

**Significance of LRINEC Score in the Diagnosis of Necrotizing Fasciitis**Raja Adeel Khan<sup>1</sup> Mohammad Kaleem<sup>2</sup> Faiza Syed<sup>3</sup> Lekhraj Mal<sup>4</sup>

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**ABSTRACT**

**Objective:** To evaluate the diagnostic justification of LRINEC score for the identification of Necrotizing fasciitis in patients having soft tissue infection using histopathology as a gold standard.

**Methods:** This cross sectional work in the Surgical Units of Dow University of Health Sciences and Civil Hospital Karachi from 23-01-2016 to 22-07-2016. A total of 156 patients diagnosed as having soft tissue infection, after fulfillment of inclusion/exclusion criteria were included in the research. Detailed informed consent taken from each patient regarding the participation in the study and for biopsy. LRINEC score parameters, final score and histopathological diagnosis were noted in the proforma. The final diagnosis was made on the basis of necrotizing changes on histopathology report.

**Results:** Rate of necrotizing fasciitis was observed in 14.7% cases confirmed by histopathology. Sensitivity, specificity, positive and negative predictive value as well as accuracy of LRINEC (>6) in diagnoses of necrotizing fasciitis were 82.6%, 76.7%, 38%, 96.2% and 77.6% respectively.

**Conclusion:** LRINEC is simple, cheap and easily available scoring system it potentially help early differentiation of non lethal soft tissue infections from lethal necrotizing fasciitis.

**Key Words:** Necrotizing fasciitis, LRINEC score, Soft tissue infection, Histopathology

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**INTRODUCTION**

The Necrotizing Fasciitis is a rare serious infection of soft tissues associated with high mortality despite modern modes of treatment<sup>1</sup>. The reported prevalence is 0.4 per 100,000 cases<sup>2</sup>. In Pakistan, the reported mortality rate is 26%<sup>3</sup>. By definition it is the infection of any of the layers within the dermis, subcutaneous tissue, superficial fascia, deep fascia or muscles, which are in association with necrotizing changes<sup>4</sup>. The disease prognosis lying on accuracy of the diagnosis and prompt suitable treatment, including wide surgical debridement with appropriate antibiotics<sup>5</sup>. At the commencement of the disease the diagnostic features on the skin are not so evident, resulting in an increase in the mortality rate<sup>6</sup>. With no specific diagnostic modality, the diagnosis of necrotizing fasciitis rests on high level of clinical suspicion, laboratory indicators, radiological findings and finally on histopathology<sup>4</sup>. Poor health resources in our country make it difficult to investigate this lethal disease using expensive MRI and not readily available frozen section biopsy.

Recently the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has drawn special attention due to its easy availability and low cost<sup>7</sup>. This score is a biochemical system based on six parameters including C-reactive protein, hemoglobin, total leukocyte count,

serum sodium, serum creatinine and blood glucose. Each variable is given score based on measured patient value. The maximum score is 13 and minimum is 0. Wang et al in his study showed that when LRINEC score is >6 it is diagnostic of Necrotizing fasciitis having positive and negative predictive values of 92% and 96% respectively<sup>8</sup>. The sensitivity and specificity are reported to be 80% and 67% respectively<sup>9</sup>. Other studies also showed similar results<sup>10-12</sup>.

This simple, cheap and easily available scoring system can potentially help early differentiation of non lethal soft tissue infections from lethal necrotizing fasciitis<sup>13</sup>. Currently, strong clinical suspicion is the only measure being used for the above mentioned purpose. This study is being conducted to provide strong local evidence that will help changing the clinical practice leading to early diagnosis of necrotizing fasciitis. No similar study has been done on this scoring system in Pakistan. Furthermore this study is expected to strengthen the assertion of applicability of LRINEC scoring and provide data for comparison with studies globally.

**METHODS:** The cross sectional work was conducted in the surgical Units of Dow University of health sciences and Civil Hospital Karachi, during six months from 23-01-2016 to 22-07-2016.

After the approval of ethical committee, a total of 156 patients diagnosed as having soft tissue infection fulfilling the inclusion criteria, visiting the outpatient / emergency surgical clinics were included in the study. Consent about the study was taken from each patient regarding the participation and for biopsy. The inclusion criteria was clinically diagnosed cases having soft tissue infection, aged >12 years, presenting to emergency / outpatient department of surgery of Civil hospital Karachi. Exclusion criteria was patients with diagnosis of soft tissue infection that have been given antimicrobial therapy before presentation. Patients with known comorbidities including Diabetes mellitus, Hypertension, Atherosclerotic vascular disease, Chronic renal failure, Cirrhosis, Polycythemia vera, anemia. Patients developing soft tissue infection during the hospital stay.

A proforma was used to document findings. It was included demographic information including

age, gender, and duration of symptoms, hospital registration number and surgical ward number. It was also included LRINEC score parameters, final score and histopathological diagnosis.

A Complete history and physical examination was done by 3<sup>rd</sup>/4<sup>th</sup> year resident of general surgery. Blood samples were taken from all patients on hospital admission for C-reactive protein, Hemoglobin, Total leukocyte count, Random blood sugar, Serum Sodium, and Serum Creatinine and sent to Central laboratory of hospital and then interpreted. A 2 X 2 cm biopsy specimen was taken by 4<sup>th</sup> year resident from all patients wounds before the administration of antibiotics and was sent to Dow laboratory for histopathological examination. Patients were managed according to hospital protocol.

The final diagnosis was made on the basis of necrotizing changes on histopathology report.

#### **LRINEC (Laboratory risk indicator for Necrotizing fasciitis) Score:**

It is a biochemical system of scoring based on variables given in table below. Each variable is given a score based on its value. The maximum score is 13 and minimum 0.

Variable	Variable	Score
C-reactive protein (mg/l)	<150	0
	> 150	4
Total Leukocyte Count (per mm <sup>3</sup> )	< 15	0
	15-25	1
	>25	2
Hemoglobin (g/dl)	>13.5	0
	11-13.5	1
	<11	2
Sodium (mmol/l)	>135	0
	< 135	2
Creatinine (mmol/l)	<141	0
	> 141	2
Glucose (mmol/l)	< 10	0
	>10	1

#### **True positive:**

LRINEC score >6 and with histopathological evidence of necrotizing fasciitis.

#### **True negative:**

LRINEC score ≤ 6 and with no histopathological evidence of necrotizing fasciitis.

#### **False positive:**

LRINEC score >6 and with no histopathological evidence of necrotizing fasciitis.

#### **False negative:**

LRINEC score ≤ 6 and with histopathological evidence of necrotizing fasciitis.

**STATISTICAL ANALYSIS PROCEDURE:**

All data was entered in statistical software SPSS-17. Mean±SD were define numerical variables including age, time span of symptoms and total LRINEC score. Frequency and percentage were used to describe categorical variables like gender, LRINEC score diagnosis, accuracy ( $\leq 6$ ,  $>6$ ) and final histological report. The sensitivity, specificity, positive and negative predictive values of LRINEC score on comparison with histological evaluation as a gold standard were calculated. Stratification done to control effect modifiers including age, gender and duration of disease to observed diagnostic accuracy through chi-square test.  $p \leq 0.05$  was accepted as significant.

**RESULTS:**

We evaluate 156 cases above the age of 12 years diagnosed as having soft tissue infection. The distribution of age is shown in figure-1. The age on average was  $37.85 \pm 11.09$  years (95%CI:

36.10 to 39.61). Similarly median duration of disease was 5(IQR= 2) days as presented in table-1.

There were 95(60.9%) were male and 61(39.1%) female. Rate of necrotizing fasciitis was observed in 14.7% cases confirmed by histopathology as given in table-2. True positive and negative as well as false positive and negative outcome were also presented in table-2. Sensitivity, specificity, positive and negative predictive value as well as accuracy of LRINEC ( $>6$ ) in diagnoses of necrotizing fasciitis was 82.6%, 76.7%, 38%, 96.2% and 77.6% respectively.

76.6% accuracy was observed for below and equal to 40 years while 78.8% for above 40 years of age as presented in tables 3 & 4.

Similarly 82.1% accuracy was observed in male patients and 70.5% was observed in female cases (table 5&6).

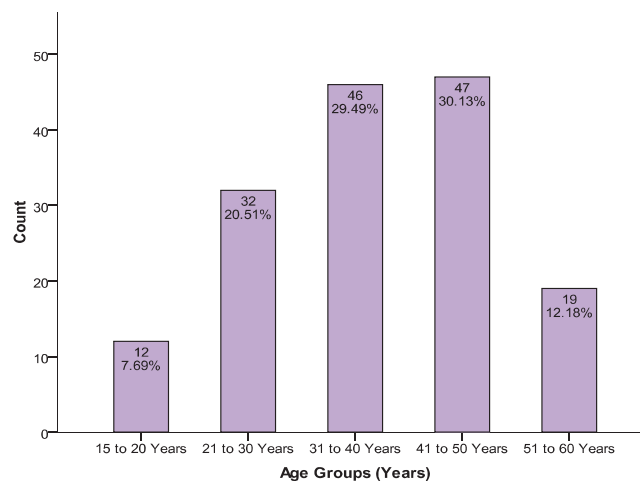


Figure 1. Age Distribution of Patients n=156

Statistics		Age (Years)	Duration of disease (days)	LRINEC Score
Mean± SD		37.85±11.09	5.42±1.79	5.08±1.68
95% Confidence Interval for Mean	Lower Bound	36.10	5.13	4.82
	Upper Bound	39.61	5.70	5.35
Median(IQR)		37(19)	5(3)	5(2)

LRINEC Score	Histopathology (Necrotizing Fasciitis)		Total
	Yes	No	
$>6$	19(TP)	31(FP)	<b>50(32.1%)</b>
$\leq 6$	4(FN)	102(TN)	<b>106(67.9%)</b>
<b>Total</b>	<b>23(14.7%)</b>	<b>133(85.3%)</b>	<b>156</b>

Sensitivity = 82.6%; Specificity = 76.7%  
 Positive Predictive value = 38%  
 Negative Predictive Value = 96.2%  
 Diagnostic Accuracy = 77.6%

Table-2. Diagnostic Accuracy of LRINEC Score in the Diagnosis of Necrotizing Fasciitis for  $\leq 40$  Years of Age

LRINEC Score	Histopathology (Necrotizing Fasciitis)		Total	P-Values
	Yes	No		
>6	10(TP)	18(FP)	28	0.0005
$\leq 6$	3(FN)	59(TN)	62	
<b>Total</b>	<b>13</b>	<b>177</b>	<b>90</b>	

Sensitivity = 76.9% Specificity = 76.6%  
 Positive Predictive value = 35.7%  
 Negative Predictive Value = 95.2%  
 Diagnostic Accuracy = 76.6%

Table-3. Diagnostic Accuracy of Lrinec Score in the Diagnosis of Necrotizing Fasciitis for 41 to 60 Years of Age

LRINEC Score	Histopathology (Necrotizing Fasciitis)		Total	P-Values
	Yes	No		
>6	9(TP)	13(FP)	22	0.0005
$\leq 6$	1(FN)	43(TN)	44	
<b>Total</b>	<b>10</b>	<b>56</b>	<b>66</b>	

Sensitivity = 90% Specificity = 76.8%  
 Positive Predictive value = 40.9%  
 Negative Predictive Value = 97.7%  
 Diagnostic Accuracy = 78.8%

Table-4. Diagnostic Accuracy of LRINEC Score in the Diagnosis of Necrotizing Fasciitis for Male

LRINEC Score	Histopathology (Necrotizing Fasciitis)		Total	P-Values
	Yes	No		
>6	12(TP)	14(FP)	26	0.0005
$\leq 6$	3(FN)	66(TN)	69	
<b>Total</b>	<b>15</b>	<b>80</b>	<b>95</b>	

Sensitivity = 80% Specificity = 82.5%  
 Positive Predictive value = 46.2%  
 Negative Predictive Value = 95.7%  
 Diagnostic Accuracy = 82.2%

Table-5. Diagnostic Accuracy of LRINEC Score in the Diagnosis of Necrotizing Fasciitis for Female

LRINEC Score	Histopathology (Necrotizing Fasciitis)		Total	P-Values
	Yes	No		
>6	7(TP)	17(FP)	24	0.003
$\leq 6$	1(FN)	36(TN)	37	
<b>Total</b>	<b>8</b>	<b>53</b>	<b>61</b>	

Sensitivity = 87.5% Specificity = 67.9%  
 Positive Predictive value = 29.2%  
 Negative Predictive Value = 97.3%  
 Diagnostic Accuracy = 70.5%

## DISCUSSION

Necrotizing Fasciitis is a scarcely progressive infection involving the subcutaneous tissues and fascia and the circulation of skin show evidence of thrombosis, first explained by Hippocrates in 500 BC<sup>14</sup>, this highly infectious disease still has a very high mortality<sup>15</sup>. The prompt management of the disease is crucial as the outcome is directly proportional with the early treatment of sepsis<sup>16</sup>.

Biochemical tests are helpful in revealing the classic changes in severe sepsis<sup>17</sup>, these are non-specific for necrotizing fasciitis, so other causes of sepsis must be excluded, but may useful in the initiation of bellicose management<sup>18</sup>.

In the year 2004 Wong et al introduced the LRINEC scoring system<sup>8</sup>, which used the biochemical laboratory data for the early recognition of necrotizing fasciitis, that includes

hemoglobin, creatinine, glucose, sodium and C-reactive protein (CRP) level with total leucocytes count. Only one study validated the score, however, and with a very small group of 28 NF patients. Most studies validated the score system for *Vibrio necrotizing soft-tissue infection*<sup>9,19</sup>. Two studies discussed its prognostic value with NF<sup>20</sup>.

We noticed an average age of 37.85±11.09 years. There were 95(60.9%) were male and 61(39.1%) female. Wong et al<sup>6</sup> in their research reported mean age of total patient was 56 years including 53 years for male and 36 years for female. In Liao et al<sup>21</sup> study average age of patient was 61.2 years.

Our study reveals the sensitivity, specificity, positive and negative predictive value and accurateness of LRINEC (>6) for diagnosing necrotizing fasciitis as 82.6%, 76.7%, 38%, 96.2% and 77.6% respectively.

Holland MJ<sup>9</sup> keep a cut-off value  $\geq 6$ , and indicates that LRINEC scoring have sensitivity, specificity, positive and negative predictive values of 80%, 67%, 57%, 86% respectively, which helps to distinguished confirmed cases of necrotizing fasciitis from advanced infections of soft tissues. The likelihood ratio of a positive and negative histopathological diagnosis were 2.4 and 0.3 respectively.

Liao et al<sup>21</sup> in their research mentioned the LRINEC score  $\geq 6$ , found the sensitivity and specificity of 59.2% (CI 52.9-65.6%) and 83.8% (CI 81.9-85.7%) respectively. They indicate a likelihood ratio 3.89, with positive and negative predictive ratio 37.9% (95% CI 32.9-42.9%), 92.5% (95% CI 91.0-94.0%) respectively. The emergency physicians have 58.4% (95% CI 52.0-64.8%) rate of clinical diagnosis of NF before admission, among these cases 97 cases were having NF, but the pre-admission clinical diagnosis was not established.

Wong et al revealed a LRINEC score of  $\geq 6$  with sensitivity, specificity, positive and negative

predictive value of 89.9%, 96.9%, 92.0%, 96.0% respectively<sup>8</sup>. In 2009, Holland studied a group of 28 patients who had received surgery because of suspected NF. Ten patients were diagnosed with NF postoperatively. The sensitivity, specificity, positive and negative predictive values were mentioned as 80%, 67%, 57%, and 86% respectively<sup>9</sup>.

The introducing of a reliable scoring system for the diagnosis of NF is a great achievement of Wong et al<sup>8</sup>, by which the early diagnosis and treatment of the risky patients is possible.

The LRINEC scoring system has some weaknesses, which are;

1. The small sample size on which the score was planned, making it less suitable to other cohorts.
2. The over-diagnosis on CRP, when elevated give score 4, in comparison to other parameters having a maximum score of 2. The CRP values are non-specific for sepsis and may be raised in other inflammatory conditions.

3. These laboratory biochemical parameters which are deranged in severe sepsis are also show derangements in diseases of longer duration. A suitable example is diabetes, in which person having impaired kidney function, if have any overload of fluids may have a score of 6 and having no any sepsis or infections of skin, though these cases are on increased risk of necrotising infection of skin.

Wong<sup>22</sup> in a review examined 234 blood samples, these cases were previously enrolled in another research on saturation of tissue oxygen for the confirmation of NF<sup>23</sup>, the LRINEC scoring of these cases was calculated. The positive and negative predictive values were 40% and 95% respectively. It was suggested that as the LRINEC system of scoring may give high false positive results, so there is a chance that majority of patients may diagnosed as NF.

The approach proposed by Wong et al<sup>6</sup>, in which calculation of LRINEC scoring was done in cases having high grade infections of soft tissues and among these the patient having a score of  $\geq 6$ , the histopathological reporting was mandatory, may well allow the initial diagnosis of NF in few cases on the histological diagnosis by surgical biopsies.

The limitation of this work is mainly the small sample size and only report data from a single center. Since data was collected for only six month and there has been no long-term follow-up of the study participants and complication.

Further use of the LRINEC system of scoring as the basis of a management algorithm, in a large prospective study generated revealing the end points such as mortality, would be very informative.

## CONCLUSION

This is simple, cheap and easily available scoring system it potentially help early differentiation of non lethal soft tissue infections from lethal necrotizing fasciitis. In patient where there is a clinical suspicion of severe soft tissue infections, the LRINEC scoring is an stirring diagnostic methodology for confirmation of NF from such infections. However it is convenient to use for the early diagnosis of necrotizing fasciitis.

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