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Biochemical Markers as Prognostic Factors in Necrotizing Fasciitis: A Prospective Study

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Abstract

Background: Necrotizing soft tissue infections are frequently associated with a fulminant presentation and fatal outcomes. A side from critical care and antibiotic therapy, aggressive surgical treatment is essential for the treatment of necrotizing fasciitis. The purpose of this study was to see if post-operative procalcitonin, lactate dehydrogenase, albumin, and culture sensitivity could be used to predict successful surgical intervention.

Methods: The study group consisted of 92 patients treated with clinical signs of sepsis caused by a necrotizing soft tissue infection. All patients received radical surgical treatment, and S.PCT, S.LDH, Albumin and wound culture and sensitivity were sent on POD3.

Results: Out of 92 patients' mortality was seen in 11 patients and amputation was done in 6 patients. The biochemical markers which were included in the study showed significant results ($p<0.01$) * that is serum procalcitonin and serum LDH were elevated and s. albumin was low in all patients who are died and amputated except in one patient. There was no significant in the microbial flora and the outcome of the patient.

Conclusions: The biochemical markers PCT, LDH, Albumin following major surgical procedures for necrotizing soft tissue infections represents a valuable clinical tool indicating successful surgical eradication of the infectious focus.

Keywords: Necrotizing Fasciitis; S.PCT, S. LDH; S. Albumin.

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INTRODUCTION

Necrotizing soft tissue infections (NSTIs) are uncommon, severe, and potentially fatal bacterial infections. The term necrotizing fasciitis was first used by Wilson[1] in 1952 to describe the primary infection, which mostly affects the fascia and subcutaneous tissue. Clinical signs such as exaggerated pain, edema, blisters, and erythema along with a systemic inflammation syndrome are characteristics of this extremely deadly infection.

Histopathologic features such as fascial necrosis, vasculitis, and thrombosis of perforating veins are also present.[2] An abundance of aerobic and anaerobic organisms can generate synergistic polymicrobial infections, which are about as prevalent as monomicrobial fasciitis.[3–5] In 50% to 80% of cases, the infection is concentrated in the extremities, with the remaining instances involving the trunk and the perineal area (Fournier's gangrene).[2,5,6] There are a number of categorization systems that have been used to classify this diverse disease based on microbial subtype or geography, but no validated classification system has been connected to outcome.[6] According to recent data, the death rate for necrotizing fasciitis has dropped from up to 32% in study groups between 1980 and 1998 to a range of 8.8% to 25%. This is most likely caused by more aggressive surgical treatment, more effective antibacterial therapy, and adjuvant treatment because advancements are based on observational data and randomised controlled trials are absent.[3,6]

There are multiple published prognostic predictors of mortality or limb loss. It has been demonstrated that a number of hematologic variables, including lactate and salt levels, can predict mortality at the time of admission.[7] In cases with infected extremities, clinical characteristics like age, heart rate, and temperature have been combined with white blood cell count, creatinine, and haematocrit to predict mortality and limb loss.[8]

Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin, which is involved in calcium homeostasis.[9,10] It has been proposed as a useful tool to characterize systemic inflammation, infection, and sepsis.[11-14]

Lactate dehydrogenase (LDH) may catalyze the conversion of pyruvate to lactate reversibly, which is the last step of aerobic glycolysis. In this study, we selected lactic dehydrogenase, which is a common biochemical marker, to confirm the relationship between glucose metabolic reprogramming and mortality in patients with sepsis.[15,16]

Nutritional biomarkers are often low in the acute phase of sepsis because of decreased protein synthesis and dilution by the systemic inflammatory response. However, it is not clear whether serial changes in nutritional markers such those as seen in progressive hypoalbuminemia reflect prognosis in patients with sepsis during their ICU stay.[17,18]

Therefore, we performed this prospective study for the purpose of examining the usefulness of PCT, S. LDH, Albumin as a prognostic marker for necrotizing soft tissue infections represents a valuable clinical tool indicating successful surgical eradication of the infectious focus.

MATERIALS AND METHODS

It is a prospective observational study of, total 92 patients between the age group of 18-70 years from Oct. 2020 - Nov. 2022 who were admitted in the Department of Surgery with features of necrotizing fasciitis were included in the study and was treated with extensive surgical debridement and was started on same antibiotics for all patients initially and later changed accordingly to culture and sensitivity. S. PCT, S. LDH, Albumin were sent on POD 3 and the outcome were seen after 1 week, 3 weeks. Patients with Age <18 yrs & >70 yrs, Pregnant women, Previously treated necrotizing fasciitis, Prolonged non-healing ulcers, Diabetic foot ulcers, Traumatic injuries were excluded from the study.

The data obtained were entered in a Microsoft Excel sheet, and statistical analysis will be performed using statistical package for the social sciences (Version 20). Results will be presented as Mean (Median) ±SD, counts and percentages and diagrams.

RESULTS

A total of 92 patients presenting with features of necrotizing fasciitis and treated for with extensive surgical debridement were included in this study. The study group consisted of 65 (70.7%) male and 27 (29.3%) female patients. The median age was 58.2+/-11.91 years (average 58, range 18 to 70 years). The most common pre-existing comorbidity was diabetes mellitus, occurring in 37 of the 92 patients (40.1%), while there was no trend observable for other comorbidities. The location and etiology of

Table 1: Geographic Variables

Geographical Parameters	Total (n=92)
Sex	
Male	65/92(70.7%)
Female	27/92 (29.3%)
Age	58 years (29–85)
Location of Infection	
Upper limb	6/38 (16%)
Lower limb	18/38 (47%)
Amputation	17/24 (71%)
Mortality	11/38 (29%)

all infections are summarized in Table 1.

All 92 patients underwent surgery on the day of admission, in this selected patient collective, the Amputation rate was 6 out of 81 patients with NSTIs of the extremities. The overall mortality in our study group was 11 of 92 patients (11.96%), with a mean survival of 5 days. Only 1 patient with high S.PCT, LDH and S. Albumin survived out of 92. Of the 92 patients treated for NSTI, 42 were sterile. Others were pseudomonas aeruginosa in 13, klebsiella pneumonia in 10, staphylococcus aureus in 8, streptococcus in 6 (32%), *E.coli* in 5, Acinetobacter in 4, proteus mirabilis in 2.

In 92 patients S.PCT which was measured on post operative day 3, the values were statistically measured using annova test and the Results of the patients who recovered were having S.PCT mean value as 2.82 +/-11.3 and the patients in whom amputation was done the mean of S.PCT was around 16.64 +/- 15.4 and the patient who were dead having a mean S.PCT of 41.4 +/- 25.5. The result were statistically highly significant (p <0.001) * (Table 2)

Table 2: Serum pct and Outcome

Outcome	N	Mean	Std. Deviation	F-value	P-value
Death	11	41.405	25.528	38.167	<0.001*
Recovered	75	2.829	11.302		
Amputation	6	16.648	15.432		
Total	92	8.342	18.717		

Similarly, while, S. LDH was measured on post-operative day 3, the values were statistically measured using ANNOVA test. The Results of the patients who recovered were having S.LDH mean value as 285.59+/-119.3 and the patients in whom amputation was done the mean of S.LDH was around 735.17 +/- 197.6 and the patient who were dead having a mean S.LDH of 878.36 +/- 156.9. The results were statistically highly significant (p <0.001) *(Table 3)

Table 3: S.LDH and Outcome

Outcome	N	Mean	Std. Deviation	F-value	P-value
Death	11	878.36	156.981	123.526	<0.001*
Recovered	75	285.59	119.391		
Amputation	6	735.17	197.666		
Total	92	385.78	249.195		

S. Albumin was measured on post operative day 3, the values were statistically measured using annova test. The Results of the patients who recovered were having S. Albumin mean value as 2.8+/-0.38 and the patients in whom amputation was done the mean of S. Albumin was around 2.33 +/-0.36 and the patient who were dead having a mean S. Albumin of 2.1 +/-0.38. The results were statistically highly significant (p <0.001) *(Table no. 4)

Table 4: S. Albumin and outcome

Outcome	N	Mean	Std. Deviation	F-value	Pvalue
Death	11	2.118	.3816	20.800	<0.001*
Recovered	75	2.815	.3812		
Amputation	6	2.233	.3615		
Total	92	2.693	.4554		

DISCUSSION

NSTIs are life threatening infections with a rapid course of inflammation and often sepsis and shock. Although the reported incidence of .4 cases per 100,000 population[19,20] makes it a rare disease and the treatment of necrotizing fasciitis has improved, its mortality remains high.

In a study done by jinn-mingwang *et. al*,[21] concluded that the disease is male predominance with a male (73.6%) and females (26.4%) which is similar to our study showing males (n=65), 70.7% were more commonly affected by Necrotising Fasciitis. Females constituted (n=27), 29.3% of the study population.

The peak incidence of NF was observed in patients aged between 51-60 years, which accounted for 24% of the study population. A study done by halukvayvada *et. al*[22] the mean age group effected was reported to be 55.9 yrs which is similar to our study where the mean age reported was 58.21.

A study done by Sigh G *et. al*[23], showed that most common sites were lower extremities seen in 70.8% of patients. Very rarely it affects the different regions of the body which is similar our study where 83% patients effected region was lower extremities.

Madhumita *et al*[24] in a prospective study had reported Type-II diabetes as the commonest co-morbidity, and has been documented as co-morbidity in 59%, (n=59%) of study population. P-Value calculated using one sample Z test was 0.0001, hence the association of type II DM and NF is statistically significant which was similar to our study seen in 37(40.2%) of the patients having T2DM.

Necrotizing fasciitis is a systemic inflammatory infectious disease where most of the patients presents with sepsis and biomedical markers like serum procalcitonin, serum Lactate dehydrogenase and serum albumin were taken as a part of our study in predicting the mortality and morbidity of patients with NF.

Procalcitonin was found to be linked with sepsis and has been part of research since the last three decades. A study done by Delevaux *et al.*[14] showed a value of procalcitonin >0.5 ng/mL is a marker of bacterial infection with sensitivity 65%; specificity 96%; positive predictive value 89%; and a negative predictive value 84%. No false positive results were reported for procalcitonin concentrations >1.2 ng/mL.

Serum LDH was reported as a predictive marker in many conditions and diseases such as sepsis, infection, acute myocardial infarction, cirrhosis, and malignancies. A study done by Lu J *et al*[15] found that serum LDH was associated with mortality in patients with sepsis and they found that the positive correlations of LDH and proinflammatory mediators as well as lactate revealed that the glucose metabolic reprogramming of immune cells contributed to the release of proinflammatory mediators and accumulation of lactate. The study also found that the elevated levels of serum LDH with higher mortality.

Inflammation reduces levels of some proteins such as albumin, which are called negative acute phase proteins (because their levels decrease with the inflammatory process). Albumin values tend to fall in the presence of an active phase reaction such as sepsis and trauma. Previous study by Mei Yin *et al*[17] in 2016, 116 patients were included in the study, the overall 28 day mortality was 26.7%. Compared with the survivor group, non-survivor patients had lower serum albumin values. The ROC curve data showed that albumin level was a strong predictor of 28 days mortality, with the optimal cut-off value being 2.92 g / dl. Similar to our study where mortality and amputation was seen in patients with albumin levels ranging from 2.23+/-0.3 mg/dl.

Our study group consisted entirely of septic patients, and all patients underwent emergency surgery on the day of admission to our hospital. Although our data do not permit us to determine an optimized time point of operation, we believe that immediate surgical treatment is essential for successful therapy.

The importance of radical surgical debridement, resection of all necrotic tissue based on the aggressiveness of the infection, and early amputation of a limb has been described in previous studies. Limited incisions, drainage as a monotherapy, and one time debridement's have been shown to be ineffective and do not decrease mortality. However, aggressive surgical resections are sometimes not radical enough, and extensive reoperations or a more proximal amputation in the further course of disease may be necessary.

CONCLUSION

Necrotizing fasciitis is a lethal soft tissue infection mostly affecting males in middle age group. Major predisposing factors age more than 50 years, and diabetes mellitus. Lower extremity is the most common site affected. The present study proved that the procalcitonin LDH, albumin helps to predict the severity and the prognosis of the infection. Sepsis and the septic shock are the major cause of death. Amputation is the replace mental therapy. Early and aggressive debridement's, often at repeated sittings, are the mainstay in the treatment of necrotizing fasciitis, supplemented by adequate antibiotics and supportive measures are important in the treatment of the necrotising fasciitis. Thus, to conclude S.PCT, S.LDH, Albumin are the important prognostic markers and are important markers indicating the adequacy of surgical resection and eradication of septic foci in patients with necrotizing fasciitis.

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