:718-728.
<https://doi.org/10.1046/j.1365-2168.2000.01497.x>