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ORIGINAL RESEARCH

Necrotizing Soft Tissue Infection: Evaluation and Management

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ABSTRACT

Aim: To determine the presentation of patients diagnosed with NSTIs and the in-hospital patient outcomes (including antibiotic treatment, surgery, and mortality) associated with this disease.

Material and methods: The study was prospective cohort study conducted from February 2020 to February 2022in patient's admitted in the department of general surgery through outpatient department/Emergency/transferred from other departments.Case of NSTI were included in the study. Viral marker for HBsAg and HCV were tested prior to surgery and informed consent for HIV testing was taken prior to HIV test.The patients were underwent debridement on the basis of extension of the infection. Tetanus vaccine was given to each patient followed by intravenous prophylactic antibiotics. Local or general anaesthesia was used according to its merit in each case. Skin was incised mainly till fascia or depending upon the depth of infection, drainage of pus and debridement of soft tissue.Patients were followed up for 1 month post-operatively with daily aseptic dressings till healthy granulation tissue appears followed by soft tissue coverage by flap or grafting and the data was collected as per the Performa attached and the data collected was tabulated and subjected to the study.

Results: It was seen thatcomorbidities like burns(p value =0.039) and cardiac diseases(p value=0.043) had statisticallysignificant association with the outcomes.A statistically significant association was seen among systemic symptoms likehypotension (p value= 0.003), and laboratory investigations like increased creatinine (pvalue=0.002) with the outcomes.

Conclusion: NSTI is a rare but highly morbid disease entity. Therefore early detection and aggressivedebridement are the cornerstones of NSTI treatment. Antibiotictherapy and intensive care support is also essentialin severe cases of NF. A high index of suspicion and timely surgical intervention, with repeated debridements and early ICU admission can minimize the morbidity and mortality of necrotizing fasciitis.

INTRODUCTION

Necrotizing soft tissue infections (NSTI) are rapidly progressive skin and soft tissue infections that cause widespread tissue necrosis and are associated with systemic illness. The term "NSTI" has been increasing used in lieu of the term "necrotizing fasciitis", originally

coined by BL Wilson in 1952, to encompass cases where necrosis extends beyond the fascia and can involve the muscle, skin and surrounding tissues.[1,2] Despite advances in the care, mortality from NSTI has remained relatively high at 25–30% for the past thirty years, and has only recently seen a decrease to just over 20%. Case fatality rates remain highest when NSTI is accompanied by shock and/or host factors such as advanced age, comorbidities or immunocompromised state[3,4].

Necrotizing soft tissue infections can be classified on the basis of microbiology, location or depth of tissue involvement. Guilianoet al[5] originally described 2 distinct microbiologic profiles in NSTI; however, the classification system has evolved over time with the recognition of additional pathogen classes.

a. Type 1 is the most common infection seen, and describes polymicrobial infections, often including anerobes,
b. Type 2 infections are monomicrobial and typically involve GAS or less commonly Staphylococcus aureus.
c. Monomicrobial NSTI can also be caused by Clostridium spp., and rarely by Vibrio vulnificans (from exposure to warm coastal seawater or consumption of raw oysters; classified by some as Type III), Aeromonashydrophila (from exposure to leech therapy or traumatic lesions in fresh water) as well as fungi (classified by some as Type IV)[6] such as Apohyphomyces spp. Certain monomicrobial etiologies have presented as local outbreaks (e.g. community-associated MRSA in Los Angeles)[7] or exhibited geographic clustering (e.g. Klebsiellapneumoniae among diabetic patients with NSTI in Taiwan)[8].

The etiology of necrotizing soft-tissue infections (NSTIs) is not always obvious. Pathogens can gain entry with a small site of inoculation, blunt trauma, cutaneous infections, post-surgical complications, hematogenous spread, burns, childbirth, or idiopathic causes.[9,10]Individuals with multiple co-morbidities are at an increased risk for NSTI. Risk factors include recent trauma (one of the most common risks[11]), intravenous drug abuse, diabetes (strongly associated with type I NSTI), steroid use, immunocompromise, peripheral vascular disease, obesity, liver disease, chronic renal failure, and alcohol use.

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has been used to gauge the likelihood of NSTI.The LRINEC score includes 6 variables associated with NSTI and are used to calculate a score correlating to the risk of NSTI. Patients with an LRINEC score of 6 or higher have been considered at highest risk for the presence of a necrotizing infection. While the score may suggest necrotizing fasciitis, it should not be used to exclude the diagnosis, as the score was retrospectively developed and demonstrates poor sensitivity in patients in the emergency department (ED). Serum lactate level, which, if elevated, should also increase concern for NSTI.[12]

Aggressive surgical debridement of all necrotic tissue is the definitive treatment of NSTIs. Studies suggest improved survival in patients undergoing surgery within 24 hours of admission, compared to those in whom surgery is delayed,[13,14] and survival further increases with operative intervention within 6 hours.[15]The present study was conducted to determine the presentation of patients diagnosed with NSTIs and the in-hospital patient outcomes (including antibiotic treatment, surgery, and mortality) associated with this disease.

MATERIALS AND METHOD

The study was prospective cohort study conducted from February 2020 to February 2022in patient's admitted in the department of general surgery through outpatient department/ Emergency/ transferred from other departments.

INCLUSION CRITERIA

All patients willing to give consent and continue with treatment

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All patients irrespective of age or gender clinically diagnosed with NSTI

EXCLUSION CRITERIA

Patient not giving consent for the study/surgery.

Patients with osteomyelitis, malignant lesions of skin, ischaemia, venous ulcers and aretrial ulcers.

The patients were worked up thoroughly and subjected to:

- Detailed history and clinical examination.
- Routine haematological investigation: Hb, TLC, DLC, PT, PTTK, INR, RBS, Blood Urea,Serum Creatinine,S.Electrolytes
- Viral markers: HCV, HBsAg, HIV 1&2
- Chest X-Ray
- Ultrasound or MRI (in selected cases)
- ECG
- PUS culture and sensitivity
- Pre-anaesthetic check-up.

PRE-OPERATIVE PREPARATION

Case of NSTI were included in the study. Viral marker for HBsAg and HCV were tested prior to surgery and informed consent for HIV testing was taken prior to HIV test. Informed consent for surgery was obtained. The patient was kept fasting after midnight with I.V. fluids for maintenance. On next morning, i/v antibiotic (Cephalosporin) as prophylactic measure was given. Pre-medication was given half an hour before the operative procedure and patient was asked to void urine just before being shifted in operating room.

OPERATIVE PROCEDURE

The patients were underwent debridement on the basis of extension of the infection. Tetanus vaccine was given to each patient followed by intravenous prophylactic antibiotics. Local or general anaesthesia was used according to its merit in each case. Skin was incised mainly till fascia or depending upon the depth of infection, drainage of pus and debridement of soft tissue. The wall of each abscess found was thoroughly curetted and all pyogenic membrane was removed. A firm dressing was applied. Pus samples and tissue samples were sent to microbiology lab for culture and sensitivity. After 24 hours the old dressing is changed with a fresh new aseptic dressing. Patients remained ambulatory during the postoperative period.

POST OPERATIVELY

Dressings were changed on daily basis, checking on how soaked the dressings become or upon the patient's pain level, until healing is complete. Patients remained ambulatory during the postoperative period. Postoperative antibiotics were used according to the report of bacterial culture and sensitivity.

FOLLOW UP

Patients were followed up for 1 month post-operatively with daily aseptic dressings till healthy granulation tissue appears followed by soft tissue coverage by flap or grafting and the data was collected as per the Performa attached and the data collected was tabulated and subjected to the study.

STATISTICAL ANALYSIS

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical

analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using chi square test and the level of significance was set at $p < 0.05$.

RESULTS

There were 79% males and 21%. The mean age of the subjects was 44.38±9.03years. Out of all the sites, 22% affected sites were in upper extremities, and 78% affected sites were inlower extremities. The mean duration of symptoms in days was4.73±2.89.Table 1 showed that 31% ofsubjects had diabetes mellitus, 3% had liver cirrhosis, 7% had burns, 28% had blunt trauma, 15% had Skin Infection, 7% had cardiac diseases, 6% had renal diseases, and 3% hadimmunosuppressant.Out of all the subjects,78% had erythema, 93% had swelling, 98% had pain, 59% had blisters, 54% had hemorrhagicbullae, 26% had crepitus, 94% had skin necrosis, and 81% had pus discharge.

Table 1: Comorbidities and symptoms/signs among the study subjects

Comorbidities	**N**	**%**
Diabetes Mellitus	31	31
Liver cirrhosis/Chronic hepatitis	3	3
Chronic Infected Burn	7	7
Blunt Trauma	28	28
Skin Infection	15	15
Cardiac Disease	7	7
Renal Disease	6	6
Immunosuppressant	3	3
Symptoms		
Erythema	78	78
Swelling	93	93
Pain	98	98
Blisters	59	59
Hemorrhagic Bullae	54	54
Crepitus	26	26
Skin necrosis	94	94
Pus Discharge	81	81

Out of total subjects, 63% subjects had leukocytosis, 42% had anaemia, and 27% had increased creatinine.11% of the subjects had bronchial pneumonia, 4% had acute renal failure, 6% had septic shock and 3% had MODS.

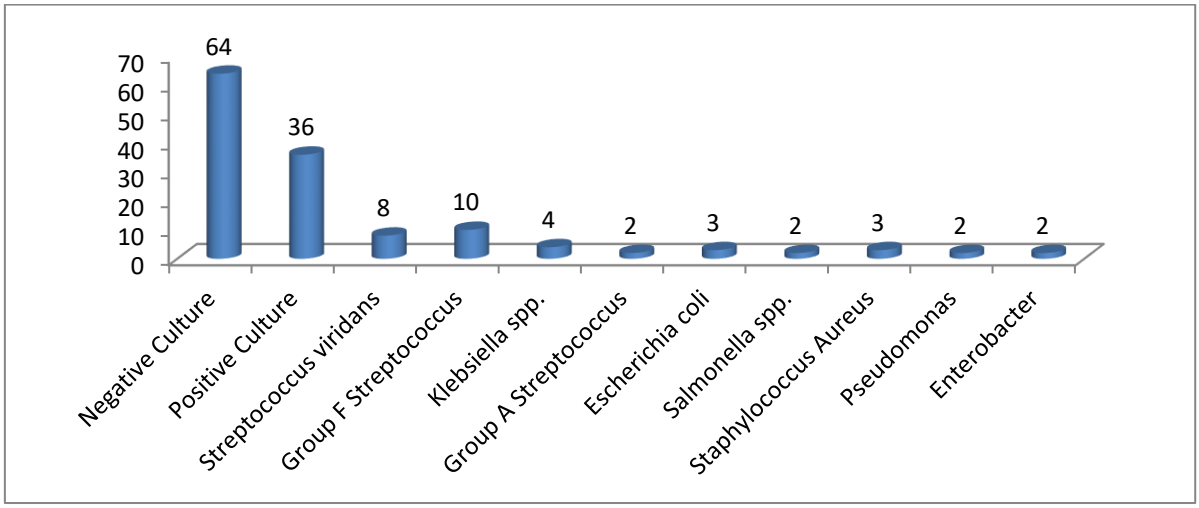
Table 2: Systemic symptoms, laboratory investigations and systemic manifestations due to NSTI among the study subjects

Parameters	**N**	**%**
Fever (> 38.0 °C)	43	43
Tachycardia (> 100 beats/min)	54	54
Hypotension (SAP < 100 mmHg)	36	36
Tachypnea (> 20/min)	51	51
Leukocytosis (>10,000 umol/L)	63	63
Anemia (<10 g/dL)	42	42
Increased creatinine (>1.2mg/dl)	27	27
Systemic manifestations		
Bronchial Pneumonia	11	11
Acute Renal Failure	4	4
Septic Shock	6	6
MODS	3	3

ISSN 2515-8260 Volume 9, Issue 3, Winter 2022

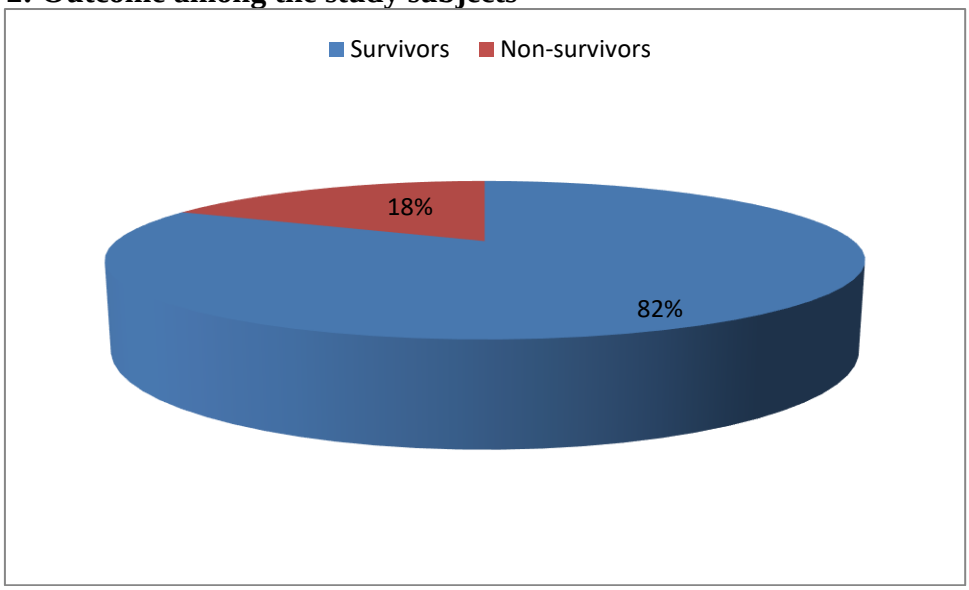
Wound cultures were depicted in graph 1. Among all the subjects, 64% had negative culture, 36% had positive culture. Most common micro-organisms isolated were streptococcus followed by Klebsiella spp. and Escherichia coli as well as Staphylococcus Aureus. In the first operation, 54% subjects had undergone debridement, 28% had amputation/disarticulation, 7% had incision and drainage, and 11% had anterior abdominal wall debridement. In thesecond operation, 4% subjects underwent debridement, 9% had amputation/ disarticulation and6% had skin grafts.

GRAPH 1: Wound cultures



It was observed that among all the subjects 82%were survivors, and 18% were non-survivors(graph 2).

GRAPH 2: Outcome among the study subjects



Association of comorbidities and outcome were seen in Table 3. It was seen thatcomorbidities like burns(p value =0.039) and cardiac diseases(p value=0.043) had statisticallysignificant association with the outcomes.

Table 3: Association of comorbidities and outcome

Comorbidities	N	Survivors	Non-survivors	p value
Diabetes Mellitus	31	30	1	0.53
Liver cirrhosis/Chronic hepatitis	3	1	2	0.11
Burns	7	3	4	0.039*

ISSN 2515-8260 Volume 9, Issue 3, Winter 2022

Blunt Trauma	28	24	4	0.36
Skin Infection	15	14	1	0.11
Cardiac Disease	7	5	2	0.043*
Renal Disease	6	4	2	0.09
Immunosuppressant	3	1	2	0.18

*: statistically significant

Statistically significant association ofsymptoms like blisters (p value=0.024) and skin necrosis (p value=0.016) was found with the outcomes (table 4).

Table 4: Symptoms/signs among the study subjects

Symptoms	N	Survivors	Non-survivors	p value
Erythema	78	62	16	0.48
Blisters	59	41	18	0.024*
Crepitus	26	19	7	0.13
Skin necrosis	94	76	18	0.016*
Pus Discharge	81	63	18	0.37

*: statistically significant

Table 5 illustrated the association of systemic symptoms and laboratory investigationswith outcome. A statistically significant association was seen among systemic symptoms likehypotension (p value= 0.003), and laboratory investigations like increased creatinine (pvalue=0.002) with the outcomes.

Table 5: Association of systemic symptoms and laboratory investigations with outcome

Parameters	N	Survivors	Non-survivors	p value
Fever (> 38.0 °C)	43	32	11	0.35
Tachycardia (> 100 beats/min)	54	39	15	0.12
Hypotension (SAP < 100 mmHg)	36	12	24	0.003*
Leukocytosis (>10,000 umol/L)	63	48	15	0.27
Anemia (<10 g/dL)	42	32	10	0.46
Increased creatinine (>1.2mg/dl)	27	14	13	0.002*

*: statistically significant

DISCUSSION

Necrotizing soft tissue infections (NSTIs) are severeinfections of any layer of soft tissue compartment includingsuperficial and deep soft tissues. Mortality in patients with NSTIs is high, ranging from 14 to 42%.Early diagnosis and treatment are essential for survival.[43]Treatment consists of broad-spectrum antibiotics, wide surgical debridement, and supportive care.Antibiotic treatment is initially broad spectrum and thentailored to antimicrobial susceptibilities of isolated organisms. Patients may require multiple debridementsor amputations to ensure adequate source control[16]. The results showed that there were 79% males and 21%. This is most possibly from the increasedincidence of Fournier's gangrene in men. The mean age of the subjects was 44.38±9.03years in this study. Christophe Mpirimbanyiet al[17]in their study found that ninetytwo(52.6%) patients were male and 83 (47.4%) patients were female. The mean age was 43.8 years(range 12 and 92 years).Jing-Chun Zhaoet al[18] in their study revealed similar age and gender disturbance. Thirty-seven patients were adults (mean age:45.6 years) and male-to-female ratiowas 4.6:1 (32 male and seven female). Our findings were in concordance with the above studies.

In our study; out of all the sites, 22% affected sites were in upper extremities, and 78% affected sites were inlower extremities. This is because of the fact that majority of NTI patients are diabetic which lead to diabetic neuropathy, hence trauma to the lower limb goes unnoticed. Evangelos P. Misiakoset al[19] too mentioned that twenty-two patients had

infectionof the lower limbs (35.5%). The upper limbs' axillary region wasinfected in only five patients (8.1%) and the infection was spreadin the abdominal wall in nine patients (14.5%). Similarly Jing-Chun Zhaoet al[18] in their study found that 33 patients had Necrotizing fasciitis (NF) of thelower limbs, and 6 patients had NF of the upperlimbs.

In our study, it was reported that 31% ofsubjects had diabetes mellitus, 3% had liver cirrhosis, 7% had burns, 28% had blunt trauma, 15% had Skin Infection, 7% had cardiac diseases, 6% had renal diseases, and 3% hadimmunosuppressant. Co-morbidities like diabetes lead to polyneuropathy and arteriopathy, causing unnoticed trauma and delayed wound healing which lead to increased chances of polymicrobial infection. Jimenez MN et al[20] in their depicted that the most common pre-existing comorbidities were diabetes (60.7%). Gohet al[11] calculated the prevalence of diabetesmellitus in patients with NF at 44.5%. Evangelos P. Misiakos et al[19] too mentioned that diabetes mellituswas the most common comorbidity, as 25 patients had deregulateddiabetes mellitus (40.3%).

Christophe Mpirimbanyiet al[17] in their study found that eighty-six (49%) patients presented with comorbiditieswith the most common being cardiac disease (n = 29,17%), diabetes mellitus (n = 28, 16%), smoking (n = 23,13%), and human immunodeficiency virus (HIV) infection(n = 20, 11%). This difference might be due to variation in study area.

Out of all the subjects,78% had erythema, 93% had swelling, 98% had pain, 59% had blisters, 54% had hemorrhagicbullae, 26% had crepitus, 94% had skin necrosis, and 81% had pus discharge.The mean duration of symptoms in days was 4.73±2.89. Due to short duration and multi-systemic involvement, early and aggressive intervention is required. Evangelos P. Misiakoset al[19] mentioned that the vast majority hadtenderness (90.3%) and pain (77.4%) on the infected site. In 46 patients, the site of infectionwas edematous (74.2%), and in 43 patients, the infected skin waserythematous (69.4%).Anaya DA[21] and Kalaivani Vet al[22] revealed similar findings too. Similarly Jing-Chun Zhaoet al[18] in their study reported that clinical characteristics on presentation includedspreading erythema, swelling, and pain. Duration ofsigns and symptoms varied from 1 to 8 days (mean4.6 days).

In the first operation, 54% subjects had undergone debridement, 28% had amputation/disarticulation, 7% had incision and drainage, and 11% had anterior abdominal wall debridement. In thesecond operation, 4% subjects underwent debridement, 9% had amputation/disarticulation, and6% had skin grafts. It was seen that 47% had Hydrogen Peroxide+Betadine dressing, 19% had EUSOL dressing, 8% had normal saline dressing, 5% had vacuum dressing, and 21% had a combination of Multiple Dressings. According to Christophe Mpirimbanyiet al[17], all patients underwentoperation, with the most common initial operationsdebridement (n = 90, 51%) and amputation or disarticulation(n = 52, 30%). A second operation was performedin 24 patients with the most common second operationsbeing skin graft (n = 12, 50%) and amputation or disarticulation(n = 5, 21%).

It was observed that among all the subjects 82%were survivors, and 18% were non-survivors.It was seen thatcomorbidities like burns(p value =0.039) and cardiac diseases(p value=0.043) had statisticallysignificant association with the outcomes. Statistically significant association ofsymptoms like blisters (p value=0.024) and skin necrosis (p value=0.016) was found with the outcomes. A statistically significant association was seen among systemic symptoms likehypotension (p value= 0.003), and laboratory investigations like increased creatinine (pvalue=0.002) with the outcomes.It was also found that all the systemic manifestations viz. bronchial pneumonia, acute renal failure, septic shock and MODS due to NSTI were significantly associated with the outcomes with p value = <0.01.

Christophe Mpirimbanyiet al[17]in their revealed that the overall mortality was46 (26%).Factorsassociated with mortality on multivariate analysis included: presence of shock at admission and renal failure. Differences in mortality may be due to differencesin practice patterns, microbiology, or epidemiology.Factors like advanced age, immunosuppression

byhuman immunodeficiency virus infection, and elevatedwhite blood count were not significantly associated with mortality in their study, which is in contrast to our study. This is likely due todifferent population demographics with a lower mean age and lower incidence of comorbidities. According to Evangelos P. Misiakoset al[16], mortality rate of their series was 17.7%. Patients' comorbidities showed no statistically significant correlation with mortality. Although not statistically significant, their results are indicative for a correlation between renalimpairment and chronic heart failure and mortality. Gohet al[11] concludedthat a median mortality ratio was 21.5%.

The CDC's most recent NF mortality rate is 15-33%. In 2013, Faraklaset al[23] quoted mortality of 13% and worked on the development and validation of necrotizing soft tissue infection mortality risk calculator using NSQIP. The criteria included: age >60, partially dependent functional status, hemodialysis, ASA-4, emergent surgery, septic shock, and low platelets. The Fournier gangrene severity index (FGSI) created in 1995, used in NF of the perineum, including temperature, heart rate, respiratory rate, sodium, potassium, hematocrit, leucocytes, bicarbonate, is a mortality predictor cited in the literature.New studies showing rates of 12-25%.

There are limitations to be considered while interpretingthe results. These data are from a single hospital. Therewere no data collected on management prior to hospitaladmission. We did not collect dataon long-term functional outcomes. The long-term complicationswould help to characterize the disease sequelae andidentify the factors related to favorable and unfavorableNSTI long-term functional outcome.

CONCLUSION

NSTI is a rare but highly morbid disease entity. Therefore early detection and aggressivedebridement are the cornerstones of NSTI treatment. Antibiotictherapy and intensive care support is also essentialin severe cases of NF. Anaerobic tissue culture and frozensection biopsy could be adopted as routine tests fordiagnosis and decision-making in NF. These findingsshould inform clinical decisions about the treatment of individual patients with NF.Regardless of ethnicity and case mix index and severity, especially in an aging population with multiple comorbidities, delay in time to surgical consultation and time to operation can occur when patients are admitted to a non-surgical service. A high index of suspicion and timely surgical intervention, with repeated debridements and early ICU admission can minimize the morbidity and mortality of necrotizing fasciitis.

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