Original Research Article

Use of serum lactate and serum sodium at admission to predict mortality in necrotising fasciitis

Sudhir S., Rachit Arora*

Department of General Surgery, J.S.S. Academy of Higher Education and Research, Mysore, Karnataka, India

*Correspondence:
Dr. Rachit Arora,
E-mail: rachitarora123@gmail.com

ABSTRACT

Background: The term necrotizing fasciitis (NF) describes a group of life-threatening infections of the skin, soft tissues, and muscles, which tend to progress rapidly through the fascia planes, causing gradual destruction of the fascia. The mortality rate for NF remains high and has not changed significantly for several decades. The prognosis depends on accurate diagnosis and immediate institution of appropriate treatment.
The current difficulty in initial diagnosis is due to the lack of obvious skin findings early on in the infection. Laboratory tests, including the laboratory risk indicator for necrotizing fasciitis, gas on imaging tests, and physical exam findings.
Methods: This is a prospective study of 100 patients of necrotising fasciitis. Serum sodium and serum lactate at time of admission were used to predict mortality.
Results: Total of 21 patients died. Above Serum lactate value of 2.95mmol/l mortality rate was 48.3%. and below it was 9.9%. Serum sodium was non significant in predicting mortality.
Conclusions: The mortality of NF remains high. A simple model using serum lactate at time of admission may help identify patients at greatest risk of death.

Keywords: Lactate, Necrotising fasciitis, Sodium

INTRODUCTION

The term necrotizing fasciitis (NF) describes a group of relatively uncommon, but life-threatening infections of the skin, soft tissues, and muscles, which tend to progress rapidly through the fascia planes, causing gradual destruction of the fascia. Developing in the lower or upper extremities, the perineum and genital area (Fournier's gangrene) and in the abdominal wall, its swift clinical course is correlated with numerous etilogies and polymicrobial infection and synergy, which usually co-exists. The majority of cases present anaerobic bacteria that proliferate in a hypoxic environment and produce gas, which accumulates in the soft tissue spaces, giving the characteristic image of gas gangrene on plain X-rays

and computed tomography (CT) scans. Early diagnosis of NF is mandatory. Any delay could prove fatal, given its association with more extensive surgery, higher rates of amputation, and higher mortality rates. Furthermore, if left untreated, the infection could lead to systemic inflammatory response syndrome (SIRS).

The incidence of NF was estimated to be 500-1000 cases per year and the

global prevalence was 0.4 cases per every 100,000 people. NF is rapidly fatal unless quickly diagnosed and aggressively treated.[1] The mortality rate for NSTI remains high, ranging from 24% to 34%, and has not changed significantly for several decades.[2] The current

difficulty in initial diagnosis is due to the lack of obvious skin findings early on in the infection. In many cases, the inciting factors are not identified. Hard clinical signs, such as crepitance, bullae, necrosis, and subcutaneous air on radiographs, help to establish the diagnosis; however, these signs are often not present at the time of initial examination. Laboratory results in necrotising fasciitis are not usually specific. However, certain laboratory findings can help to differentiate NF from other skin diseases. Blood lactate levels have been found to be the earliest predictor of mortality in sepsis and identify survivors from non-survivors as early as 12 hrs after admission. Levraut et al, showed that blood lactate levels >27mg/dl at 12 hrs of admission had a positive predictive value for survival of 44% and <27mg/dl has a positive predictive value for survival of 84%.[3] Some studies have shown that in specific patient groups, lactate levels are better predictors of survival and development of organ failure than complex scoring systems such as Acute Physiology and Chronic Health Evaluation (APACHE II).[4] Smith et al, showed that by using blood lactate levels, patients with high risk of morbidity and mortality can be discriminated from patients with relative low risk.[5]

The aim of the present study was to determine the role of Serum Lactate and Sodium levels at time of admission in predicting mortality in necrotising fasciitis.

METHODS

The patients admitted with Necrotizing Fasciitis in Surgery Department in J.S.S. Medical College and Hospital, Mysore. All patients with necrotising fasciitis fulfilling inclusion criteria admitted in surgery ward will be included in study.

A detailed history and clinical examination will be carried out for each patient.

A written informed consent will be taken for each patient enrolled in this study. It is an explorative study and total 100 patients were included in the study. The duration of the present study was 2016 to 2018.

Inclusion criteria

All cases of necrotising fasciitis willing to be part of study.

Exclusion criteria

All patients who are known case of Chronic Renal Disease.

Investigations and interventions to be conducted on patients

- To collect Arterial Blood Gas and Serum Electrolytes at time of admission.

- Clinical examination and appropriate treatment which includes
- Broad spectrum antibiotics
- Wide surgical debridement.

Stastical analysis

- The collected data will be evaluated using appropriate statistical tests.
- Descriptive statistics
- Chi-square test
- Independent t test
- Mann Whitney test.

RESULTS

Age distribution of patients studied. As shown in Table 1, in present study age variation was from 20 years to 90years. Majority of patients were in age group of 61-70years that included 32 patients.

Age group (years)	Count	Column N %
<40	7	70%
41-50	13	13.0%
51-60	23	23.0%
61-70	32	32.0%
71-80	16	16.0%
>81	9	9.0%

Table 2: Gender distribution of patients studied.

Age category	Sex					
	F		M		Total	
	Count	Column N %	Count	Column N %	Count	Column N %
<40	1	7.7%	6	6.9%	7	7.0%
41-50	1	7.7%	12	13.8%	13	13.0%
51-60	3	23.1%	20	23.0%	23	23.0%
61-70	2	15.4%	30	34.5%	32	32.0%
71-80	4	30.8%	12	13.8%	16	16.0%
>81	2	15.4%	7	8.0%	9	9.0%
Total	13	100.0%	87	100.0%	100	100.0%

Table 3: Co- morbidities and site of involvement.

		Count	Column N %
T2DM	No	53	53.0
	Yes	47	47.0
HTN	No	69	69.0
	Yes	31	31.0
Site	Back	1	1.0
	Fourniers	12	12.0
	Fourniers/LL	1	1.0
	LL	84	84.0
	UL	2	2.0

As shown in Table 2, majority of subjects in the present study were males (87%) as compared to females (13%). As shown in the table 3, 47% patient were diabetic and 31% were hypertensives.

As shown in Table 3, The most common site was lower limb (84%). The number of patients with Fourniers gangrene were 12. 2 patients had necrotising fasciitis of upper limb. 1 patient had both lower limb involvement and fourniers gangrene. One patient had necrotising fasciitis of back.

Table 4: Modalities of management.

		Count	Column N %
Debridement	No	6	6.0%
	Yes	94	94.0%
	Total	100	100.0%
Amputation	No	91	91.0%
	Yes	9	9.0%
	Total	100	100.0%

As shown in Table 4, 94 patients underwent surgical debridement. 9 patients underwent amputation.

Table 5: Mortality.

		Count	Column N %
Mortality	No	79	79.0%
	Yes	21	21.0%
	Total	100	100.0%

Table 6: Type of discharge.

		Mortality			
		No		Yes	
		N	Column N %	N	Column N %
Discharge type	Planned discharge	66	83.5%	20	95.2%
	AMA total	13 79	16.5%	1	4.8%

As shown in Table 5 and 6, In this study out of 100 patients, 21 patients died. 13 patients were discharged against medical advice.

As shown in Table 7 In this study the mean value of sodium was 131.4 in the patients who survived and 131.8 in the patients who died. p value of 0.9 which is statistically non-significant.

The mean value of sodium in patients who underwent amputation was 130.2 and patients who did not underwent amputation was 131.6. p value of 0.7 which is statistically non-significant.

The mean value of patients who underwent surgical debridement's (91 patients) was 131.5 and who did not

undergo debridement was 132.5. p value of 0.9 which is statistically non-significant.

Table 7: Role of sodium.

	Mortality		
Sodium	No	Yes	P
	Mean±SD	Mean±SD	
	131.4±13.9	131.8±8.0	0.9
Amputation			
Sodium	No	Yes	P
	Mean±SD	Mean±SD	
	131.6±131.5	131.6±3.0	0.7
Surgery			
Sodium	No	Yes	P
	Mean±SD	Mean±SD	
	132.5±5.5	131.5±13.2	0.9

As shown in Table 8, for lactate median value was taken because data was not normally distributed.

Table 8: Role of lactate.

		Lactate			
		Median	Q1	Q3	p
Mortality	No	1.70	1.20	2.50	0.001
	Yes	3.30	2.20	4.60	
Amputation	No	2.10	1.30	3.30	0.02
	Yes	1.10	1.10	1.50	
Surgery	No	4.00	2.00	6.40	0.034
	Yes	1.80	1.20	3.20	

The median value of lactate in patients who died was 3.30, while it was 1.70 in patients who survived. p value 0.001 which is statistically significant.
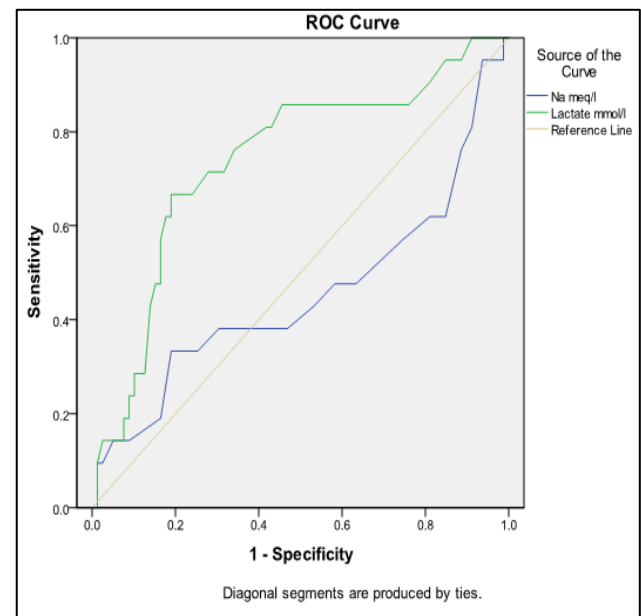

Figure 1: ROC curve.

The median value of lactate who underwent amputation was 1.1, while it was 2.1 in patients who did not undergo amputation with p value of 0.02 which is statistically significant.

Table 9: Area under the curve.

Test result variable(s)	AUC	p	Asymptotic 95% Confidence Interval	
			Lower bound	Upper bound
Sodium	0.454	0.515	0.294	0.614
Lactate	0.740	0.001	0.615	0.864

The test result variable(s): Sodium, Lactate has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. a. Under the nonparametric assumption b. Null hypothesis: true area = 0.5.

The median value of lactate in patients who underwent debridement was 1.80 while who did not undergo surgery was 4. p value of 0.03 which is statistically significant which shows patient who were unfit for surgery had higher lactate value.

Table 10: Lactate cut off.

		Mortality			
		No		Yes	
		Count	Column N %	Count	Column N %
Lactate cut off	No	64	90.1	7	9.9
	Yes	15	51.7	14	48.3

2.95 cut off for lactate; P <0.001

As shown in Table 9 and Figure 1, The area under curve for serum sodium value at time of admission in predicting mortality was 0.454 which was fair. However, this was statistically non significant (p=0.515).
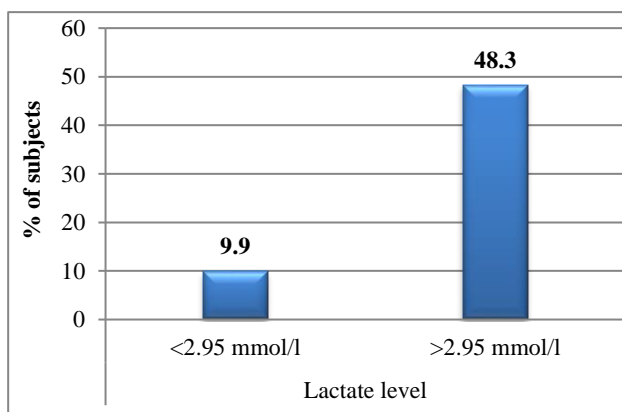

Figure 2: Lactate cut off for mortality.

The area under curve for serum lactate at time of admission in predicting mortality was 0.740 which was good. This was statistically significant also (p=0.001).

This indicated serum lactate as a better predictor of mortality.

Table 11: Sensitivity and specificity.

Parameter	Estimate	Lower-Upper 95% CIs
Sensitivity	66.67%	(45.37, 82.81)
Specificity	81.01%	(71.01, 88.14)
Positive predictive value	48.28%	(31.39, 65.57)
Negative predictive value	90.14%	(81.02, 95.14)
Diagnostic accuracy	78%	(68.93, 85)

As shown in Table 10 and Figure 2, The serum lactate cut off of 2.95mmol/l was significantly associated with mortality rate at the time of admission. The mortality rate of serum lactate >2.95mmol/l was 48.3%, significantly higher than 9.9% for <2.95mmol/l. That is almost 5 times higher mortality.

As shown in Table 11 The sensitivity of 66.67%, specificity of 81.07%, Positive predictive value of 48.28%, negative predictive value of 90.14% and diagnostic accuracy of 78%.

As shown in Table 12, There was no statistically significant relation of mortality with age and co morbidities in the present study.

DISCUSSION

Necrotizing fasciitis (NF), which is characterized by progressive necrosis of the fascia, subcutaneous tissue and skin, is a life-threatening soft tissue infection. Diagnosis is made by physical examination but may be difficult since it is frequently confused with the other skin and soft tissue infections. For this reason, various laboratory indicator serum sodium, serum lactate, serum glucose, CRP, hemoglobin of patients are evaluated at admission and used for diagnosis and prediction of mortality.

Also, other co morbid condition like old age, diabetes, hypertension, malnutrition are used to support diagnosis and evaluate for prognosis.

Sepsis leads to increased muscle glucose uptake, increased lactate production and decreased utilization, an increase in the calculated ratio of muscle membrane permeabilities to Na^+ and K^+, and an increased intracellular Na^+ concentration. These effects may be mediated by complement activation. In addition, sepsis has been linked to an increase in antidiuretic hormone level as well as adrenocortical insufficiency, both of which may lead to hyponatremia. Finally, severe NSTIs lead to marked third spacing of fluids, which may be

replaced by free water, leading to hypovolemic hyponatremia.

Blood lactate levels have been found to be the earliest predictor of mortality in sepsis. This increases as a result of hypermetabolism.

Therefore, early diagnosis of necrotising fasciitis require high level of suspicion and similarity with clinical findings. Establishing the diagnosis at earliest time point presents a major challenge.

Table 12: Role of co-morbidities.

		Mortality				
		No		Yes		
		Count	Row N %	Count	Row N %	p
T2DM	No	43	81.1%	10	18.9%	0.6
	Yes	36	76.6%	11	23.4%	
HTN	No	54	78.3%	15	21.7%	0.8
	Yes	25	80.6%	6	19.4%	
Age category	<40	6	85.7%	1	14.3%	0.7
	41-50	9	69.2%	4	30.8%	
	51-60	18	78.3%	5	21.7%	
	61-70	25	78.1%	7	21.9%	
	71-80	15	93.8%	1	6.3%	
	>81	6	66.7%	3	33.3%	
Co-morbidity	None	33	82.5%	7	17.5%	0.7
	DM	21	72.4%	8	27.6%	
	HTN	10	76.9%	3	23.1%	
	Both	15	83.3%	3	16.7%	

Therefore, this study was conducted to evaluate the role of lab parameters like serum lactate and serum sodium and other co morbid conditions in role of necrotising fasciitis.

The following were the objectives of study

- To determine the role of serum lactate and sodium levels in predicting mortality in necrotising fasciitis.
- To predict the Need for major extreme amputation.

Demographic profile of the group

During this 2 year study period total of 100 admissions were recorded for necrotising fasciitis.

Majority of patients were males (87%) as compared to females (13%). Mean age was 61.7±14.15 Majority of patients were in group 61-70 years.

The mortality rate seen in more than 81 years was 33%, which was more than that seen in any other age group. However, there was no statistical correlation in mortality with respect to age. Also, the two groups of survivors and non survivors were comparable with respect to gender.

This observation was comparable to study done by Yaghoubian A, MD et al, in which the co relation between age and mortality rate was statistically non-significant.[6]

Another study done by Colak E et al, who compared various associations with mortality in patients with necrotising fasciitis showed no statistical co relation between survivors and non survivors with respect to age (p=0.7) and gender.[7]

Site of infection

Out of 100 patients, 84 patients had lower limb involvement, 12 patients had fourniers gangrene. 2 patients had upper limb involvement and 1 had both fourniers gangrene and lower limb involvement and 1 patient back. This observation was comparable to study done by Yaghoubian A et al.[6]

Assessment of co morbidities

In present study while evaluating for co morbidities the incidence of Diabetes mellitus was seen higher (47%) then hypertension (31%). However, this is not statistically significant. This is in co-relation with study done by Colak et al, in which the most frequent co morbid disease was diabetes mellitus.[7] This finding could be attributed in part to hyperglycaemic status that

compromises immunity status and fosters bacterial growth.

In contrast another study done by Jabbour G et al, patients with a history of diabetes mellitus showed considerably rapid progress of the severity of NF and mortality.[8]

Laboratory findings

In present study initial serum lactate levels at time of admission of more than 2.95 had a mortality rate of 48%. Thus, there is a statistically significant correlation between high lactate levels and mortality rate with p=0.001. This is in correlation with study done by Elliott DC et al, (p<0.0001).[9]

Another study done by Martinschek A et al, showed increase in serum lactate at time of admission prove to be a significant factor for fatal prognosis (p=<0.001).[10]

However, in the study done by Yaghoubian A et al, lactate was not significant (p=0.2).[6]

In present study serum sodium levels at time of admission in predicting mortality was not significant (p=0.5). The results were comparable with study done by Yaghoubian A et al, (p=0.3).[6]

Another study by Jabbour G et al, shows in univariate analysis serum sodium levels was not significant in predicting mortality (p= 0.43).[8]

Surgical management

NSTI requires a combined therapy consisting of early operative debridement, intensive care medicine, and combined antibiotic therapy.

Aggressiveness remains the key to successful outcome in necrotizing fasciitis. Aggressive debridement, often in multiple sittings, was the primary operative procedure used as curative procedures. in this study 94 patients underwent surgical debridement. 9 patients underwent amputation. The mortality of patients who underwent amputation was 1 (11%) p=0.44 which was not significant. The results were comparable with the study done by Yaghoubian A et al.[6]

Another study by Misiakos P et al, has also shown that early and meticulous debridement is the mainstay of treatment.[11]

CONCLUSION

Age and sex are not significant in predicting mortality of patient. There is no significant correlation between Diabetes and Hypertension in predicting mortality of patient. Serum sodium at the time of admission is not significant in predicting mortality. Serum Lactate at time

of admission is significant in predicting mortality of patients. Serum lactate levels above 2.95mmol/l have significantly higher mortality. Amputation is not significant in predicting mortality however early operative debridement, intensive care medicine, and combined antibiotic therapy is the key to successful outcome in necrotising fasciitis.

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