To Correlate The Laboratory Risk indicators For Necrotizing Fasciitis (LRINEC)Score With The Clinical Features And Surgical Management Of Necrotizing Soft Tissue Infections

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Abstract: *Necrotizing soft tissue infection (NSTI) is a life-threatening disease with an increased incidence in African and Asian countries as compared to West. Despite advances in modern medical care, mortality ranges from 6 to 76 %[11].NSTI are less common than subcutaneous abscess and cellulitis but are much more seriousconditions whose severity initially may go unrecognized. My study aim Toexplore the relation between the laboratory risk indicators for necrotizing fasciitis (LRINEC) score with the clinical features and surgical management of necrotizing soft tissue infections.This Hospital-based, open, case-control, observational studywasconducted in the department of Surgery over a period of 18 months. A total of 60 patients with severe soft tissue infections requiring admission and 48 hours antibiotics presenting to our Emergency/Outpatient department (OPD). I my study the Calculation of the LRINEC score done after using the following six parameters Haemoglobin, Total leukocyte count Blood glucose ,Serum creatinine, Serum sodium-reactive protein. Correlation of the management and severity of infections with respective LRINEC score were found out. The study result shows that a higher LRINEC score was found to significantly correlate with a longer time to operation (correlation coefficient of 0.56, p value <0.0001) and longer duration of hospitalization (correlation coefficient of 0.345, p value 0.0069).*

I. Introduction

NSTI is a bacterial infection characterized by rapidly spreading inflammation and necrosis of skin, subcutaneous tissue and superficial fascia [2,3].NSTI is a severe life threatening soft tissue infection characterized by a fulminant course and a high mortality. Thedifferentiation of necrotizing fasciitis from other soft tissue infections are therefore critically important. However, earlyclinical recognition of necrotizing fasciitis is difficult, as thedisease is often indistinguishable from cellulitis or abscesses early in its evolution. Although modalities such as ultrasonography, computed tomography, magnetic resonance imaging and frozen section biopsy have been shown to be useful in the early recognition of necrotizing fasciitis, routine application of these modalities in the evaluation of soft tissue infections has been limited by cost and availability. The Laboratory Risk Indicator for Necrotizing Fasciitis(LRINEC) score described by Wong et al is one of the recently described diagnostic adjuncts for discriminating between necrotizing soft tissue infections and non-necrotizing soft tissue infections[10]. It is based on routinely available laboratory investigations (Haemoglobin, Total Leukocyte Count, Blood Glucose, Serum Creatinine, Serum Sodium, C-reactive protein). Each variable if present provides a specific number of points towards the final score. The mainstay of treatment of NSTI is early complete surgical debridement with broad spectrum antibiotics, physiological support and a close intensive monitoring[11]. Treatment strategies like hyperbaric oxygen therapy and intravenousimmunoglobulins have been proposed but their role still remains debatable, Early recognition and aggressive debridement of all necrotic fascia and subcutaneous tissue are major prognostic determinants, and delay in operative debridement has been shown to increase morbidity and mortality.

II. Material And Methods

Hospital-based, open, case-control, observational study was conducted in the department of Surgery in Calcutta National Medical College & Hospital, over a period of 18 months. A total of 60 patients with severe soft tissue infections requiring admission and 48 hours antibiotics presenting to our Emergency/Outpatient department (OPD) meeting the inclusion criteria for the study were taken for the study.
Study Design: Hospital-based, open, case-control, observational study.

Study Location: Case selection and research analysis will be done in the Department of General Surgery in Calcutta National Medical College and Hospital, Kolkata, West Bengal.

Study Duration: 18 months, starting after getting clearance from hospital ethical committee and acceptance from the West Bengal University of Health Sciences.

Sample size: 60 patients.

Sample size calculation: All patients presenting to our Emergency/Outpatient department with severe soft tissue infections requiring admission and 48 hours of IV antibiotics will be taken up for study. According to this sample size was selected. The sample size actually obtained for this study was 60.

Subjects & selection method: All patients presenting to our Emergency/Outpatient department with severe soft tissue infections requiring admission and 48 hours of IV antibiotics will be taken up for study. Patient with less than 12 years or having simple boils, carbuncle, small abscesses, diabetic foot, and collagen vascular disease, any associated malignancy and female patients having pregnancy will be excluded.

Inclusion criteria:
Data for present study was collected from severe soft tissue infections patients requiring admission and 48 hours intravenous antibiotics coming to emergency and OPD of Calcutta National Medical College & Hospital.

Exclusion criteria:
1. Patients with age less than 13 years.
2. Patients having simple boil, carbuncle, small abscesses.
3. Patients having diabetic foot.
4. Patients having collagen vascular disease.
5. Patients having any associated malignancy.
6. Female patients having pregnancy.

Procedure methodology
After written informed consent was obtained, a well-designed preforma was used to collect the data of the recruited patients .in this proforma preliminary data was collected , these are demographic profile like Name, Age, Sex ,Address ,Occupation, PA No ,Reg No ,Unit ,DOA,DOD, after that history, chief complain, investigation and treatment. Correlation of the management and severity of infections with respective LRINEC score. The following symptoms and sign were assessed in these patients at the time of admission: -

- Pain
- Erythema
- Induration
- Crepitus
- Blistering
- Skin discoloration
- Fever
- Tachycardia
- Hypotension

The following hematological, biochemical & microbiological parameters were assessed in these patients at the time of admission –
- Complete blood count
- Blood glucose
- Renal function test
- Serum sodium and potassium
- C-reactive protein
- Culture and sensitivity of pus if present and biopsy of the infected tissue

Calculation of the LRINEC score done after using the following six parameters-
- Hemoglobin
- Total leukocyte count
- Blood glucose
- Serum creatinine
- Serum sodium
- C-reactive protein

After the above factors were assessed the patients were managed according to the severity of infection that is aggressive fluid therapy and IV antibiotics, early and prompt debridement, fasciotomy, serial debridement, daily dressings, amputations, skin grafting, secondary closure and improvement of general condition.

Statistical analysis

Data was fed into Microsoft Excel format in computer and was analyzed using SPSSstatistical software, version 21. Categorical variables were presented as numbers and continuous data was presented as Mean *(+/-standard deviation)* or, median (min/max) as appropriate. The comparison between qualitative data was determined by applying Chi-square or Fischer exact test. Continuous data was compared by Student T-test/Mann Whitney U-test wherever required. Correlation of LRINEC score with other variables ware determined using Pearson correlation test. P-value less than 0.05 was considered significant.

III. Result

Age Distribution	Frequency	Percentage
1)<=30	8	13.33%
2)31-40	11	18.33%
3)41-50	17	28.33%
4)51-60	20	33.33%
5)61-70	4	6.67%
Total	60	100.00%
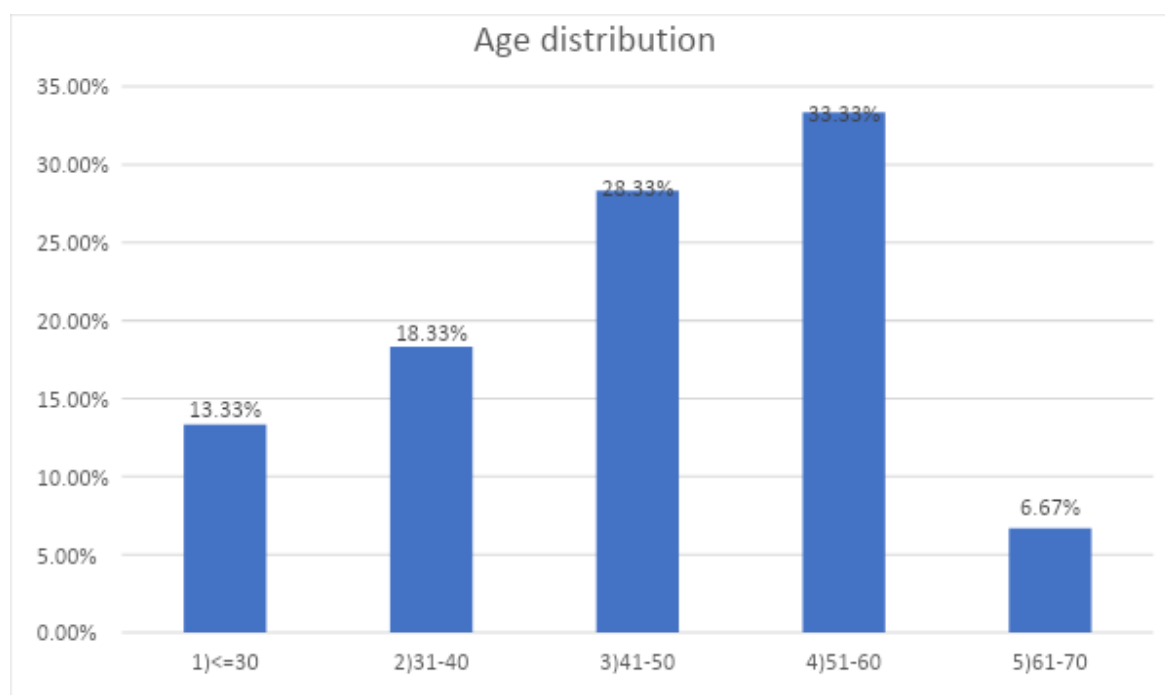
Figure 6 - showing frequency distribution in different age groups

Sex	Frequency	Percentage
F	15	25.00%
M	45	75.00%
Total	60	1000.00%
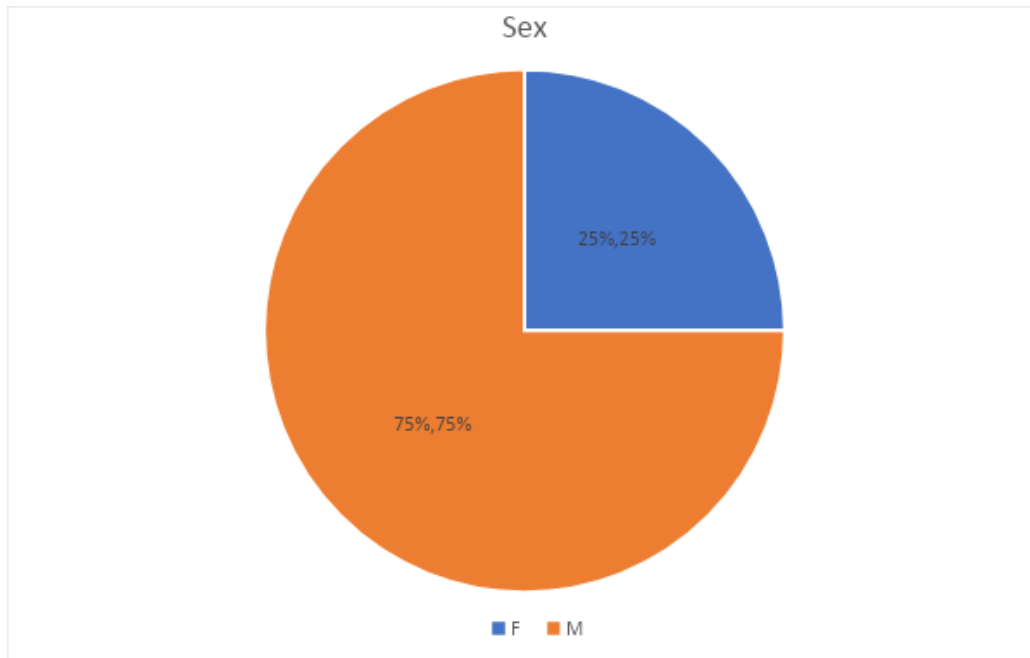
Figure 7 - showing sex distribution

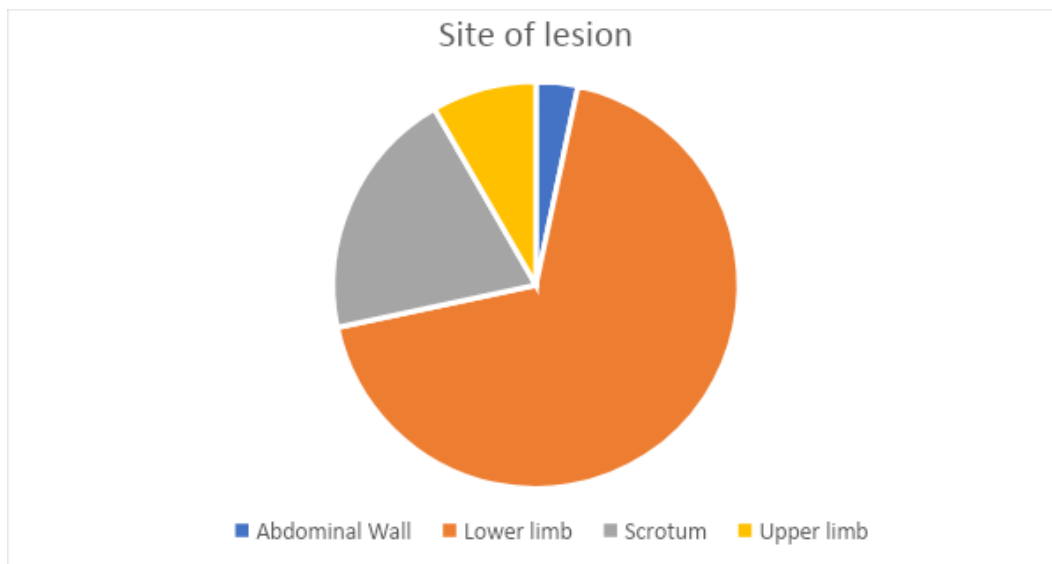| Site of lesion	Frequency	Percentage
Abdominal Wall	2	3.33%
Lower limb	41	68.33%
Scrotum	12	20.00%
Upper limb	5	8.33%
Total	60	100.00%

Figure 8 – Distributions of lesions in different parts of body

Risk factors	Frequency (Out of 60 patients)	Percentage
Trauma	26	43.33%
Smoking	48	80.00%
Alcohol	35	58.33%
Renal Disease	7	11.67%
Liver Disease	5	8.33%
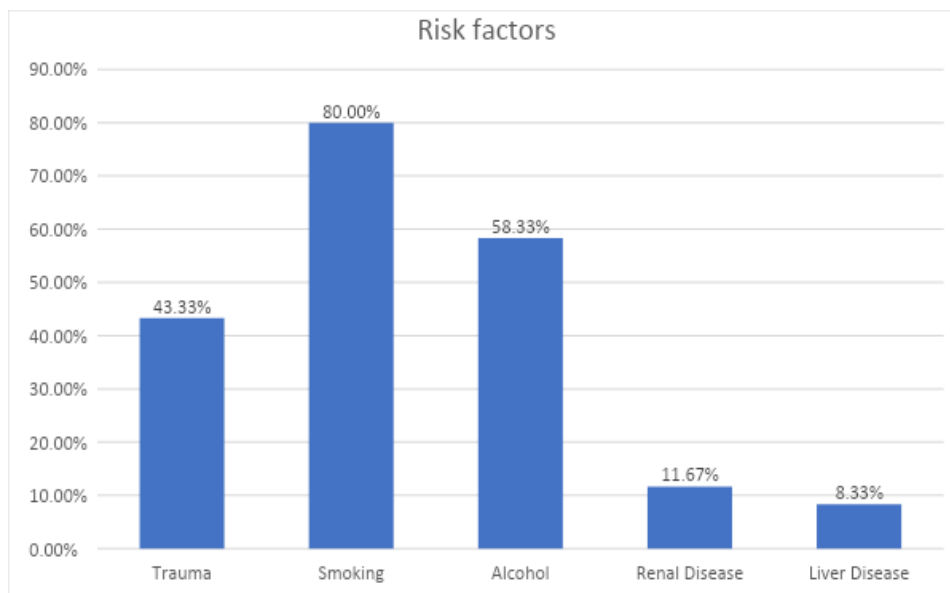
Figure 9 – Risk factors for development of NSTI

Symptoms & Sign	Frequency (Out of 60 patients)	Percentage
Tenderness	47	78.33%
Erythema	44	73.33%
Blackish discoloration	37	61.67%
Fever	52	86.67%
Tachycardia	32	53.33%
Bullae	23	38.33%
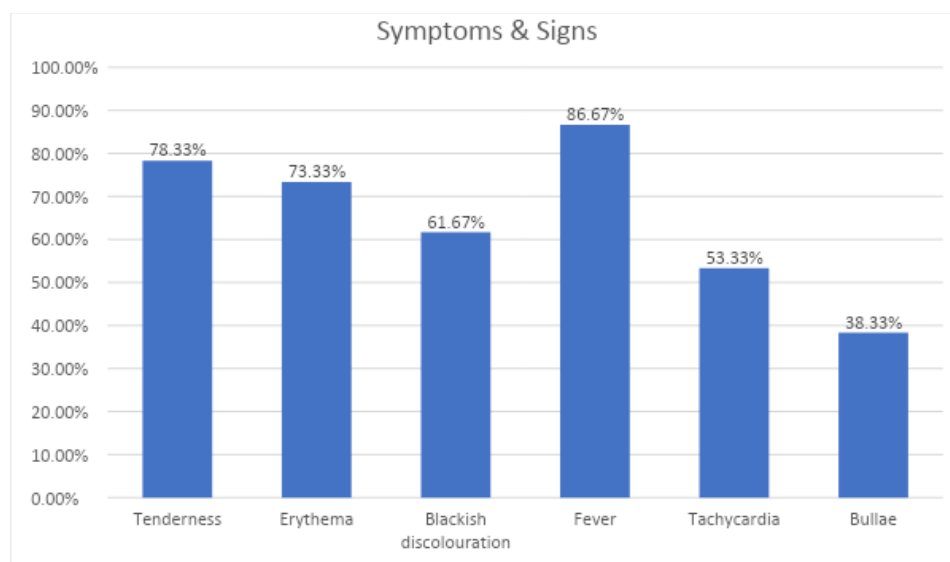
Figure 10 – Symptomatology of NSTIManagement

	Only	Skin Grafting (SG)	Secondary Closure (SC)	SG + SC	Total	Percentage
Conservative	11	-	-	-	11	18.33%
Debridement	11	7	-	-	18	30.00%
Fasciotomy	3	-	4	8	15	25.00%
Amputation	14	1	1	-	16	26.67%
Total	39	8	5	8	60	100.00%

Total skin grafting	16	26.67%
Total secondary closure	13	21.67%
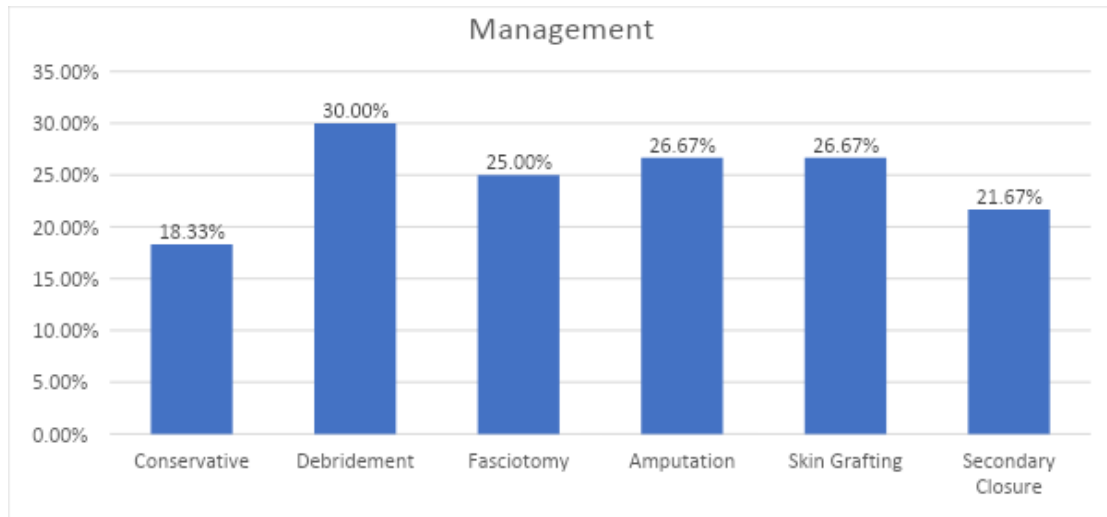
Figure 11 – Treatment modalities for NSTI Management

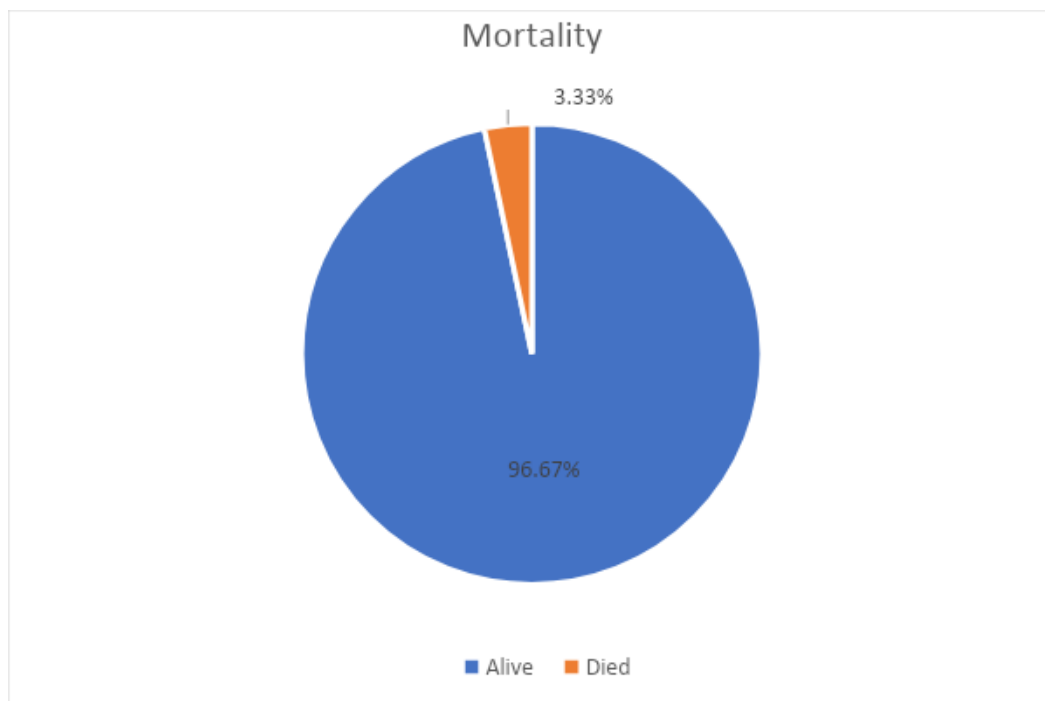| Mortality	Frequency	Percentage
Alive	58	96.67%
Died	2	3.33%
Total	60	100.00%

Figure 12 – Mortality in NSTI
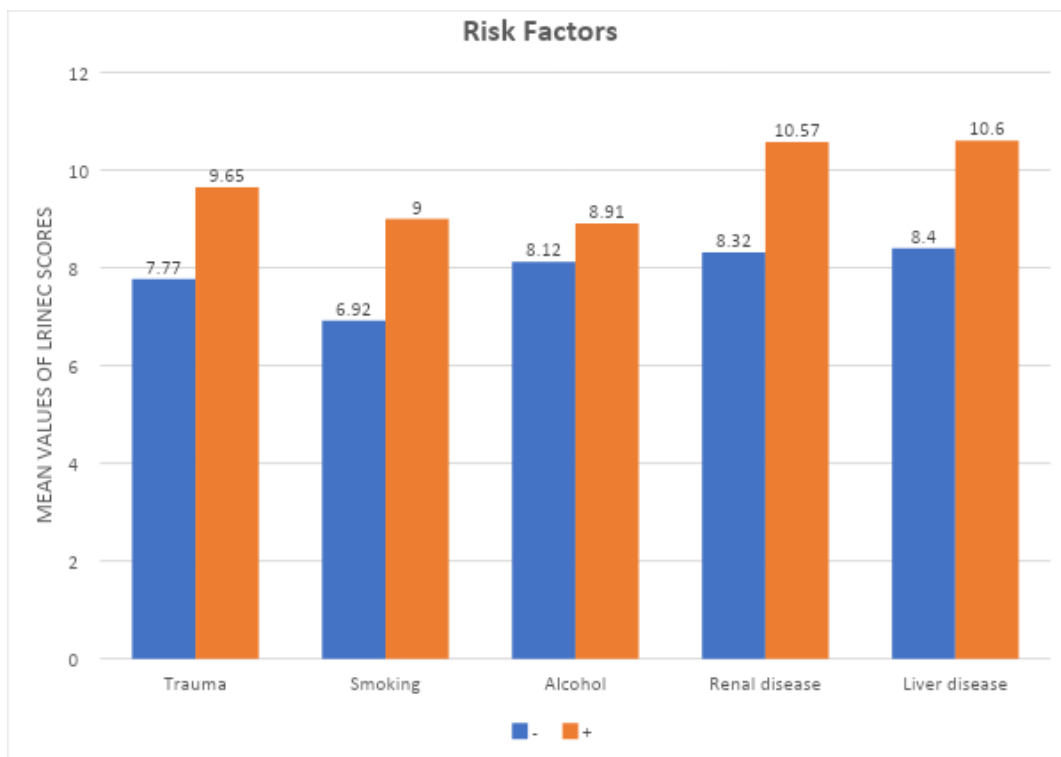
Figure 13 – Correlation of mean LRINEC score with various risk factors

Risk Factors	-	+	P Value
Trauma			
Sample size	34	26	
Mean ± Stdev	7.77 ± 2.18	9.65 ± 1.41	0.001
Median	8	9	
Min – Max	5-13	7-12	
Inter quartile Range	5 – 9	9 - 11	
Smoking			
Sample size	12	48	
Mean ± Stdev	6.92 ± 2.5	9 ± 1.77	0.005
Median	6	9	
Min – Max	5-12	5-13	
Inter quartile Range	5 – 8	8 – 10	
Alcohol			
Sample size	25	35	
Mean ± Stdev	8.12 ± 2.24	8.91 ± 1.95	0.207
Median	8	9	
Min – Max	5-12	5-13	
Inter quartile Range	6.5 - 10	8 - 10	
Renal disease			
Sample size	53	7	
Mean ± Stdev	8.32 ± 2.05	10.57 ± 1.27	0.005
Median	9	10	
Min – Max	5-12	9-13	
Inter quartile Range	7 - 10	10 - 11	
Liver disease			
Sample size	55	5	
Mean ± Stdev	8.4 ± 2.07	10.6 ± 1.14	0.015
Median	9	11	
Min – Max	5-13	9-12	
Inter quartile Range	7 -10	9.75 - 11.25	

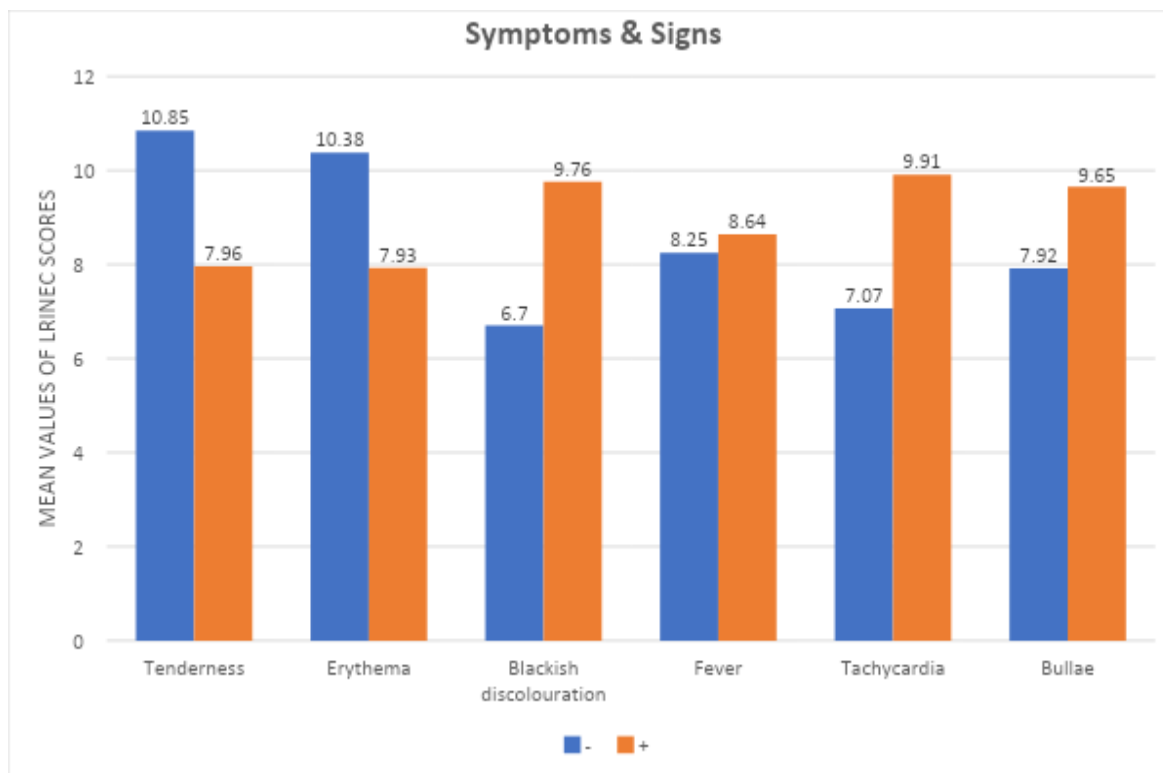**Table showing correlation of mean LRINEC score with various risk factors**

Figure 14 – Correlation of mean LRINEC score with various symptoms & signs of NSTI

Symptoms & Signs	-	+	P Value
Tenderness			<0.0005
Sample size	13	47	
Mean ± Stdev	10.85 ± 1.21	7.96 ± 1.84	
Median	11	8	
Min – Max	9-13	5-11	
Inter quartile Range	10 -12	7 - 9	
Erythema			<0.0005
Sample size	16	44	
Mean ± Stdev	10.38 ± 1.31	7.93 ± 1.95	
Median	10.5	8	
Min – Max	7-12	5-13	
Inter quartile Range	10 – 11	7 - 9	
Blackish discoloration			<0.0005
Sample size	23	37	
Mean ± Stdev	6.7 ± 1.61	9.76 ± 1.38	
Median	7	10	
Min – Max	5-10	7-13	
Inter quartile Range	5 – 8	9 - 11	
Fever			0.635
Sample size	8	52	
Mean ± Stdev	8.25 ± 2.55	8.64 ± 2.04	
Median	8.5	9	
Min – Max	5-12	5-13	
Inter quartile Range	6 – 10	7 - 10	
Tachycardia			<0.0005
Sample size	28	32	
Mean ± Stdev	7.07 ± 1.68	9.91 ± 1.42	
Median	7	10	
Min – Max	5-10	7-13	
Inter quartile Range	5 - 8.5	9 - 11	
Bullae			0.003
Sample size	37	23	
Mean ± Stdev	7.92 ± 2.05	9.65 ± 1.72	
Median	8	10	
Min – Max	5-12	7-13	
Inter quartile Range	5.75 - 9	9 - 11	

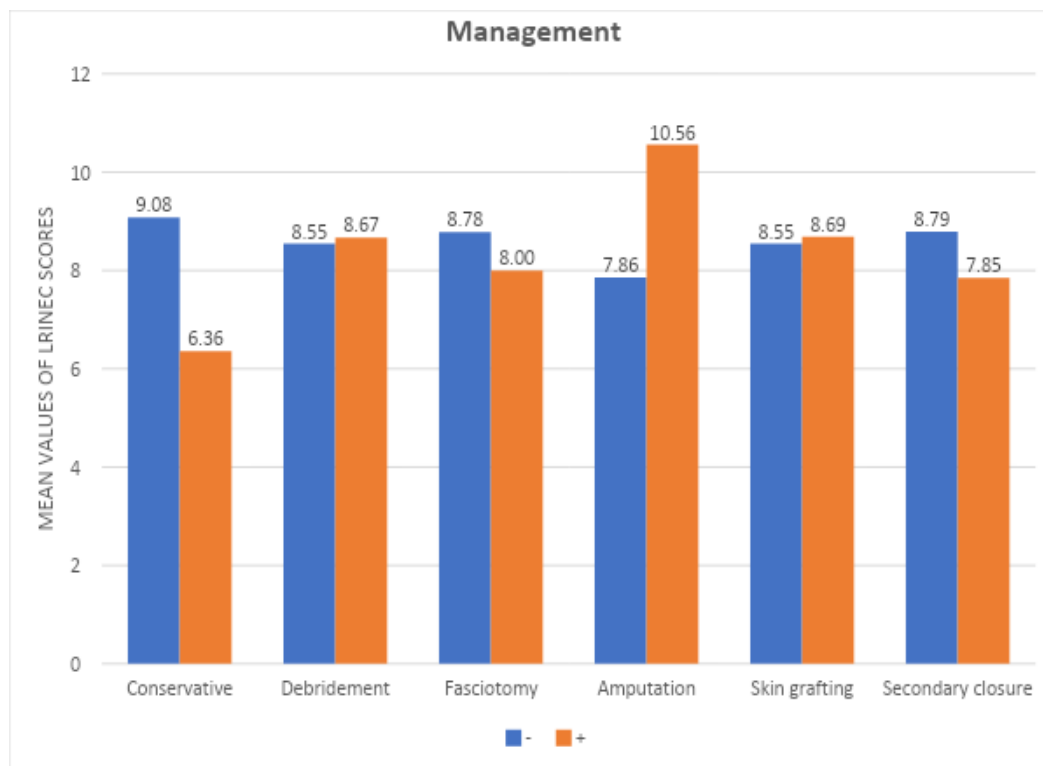**Table showing correlation of mean LRINEC score with various symptoms of NSTI**

Figure 15 – correlation of mean LRINEC score with various treatment modalities of NSTI

Management	-	+	P value
Conservative			
Sample size	49	11	0.001
Mean ± Stdev	9.08 ± 1.53	6.36 ± 2.84	
Median	9	5	
Min – Max	5-12	5-13	
Inter quartile Range	8 -10	5 - 5.75	
Debridement			
Sample size	42	18	0.948
Mean ± Stdev	8.55 ± 2.37	8.67 ± 1.28	
Median	9	9	
Min – Max	5-13	5-10	
Inter quartile Range	7 – 11	8 - 9	
Fasciotomy			
Sample size	45	15	0.053
Mean ± Stdev	8.78 ± 2.33	8 ± 0.93	
Median	9	8	
Min – Max	5-13	7-10	
Inter quartile Range	7 - 10	7- 8	
Amputation			
Sample size	44	16	<0.0005
Mean ± Stdev	7.86 ± 1.91	10.56 ± 1.03	
Median	8	11	
Min – Max	5-13	9-12	
Inter quartile Range	7 - 9	10 - 11	
Skin grafting			
Sample size	44	16	0.859
Mean ± Stdev	8.55 ± 2.32	8.69 ± 1.35	
Median	9	9	
Min – Max	5-13	5-10	
Inter quartile Range	7 - 10.5	8.5 - 9.5	
Secondary closure			
Sample size	47	13	0.024
Mean ± Stdev	8.79 ± 2.3	7.85 ± 0.69	
Median	9	8	
Min – Max	5-13	7-9	
Inter quartile Range	7 – 10	7 – 8	

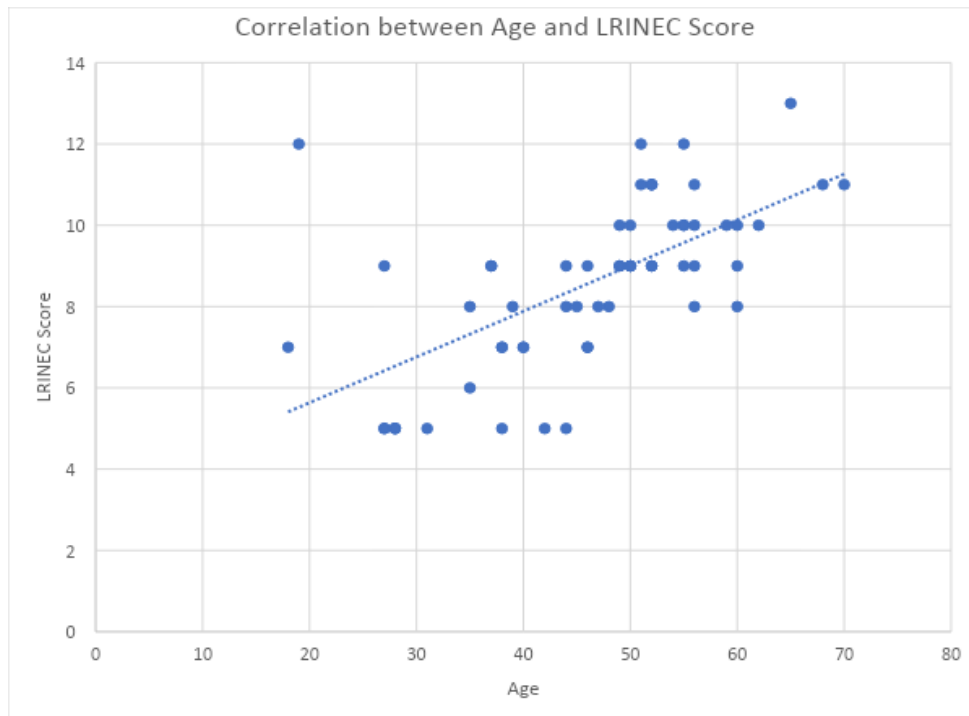**Table showing correlation of mean LRINEC score with various treatment modalities of NSTI**

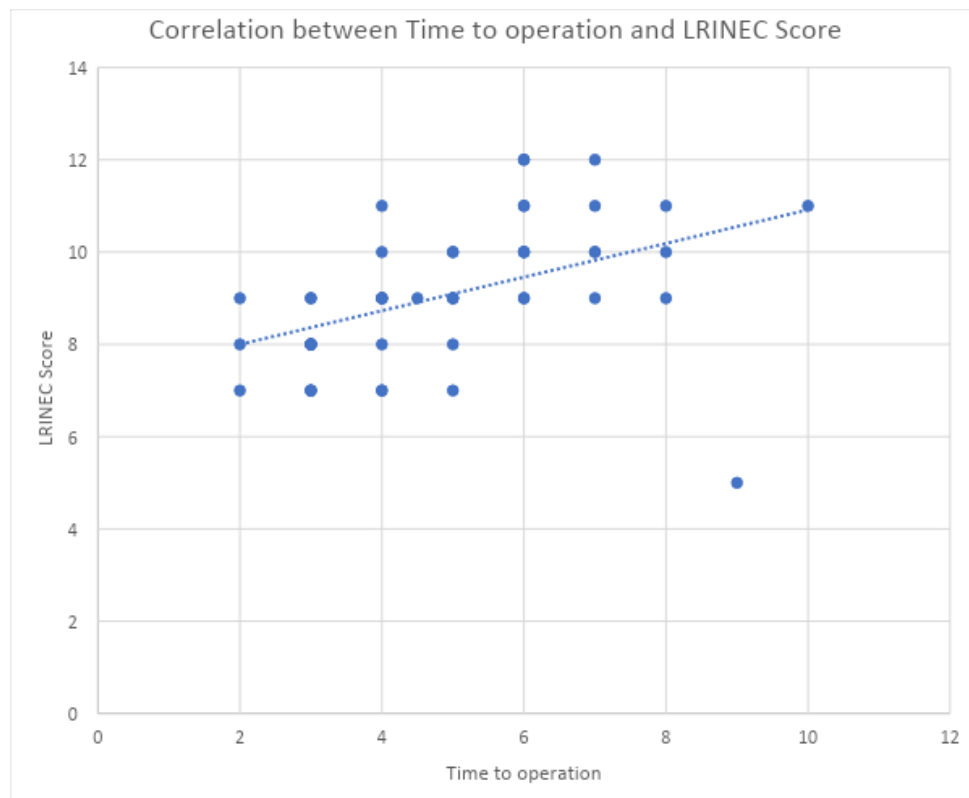**Figure 16 –** correlation of LRINEC score with age of the patients

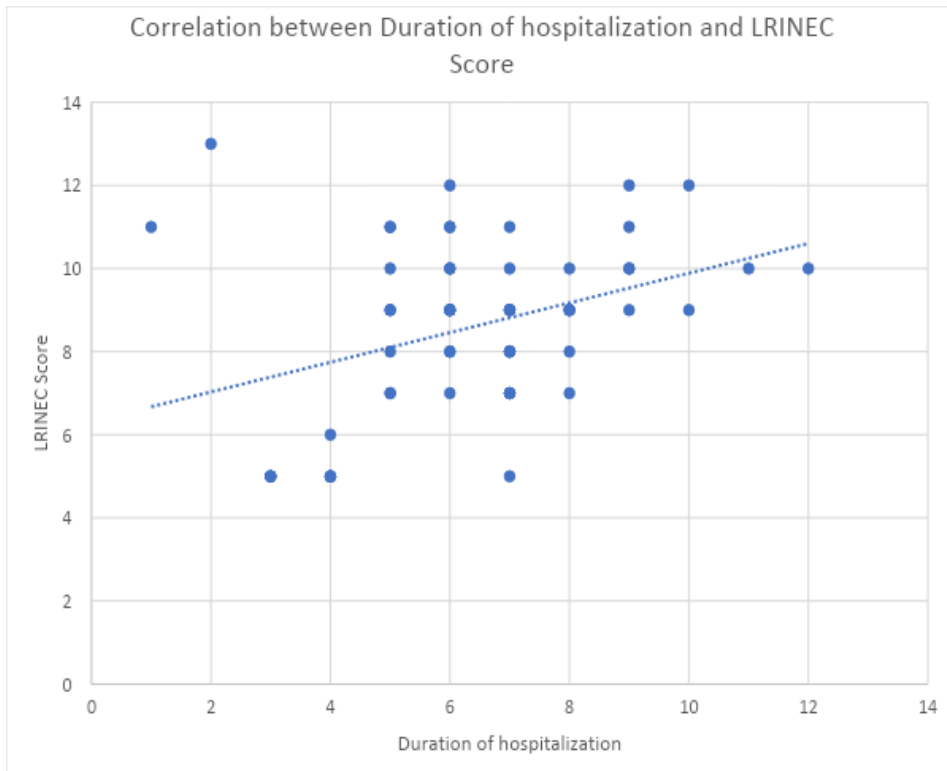**Figure 17 –** Correlation of LRINEC score with time of operation

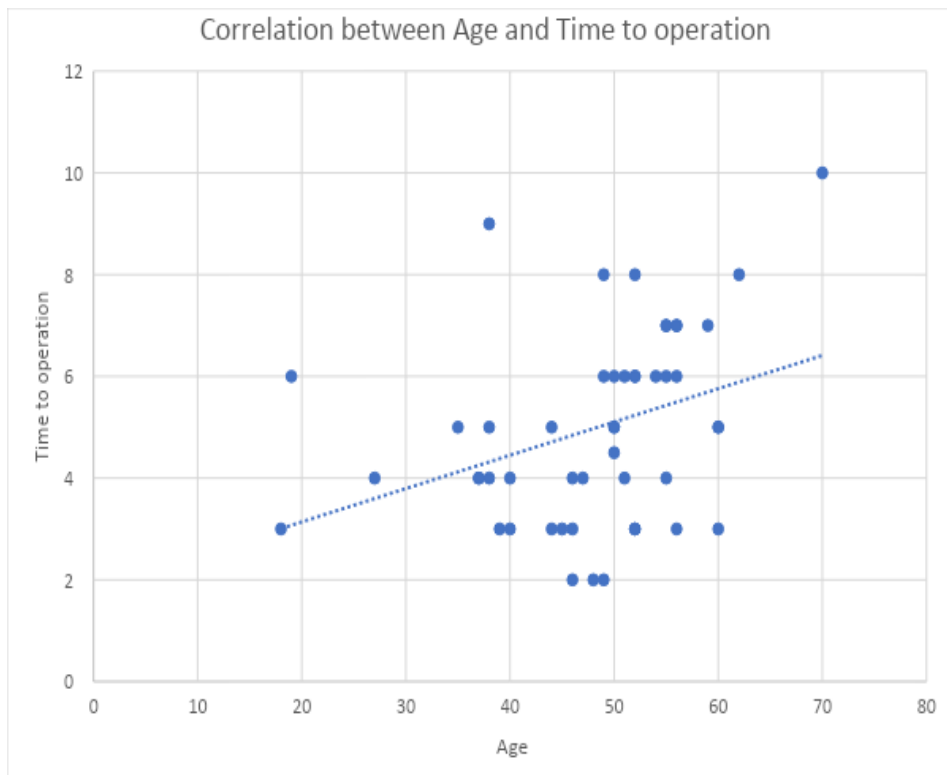**Figure 18 –** Correlation of LRINEC score with duration of hospitalization

Figure 19 – Correlation of time to operation with age
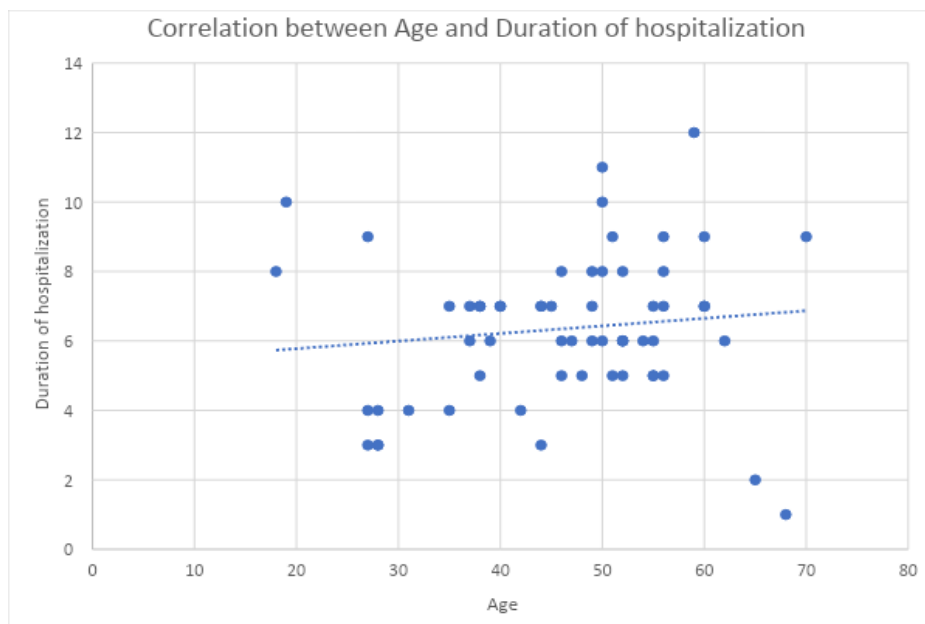
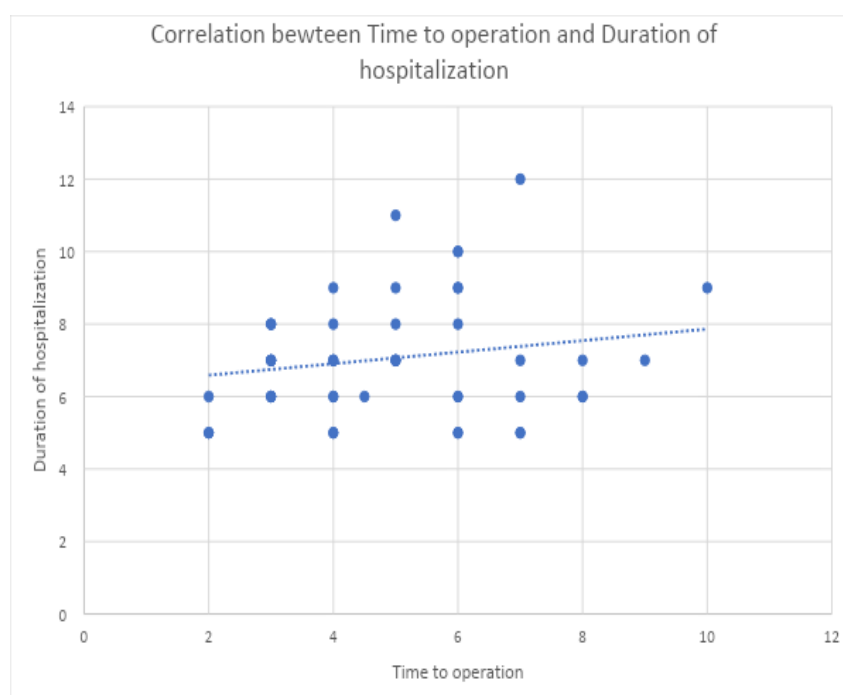**Figure 20 –** Correlation of duration of hospitalization with age

Figure 21 – Correlation of duration of hospitalization with time to operation

		Age	LRINEC score	Duration of hospitalization	Time of operation
Age	Correlation Coefficient		0.678	0.162	0.399
	Significance Level P		<0.0001	0.2154	0.0045
	N		60	60	49
LRINEC score	Correlation Coefficient	0.678		0.345	0.6
	Significance Level P	<0.0001		0.0069	<0.0001
	N	60		60	49
Duration of hospitalization	Correlation Coefficient	0.162	0.345		0.128
	Significance Level P	0.2154	0.0069		0.382
	N	60	60		49
Time of operation	Correlation Coefficient	0.399	0.6	0.128	
	Significance Level P	0.0045	<0.0001	0.382	
	N	49	49	49	

Table showing correlation between age, LRINEC score, duration of hospitalization and time to operation
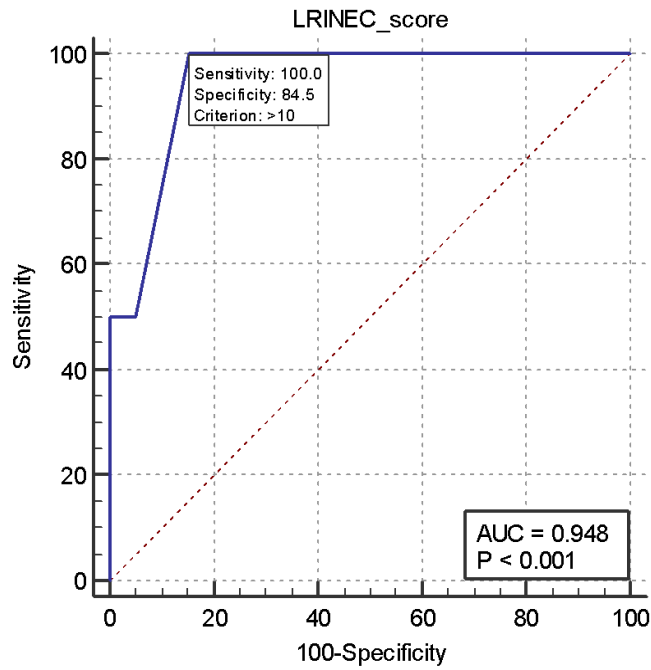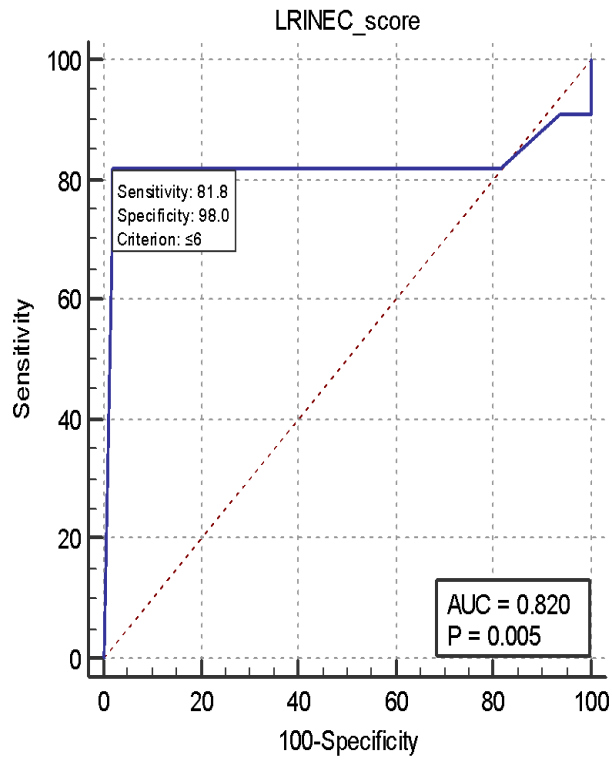
Figure 22 – AUC for mortality
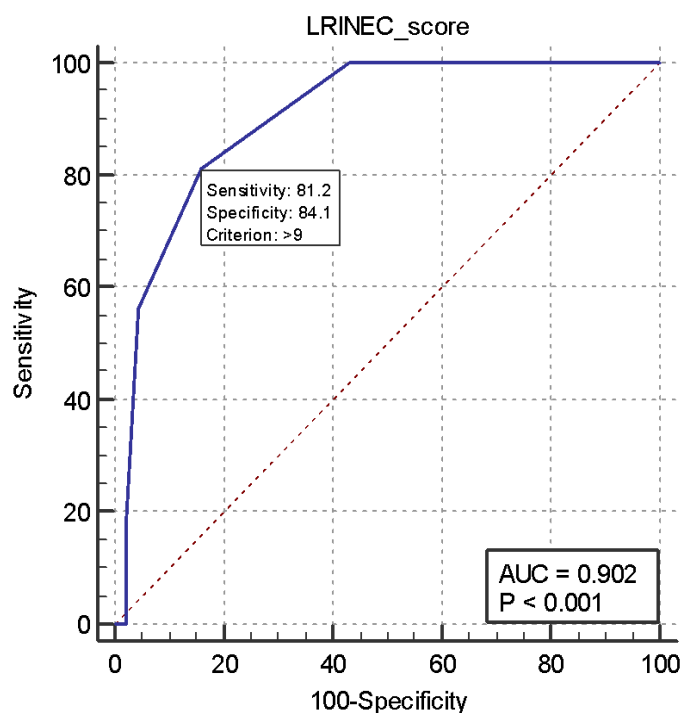

Figure 23 – AUC for conservative management

Figure 24 – AUC for amputation

	Area under the ROC curve(AUC)	Standard Error A	95% Confidence interval B	P Value	Cut off point	Sensitivity	Specificity
Cut off point of LRINEC score for amputation	0.901989	0.0385	0.797441 to 0.963636	<0.0001	>9	81.25	84.09
Cut off point of LRINEC score for conservative	0.820037	0.114	0.699459 to 0.907278	0.0049	≤6	81.82	97.96
Cut off point of LRINEC score for mortality	0.948276	0.0545	0.858355 to 0.988802	<0.0001	>10	100	84.48

Table showing AUC and cut-off LRINEC score for conservative management, amputation and mortality

IV. Discussion

In the present study, 60 patients of severe soft tissue infections presenting to CNMCH over the period of 18 months were studied tor various parameters. All the patients were studied according to the annexure 1. The results are discussed below:

Age distribution

Patients presented between the age group of 14- 70 years old.

Study	Common age group (in years)
Anaya et al [16]	41-50
Paramythiotis et al [33]	51-60
Yi - Chun Su et al [1]	51-60
Present study	51-60

In our study, most of the patients were in the age group of 51 - 60 years which is comparable to studies conducted by Paramythiotis et al [33] and Yi - Chun Su et al [1].Mean age of presentation in our study was 46.22 ± 11.706 years.

Sex distribution

There were definite male preponderance 45 patients (75%) over 15 female patients(25%).

Study	Males (%)	Females (%)
Anaya et al [16]	60	40
Paramythiotis et al [33]	61	39
Well et al [57]	77	23
Present study	75	25

Male to female ratio is 3:1 which is comparable with the study conducted by Wall et al [57]. The reason for this male preponderance in patients of necrotizing fasciitis is not known.

Site of lesion

In our study, the most common site involved by NSTI is lower limb (68.33%) followed by scrotum/perineum (20%), upper limb (8.33%), and abdominal wall (3.33%).

Study	Most Common site (%)
Elliot et al [18]	Perineum (36%)
Wall et al [57]	Upper limb (48%)
Present study	Lower limb (68%)

The disparity between our study and that by Wall et al is attributed to the fact that most of the patients in the study by Wall et al were iv drug abusers (71 %).

Risk factors

Most common risk factor in our study is smoking (80%) followed by alcohol (58.33%), trauma (43.33%), renal disease (11.67%) and liver disease (8.33%). Compared to this, the most common risk factor in the study conducted by Wall et al [57] was iv drug abuse (71%) while in the study by Yi - Chun Su et al[1], diabetes mellitus was the commonest predisposing factor.

Symptomatology

In our study, patients presented with many clinical features, most common being fever 52 patients (86%), tenderness 47 patients (78%), erythema 44 patients (73%), blackish discoloration 37 patients (61%), tachycardia 32 patients (53%) and bullae 23 patients (38%). Most of the patients presented with more than one symptom, Compared to this, inthe study by Yi - Chun Su et al [1], the most common feature was tenderness (86%), erythema (85%), tachycardia (47%), bullae formation (44%) and fever (33%).

LRINEC Score and Its correlation with management

The median LRINEC score In our study is 9. Of the 60 patients in our study, 11 patients (18.3%) were treated conservatively with a mean LRINEC score of 6.36 ± 2.84. 18 patients (30%) underwent extensive/serial debridement with a mean score of 8.67 ± 1.28. 15 patients (25.00%) had to undergo fasciotomy with a mean score of 8 ± 0.93. Amputation was performed in 16 patients (26.67%) with a high mean score of 10.56 ± 1.03.

Reconstructive procedure. Were performed in 29 patients with secondary closure in 13 patients (21.67%) and skin grafting in 16 patients (26.67%). Mean LRINEC in patients with secondary closure was lower than those with skin grafting (7.85 vs 8.69).

After applying Pearson correlation test, a higher LRINEC score was found to significantly correlate with a longer time to operation (correlation coefficient of 0.56, p value <0.0001) and longer duration of hospitalization (correlation coefficient of 0.345, p value 0.0069).

ROC analysis

Receiver operator curve for LRINEC score for predicting conservative management shows a cut-off value of LRINEC score ≤ 6 with Area under the ROC (AUC) of 0.820, sensitivity of 81.8% and specificity of 98%.

Similarly, ROC for LRINEC score for predicting amputation shows a cut off value of LRINEC score > 9 with AUC of 0.901, sensitivity of 81.2% and specificity of 84%.

Finally, ROC for LRINEC score for predicting mortality shows a cut-off value of LRINEC score > 10 with AUC of 0.948, sensitivity of 100% and specificity of 84.5%.

The study by Yi - Chun Su et al shows a cut-off value of LRINEC score of 6 for predicting amputation and AUC of 0.75. In terms of mortality, cut-off value of LRINEC score of 6 and AUC of 0.61 was reported by the researchers.

V.   Conclusion

LRINEC score greatly helped in categorization of patients into different risk groups, planning of treatment modality and prediction of outcome. the management of NSTI and LRINEC score will greatly help in predicting necrotizing son tissue infections. Because of its cost effectiveness, availability and ease or use, it is recommended to be a part in the holistic approach of treatment of necrotizing soft tissue infections.

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