"LRINEC – An Objective Scoring System as a tool for early diagnosis of Necrotizing Fasciitis"

Dissertation submitted in
Partial fulfilment of the regulations required for the award of
M.S. DEGREE
In
General Surgery Branch - I

THE TAMILNADU
DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI
APRIL, 2014.

Certificate

CERTIFICATE

This is to certify that this dissertation titled **"LRINEC – An Objective Scoring System as a tool for early diagnosis of Necrotizing Fasciitis"** submitted to the Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of M.S Degree Branch - I (General Surgery) is a bonafide work done by Dr.VISHVAK CHANTHAR K.M.M., post graduate student in General Surgery under my direct supervision and guidance during the period of November 2012 to November 2013.

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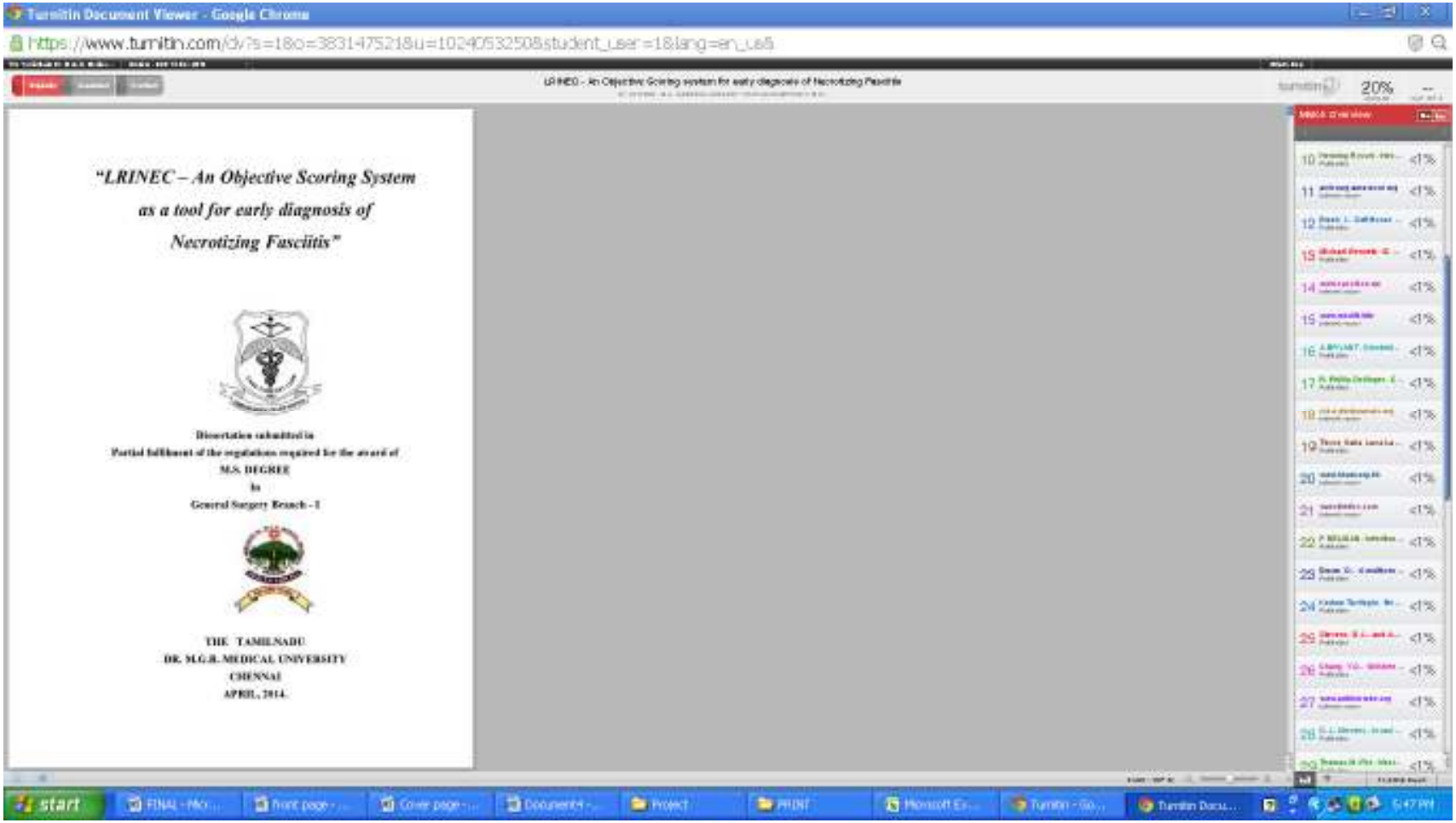
"LRINEC – An Objective Scoring System as a tool for early diagnosis of Necrotizing Fasciitis" Dissertation submitted in Partial fulfilment of the regulations required for the award of M.S. DEGREE In General Surgery Branch - I THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI APRIL, 2014. INTRODUCTION Skin and/or subcutaneous tissue infections are highly diverse with regard to etiology, predisposing organisms, incidence, clinical features, severity and complications. They may occur as single or recurrent episodes. The spectrum of deep soft tissue infections ranges from localized bacterial, viral and parasitic lesions to rapidly spreading, tissue destructive infections such as necrotizing...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I express my thanks to my family and friends and all others who have helped me in the preparation of this dissertation.

Last but not the least; I heartily thank all the patients for their kind support without whom this study could never be done.

Declaration

DECLARATION

I hereby declare that the dissertation entitled **"LRINEC – An Objective Scoring System as a tool for early diagnosis of Necrotizing Fasciitis** "was done by me at Coimbatore Medical College Hospital Coimbatore – 641018 during the period of my post graduate study for M.S. Degree Branch-1 (General Surgery) from 2012 to 2013.

This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the University regulations for award of M.S., Degree in General Surgery.

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LRINEC – AN OBJECTIVE SCORING SYSTEM AS A TOOL FOR EARLY DIAGNOSIS OF NECROTIZING FASCIITIS

BACKGROUND

Skin and/or subcutaneous tissue infections are highly diverse with regard to etiology, predisposing organisms, incidence, clinical features, severity and complications.The spectrum of deep soft tissue infections ranges from localized lesions to rapidly spreading, tissue destructive infections such as necrotizing fasciitis and myonecrosis. Necrotizing soft tissue infections are often fatal, characterized by extensive necrosis of thesubcutaneous tissues and fascia.The reported mortality of 30-40% reflects the inadequacy of early recognition of Necrotizing soft tissue infections. This study emphasizes on the search for a tool that reliably and rapidly identifies patients with NF and helps to decide for earlier effective therapy to modify clinical outcome.

AIM OF THE STUDY

To Validate the LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score as a tool for early distinguishing of Necrotizing Fasciitis from other infections of the soft tissues.

METHODS

Sixty of patients with soft tissue infections were evaluated prospectively on the basis of Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC). Based on their LRINEC score, the patients were categorised as Low, Intermediate and High Risk for the onset of Necrotizing fasciitis. Patients in each category were appropriately managed. All variables in terms of progression of the disease, associated co-morbidity, onset of necrotizing fasciitis, number of debridement, outcome of the disease in each category were documented and statistically analysed to evaluate the significance of LRINEC score in predicting the onset of Necrotizing fasciitis and its clinical outcomes.

RESULTS

A total of 60 patients with soft tissue infections were prospectively evaluated in this study and categorised on the basis of LRINEC score – 45 patients in Low risk category, 7 in Intermediate risk and 8 patients in High risk group.This study included forty two males (70%) and eighteen females (30%). Diabetes mellitus was the most common co-morbidity (23 cases). Tissue diagnosis was positive for necrotizing fasciitis in 7 cases of low risk, 1 case in intermediate risk and 3 cases in high risk group. Required mean number of debridement is 1.6 times . In terms of outcome, all cases (including positive tissue diagnosis cases) in low risk and intermediate risk groups and 2 cases in high risk group were improved with surgical dedridement/fasciotomy.

2 cases required amputation and 3 cases were dead. There is no statistically significant difference between the mean age between the groups of severity. The cut off of LRINEC ≥ 6 has better sensitivity and specificity in identifying the risk of the patient. The p-value (0.001) reveals that there is an association between Diabetes Mellitus and the severity of risk. The p-value(0.08) for the comparison of mean hospital days among the group of severity indicates that there is no difference between the mean of hospital stay.

CONCLUSION

LRINEC scoring system has a better positive predictive value in identifying the onset of necrotizing fasciitis and risk strategizing of the patients with severe soft tissue infections.There is a statistically significant association between Diabetic Mellitus and the severity of risk. The significance of LRINEC score in predicting the clinical outcome of the disease could not be outlined because of limited population included in this study. Further studies are needed to determine whether additional interventions targeted to the high mortality risk group can lead to improved outcomes.

KEY WORDS

NF - Necrotizing Fasciitis

LRINEC - Laboratory Risk Indicator for Necrotizing Fasciitis

Introduction

Skin and/or subcutaneous tissue infections are highly diverse with regard to etiology, predisposing organisms, incidence, clinical features, severity and complications.

They may occur as single or recurrent episodes. The spectrum of deep soft tissue infections ranges from localized bacterial, viral and parasitic lesions to rapidly spreading, tissue destructive infections such as necrotizing fasciitis and myonecrosis.

When a patient presents with soft tissue infection, the clinician faces the challenge of establishing a specific diagnosis and prescribing definitive treatment. Even the experienced clinician may have difficulty distinguishing between the different forms of deep soft tissue infection during the early stages.

Necrotizing soft tissue infections are often fatal, characterized by extensive necrosis of the subcutaneous tissues and fascia. Perhaps it is the most severe form of soft tissue infection potentially limb and life threatening. These infections often are mistaken for cellulitis or innocent wound infections and hence, diagnostic delay. Inspite of advances in antibiotic therapy and intensive care, the mortality of necrotizing soft tissue infections is still high. The reported mortality of 30-40% reflects the inadequacy of early recognition of Necrotizing soft tissue infections.

This study emphasizes on the search for a tool that reliably and rapidly identifies patients with NF and helps to decide for earlier effective therapy to modify clinical outcome.

Aims and Objectives

AIM OF THE STUDY:

To Validate the LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score as a tool for early distinguishing of Necrotizing Fasciitis from other infections of the soft tissues.

OBJECTIVES:

1. To determine whether laboratory risk indicators based on LRINEC score among patients with severe soft tissue infectionswould predict the onset and presence of an early stage of necrotizing fasciitis.
2. To evaluate whether risk categorization using LRINEC score is appropriate.
3. To identify the significance of LRINEC score in predicting the clinical outcomes.
4. To interpret the accuracy of score in the presence of co-morbid conditions

Review of Literature

EPIDEMIOLOGY

Necrotizing fasciitis (NF) is a well-defined, persistent, and pervasive disease in which the fascia is the primary site of infection. Necrotizing fasciitis has been described in medical texts since 1871[1] and in the surgical literature since 1924[2].

Although the exact incidence of these infections in the general population is unknown, they are among the most common infections occurring in all age groups. Some are age-related, for example impetigo commonly in children and erysipelas common in older adults.

Until the mid-of 20th century, wartime injuries were commonly complicated by gas gangrene caused by Clostridium spp. Those were the time of civil war in USA, when nearly 50% of soldiers who sustained gunshot injuries developed infection and most of them developed gas gangrene. Clostridial gangrene is typically a sporadic infection but during the Civil War apparent epidemics of 'hospital gangrene' were described. Contributing factors included severe trauma, grossly contaminated wounds, crowded and dirty conditions, application of soiled dressings (often recycled from patients who had just died of infection) and primitive surgical techniques for debridement and fixation of open fractures.

Group A streptococci undoubtedly caused some of these infections but other major bacterial pathogens, including Clostridium perfringens, Gram-negative bacteria and mixed aerobic-anaerobic bacteria, also contributed.

Gas gangrene was also common during the First World War, particularly in the European theatre, where the soil was rich and well fertilized with animal faeces containing large numbers of vegetative spores of clostridia. In contrast, in North Africa, cases of gangrene following gunshot wounds were far less common, presumably because the desert sand contained few Clostridial spores[3].

In modern warfare, gas gangrene has become uncommon because wounded soldiers are evacuated rapidly to well-equipped hospitals for surgical intervention, arterial reconstruction and antibiotic treatment, all of which have greatly reduced the prevalence of this feared disease.

In modern times, these serious deep soft tissue infections have become less common. Sporadic cases in the general population most often occur as occasional complications of penetrating trauma, compound fractures or septic abortions. For the first time in history, spontaneous gas gangrene caused by Clostridium septicum may be more common than trauma-associated gas gangrene caused by C. histolyticum, C. perfringens or other Clostridium spp.

Recently, severe soft tissue infections due to C. sordellii, C. perfringens, and C. novyi have been described among intradermal ('skin popping') and intravenous drug users.[4, 5]

Necrotizing fasciitis, a life-threatening soft tissue infection, can occur in association with gas gangrene as a part of generalized tissue necrosis or as a separate clinical entity.

PATHOGENESIS

The skin is an organ that reacts to infectious, noxious, external and internal stimuli in a limited number of ways. The rich plexus of capillaries beneath the dermal papillae provides nutrition to the stratum germinativum and the dermatocytes, which are bound together by tight junctions and form the barrier to microbial invasion. Once microbes have penetrated this barrier through a hair follicle, cut or bite, the dermal plexus of capillaries delivers the components of the host's defence — oxygen, complement, immunoglobulins, macrophages, lymphocytes and granulocytes — to the site of infection.

Release of proinflammatory cytokines such as IL-1, IL-6 and tumor necrosis factor- alpha, results in an augmentation of the immune functions described above. These cytokines induce fever, prime neutrophils, and increase antibody production and the synthesis of acute phase reactants, such as C-reactive protein. Cytokine driven stimulation of endothelial cells also results in the generation of nitric oxide and prostaglandins, both of which cause vasodilation. The net physiologic effect is greater blood flow to the tissue.

These processes result in the cardinal features of inflammation (Fig.1):

¦ Erythema,

¦ Swelling,

¦ Heat and

¦ Tenderness or pain.

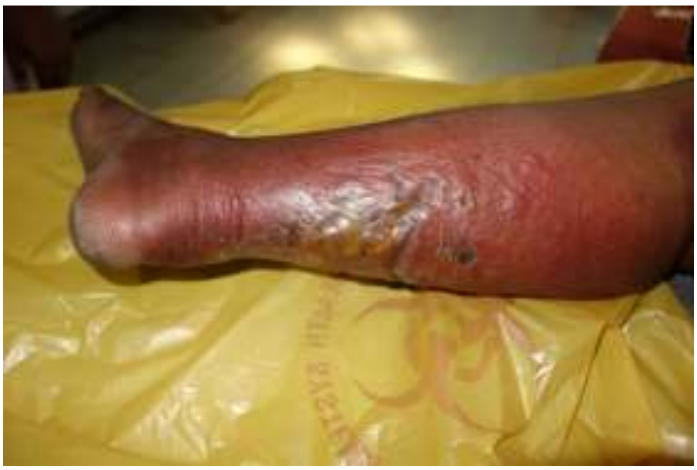


Fig.1 Signs of Inflammation

If tissue perfusion is moderately attenuated, tissues may remain viable, but the threshold for progression of infection may be lowered.

Predisposing conditions in this category include:

- peripheral vascular disease affecting large arteries,
- diabetes mellitus causing microvascular disease, and
- Chronic venous stasis causing post capillary obstruction.

Most fungi and bacteria multiply in the viable tissue, but the spread of infection is limited by the fibrous attachments in between subcutaneous tissues and fascia. The natural lack of fibrous attachments facilitates wide spread infection especially in the trunk or extremities. The superficial fascia being the primary site of such pathology; the attributed mechanism of spread is expression of hyaluronidase like bacterial enzymes that helps to degrade the fascia. Unregulated multiplication of bacteria results in angiothrombotic microbial invasion with liquefactive necrosis of the superficial fascia. Thus the infection usually spreads along fascial planes. This leads to thrombosis of perforating nutrient vessels to the skin and progressive skin ischemia.

This pathogenesisis responsible for the skin manifestations of evolving necrotising fasciitis[6]. Initially a radial phase with abrupt spread through the fascia predominates, followed by extensive undermining of apparently normal looking skin.

As the condition progresses, ischaemic necrosis of skin evolves and ensues gangrene in subcutaneous fat, dermis and the epidermis, with progressive bullae formation, ulceration, and skin necrosis (Fig.2).

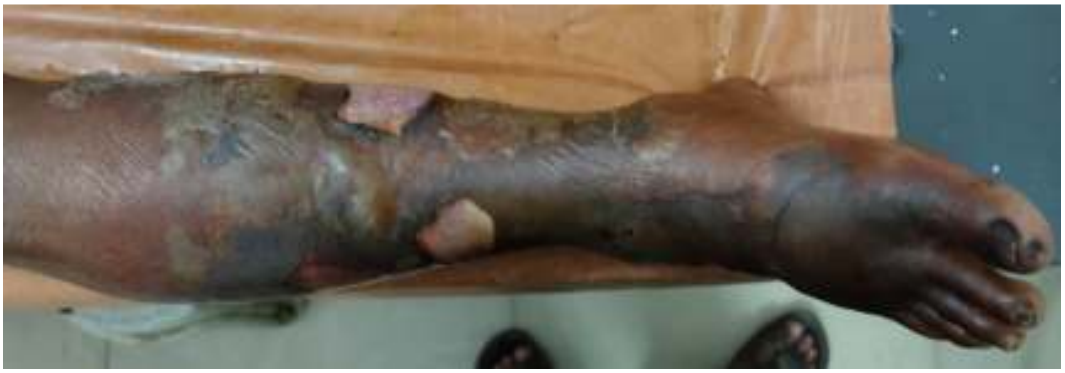


Fig.2 Skin Necrosis with Ulceration

Necrosis of the skin and deeper tissue may occur if there is severe hypoxia. Two examples are:

- pressure necrosis resulting in decubitus ulcers, and
- Compartment syndromes resulting in hypoxia and then necrosis in muscles confined within tight fascial bundles.

CLASSIFICATION OF DEEP SOFT TISSUE INFECTION

Clinical types are two:

Type I:

Type I necrotizing fasciitis refers to a mixed aerobic and anaerobic bacterial infection occurring most commonly in diabetic patients, following surgical procedures, and in those with peripheral vascular disease.

Although the risk for an individual diabetic patient is low, this type of deep soft tissue infection is the most common form in the general population because the total number of people who have diabetes is large.

Non-clostridial anaerobic cellulitis and synergistic necrotizing cellulitis are both variants of the same syndrome. It may not be important to distinguish these entities from one another because all occur in diabetic patients and are caused by mixed anaerobic and aerobic bacteria.

Type II

Type II is caused by group A streptococci and was earlier labelled as streptococcal gangrene.[7]

Of recent years, there has been a dramatic rise in the number of invasive infections, caused by group A streptococci including necrotizing fasciitis. In contrast to type I, this type may occur in any age group. Moreover Patients who do not have complicated medical illnesses may develop Type II necrotizing fasciitis.

Predisposing factors include:

¦ Intravenous drug abuse,

¦ History of blunt trauma,

¦ Non-steroidal anti-inflammatory agents,

¦ Childbirth,

¦ Chickenpox,

¦ Muscle strain, or

¦ wounds such as caused by a laceration or a surgical procedure.

Based on the etiology

NF with a known aetiology are classified as **secondary NF.** Bacterial entry occurs following some predisposing events such as cuts, abrasions, contusions, lacerations, burns, subcutaneous injections, bites, or operative incisions that causea break in the epidermis. In circumstances of occult infection such as an infected Bartholin cysts, perforated hollow viscus or as a complication of peri-rectal abscess, secondary NF can also occur.

Idiopathic or Primary NF, occurs in the presence of a unknown or un-identifiable etiologic factor. The exact pathogenesis still unknown. In view of early diagnosis and management, it is wiser to consider that idiopathic NF exists, and is a distinct clinical entity.

CLINICAL FINDINGS

Necrotizing fasciitis is a severe infection of subcutaneous soft tissues, principally the superficial and often the deep fascia. Usually it is an acute process but rarely may follow a sub-acute progressive course.

Any part of the body can be affected by Necrotizing fasciitis but is most common on the extremities, especially the legs. Other sites of predilection are the perianal and groin areas, abdominal wall, and postoperative wounds.

The gateway of infection usually is from a site of trauma such as an abrasion, laceration, insect bite, burn, a laparotomy performed in the presence of peritoneal soiling(e.g., penetrating abdominal trauma or perforated viscus) or

another surgical procedure (e.g., haemorrhoidectomy, vasectomy), perirectal abscess, decubitus ulcer, or intestinal perforation. The intestinal perforation may be due to occult diverticulitis, recto sigmoid neoplasm, or a foreign body such as a chicken bone or toothpick. Necrotizing fasciitis of such intestinal sources may occur in the lower extremity, in the groin or abdominal wall. The spread of infection from intestinal sources to the lower extremity is via extension along the psoas muscle and to that of abdominal wall is via a colo-cutaneous fistula. In particular necrotizing fasciitis may develop in the clinical setting of alcoholism, diabetes mellitus, and parenteral drug abuse.

The affected region is initially swollen, erythematous, shiny, without sharp margins, hot, exquisitely tender, and painful. Lymphangitis and lymphadenitis are uncommon.

The process progresses rapidly over several days, with sequential integument colour changes from patches of red-purple to blue-grey. In 3 to 5 days after onset, skin breaks down with the formation of bullae (containing thick pink or purple coloured fluid) and frank cutaneous gangrene (resembling a thermal burn) can be seen. (fig.3)

Fig.3 Skin broken down with Thermal burn appearance

The involved area by this time is no longer tender and becomes anaesthetic due to thrombosis of micro vasculature and destruction of superficial nerves that are normally located in the necrotic, undermined subcutaneous tissue. The onset of anaesthesia may precede the appearance of skin necrosis and suggests that the process is necrotizing fasciitis and not a simple cellulitis. Marked swelling and edema may cause a compartment syndrome with resultant extensive myonecrosis requiring prompt fasciotomy. Measurement of compartment pressure may aid the evaluation in early situations in which marked pain and swelling are present without concomitant skin changes that would indicate the diagnosis.

Subcutaneous gas is often present in the polymicrobial form of necrotizing fasciitis, particularly in patients with diabetes mellitus. Systemic toxicity is prominent, and the temperature is elevated in the range of 38.9° to 40.5°C (102°to105° F).On probing of the lesion with a haemostat through a small incision, the instrument passes easily along a plane just above the deep fascia. Such easy passage would not occur with ordinary cellulitis.

The Centre for Disease Control and Prevention and The National Necrotizing Fasciitis Foundation has compiled the following as symptoms of NF:

Early symptoms (usually within 24 hours):

1. Commonly a trivial trauma or breech of skin has occurred (not necessarily appear infected)
2. Pain at the site of injury. Pain may be sometimes in the same region or limb of the body
3. Pain often disproportionate to the grade of injury
4. Flu like illness then faces up with symptoms such as nausea, diarrhoea, dizziness, weakness, fever, confusion, and malaise
5. Dehydration
6. The biggest symptom is combined of all these symptoms.

Advanced symptoms (usually occurs within 3–4 days):

1. The affected area swells, and may develop a purplish rash
2. Formation of blisters filled with blackish fluid
3. The wound may appear necrotic, associated with a dark mottled, flaky appearance.

Critical symptoms (usually within 4–5 days):

1. Hypotension
2. State of septic shock from the toxins released by the bacteria.
3. Unconsciousness.

CLINICAL DIAGNOSIS

Recognition of the characteristic features and the rapidly progressive clinical course of the disease aids in the diagnosis of necrotising fasciitis.[8]

Table.1 **Clinical stages of necrotising fasciitis**

Stage 1	Stage 2	Stage 3
Tenderness	Blisters and bullae formation	Tissue necrosis
Erythema		Hyposensitivity
Oedema		Anaesthesia
Warm skin		Tissue crepitation
Fever		Haemorrhagic bullae

Preceding history of soft tissue injury could be there commonly, from a blunt or penetrating trauma, animal or insect bite, postoperative infection, minor skin infection, or even injections that the patient has received as in subcutaneous insulin or illicit drugs.

Overlapping diagnostic characteristics among cellulitis and necrotising fasciitis, often initially mislead the diagnosis to cellulitis, resulting in delayed management of much severe condition underneath. Not uncommonly, pain out of proportion to the elicited sign is the only early differentiating feature. In cellulitis, infection starts at the junction of dermis and superficial fascia, but in necrotising fasciitis it begins at the level of subcutaneous fat and deep fascia. The early stages of NF spares the epidermal and dermal layers.[9] Erythema of skin and edema of the epidermal and dermal layers are therefore not obvious initially. Hypocalcemia (without tetany) may occur if subcutaneous fat necrosis is extensive.

A number of symptoms and signs, however have been proposed that may help differentiate the two mentioned conditions. A Canadian study outlined patients with necrotising fasciitis as more likely to have a generalised erythematous rash and a toxic appearance.[10] The pyogenic exotoxins and cytolysin produced by organisms are responsible for hypotension, disseminated intravascular coagulation and multi-organ failure.

This study also described that patients with necrotising fasciitis were more likely to have thrombocytopenia at presentation (mean, 194.0 x 10^9/L for necrotising fasciitis Vs 299.3 x 10^9/L for cellulitis=0.03).[10]

Radiological studies help in assessing the extent of tissue infection, the presence of sub cutaneous gas aids in determining the extent of infection, especially in mixed aerobic – anaerobic or Clostridial infections. Plain radiographs may detect gas in soft tissues (fig.4), but Magnetic Resonance Imaging and Computed Tomography are superior at revealing the extent of affected area.

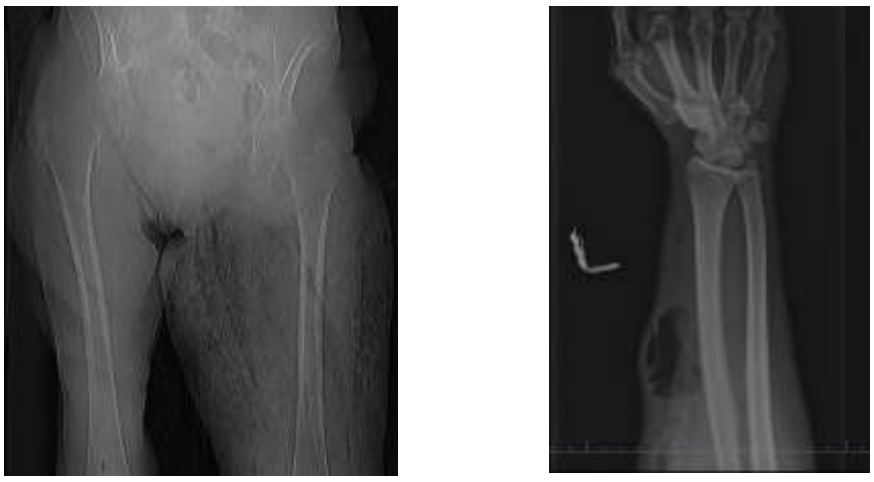


Fig.4 Plain Radiographs showing subcutaneous gas

CT scan features of Necrotizing Fasciitis include thickening and enhancement of deep fascia, fluid and gas in the soft tissue planes in and around the superficial fascia. (fig.5)

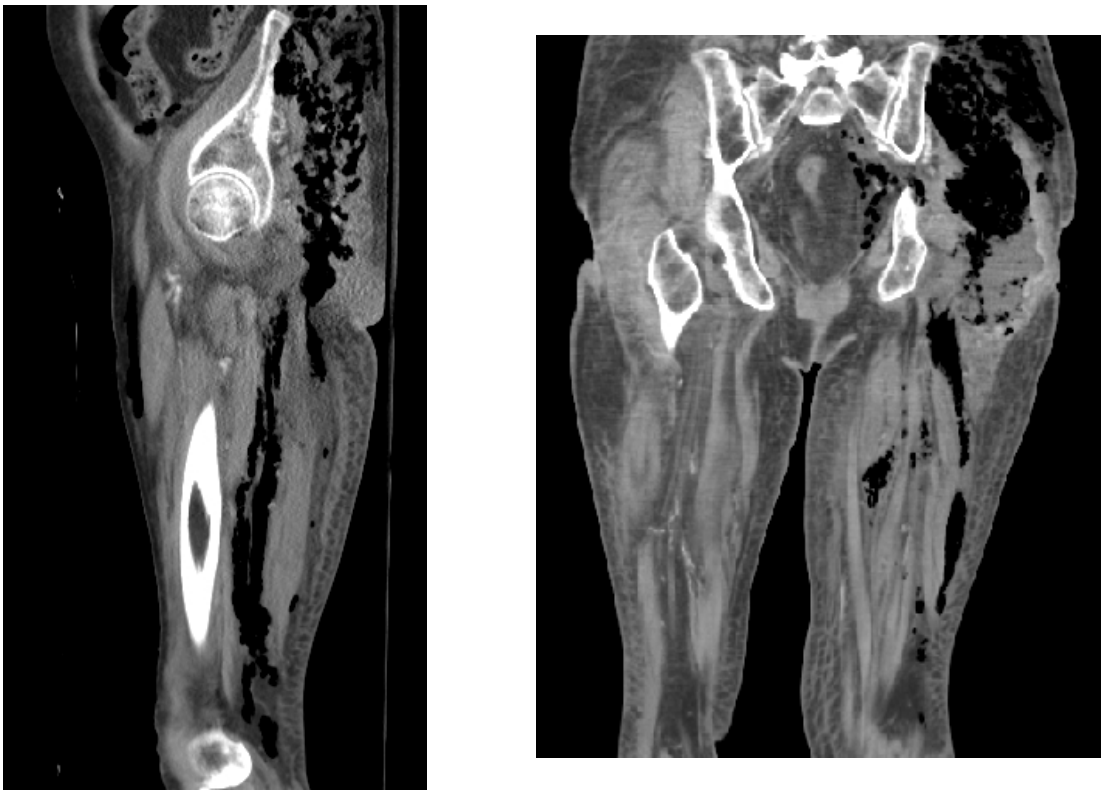


Fig.5 CT Image showing impressive amount of gas extending up the fascial planes in the upper left leg and gluteal area.

The features indicative of NF in USG include distortion and thickening of the deep fascia and fluid collections along the deep fascia.

MRI is better to CT in distinguishing healthy and necrotic tissue. Features in MRI that are distinct for NF includes deep fascial fluid collections and thickening, and hyperintense T2W signal within the muscles.

In MRI the sensitivity often exceeds its specificity that ensues in overestimation of extent of deep fascial involvement. Despite, a negative deep fascial involvement on MRI almost certainly excludes NF.

However, routine application of Computed Tomography, Magnetic Resonance Imaging and frozen section biopsy in the evaluation of soft tissue infections is limited by cost and availability. Hence, Wong et al designed a simple scoring system, the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC), which is based on routine laboratory investigations that are readily available at most centres, and that can help distinguish Necrotizing Fasciitis from other soft tissue infections. [11]

The LRINEC score is calculated based on points assigned for six laboratory variables at the time of presentation including: C-reactive protein, haemoglobin, total leukocyte count, serum glucose, serum sodium, serum creatinine.

Table.2 **Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score**

Variable	***Score***
C- Reactive Protein, mg/L	
< 150	0
≥ 150	4
Total White cell count, per mm^3	
< 15	0
15 – 25	1
> 25	2
Hemoglobin, gm/dl	
> 13.5	0
11 – 13.5	1
< 11	2
Sodium , mmol/L	
≥ 135	0
< 135	2
Creatinine , mg/dl	
≤ 1.6	0
> 1.6	2
Glucose , mg/dl	
≤ 180	0
> 180	1

The maximum score is 13.

LRINEC Score	Inference
≥ 6	Suspicious of NF
≥ 8	Strong prediction of NF

The LRINEC score stratifies patients with softtissue infection into low, moderate and high risk categories of necrotizing fasciitis even when the clinical picture is equivocal. (fig.6)

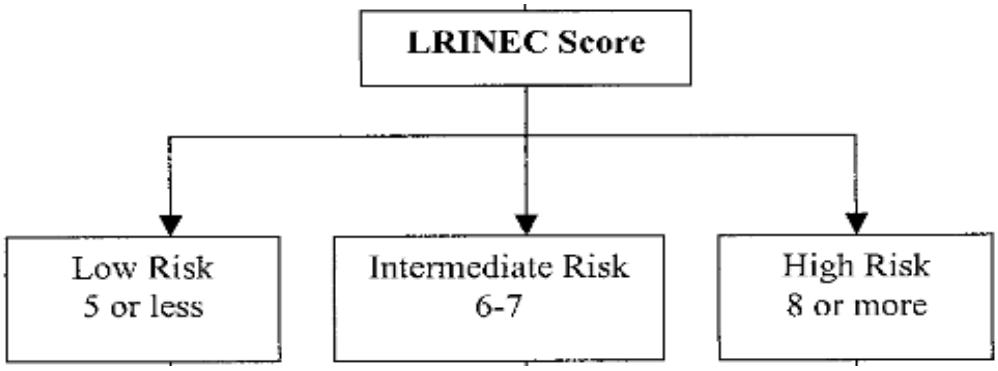


Fig.6 Risk Stratification using LRINEC Score

Although Wong et al suggested LRINEC score as capable of detecting even clinically early cases of NF, other studies[12-15] did not yielded satisfactory results so far to validate LRINEC score for routine use.

Limitations in earlier studies:

1. Earlier studies were retrospective one. All variables of research interest may not be included in medical records since they might not be designed for research purposes or may contain inaccurate descriptions.

However, to recommend the score for its routine use in the evaluation of soft tissue infections, LRINEC needs to be prospectively validated.

2. The study cohort might include the subjects by the discharge diagnosis of necrotizing fasciitis. Less severe forms of the disease where the diagnosis was not made might have preferentially been missed. However, there may be some cases that are so fulminant where the diagnosis was unclear, would also affect their sample either way.
3. Antibiotic therapy in other hospitals before the presentation to their ED might had an influence on the clinical course of disease.
4. The inflammatory response may be blunted in patients with multiple comorbidities, thereof, the accuracy of the score had not been interpreted in such a cohort
5. Unclear significance between the LRINEC score and the outcomes of necrotizing fasciitis, especially in terms of its predictability in limb loss and mortality

SURGICAL DIAGNOSIS

Tissue biopsy obtained at wound exploration and surgical debridement has remained the gold standard for detecting necrotising soft tissue infection. Biopsy diagnosis of NF is made when it shows infiltration of fascia by polymorphonuclear leukocytes.

Integrity of tissue and depth of invasion during wound exploration can also be evaluated. Evidence of myonecrosis and fascial necrosis are indicative of necrotising infection. Definitive features of loss of fascial integrity along the tissue planes and presence of involvement of muscles are also diagnostic.

A bedside procedure that helps in diagnosis is the 'finger test'. Under local anaesthesia, a 2-cm incision is made down to the deep fascia and a gloved finger is then probed at the level of the superficial fascia. Foul-smelling 'dishwater' pus, lack of bleeding and least tissue resistance to finger dissection signifies a positive finger test, and are considered to be diagnostic of necrotising fasciitis.[16, 17]

MICROBIOLOGY

The exudate from wound, on gram staining usually reveals a mixture of organisms or chains of gram-positive cocci in the case of streptococcal gangrene. Infection with a single pathogen occurs in only 15% to 29 % of patients.[18] NSTI s are typically polymicrobial in nature.

Staphylococcal and Streptococcal species are relatively common causative organisms in combination with anaerobes. Vibrio and fungal pathogens have also been described as causing NSTI.

Clostridial infections are typically monomicrobial, although they can be seen in combination with other bacteria. They are often characterised by myonecrosis and associated with a significantly worse prognosis. The most common organisms associated with Clostridial infections are clostridium perfringens, C.novyi and C. septicum.[18] In most studies Clostridium difficile has also been isolated along with several members of Enterobacteriaceae from the wound drainage material.

Commonly cultured gram positive organisms include coagulase negative staphylococci, group A haemolytic streptococci, Staphylococcus aureus, Staph. Epidermidis, enterococci, and Clostridial species. Mixed gram positive infections are present in approximately 10% of patients. Gram negative organisms such as Enterobacter species, Escolar, proteus sp, Pseudomonas, bacteroides sp, Serratia sp and mixed gram negative organisms are also common. The only other bacteria commonly reported as the sole cause of non Clostridial NSTI is β- haemolytic Streptococcus pyogenes, so called flesh eating bacteria and it does cause a rapidly spreading NSTI.[18]

COMPLICATIONS

1. Delay in diagnosis
2. Bacteraemia
3. Delay in first debridement
4. Acute renal failure
5. ARDS/other respiratory failure
6. Multiorgan system dysfunction
7. Inadequate debridement
8. Other infection (e.g., pneumonia, UTI)
9. Clostridium difficile colitis
10. Wound infection
11. Decubitus breakdown/ulcer
12. latrogenic source of necrotizing infection
13. Seizure
14. Antibiotic reaction
15. Osteomyelitis
16. Cardiopulmonary resuscitation
17. Fecal wound soilage
18. Heart failure
19. Complications from HBO therapy

Acute renal failure is defined as a rise in serum creatinine level to more than twice the baseline level or at least greater than 2 mg/dl.

Adult respiratory distress syndrome can be defined as radiographic evidence of diffuse pulmonary edema, not found to be cardiogenic, and is associated with a PaO2/FiO2 ratio of less than 150 and decreased pulmonary compliance.

Multiorgan system dysfunction, defined as objective evidence of acutely diminished function in two or more organ systems that requires urgent medical or surgical intervention.

Complications from HBO therapy were uncommon which includes hypoglycemia, seizures, hemotympanum, and claustrophobia

PREVENTION

Centre for Disease Control has reported the following list of recommendations to prevent the disease:

- Patients with sore throats should consult a doctor.
- Patients with streptococcal throat infections should stay home until 24 hours after their last antibiotic dose.
- Proper hand wash do prevent the spread of Group A Streptococcus (GAS) infection, especially before preparing food or eating, after sneezing and coughing.
- Keeping the skin intact is essential.

- Patients with infected wounds and fever should seek early medical care.
- Wounds should be cleaned and monitored regularly for signs of infection (redness, swelling, drainage, pain).

MANAGEMENT

The three essential themes in treatment are surgical debridement, intensive supportive care and appropriate antibiotics. Some patients require mechanical ventilation and others need hemodialysis. Gross hypotension and diffuse capillary leak often necessitates vigorous amounts of intravenous fluids (10–20 litres per day), although anasarca is a common complication. In some patients blood pressure improves with intravenous fluid alone. Vasopressors such as dopamine may be useful, but there is meagre information from clinical studies in this specific infection. Although potent vasoconstrictors like epinephrine may improve blood pressure, symmetric gangrene may ensue, partly as a result of the drug and partly as a result of poor perfusion caused by the bacteria, toxins and endogenous mediators.

The "Surviving Sepsis Campaign," a multidisciplinary group that worked to develop treatment recommendations, has published guidelines incorporating evidence-based treatment strategies most recently in 2008.[19]

These guidelines are summarized below:

Initial evaluation and infection issues

Initial resuscitation:		Begin resuscitation immediately in patients with hypotension or elevated serum lactate with resuscitation goal of CVP 8-12mmHg, mean arterial pressure of ≥ 65 mmHg, and urine output of ≥ 0.5ml/kg per hour
Diagnosis	:	Obtain samples for cultures before antibiotic but antibiotic therapy not be delayed.
Antibiotic Therapy	:	Begin IV antibiotic therapy as early as possible: should be within the first hour after recognition of severe sepsis / septic shock; use broad spectrum antibiotic regimen with penetration into presumed source; reassess regimen daily; discontinue antibiotics in 7- 10 days for most infections; stop antibiotics for non-infectious issues.
Source control:		The anatomic site of infection should be established earlier. After initial resuscitation implement source control measures as soon as possible. Potentially

infected intra vascular access devices need to be removed.

HEMODYNAMIC SUPPORT AND ADJUNCTIVE THERAPY

Fluid Therapy :Fluid resuscitate using crystalloid or colloid, using fluid volumes of 1000 mL (crystalloid), target CVP of 8–12 mmHg.

Vasopressors/inotropic therapy: Maintain MAP of ≥65 mmHg; centrally administered nor epinephrine or dopamine are first-line choices; dopamine should not be used for "renal protection"; insert arterial catheters for patients requiring vasopressors. Do not increase cardiac index to predetermined supranormal levels.

Steroids : Consider IV hydrocortisone (adult dose ≤300 mg/d) for septic shock when hypotension is refractory to fluids and vasopressors.

Recombinant human activated protein C:

Consider rhAPC in adult patients with sepsis-induced organ dysfunction and high risk of death.

OTHER SUPPORTIVE THERAPY

Administration of Blood product:

Packed cell transfusion if hemoglobin decreases to <7.0 g/dL.

Mechanical ventilation : Target an initial tidal volume of 6 mL/kg body weight and plateau pressure of ≤30 cm H2O in patients with acute lung injury. Use PEEP to avoid lung collapse. Use a weaning protocol to evaluate the potential for discontinuing mechanical ventilation. Pulmonary artery catheter is not indicated for routine monitoring.

Glucose control : Control hyperglycemia in patients with severe sepsis with IV insulin.

Prophylaxis : Use stress ulcer (proton pump inhibitor or H2 blocker) and deep venous thrombosis (low-dose unfractionated or fractionated heparin) prophylaxis.

Limitation of support: Patients and families need to be aware of advance care planning.

CVP = central venous pressure; MAP = mean arterial pressure;

PEEP = positive end-expiratory pressure;

rhAPC = recombinant human activated protein C.

Aggressive nutritional support is mandatory in all patients after debridement. Recommended allowances of calories would be double their basal caloric requirements given orally or parenterally. Nutritional support runs the risk of fewer complications with lower morbidity and mortality rates. Pre and post-operative pain control is also an important part of management and should be individualised for each patient.

PHARMACOTHERAPY

Antibiotic selection is difficult in patients who have rapidly progressing infection. Antibiotic therapy of NSTI is specifically directed to provide broad spectrum coverage for gram positive organisms, gram negative organisms and anaerobes.

The choice of empiric antibiotics is controversial and is dependent primarily on personal preference. Many of the most commonly used regimens include (1) penicillin and an aminoglycoside plus clindamycin, (2) imipenem-cilastatin, or (3) ampicillin plus sulbactam (Unasyn) plus an aminoglycoside.

Some practitioners select an antipseudomonal penicillin or, in the patient who is allergic to penicillin, vancomycin. Initial empiric treatment can subsequently be adjusted according to bacterial sensitivities on tissue cultures.

Recent studies describes that clindamycin is better to penicillin for treatment of experimental necrotizing fasciitis or myonecrosis caused by group A streptococci.[20] It seems likely that penicillin failure is due to the decreased expression of penicillin-binding proteins during the stationary phase of bacterial growth.

Clindamycin may be more efficacious because:

- it suppresses toxin production,
- it has a long post antibiotic effect.
- it is not affected by inoculum size or stage of growth
- it inhibits M-protein synthesis and facilitates phagocytosis of Streptococcus pyogenes

Neutralization of streptococcal toxins is a desirable therapeutic goal and is advocated by some experts.[21] Some authorities recommend also giving immune globulin (400 mg/kg/d intravenously for 5 days) for documented streptococcal toxic shock syndrome.[21]

SURGICAL INTERVENTION

The major emphasis in treatment is inevitably surgical. Suspicion should be directed toward any wound incurred out of doors and contaminated with a foreign body, soil, or faeces and any wound in which tissue (particularly muscle) has been extensively injured. This type of wound should be carefully examined, with the patient under sufficient anaesthesia to permit full inspection and debridement of devitalized tissue, including muscle.

It is often difficult to distinguish necrotic from edematous tissue. Careful daily inspections of the wound will determine whether repeated debridement will be necessary. Daily debridement under anesthesia may be required, since these lesions are extensive and the degree of tissue viability is often difficult to assess in the operating room (fig.7). Tight fascial compartments must be decompressed. Wide-open drainage is essential and may require extensive denudation.

A functional extremity can usually be salvaged in fasciitis; if not, amputation can be safely performed later.

Fig.7 Raw area right leg after surgical debridement

It is important to avoid confusing fasciitis with deep gangrene. It is a tragic error to amputate an extremity when removal of dead skin and fascia will suffice. Immediate amputation is necessary when there is diffuse myositis with complete loss of blood supply or when adequate debridement would clearly leave a useless limb.

When viability of the remaining tissue is assured and the infection has been controlled, soft tissue deficits can be covered with skin grafts.(fig.8)

Fig.8 Skin graft applied to cover the soft tissue deficit

The following factors favours limb salvage surgery:

Table.3 **Factors favouring limb salvage surgery versus amputation**

Limb salvage surgery	Amputation
Good past health Not life-threatening state Multiple sites Responsive to inotropic support	Concurrent medical disease with high anaesthetic risk from multiple operations (eg poorly controlled diabetes mellitus, valvular heart disease) Myonecrosis Unremitting shock Concurrent peripheral vascular insufficiency Rapidly progressive infection Large area of tissue necrosis (heel pad and sole skin loss)

HYPERBARIC OXYGEN THERAPY

Hyperbaric oxygen (HBO) is generally regarded as an important adjunct that can be used in the management of Clostridial myonecrosis or gas gangrene.[22] The principle of hyperbaric oxygen therapy is that all necrotizing infections have reduced oxygen tension in the tissues, ischemia and subsequent reduction in the host cellular immunity. Increased oxygen partial pressure has been associated with the reversal of basic pathophysiologic mechanism of necrosis. Increased oxygen tension also reverses ischemia and thereby improves host defence mechanisms. Furthermore, it facilitates the transport of drugs across the bacterial cell wall and thus enhances the action of various antibiotic agents.[22-24]

Despite these facts, the efficacy of HBO for other NSTIs remains controversial. The studies on the efficacy of HBO therapy and its outcome with respect to length of hospitalisation and mortality have failed to show statistically significant differences. As a result, HBO is not a mandatory component of therapy, but its use should never delay definitive surgical care.

An HBO treatment regimen usually consists of wound exposure at 2.5 to 3.0 atmospheres and breathing 100% oxygen for 90 minutes every 8 hours in the first 24 hours of infection, and then twice daily. HBO treatment is continued for a minimum of 5 days and is discontinued when the patient is stable and has no evidence of ongoing necrosis.

PROGNOSIS AND OUTCOME

The mortality associated with NSTI has been in the range of 16% to 45%. Multiple prognostic factors have been identified, including the presence of clostridial infection.[25]

For patients who survive no matter what their premorbid state – major disfigurement and lengthy rehabilitation are common.

Table.4 **Prognostic score to predict mortality in patients with NSTI at the time of first assessment**

VARIABLE (on admission)	NO. OF POINTS
Heart Rate > 110 beats/min	1
Temperature <36 ° C	1
Creatinine > 1.5mg/dl	1
Age	3
WBC > 40,000	3
Hematocrit> 50	3

From Anaya DA, Bulger EM et al: Predicting mortality in Necrotizing Soft Tissue Infections : A clinical score. Paper presented at the 25th Annual Meeting of the Surgical infection Society, May 2005

NO. OF POINTS	MORTALITY RISK
0- 2	6%
3-5	24%
≥ 6	88%

CLINICAL FORMS OF NECROTIZING FASCIITIS

Fournier's gangrene

'Fournier's gangrene' may be caused by the penetration of the GIT or urethral mucosa by bacteria. It is an aggressive infection caused by Gram-negative, aerobic bacteria, enterococci and anaerobic bacteria such as Bacteroides spp. and peptostreptococci. Extremes of pain may herald the onset of infection which spreads to the anterior abdominal wall and muscles of the gluteal region; in males, infection frequently extends to the scrotum and penis.(fig.9) Surgical inspection, placement of drains and appropriate surgical debridement are necessary for both diagnosis and treatment. Antibiotic treatment should be based upon culture and sensitivity and Gram staining information when available. An appropriate empiric regimen would be either ampicillin or ampicillin and sulbactamin combination with metronidazole or clindamycin. Alternatively, Gram-negative coverage is advisable if the patient had been hospitalised in the past or antibiotics have been used recently. This could be alleviated by substitution of ticarcillin-clavulanic acid or piperacillin-tazobactam for ampicillin or by addition of a fluorinated quinolone or aminoglycoside.

Fig.9 Fournier's gangrene

Meleney's synergistic gangrene

This is a rarer variety occurring in postsurgical state of patients. The lesions are slowly expanding, ulcerated and limited to the superficial fascia resulting in a combination between Staph. aureus and microaerophilic streptococci synergism. As in other forms of necrotizing infection, antibiotic therapy together with surgical debridement is the mainstay of treatment.

Non-Clostridial anaerobic cellulitis

In non-Clostridial anaerobic cellulitis, infection is associated with tissue gas producing aerobic organisms and mixed anaerobes. This foul smelling infection is associated with Diabetes Mellitus and differs from Clostridial cellulitis. Surgical exploration is required to distinguish this condition from necrotizing cellulitis, myonecrosis and necrotizing fasciitis by Clostridium spp.

Clostridial cellulitis

In Clostridial cellulitis, recent surgery or local trauma precedes infection. Clostridium perfringens is the most common species causing this entity. The fascia and deep muscle are spared whereas gas is invariably found in the skin; although clostridial cellulitis is different from clostridial myonecrosis in that there is less systemic toxicity, it is mandatory that thorough debridement and surgical exploration be performed to distinguish these entities. MRI or CT scans as well as a serum creatinine phosphokinase assay may also be useful for determining whether muscle tissue is involved. Treatment is discussed below under gas gangrene.

Clostridial gas gangrene

The following are types of Clostridial soft tissue infections [3]:

1. Simple wound contamination or colonization,
2. Cellulitis by anaerobic organisms
3. Clostridial gas gangrene.

The first type, simple wound contamination or colonization, does not progress to true infection for various reasons (e.g. there may be insufficient devitalized tissue to promote infection or there may be effective host responses or effective medical and surgical management). Contamination is a very common occurrence; 30–80% of open wounds has species of clostridial origin.[26]

Anaerobic cellulitis occurs in the presence of devitalized tissue in wound, sufficient for growth of Clostridium perfringens or other strains. Although gas extends along fascial planes, bacteremia and healthy tissue invasion do not occur. Appropriate removal of devitalized tissue at the prompt time, is all that is necessary for cure and nearly nil mortality.

The third type is myonecrosis or clostridial gas gangrene. This is defined as an acute invasion of muscle that is healthy and not damaged by previous ischemia or trauma.

It is divided into three different subtypes:

1. Traumatic gas gangrene,
2. Spontaneous or non-traumatic gas gangrene, and
3. Recurrent gas gangrene caused by C. perfringens.

Gas gangrene caused by trauma is the most common (70%)subtype. It develops when a deep, penetrating injury compromises perfusion that creates an anaerobic environment which is ideal for proliferation of clostridial organisms.

80% of such infections contain Clostridium perfringens; and the remaining cases reveal other strains such as Clostridium histolyticum, Clostridium septicum, Clostridium bifermentans, Clostridium novyi, Clostridium tertium and Clostridium fallax. Other predisposing conditions of traumatic gas gangrene are biliary tract and bowel surgery, intramuscular injection of adrenaline, illegal

abortion, retained placenta, prolonged rupture of the membranes and intrauterine foetal demise or missed abortion in postpartum patients.

Spontaneous or non-traumatic gas gangrene is less common. This is often caused by the aerobic species Clostridium septicum.

Recurrent gas gangrene caused by Clostridium perfringens is the least common type. This occurs in non-penetrating injuries at sites of previous gas gangrene.[27]

Traumatic gas gangrene

Pathogenesis

The initial trauma introduces organisms into the deep tissues and produces an anaerobic niche with a sufficiently low redox potential and acid pH for optimal growth of clostridial organisms. Necrosis progresses within hours. At the junction of normal tissues and necrotic, few polymorpho nuclear leukocytes are present, yet pavementing of these cells along the endothelium is apparent within capillaries and smaller arterioles and post capillary venules. Later in the course of the illness there is leukostasis within large vessels. Thus, the unique histopathology appearance in clostridial gas gangrene is an early influx of abundant polymorpho nuculear leukocytes without adjacent tissue or vascular destruction. This picture is in contrast to that seen in pyogenic organisms causing infection. Of late, it is suggested that s-toxin, at the site of infection, destroys host tissues and inflammatory cells.

The s-toxin promotes dysregulated adhesive interactions between polymorpho nuclear leukocytes and endothelial cells within circulation or in adjacent tissues and primes leukocytes for increased respiratory burst activity.

This results in injury to the endothelial layer, vascular leukostasis and regional hypoxia of tissues. Such hypoperfusion creates an anaerobic environment and contribute to the increased rate of tissue margin destruction. This is characteristic of clostridial gangrene.

Shock associated with gas gangrene may be attributed to the effects of released toxins. This effect may be a direct or indirect effect. Alpha toxin, a phospholipase C, suppresses cardiac contractility ex vivo and may contribute to hypotension. Theta toxin (a cholesterol-binding cytolysin) causes 'warm shock', which is defined as a markedly reduced systemic vascular resistance combined with a markedly increased cardiac output.[28]

Theta toxin accomplishes this by enhancing the release of endogenous mediators that cause relaxation of blood vessel smooth muscle, such as the lipid autacoids prostacyclin or platelet-activating factor. Tone of vessels reduces rapidly. A compensatory increase in cardiac output or rapid expansion of the intravascular blood volume occurs in order to maintain adequate tissue perfusion. This adaptive mechanism is markedly seen in Gram-negative sepsis, however similar compensatory mechanism may not be adequately possible in

shock induced by C. perfringens as because of alpha toxin directly suppresses on myocardial contractility.

Prevention

- Aggressive debridement of devitalized wound and early repair of any compromised blood supply helps to reduce the onset of gas gangrene in contaminated deep wounds.
- Prolonged tourniquet duration, Intramuscular adrenaline and surgical closure of dirty traumatic wounds should be avoided.
- Patients with compound fractures are at particular risk of gas gangrene especially if the wound is surgically closed immediately.
- Patients who have contaminated wounds should receive adequate and appropriate prophylactic antibiotic cover.

Clinical findings

The initial symptom is abrupt onset of severe pain in the site of recent surgery or trauma. The mean incubation period is often less than 24 hours, but may vary probably depending on the degree of wound contamination or bowel contents spillage and the extent of vascular injury with low tissue oxygen tension.

Initially pallor skin changes to bronze, then purplish red, becoming tense and tender. Bullae may beclear, red, blue or purple.

Gas in tissue may be obvious from clinical examination and soft tissue imaging. Interestingly, none of the CT, MRI has proved to be more sensitive or specific than the physical finding of crepitus in the soft tissue. However, imaging procedures are particularly useful for demonstrating gas in deeper tissue such as the uterus.

Features of systemic toxicity develop rapidly; these include diaphoresis, fever, tachycardia, followed by shock and multiple organ failure. Shock is present in 50% of patients at the time they present to the hospital. Bacteremiais seen in 15% of patients and can be associated with brisk hemolysis. Not all cases of C. perfringens bacteremia are associated with gas gangrene. Isolates from blood showing C. perfringens and C. septicum were associated with clinically significant wound infection.

Further complications of clostridial myonecrosis include hypotension, liver necrosis with jaundice and renal failure. Hemoglobinuria and myoglobinuria, causes renal failure but it can be a result of hypotension induced acute tubular necrosis. Renal tubular cells are probably directly affected by toxins, but this has not been proved.

Diagnosis

Factors supporting the diagnosis are worsening of pain at the site of previous injury or surgery, together with signs of systemic toxicity and gas in the tissues.

Definitive diagnosis is done by demonstrating Gram-variable rods at the affected site. Although clostridia stain Gram positive when obtained from bacteriologic media, when visualized from infected tissues they often appear both Gram positive and Gram negative. C. perfringens may appear to be encapsulated in fresh specimens.

Surgical exploration is inevitable. The exposed muscle appears edematous, may be an abnormal reddish-blue to black colour and does not bleed or contract when stimulated. Usually, some degree of fascial and cutaneous necrosisis also present. Organisms amongst degenerating muscle bundles with absence of acute inflammatory cells are evident in microscopic examination.

Management

Excellent in vitro activity against C. perfringens and other clostridia have been demonstrated in Penicillin, tetracycline, chloramphenicol, metronidazole, clindamycin, and numerous cephalosporins.

Randomized trials in humans to compare the efficacy of different antibiotics yet to be conducted. Most literature, based on in-vitro data states that penicillin is the drug of choice. However, experimental studies in mice have shown greatest efficacy for clindamycin and least for penicillin.

Erythromycin, rifampin, chloramphenicol, tetracycline and metronidazole are agents with efficacy greater than penicillin. Survival advantage was observed in animals receiving both clindamycin and penicillin; in contrast,

antagonistic effect was observed with combination of penicillin and metronidazole. A combination of penicillin and clindamycin is advisable since upto5% of strains would be resistant to clindamycin. Use of combination of tetracycline and penicillin is also advocated based on various experimental studies. Thus, in the absence of clinical trial in humans, the best treatment would be to administer a combination of clindamycin or tetracycline with penicillin. Thorough surgical debridement is always mandatory to improve survival, preserve limbs and prevent further complications.

Although some studies have reported better efficacy with HBO therapy when combined with antibiotics and surgical debridement, the use of hyperbaric oxygen is controversial. The Hyperbaric oxygen therapy, of theoretically, inhibits bacterial growth, preserve marginally perfused tissue and inhibit toxin production. Animal studies have demonstrated that HBO alone can be effective treatment if the inoculum is small and treatment is begun immediately. On contrary, other studies have reported that HBO when combined with penicillin was only of slight benefit. However, survival was better with clindamycin alone than with HBO alone, penicillin alone or HBO plus penicillin together.

Strategies in therapy have been directed against toxin expression and proadhesive molecules. Target of toxin expression is accomplished in vivo, by neutralization with specific antitoxin antibody or by toxin synthesis inhibition. Currently, antitoxin is no longer available. Endogenous proadhesive molecules

may be the promising future targeted strategy in attenuating toxin induced tissue injury.

Prognosis

Gas gangrene of an extremity have a better prognosis than those e truncal or intra-abdominal gas gangrene, because it is hardly feasible to debride such lesions adequately.[29] Truncal gangrene with associated bacteraemia and intravascular hemolysis have the greatest likelihood of progressing to shock and death.[33, 34]

Spontaneous, non-traumatic gas gangrene due to Clostridium septicum

Pathogenesis

Predisposing factors include:

¦ Leukemia,

¦ Cancer chemotherapy,

¦ Colonic carcinoma,

¦ Diverticulitis,

¦ Lymphoproliferative disorders,

¦ Gastrointestinal surgery,

¦ Radiation therapy, and AIDS

Neutropenia associated with spontaneous gas gangrene is due to C. septicum and in such cases commonly found lesions are necrotizing enterocolitis, cecitis or distalileitis. These factors allows bacteremia; consequently, the aero tolerant C. septicum can establish in healthy tissues.[30]

The distinct feature of C. septicum from the toxin of C. perfringensis that a- toxin of C.septicum has no phospholipase activity. Active immunization against a-toxin significantly protects against viable C. septicum experimentally. however, the recent cloning and sequencing of this toxin may facilitate further studies in this area.

Clinical features

The disease has often abrupt onset, with excruciating pain, although the symptoms of the patient usually is heaviness or numbness. Sometimes, confusion or malaise may be the initial presentation. Rapid progression of gangrene frequently sets in. Haemorrhagic or purplish fluid filled bullae make their appearance. Vascular compromise of the surrounding area also causes a purple hue of the skin.

Diagnosis

Histopathology of muscle and connective tissues reveals cell lysis and gas formation; with conspicuous absence of inflammatory cells.

In Spontaneous gangrene, the onset of bacteraemia usually precedes cutaneous manifestations unlike the traumatic gangrene.

Other common conditions presenting with fever and extremity pain in the absence of cutaneous signs of gas gangrene that should be considered are deep vein thrombophlebitis or cellulitis.

Management

Human trials evaluating the efficacy of Hyperbaric Oxygen or various antibiotics for treating spontaneous gas gangrene is yet to be done. Study data indicates C.septicumas susceptible to penicillin, tetracycline, erythromycin, clindamycin and metronidazole. The aero tolerance of C. septicum mayreduce the likelihood that HBO therapy would be effective.

Prognosis

The first 24 hours being the most crucial period comprising of majority of deaths with the mortality ranges from 67% to 100%,.[31, 32] Unfavourable factors include underlying malignancy and conditions causing compromised immune status. Survivors of bacteraemia or spontaneous gangrene caused by C. septicum should undergo appropriate diagnostic studies of the gastrointestinal tract. Occasionally, this has led to detection and cure of an unsuspected malignancy that might otherwise have been fatal.

Clostridium sordellii infections

The characteristic clinical features of C. sordellii infection are edema, leukemoid reaction, hemoconcentration, absence of fever and even shock in later stages combined with multiple organ failure. Often C. sordellii infections develop after gynaecologic procedures or in postpartum period and mostly represent endometrial infection. Rarely, other cases have occurred at sites of minor injuries such as lacerations of the soft tissues of an extremity. Recently, outbreaks of C. sordellii and C.novyi infections have been described among intravenous drug users in Scotland, Ireland and England. Patients have presented with severe soft tissue infections with shock with a case fatality rate of 20–30%. Absence of pain in C.sordellii is typical feature. The absence of fever and the paucity of signs and symptoms make early diagnosis difficult in such infections

Clostridium tertium infections

Clostridium tertium has been associated with spontaneous myonecrosis; however, bacteremia in immuno compromised hosts is more common with this infecton. Bacteremia probably arises from bowel sources, and the presence of the organism in the bowel may be partly related to its relative resistance to penicillin, clindamycin and cephalosporins. Clostridium tertium usually responds to metronidazole, chloramphenicol and vancomycin.

Because this organism can grow in an aerobic environment, it can be by mistake disregarded as a contaminant.

Pyomyositis

Most cases of pyomyositis occur in tropical areas. Local trauma is a common predisposing factor. Initially, seeding of traumatized muscle occurs and physical findings are not usually helpful. Within 10–20 days, fever, chills, muscle pain and tenderness are manifest. Most patients seek medical care at this stage and a diagnosis can be established by appropriate imaging studies, needle aspiration or exploration. Patients in whom a diagnosis has not been made may progress to shock and organ failure, though these complications are uncommon. Staphylococcus aureus is the most common cause of pyomyositis in tropical and non-tropical areas, and among HIV-positive patients.

Hospitalized immuno compromised patients who are HIV negative occasionally develop pyomyositis caused by Gram negative bacteria.

Surgical drainage of the abscess and empiric administration of parenteral antibiotics such as nafcillin or cephalosporins are reasonable treatments since most cases are caused by Staph. aureus. Definitive treatment can then be established based on cultures and sensitivities. Due to an increase in the prevalence of methicillin-resistant Staph. aureus, it may be necessary to use vancomycin or linezolid empirically pending sensitivity results.

Materials and Methods

A Prospective Observational study was conducted in Coimbatore Medical College Hospital from November 2012 to November 2013 among Patients admitted to the surgical wards with severe soft tissue infections.

Inclusion Criteria:

All Patients above 18 years of age with severe soft tissue infections.

Exclusion Criteria:

1. Patients ≤ 18 years age
2. Patients referred from other institutions
3. Patients who needs multiple admissions due to soft tissue infection, only the first admission be considered.
4. Patients with features of Necrotizing Fasciitis on presentation.
5. Patients with Surgical site infections.

Interventions:

- Age, sex, clinical manifestations, site and aetiology of infection, predisposing factors, comorbidities, vital signs, laboratory parameters at the time of admission, medication being taken at the time of admission and microbiology of wound and blood cultures had been recorded.
- Aggressive surgical debridement, culture of pus, tissue biopsy, radiological imaging, antibiotic therapy, treatment of complication, amputation or skin grafting were strategized for management.

- The interval between contact and admission, LRINEC score(Table -2), risk categorization (Fig 6), time interval between admission and first surgery, the number of surgical procedures, the need for amputation, the length of hospital stay and the mortality rate had been documented.
- All variables were statistically analysed further to evaluate the significance of LRINEC score in predicting the clinical outcomes.

Observation and Results

Total of 60 patients with soft tissue infections were included in this study. They were evaluated on the basis of Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC). Based on their LRINEC score, the patients were categorised as Low, Intermediate and High Risk for the onset of Necrotizing fasciitis. Patients in each category were appropriately managed and their outcomes are discussed below.

Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score

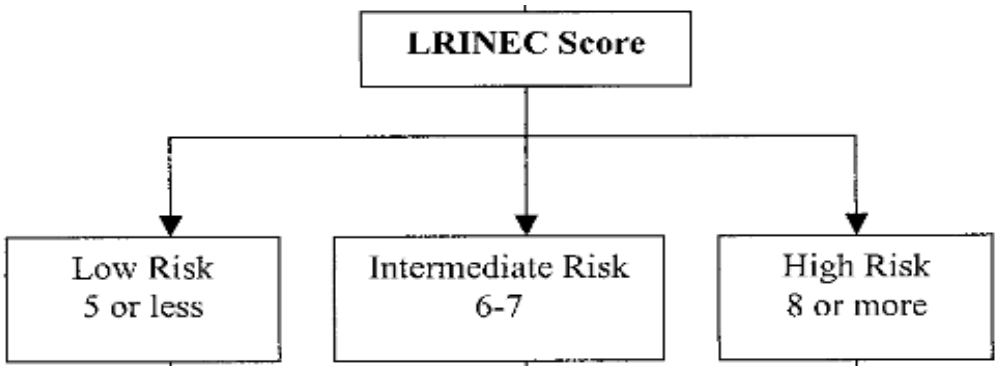
Variable	***Score***
C- Reactive Protein, mg/L	
< 150	0
≥ 150	4
Total White cell count, per mm^3	
< 15	0
15 – 25	1
> 25	2
Hemoglobin, gm/dl	
> 13.5	0
11 – 13.5	1
< 11	2
Sodium , mmol/L	
≥ 135	0
< 135	2

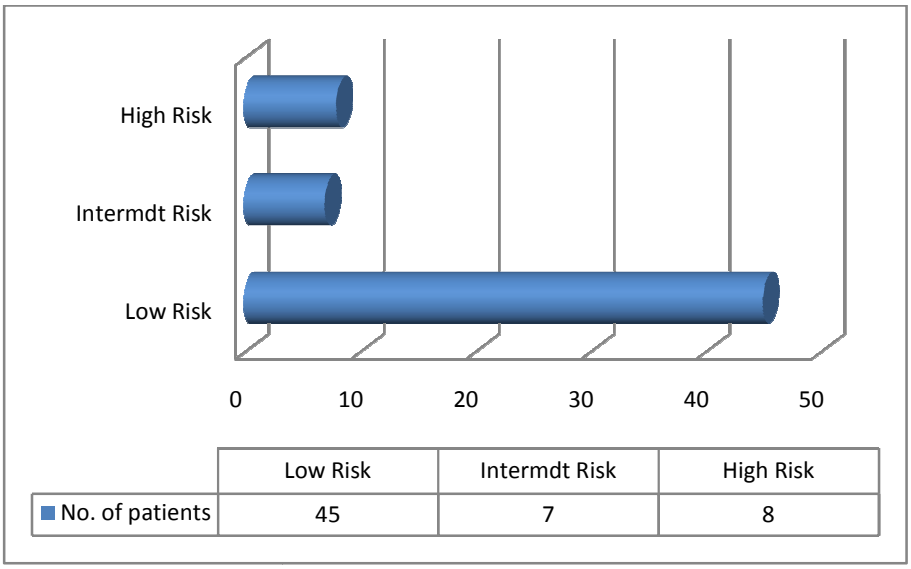
Creatinine , mg/dl	
≤ 1.6	0
> 1.6	2
Glucose , mg/dl	
≤ 180	0
> 180	1

The maximum score is 13.

RISK CATEGORIZATION OF PATIENTS BASED ON LRINEC SCORE

The study population of 60 patients were categorised based on the LRINEC risk stratification as mentioned below :

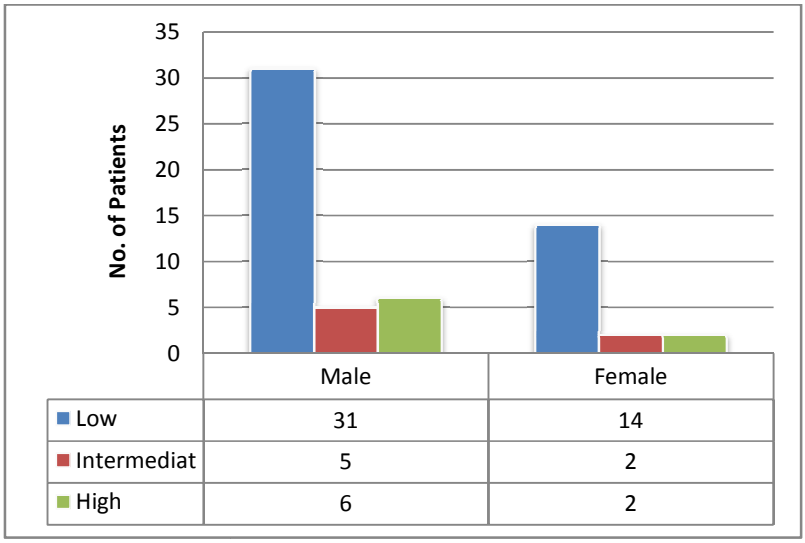




LRINEC SCORE	NO. OF PATIENTS	RISK CATEGORY
5 OR LESS	45	LOW
6 - 7	7	INTERMEDIATE
8 OR MORE	8	HIGH

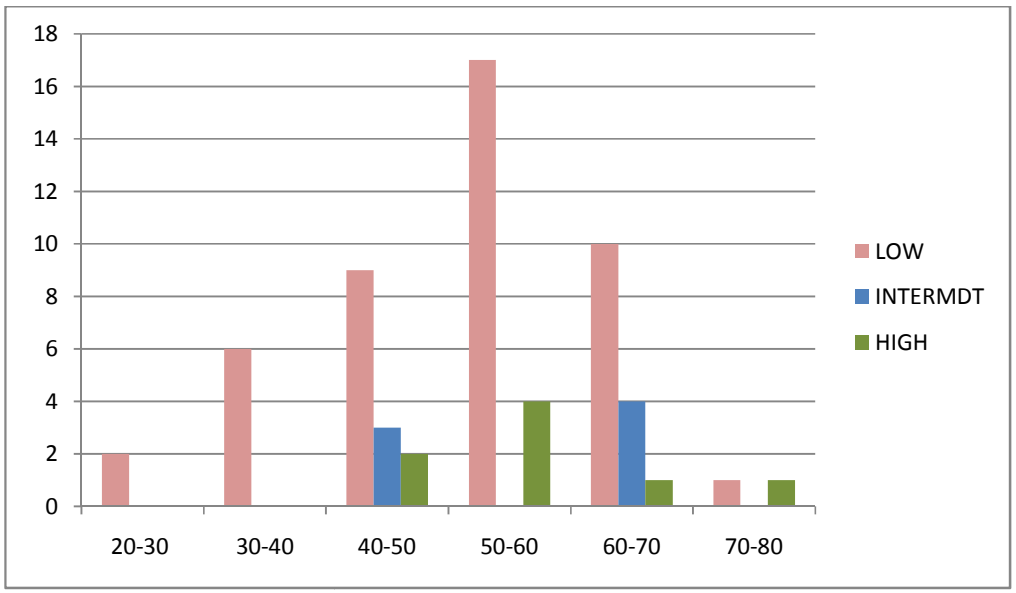
About 75% of patients with soft tissue infections were categorized as low risk for progression to Necrotizing Fasciitis. About 12% and 13% of patients with soft tissue infections were categorized as intermediate and high risk for progression to Necrotizing Fasciitis respectively.

SEX WISE DISTRIBUTION



The study population with soft tissue infections comprises 70% males and the rest being females.

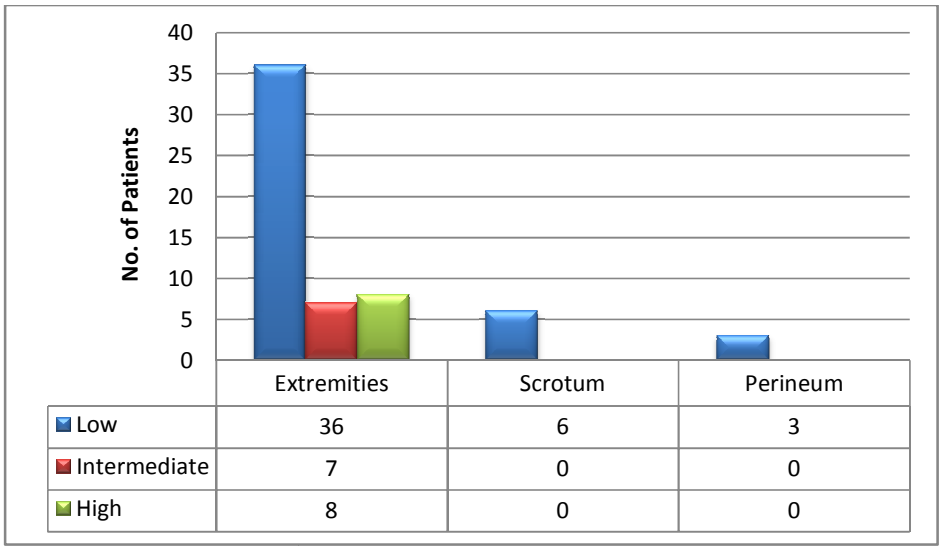
AGE WISE RISK DISTRIBUTION



The Patients with soft tissue infections were categorized by their LRINEC Score as Low, Intermediate and High risk for the occurrence of

Necrotizing Fasciitis. It was found in this study that larger proportion of soft tissue infections had been in 5th to 6th decade. Moreover, Patients with soft tissue infections in their 50s and 60s were more at low risk for Necrotizing Fasciitis than those at the rest of age. However age beyond 50 years confers the high risk for Necrotizing Fasciitis, as evident in this study.

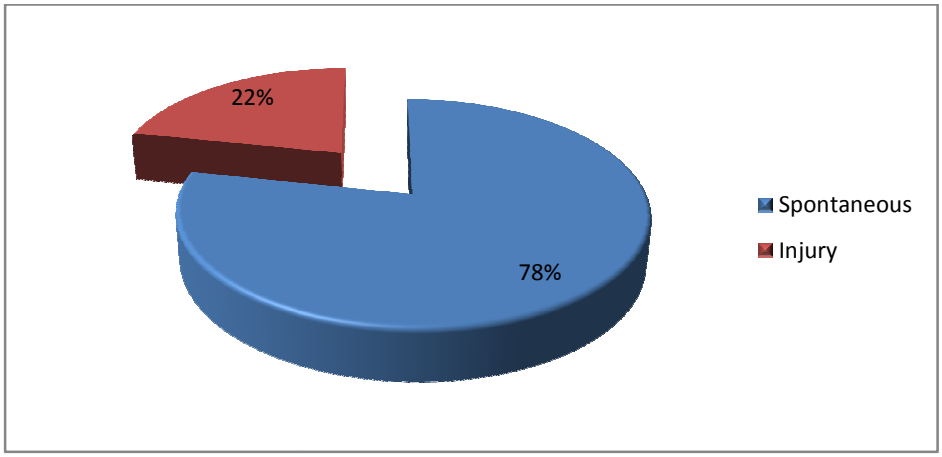
SITE DISTRIBUTION OF SOFT TISSUE INFECTIONS



	Extremities	Scrotum	Perineum
Low	36	6	3
Intermediate	7	0	0
High	8	0	0

Extremity was the most common site involved in soft tissue infections followed by scrotum and perineum. Lower limb was the more common site of infection than Upper limb.

ETIOLOGY FOR SOFT TISSUE INFECTIONS

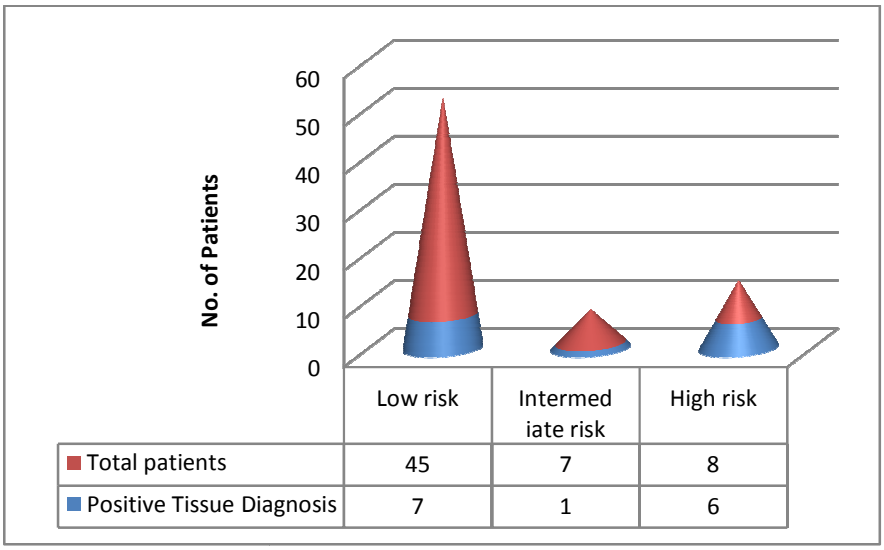


Among the Patients studied, about 78 % of the patients had their illness of spontaneous onset and 22% had a preceding history of injury, more often a thorn / nail prick or a road traffic accident or a history of fall.

TISSUE DIAGNOSIS OF NF IN EACH CATEGORY

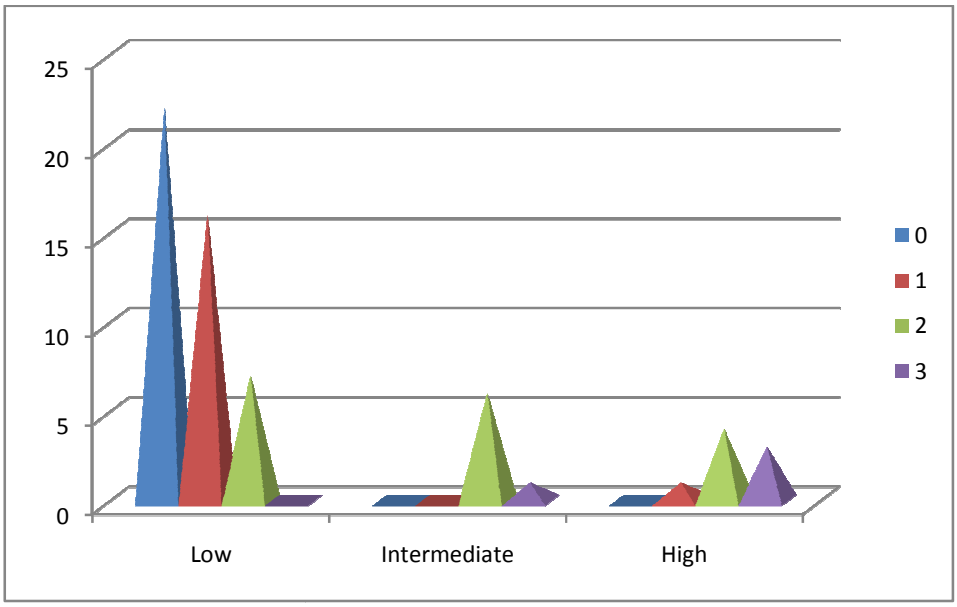
The tissue biopsy obtained during wound exploration and surgical debridement is the gold standard for diagnosing necrotising soft tissue infections. Biopsy diagnosis of NF is made when it shows infiltration of fascia by polymorpho nuclear leukocytes.

Tissue biopsy had been obtained in all patients in the study group and the results of biopsy is summarised below:



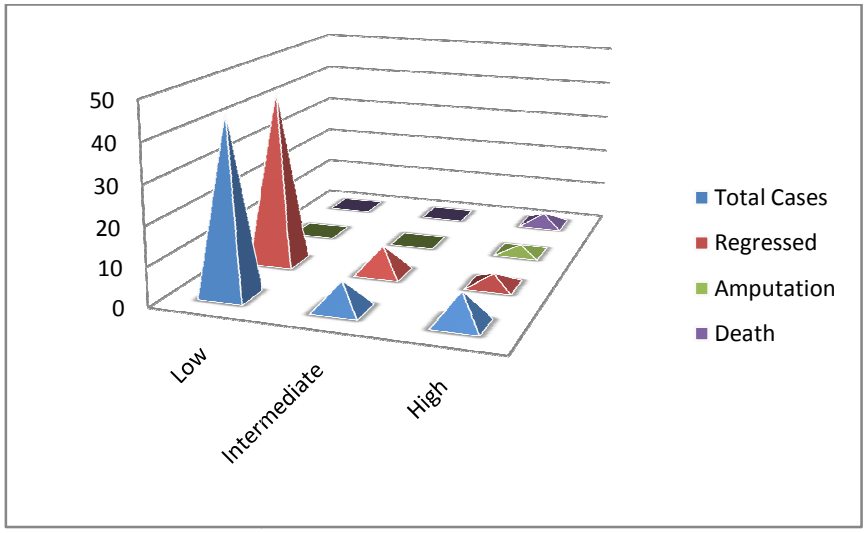
NUMBER OF DEBRIDEMENT REQUIRED FOR EACH CATEGORY

The number of surgical debridement that were required for patients in each category is summarised below:



The Patients under high risk category required higher number of surgical debridement than the low and intermediate risk groups. And nearly 50% of patients in low risk group did not require debridement. Patients in Intermediate risk group had required at least two debridement for the regression of their soft tissue infection.

OUTCOME IN EACH CATEGORY



	Low	Intermediate	High
Total Cases	45	7	8
Regressed	45	7	3
Amputation	0	0	2
Death	0	0	3

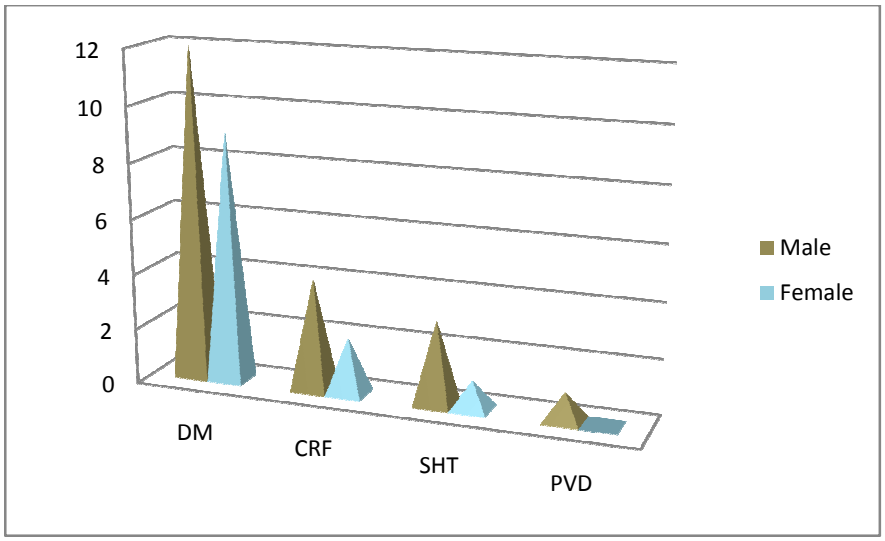
Forty five Patients in Low risk category had their soft tissue infection regressed with IV antibiotics, anti-inflammatory measures, Limb elevation in 22 cases and surgical debridement in 23 cases. Of them, Skin grafts were applied in eight patients.

All seven patients in Intermediate risk were improved with no morbidity or mortality. Three of them required split skin graft.

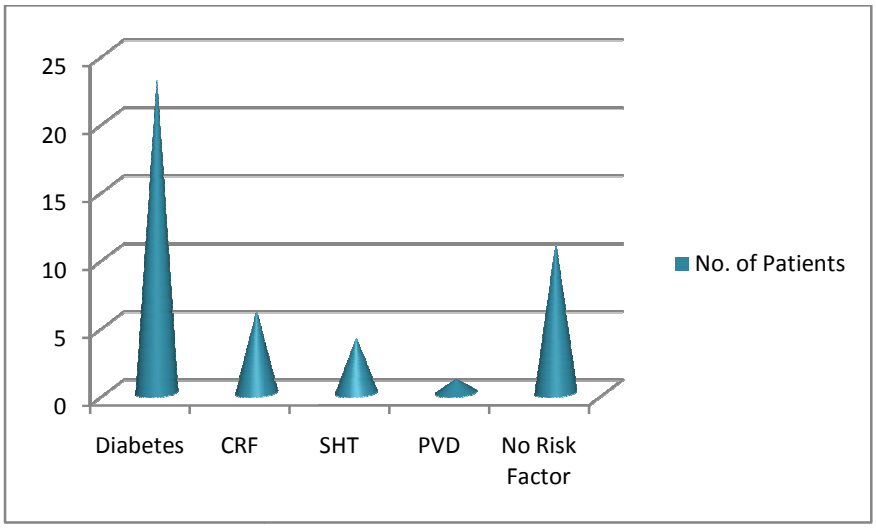
Three of eight patients in High risk category improved with multiple surgical debridement along with graft application. Two Patients required amputation and three died despite all resuscitative measures.

CO MORBID FACTORS

SEX DISTRIBUTION FOR COMORBIDITIES



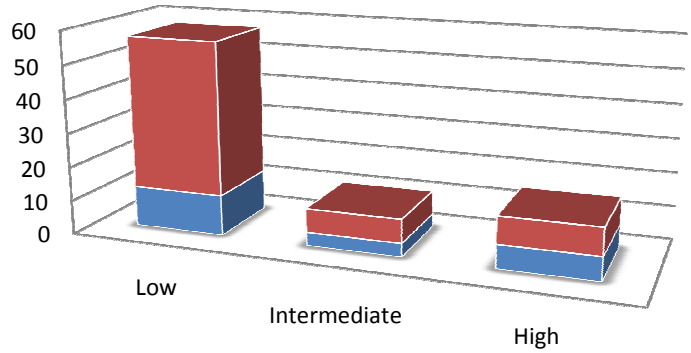
Comorbidities such as Diabetes Mellitus, Chronic Renal Failure, Systemic Hypertension, Peripheral Vascular disease were more commonly found in males than females.



DM was the leading comorbid factor in both primary and secondary NF in our study population.

RISK CATEGORIZATION AMONG DIABETIC PATIENTS

Patients with pre-existing or currently diagnosed Diabetes Mellitus were categorised based on their LRINEC score.

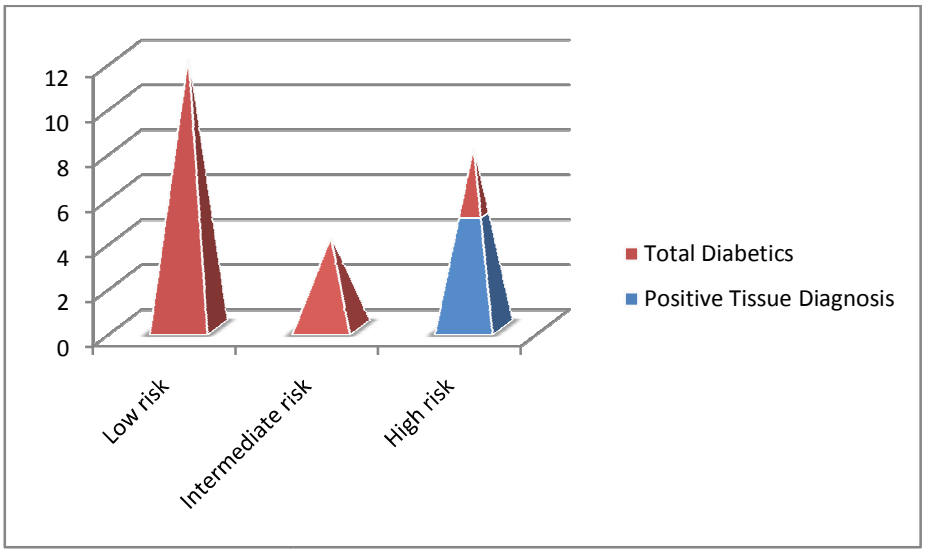


	Low	Intermediate	High
Total Patients	45	7	8
Diabetics	12	4	7

Seven of eight patients in high risk group were diabetics. Twelve and four patients were diabetics in Low and Intermediate risk groups respectively.

POSITIVE TISSUE DIAGNOSIS IN DIABETICS

Tissue biopsy had been obtained in all diabetic patients with severe infections of soft tissue and the results are summarised below:

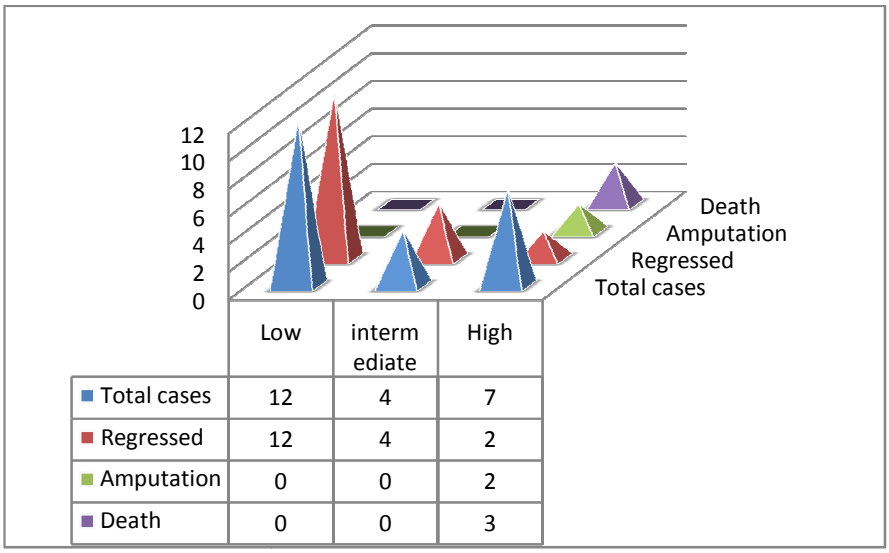


	Low risk	Intermediate risk	High risk
Total Diabetics	12	4	7
Positive Tissue Diagnosis	0	0	5

None of the diabetics in low and intermediate risk showed positive for tissue diagnosis. Five of seven diabetics in high risk group had positive tissue diagnosis for necrotizing fasciitis.

OUTCOME OF DISEASE AMONG DIABETIC PATIENTS

Disease outcome among diabetics with soft tissue infections is summarised below:

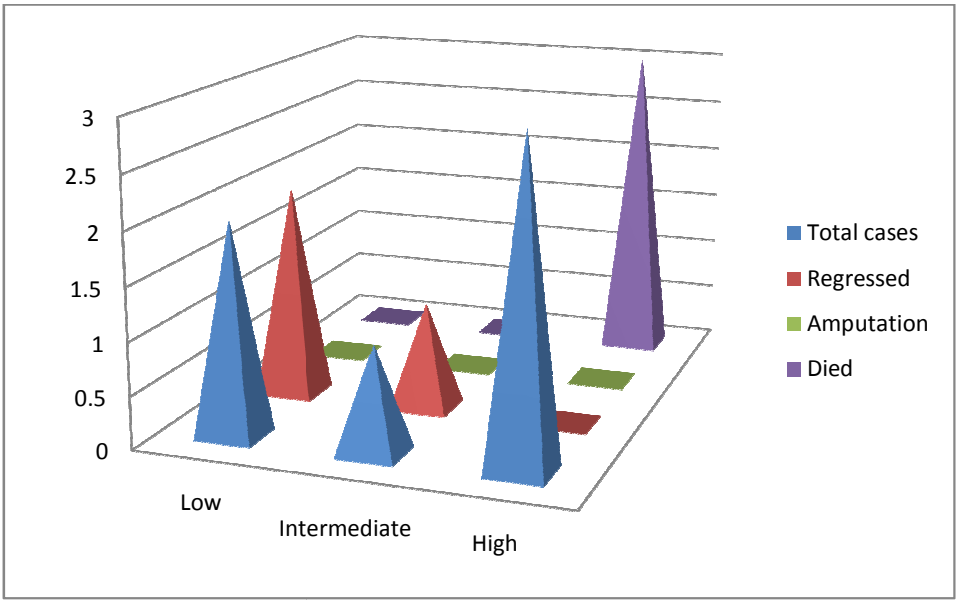


	Low	interm ediate	High
Total cases	12	4	7
Regressed	12	4	2
Amputation	0	0	2
Death	0	0	3

All twelve diabetics in low risk group had improved with appropriate management. All of the diabetics in intermediate group have improved with IV antibiotics and surgical debridement.

Among the diabetic patients in high risk group, two got improved with resuscitative measures and multiple surgical debridement; two required amputation of the affected part and three (as in entire study group) succumbed to death.

OUTCOME OF DISEASE AMONG PATIENTS WITH CRF



	Low	Intermediate	High
Total cases	2	1	3
Regressed	2	1	0
Amputation	0	0	0
Died	0	0	3

Three patients with coexisted Diabetes and CRF were dead. CRF alone did not found to influence the outcome of necrotizing fasciitis.

Discussion

Necrotizing soft tissue infections are fatal progressive infectious processes, most prevalent among alcoholics, impoverished obese diabetic patients and injection drug users, with a varied spectrum of clinical course associated with severe sepsis. The associated systemic inflammatory response syndrome in the setting of sepsis causes changes in the biochemical parameters in a predictable manner.

The LRINEC score is a measure of these changes and predicts the presence of necrotizing fasciitis. Other soft tissue infections (e.g. cellulites and abscesses) rarely cause an inflammatory state severe enough to cause such disturbances in the laboratory variables.

This Prospective study of 60 patients with soft tissue infections included forty two males (70%) and eighteen females (30%). The mean age was 55.3 years. Diabetes mellitus was the most common co-morbidity (23 cases). Other comorbidities included Chronic Renal Failure (6 cases), Systemic Hypertension (4 cases), Peripheral vascular disease (1 case). The important manifestations at presentation were erythema, edema, tenderness, bullae, necrosis tachycardia and hypotension. Extremity was the most common site involved (51 cases) followed by scrotum (6cases) and perineum (3 cases). About 78% of patients had soft tissue infection of unknown origin and 22% were attributed injury as a cause.

Table.5**The characteristics of the study group**

RISK CATEGORY	NO. OF CASES	TISSUE DIAGNOSIS	NO. OF CASES	M	F	SITE			TREATMENT GIVEN	OUTCOME
						SCROTUM	PERINEUM	EXTREMITY		
LOW RISK	45	+	7	7	0	5	0	2	WOUND DEBRIDEMENT, GRAFT IN 2 CASES. 2° SUTURING IN 2 CASES, FASCIOTOMY IN 2 EXTREMITY,	ALL 7 CASES IMPROVED
		-	38	24	14	1	3	34	DEBRIDEMENT IN 9 CASES, FASCIOTOMY IN 7 CASES, GRAFT IN 6 CASES, 2° SUTURING IN 3 CASES, CONSERVATIVE IN 22 CASES	ALL 38 CASES IMPROVED
INTERMDT RISK	7	+	1	1	0	0	0	1	DEBRIDEMENT AND GRAFT APPLIED	IMPROVED
		-	6	4	2	0	0	6	DEBRIDEMENT IN 3 CASES, FASCIOTOMY IN 3 CASES GRAFT IN 2 CASES , 2° SUTURING IN 1 CASE	IMPROVED
HIGH RISK	8	+	6	4	2	0	0	6	DEBRIDEMENT IN 6 CASES, GRAFT IN 2 CASES	2 CASE IMPROVED, AMPUTATION IN 2 CASES, 2 CASES DEAD
		-	2	2	0	0	0	2	DEBRIDEMENT AND GRAFT IN 1 CASE	1 CASE IMPROVED, 1 CASE DEAD

Sensitivity, Specificity, PPV and NPV betweenRisk and LRINEC

		Scores	
		>=6	<6
Risk	Inter/high	15	0
		100	0
		100	0
	Low	0	45
		0	100
		0	100

Yellow - Sensitivity
Blue - Specificity
Red - PPV
Pink - NPV

LRINEC scoring system has a better sensitivity and positive predictive value in identifying the onset of necrotizing fasciitis in soft tissue infections.

Of all the comorbidities Diabetes Mellitus was the most frequent predisposing factor followed by chronic renal failure in both primary and secondary NF in this study group.

Table. 6 **Clinical outcome in patients with co-morbidities**

CO-MORBIDITY	NO. OF CASES	RISK CATEGORY	NO. OF CASES	TISSUE DIAGNOSIS	NO. OF CASES	M	F	SITE			OUTCOME
								SCROTUM	PERINEUM	EXTREMITY	
DIABETES	23	L	12	+	0	0	0	0	0	0	ALL CASES IMPROVED
				-	12	6	6	0	2	10	
		I	4	+	0	0	0	0	0	0	ALL CASES IMPROVED
				-	4	3	1	0	0	4	
		H	7	+	5	3	2	0	0	5	2 CASES IMPROVED, AMPUTATION IN 2 CASES, 3 CASES DEAD
				-	2	2	0	0	0	2	

CRF	6	**L**	2	+	1	1	0	1	0	0	ALL CASES IMPROVED
				-	1	0	1	0	0	1	
		I	1	+	1	1	0	0	0	1	IMPROVED
				-	0	0	0	0	0	0	
		H	3	+	2	1	1	0	0	2	3 CASES DEAD
				-	1	1	0	0	0	1	

L - Low risk

I - Intermediate risk

H - High risk

Comparing hospital stay among DM

DM	Hospital stay				p-value
	n	Min	Median	Max	
Absent	37	6	9	40	0.37
Present	23	6	10	30	

The Length of Hospital stay in those with Diabetic Mellitus was not statistically significant when compared to patients without DM.

Table.7 **Characteristics in patients with LRINEC score < 6 and patients with ≥ 6**

VARIABLES	LRINEC < 6 (n = 45)	LRINEC > 6 (n = 15)	p VALUE
AGE ,years (mean)	53.24	56.33	0.37
MALE SEX	31	11	0.74
NECROSIS	8	10	0.000
CREPITUS	0	5	0.001
VITALS UNSTABLE	1	8	0.000
INJURY	11	2	0.366
UNKNOWN ETIOLOGY	34	13	0.366
DM	12	11	0.001
CRF	2	4	0.013
DM WITH CRF	1	3	0.305
SHT	4	0	0.232
PVD	0	1	0.081
NO. OF DEBRIDEMENT(min/median/max)	1/2/3	0/ 1/ 2	0.00
TIME FOR SURGERY (min/median/max)	1/ 2/ 28	0/ 1/24	0.26
AMPUTATION	0	2	0.013
MORTALITY	0	3	0.013
HOSPITAL STAY ((min/median/max)	7/13/24	6/11/40	0.05

(p- value calculated by using Fisher's exact and Pearson chi square methods.)

In the above table the p-value (0.745) suggests that there is no association between gender and the severity of risk. There is no statistically significant difference between the mean age between two groups of severity. The cut off of LRINEC ≥ 6 has better sensitivity and specificity in identifying the risk of the patient.

The p-value (0.001) reveals that there is an association between Diabetes Mellitus and the severity of risk. The proportion of high/intermediate risk is more in DM group(73.33) compared to the Non-DM group(26.66). The p-value(0.08) for the comparison of mean hospital days among the group of severity indicates that there is no difference between the mean of hospital stay. A multi variate comparison could not be done using death as an outcome since there were only three deaths occurred and hence a good value of predictor could not be obtained in this study.

Conclusion

Necrotizing soft tissue infections are often fatal, characterized by extensive necrosis of the fascia and subcutaneous tissues. It is perhaps the most severe form of soft tissue infection potentially limb and life threatening. Early diagnosis of necrotizing fasciitis is essential to advocate timely management for the better wellbeing of the patient.

LRINEC - Laboratory Risk Indicator for Necrotizing Fasciitis score is based on routine laboratory investigations that are readily available, at most centres that can help distinguish Necrotizing Fasciitis from other soft tissue infections.

LRINEC scoring system has a better positive predictive value in identifying the onset of necrotizing fasciitis and risk strategizing of the patients with severe soft tissue infections.

There is a statistically significant association between Diabetic Mellitus and the severity of risk.

The significance of LRINEC score in predicting the clinical outcome of the disease could not be outlined because of limited population included in this study.

Further studies are needed to determine whether additional interventions targeted to the high mortality risk group can lead to improved outcomes.

Finally, Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score can be used as an adjunct in the management of soft tissue infections especially in secondary care hospitals and may prevent delayed referral to tertiary centres where experienced surgeons, infectious disease and hyperbaric specialists may guide immediate operative and ancillary management, thereby improving the clinical outcome of the patient.

Appendices

APPENDIX – I
ABBREVIATIONS

C.	-	Clostridium
CRF	-	Chronic Renal Failure
CRP	-	C Reactive Protein
CT	-	Computed Tomography
DM	-	Diabetics Mellitus
ED	-	Emergency Department
GIT	-	Gastro Intestinal Tract
GAS	-	Group A Streptococci
HBO	-	Hyperbaric oxygen
IV	-	Intravenous
LRINEC	-	Laboratory Risk Indicator for Necrotizing Fasciitis
MRI	-	Magnetic Resonance Imaging
NF	-	Necrotizing Fasciitis
NSTI	-	Necrotizing soft tissue infection
PVD	-	Peripheral Vascular Disease
SHT	-	Systemic Hypertension
sp.	-	Species
USG	-	Ultrasonogram

APPENDIX – II

CONSENT FORM

It has been explained to me in my mother tongue and I completely understand my condition, its related complications and the treatment options available. I have been explained in detail regarding this study- **"LRINEC – An Objective Scoring System as a tool for early diagnosis of Necrotizing Fasciitis."**I hereby give my consent to participate in the above mentioned study.

Date:

Place:

Signature of the relative

with name:

Signature of the patient

with name:

Signature of the witness

with name:

APPENDIX - III
PROFORMA

1) NAME -

2) AGE -

3) SEX -

4) IP NO. -

5) D.O.A -

6) D.O.P -

7) D.O.D -

8) CLINICAL FINDINGS

   a) SITE & EXTENT -

   b) INFLAMMATION -

   c) INDURATION -

   d) NATURE OF DISCHARGE

9) VITALS ON ADMISSION

   a) TEMP -

   b) PULSE RATE -

   c) BP -

   d) RR -

10) CO-MORBID FACTORS

a) RECENT H/O INJURY OR SURGERY

b) SMOKING

c) ALCOHOL

d) IF ON STEROIDS

e) IMMUNO SUPPRESSORS

f) IV DRUG USE

11) CO-MORBID DISEASES

a) DIABETES

b) MALIGNANCY

c) CARDIAC DISEASE

d) PVD

e) HIV/AIDS

12) INVESTIGATIONS

a) TOTAL COUNT -

b) BLOOD SUGAR -

c) HB -

d) SR.CREATININE -

e) SR.SODIUM -

f) CRP -

g) LRINEC SCORE -

h) PUS C&S -

i) X-RAY LOCAL REGION -

j) HIV / HBsAgSTATUS -

13) MANAGEMENT

a) DEBRIDEMENT

NO. OF DEBRIDEMENTS -

FREQUENCY & TOTAL -

b) AMPUTATIONS

c) SKIN GRAFTING

14) FINAL OUTCOME

a) STATUS OF DISEASED PART

b) MORBIDITY/MORTALITY

APPENDIX – IV

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APPENDIX - V

MASTER CHART

SI.NO.	NAME OF THE PATIENT	IP.NO.	AGE IN YRS	SEX	SITE	CLINICAL FINDING			VITALS	ETIOLOGY		COMORBIDITY				SMOKING	LRINEC PARAMETERS						LRINEC SCORE	RISK CATEGORY	NO. OF DEBRIDEMENT	MEAN DURATION OF SURGERY	TISSUE BIOPSY	PUS C&S	OUTCOME					
						INFLAMMATION	NECROSIS	CREPITUS		INJURY	SPONTANEOUS	DM	SHT	CRF	PVD		TOTAL COUNT	RBS	HB	CREATININE	SODIUM	CRP							PROGRESSED	REGRESSED	SKIN GRAFT	AMPUTATION	HOSPITAL STAY	DIED
1	ARUMUGAM	36997	45	M	RT. LL	1	0	0	S	0	1	1	0	0	0	0	20000	363	8.1	1.7	127	60	8	H	1	28	0	1	0	1	1	0	18	0
2	MURUGESHAN	44764	43	M	RT.UL	1	1	1	S	0	1	0	0	0	1	1	9100	139	9	1.9	121	30	6	I	2	1	0	1	0	1	1	0	8	0
3	NANDHA KUMAR	46306	29	M	LT.FA	1	0	0	S	1	0	0	0	0	0	1	23000	80	10	0.9	125	55	5	L	1	4	0	0	0	1	1	0	8	0
4	ANAND	51079	32	M	SCROTUM	1	1	0	S	0	1	0	0	0	0	1	12400	88	6.4	1.5	131	66	4	L	1	1	1	1	0	1	1	0	10	0
5	MALLAR	49312	66	F	LT.LEG	1	0	0	S	0	1	0	0	0	0	0	12800	138	11.4	0.5	138	60	1	L	0	0	0	0	0	1	0	0	8	0
6	SURESH	58755	49	M	RT. LL	1	1	0	US	0	1	1	0	1	0	1	25100	218	7.4	3.8	123	160	12	H	2	8	1	1	1	0	0	0	10	1
7	SHANMUGAM	70869	70	M	LT. LEG	1	0	0	S	0	1	0	0	0	0	1	14100	175	10	1.9	143	80	4	L	1	4	0	0	0	1	1	0	9	0
8	ESWARAN	52606	32	M	RT. LL	1	1	0	S	1	0	0	1	0	0	1	11500	92	10	0.6	141	90	2	L	1	5	1	0	0	1	1	0	14	0
9	PALANISAMY	54027	78	M	LT. LL	1	0	0	S	0	1	1	0	0	0	1	12600	260	12	1	137	40	2	L	0	0	0	0	0	1	0	0	9	0
10	JAMES WILLIAM	72534	70	M	RT. LEG	1	0	0	S	0	1	1	1	0	0	1	5000	141	13	1.1	134	80	3	L	0	0	0	0	0	1	0	0	7	0
11	PALANIAMMAL	72380	50	F	RT. FOOT	1	0	0	S	1	0	0	0	0	0	0	11800	90	12.6	1	130	30	3	L	1	3	0	0	0	1	0	0	6	0
12	MURUGAN	71391	48	M	BOTH LEGS	1	1	0	US	0	1	0	0	1	0	1	14600	102	9.4	2.8	133	96	6	I	3	2	1	1	0	1	1	0	19	0
13	MANI	72266	53	F	LT. FOOT	1	0	0	S	0	1	1	0	1	0	0	6200	109	13.2	2.8	139	30	3	L	1	4	0	0	0	1	0	0	6	0
14	MURUGESHWARI	72461	41	F	LT. FOOT	1	0	0	S	0	1	1	0	0	0	0	7800	323	10	1.5	134	55	5	L	1	24	0	0	0	1	1	0	6	0
15	SUBRAMANI	66638	53	M	RT. THIGH	1	1	0	US	1	0	0	0	0	0	1	13700	132	8.1	0.8	142	104	2	L	2	6	1	1	0	1	0	0	40	0
16	ARUL RAJ	70440	44	M	SCROTUM	1	1	0	S	0	1	0	0	1	0	1	13600	74	8.3	2.3	137	86	4	L	2	7	1	1	0	1	0	0	20	0
17	SRI RAMULU	70568	70	M	LT. FOOT	1	0	0	S	0	1	1	0	0	0	0	12600	161	12.3	0.9	136	30	1	L	0	0	0	0	0	1	0	0	7	0
18	MAHESH	37012	68	M	RT.FOOT	1	0	0	S	0	1	0	0	0	0	0	11200	123	11.2	0.8	132	68	3	L	0	0	0	0	0	1	0	0	7	0
19	RANI AMMAL	43786	56	F	RT. HAND	1	0	0	S	1	0	0	0	0	0	0	14100	106	9	1.1	128	54	4	L	1	6	0	0	0	1	0	0	8	0
20	MALLIKA	60241	60	F	LT. FOOT	1	1	0	S	0	1	1	0	0	0	0	16100	226	8	1.2	134	90	4	L	2	7	0	0	0	1	0	0	10	0
21	RAJA	58210	55	M	PERINEUM	1	1	0	S	0	1	1	0	0	0	1	13300	320	11.3	1.4	128	110	4	L	2	5	0	1	0	1	0	0	11	0
22	KUMARI	60414	67	F	RT. LEG	1	0	0	S	0	1	0	0	0	0	0	9800	120	9.2	0.9	132	60	4	L	0	0	0	0	0	1	1	0	6	0
23	RANJITH	54302	37	M	SCROTUM	1	0	0	S	0	1	0	0	0	0	1	12200	96	13	1.1	134	40	3	L	1	7	0	1	0	1	1	0	24	0
24	RAMANI	30421	55	M	RT. FOOT	1	1	1	US	0	1	1	0	0	0	1	23100	210	7.6	2.3	126	145	8	H	2	2	1	1	1	0	0	1	23	0
25	MURUGESH	44729	67	M	RT. LEG	1	0	0	S	0	1	0	0	0	0	0	7800	87	10	0.6	132	40	4	L	0	0	0	0	0	1	0	0	9	0
26	MAYILAL	70353	64	F	RT. LEG	1	1	0	S	0	1	1	1	0	0	0	8800	146	9	1	132	50	4	L	0	0	0	0	0	1	0	0	9	0
27	NARAYANAN	45622	42	M	RT. HAND	1	0	0	S	1	0	0	0	0	0	1	11100	88	12	0.8	135	60	3	L	1	6	0	0	0	1	0	0	7	0
28	KANDASAMY	53621	55	M	LT. FOOT	1	0	0	S	0	1	0	0	0	0	0	8800	96	11.5	0.9	142	98	1	L	0	0	0	0	0	1	0	0	8	0
29	MAHENDRAN	40300	61	M	RT. LEG	1	1	0	US	0	1	1	0	0	0	1	21000	132	8	2.2	128	140	7	I	2	4	0	1	0	1	1	0	7	0
30	KUMARAVELU	62111	56	M	LT. FOOT	1	0	0	S	0	1	0	0	0	0	1	14400	124	11	1	134	90	3	L	0	0	0	0	0	1	0	0	11	0

						CLINICAL FINDING				ETIOLOGY		COMORBIDITY					LRINEC PARAMETERS												OUTCOME				
SI.NO.	NAME OF THE PATIENT	IP.NO.	AGE IN YRS	SEX	SITE	INFLAMMATION	NECROSIS	CREPITUS	VITALS	INJURY	SPONTANEOUS	DM	SHT	CRF	PVD	SMOKING	TOTAL COUNT	RBS	HB	CREATININE	SODIUM	CRP	LRINEC SCORE	RISK CATEGORY	NO. OF DEBRIDEMENT	MEAN DURATION OF SURGERY	TISSUE BIOPSY	PUS C&S	PROGRESSED	REGRESSED	SKIN GRAFT	AMPUTATION	HOSPITAL STAY
31	GOPALAKRISHNAN	67048	23	M	LT. LEG	1	0	0	S	1	0	0	0	0	0	1	10400	129	11	1	132	100	3	L	1	7	0	1	0	1	0	0	8
32	RANGASAMY	72600	68	M	LT. FOOT	1	0	0	S	0	1	1	0	0	0	1	10600	85	10.6	2.5	136	120	3	L	0	0	0	0	0	1	0	0	11
33	SAMYNATHAN	15137	78	M	LT. LL	1	0	0	S	1	0	1	0	1	0	0	20100	178	11.1	3.5	125	160	10	H	2	6	0	1	1	0	0	0	22
34	ABUTHAHEER	18229	48	M	BOTH LEGS	1	0	0	S	0	1	0	0	0	0	0	8700	67	13.5	0.9	134	66	2	L	0	0	0	0	0	1	0	0	7
35	RAMALINGAM	35543	63	M	RT. HAND	1	0	0	S	0	1	1	1	0	0	1	11000	327	9	0.9	127	100	5	L	1	6	0	0	1	1	0	0	30
36	MUTHUKUMAR	44253	34	M	LT. HAND	1	0	0	S	1	0	0	0	0	0	1	9900	74	12	0.8	134	80	3	L	0	0	0	0	0	1	0	0	10
37	VELLACHI	65439	64	F	RT.FOOT	1	1	0	S	0	1	0	0	0	0	0	17600	104	8	1.8	129	135	7	I	2	2	0	1	0	1	0	0	9
38	RAJESWARAN	54306	56	M	SCROTUM	1	1	0	S	0	1	0	0	0	0	0	20100	110	9	1.5	130	120	5	L	2	7	1	1	0	1	0	0	22
39	RAVI SHANKAR	64021	54	M	BOTH LEGS	1	0	0	US	0	1	0	0	0	0	1	26100	146	7.6	2	128	150	12	H	3	1	1	1	0	1	1	0	18
40	GOWRI AMMAL	34208	67	F	RT. FOOT	1	0	0	S	0	1	0	0	0	0	0	8400	86	9	0.8	135	80	2	L	0	0	0	0	0	1	0	0	8
41	LAKSHMI	64902	54	F	LT. HAND	1	0	0	S	1	0	0	0	0	0	0	10100	91	9	0.9	135	110	2	L	0	0	0	0	0	1	0	0	9
42	RANI	72100	48	F	PERINEUM	1	0	0	S	0	1	1	0	0	0	0	14600	120	8	1	136	88	2	L	1	5	0	1	0	1	0	0	12
43	MURALI	38154	63	M	RT. LEG	1	1	0	S	0	1	1	0	0	0	1	17300	340	10	1.6	130	120	7	I	2	3	0	1	0	1	0	0	13
44	VIJAYARAJ	63820	45	M	LT. FOOT	1	0	0	S	0	1	0	0	0	0	0	7700	96	12	0.9	135	90	1	L	0	0	0	0	0	1	0	0	11
45	MAHARANI	45320	56	F	RT. FOOT	1	0	0	S	0	1	0	0	0	0	0	6800	98	11	0.8	135	30	1	L	0	0	0	0	0	1	0	0	9
46	KIRAT RAJ	32981	54	M	LT. LEG	1	0	0	S	1	0	0	0	0	0	1	13300	124	13	1	132	60	3	L	0	0	0	0	0	1	0	0	8
47	SIVA	64010	45	M	BOTH LEGS	1	0	0	S	0	1	1	0	0	0	1	20100	220	10	1.7	128	120	8	I	2	3	0	1	0	1	0	0	7
48	SUNDARI	43010	54	F	RT. HAND	1	0	0	S	1	0	1	0	0	0	0	11300	340	8	1.4	133	140	5	L	1	6	0	0	0	1	0	0	14
49	MAHESHWARAN	50201	60	M	RT. FOOT	1	0	0	S	0	1	0	0	0	0	1	8800	140	12	1.4	136	120	1	L	0	0	0	0	0	1	0	0	12
50	SARASWATHY	32012	55	F	RT. LL	1	1	1	US	1	0	1	0	0	0	0	27400	450	8	2.8	124	160	13	H	3	2	1	1	1	0	0	1	22
51	SIVARAM	53010	54	M	LT. LEG	1	0	0	S	0	1	0	0	0	0	0	6600	86	12	0.7	136	30	1	L	0	0	0	0	0	1	0	0	11
52	KRISHNA	30102	43	M	SCROTUM	1	0	0	S	0	1	0	0	0	0	1	13200	108	10	1.2	134	90	3	L	2	6	1	1	0	1	0	0	9
53	PRABHU	45201	37	M	PERINEUM	1	0	0	S	0	1	0	0	0	0	1	12100	74	12	0.8	133	30	3	L	1	6	0	0	0	1	0	0	7
54	VIJAYA LAKSHMI	65301	60	F	LT. FOOT	1	0	0	S	0	1	0	0	0	0	0	5400	102	12	0.9	136	40	1	L	0	0	0	0	0	1	0	0	10
55	JEYARANI	30265	64	F	BOTH LEGS	1	1	1	US	0	1	1	0	1	0	0	24300	324	7	5.6	124	180	12	H	2	2	1	1	1	0	0	0	10
56	SUNIL	47209	40	M	SCROTUM	1	0	0	S	0	1	0	0	0	0	0	12300	98	10	1.4	133	90	3	L	2	7	1	1	0	1	0	0	12
57	SUNDARA PANDIAN	42302	60	M	RT. LEG	1	0	0	S	0	1	0	0	0	0	1	6000	78	11	0.6	135	30	1	L	0	0	0	0	0	1	0	0	15
58	MANIAN	53012	58	M	LT. LL	1	1	1	US	0	1	1	0	0	0	1	28100	320	8	2.6	114	180	13	H	3	2	1	1	0	1	1	0	24
59	KUMARAVEL	72310	54	M	RT. FOOT	1	0	0	S	0	1	0	0	0	0	1	18100	160	11	1.6	130	100	4	L	1	7	0	0	0	1	1	0	8
60	MURUGAVALLI	32540	64	F	LT. LEG	1	0	0	S	0	1	1	0	0	0	0	21000	320	9	1.8	130	140	8	I	2	3	0	1	0	1	0	0	9

APPENDIX - VI

KEY WORDS TO MASTER CHART

INFLAMMATION, NECROSIS, CREPITUS, INJURY, SPONTANEOUS, DM, CRF, SHT, PVD, SMOKING

0 - ABSENT

1 - PRESENT

VITALS

S - STABLE

US - UNSTABLE

RISK CATEGORY

L - LOW RISK

I - INTERMEDIATE RISK

H - HIGH RISK

TISSUE BIOPSY

0 - NEGATIVE

1 - POSITIVE FOR NF

PUS C & S

0 - GROWTH ABSENT

1 - GROWTH PRESENT

OUTCOME

PROGRESSED

0 - NO PROGRESSION

1 - PROGRESSION

REGRESSED

0 - NO REGRESSION

1 - REGRESSION

SKIN GRAFT

0 - NOT APPLIED

1 - APPLIED

AMPUTATION

0 - NOT DONE

1 - AMPUTATION DONE

DIED

0 - ALIVE

1 - DEAD

DM - DIABETES MELLITUS

CRF - CHRONIC RENAL FAILURE

SHT - SYSTEMIC HYPERTENSION

PVD - PERIPHERAL VASCULAR DISEASE

RBS - RANDOM BLOOD SUGAR

HB - HEMOGLOBIN

CRP - C - REACTIVE PROTEIN

NF - NECROTIZING FASCIITIS

MEAN DURATION OF SURGERY IN HOURS

HOSPITAL STAY IN DAYS