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Laboratory risk indicator for necrotising fasciitis [LRINEC] score as a tool for differentiating necrotising fasciitis from other soft tissue infections

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Abstract

Necrotizing fasciitis (NF) is often fatal, characterized by extensive necrosis of the subcutaneous tissues and fascia. The present study was aimed to validate the Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) score as a tool to predict/diagnose NF and to differentiate it from other soft tissue infections depending on the score. A Prospective Observational study was conducted in ESICMC PGI MSR, Medical College Hospital, Rajajinagar, Bengaluru, from Jan 2019 to June 2020. Patients ≥18 years of age with severe soft tissue infections were included in the study. Based on the LRINEC score, the patients were categorised as low (≤5), moderate (6-7) and high risk (≥8) for the prediction of onset or diagnosis of NF. Data analysis was performed using SPSS version 21.0. A total of 55 patients were included in the study. A significant association was observed with age (p=0.042), LRINEC score (p=0.0001), C Reactive Protein (CRP; p=0.0001), haemoglobin (p=0.008), serum sodium levels (p=0.004), serum creatinine (0.001), and amputation (p=0.004). Amputation was done in 5 cases. Only 1 mortality was observed in LRINEC high risk group with NSSTI. To conclude, LRINEC scoring system showed a better positive predictive value in identifying the onset of NF and risk strategizing of the patients with severe soft tissue infections.

Keywords: debridement, LRINEC score, necrotizing fasciitis, soft tissue infections

1. Introduction

Skin and soft tissue infections (SSTIs) are caused by microbial invasion of the skin and underlying soft tissues (1). In few cases, severe infection causes skin necrosis leading to necrotizing skin and soft tissue infections (NSSTIs). NSSTI is also referred as Fournier gangrene, necrotizing fasciitis, necrotizing skin and skin structure infections, and meleneys gangrene (2). Among all variants, necrotizing fasciitis (NF) is a rare, rapidly progressive, potentially life-threatening, inflammatory infection of the soft tissue that cause necrosis of the muscle fascia and subcutaneous tissues (3, 4). Even with optimal treatment, the morbidity and mortality rate was reported to be 25% to 35% (4). The most common cause and route of infection is microorganism invasion of the subcutaneous tissue through a cut in the skin, open wound or surgical wound and insect bite. Once the pathogens enter the subcutaneous tissues, the pathogens releases exotoxins causing tissue necrosis. Patients with co-morbidities such as diabetes mellitus (DM), peripheral vascular diseases, malnutrition, liver disease, kidney disease, human immunodeficiency virus, and alcohol abuse were reported to be more susceptible to the disease (5).

The key to successful treatment and prognosis in patients with NF lies in early diagnosis, early operative debridement and appropriate antibiotic therapy. If not, it may lead to sepsis, systemic inflammatory response syndrome [SIRS] or Multi Organ Dysfunction Syndrome [MODS], and eventually causing mortality. The major challenge faced by clinicians is differentiation of NF from other soft tissue infections like cellulites or abscesses early in its evolution (6). Delayed diagnosis is one of the main reasons for the high mortality rate (7). However, diagnosis solely based on physical examination is highly impossible, though modalities such as magnetic resonance imaging (MRI), computed tomography (CT), and frozen section biopsy help in the early diagnosis of NF, cost and availability limits their use in routine application in the evaluation of soft tissue infections (8-10). To overcome these limitations, Wong et al., developed a scoring system from a clinical tool called as The Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC). The tool is based on six routine laboratory variables: glucose, creatinine, serum sodium, haemoglobin, total white cell count, and C-reactive protein (CRP) (6).

The aim of the present study was to validate the Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) score as a tool to predict/diagnose NF and to differentiate it from other soft tissue infections depending on the score. This data can be vital in guiding clinicians to help and identify the disease, which can further help the patients in receiving definitive therapeutic interventions without much delay.

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2. Materials and methods

This prospective observational study was conducted at ESICMC PGI MSR Hospital, India, from January 2019 to June 2020. All ethical approvals were procured from Institute Ethics Committee (IEC) prior to study commencement. Written informed consent was obtained from all patients. Patients ≥18 years of age with severe soft tissue infections were included in the study. Patients ≤18 years of age, pregnant women, and patients refused to provide consent were excluded from the study. Ethics committee approval was received for this study from the Institutional Ethics Committee of ESIC Medical College & Post Graduate Institute of Medical Sciences & Research, India (Protocol No.– 532/L/11/12/Ethics/ESICMC & PGIMSR/Estt. Vol. IV).

Patients' age, sex, site and aetiology of infection, clinical manifestations, comorbidities, predisposing factors, vital signs, laboratory parameters at the time of admission were recorded in a prespecified proforma. In the present study, culture of pus was done to all patients admitted with soft tissue infection before giving antibiotics. Based on the LRINEC score, the patients were categorised as low (≤5), moderate (6-7) and high risk (≥8) for the prediction of onset or diagnosis of NF. LRINEC score risk categorization, the time interval between the admission and first surgery, the number of surgical procedures, the need for amputation and the mortality rate had been documented. All variables were statistically analyzed further to evaluate the significance of LRINEC score in predicting the clinical outcomes. On admission, general and medical treatment of necrotizing fasciitis, followed by wound debridement was done as the definitive procedure. Later, regular wound dressing, administration of antibiotics, and supportive therapy for maintenance of blood pressure and renal status and in few cases vacuum assisted dressings were done for faster healing. Once the wound was healthy, split skin grafting and secondary suturing was done in most cases. Some cases healed by secondary intention while some cases had to undergo major amputations for control of infection and its spread. Regular dressings and water beds were given to patients that had bed sores as a complication of necrotizing fasciitis. Patients that developed septicaemia were managed in intensive care units on ventilators under the guidance of anaesthetists and physicians. Post discharge patients were followed up to one month regularly for dressing, and also to review liver and renal parameters. Major amputation patients were advised for clutches.

2.1. Statistical analysis

Data analysis was performed using SPSS version 21.0. Data analysed by descriptive statistics was represented as mean ± standard deviation (SD) or percentages. Chi-square test and independent T-test was used to determine qualitative variables and significance difference between the two groups. P≤0.05 was considered as statistically significant.

3. Results

The study included a total of 55 patients, of which 12 (21.81%) were female and the rest 43 (78.18%) were male. Diabetes mellitus was observed to be most common comorbidity (89.09%) followed by systemic hypertension (50.91%), chronic renal failure (12.73%) and peripheral vascular disease (7.27%). The most common site of infection was extremity followed by scrotum and perineum. In 55 patients, 12 had soft tissue infections of unknown origin and the remaining 43 cases infection were attributed to injury as a cause; 12 were treated conservatively while 43 were debrided.

Based on LRINEC score, 17 patients were diagnosed with necrotizing fasciitis and 38 patients with other soft tissue infections (Table 1). Out of 17 patients with necrotizing fasciitis, one patient had low risk and the other 16 had high risk disease whereas among 38 patients with soft tissue infections, 19 were of low, 17 of moderate, and two were from high risk category. All the 16 NSSTIs cases underwent more than three debridement's (Figs. 1 and 2), 13 cases were treated with split skin graft (SSG), and five cases underwent major amputation to prevent septicaemia and its complications (Fig. 3). Out of five amputations, four patients had LRINEC high risk group with NSSTIs while only 1 had other soft tissue infection.

Fig. 1. Necrotising fasciitis of right lower limb [thigh] on arrival (A), after second debridement (B), and after negative pressure wound therapy or VAC dressing (C)

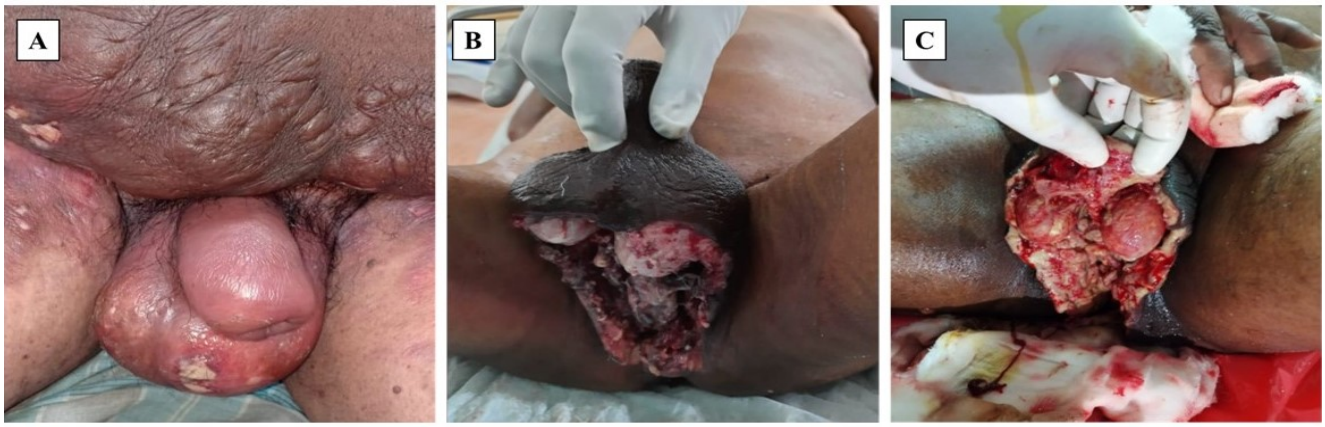

Fig. 2. A case of fournier's gangrene associated with meleneys gangrene (A), fournier's gangrene after second (B) and fourth debridment (C).

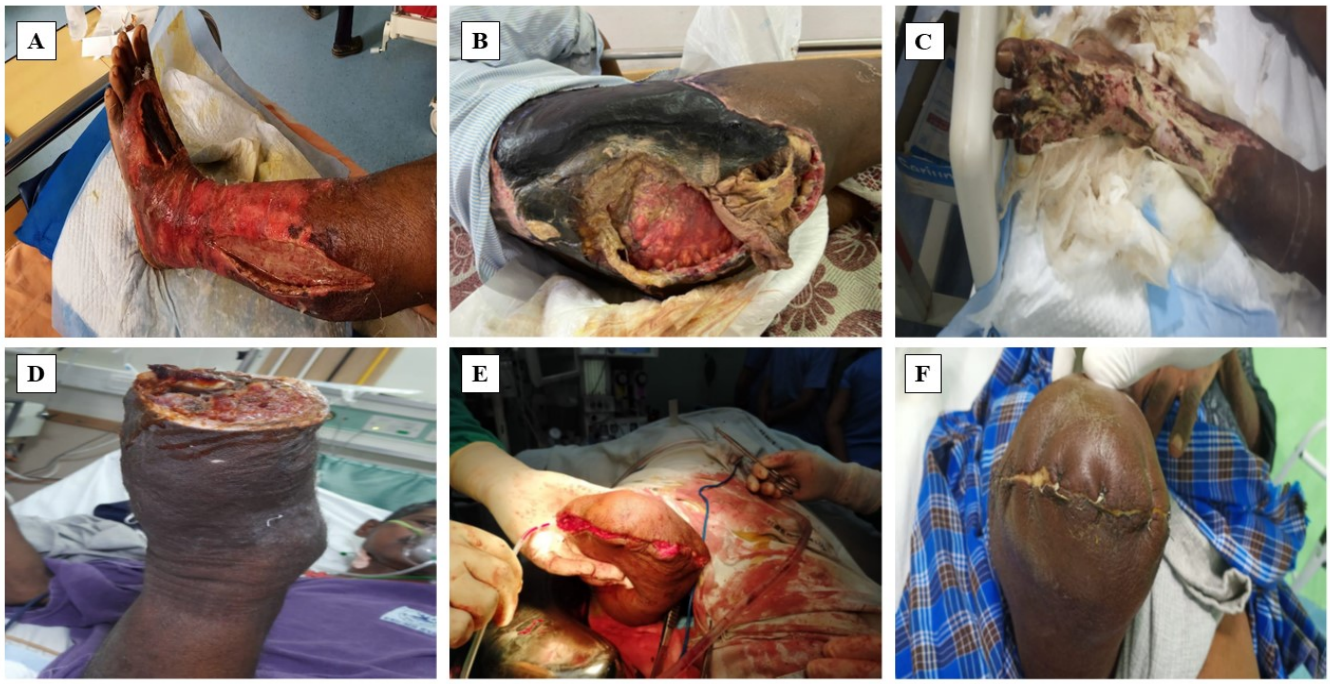

Fig. 3.

(A) A case of left lower limb cellulites with fasciotomy later developed necrotizing fasciitis
(B) A case of necrotizing fasciitis of right hip, gluteal region and upper thigh with maggots.
(C) A case of left lower limb necrotizing fasciitis did not heal with aggressive treatment and underwent above knee amputation.
(D) A case of right lower limb necrotizing fasciitis underwent emergency guillotine amputation
(E) Amputation stump on post op day 4 in a necrotizing fasciitis case
(F) Amputation stump immediate post-surgery on table in a necrotizing fasciitis case of right leg

Table 1. Association between LRINEC score and diagnosis

Risk category	Diagnosis		p
	Necrotising fasciitis	Other soft tissue	
Low	01(5.9)	19(50.0)	0.0001
Moderate	0(0.0)	17(44.7)	
High	16(94.1)	02(5.3)	
Total	17(100.0)	38(100.0)	

Table 2. Comparison of age by LRINEC score

Parameters	LRINEC Score			p
	Low	Moderate	High	
Age	51.00±14.89	62.94±13.27	55.94±13.44	0.042
LRINEC Score	4.75±2.07	6.76±0.56	9.61±1.38	0.0001

Table 3. Association between various parameters and their Laboratory Risk Indicator for Necrotising Fasciitis score

Parameters	LRINEC Score			p
	Low (n=20)	Moderate (n=17)	High (n=18)	
Male	17 (85.0)	12 (70.6)	14 (77.8)	0.571
Female	03 (15.0)	05 (29.4)	04 (22.2)	
	C Reactive Protein (CRP)			
Negative (≤150mg/dlL)	19 (95.0)	17 (100.0)	03 (16.7)	0.0001
Positive (≥150mg/dL)	01 (5.0)	0 (0.0)	15 (83.3)	
	White blood cells (cmm)			
15-25	04 (20.0)	03 (17.6)	08 (44.4)	0.135
>25	16 (80.0)	14 (82.4)	10 (55.6)	
	Haemoglobin (gm/dL)			
>13.5	01 (5.0)	0 (0.0)	0 (0.0)	0.008
11-13.5	12 (60.0)	2 (11.8)	4 (22.2)	
<11	07 (35.0)	15 (88.2)	14 (77.8)	
	Serum sodium (mmol/L)			
≥135	16 (80.0)	11 (64.7)	05 (27.8)	0.004
<135	04 (20.0)	06 (35.3)	13 (72.2)	
	Serum creatinine (mg/dL)			
≤1.6	18 (90.0)	05 (29.4)	12 (66.7)	0.001
>1.6	02 (10.0)	12 (70.6)	06 (33.3)	
	Blood glucose (mg/dL)			
≤180	04 (20.0)	01 (5.9)	2 (11.1)	0.425
>180	16 (80.0)	16 (94.1)	16 (88.9)	
	Diabetes mellitus			
Yes	17 (85.0)	16 (94.1)	16 (88.9)	0.675
No	03 (15.0)	01 (5.9)	02 (11.1)	
	Hypertension			
Yes	06(30.0)	10 (58.8)	12(66.7)	0.057
No	14(70.0)	07 (41.2)	06(33.3)	
	Amputation			
Yes	0 (0.0)	0 (0.0)	05 (27.8)	0.004
No	20 (100.0)	17 (100.0)	13 (72.2)	

Patients aged 55 years were found to be at higher risk with a LRINEC score of 9.61 (Table 2). Table 3 represents association between various laboratory parameters and their LRINEC scores. A significant association was observed with age (p=0.042), LRINEC score (p=0.0001), C Reactive Protein (CRP; p=0.0001), haemoglobin (p=0.008), serum sodium levels (p=0.004), serum creatinine (0.001), and amputation (p=0.004). No significant association was observed with gender, white blood cells (WBC), blood glucose, DM and hypertension. Only one mortality was observed in LRINEC high risk group with NSSTI.

4. Discussion

NF is one of the most difficult disease processes encountered by physicians and surgeons (11). It can often progress within a few hours, and is an invasive infection that complicates the skin, subcutaneous tissue, deep fascia (12). NF poses a challenge to clinicians by encompassing a wide range of infections that share the same diagnostic and treatment principles. Therefore, establishing the diagnosis itself is one of the biggest challenge to clinician. To distinguish the NF from other soft tissue infections, Wong et al. developed a novel diagnostic scoring system called LRINEC score (6). This LRINEC score was calculated from the routine laboratory investigations and such tests are easy to access, readily available, and cost-effective. This LRINEC score was calculated from the patient's glucose, creatinine, sodium level, haemoglobin, WBC count, and CRP values. The maximum score is 13. A score of ≥6 raise suspicion for NF, and a score of ≥8 is highly predictive of NF (6, 13, 14).

The present study was aimed to validate the Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) score as a tool to predict/diagnose NF and to differentiate it from other soft tissue infections depending on the score. In this study, ratio of male over female was predominant and the more common age group was found to be ~ 55 years. Similar male predominance was reported in a prospective study conducted by Espander et al. (12). In a recent retrospective study by Rampal et al, 60% of patients were male (15). Many reported studies showed the male predominance with highest number of cases among age groups between 50 and 60 years (5, 12, 15-17).

In the present study, the most common site of NF infection was extremities followed by scrotum and perineum which was in accordance with a study by Singh et al. The study reported most common anatomical sites with NF was lower extremities, followed by the upper extremity, and perineum (18). A prospective, cross sectional study also showed lower extremity, followed by

upper extremity, and other sites such as perineum, chest, buttocks as the most common anatomical sites infected (5).

The most pre-disposing factors observed from this study group were age, DM, and hypertension, which was in par with other reported studies (5, 18-20). In patients with DM, a delay in diagnosis of NF was apparent, especially in early stages. Due to these age related co-morbidities and progressive decrease in immunity, patients become more susceptible to infections. In some patients, diabetes related issues increases the risk of injuries which may act as triggering factors for infection (18). Kwan et al. and Shaikh et al. have also reported age, DM and hypertension as the most common co-morbid conditions making NF patients much more susceptible and immunocompromised (19, 20). Amputation rate was high in DM patients compared with other comorbidities, similar results were reported in a previous study by Espander et al (12). Such high rate of amputations in DM patients might be due to the development of severe atherosclerosis, especially in small-caliber arteries which results in ischemia and gangrene (16, 21).

In the present study, we have employed LRINEC score to differentiate NF from other SSTIs. The serum creatinine levels are often elevated in patients with septic shock and renal dysfunction, where, creatinine clearance is compromised with early signs of acute renal failure (16, 18). Overall, a strong positivity for NF from laboratory findings was observed with elevated CRP, elevated WBC, low haemoglobin, decreased sodium, and increased creatinine. Depending on the severity, treatment differed from patient to patient. Still the essential steps in the treatment is early diagnosis, surgical debridement, amputation of extremity in high risk patients, wound care, antimicrobial therapy, and intensive supportive care. According to our findings, the presence of multiple predisposing factors such as DM, low haemoglobin, high serum creatinine levels, gangrene, and skin necrosis were proven lethal.

To conclude, LRINEC score has shown a better positive predictive value in identifying the onset of NF and risk strategizing of the patients with severe soft tissue infections. The risk stratification was an important tool in differentiating NSSTI from other forms of SSTIs.

Conflicts of interests

None.

Acknowledgments

All patients provided written informed consent.

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