

CLINICO-PATHOLOGICAL STUDY MANAGEMENT AND OUTCOME OF NECROTIZING SOFT TISSUE INFECTIONRajesh Kumar Maurya¹, G. D. Yadav², Sanjay Kala³, R. K. Johari⁴, Chayanika Pantola⁵**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: INTRODUCTION: Necrotizing soft tissue infection (NSTI) is a broad term applied to infections of "flesh eating bacteria" that may cause cellulitis, fasciitis, or myositis. NSTI's can rapidly progress to systemic toxicity, resulting in major morbidity and mortality without prompt recognition and treatment. **MATERIAL & METHODS:** In the present study, all the cases of necrotizing soft tissue infection attending OPD, emergency & admitted in ward of L. L. R. And associated hospitals from Dec. 2012 to June 2014 were selected for the study. The general condition of the patient was noted with special reference to temperature, respiratory rate, pulse rate, blood pressure and signs of toxemia. All routine hematological and biochemical tests were done. Pus and excised tissue sent in sterile container for Gram staining and culture & Histopathological examination. **RESULTS:** In our study we have found that with increasing age the incidence of necrotizing soft tissue infection rises and 9 out of 44 patients expired which is 20.45% of total patient studied. Most common bacteria identified in this study was Group-A β hemolytic streptococcus (52.27%). In most of the case (72.72%) infection was found to be poly-microbial (32 out of 42) and only ten out 42(22.72%) were mono microbial. Increased mortality was seen in patient associated with diabetes mellitus shock renal dis-function anemia and coagulopathy. **CONCLUSION:** Earliest possible patient should be treated by extensive debridement broad spectrum antibiotics. Wound closure or grafting should only be performed when there is no longer evidence of necrotic tissue and the patient has been adequately resuscitated.

KEYWORDS: Necrotizing fasciitis, Necrotising soft tissue infection, Antibiotic sensitivity.

INTRODUCTION: Soft tissue infections are one of the most common causes of morbidity and mortality worldwide. These infections are more prevalent in tropical countries like India. Necrotizing fasciitis are highly lethal infections. They can be defined as infections of any of the layers within the soft tissue compartment (Dermis, subcutaneous tissue, superficial fascia, deep fascia, or muscle) that are associated with necrotizing change.¹

The first recorded modern description of NSTI in the United States was by Joseph Jones, a Confederate Army surgeon, who reported 2,642 cases of "hospital gangrene" with a mortality approaching 50%.² The French physician, Jean Alfred Fournier, described necrosis of the perineum in five men in 1883, and perineal NSTIs continue to bear the eponym of Fournier's gangrene.³ Brewer and Meleney⁴ noted an association between hemolytic streptococcal infection and fascial gangrene, and proposed that the synergistic effects of various bacteria involved in these infections was responsible for their rapid progression. The term "necrotizing fasciitis" was proposed by Wilson⁵ in 1952, and depicts the most common feature of these infections, that is, fascial necrosis. More recently, the term "necrotizing soft-tissue infection" (NSTI) has been proposed for this collection of infectious diseases since it encompasses all forms of this disease process regardless of anatomical location or depth of infection.

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In early stages pain and fever is the presenting manifestation, swelling then develops followed by brawny edema and tenderness with progression of disease along with bullae with blue or purple fluid.⁶ Later the skin becomes friable and takes on a maroon or black colour. At this stage thrombosis of blood vessels in dermal papillae is extensive resulting in rapid spread along the fascial planes through venous channels & lymphatics.^{7,8} Patients in later stage are toxic and frequently manifest shock and multi organ failure⁹.

In the present study we have tried to evaluate different bacterial flora involved in necrotizing soft tissue infection, different clinical presentation and its co-relation with microbiological diagnosis, the effect of various co-morbid conditions on the disease process for example diabetes mellitus, coagulopathy, renal dysfunction, advanced age, multiple organ system involvement on prognosis and to help in selecting antibiotics in patients diagnosed as having necrotizing soft tissue infection.

MATERIAL AND METHOD: In the present study "Clinicopathological study management & outcome of necrotizing soft tissue infection" was done in following manner. All the cases of necrotizing soft tissue infection attending OPD, emergency & admitted in ward of L. L. R. and associated hospitals from Dec. 2012 to June 2014 were selected for the study.

The predilection to develop NSTI increases with age. Detailed history with particular reference to any major or minor trauma, previous surgical procedures, cutaneous or disabling disease leading to immuno suppression, perineal abscess or sub cutaneous injections etc. and the time elapsed since the onset of symptoms was noted. Thorough physical examination including local examination for swelling painful erythema, bullae formation, gangrenous necrosis, crepitus and pain (Which may be out of proportion to clinical signs') was done.

The general condition of the patient was noted with special reference to temperature, respiratory rate, pulse rate, blood pressure and signs of toxemia. The patient was described as having systemic sepsis if their temperature was greater than 38°C (100.4°F), pulse rate more than 90 per minute, respiratory rate greater than 21 per minute and white blood cell count greater than 12000 per cubic mm. Associated disease like diabetes mellitus, arterial or venous disorders, ischiorectal fossa abscess history of immunosuppressive drugs or any other immunosuppressive disorder if present thoroughly studied and its effect on mortality was tabulated and studied.

GENERAL INVESTIGATION: All routine hematological and biochemical tests Hb%, TLC, DLC & CRP, Creatinine and urea nitrogen, RBS, Coagulation profile including P. T. T. , P. T. , platelet count & liver function, Serum electrolyte were done in admitted patient. Pus culture and sensitivity and excised tissue sent in sterile container for Gram staining and culture & Histopathological exam, X-ray of affected organs and X-ray chest, Doppler study of limb for arterial or venous disorders.

SPECIFIC INVESTIGATIONS BACTERIOLOGICAL: Smears were made of the pus obtained from wounds on glass slides and they were stained by Gram's staining method. The best specimen for anaerobic culture is obtained by using a needle and syringe. Tissue samples and biopsy samples were taken for anaerobic culture.

ANTIBIOTIC SENSITIVITY TESTS: Isolated organisms were tested for their antibiotic sensitivity. The antibiotics tested were Ceftriaxone, Gentamycin, Amikacin, Cefuroxime, Piperacillin/Tazobactam, Cefoperazone/Sulbactam, Amoxycillin/Clavulanic acid, Ofloxacin, Ceftazidime, Azithromycin, Imipenem.

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RESULT: A series of 44 cases with different clinical presentation were studied and following results have been made.

In our study we have found that with increasing age the incidence of necrotizing soft tissue infection rises (Table 1). Overall 61% of the total cases studied were above the age group of 40 years. Percentage of male patient was 84% in comparison to female patients 16%. We found that mortality due to necrotizing soft tissue infection is still high 9 out of 44 patients expired, which is 20.45% of total patient studied (Table-1). Most common site involved in necrotizing fasciitis was found lower limb in 77.27% patients.

Age Group (years)	Male	Female	Total No. of Patients	Percentage	No. of Patient Exp.	Percentage %
0-10	2	0	2	4.54%	0	0%
11-20	4	0	4	9.99%	1	25%
21-30	4	2	6	13.63%	1	16.6%
31-40	4	1	5	11.36%	0	0%
41-50	6	3	9	20.45%	1	11.1%
>50	17	1	18	40.90%	6	33%
Total	37	7	44	100%	9	100%

Table 1: Incidence of Disease According to Age Group & Mortality

Most common bacteria identified in this study was Group-A β hemolytic streptococcus (52.27%). (Table-2). In most of the case (72.72%) infection was found to be poly microbial (32 out of 42) and only ten out 42(22.72%) were monomicrobial. Most common organism found in monomicrobial infection was group A, β hemolytic Streptococci 4 out 10(40%) second most common was Staphylococcus aureus 3 out of 10(30%). In our study we found that the infection which was poly microbial showed many combination of different organism (Range 2-3 per case). Anaerobic culture was done in 14 cases out of which 6 cases came out to be positive.

Bacteria isolated	Total No. of Patients	Percentage
Staphylococcus Aureus	20	45.45%
Staphylococcus Albus	1	2.27%
Group A β hemolytic streptococcus	23	52.27%
Non hemolytic streptococcus	3	6.81%
E-coli	14	31.81%
Pseudomonas	4	9.09%
Klebsiella species	2	4.54%
Bacillus proteus	6	13.6%
Anaerobes	6	13.6%
Sterile	2	4.54%

Table 2: Bacteria Isolated by Swab and Tissue Culture Including All Monomicrobial and Poly microbial Infection

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Empiric antibiotic therapy can be employed until wound culture isolates are identified. Depending on the culture results, antibiotic selection can be modified. In our study 70% Staphylococcus Aureus were sensitive to Ceftriaxone & 45% Azithromycin. Incidence of Staphylococcus resistance to Gentamycin was 70%. Staphylococcus was sensitive to Amikain in 40% patients. Staphylococcus albus was found to be sensitive to ceftraixone, Gentamycin, Amikacin, Azithromycin, Piperacillion/Tazobactam & Imipenem. Streptococci sensitivity with Amoxycillin/Clavulanic was done and it was found that they are 78% sensitive to Amoxycillin/Clavulanic. E-coli were found most sensitive to Amikacin among the drugs tested (After imipenem (100%)). Cefoperazone/Sulbactam and Ceftazidime was next effective drug. Pseudomonas was found to be most resistant organism to treat. Pseudomonas was most sensitive to Amikacin (75%), Ceftrazidime 75% (After imipenem (100%) of the drug studied. Bacillus proteus & Klebsiella both were sensitive to Amikacin & Ceftrazidime.

In this study we found that there is increase in incidence of disease with increasing age also there is higher mortality in age group more than 40 years (25.92%) (Table 3). If the interval between first symptoms and surgical intervention is increased, the mortality increases. According to this study patient operated in first 24 hrs. Had, mortality 16.66% whereas after 120 hrs. (5 days) it was 33% (Table 4).

Age Group Year	No. of patient	No. of patient Exp.	Percentage %
0-40	17	2	11.76%
>40	27	7	25.92%

Table 3: Showing Age Distribution & Relation to Mortality in 0-40yrs & >40yrs Age Group

Duration in Hrs.	No. of Patients	No. of patients expired	Percentage
1-24	6	1	16.66%
25-48	2	0	0%
49-72	3	0	0%
72-96	11	2	18.18%
96-120	13	3	23.07%
>120	9	3	33%

Table 4: Duration between Appearance of First Symptom and Surgical Intervention and Its Relation to Mortality

Prevalence of diabetes mellitus was found to be much more in patients of necrotizing soft tissue infection (10 of 44 i.e. 22.72%) than general population (1-2%). In total 10 patients diagnosed as diabetics 4 patients expired (40%) which is much higher than overall mortality in the study (20.45%), from this conclusion was drawn that diabetics have bad prognosis. We found that 2 patient out of 44 had coagulopathy. In these 2 patients who were having coagulopathy all expired, mortality

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was 100%. 50% mortality was seen in patients with shock on admission. This is two and half times the overall mortality seen. In this study we found that S. creatinine level was between 1-3mg/dl in 25 out of 44 patient the mortality rate increased with increasing S. creatinine level, i.e., With increasing renal dis-function. Mortality was 66.66% in patient with S. Creatinine more than 3 mg/dl. In this study on analysis it was found that relevance of anemia (55.7%) was high in patients of necrotizing soft tissue infection. Mortality in patients of moderate severe anemia was seen to be very high (35.7%).

DISCUSSION: In the present study we found an increase in incidence of necrotizing soft tissue infection with age, as more than 61% of cases were above the age of >40 years. Steep rise in incidence was seen above age of 40. K. Moorthy¹⁰ studied 8 patients with necrotizing, perineal infection in which it was found that the mean age of the patient was 50.6±10.3 years. As regarding sex distribution the percentage of male patients in our study was 84% in comparison to females (16%). In comparison to a study conducted by Kujath¹¹ where 21 cases were reviewed of which 10 were males (48%).

BACTERIOLOGY: In this study we were able to perform culture of 42 out of 44 patients of which 2 were sterile even after repeated cultures. Culture report's showed presence of poly microbial flora in most of the cases 72.72% (32 out of 42 cases). 10 out of 42(22.72%) culture reports' showed monomicrobial infection. 2-3 microorganisms were found in poly microbial cultures.

A similar report was seen by Elliot⁷ where he studied 182 patients and found 154 cultures (84.61%) to be positive for poly microbial flora. Only 28 cultures (15.38%) were found to be pure cultures. On an average 4. 4 microbes per wound culture were detected. Voros D.¹² (1993) reviewed 43 patients of necrotizing soft tissue infection and he found that bacterial culture revealed 2-7 microbes in each patient.

Out of all 42 cultures which showed growth of different bacteria Group-A β hemolytic streptococcus was seen to be most frequent. 23 out of 42 (52.27%) cultures grew Group-A β hemolytic streptococcus either as pure or poly microbial flora. Next were Staphylococcus Aureus 45. 45%.

SENSITIVITY OF ORGANISM TO ANTIBIOTICS: Group-A β hemolytic streptococcus which was found to be most prevalent organism in this study was found to be 78.26% sensitive to amoxycillin/Clavulanic acid and 69.56% sensitive to Ceftriaxone.

Sensitivity of organism to antibiotics: Group-A β hemolytic streptococcus which was found to be most prevalent organism in this study was found to be 78.26% sensitive to amoxycillin/Clavulanic acid and 69.56% sensitive to Ceftriaxone. Staphylococcus Aureus was found 2nd most prevalent organism (44.45%) and 70% sensitivity to ceftriaxone. E. Coli was found most sensitive to Amikacin followed by Cefoperazone/sulbactam and Piperacillin/Tazobactam least to Cefuroxime in our study.

MORTALITY AND RELATED COMORBID CONDITIONS: Mortality of necrotizing soft tissue infections is still high all over the world. In spite of availability of higher antibiotics, improvement in critical care, diagnostic procedures & surgical techniques. High mortality is due to multiple factors and depends on age of patient, time duration between appearance of like diabetes mellitus, renal

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dysfunction, coagulopathies, alcoholism, intra venous drug abuse and other immune compromised states. In the present study 9 out of 44 patient were expired. Mortality was found to be 20.45 per cent in this series. In a similar study conducted by Hsiago GH, Chang CH.¹³ he reviewed 34 cases with necrotizing soft tissue infection and found that overall mortality was 26.5%.

The single most common factor associated with increased mortality was delay to operative debridement.^{14,15} In this study it was seen that if the time interval between the first symptom and surgical intervention is increased the mortality is increased. On analysis the result was that the patients who were managed surgically in first 24 hrs. Of appearance of symptoms had mortality of 16.66% but those patients who were operated after 5 days the mortality was 33%. Voros D.¹² (1993) reviewed 45 patients with necrotizing soft tissue infection and found that in 30 patients early diagnosis and treatment resulted in only 2 deaths and delayed surgical intervention in 12 patients was followed by 9 deaths.

Diabetes mellitus predisposes to infection by three mechanisms one due to peripheral neuropathy where patient is unaware of minor trauma to limb which help in colonization of bacteria also increased blood sugar level predisposes to bacterial cultivation the condition has a fulminant had fatal course because of inherent neutrophil dysfunction with decreased phagocytic and intracellular bactericidal activity in diabetes mellitus. Moorthy¹⁰ studied 8 patients of necrotizing perineal infection of which 5 were found to be diabetics of whom 4 died (80% mortality), all the non-diabetics survived. In our study out of 44 patient 10 were found be suffering from diabetes mellitus out of which, 6 were successfully treated but 4 patient expired. Mortality in diabetic patient was 40%. In comparison overall mortality in this study was 20.45%. We found that diabetes increases the mortality when present in these patients.

In our study coagulation profile was done only in 26 out of total 44 patients. Out of these 2 patients had all the three parameter's (Platelet count, prothrombin time, partial thromboplastin time) deranged, all of them died and the mortality was 100%. Similar study was done by K. Moorthy.¹⁰ Who studied 8 patients with necrotizing perineal infection out of which coagulant profile was deranged in 1 patient diagnosed as having disseminated intravascular coagulopathy and this patient expired.

In this series we found that out of 44 patient 8 patient were admitted in shock, of which 4 patients expired, overall mortality was 50% in patient with shock. In this study we found that S. creatinine level was between 1-3mg/dl in 25 out 44 patients the mortality rate increased with increasing S. creatinine level, i.e. With increasing renal dysfunction, mortality was 66.6% in patient with S. Creatinine more than 3mg/dl. De Polavieja.¹⁶ Studied retrospectively 24 patients diagnosed of necrotizing soft tissue infection and came to a conclusion that high level of blood urea at admission is associated with a worse outcome.

In this study we found that prevalence of anemia (55.7%) was high in patients of necrotizing soft tissue infection & Mortality in patients with moderate and severe anemia was seen to be very high (35.7%). In the patients with anemia the oxygenation of the tissues are poor who leads to delayed wound healing and due to which disease takes a fulminant course.

CONCLUSION: Necrotizing soft tissue infections are true surgical emergencies and wide debridement must be undertaken. Multiple studies have shown that the elapsed time between onset of symptoms and initial operative debridement is the most important factor affecting morbidity and mortality.

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All debrided areas should be re-examined routinely with repeat debridement performed as needed. Delaying repeat debridement increases mortality and risk of acute kidney injury, thus should be performed as early as feasible. Wound closure or grafting should only be performed when there is no longer evidence of necrotic tissue and the patient has been adequately resuscitated.

To summarize, it is a poly microbial synergistic infection and a multipronged aggressive approach with intensive monitoring, broad spectrum antibiotics coverage guided by intraoperative cultures and plastic reconstructive techniques will bring down the mortality to an acceptable rate in these patients.

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AUTHORS:

1. Rajesh Kumar Maurya
2. G. D. Yadav
3. Sanjay Kala
4. R. K. Johari
5. Chayanika Pantola

PARTICULARS OF CONTRIBUTORS:

1. Junior Resident, Department of Surgery, G. S. V. M Medical College, Kanpur.
2. Professor & HOD, Department of Surgery, G. S. V. M. Medical College, Kanpur.
3. Professor, Department of Surgery, G. S. V. M. Medical College, Kanpur.

FINANCIAL OR OTHER**COMPETING INTERESTS:** None

4. Assistant Professor, Department of Surgery, G. S. V. M. Medical College, Kanpur.
5. Lecturer, Department of Pathology, G. S. V. M. Medical College, Kanpur

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Rajesh Kumar Maurya,
Room No. 36,
NRH Married Boys Hostel,
G. S. V. M, Medical College, Kanpur.
E-mail: merajeshm@gmail.com

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