International Surgery Journal
Harikrishnan CP et al. Int Surg J. 2017 Mar;4(3):883-889
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20170610

Original Research Article

Necrotizing soft tissue infections: a clinical profile

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Received: 01 February 2017
Accepted: 14 February 2017

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ABSTRACT

Background: Necrotizing soft tissue infections (NSTIs) are a rapidly progressing fatal disorder and the prognosis of which depends on early diagnosis and management.
Methods: This was a prospective observational study carried out in the surgical department of Jubilee Mission Medical College and Research Institute from August 2010 to August 2012 in 75 patients presented with NSTIs having extensive tissue necrosis. The following parameters were analyzed: demographics, infection site, laboratory findings, isolated microorganisms, antibiotics used, total hospital stays, predisposing factors, associated comorbidities and secondary management performed.
Results: 75 patients with NSTIs were enrolled in this study. Youngest in this series is 3 years and oldest patient was 89 years old, with most-commonest age group being 41 to 60 years. Average age of patients is 55 years. Male: Female is in the ratio 9:1. Diabetes mellitus was seen as the common underlying disease in 20 patients. Lower limb (85%) was the most commonly affected site. Most of the patients (69) arrived with a delay in intervention of more than 3 days. Average delay in intervention from onset of symptoms of patients is 10 days. After analyzing, 26 patients were categorized in to Group 1 (survival) and the remaining 49 were into Group 2 (morbidity/mortality). In death patients Creatinine is very high 2.3 mg/dl and it is least in non-morbidity. In cases with morbidity it varies from 1.27-1.87 mg/dl. The incidence ratio of monomicrobial: polymicrobial: sterile microbial culture was 2:2:1. E. coli is the highest seen organism in monomicrobial and polymicrobial cases. Klebsiella is mostly seen in poly organism. *Staphylococcus aureus* is seen reasonably in polymicrobial and monomicrobial cases. Meropenem and imipenen are instituted as the most sensitive drugs with sensitivity above 90%. Most patients where managed by healing with secondary intention or split skin grafting. The average number of debridement is 1.2. The average duration of hospital stay is 26 days. 12 patients developed septicemia with multi organ dysfunction syndrome (MODS) as complications. Of these three patients survived. Mortality rate was 12%.
Conclusions: NSTI is a lethal disease and early diagnosis based on high index of clinical suspicion and prompt and aggressive surgical, antibiotic and supportive therapy is essential for the better prognosis and early recovery of the disease.

Keywords: Blood parameters, Mortality, Microbial culture pattern, Necrotizing soft tissue infections

INTRODUCTION

Necrotizing soft tissue infections (NSTIs) are fulminant infections of any layer of the soft tissue compartment associated with widespread necrosis, systemic toxicity and a high mortality rate if not treated early. Establishing the diagnosis of NSTI can be the main challenge in treating patients with NSTI, and knowledge of all available tools is the key for early and accurate diagnosis.[1] Aggressive soft tissue infections are rare, difficult to diagnose, and require immediate surgical intervention plus administration of antimicrobial agents. Failure to do so result in an extremely high mortality rate

(80 to 100%), and even with rapid recognition and intervention, current mortality rates remain approximately 30 to 50%.[2]

The Food and Drug Administration (FDA) has classified skin and soft tissue infections in to two categories based on the microbiological characteristics.[3,4] Type I infections are the most common forms accounting for 80% or more of all the NSTIs, for example, Fournier's gangrene and Ludwig's angina.[5] These are mostly polymicrobial infections (caused by both aerobes and anaerobes). Type II infections are usually mono-microbial (caused by Streptococcus or the S. aureus) and usually follow a minor injury accounting for 10-15% of all NSTIs.[6,7]

Individual factors that have been implicated to increased mortality from NSTI includes increasing age, diabetics mellitus, peripheral vascular disease, obesity, chronic renal failure, HIV, alcohol abuse, IV drug abuse, abscess, blunt or penetrating trauma, insect bite, surgical incision and delaying surgical debridement etc. Unfortunately, the small number of patients reported in most series of NSTIs has precluded the definitive identification of risk factors for mortality.[8] The aim of this study was to determine the clinical characteristics, predisposing factors, microbial culture pattern involved in the pathogenesis of NSTI and to analyze the outcome and its management.

METHODS

This prospective observational study was carried out in the surgical department of Jubilee Mission Medical College and Research Institute from August 2010 to August 2012. 75 patients who presented with necrotizing soft tissue infections having extensive tissue necrosis, that followed a rapid, progressive, course was evaluated in the study. Patients with pyaemic abscesses, cellulitis, impetigo, furuncles, carbuncles and erysipelas were excluded.

Name, age, occupation, socioeconomic status, residence, onset of symptoms, predisposing factors, and co morbidities were recorded in the proforma case sheet. The presenting complaints and details were recorded in the chronological order.

Laboratory tests were performed immediately after admission. They included complete blood count (hemoglobin level, WBC and platelet [PLT] count), blood sugar-fasting and post prandial (FBS, PPBS) and corresponding urine sugar on regular basis, routine urinalysis: albumin, sugars, ketones' and microscopy, blood urea and serum creatinine, serum electrolytes, lipid profile, radiograph of affected part (lower limbs), wound discharge for culture and sensitivity, arterial and venous doppler study (optional), liver function test, arterial blood gas analysis and C- reactive protein.

All patients were treated according to a uniform protocol. After complete clinical assessment resuscitation was initiated and continued until cardiovascular stabilization had been achieved. An assessment was made of the extent of infection and all patients had prompt and thorough surgical debridement of all necrotic tissue. The digits or limbs were amputed where necessary. Intensive care was provided and included mechanical ventilation, invasive monitoring and inotropic support as indicated by the condition of the patient.

All patients were initially given cephalosporin and metronidazole and when found necessary aminoglycosides were given with subsequent modifications according to culture and sensitivity. Blood, surface swabs and debrided tissues were cultured for bacteria. All wounds were inspected within 24 hours after debridement and a decision made regarding further debridement.

Wounds were cleaned twice daily with hydrogen peroxide and povidone iodine solution. The raw areas were covered with split skin graft once they were healthy and granulating. Some cases healed by secondary intention. Some cases had to undergo major amputations for control of infection and its spread. In few cases, plastic reconstruction of the deformities had been undergone. The hospital course and mortality were recorded for all patients.

Diabetic patients were managed by diabetic treatment like diabetic diet, sugar restriction and anti-diabetic treatment were given with oral hypoglycemic drugs and insulin. Patients who developed renal complications were managed by salt restrictions, dialysis and supportive renal treatment. Supportive treatment was given for patients who had bed sores as complications of NSTIs by regular dressings and water/ air beds. Patients who went into septicemia were managed in intensive care units on ventilators under guidance of anesthetist and physicians.

In this study patients were divided into two groups. In the first group, there is minimal morbidity (Group 1: survival) and in the second group there is greater morbidity and also some mortality (Group 2: morbidity/mortality). After discharge, follow up was done up to 3 months regularly on outpatient basis for dressing, further management of diabetes and hypertension and also to review liver and renal parameters. Major amputation patients were advised for crutches and artificial prosthesis after 2 months after surgery. On mean time patients had physiotherapy exercises of the stump.

Statistical analysis

Statistical analysis is conducted based on Manifold classification and further testing of hypothesis. Two way and three way tables are prepared to compare the influence of blood parameters, age, intervention delay and associated co morbidities on morbidity and mortality. Suitable graphs like subdivided bar diagrams, pie

diagrams, circles and cones were used to present the data. The significance of statistical parameters is tested using normal tests, T - test, analysis of variance level of significance.

RESULTS

Table 1: Patient details.

Age in years	No. of cases	Percentage
<=15	3	4
16-40	12	16
41-60	42	56
61-80	13	17.3
>80	5	6.6
Sex		
Male	68	90.7
Female	7	9.3
Site involved		
Lower limb	64	85
Upper limb	5	7
trunk	2	3
Fournier's gangrene	4	5
Co morbidities		
Diabetes mellitus	20	39
Hypertension	9	18
Peripheral vascular disease	5	10
Chronic renal failure	5	10
Liver diseases	0	0
Immunosuppressed/ on steroids	2	4
Others (IHD, stroke)	10	19
Intervention delay		
<=3 days	6	8
4-7 days	27	36
8-14 days	30	40
15-28 days	10	13.33
29-32 days	2	2.6

Table 1 presents the patient details participated in the study. The study enrolled 75 patients diagnosed with NSTI. They are all treated together following a uniform protocol. 68 patients (91%) were males and 7 (9%) were females. The youngest patient of this study is of 3 years age and eldest one is 89 years old. More than 50% of patients had an age 40-60 years and the disease is distributed symmetrically in lower and above of this age group. Most of the patients (69) arrived with a delay in intervention of more than 3 days. Only 2 patients exceeded the intervention beyond one month of about a period of 4-7 days or 1week to 2 weeks. Average intervention delay period of patients is 10 days. The most common site involved is the lower limb followed by upper limb followed by perineum/genitalia i.e. Fournier's gangrene. Diabetes mellitus is the most common co morbidity found in association with necrotizing soft tissue infections followed by hypertension and peripheral vascular disease.

After analyzing, out of 75, 26 patients were categorized in to group 1 and the remaining 49 were into group 2. The mean value of HB was decreased in group 2 and the remaining bold parameters were increased in the same group when compared to group 1 but this difference is statistically not significant. But a significant increase in creatinine level was observed in group 2 patients when compared to group 1 as tabulated in Table 2.

Table 2: Analysis of blood parameters in two groups.

Parameters	Group 1 (Survival)	Group 2 (morbidity /mortality)	P value
HB	12.20±1.41	11.82±2.21	0.4318
TC	15594.23±4406.99	19059.18±10122.48	0.1012
ESR	64.27±39.96	73.18±31.99	0.2962
RBS	189.77±126.10	197.65±154.86	0.8241
Creatinine	1.20±0.45	1.57±0.82	0.0378

Table 3: Age wise outcome of NSTI patients.

Age (in years)	Outcome (morbidity/mortality)					
	Large ulcer	Toe disarticulation	Amputation	Death	Nil (Group1)	Total
<=15	1	-	-	-	2	3
16-40	8	-	-	-	4	12
41-60	12	3	7	5	15	42
61-80	3	1	1	3	5	13
>80	2	-	2	1	-	5
Total	**26**	**4**	**10**	**9**	**26**	**75**

Table 3 presents the age wise outcome of NSTI patients. In group 2 large ulcers was observed in 26 patients and high number under the age group of 41-60 years. Mortality was seen in 9 patients from group 2 and found large ulcers are the main morbidity in 5 patients. Amputation is high in late 80 years in 2 out of 10 cases. The ratio of occurrence of large ulcer: toe disarticulation: amputation: death: no mortality or morbidity was 5:1:2:2:5 and p value = 0.9840. Table 4 presents the association of morbidities with blood parameters. Out of all 75 cases, 69 patients had high ESR. In 10 cases of amputation, total count and ESR are high in all patients and RBS and creatinine is also abnormal except in 1 or 2 cases. Large ulcer is associated with high ESR and total counts and all toe disarticulation patients had abnormal ESR, RBS and creatinine values.

Table 4: Analysis of outcome in relation to blood parameters.

Outcome	HB	TC	ESR	RBS	Creatinine
Nil (Group1)	12.20±1.41	15594.23±4406.99	64.27±39.96	189.77±126.10	1.20±0.45
Amputation	11.11±2.73	27548±12798.19	79.00±39.16	330.4±239.64	1.87±0.71
Large ulcer	12.51±1.47	18066.15±7986.49	68.54±31.96	139.00±88.53	1.27±0.46
Toe disarticulation	12.08±2.09	11115.00±882.93	86.00±26.09	252.75±56.62	1.48±0.81
Died	10.72±2.59	19667.78±14354.65	73.78±26.14	181.22±127.83	2.30±1.26

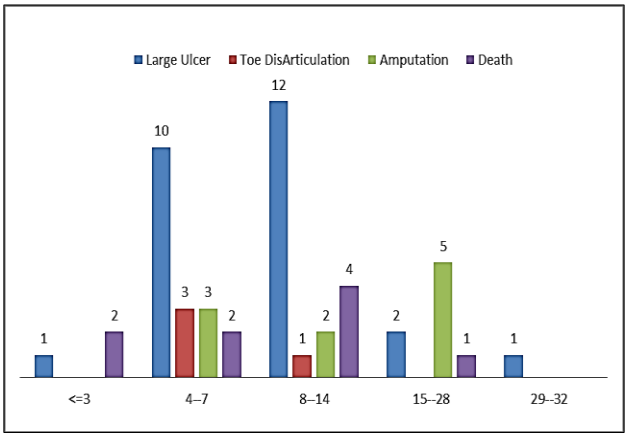

Figure 1: Intervention delay versus morbidities in NSTI patients.

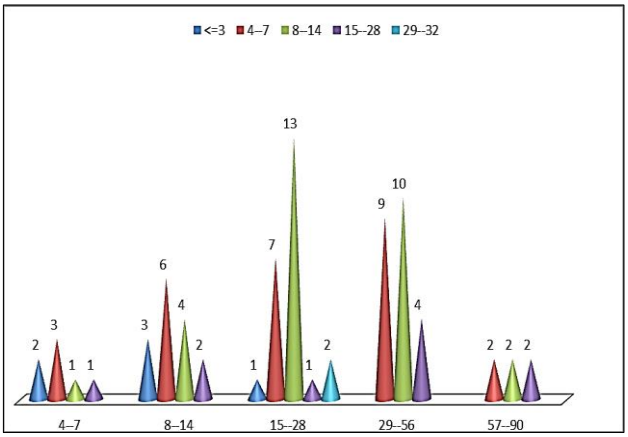

Figure 2: Intervention delay versus hospital stay.

Figure 1 explains the interventional delay in various cases of morbidities. Symptom onset intervention time had no much effect in the cases of large ulcer patients as 22 out of 26 patients has only intervention delay of 4-14 days. Among toe disarticulation patients the intervention period is 4-7 days in ¾ patients. Amputation patients have intervention delay period. 5 out of 10 patients had delayed intervention by 2-4 weeks and 2 out of 10 patients by 1-2 weeks.

If symptom onset intervention time is <=3 days average hospital stay is 10 days only and if it is 4-7 days average hospital stay is 1 month. About 2-4 weeks is needed as hospital stay for a delay in intervention of 8-14 days in 45% patients and another 33% needed 1month to 2 months hospital stay. If average intervention delay is 15-28 days the average hospital stay is 29-56 days as depicted in Figure 2 and on comparison of these parameters the difference was found to be insignificant with each other (p value = 0.9984).

Average hospital stay is too high in Amputation patients with high variability in each patient and minimum in death cases. Toe disarticulation cases required additional 6 days compared to non-morbid cases and Large Ulcer cases needed additional 15 days. The average hospital stay in case of death patients is lower because of two early deaths, due to missed diagnosis of cellulitis instead of life threatening necrotizing soft tissue infections and improper selection of narrow spectrum antibiotics instead of broad spectrum antibiotics.

The pattern of organisms cultured from wounds was given in Table 6. The number of patients infected with one type of microorganism in the wound culture was 32, whereas multiple infected organisms was seen in 30 patients. No microorganisms were found in 13 cases. *E. coli* was the most common seen organism in monomicrobial and polymicrobial cases. *Klebsiella* is mostly seen in polymicrobial isolates and *Staphylococcus aureus* is seen reasonably in polymicrobial and

monomicrobial cases as represented in Figure 3. Fungi and other organisms were not isolated.

Out of 75 cases, 62 patients were infected with different microorganisms. All the 62 wound cultures were tested for antibiotic sensitivity, and the result was as depicted in Figure 4. Meropenem and imipenem is among the most sensitive drugs with sensitivity above 90% for most of the microorganisms. Colistin, tigeycycline, amikacin, gentamycin, piperacillin tazobactum, linezolid and cefoperzone sulbactum are the other drugs which is sensitive in about 50% of the cases in the present study.

Table 5: Analysis of hospital stays in various outcome groups.

Hospital stay	Amputation	Death	Large ulcer	Toe disarticulation	Nil (Group 1)
Mean (days)	41.6	11.11	32.69	24.75	18.80
SD	16.31	9.57	21.17	5.18	7.99

Table 6: Microbial culture pattern of the study.

Organism	Patients
Monomicrobial	32
Polymicrobial	30
Sterile	13
Total	**75**

The main predisposing factor for NSTI in the presnt study was identified as trauma in 26 patients followed by bites in 24 patients, poorly treated in pre-existing lesions in 13 cases and idiopathic in 9 cases as given in Table 7.

Table 7: Predisposing factors in study participants.

Predisposing factors	Patients	Percentage
Trauma	26	35
Bites	24	32
Preexisting lesions (ulcers/ wounds/lymphedema etc.)	13	17
Idiopathic	9	12
Postsurgical/ intervention	3	4
Total	**75**	**100**

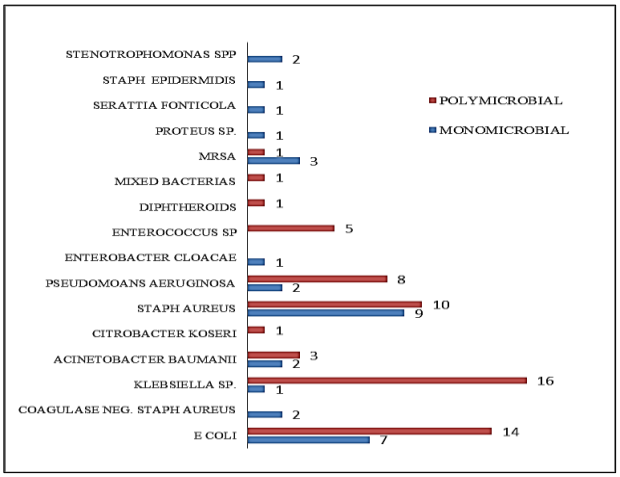

Figure 3: Microorganisms growth in polymicrobial and monomicrobial cases.

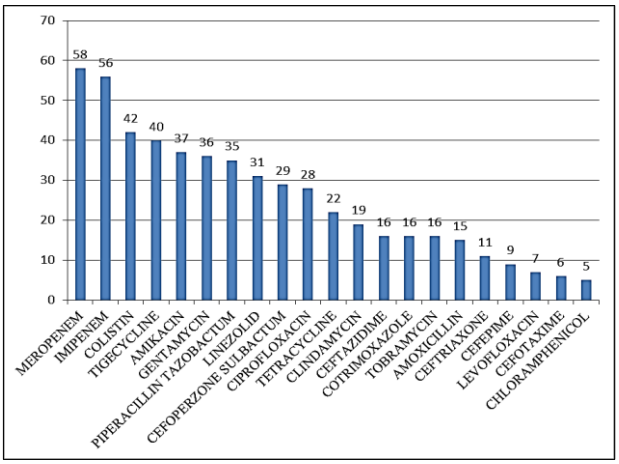

Figure 4: Antibiotics sensitivity towards microorganisms in 62 study cases.

Different types of surgical procedures were adopted in the present study. The number of debridement's done in our patients was 93, disarticulation in 14 cases, amputations in 10 cases and fasciotomy in 33 cases. Ten patients out of 75 were died. It was 10.3% among males and 28.6% among females. 66 patients who survived were treated with various types of secondary managements in the form of secondary suturing and skin grafting as shown in Table 8.

Table 8: Secondary management.

Procedures	Numbers	Percentage
Secondary suturing	8	11
Skin grafting/ plastic reconstruction	25	33
Amputation	10	13
Secondary intention	23	31
Death during resuscitation	9	12
Total	**75**	**100**

Table 9 presents the complications during follow up. 19 patients developed complications. The most common complication being septicemia with MODS. Three septicemia with MODS patients survived after intensive care unit treatment and higher generation antibiotics like colistin and meropenem.

Table 9: Complications.

Complications	Number	Percentage
Chronic renal failure	6	29
Bed sores	2	9
Osteomyelitis	1	5
Septicaemia	12	57
Total	**19**	**100**

DISCUSSION

Necrotizing soft tissue infections rapidly progresses along the deep fascia. It becomes a fatal with high mortality rate if treatment is delayed. Early diagnosis for emergency surgical debridement and broad-spectrum antibiotic therapy were the optimal treatments to reduce the mortality rate of NF.[9]

In our study 75 patients diagnosed with NSTI were enrolled. The mean average age of the patients were 55±17 years ranging from 3-89 years. This was almost similar to the mean age group of patients participated in a study conducted by Park et al.[10] Male preponderance was seen in the study that was in accordance with the studies of Park et al.[10] It was observed that lower limb was the most common affected site in most of the cases (64; 85%). This observation was similar with the previous studies of Khamnuan et al.[9] Diabetes mellitus was found to be major co-morbidity in NSTI patients which was similar to the observations of Mishra et al and Khamnuan et al, where as in a study done by Garg et al Pulmonary diseases was the major comorbidity associated with NSTI.[1,9,11]

In different reports, changes in serum levels of hematocrit, leukocyte count, blood urea nitrogen, creatinine, serum sodium, potassium, magnesium, calcium, serum albumin, lactate dehydrogenase, and alkaline phosphatase are reported to be predictors for higher mortality.[12-14] In our series, there were 2 or more abnormal values in the observed blood parameter at the time of admission. They are hemoglobin, total leukocyte count, erythrocyte sedimentation rate, random blood sugar and serum creatinine.

Several studies have revealed that the most important mortality factors of NSTI are the time to first surgical intervention and its adequacy.[15] Early diagnosis and intervention are essential because mortality is directly affected by time to initial intervention.[15-18] As the interventional delay was increased the duration of hospital stay was also increased respectively. In the present study, the average intervention delay was 15-28 days and the average hospital stay was 29-56 days.

In this study ulcers was seen in 56 patients, toe disarticulation in 14 and amputations in 10 patients and death in 9 patients. Rouse et al found that 45% of deaths from NSTI occurred within 10 days of initial debridement and resulted from either persistent infection after inadequate debridement or rapidly progressive septicemia.[19] In our series 12% (n = 9) of the patients had died within 11 days due to overwhelming sepsis. This was comparable with the studies of Garg et al in which mortality was seen in 10 (17.2%) cases out of 58 patients.[11] More recently Yanar et al reported a mortality of 40% in a series of 35 patients.[20]

In the present study, various bacteriologic agents have been identified in patients with NSTI. The organisms isolated from the tissue were most commonly *E. coli* (n = 21) either alone when monomicrobial infections occurred or in association with other organisms when polymicrobial infections were present especially when the lower limb was involved. *Staphylococcus aureus* is seen reasonably in polymicrobial and monomicrobial cases. This observation was in accordance with the findings of Kalaivani et al.[8]

Prompt use of empirical broad-spectrum antibiotics is essential for treatment. In this study, all patients were administered broad-spectrum antibiotics within 24 hours.[21] Meropenem and imipenem found as the most sensitive drugs in most of the cases with sensitivity above 90%.

Patients with NSTI usually have some predisposing factors such as trauma, bites, preexisting lesions or postsurgical infections.[22] In our study most of the patients developed NSTI due to trauma which is in accordance with the observations of Kalaivani et al.[8]

Patients who survived were treated with various types of secondary management in the form of secondary suturing, skin grafting and healing by secondary intention. In this study most the cases underwent skin grafting (25) as secondary therapy. This similar type of secondary management was seen in NSTI patients in the study done by Garg et al.[11]

CONCLUSION

Necrotizing soft tissue infections is a surgical emergency. High clinical suspicion of such infection in its early course and initial and aggressive surgical treatment constitutes the principles for successful management. Whenever NSTI suspected and intravenous antibiotics fails to adequately control the infective process within 24 hours, an aggressive therapy should start immediately in order to achieve a favorable outcome.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Harikrishnan CP, Vakayil HJ. Necrotizing soft tissue infections: a clinical profile. Int Surg J 2017;4:883-9.