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Necrotizing Soft Tissue Infection: Evaluation and Management

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ABSTRACT:
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 incidence and prevalence of NSTI varies by season, location and patient population. 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[1,2,3,4].
Aim: To evaluate and manage patients suffering from necrotizing soft tissue infection.
Materials and Methods: The study was prospective cohort study conducted from October 2019 to August 2021 to study 'Necrotizing soft tissue infection: its evaluation and its management' in 100 patients admitted through surgery Outpatient department / Emergency / transferred from other departments in Chhatrapati Shivaji Subharti Hospital, Meerut.
Results: The results showed that there were 79% males and 21% were females. The mean age of the subjects was 44.38±9.03 years .It was found that maximum subjects were from the middle class (53%). In our study; most commonly affected site was lower extremities. The most common underlying co morbidity was diabetes mellitus. The most common presentation was pain (98%) and least common was skin crepitus (26%). Most common micro-organisms isolated were streptococcus followed by Klebsiella spp. 54% subjects had undergone debridement as the first surgery.

I. 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 incidence and prevalence of NSTI varies by season, location and patient population. 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[1,2,3,4].

Necrotizing soft tissue infections can be classified on the basis of microbiology, location or depth of tissue involvement. **Guiliano et 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.

- Type 1- It is the most common infection seen, and describes polymicrobial infections, often including anerobes,
- Type 2- These infections are monomicrobial and typically involve GAS or less commonly Staphylococcus aureus.

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), Aeromonas hydrophila (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. Klebsiella pneumoniae among diabetic patients with NSTI in Taiwan)[8].

The etiology of necrotizing soft-tissue infections (NSTIs) is not always obvious. Pathogens **(Figure 1)** can gain entry with a small site of inoculation, blunt trauma, cutaneous infections, post-surgical complications, hematogenous spread, burns, childbirth, or idiopathic causes.[9]

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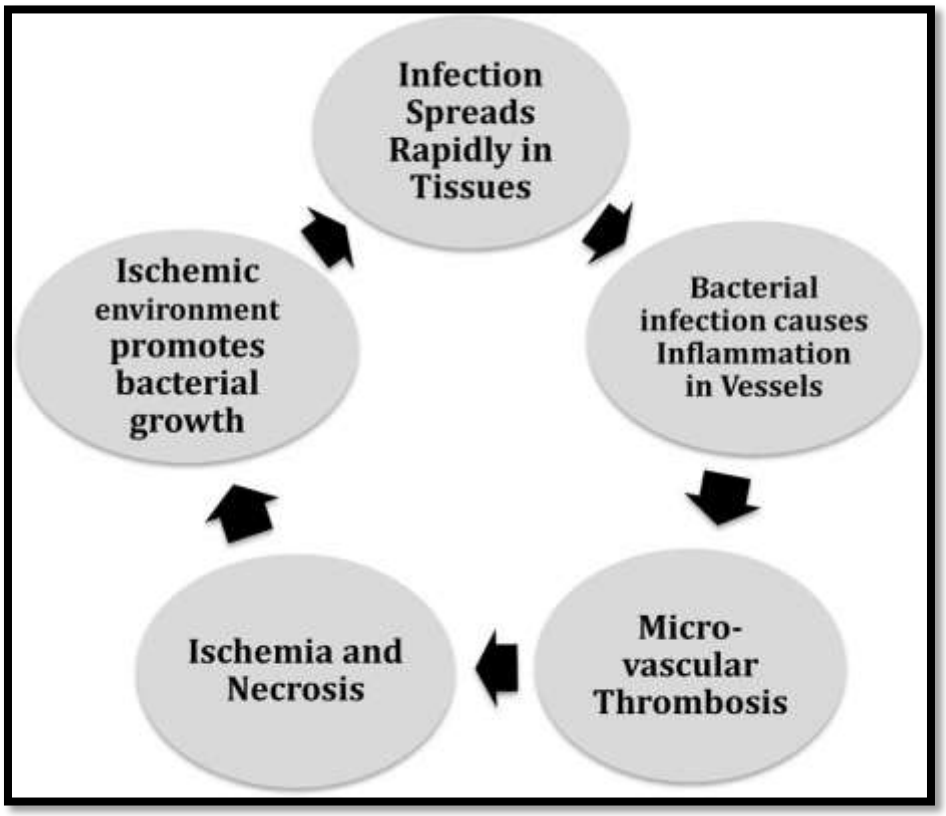

Figure 1[10]: Vicious cycle of necrotizing soft tissue infection

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. IVDU is one of the most common risk factors associated with community-acquired NSTI. Nonetheless, healthy people without these risk factors may also be susceptible, [12] especially for type II NSTI.[13,14] In fact, up to half of patients have no inciting event. [15]

NSTI is pathophysiologically characterized by effects of bacterial toxins and enzymes (e.g., hyaluronidase) that enable horizontal extension through the fascial planes, leading to intravascular thrombosis and ischemic necrosis with disturbance of the host's humoral and cellular immune response. [16]

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has been used to gauge the likelihood of NSTI. [17] The LRINEC score includes 6 variables associated with NSTI and are used to calculate a score correlating to the risk of NSTI **(Figure 2)**.

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Laboratory Risk Indicator for Necrotizing Fasciitis		
CRP (mg/dL)	<15	0
	≥15	4
WBC (per mm³)	<15	0
	15-25	1
	>25	2
Hemoglobin (g/dL)	>13.5	0
	11-13.5	1
	<11	2
Sodium (mEq/L)	≥135	0
	<135	2
Creatinine (mg/dL)	≤1.6	0
	>1.6	2
Glucose (mg/dL)	≤180	0
	>180	1
Composite Score	Score < 6	Low Risk
	Score 6-7	Intermediate
	Score ≥ 8	High Risk

Figure 2 - The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score

The current Infectious Disease Society of America (IDSA) guidelines recommend broad-spectrum coverage (vancomycin or linezolid plus [1] piperacillin-tazobactam or a carbapenem or [2] ceftriaxone and metronidazole).[18] One of the antibiotics should be a toxin-suppressing and cytokine-modulating medication, such as clindamycin or linezolid.[19,20]

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,[21,22] and survival further increases with operative intervention within 6 hours.[23]

II. AIM:

To evaluate and manage patients suffering from necrotizing soft tissue infection.

III. MATERIALS AND METHODS:

The study was prospective cohort study conducted from October 2019 to August 2021 to study 'Necrotizing soft tissue infection: its evaluation and its management' in 100 patients admitted through surgery Outpatient department / Emergency / transferred from other departments in Chhatrapati Shivaji Subharti Hospital, Meerut.

IV. RESULTS:

The results showed that there were 79% males and 21% were females. The mean age of the subjects was 44.38±9.03 years in this study. It was found that maximum subjects were from the middle class (53%). In our study; out of all the sites, 22% affected sites were in upper extremities, and 78% affected sites were in lower extremities. The mean duration of symptoms in days was 4.73±2.89. It was reported that 31% of subjects had diabetes mellitus, 3% had liver cirrhosis, 7% had chronic infected burns, 28% had blunt trauma, 15% had skin Infection, 7% had cardiac diseases, 6% had renal diseases, and 3% had immunosuppression. Out of all the subjects, 78% had erythema, 93% had swelling, 98% had pain, 59% had blisters, 54% had hemorrhagic bullae, 26% had crepitus, 94% had skin necrosis, and 81% had pus discharge. Among all the subjects, 43% had fever, 54% had tachycardia, 36% had hypotension, and 51% had tachypnea. 63% of the subjects had leukocytosis,

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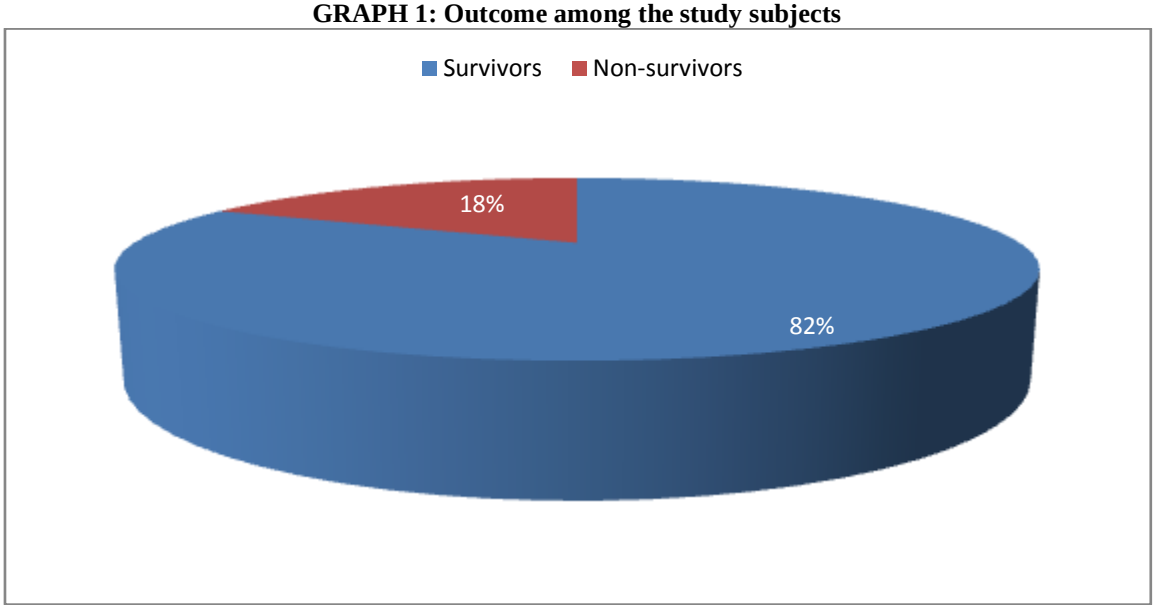
42% had anaemia, and 27% had increased creatinine. It was depicted that 11% subjects had developed bronchial pneumonia, 4% had developed acute renal failure, 6% had developed septic shock and 3% had developed MODS. Among all the subjects, 64% had negative culture and 36% had positive culture. Most common micro-organism isolated were streptococcus followed by Klebsiella spp. ,Escherichia coli and 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 the second operation, 4% subjects underwent debridement, 9% had amputation/disarticulation, and 6% 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. It was observed that among all the subjects 82% were survivors, and 18% were non- survivors (**GRAPH 1**). It was seen that comorbidities like chronic infected burns (p value =0.039) and cardiac diseases (p value =0.043) had statistically significant association with the outcomes. Statistically significant association of symptoms 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 like hypotension (p value= 0.003), and laboratory investigations like increased creatinine (p value=0.002) with the outcomes. It was also found that all the systemic manifestations due to NSTI were significantly associated with the outcomes with p value = <0.01.

GRAPH 1: Outcome among the study subjects



V. DISCUSSION:

Necrotizing soft tissue infections (NSTIs) are severe infections of any layer of soft tissue compartment including superficial and deep soft tissues. Mortality in patients with NSTIs is high, ranging from 14 to 42%. Early diagnosis and treatment are essential for survival[24]. Treatment consists of broad-spectrum antibiotics, wide surgical debridement, and supportive care. Antibiotic treatment is initially broad spectrum and then tailored to antimicrobial susceptibilities of isolated organisms. Patients may require multiple debridements or amputations to ensure adequate source control[27].

The study was prospective cohort study conducted from October 2019 to August 2021 in the department Outpatient department/Emergency/transferred from other departments in Chhatrapati Shivaji Subharti Hospital, Meerut among 100 patients irrespective of age or gender clinically diagnosed with NSTI.

1. Gender and Age:

The results showed that there were 79% males and 21% females. This is most possibly from the increased incidence of Fournier's gangrene in men. The mean age of the subjects was 44.38±9.03years in this study.

Christophe Mpirimbanyi et al[25] in their study found that ninety two (52.6%) patients were male

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and 83 (47.4%) patients were female. The mean age was 43.8 years (range 12 and 92 years). Our findings were in concordance with the above studies.

2. Affected Sites:

In our study; out of all the sites, 22% affected sites were in upper extremities, and 78% affected sites were in lower extremities. This is because of the fact that majority of NSTI patients are diabetic which lead to diabetic neuropathy, hence trauma to the lower limb goes unnoticed. The most commonly involved body parts were lower extremities (n = 94, 54%) and trunk (n = 44, 25%) as mentioned by **Christophe Mpirimbanyi et al**[25], which is similar to the present study.

3. Comorbidities:

In our study, it was reported that 31% of subjects had diabetes mellitus, 3% had liver cirrhosis, 7% had chronic infected burns, 28% had blunt trauma, 15% had Skin Infection, 7% had cardiac diseases, 6% had renal diseases, and 3% had immunosuppression. 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[26] in their depicted that the most common pre-existing comorbidities were diabetes (60.7%).

Christophe Mpirimbanyi et al[25] in their study found that eighty-six (49%) patients presented with comorbidities with 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.

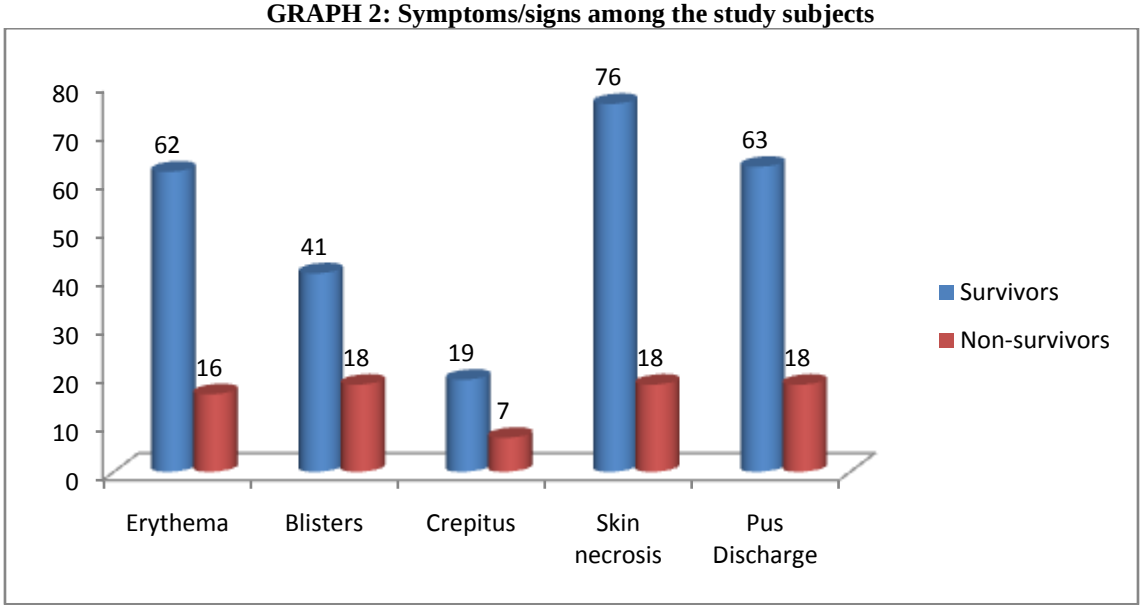
4. Symptoms/Signs and Duration of Symptoms:

Out of all the subjects, 78% had erythema, 93% had swelling, 98% had pain, 59% had blisters, 54% had hemorrhagic bullae, 26% had crepitus, 94% had skin necrosis, and 81% had pus discharge **(Graph 2)** . 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. Misiakos et al[27] mentioned that the vast majority had tenderness (90.3%) and pain (77.4%) on the infected site. In 46 patients, the site of infection was edematous (74.2%), and in 43 patients, the infected skin was erythematous (69.4%).

Anaya DA et al[28] and **Kalaivani V et al**[29] revealed similar findings too.

GRAPH 2: Symptoms/signs among the study subjects



5. Systemic Symptoms and Manifestations:

Among all the subjects, 43% had fever, 54% had tachycardia, 36% had hypotension, and 51% had tachypnea. It was depicted that 11% subjects had developed bronchial pneumonia, 4% had developed acute renal failure, 6% had developed septic shock and 3% had developed MODS in our study **(Graph 3).**

Jing-Chun Zhao et al[30] in their study revealed similar findings too.

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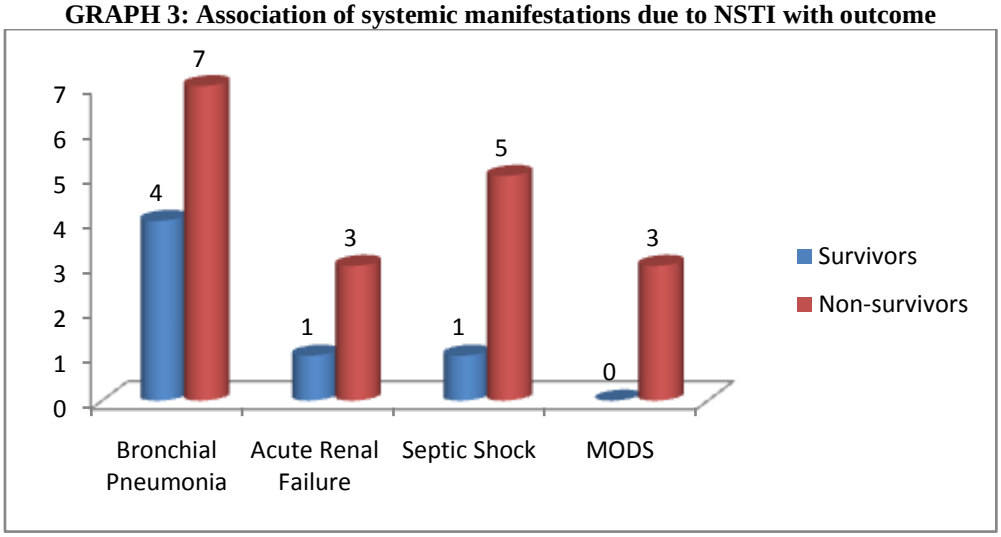
GRAPH 3: Association of systemic manifestations due to NSTI with outcome



6. Laboratory Investigations:

Out of total subjects, 63% subjects had leukocytosis, 42% had anaemia, and 27% had increased creatinine.

Christophe Mpirimbanyi et al[25] and **Evangelos P. Misiakos et al**[27] in their study reported similar laboratory profile.

7. Wound cultures:

Among all the subjects, 64% had negative culture, 36% had positive culture. The negative cultures could be because the patient had already been started on antibiotics prior to sending the cultures. Most common micro-organisms isolated were streptococcus followed by Klebsiella spp. , Escherichia coli as well as Staphylococcus Aureus (**Table 1**).

Jimenez MN et al[26] similarly revealed that blood cultures were drawn in 96% of patients and 32% were positive. Streptococcus viridans and Group F streptococcus were the most common organisms isolated.

Table 1: Wound cultures

Parameters	**N**	**%**
Negative Culture	64	64
Positive Culture	36	36
1. Streptococcus viridans	8	8
2. Group F Streptococcus	10	10
3. Klebsiella spp.	4	4
4. Group A Streptococcus	2	2
5. Escherichia coli	3	3
6. Salmonella spp.	2	2
7. Staphylococcus Aureus	3	3
8. Pseudomonas	2	2
9. Enterobacter	2	2

8. Operative Management:

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 the second operation, 4% subjects underwent debridement, 9% had amputation/disarticulation, and 6% had skin grafts (**Table 2**). According to **Christophe Mpirimbanyi et al**[25], all patients underwent operation, with the most common initial operations debridement (n = 90, 51%) and amputation or disarticulation (n = 52, 30%). A second operation was performed in 24 patients with the most common second operations being skin graft (n = 12, 50%) and amputation or disarticulation (n = 5, 21%).

Table 2: Operative Management

Parameters	N	%
First operation		
• Debridement	54	54
• Amputation/disarticulation	28	28
• Incision and drainage	7	7
• Anterior Abdominal Wall Debridement	11	11
Second operation		
• Debridement	4	4
• Amputation/disarticulation	9	9
• Skin graft	6	6

9. Outcome:

It was observed that among all the subjects 82% were survivors, and 18% were non-survivors. It was seen that comorbidities like burns (p value =0.039) and cardiac diseases (p value=0.043) had statistically significant association with the outcomes. Statistically significant association of symptoms 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 like hypotension (p value= 0.003), and laboratory investigations like increased creatinine (p value=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 Mpirimbanyi et al[25] in their revealed that the overall mortality was 46 (26%). Factors associated with mortality on multivariate analysis included: presence of shock at admission and renal failure. Differences in mortality may be due to differences in practice patterns, microbiology, or epidemiology. Factors like advanced age, immunosuppression by human immunodeficiency virus infection, and elevated white blood count were not significantly associated with mortality in their study, which is in contrast to our study. This is likely due to different population demographics with a lower mean age and lower incidence of comorbidities.

According to **Evangelos P. Misiakos et al**[27], 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 renal impairment and chronic heart failure and mortality.

Goh et al[11] concluded that a median mortality ratio was 21.5%.

The CDC's most recent NF mortality rate is 15-33%. In 2013, **Faraklas et al**[31] 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%.

VI. CONCLUSION:

NSTI is a rare but highly morbid disease entity. Therefore early detection and aggressive debridement are the cornerstones of NSTI treatment. Antibiotic therapy and intensive care support is also essential in severe cases of NF. Anaerobic tissue culture and frozen section biopsy could be adopted as routine tests for diagnosis and decision-making in NF. These findings should 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. Multi-centered studies of this entity in India will help to create an evidence-based assessment and management algorithm.

BIBLIOGRAPHY:

[1]. Nelson GE, Pondo T, Toews KA, et al. Epidemiology of Invasive Group A

Streptococcal Infections in the United States, 2005–2012. Clin Infect Dis. 2016; 63(4): 478–86.
[2]. Yilmazlar T, Ozturk E, Alsoy A et al. Necrotizing soft tissue infections: APACHE II score, dissemination, and survival. World J Surg. 2007; 31:1858–1862.
[3]. Miller AT, Saadai P, Greenstein A et al. Postprocedural necrotizing fasciitis: A 10-year retrospective review. Am Surg. 2008; 74:405–409.
[4]. Lee TC, Carrick MM, Scott BG, et al. Incidence and clinical characteristics of methicillin-resistant Staphylococcus aureus necrotizing fasciitis in a large urban hospital. Am J Surg. 2007; 194:809– 812.
[5]. Giuliano A, Lewis F, Hadley K et al. Bacteriology of necrotizing fasciitis. Am J Surg. 1977; 134:52–57.
[6]. Sartor C, Limouzin-Perotti F, Legré R et al. Nosocomial Infections with Aeromonas hydrophila from Leeches. Clin Infect Dis. 2002; 35(1): E1–5.
[7]. Miller LG, Perdreau-Remington F, Rieg G et al. Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles. N Engl J Med. 2005; 352(14):1445–53.
[8]. Cheng NC, Yu YC, Tai HC et al. Recent trend of necrotizing fasciitis in Taiwan: focus on monomicrobial Klebsiella pneumonia necrotizing fasciitis. Clin Infect Dis. 2012; 55(7):930–9.
[9]. Bosshardt TL, Henderson VJ, Organ CH. Necrotizing soft-tissue infections. Holzheimer RG, Mannick JA, eds. Surgical Treatment: Evidence-Based and Problem-Oriented. Munich: Zuckschwerdt 2001: 221-25.
[10]. Anaya DA, McMahon K, Nathens AB, Sullivan SR, Foy H, Bulger E. Predictors of mortality and limb loss in necrotizing soft tissue infections. Arch Surg 2005; 140(2):151–7.
[11]. Goh T, Goh LG, Ang CH, Wong CH. Early diagnosis of necrotizing fasciitis. Br J Surg 2014; 101 (1): e119-25.
[12]. Hakkarainen TW, Kopari NM, Pham TN, Evans HL. Necrotizing soft tissue infections: review and current concepts in treatment, systems of care, and outcomes. Curr Probl Surg. 2014 Aug. 51 (8):344-62.
[13]. Roje Z, Roje Z, Matić D, Librenjak D, Dokuzović S, Varvodić J. Necrotizing fasciitis: literature review of contemporary strategies for diagnosing and management with three case reports: torso, abdominal wall, upper and lower limbs. World J Emerg Surg 2011; 6 (1):46.
[14]. Phan HH, Cocanour CS. Necrotizing soft tissue infections in the intensive care unit. Crit Care Med 2010; 38 (9):S460-8.
[15]. Marx J, Hockberger R, Walls R. Rosen's Emergency Medicine - Concepts and Clinical Practice. 8th ed. Philadelphia: Elsevier Saunders; 2014:751-67.
[16]. Sunderkötter C, Becker K. Frequent bacterial skin and soft tissue infections: diagnostic signs and treatment. J Dtsch Dermatol Ges. 2015;13 (6):501-24.
[17]. Brucato MP, Patel K, Mgbako O. Diagnosis of gas gangrene: does a discrepancy exist between the published data and practice. J Foot Ankle Surg 2014 53 (2):137-40.
[18]. Stevens DL, Bisno AL, Chambers HF et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis 2014; 59 (2): e10-52.
[19]. Mallikarjuna MN, Vijayakumar A, Patil VS, Shivswamy BS. Necrotising fascitis. ISRN Surg. 2012; 20(12): 942437.
[20]. Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. J Hosp Infect. 2010; 75 (4): 249-57.
[21]. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for necrotizing soft-tissue infections. Ann Surg. 1995; 221 (5):558-63.
[22]. Freischlag JA, Ajalat G, Busuttil RW. Treatment of necrotizing soft tissue infections. The need for a new approach. Am J Surg. 1985; 149 (6):751-5.
[23]. Hadeed GJ, Smith J, O'Keeffe T et al. Early surgical intervention and its impact on patients presenting with necrotizing soft tissue infections: A single academic center experience. J Emerg Trauma Shock. 2016; 9 (1):22-7.
[24]. Anaya DA, and Dellinger EP. Necrotizing Soft-Tissue Infection: Diagnosis and Management. Clin Prac 2007:44 (1): 705-710.
[25]. Mpirimbanyi C, Rickard J, Furaha C. Necrotizing Soft Tissue Infections at a Tertiary Referral Hospital in Rwanda: Epidemiology and Risk Factors for Mortality. World J Surg 2018; 42: 2314–2320.

[26]. Jimenez MN, Seltzer ES, Devanabanda B, Louis M, Mandava N. Necrotizing fasciitis: presentation, microbiology and outcomes in a community hospital. Int Surg J 2020; 7: 2471-9
[27]. Misiakos EP, Bagias G, Papadopoulos I et al. Early diagnosis and management of Necrotizing fasciitis: A Multicenter Study. Front Surg 2017; 4:5.
[28]. Anaya DA, and Dellinger EP. Necrotizing Soft-Tissue Infection: Diagnosis and Management. Clin Prac 2007:44 (1): 705-710.
[29]. Kalaivani V, Hiremath BV, Indumathi VA. Necrotising Soft Tissue Infection–Risk Factors for Mortality. J Clin Diagnostic Res 2013; 7(8): 1662-1665.
[30]. Zhao JC, Zhang BR, Shi K. Necrotizing soft tissue infection: clinical characteristics and outcomes at a reconstructive center in Jilin Province. BMC Infect Dis 2017; 17: 792.
[31]. Faraklas I, Stoddard GJ, Neumayer LA. Development and validation of a necrotizing soft-tissue infection mortality risk calculator using NSQIP. J Am Coll Surg. 2013;217(1):153-60.