A STUDY OF CLINICAL PRESENTATIONS, BIO CHEMICAL MARKERS AND MICROBIAL FLORA IN OUTCOME OF NECROTIZING FASCIITIS

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LIST OF ABBREVATIONS

ABBREVATIONS	FULL FORM
NF	NECROTIZING FASCIITIS
NSTI	NECROTIZING SOFT TISSUE INFECTIONS
HBOT	HYPERBARIC OXYGEN THERAPY
VACT	VACUUM ASSISTED CLOSURE THERAPY
DM	DIABETES MELLITUS
HTN	HYPER TENSION
S.PCT	SERUM PROCALCITONIN
S.LDH	SERUM LACTATE DEHYDROGENASE
S.ALB	SERUM ALBUMIN
LRINEC	LABORATORY RISK INDICATOR OF NECROTIZING FASCIITIS
MODS	MULTI ORGAN DYSFUNCTION SYNDROME
PBSG	PROGRESSIVE BACTERIAL SYNEGISTIC GANGRENE
SSSS	STAPHYLOCOCCAL SCALDED SHOCK SYNDROME
TEN	TOXIC EPIDERMAL NECROLYSIS
CT	COMMUTED TOMOGRAPHY

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ABSTRACT:

INTRODUCTION: Necrotizing fasciitis is a rapidly advancing infection that primarily affects the fascia and subcutaneous tissue. It is the most severe type of soft tissue infection and can result in limb and life loss. Although clinical modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and frozen section biopsy have been shown to be useful in the early detection of necrotizing fasciitis, their routine use in the evaluation of soft tissue infections has been limited due to cost and availability.[2]Hence there is an obvious need for biomarkers of inflammation to detect bacterial infections in patients with sepsis.

AIMS AND OBJECTIVES: To study the influence of Serum Ldh, Serum Albumin, Serum Procalcitonin, Microbial Flora In predicting the outcome of necrotizing fasciitis.

MATERIAL AND METHODS: This is a prospective observational study of 92 patients admitted with diagnosis of necrotizing fasciitis in B.L.D.E (DU)'S Shri B.M. Patil Medical College.

RESULTS: Out of 92 patients' mortality was seen in 11 patients and amputation was done in 6 patients. Patients 60-70 years age group was predominant 58(63%) in the present study. The male predominance was almost three-fold compared to the females. Type 2 diabetes mellitus being the most common co-morbidity accounting for around 40.2%. The biochemical markers which where

included in the study showed significant results ($p<0.05$) * that is serum procalcitonin and serum LDH were elevated and s. albumin was low in all patients who are died and amputated except in one patient. There was no significant in the microbial flora and the outcome of the patient.

CONCLUSION: Thus, to conclude S.PCT, S.LDH, Albumin are the important diagnostic markers for diagnosing the severity and prognosis of the patient with necrotizing fasciitis. Early and aggressive debridement's, often at repeated sittings, are the mainstay in the treatment of necrotizing fasciitis, supplemented by adequate antibiotics and supportive measures are important in the treatment of the necrotising fasciitis.

INTRODUCTION:

Necrotizing fasciitis is a rapidly advancing infection that primarily affects the fascia and subcutaneous tissue. It is the most severe type of soft tissue infection and can result in limb and life loss. It is caused by a synergistic, polymicrobial infection of streptococcal species (Group A beta - haemolytic) in combination with Staphylococcus, Escherichia coli, Pseudomonas, Proteus, Bacteroides, or Clostridia. Over 80% have a history of previous trauma/infection, and more than 60% begin in the lower extremities. Diabetes, smoking, penetrating trauma, pressure sores, immunosuppression, intravenous drug abuse, perineal infection, and skin damage are all risk factors.[1]

Although clinical modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and frozen section biopsy have been shown to be useful in the early detection of necrotizing fasciitis, their routine use in the evaluation of soft tissue infections has been limited due to cost and availability.[2]

Hence there is an obvious need for biomarkers of inflammation to detect bacterial infections in patients with sepsis. The conventional markers of inflammation and they may be slowly released during the progression of an infection may be influenced by parameters other than infection.[3]

The definition of a sepsis marker is "a measure that identifies a normal biologic state or predicts the presence or severity of a pathologic process or disease."

Estimating serum procalcitonin levels may aid in the early diagnosis and treatment of sepsis. Procalcitonin levels rise in response to organ dysfunction and the severity of sepsis.[4]

Serum LDH levels that are elevated are indicative of cellular damage and dysfunction. LDH is an intracellular enzyme that converts pyruvic acid to lactic acid. Serum LDH can be used as a biochemical marker because it reflects disease severity.[5]

Inflammation reduces levels of some proteins such as albumin, which are called negative acute phase proteins (because their levels decrease with the inflammatory process). Albumin values tend to fall in the presence of an active-phase reaction such as sepsis with a mean decrease ranging from 10-15 g / L in the first week. There are several causes for the occurrence of hypoalbuminemia in septic patients, namely, decreased albumin synthesis in the liver, reduced intake of amino acids, increased fluid transfer to the interstitial (plasma leakage), and increased tissue catabolism. So, it is ideal to look at acute phase protein levels as a diagnostic tool for the sepsis process.

Thus, the biochemical markers procalcitonin, LDH, and albumin, as well as microbial flora, are evaluated in the morbidity and mortality of necrotizing fasciitis in this study.

AIM AND OBJECTIVE OF THE STUDY

To study the influence of the following factors on the outcome of patients with Necrotizing Fasciitis:

1. SERUM LDH
2. SERUM ALBUMIN
3. SERUM PROCALCITONIN
4. MICROBIAL FLORA

The above factors were analysed in this study to predict the diagnosis outcome of necrotizing fasciitis which has got a high degree of morbidity and significant mortality so that the analysis would help bring down the morbidity of the disease.

REVIEW OF LITERATURE

HISTORIGICAL ASPECTS: -

- Hippocrates[6] described Necrotizing soft tissue infection (NSTI) as a complication of acute streptococcal infection in the fifth century BC, writing, "Many were attacked by the erysipelas all over the body when the exciting cause was a trivial accident or a very small wound. Many people suffered from severe inflammations even while receiving treatment, and the erysipelas spread rapidly in all directions. Large amounts of flesh, sinew, and bone fell away. There were numerous fluxes and the bones were bared and fell away. Fever was sometimes present and sometimes absent. There were numerous fatalities. The disease took the same path in every part of the body where it spread. Many lost the arm and the entire forearm. In some cases, the entire thigh was borne or the shin and the entire foot. But the most dangerous cases of all such cases were when the pubes and genital organs were attacked".
- In the late 18th century, English descriptions similar to NSTIs were given by the Naval surgeon Leonard Gillespie and Naval physicians Gilbert Blaine and Thomas Trotter. Phagedenic ulcer, phagedaena gangrenous, gangrenous ulcer, malignant ulcer, putrid ulcer, or hospital gangrene[7] were all names for NSTI.

- In 1871, during US Civil War, Confederate Army surgeon Joseph Jones described this infection as "hospital gangrene" during which mortality rate 46% of the 2,642 soldiers afflicted died from its complications[8] .
- "In 1883, Dr Jean-Alfred Fournier[9] described a necrotizing infection of the perineum and scrotum, and the term Fournier gangrene is still in common usage"
- Dr.B.R.Wilson coined the term necrotizing fasciitis in 1952, recalling the key feature of necrosis extending beyond fascia to muscles, skin, and surrounding structures[10].
- Between January 1997 and August 2002, Wong et al (2004)[11] conducted a retrospective observational study for necrotizing fasciitis at Changi General Hospital and developed a novel diagnostic scoring system for distinguishing necrotizing fasciitis from other soft tissue infections based on laboratory tests routinely performed for the evaluation of severe soft tissue infections: the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score. And has concluded that "LRINEC score is a robust score capable of detecting even clinically early cases of necrotizing fasciitis".

- In 2008, Yi-chun Su et al. began a retrospective observational cohort study[12] of 209 patients in one tertiary academic centre and one community, university affiliated hospital, and concluded that the LRINEC score is associated with the outcomes of NSTI patients (Necrotizing soft tissue infection). Patients with an LRINEC score greater than or equal to 6 have a higher risk of death and amputation.
- V Corbin et al. began a prospective study[13] for fifty patients at the Clermont-Ferrand University Hospital's Department of Infectious Diseases and Dermatology in 2010. Time from antibiotic initiation to erythema regression, fever duration, and complications were the evaluation criteria (abscess, surgery, septic shock, necrotizing fasciitis, death, and transfer to intensive care). Other potential variables included: LRINEC score greater than 6, comorbidities, clinical presentation, and soft tissue ultrasound results. Patients with moderate to severe soft tissue infections should be carefully evaluated, and the LRINEC score is a useful tool for detecting infections.
- In 2017 J Bechar, S Sepehripour, J Hardwicke, and G Filobbos conducted a systematic review of English-language literature[14] articles from 2004 to 2014, about the use of the LRINEC score and the incidence of Necrotizing fasciitis. The LRINEC score was found to be a useful tool in the diagnosis and surgical treatment of patients with necrotizing fasciitis, with a statistically significant positive correlation.

- In 2019 Abdullah M, McWilliams B, and U. Khan S conducted a systemic review[15] of eighteen clinical studies published between 2004 and 2018. Furthermore, there is Level 3 evidence that the LRINEC score is a reliable tool in risk stratification of patients with severe soft tissue infections.
- In 2021 a study done by Takaaki Kishino et.al from 2014-2019 in 25 patients with necrotizing fasciitis has concluded that Serum-PCT could be a useful diagnostic marker for differentiating diagnosis of NF from cellulitis.[16]

ANATOMY OF SKIN:

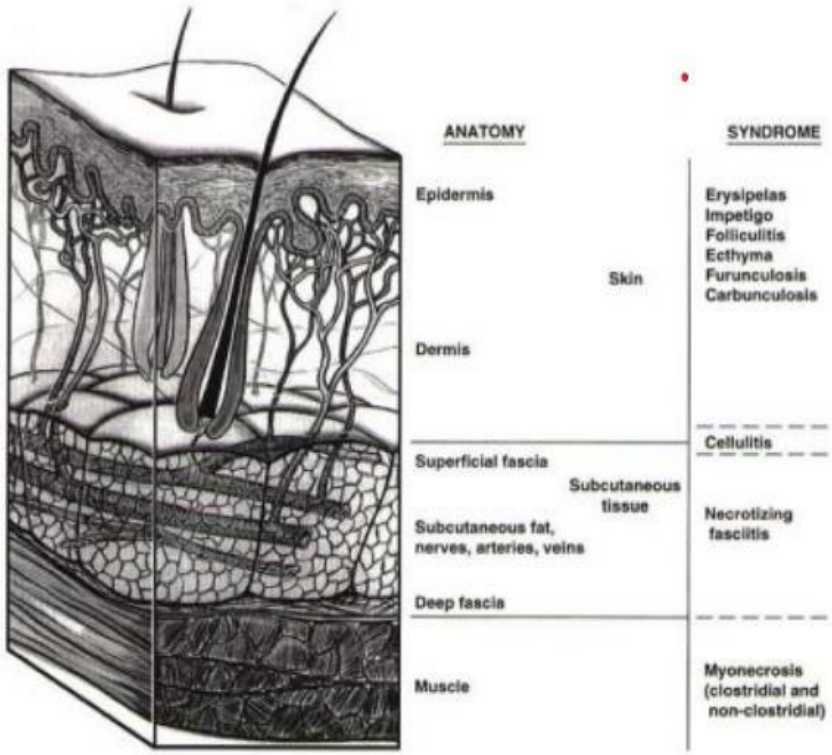


FIGURE:1 ANATOMY OF SKIN

Because the epidermis lacks blood vessels, it is protected from infection by the mechanical barrier provided by stratum corneum. Bites, abrasion, burns, foreign bodies, primary dermatological disorders (herpes simplex, varicella, and ecthyma gangrenosum), surgery, vascular or pressure ulcers all cause erosion or disruption of this layer, allowing bacteria to enter the underlying structures.

The hair follicle can also act as a portal for either normal flora (staphylococcus) or extrinsic bacteria (Pseudomonas in hot tub folliculitis). Bacteria that infect the epidermis are transmitted to deeper structures via the lymphatics, resulting in the rapid superficial spread of erysipelas.

The capillary plexus beneath the dermal papillae serves as a nutritional reservoir for the stratum germinativum, and its physiological responses produce significant signs and symptoms. The plexus allows bacteria to enter the circulation, eventually leading to local spread or bacteraemia.

Leucocytosis, venous occlusion, and pitting oedema are brought on by the exaggeration of any of these physiological processes by excessive quantities of cytokines or bacterial toxins. Exploration of the deeper structures is necessary to look for signs suggestive of necrotizing fasciitis or myonecrosis in cases of oedema with purple bullae, ecchymosis, and cutaneous anaesthesia. Even in the absence of acute cutaneous inflammation, an early diagnosis is warranted in cases of unexplained fever, discomfort, and soreness in the soft tissue.

EPIDEMIOLOGY:

The incidence of necrotizing fasciitis is thought to be 0.001% worldwide. According to some studies, 0.4-0.53 incidents per 100,000 people. In comparison to women, men are more likely to have it. Patients with diabetes mellitus have a greater incidence rate. Although NF can develop everywhere on the body, it most frequently affects the extremities, followed by the perineum and trunk. According to reports, the mortality rate is 17–34%.

PATHOPHYSIOLGY

Because necrotizing fasciitis (NF) affects the deeper tissues, the muscle fascia and subcutaneous fat that lies above it are always gradually destroyed.

As a result of its abundant blood supply, muscle tissue is typically spared. In NF, the infection typically progresses along the muscle fascia and the surrounding tissue, which at first glance seems untouched. Due to this distinct characteristic, identifying NF without surgical intervention is more challenging[17].

Microbes enter the subcutaneous tissues either directly via a perforated viscus or indirectly by external injuries, most frequently from the colon, rectum, or urogenital organ. The release of a mixture of enzymes, endotoxins, and exotoxins as a result of rapid bacterial growth inside the superficial fascia spreads infection across the fascia.[18]

Extension is restricted to places like the scalp, hands, and feet due to fibrous linkages between subcutaneous tissues and fasciae.

Despite this, there is significant infection and tissue death due to a lack of fibrous attachments in the limbs and trunk. Oedema is a side effect of infection that spreads to the lymphatic and venous systems. This bacterial spread causes the blood vessels in the dermal papilla to thrombose, which results in ischemia necrosis and gangrene of the dermis and subcutaneous fat. Deep skin ischaemia is caused by the thrombosis of tiny veins and arteries that penetrate through the fascia.[19]

Therefore, inadequate microcirculation, ischaemia in afflicted tissues, and cell loss and necrosis are the end results. The progression of the necrotizing soft tissue infection is characterised by this skin ischaemia. Despite widespread infection of the underlying fascia, the skin initially seems to be normal. Following further structural involvement, haemorrhagic bullae, ulceration, and skin necrosis are the subsequent signs. Even though thrombosis of penetrating veins to the skin is the distinctive feature in the pathogenesis of NSTI, the initial clinical skin signs cause underestimate of the tissue infection present. Before skin alterations indicative of necrosis appear, thrombosis of several dermal capillary beds is required. Myositis develops when the fascia is torn, which causes a muscle infection[20]

Vascular blockage results in skin infarction and necrosis, promotes the growth of obligatory anaerobes like Bacteroides, and aids in the anaerobic metabolism of facultative organisms like Escherichia coli, which causes gangrene. Gases like hydrogen and nitrogen, which are comparatively insoluble gases that accumulate in subcutaneous tissues, are produced as a result of anaerobic metabolism.[21]

Additionally, gas-producing microbes like Clostridium species can cause an accumulation of subcutaneous gas, which is why the phrase "gas gangrene" has been coined. Toxic shock-like syndrome can result from infections brought on by toxin-producing bacteria such Staphylococcus aureus and Streptococcus pyogenes. Thus, apparently confined infection can result in septic shock and multi-organ failure.[22] There are two distinct clinical presentations:

(a) Those with no portal of entry and

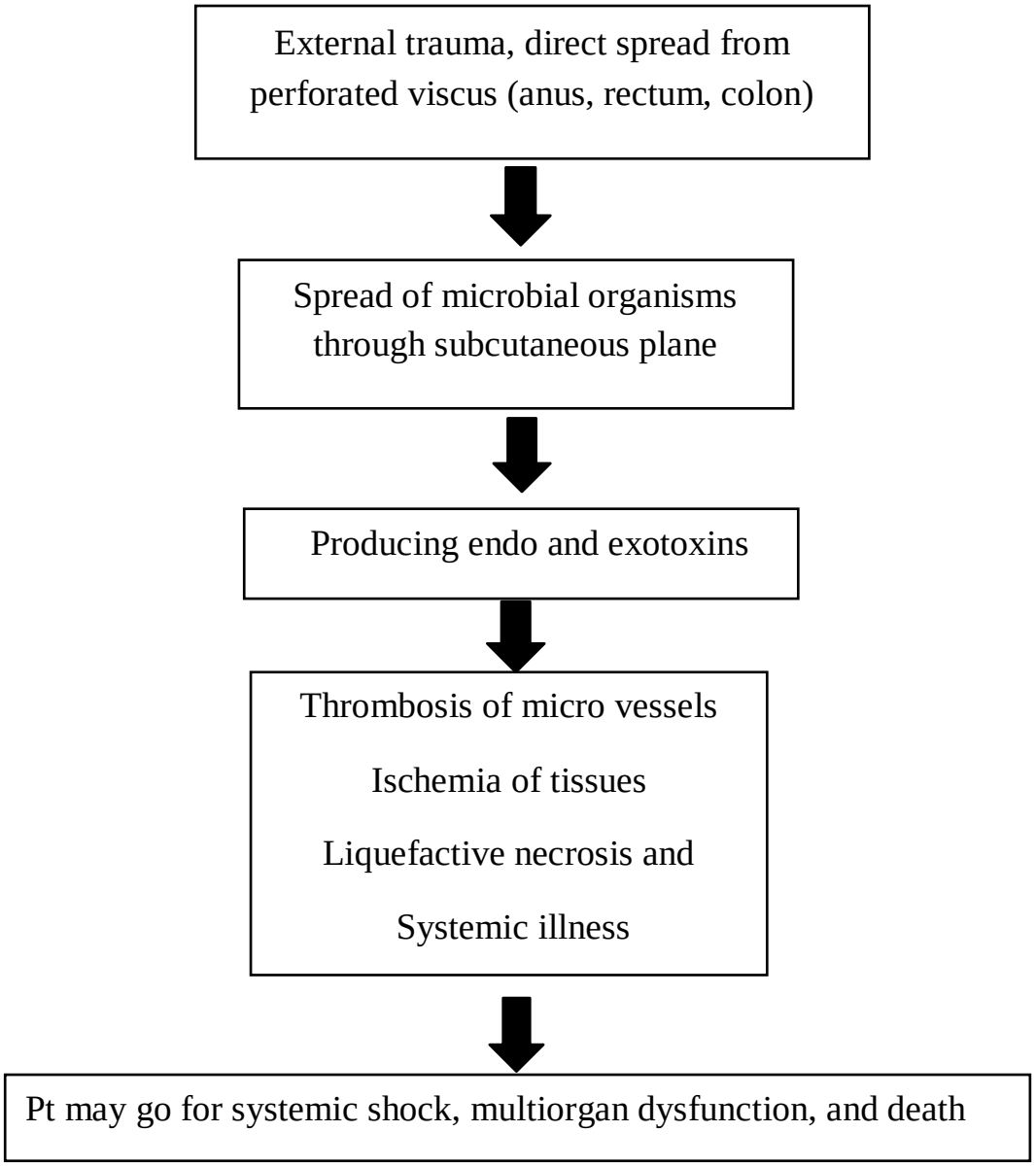
(b) Those with a defined portal of entry.

The first type of infections frequently starts deep at the site of a nonpenetrating mild injury, like a bruise or a muscle strain. Although the majority of patients deny having had a prior streptococcal infection, it is likely that transitory bacteraemia seeded the location. Just intense pain and fever are present in these patients. The characteristic necrotizing fasciitis symptoms, such as purple (violaceous) bullae, skin sloughing, and increasing poisoning, appear later in the course. Streptococcus pyogenes may enter the deep fascia in infections of the second kind via a site of cutaneous infection or penetrating trauma.

Early superficial skin infection symptoms in these patients lead to necrotizing fasciitis.

In either scenario, the toxicity is substantial, and shock may first emerge due to renal failure. Myositis co-occurs in 20–40% of patients, and similar to gas gangrene, serum creatine phosphokinase levels may be noticeably raised. When Streptococcus pyogenes or Methicillin-Resistant Staphylococcus aureus are the culprits, gas is typically not a problem.

FLOW CHART



CLASSIFICATION:

The following criteria serve as the main basis for this infection's current classification:

The following factors must be considered:

(a) the anatomical site,

(b) the extent of invasion, and

(c) the pathogens responsible.

Necrotizing fasciitis and necrotizing myositis are two different categories for deep soft tissue infections.

A rapid, widespread infection of the fascia beneath the adipose tissue is called necrotizing fasciitis.

Necrotizing myositis mostly affects the muscles, although it can also extend to nearby soft tissue.[23]

CLASSIFICATION OF SOFT TISSUE NECROTIZING INFECTIONS

TABLE 1:

Classification	Comments
Anatomic location	Cervical, thoracic, abdominal (Meleney's), pelvis, Fournier's gangrene
Depth of infection	
(a)Epidermis and dermis	Erysipelas Impetigo Folliculitis Ecthyma Furunculosis Carbunculosis Cellulitis
(b) Superficial fascia, subcutaneous tissue, subcutaneous fat, nerves, arteries, veins, deep fascia.	Necrotising fasciitis
(c) Muscle	Myonecrosis
Microbial causes	Types I, II, III, IV

Classification of soft tissue infections by Lewis. [24]

Infections of skin and subcutaneous tissue

Progressive synergistic bacterial gangrene

Chronic undermining burrowing ulcer (Meleney's ulcer)

Idiopathic scrotal gangrene (Fournier's gangrene)

Infections involving subcutaneous tissue and fascia

Haemolytic *streptococcal* gangrene

Necrotizing fasciitis

Gram-negative synergistic necrotizing cellulitis

Clostridial cellulitis

Infections involving muscle

Clostridial myonecrosis

Streptococcal myositis

Classification based on Microbiology: Table 2

Types of NF	Aetiology	Organisms
Type I	Polymicrobial, synergistic, commonly bowel derived	Mixed aerobes and anaerobes
Type II	Monomicrobial, skin or throat derived	Group A-β haemolytic Gram-negative Streptococcus (GAS) and Staphylococcus aureus
Type III	marine related organisms	Vibrio spp
Type IV(fungal)	Trauma associated	Candida spp immunocompromised, zygomycetes – immunocompetent

TYPE I NECROTIZING FASCIITIS:

Type I, or polymicrobial NF, typically results from synergistic infection and gut flora. Anaerobes and aerobes will coexist in cultures of tissue. It is a typical form that is usually seen in people with diabetes mellitus. Perineum and the body's trunk are the typical sites for Type I NF. [25]

TYPE II NECROTIZING FASCIITIS

Usually, skin or throat infections lead to type II mono-bacterial illnesses.

The infectious agent will either be Staphylococcus aureus alone or in combination with Group A/B haemolytic Streptococci. Type II infections may only be brought on by Staphylococcus aureus.

Type II NF often affects young, immuno-competent individuals. MRSA increases the incidence of Type II NF. Certain MRSA strains have been shown to produce the Panton-Valentine leucocidin (PVL) toxin, which causes necrotizing fasciitis. This virus typically affects the body's extremities. These patients are at risk for toxic shock syndrome and multi organ failure syndrome (MODS).[26]

TYPE III NECROTIZING FASCIITIS

The most serious type of NF, which is often caused by gram-negative bacteria found in marine environments, manifests itself in this way. This typically occurs following a fish puncture wound, a cut, or an insect bite when exposed to sea water. The very acute infection produces septic shock and Multi Organ Dysfunction Syndrome within 12 to 24 hours following the damage. Early detection is essential for effective care, and any delay in diagnosis always has a 100% death rate[27]. 83% of all instances of NF were caused by type III infections, according to data from Hong Kong.

TYPE IV NECROTIZING FASCIITIS

People with compromised immune systems and those who are under a lot of stress are at risk of developing type IV NF. Various fungi are the main infectious agents. It can cause significant NF and spread swiftly. frequently caused by Rhizopus, mucor, and candida species[28].

CLINICAL MANIFESTATION:

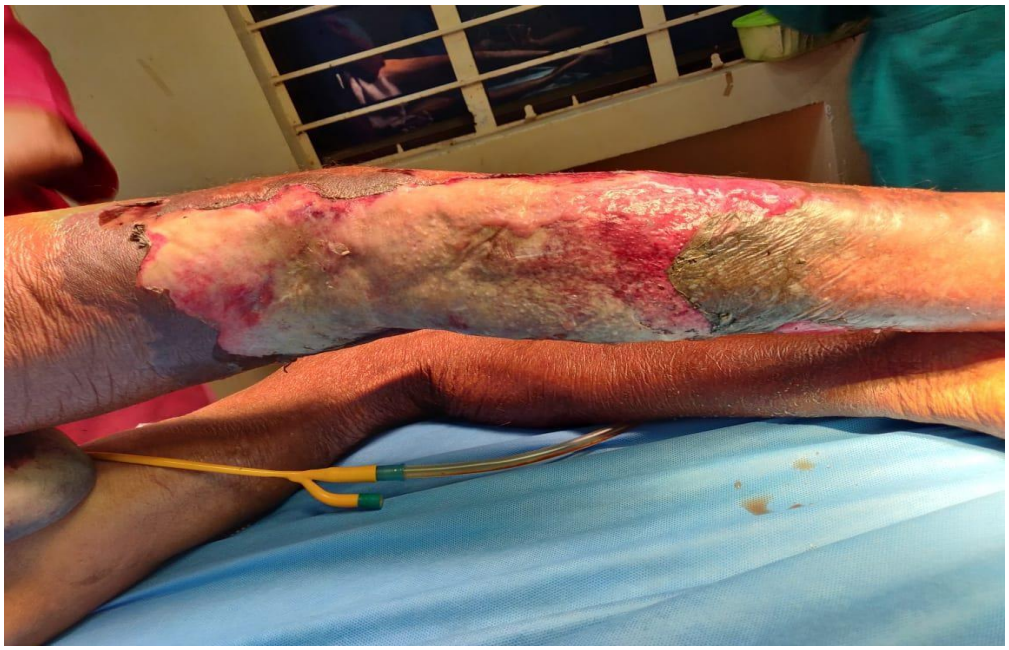


FIGURE 2: NF of right lower limb

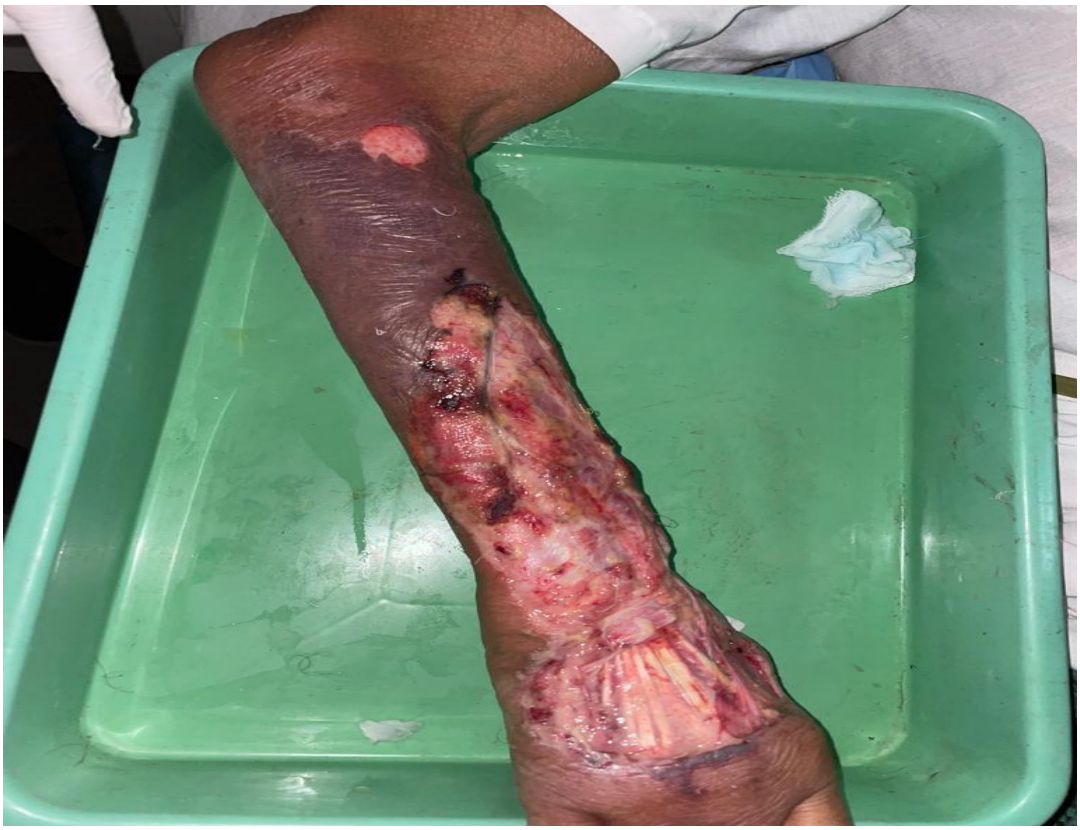


FIGURE 3: NF of right upper limb

CLINICAL FEATURES SUGGESTIVE OF NECROTISING FASCIITIS:

NSTI can happen anywhere on the body, however they frequently do so in the groin, perineum, belly, and extremities. Since the infection begins in the deep tissue planes, only the epidermis may be impacted. It becomes difficult because NF must be distinguished from cellulitis and non-necrotizing skin disorders. Minor trauma-related cellulitis may have deeper plane spread and initially go unrecognised. [29]

Because erysipelas is an infection of the superficial dermis, it has distinct borders and frequently boils. Erythema and lymphangitis are common in cellulitis, but there is little blistering.

While necrotizing fasciitis has a distinct boundary and is not connected to lymphangitis, it often presents as a patchy skin discoloration followed by pain and swelling[30]. As the sickness worsens, it becomes more obvious when tight oedema, a greyish-brown discharge, vesicles, bullae, necrosis, and crepitus emerge[31].

table 3

Skin	Pain	General
Erythema with ill-defined margins	Pain that extends past margin of apparent infection	Fever with toxic appearance
Tense oedema with or brown discharge	Severe pain, out of proportion to dermal involvement or physical findings	Altered mental state
Lack of lymphangitis or lymphadenopathy	Decreased pain or anaesthesia at apparent site of infection	Tachycardia, tachypnea due to acidosis
Vesicles or bullae, haemorrhagic bullae		Dehydration
Necrosis		Decreased urine output
Crepitus		Presentation with diabetic ketoacidosis.

Crepitus and haemorrhagic bullae are severe signs that affect the underlying fascia and muscle[32]. Crepitus is only a late sign in 18% of NF cases[33]. Typically, there is no pus collection, which prompts the surgeon to eventually defer a surgical consultation or intervention.

Elliot et al. and Wang et al. discovered that blisters were missing at the time of initial presentation in 76% to 95% and 62% to 73% of cases, respectively, in their two-retrospective case series[34, 35]. Patients with diabetic neuropathy cannot feel particularly uncomfortable, which might lead to a missed diagnosis. Oddly, this occurs in sites of hidden infection, including the perineum or oral cavity. Occasionally, an anaesthetic patch over the erythema site is also mentioned in NF. Soft tissue cutaneous nerve infarction and necrotic subcutaneous fascia are hypothesised to be the cause of this[36]

Following are some distinct varieties of necrotizing fasciitis and their distinguishing traits:

(a) Necrotizing cellulitis, sometimes referred to as haemolytic streptococcal gangrene, commonly appears shortly after a minor injury. Erythema, warmth, and edema are signs that the patient likely has cellulitis. Typical symptoms of this kind of cellulitis include severe discomfort. Further potential developments include gas build-up distant from the location and blebs with black serous fluid.

(b) Streptococcal Myositis: Streptococcal myositis frequently causes serious local pain and toxaemia. Wounds smell bad, are discoloured, and have edema. Patients frequently have gangrene of the underlying skin and blebs, but the disease typically advances slowly. Since the muscle beneath is no longer functioning, excision is always required.

(c) Clostridial Cellulitis: Severe pain that starts days after local tissue damage is the most important historical presentation linked to clostridial cellulitis. Skin blebs packed with a reddish-brown, foul-smelling fluid eventually result from this. Within hours, cellulitis advances quickly, and the patients become toxic. Crepitus is not always found, despite the possibility.

(d) Progressive Bacterial Synergistic Gangrene or Meleney's Gangrene: According to Baxter, Meleney's ulcer and Progressive Bacterial Synergistic Gangrene (PBSG) are two distinct diseases that share a common disease process but appear in different ways. Clinical profiles were discovered to be comparable despite all of the variances.

PBSG, a non-haemolytic streptococcal infection that rapidly progresses and most frequently occurs after abdominal procedures with infected wounds, is frequently linked to gram-negative bacteria or haemolytic Staphylococci. This wound has purple, erythematous zones of skin surrounding a core necrotic region. Additionally, wounds have necrotic tracts that penetrate the underlying tissue and eventually result in ulcerations at locations remote from the main lesion.

(e) **Fournier's Gangrene:** Fournier's gangrene is an acute, fast progressing, and possibly fatal infection necrotizing fasciitis that most commonly affects men but can also affect women and children. It affects the external genitalia, perineum, or perianal regions. Sudden discomfort in the scrotum, prostration, pallor, and pyrexia are the symptoms of Fournier's Gangrene. Cellulitis begins in the scrotum and spreads unchecked until the entire scrotal coverings slough off, leaving the testes exposed but healthy. The intense "repulsive, foetid stench" that is connected to this disease is one subtle aspect of the presentation. Symptoms and indicators that patients typically exhibit include fever over 380°C, scrotal enlargement, erythema, purulent wound discharge, and crepitation[37].

PREDISPOSING FACTORS AND CO-MORBID CONDITIONS

Pathogens can enter the body through trauma, insect bites, surgical incisions, and homogenous dissemination from far-off infection sites, according to reports[38]

Odontogenic infections, varicella lesions, intramuscular injections, and bruises are a few more risk factors[39]. Even in cases when there has been no trauma, NF has been recorded. Even NF following acupuncture has been documented [40]. Indirect queries from the doctor are frequently the only way to collect this kind of detailed history; otherwise, patients are likely to neglect or forget to mention it.

The usage of non-steroidal anti-inflammatory drugs has been a contributing factor in the development of severe necrotizing streptococcal infections. Non-steroidal anti-inflammatory medicines are thought to affect lymphocyte activity[41]. Nevertheless, the reason for the delay in diagnosis, particularly in cases when patients present with ambiguous symptoms at an early stage, may be attributable to the suppression of symptoms and signs of inflammation. Malnutrition and skin diseases like varicella are risk factors for NF in children [42]

It is important to stress that doctors should not rule out NF in healthy, normal persons who have mild skin injuries. These are the patients who frequently are overlooked.

RISK FACTORS FOR NECROTIZING FASCIITIS

- Diabetes
- Chronic disease
- Immunosuppressive drugs (eg, prednisolone)
- Age above 60 years
- Malnutrition
- Peripheral vascular disease
- Intravenous drug misuse
- Renal failure
- Underlying malignancy
- Obesity

PRECIPITATING EVENTS CAUSING NECROTIZING FASCIITIS

Table:4

Traumatic	Non traumatic
Surgery	Soft tissue infections
Minor invasive procedures (joint aspiration, acupuncture)	Burns
Intravenous drug abuse	Childbirth
Penetrating injuries (insect and animal bites)	

DIAGNOSIS:

Important diagnostic cues include the how lesions look physically and where they are located inside the soft tissues. In addition to the progression of the lesions, it's also important to take into account the patient's travel history, history of animal exposure or bites, age, the presence of underlying diseases, and lifestyle choices when reducing the list of possible diagnoses.

However, a history and physical examination alone cannot reliably rule out all infections of the soft tissues. If the patient has quickly developed lesions or indications of a systemic inflammatory response syndrome, soft tissue radiography, CT, and MRI should be carried out in order to assess the depth of infection. These examinations are crucial for identifying a localised abscess or spotting gas in tissue. [43]

They are not, however, specific for fulminant infections such necrotizing fasciitis or myonecrosis caused by group A Streptococcus, where gas may not be present in lesions and only soft tissue edema may be revealed.

If the results of the imaging tests are positive, aspiration of the leading edge or punch biopsy with frozen section may also be beneficial, however false negative results happen in about 80% of instances. Injection with aspiration with regular saline may not be as effective as aspiration alone. In situations of necrotizing fasciitis, frozen sections are very helpful in separating Staphylococcal Scalded Skin Syndrome (SSSS) from Toxic Epidermal Necrolysis (TEN)[44].

type I: Typically, this kind is polymicrobial (aerobes and anaerobes).

As opposed to Klebsiella pneumonia, Escherichia coli, Proteus mirabilis, and Pseudomonas aeruginosa, Enterobacteriaceae are the most often isolated bacteria. the widespread gram-negative bacteria. Staphylococcus aureus, Enterococcus species, and Streptococcus pyogenes are frequently found in Gram-positive bacteria[45]. Known also as necrotizing cutaneous myositis and synergistic necrotizing cellulitis, synergistic non-clostridial anaerobic myonecrosis is a type of necrotizing fasciitis that is brought on by mixed aerobic and anaerobic bacteria but not clostridial organisms.

Anaerobes: Among isolated organisms, Bacteroides fragilis is the most prevalent. Other species discovered in NF wounds include Clostridium spp. and Pepto streptococcus spp. The other less frequent anaerobes that cause NF are Porphyromonas spp., Viellonella parvula, Prevotella brivia, and Fusobacterium spp[46]

Bacteroides: included under the heading of Gram-negative anaerobic non-sporing bacteria. are stationary, stringent anaerobes. Pleomorphic, thin rods, they can be organised single, in pairs, or in short chains. The typical flora of the human intestine includes bacteria.

The most prevalent isolate in clinical specimens is Bacteroides fragilis. belongs to the Bacteroidaceae family. An infection of the soft tissues is more frequently isolated from wounds, pleural fluid, blood, brain abscesses, peritoneal fluid, and

urogenital infections. The Bacteroides fragilis group typically develops below the diaphragm.

A compromise in the mucosal integrity is necessary for the majority of infections, allowing the ability of the germs to enter deeper tissues. The creation of a bad odour is a defining characteristic of most illnesses, albeit not all.[47]

They produce a capsule, endotoxin, and succinic acid as virulence factors.

can block phagocytosis and a number of enzymes involved in tissue injury[47] .

IDENTIFICATION

White to grey white, whole convex transparent to semi-opaque, non-haemolytic colonies can be found on anaerobic blood agar.

Colonies on Bacteroides Bile Esculin agar (BBE) are >1mm in diameter, round, complete, and either (a) have a dark grey zone (esculin hydrolysis) or are (b) low convex and occasionally precipitate bile. (b) shiny, convex, light to dark grey, and encircled by a grey zone.

Gram Stain: Gram negative, pale-staining, pleomorphic rods with rounded ends that can appear single or in pairs and are sometimes compared to the look of safety pins.

Pepto streptococcus: Anaerobic Cocci with Gram Positive. normal intestinal, vaginal, skin, and oral flora. These have recovered from a variety of clinical diseases, including puerperal sepsis, soft tissue infections of the skin and body, and brain abscesses.

Peptostreptococcus Anaerobius**:** Anaerobic blood agar colonies: Colonies have a sweet, foetid odour, are opaque and grey-white in colour, and are often larger than most anaerobic cocci.

Gram Stain: Large, Gram-positive coccobacilli are frequently found in chains.

Type II: It is a single bacterial infection that affects the skin or throat. Group A/B haemolytic streptococci alone or in conjunction with Staphylococci will be the pathogenic organism. This kind of NF can also be brought on just by staphylococci.

The most frequent cause of NF, accounting for about 60% of all cases, is group A streptococci. Common serotypes that produce streptococcal pyrogenic exotoxins are M types 1 and 3.[48]

Type III: The Clostridium species, anaerobic bacteria that enter through deep wounds or crush injuries that cause local devascularization, or surgical wounds, notably intestinal and obstetric, are included in Type III monomicrobial infections. The most common bacterium causing type III NF is Clostridium perfringens, and drug addicts are currently more likely to get clostridium infections [49]than the general population.

The marine bacterium Vibrio vulnificus is regularly isolated throughout Asia. Additionally, Vibrio vulnificus produces lipopolysaccharides, metalloproteases, cytolysin, toxins, enzymes, and capsular polysaccharides. In retrospective research, Shiuan-Chih Chen et al. recorded 89 cases of necrotizing fasciitis brought on by Vibrio vulnificus.[50]

In addition to soil, Aeromonas hydrophilia can be found in freshwater or low-salinity water. These two bacteria both induce comparable clinical signs. 83% of the overall NF in a study from Hong Kong was type III [51]. A case of Aeromonas sabori-related type III NF of the forearm had been reported.

Type IV: These infections are fungi, primarily caused by Zygomycetes and Candida spp. This kind is primarily present in immunosuppressed hosts. These fungal infections happen after trauma, and the clinical picture is aggressive and spreads quickly, especially in immuno-compromised patients. Zygomycetes like Mucor and Rhizopus are widespread.

Deepali Jain et al in a retrospective study has reported 18 cases of fungal necrotising fasciitis, out of which five were positive for *Apophysomyces elegans* and fifteen patients were immune competent[52].

PROCALCITONIN:

Procalcitonin, one of the 116 amino acids that make up the hormone calcitonin, is generally produced by the thyroid's C-cells. In cases of bacterial infection, procalcitonin's blood level will rise due to synthesis from extra-thyroidal parenchymal cells, particularly neuro endocrine tissues, which is lower than 0.05 ng/ml under normal physiological settings. Cytokines as well as bacterial endotoxin or lipopolysaccharide will induce the production of procalcitonin. The systemic response includes the rise in procalcitonin, which is particularly specific to bacterial infections[53]. Procalcitonin not only rises quickly but also undergoes rapid cleavage when infection is controlled by the immune system

with effective antibiotic therapy. Infection with a virus will result in a downregulation of procalcitonin. With little to no increase in viral infections, localised infections, or intracellular infections, the level of serum procalcitonin will be highest in cases of bacterial infection. Blood levels of procalcitonin peak between 8 and 24 hours following the start of the systemic reaction, at which point they start to climb at 4 hours. The most popular biomarker, CRP, rises gradually and peaks 36 hours after the start of the systemic response, whereas this occurs earlier[54]. Due to its dual role as a precursor to the hormone calcitonin and as a mediator of cytokines that are raised in response to systemic bacterial infection, procalcitonin is known as a hormone mediator. Procalcitonin production does not appear to be affected by non-steroidal and steroidal anti-inflammatory medicines, unlike other biomarkers (such as CRP). An experiment with rats revealed that procalcitonin peak values were significantly higher in rats stimulated with lipopolysaccharide, a component of gramme negative bacteria's outer membrane, compared to rats stimulated with muramyl dipeptide, a component of gramme positive bacteria's outer membrane, demonstrating a relationship between the rise in procalcitonin level and the type of pathogenic microbes. Patients with pancreatitis, post-surgical or trauma, and renal impairment will have higher procalcitonin levels. Procalcitonin can be delivered to a lab for investigation together with other tests because its half-life is 24 hours.[55]

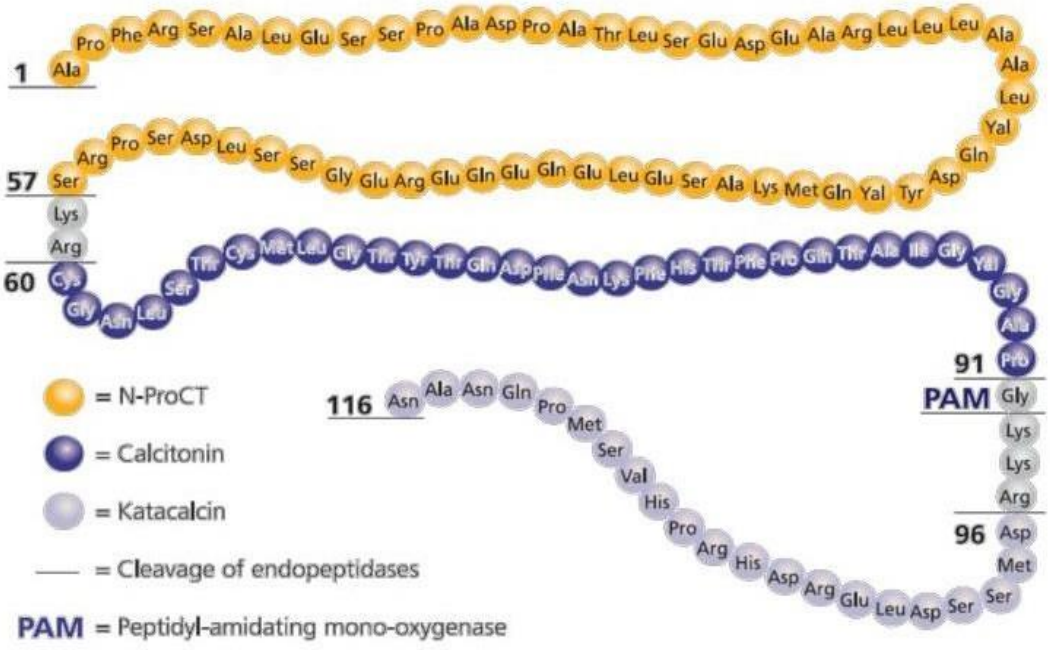


Figure 4: structure of procalcitonin

ALBUMIN

I. i)The name comes from the white precipitate that forms when eggs are boiled (albus = white in Latin). Plasma proteins primarily consist of albumin.

II. ii One polypeptide chain of 585 amino acids makes up the substance. It has a 69,000 D molecular weight. Its form is elliptical.

III. Since hepatocytes are responsible for its synthesis, measuring albumin serves as a liver function test. Albumin is created as a precursor, and when it moves through the endoplasmic reticulum, the signal peptide is taken out.

IV. Vascular compartments can allow albumin to escape. So, CSF and interstitial fluid both include albumin.

V. Albumin has a half-life of roughly 20 days. About 25% of the total protein synthesis in the liver, or about 12 g per day, is produced by the liver.[56]

Functions of Albumin

1) Colloid osmotic pressure of plasma:

i. Total serum osmolality ranges from 278 to 305 m osmol/kg (about 5000 mm of Hg). But salts, which can easily flow from intravascular to extravascular space, are what primarily create this. The osmotic pressure that electrolytes exert both inside and outside of the vascular compartments will therefore cancel out. However, proteins impose "effective osmotic pressure" since they cannot easily leave blood vessels. It is roughly 25 mm Hg, and albumin is responsible for 80% of it. This effective osmotic pressure is necessary to maintain blood volume.[57]

ii. According to Starling's theory, water is taken into the vascular compartment by effective osmotic pressure (EOP) and ejected out of the capillary end by blood pressure (BP) or hydrostatic pressure.

iii. Water is evacuated by a pressure of 10 mm Hg at the arterial end of the capillary where BP is 35 mm Hg and EOP is 25 mm of hg. Water is ingested at a pressure of 10 mm of hg because the capillary's venous end has an EOP of 25 mm and a BP of 15 mm of hg. As a result, the amount of water molecules exiting from the artery side and those returning from the venous side will be exactly equal, keeping the blood volume constant.

iv. The EOP decreases in direct proportion to the reduction in serum protein content. Water then builds up in tissues as a result of decreased water return to blood vessels. We refer to this as oedema. Edema is seen in conditions where albumin level in blood is less than 2g/dl.

2) Transport Mechanism[58]

Different hydrophobic compounds are transported by albumin in the blood. Blood cannot solubilize lipid components since it is a watery medium.

i. Albumin transports bilirubin and non-esterified fatty acids in particular.

Drugs (sulpha, aspirin, salicylate, dicoumarol, phenytoin) and hormones (steroid hormones, thyroxine) are included in item number two.

iv. Metals: Copper is transported through albumin. Albumin is a general carrier of calcium and heavy metals. Only the portion of medicines that are unbound is physiologically active.

3) Buffering function: There is a buffering ability in every protein. The highest amount of buffering power is provided by albumin due to its high blood content. The 16 histidine residues in albumin work together to provide this buffering effect.

4) Nutritive Function.

Pinocytosis allows albumin to be taken up by all tissue cells. Then it is reduced to the level of amino acids. Therefore, albumin may be thought of as the vehicle that carries important amino acids from the liver to cells outside the liver. Clinically, human albumin is helpful in the treatment of liver conditions, haemorrhage, shock, and burns.[59]

LDH:

An intracellular enzyme called lactate dehydrogenase is present in body tissues like the lungs, kidneys, liver, heart, muscles, and blood cells. It stimulates the interaction between NADH and NAD+. Pyruvate, the end result of glycolysis, is transformed into lactate. Because the respiratory chain cannot re-oxidize NADH in anaerobic conditions, pyruvate is converted to lactate, which is catalysed by the lactate dehydrogenase enzyme. This enables the oxidation of NADH, enabling the glycolysis of an additional glucose molecule.[60] Due to the lack of mitochondria, glycolysis in erythrocytes invariably results in the generation of lactate; however, other tissues such the brain, renal medulla, retina, and skin obtain a significant portion of their energy from glycolysis and oxidise lactate. Serum lactate levels also rose in cachexia and septic shock. Under hypoxic conditions, the liver, kidney, and heart normally absorb lactate and oxidise it. When there is tissue hypoxia and cellular damage, LDH levels rise[61]. Adult normal range is 0-250 U/L. Since there was widespread cellular hypoxia, tissue

damage from vasospasm, and endothelial cell destruction in necrotizing fasciitis, there will be a rise in serum lactate dehydrogenase levels. The severity of cellular damage, multiorgan damage, and subsequent problems can therefore be predicted by measuring serum LDH levels, as was done in our study[62]. Serum LDH levels were shown to be elevated in patients with necrotizing fasciitis.

IMAGING STUDIES: -

Radiography: -

It comprises soft tissue thickening and opacity, which at first resemble cellulitis. When gas-forming organisms are present, the classic finding is the presence of gas along the fascial planes.

ultrasound imaging: Due to the inability to resolve deeper structures, ultrasonography has a limited function in the treatment of necrotizing fasciitis. Compared to X-ray images, the presence of soft tissue gas may be more visible on ultrasound. A layer of gas that is echogenic and with posterior filthy acoustic shadowing is discovered above the deep fascia. The aberrant echogenicity, increased dermal thickness, unclear "haziness," increased subcutaneous tissue echogenicity, and "COBBLE STONE Appearance" (caused by subcutaneous edema) are hallmarks of NF. Hypervascularity may not be detected by a colour doppler evaluation. Specifically, irregularities in the fascia, aberrant fluid accumulation along fascial planes, and diffuse fascia thickening as compared to

the contralateral unaffected side are helpful in separating necrotizing fasciitis from cellulitis.[63]

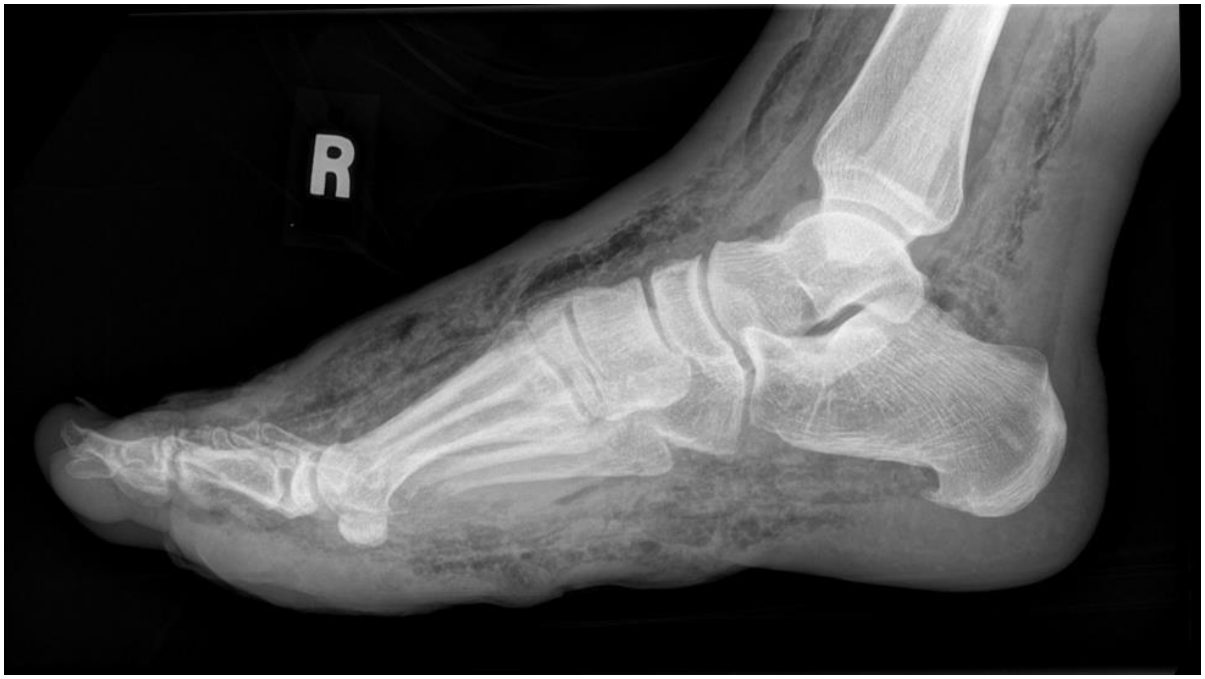


Figure 5: X-RAY findings of right foot showing gas in subcutaneous plane.

CT SCAN (Computerized Topography): Due to its greater accessibility and superior spatial resolution as compared to X-RAY and Ultrasound, it is one of the key modalities in the diagnosis of NF. The previously mentioned characteristic of the NF is gas inside fascial planes. On a contrast-enhanced CT, the fascia's thickening and lack of enhancement may help to distinguish it from non-necrotizing fasciitis. Other findings are increase soft tissue attenuation, fat stranding, etc. It is helpful in identifying potential complications like vessel injury.[64]

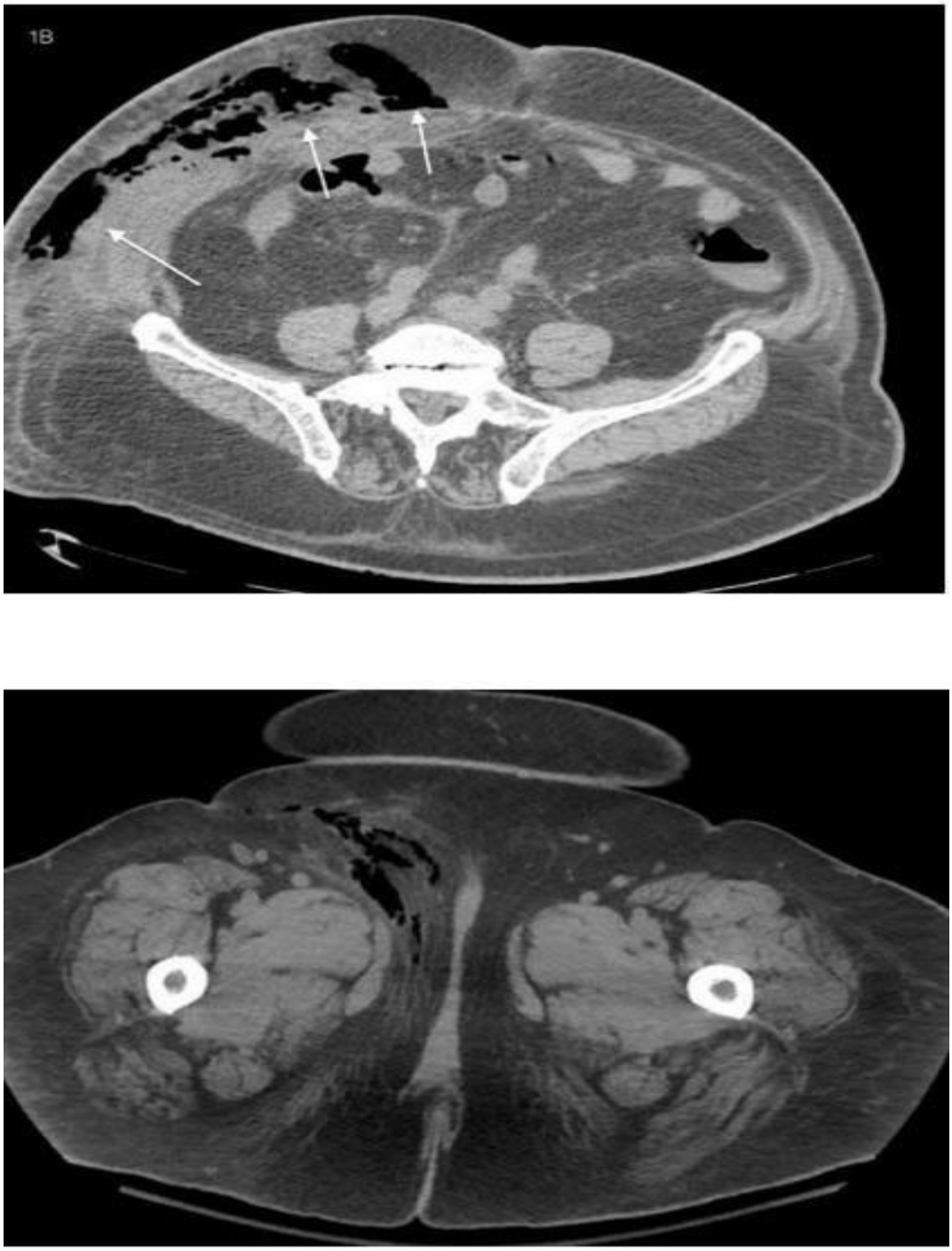
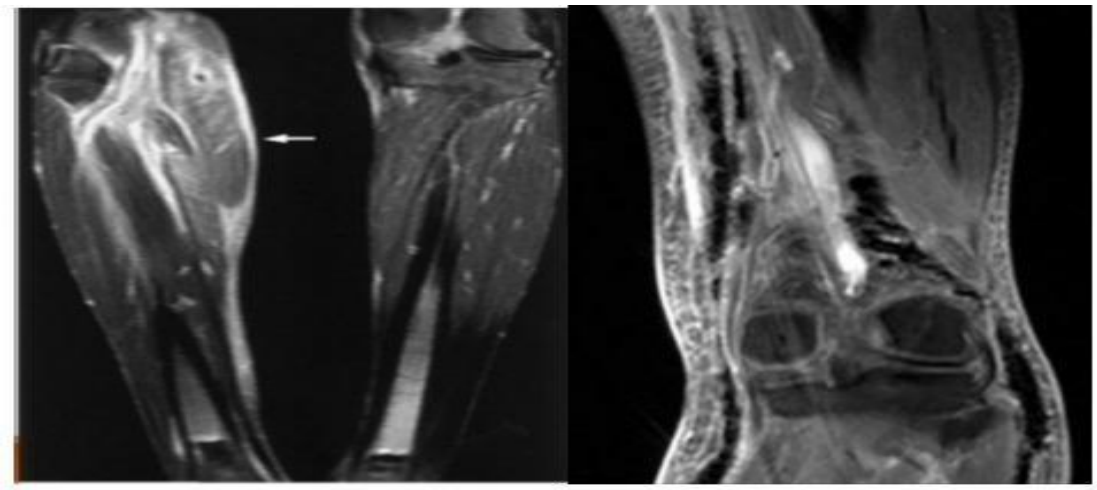


Figure 6: CT shows Necrotising fasciitis of right lower limb extending to abdominal wall shows gas within tracing along the fascial plane.

Magnetic Resonance Imaging (MRI): - It exhibits exceptional soft tissue resolution, making it the gold standard for infections of soft tissues. T1 weighted imaging is used to evaluate the anatomy, while T2 weighted imaging is used to check for fascial thickness and edema. "A sensitive result to imply necrotizing fasciitis is hyperintensity and thickness of the fascia greater than or equal to 3 mm on fat saturated T2 weighted or short T2 inversion-recovery images with involvement of three or more compartments." Because sensitivity surpasses specificity in MR imaging, it tends to overstate the depth of deep fascial involvement; as a result, the therapeutic plan should be based on both clinical findings and MR imaging[65] .



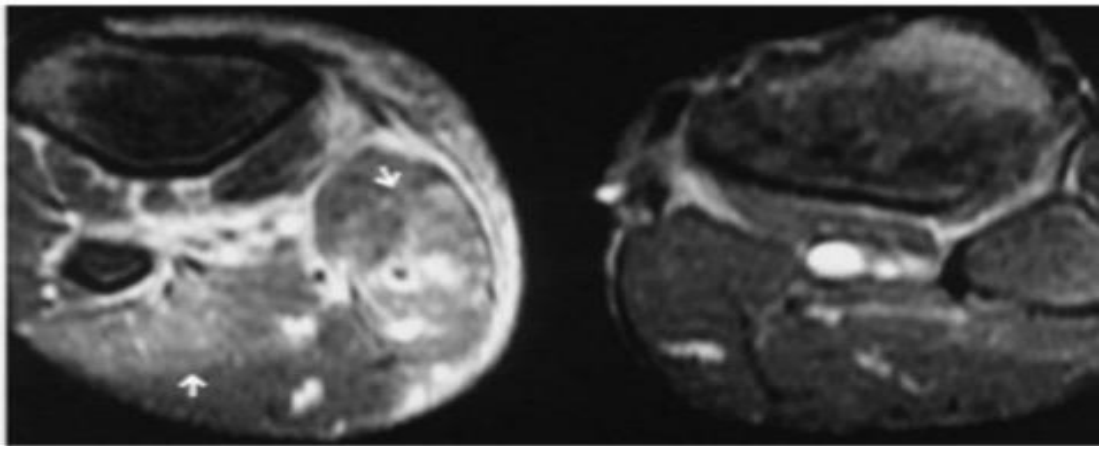


Figure 7: MRI shows Necrotising fasciitis of right lower limb shows fascial thickening and hyper intensity, starting in the superficial fascia involving deep muscular fascia in multiple compartments, sub-fascial and inter-fascial fluid collection, low signal foci of gas and subcutaneous edema.

Treatment:

Resuscitation and supportive care:

Restoring adequate oxygen supply and tissue perfusion is the primary goal of resuscitation. The Surviving Sepsis Campaign advises hemodynamic resuscitation in patients presenting with sepsis owing to NF; invasive arterial pressure monitoring and central venous access may be necessary.

Treatment of nosocomial infections and adequate nutritional assistance are crucial. Given the fast clinical course, high likelihood of multiple organ failure, and considerable death rate, admission to critical care is strongly advised.

In cases of suspected necrotizing fasciitis, myositis, or gangrene, early and aggressive surgical exploration is necessary to[66]

(1) visualise the deep structures,

(2) remove necrotic tissue

(3) lower compartment pressure, and

(4) obtain suitable material for Gram's staining and aerobic and anaerobic cultures.

Debridement: - It involves clearing the wound of necrotic tissue. The presence of necrotic or dead tissue delays healing, prevents the growth of healthy granulation tissue, and creates an ideal environment for the growth of more bacteria, raising the risk of sepsis. [67]By applying a wet wound dressing, autolytic debridement, which removes necrotic tissue, may be aided.

FIGURE 8: post op debridement pictures of left lower limb necrotizing fasciitis

Other types of debridement

- Enzymatic (agent impregnated either on wound or dressing)
- Mechanical (physical removal of dead tissue either using dry gauze or DE sloughing solutions) (physical removal of dead tissue either using dry gauze or DE sloughing solutions) and
- precise surgical debridement the more thorough removal of tissue under anaesthesia (when a surgeon removes enough tissue until tissue with a healthy bleeding capillary foundation is detected) and the debridement of completely dead or necrotic tissue using a scalpel or scissors Incisions are carried out parallel to Langer's lines to prevent less scarring and promote faster wound healing. and extend at least past the indurated area. Induration is a sign of clogged dermal lymphatics and thrombosed post-capillary venules, which results in tissue necrosis. Excision should be continued until the tissue is healthy; bleeding tissue is evident at all margins. It is necessary to examine the wound again. re-debridement, if it's necessary.[6]

Antibiotic therapy: Ischemia and hypoxia result in insufficient antibiotic administration to the infection site. Therefore, BROAD SPECTRUM ANTIBIOTICS should be started right once following surgical care of the NSTI. First, third- or fourth-generation Cephalosporins, Carbapenems, Amoxicillin-Clavulanate acid, Ampicillin-Sulbactam, Piperacillin-Tazobactam,

and Ticarcillin-Clavulanate acid are utilised. subsequently modified in response to a microbiological culture sensitivity report. For anaerobic coverage of type I infections, metronidazole and clindamycin are beneficial. Cephalosporins of the first or second generation are used to treat type II infections. Vancomycin is the drug of choice for Methicillin Resistant Staphylococcus aureus (MRSA) infections. Daptomycin is another option. When Staphylococcus aureus is vancomycin-resistant, linezolid is employed.[69]

Table:5

Condition	Primary Treatment	Alternative treatment
Necrotising fasciitis (group A Streptoccocal)	Clindamycin, 600- 900mg IV q6-8h, + Penicillin G, 4 million units IV q4h.	Clindamycin, 600- 900mg IV q6-8h, + Cephalosporin (first or second generation).
Necrotising Fasciitis (mixed aerobes and anaerobes)	Ampicillin,2g IV q4h, + Clindamycin, 600-900 mg IV q6-8h, + Ciprofloxacin, 400mg IV q6-8h.	Vancomycin, 1g IV q6h, + Metronidazole, 500 mg IV q6h, + Ciprofloxacin, 400mg IV q6-8h.
Gas gangrene	Clindamycin, 600- 900mg IV q6-8h, + Penicillin G, 4 million units IV q4h	Clindamycin, 600- 900mg IV q6-8h, + Cefoxitin, 2g IV q6h

Other treatment modalities: -

Hyperbaric oxygen therapy (HBOT)[70]

inhaling oxygen under high atmospheric pressure is a component of hyperbaric oxygen therapy. Increased leucocyte killing, anaerobe killing, reduced oedema, stimulation of fibroblasts, and improved collagen production are all effects of tissue-level hyperoxia. It ought to begin as soon as possible and shouldn't postpone surgical therapy.

100% oxygen is delivered through a pressure chamber with a pressure higher than that of the atmosphere.

After surgical debridement, HBOT was administered at a rate of 2.5 to 3.0 atmospheres for 90 minutes twice daily. Both healthy and devitalized tissue benefit from an improved level of tissue oxygenation.[71]

It can be used in:

- gas embolism
- gas gangrene,
- carbon mono oxide poisoning.

Indication of HBOT:

1. Despite receiving adequate medical and surgical care, the patient with necrotizing fasciitis does not recover.

2. a person infected with clostridium.

3. infiltration of deeper tissues and muscle gangrene.

Benefits of HBOT

1. By giving the tissue 100% oxygen, HBOT prevents the growth of anaerobic microbes.

2. fibroblast multiplication and angiogenesis

3. enhanced neutrophil phagocytic function

4.reduces edema by vasoconstriction and enhanced intracellular antibiotic delivery.

5.HBOT aids in the action of medicines. An example of an oxygen-dependent pump is an aminoglycoside.

6. It promotes collagen formation.

A Drawback Of HBOT: Absolute prohibition:

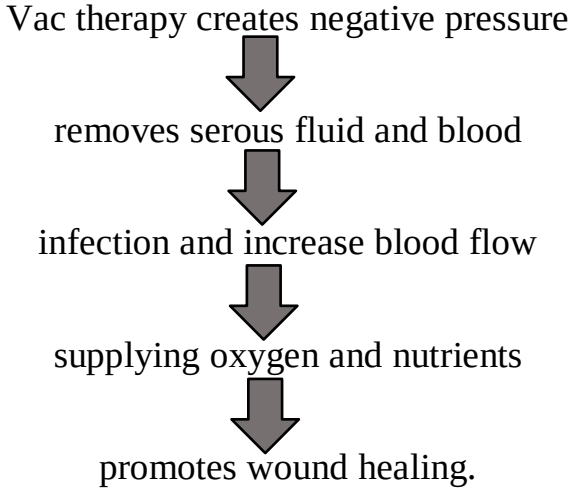
1. Untreated tension pneumothorax is number one.

Relative contraindications:

1. Middle ear cavity barotrauma
2. heart disease
3. 3. malignancy
4. URTI emphysema with retention of carbon dioxide

However, the utility of HBOT is still debatable; it can be utilised if standard medical and surgical management fail. Six studies were done to determine whether HBOT was effective in treating necrotizing fasciitis; four of them found that HBOT increased patient survival, whereas the other two did not. No research have proven that hyperbaric oxygen therapy is effective

vacuum assisted closure: vacuum assisted closure was created by Dr. Louis Argenta and Dr. Michael. It operates through negative pressure, also known as topical negative pressure/sub atmospheric pressure.[72]



Steps in vac :

1. prepration of the wound
2. placement of foam
3. sealing with drapes
4. application of negative pressure

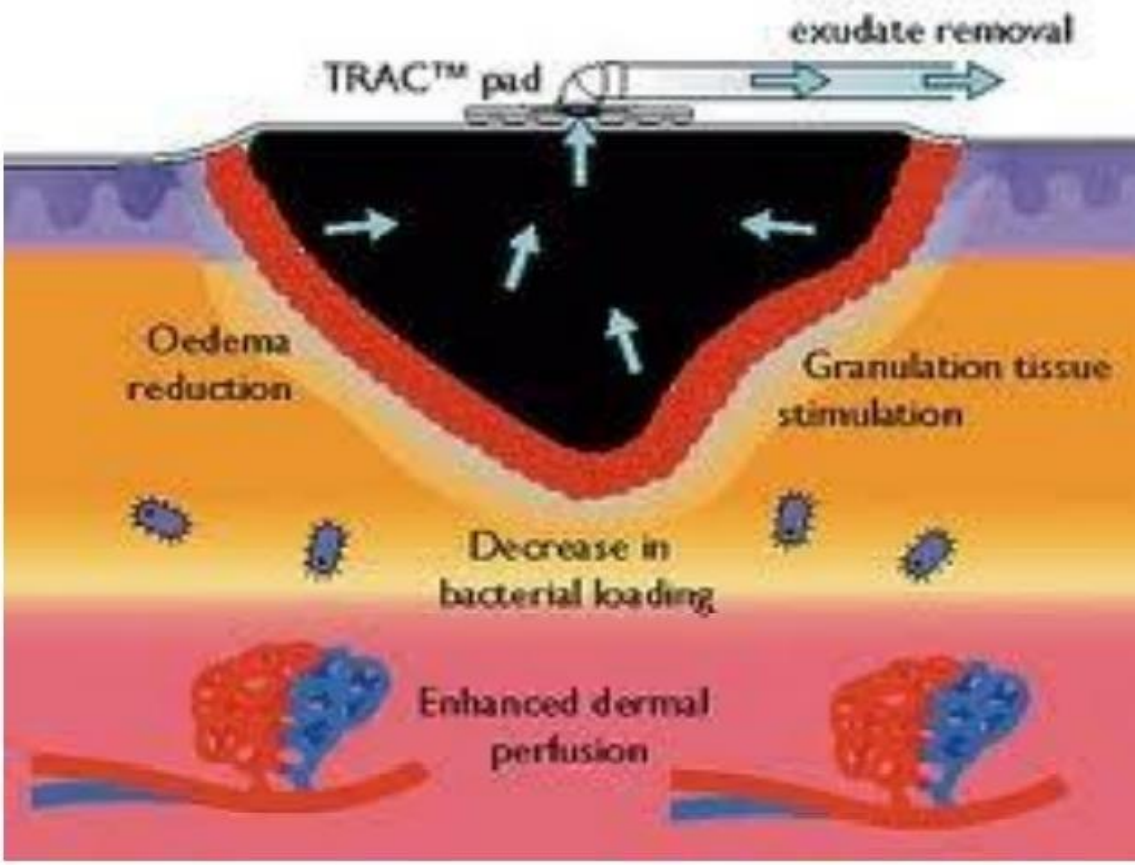


FIGURE 9: VAC ASSISTED DRESSING

Intravenous immunoglobulin (IVIg): -

It entails administering pooled IVIg from human donors, which binds to exotoxins produced by type II infections and limits the systemic inflammatory response. According to research, IVIg therapy should only be considered for critically ill patients with TYPE II infections.

Anaya et al. investigated the role of IVIG in the treatment of type II NSTI. The authors concluded that IVIG was beneficial in patients with group A streptococcal infection who developed streptococcal toxic shock syndrome, as well as those with a high mortality risk (advanced age, hypotension, and bacteraemia). The majority of the studies are non-randomized or underpowered, implying weak evidence for patient benefit.

Wound management: - A moist environment has been shown to aid in wound healing, and a bandage acts as a barrier. The type of dressing used depends on factors such as depth, size, location, and wound surface.

Dressings: Films, composites, hydrogels, hydrocolloids, alginates, foam, and other absorptive dressings, including NPWT-Negative Pressure Wound Therapy, can be classified.[73]

Skin transplantation: It is the transfer of tissue from the donor to the recipient without any blood or nerve supply. It is used to treat clean granulated ulcers where the defect cannot be opposed.

It is classified into several categories based on the composition of the graft: - STSG (split-thickness skin grafts): Thiersch graft is another name for it. They are made up of the epidermis and a thin layer of the dermis.

Full-thickness skin grafts (FTSG) contain both the full epidermis and dermis.

Composite grafts contain skin and another type of tissue, usually cartilage.

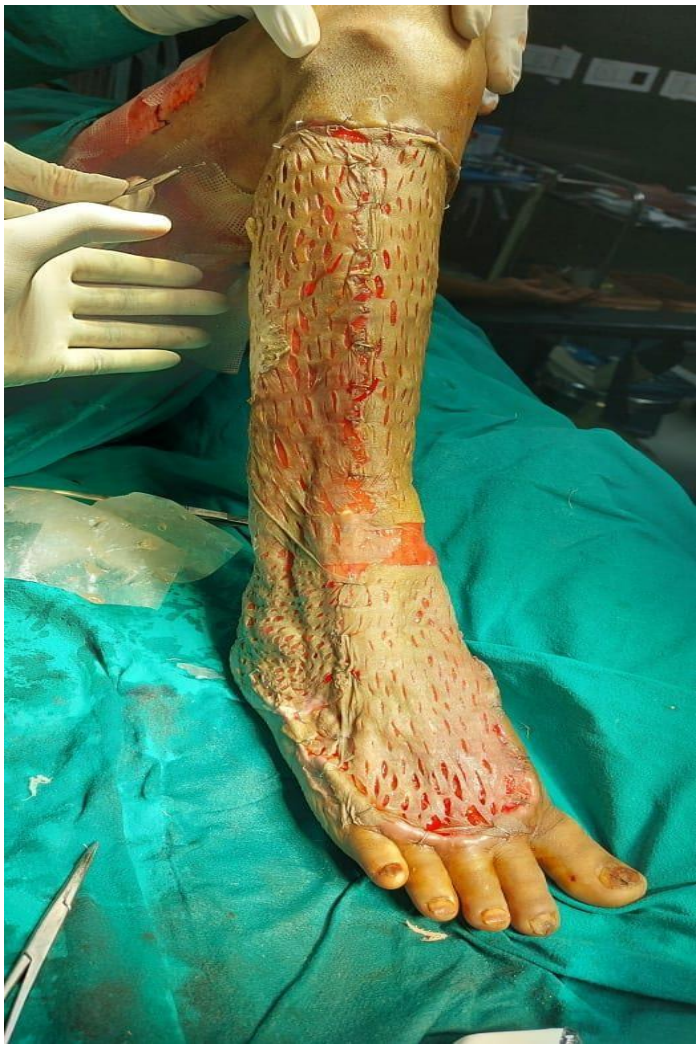


FIGURE 10: split thickness skin grafting of right lower limb necrotizing fasciitis

AMPUTATION: -It is defined as the surgical removal of a limb or part of the body. It is usually done when a patient with necrotizing soft tissue infections presents late (i.e gangrene of limbs).

Ray's amputation is one type of amputation.

Amputation below the knee

Amputation above the knee

Disarticulation of the hip

Amputation of the hindquarters.

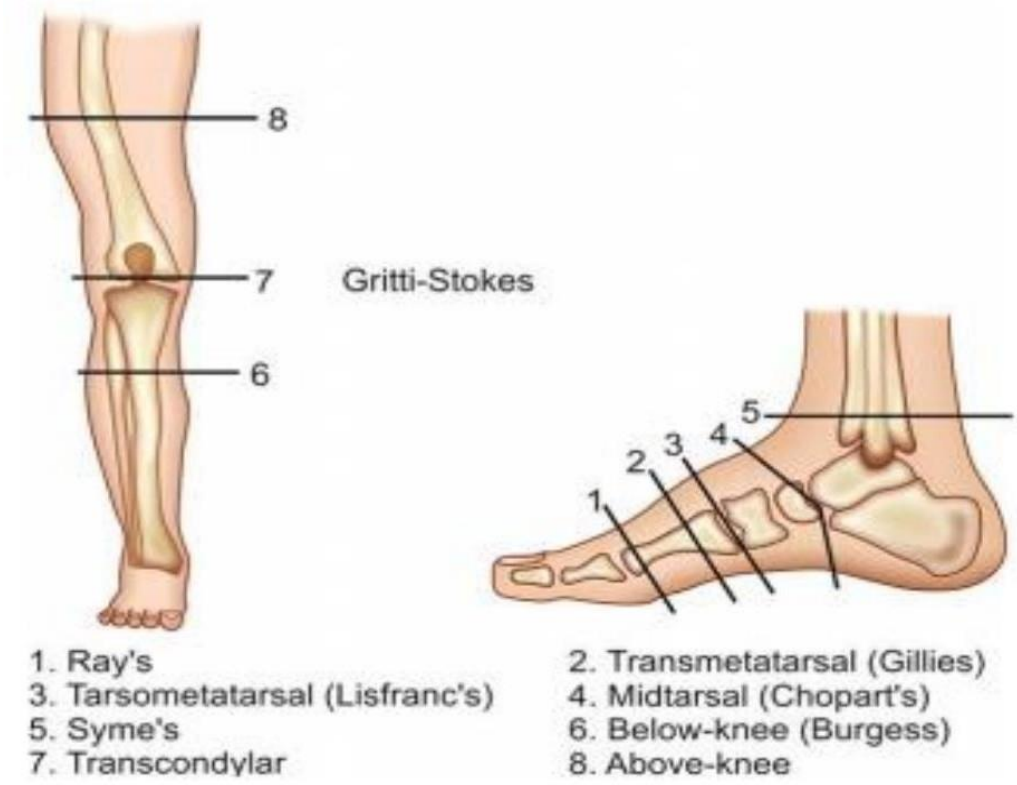


Figure11: different types of amputation

Most NSTIs of the lower extremities involve below-knee and above-knee amputations.

In a retrospective cohort study at a tertiary teaching hospital in Taiwan, Chang et al 2018 concluded that "patients with haemorrhagic bullae, comorbidity with peripheral vascular disease, and the presence of bacteraemia should receive early and primary amputation in order to prevent mortality."[74]

According to Khamanuan et al. (2015)[75]patients with clinical predictors for amputation such as diabetes mellitus, soft tissue swelling, skin necrosis, gangrene, and serum creatinine values greater than 1.6 mg/dL on admission should be closely monitored for progression and receive early aggressive treatment to avoid amputation.

GLYCEMIC CONTROL: Patients with Diabetes Mellitus have decreased wound healing and are more susceptible to infections due to an increase in blood sugar levels. Insulin will frequently be required in those who have never received it before, even if only temporarily**.**

PREVENTION: -

1. Streptococcus infection is easily avoided with proper hand washing.

2. Necrotizing fasciitis can be avoided by keeping the skin intact.

3. A patient with a rapidly spreading wound infection with toxic features should seek medical attention right away.

4. The wound should be dressed on a regular basis, and through dressing should be done daily, and the patient should be on the lookout for any signs of infection, such as erythema, swelling, tenderness, and discharge from the wound.

5. Patients with streptococcal throat infection should stay at home for 24 hours following their last antibiotic dose.

MORTALITY:

Mortality due to necrotizing fasciitis in untreated condition is very high. Mortality rate has changed little since Meleney first recognized that early intervention needed in case of necrotizing fasciitis. Mortality rate ranges from 29% to 76%. There are other comorbid conditions that increases the mortality in case of necrotizing fasciitis they are diabetes mellitus, peripheral vascular disease and poor nutritional status.

The mortality in necrotizing fasciitis is due to sepsis or multiorgan dysfunction. Early cause of death was due to sepsis syndrome and late death were due to multiple organ dysfunction.

7. MATERIALS AND METHODS:

SOURCE OF DATA:

The patients attending the outpatient department and who are admitted in B.L.D.E(DU)'s Shri. B. M. Patil Medical College, Hospital and Research Centre Vijayapura in the Department of Surgery.

METHOD OF COLLECTION OF DATA:

The patients attending outpatient department and who are admittedin the Department of Surgery during in B.L.D.E(DU)'sShri. B. M. Patil Medical College Hospital and Research Centre Vijayapura. Period of study between oct **2020-nov 2022** with a sample size of total of **92 patients**.

Details of cases will be recorded including history, clinical examination, and investigations are done. Following parameters of each patient will be recorded initially at the first consultation post-treatment (after1week,3 weeks, and 6 weeks).

- Patients who were diagnosed clinically with necrotizing fasciitis, affected body region,
- The severity of the disease assessed
- Patients' comorbidities are diagnosed
- Initial blood investigations have done
- Surgical debridement
- Microbiological investigations S.Procalcitonin, S.Ldh, S.Albumin, wound culture and sensitivity were sent on POD3

- Outcomes of patients after treatment

POST- TREATMENT PARAMETERS:

1. The picture of the wound debrided by surgical management

2. Relief of symptoms

3.final outcome of the patient

INCLUSION CRITERIA

All patients with features of necrotizing fasciitis admitted in B.L.D.E(DU)'s Shri. B. M. Patil Medical College Hospital and Research Centre Vijayapura between the age group of 18-70 years

EXCLUSION CRITERI

- Age <18yrs&>70 yrs
- Pregnant women
- Previously treated necrotizing fasciitis
- Prolonged non-healing ulcers
- Diabetic foot ulcers
- Traumatic injuries

SAMPLING:

Sample size

With anticipated Sensitivity and specificity of PCT83.3% and 71.4% (REF) respectively, considering the prevalence of sepsis 25% at precision of 2% and 98% confidence, the required sample size is **57.**

Formula used is—

$$N=\frac{Z^2P(1-p)}{\Delta^2}$$

N will be (a+c) if we use sensitivity as p

N= (a+c)/Prevalence

Statistical Analysis

- The data obtained will be entered in a Microsoft Excel sheet, and statistical analysis will be performed using statistical package for the social sciences (Version 20).
- Results will be presented as Mean (Median) ±SD, counts and percentages and diagrams.

RESULTS

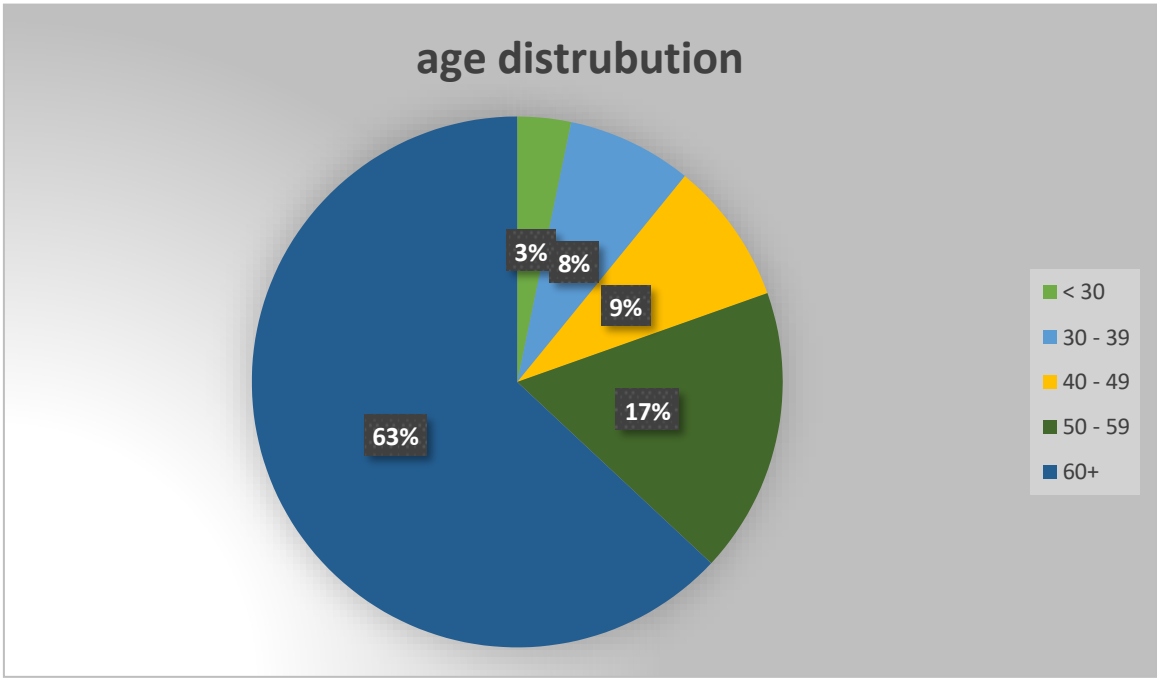
1) MEAN AGE OF THE SUBJECTS

AGE DISTRUBUTION	frequency	PERCENT	VALID PERCENT	CUMULATIVE PERCENT
< 30	3	3.3	3.3	3.3
30 - 39	7	7.6	7.6	10.9
40 - 49	8	8.7	8.7	19.6
50 - 59	16	17.4	17.4	37.0
60+	58	63.0	63.0	100.0
Total	92	100.0	100.0	

N	Mean	Std. Deviation
92	58.21	11.910

TABLE:6

Mean± SD age of subjects was (58.21±11.910).

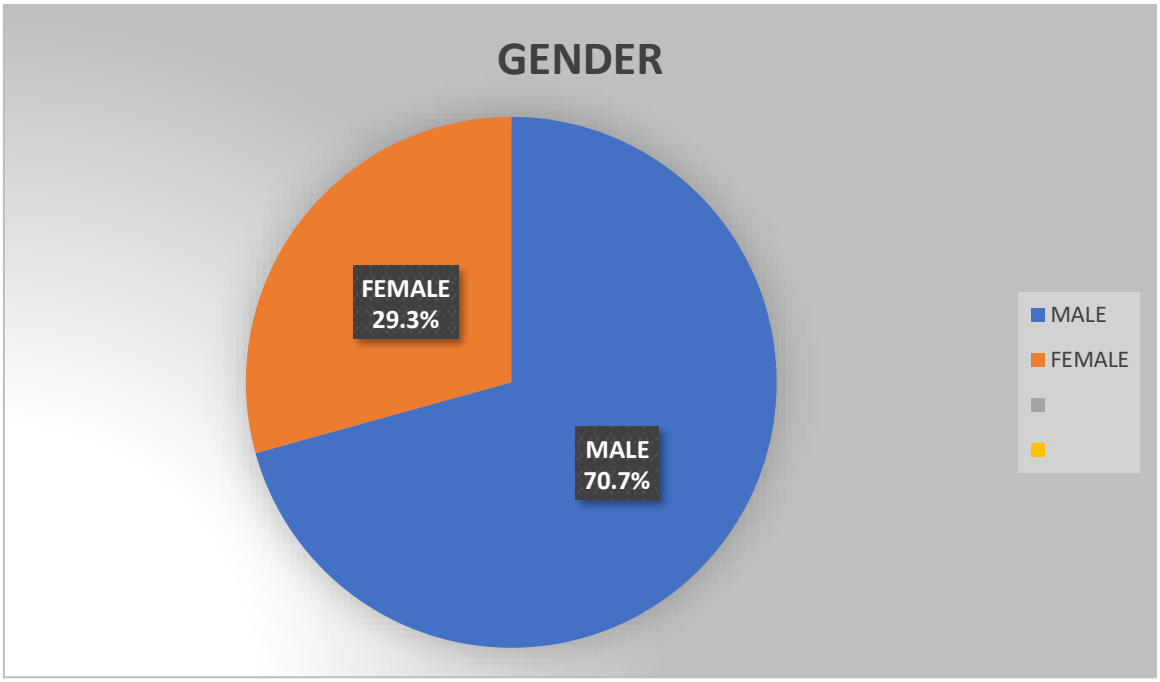


Graph 1: age distribution

2) GENDER WISE DISTRIBUTION OF THE SUBJECTS

GENDER	Frequency (N)	Percent (%)
MALE	65	70.7
FEMALE	27	29.3
TOTAL	92	100.0

TABLE:7



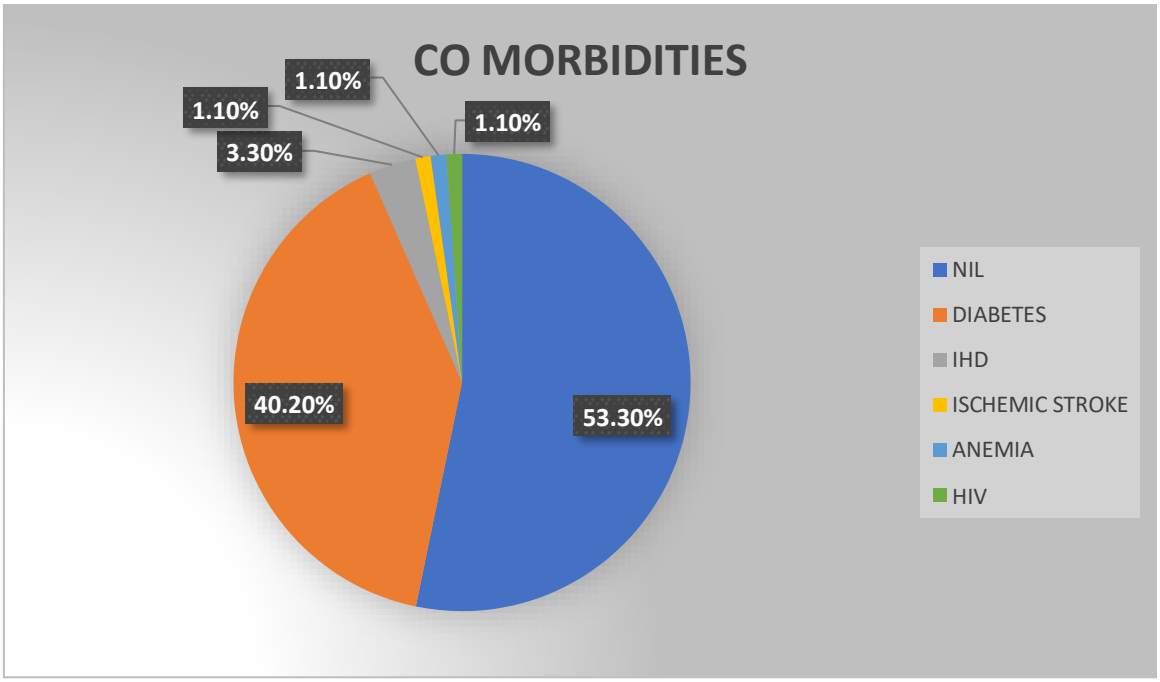
GRAPH:2

Among the total subjects maximum subjects were male 65(70.7%) and females was 27(29.3%).

3) DISTRIBUTION OF COMORBIDITIES AMONG SUBECTS

CO MORBIDITIES	Frequency	Percent
NIL	49	53.3
DIABETES	37	40.2
IHD	3	3.3
ISCHEMIC STROKE	1	1.1
ANEMIA	1	1.1
HIV	1	1.1
Total	92	100.0

TABLE:8



GRAPH 3

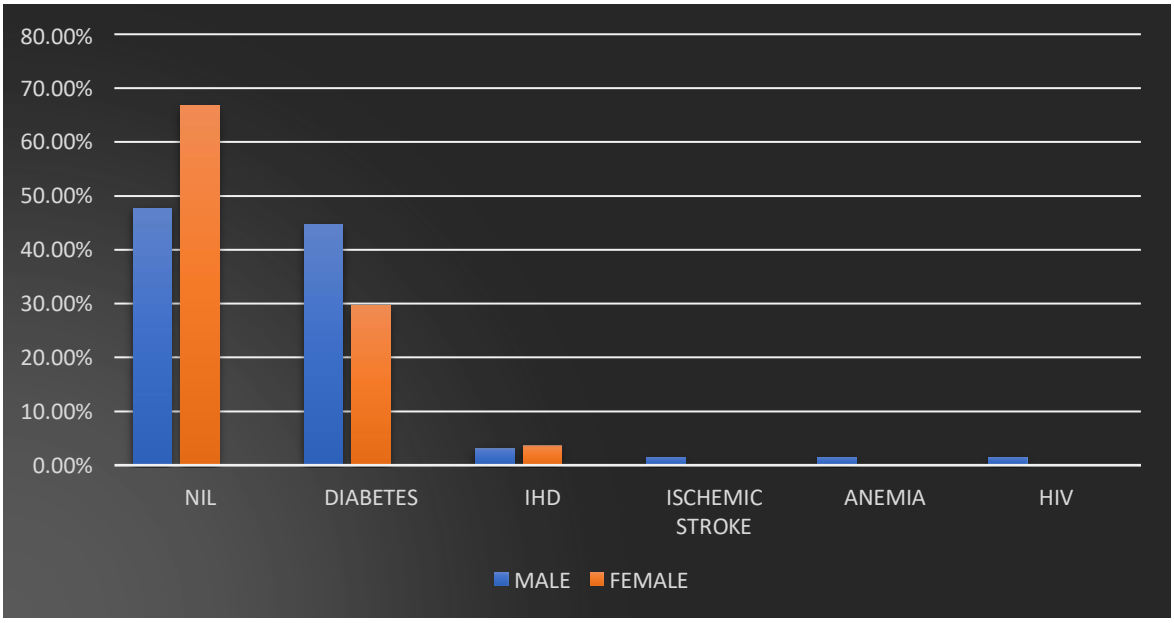
among the total subjects, Comorbidities was nil in 49(53.3%) subjects, diabetes in 37(40.2%) subjects, IHD in 3(3.3%) subjects , ischemic stroke , anaemia and HIV in 1(1.1%), 1(1.1%) and 1(1.1%) subjects

4) GENDER WISE DISTRIBUTION OF COMORBIDITIES AMONG SUBECTS

TABLE:9

CO MORBIDITIES	MALE	FEMALE	TOTAL	CHISQUARE VALUE	P VALUE
NIL	31 47.7%	18 66.7%	49 53.3%	3.624	.605
DIABETES	29 44.6%	8 29.6%	37 40.2%		
IHD	2 3.1%	1 3.7%	3 3.3%		
ISCHEMIC STROKE	1 1.5%	0 0.0%	1 1.1%		
ANEMIA	1 1.5%	0 0.0%	1 1.1%		
HIV	1 1.5%	0 0.0%	1 1.1%		
Total	65 100.0%	27 100.0%	92 100.0%		

Test used- chi square, p>0.05 insignificant



GRAPH:4

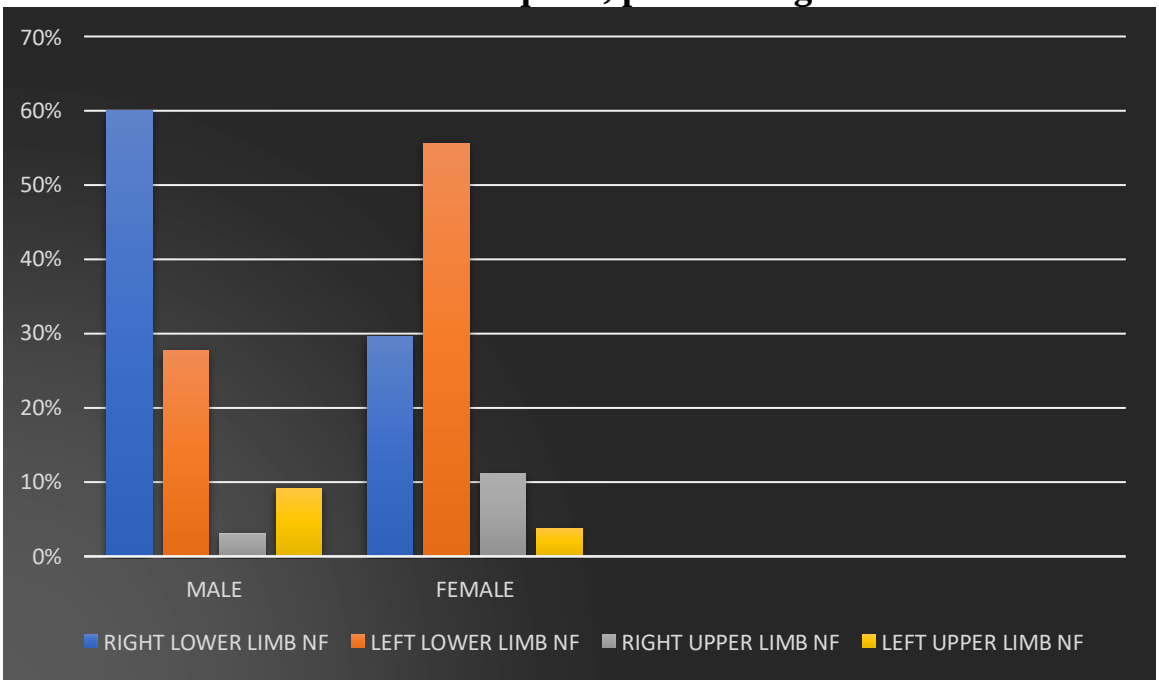
Results were found to be statistically insignificant when comparing gender wise distribution of comorbidities.

5) GENDER WISE DISTRIBUTION OF DIAGNOSIS AMONG SUBJECTS

TABLE:10

GENDER	Right lower limb NF	Left lower limb NF	Right upper limb NF	left upper limb NF	TOTAL	Chi value	P value
MALE	39 60.0%	18 27.7%	2 3.1%	6 9.2%	65 100.0%	10.604	.01*
FEMALE	8 29.6%	15 55.6%	3 11.1%	1 3.7%	27 100.0%		
TOTAL	47 51.1%	33 35.9%	5 5.4%	7 7.6%	92 100.0%		

Test used- chi square, p<0.05 insignificant



GRAPH:5

Among the subjects, 65(100%) were males in which 39(60%), 18(27.7%), 2(3.1%) and 6(9.2%) subjects were diagnosed of right lower limb nf, left lower limb nf, right upper limb nf and left upper limb nf in males. , 27(100%) were females in which 8(29.6%), 15(55.6%), 3(11.1%) and 1(3.7%) subjects were diagnosed of right lower limb nf, left lower limb nf, right upper limb nf and left

upper limb nf in females. Results were found to be statistically significant when comparing diagnosis with gender. It was clear in graph less subjects were diagnosed with right upper limb nf in males and less subjects were diagnosed with left upper limb nf in females.

6) GENDER WISE DISTRIBUTION OF SERUM PROCALCITONIN

TABLE:11

GENDER	Mean	Std. Deviation	Mean diff	P value
MALE	7.818	14.94	-1.784	.74
FEMALE	9.602	25.96		

test used- independent t test, p>0.05 insignificant.

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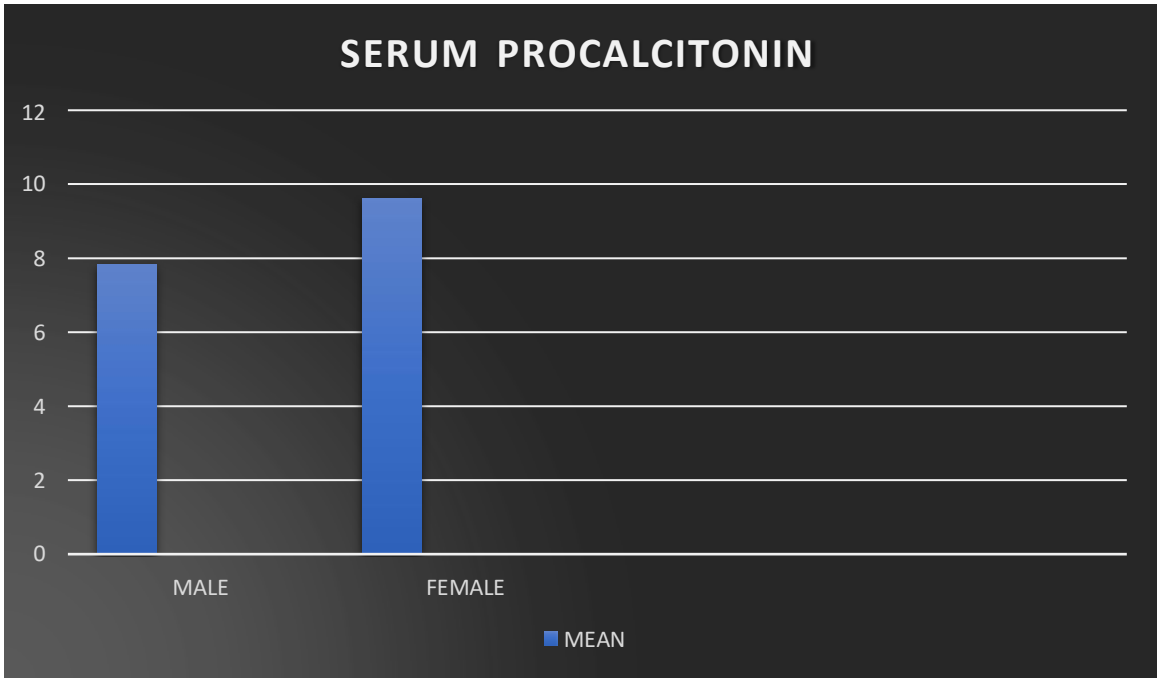


GRAPH:6

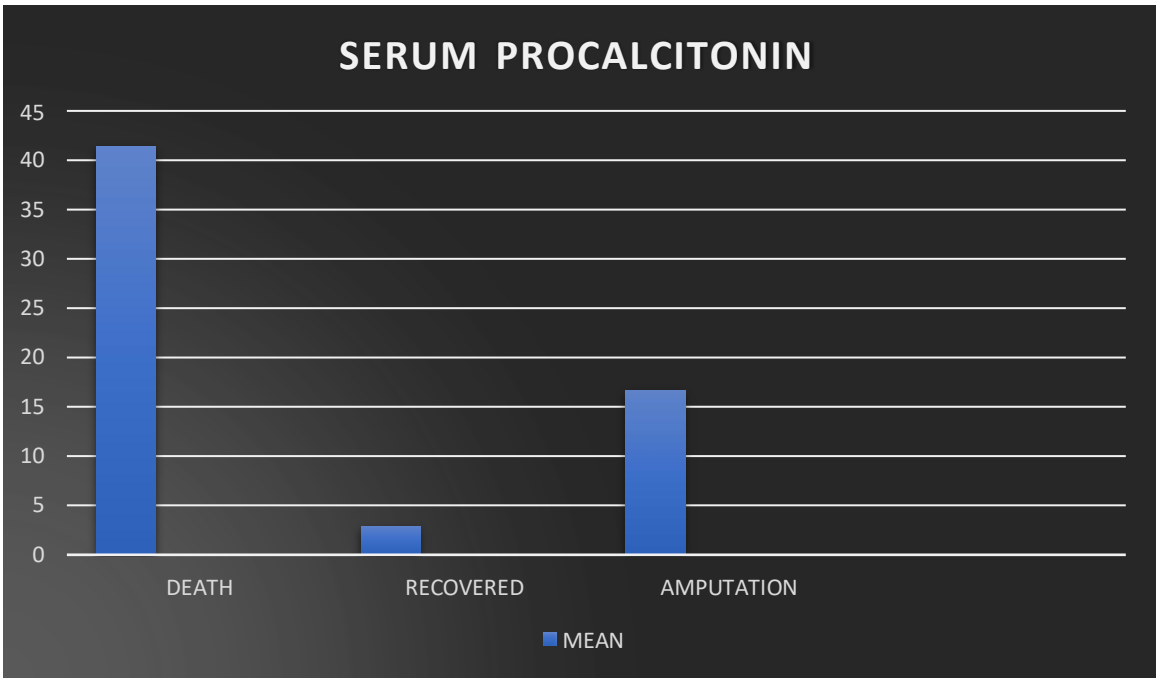
It was clear from graph and table serum procalcitonin was slightly more in female in comparison to male and results were found to be statistically insignificant.

7) MEAN OF SERUM PROCALCITONIN OUTCOME OF PATIENT WITH NECROTIZING FASCIITIS

TABLE:12

OUTCOME	N	MEAN	Std. Deviation	F VALUE	P value
DEATH	11	41.40482	25.527767	38.167	<0.001*
RECOVERED	75	2.82853	11.302481		
AMPUTATION	6	16.64833	15.432197		
Total	92	8.34221	18.716842		

Test used- ANOVA, p<0.05 statistically significant



GRAPH:7

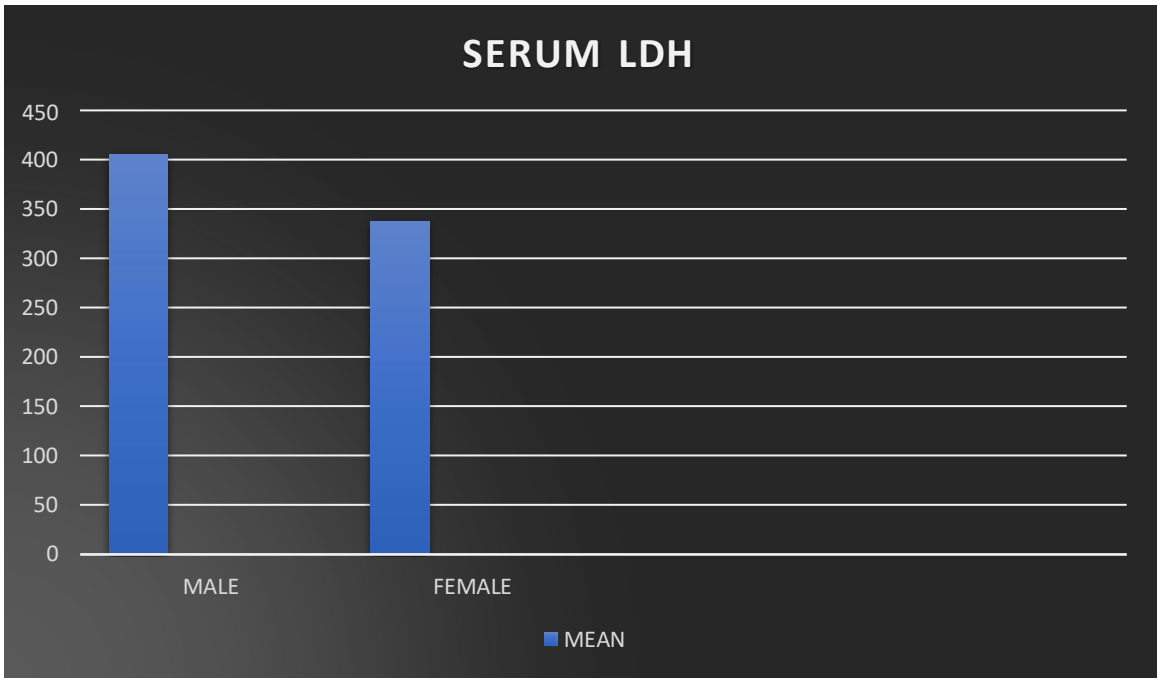
It was clear in table and graph that recovered patient having less serum procalcitonin and death patients having more. And results were found to be highly statistically significant.

8) GENDER WISE DISTRIBUTION OF SERUM LDH

TABLE:13

GENDER	Mean	Std. Deviation	Mean diff	P value
MALE	405.71	265.75	67.893	.18
FEMALE	337.81	200.03		

test used- independent t test, p>0.05 insignificant.



GRAPH:8

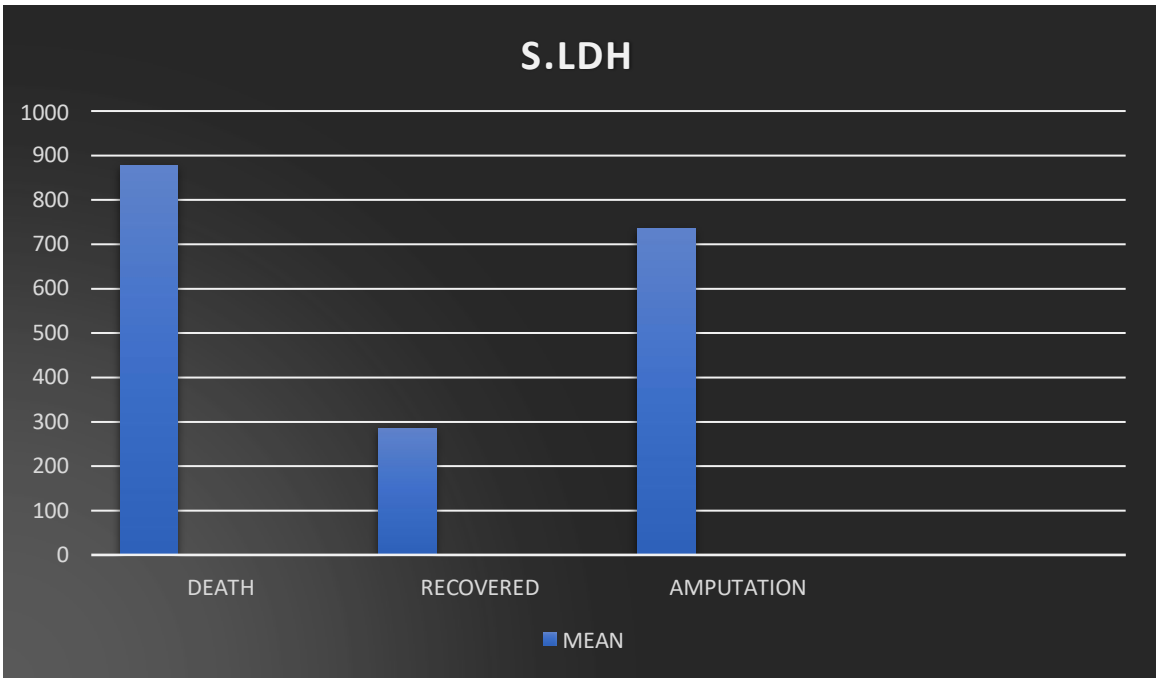
It was clear from graph and table serum LDH was slightly more in male in comparison to Females and results were found to be statistically insignificant.

9) MEAN OF SERUM LDH OUTCOME OF PATIENT WITH NECROTIZING FASCIITIS

TABLE:14

OUTCOME	N	MEAN	Std. Deviation	F VALUE	P value
DEATH	11	878.36	156.981	123.526	<0.001*
RECOVERED	75	285.59	119.391		
AMPUTATION	6	735.17	197.666		
Total	92	385.78	249.195		

Test used- ANOVA, p<0.05 statistically significant



GRAPH:9

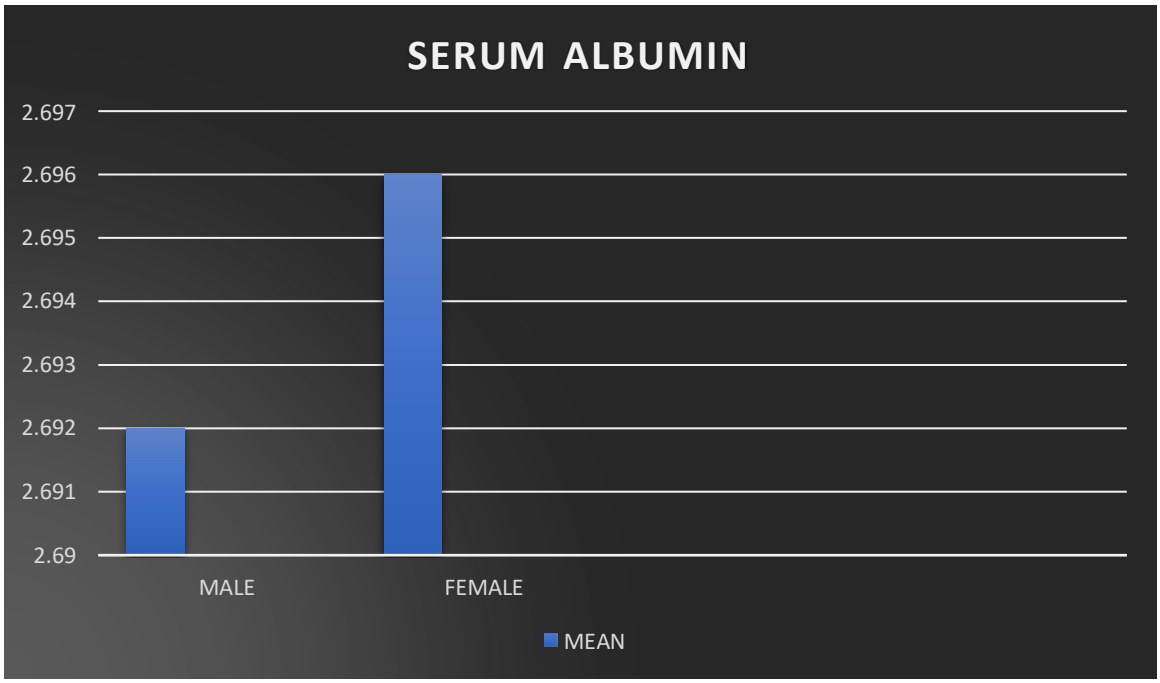
It was clear in table and graph that recovered patient having less serum LDH and death patients having more. And results were found to be highly statistically significant.

10) GENDER WISE DISTRIBUTION OF SERUM ALBUMIN

TABLE:15

GENDER	Mean	Std. Deviation	Mean diff	P value
MALE	2.692	.47	-0.004	.96
FEMALE	2.696	.40		

Test Used- Independent T Test, P>0.05 Insignificant.



GRAPH:10

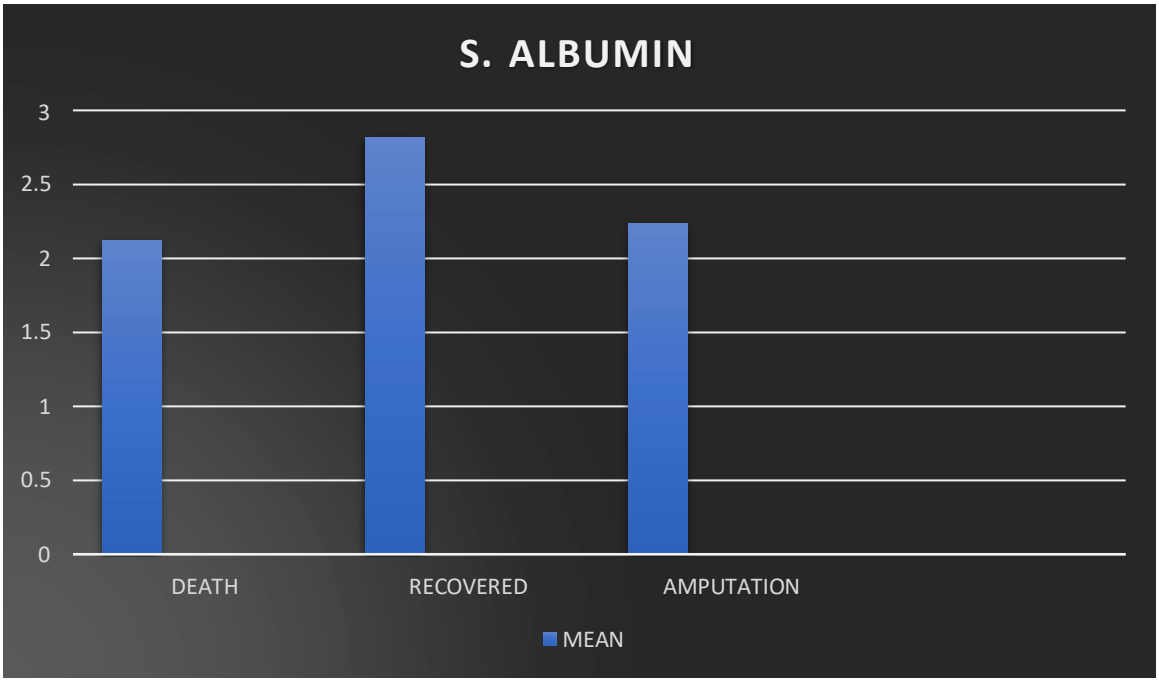
It was clear from graph and table serum albumin was slightly more in female in comparison to male and results were found to be statistically insignificant.

11) MEAN OF SERUM ALBUMIN OUTCOME OF PATIENT WITH NECROTIZING FASCIITIS

TABLE:16

OUTCOME	N	MEAN	Std. Deviation	F VALUE	P value
DEATH	11	2.118	.3816	20.800	<0.001*
RECOVERED	75	2.815	.3812		
AMPUTATION	6	2.233	.3615		
Total	92	2.693	.4554		

Test used- ANOVA, p<0.05 statistically significant



GRAPH:11

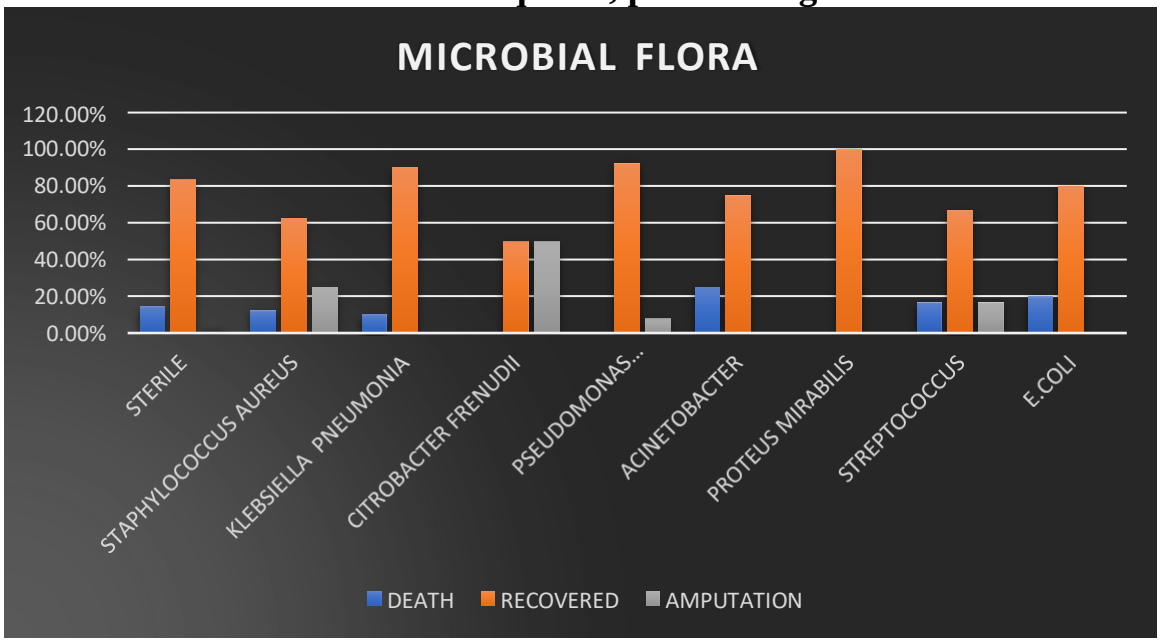
It was clear in table that recovered patient having slightly more serum albumin and death patients having less And results were found to be highly statistically significant.

12) OUTCOME OF MICROBIAL FLORA OF NECROTIZING FASCIITIS PATIENTS

TABLE:17

MICROBIAL FLORA	DEATH	RECOVERED	AMPUTATION	TOTAL	Chi value	pvalue
STERILE	6 14.3%	35 83.3%	1 2.4%	42 100.0%	17.800	.336
STAPHYLOCOCCUS AUREUS	1 12.5%	5 62.5%	2 25.0%	8 100.0%		
KLEBSIELLA PNEUMONIA	1 10.0%	9 90.0%	0 0.0%	10 100.0%		
CITROBACTER FRENUDII	0 0.0%	1 50.0%	1 50.0%	2 100.0%		
PSEUDOMONAS AERUGINOSA	0 0.0%	12 92.3%	1 7.7%	13 100.0%		
ACINETOBACTER	1 25.0%	3 75.0%	0 0.0%	4 100.0%		
PROTEUS MIRABILIS	0 0.0%	2 100.0%	0 0.0%	2 100.0%		
STREPTOCOCCUS	1 16.7%	4 66.7%	1 16.7%	6 100.0%		
E.COLI	1 20.0%	4 80.0%	0 0.0%	5 100.0%		
TOTAL	11 12.0%	75 81.5%	6 6.5%	92 100.0%		

Test used- chisquare , p>0.05 insignificant



GRAPH:12

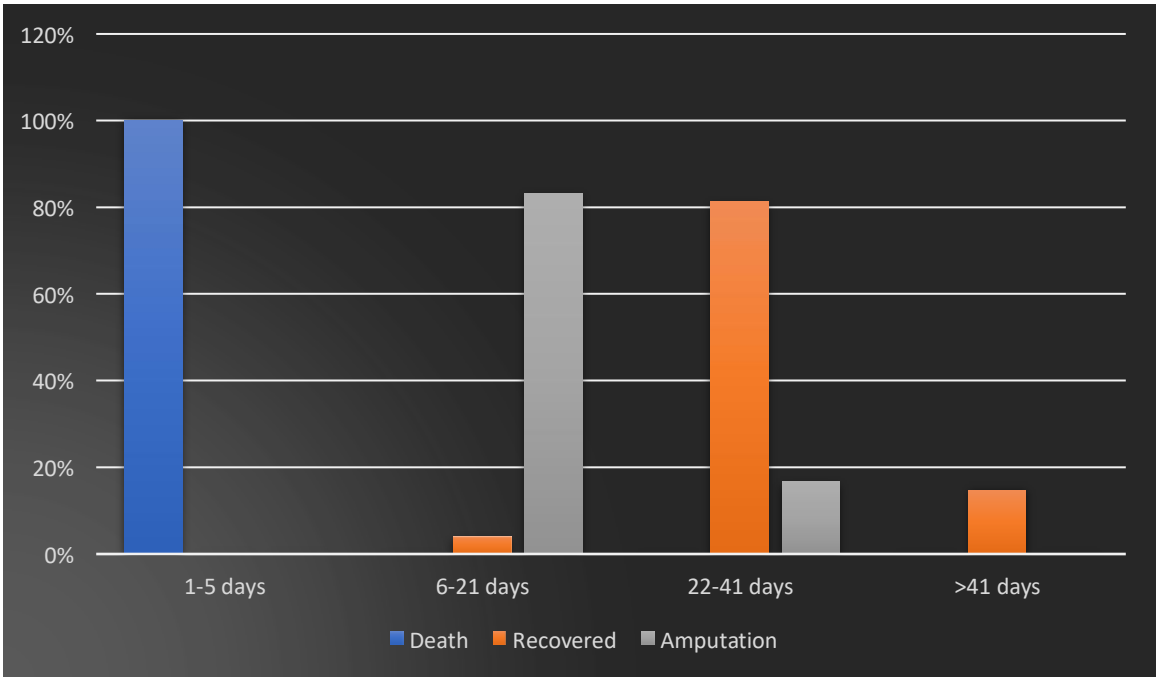
Among the total 92(100%), 42(100%) were sterile in which 6(14.3%) subjects were death, 35(83.3%) subjects were recovered and 1(2.4%) subjects were amputated. 8(100%) were staphylococcus aureus in which 1(12.5%) subjects were death, 5(62.5%) subjects were recovered and 2(25%) subjects were amputated. 10(100%) were klebisella pneumonia in which 1(10%) subjects were death, 9(90%) subjects were recovered and none subjects were amputated. 2(100%) were citrobacter frenudii in which none subjects were death, 1(50%) subjects were recovered and 1(50%) subjects were amputated. 13(100%) were pseudomonas aeruginosa in which none subjects were death, 12(92.3%) subjects were recovered and 1(7.7%) subjects were amputated. 4(100%) were acinetobacter in which 1(25%) subjects were death, 3(75%) subjects were recovered and none subjects were amputated. 2(100%) were proteusmirabalis in which none subjects were death, 2(100%) subjects were recovered and none subjects were amputated. 6(100%) were streptococcus in which 1(16.7%) subjects were death, 4(66.4%) subjects were recovered and 1(16.7%) subjects were amputated. 5(100%) were E.coli in which 1(20%) subjects were death, 4(80%) subjects were recovered and none subjects were amputated. Results were found to be statistically insignificant when comparing microbial flora with outcome.

13) COMPARISON OF HOSPITAL STAY WITH OUTCOME OF NECROTIZING FASCIITIS PATIENTS

TABLE:18

Outcome	HOSPITAL STAY				Total	Chi value	pvalue
	1-5 days	6-21 days	22-41 days	>41 days			
Death	11 100.0%	0 0.0%	0 0.0%	0 0.0%	11 100.0%	136.657	<0.001**
Recovered	0 0.0%	3 4.0%	61 81.3%	11 14.7%	75 100.0%		
Amputation	0 0.0%	5 83.3%	1 16.7%	0 0.0%	6 100.0%		
Total	11 12.0%	8 8.7%	62 67.4%	11 12.0%	92 100.0%		

Test used- chi square, p<0.05 statistically significant.



GRAPH:13

Among the subjects , death of 11(100%) subjects occurred who stay hospital only 1-5 days, 3(4%) , 61(81.3%) and 11(14.7%) subjects recovered who stay in hospital around 6-21 days, 22-41 days and >41 days. 5(83.3%) and 1(16.7%) subjects were having amputation who stay in hospital around 6-21 days and 22 41 days. Results were found to be statistically significant when comparing hospital stay.

DISCUSSION:

This is a cross sectional study done at B.L.D.E(DU) 's Shri. B. M. Patil Medical College, Hospital and Research Centre Vijayapura in the Department of Surgery. Duration of the study was between Nov 2020–June 2022 with a sample size of a total of 92 patients.

In a study done by jinn-ming wang et al[56],concluded that the disease is male predominance with a male (73.6%) and females(26.4%) which is similar to our study showing males (n=65), 70.7% were more commonly affected by Necrotising Fasciitis. Females constituted (n=27), 29.3% of the study population.

Study	Results
Jinn-Ming Wang et al	Males (73.6%) female (26.4%)
Our study	Males 70.7% Females 29.3%

The peak incidence of NF was observed in patients aged between 51-60 years, which accounted for 24% of the study population. A study done by haluk vayvada et al[58] the mean age group effected was reported to be 55.9 yrs which is imilar to our study where the mean age reported was 58.21.

Study	Results
Haluk Vayvada et al	Mean age was 55.9 years
Our study	Mean age was58.21 years.

When Comorbidities (table 3, fig 2) were compared it was nil in 49(53.3%) subjects, diabetes in 37(40.2%) subjects, IHD in 3(3.3%) subjects, ischemic stroke, anaemia and HIV in 1(1.1%), 1(1.1%) and 1(1.1%) subjects. And on comparing gender wise distribution of comorbidities, it was insignificant.

When serum prolactin distribution gender wise done serum procalcitonin was slightly more in female in comparison to male and results were found to be statistically insignificant. The mean of serum procalcitonin outcome of patient with necrotizing fasciitis shows patient having less serum procalcitonin and death patients having more. And results were found to be highly statistically significant.

Recent reports documented that different pathogens could induce different levels of PCT. Many studies reported that serum-PCT levels tend to be higher in gram negative than gram-positive bacteraemia regardless of the presence of

shock. Especially, Staphylococcus aureus, Streptococcus pyogenes, S. agalactiae, Escherichia coli and Klebsiella pneumoniae could induce high levels of PCT.

Previous studies also demonstrated that many cases of cellulitis were possibly not due to infection, and that cellulitis-induced inflammation is likely due to the effects of bacterial toxins or other factors that diffuse into affected tissue via lymphatics or interstitial fluid, and that bacterial burden at the affected site is less influential While cellulitis is a focal infection confined in the skin, NF is a systemic inflammatory infectious disease. While the positive blood culture rate was previously reported to be 4% in cellulitis cases, 22% and 45% of cellulitis and NF patients respectively had a positive blood culture in our study. This means most NF patients could be in septic condition, even though more than half of their blood culture were negative.

Procalcitonin was found to be linked with sepsis and has been part of research since the last three decades. Patients with procalcitonin concentration of <0.5 ng/mL are unlikely to have sepsis. However, this concentration does not exclude infection, because localized infections without systemic signs are still possible.

Assicot et al.[9] showed that high procalcitonin concentrations were related to acute septic episodes in children, but the reference range used was different. They demonstrated that a range of 0.1–120 ng/mL was closely related to infectious complications and acute septic episodes. High serum procalcitonin

(range6–53 ng/mL) at diagnosis was reported in 24% of patients with severe bacterial infections. Park et al. [10] also demonstrated increased severity of infection with high procalcitonin concentrations. Delevaux et al. [11] showed a value of procalcitonin >0.5 ng/mL is a marker of bacterial infection with sensitivity 65%; specificity 96%; positive predictive value 89%; and a negative predictive value 84%. No false positive results were reported for procalcitonin concentrations >1.2 ng/mL.

Study	**Results**
Assicot et al	19 patients s.pct(6-53) Patients were in severe sepsis and death 11 patients s.pct(0.5-1.5) Patients recoverd
Our study	11 patients s.pct >12the out-come was death 6 patients with serum pct 5-12 has undergone amputation <5 all patients has recovered

The gender wise distribution of serum LDH, shows serum LDH was slightly more in male in comparison to Females and results were found to be statistically insignificant. When mean of serum LDH outcome of patient with necrotizing fasciitis shows recovered patient having less serum LDH and death patients having more. And results were found to be highly statistically significant.

As an enzyme is expressed in several tissues, the LDH may catalyse the conversion of pyruvate to lactate, which is the final step of aerobic glycolysis. Serum LDH was reported as a predictive marker in many conditions and diseases such as sepsis, infection, acute myocardial infarction, cirrhosis, and malignancies. Serum LDH was also observed to associate with mortality in patients with metabolic syndrome. A study done by Lu J et al [12] found that serum LDH was associated with mortality in patients with sepsis and they found that the positive correlations of LDH and proinflammatory mediators as well as lactate revealed that the glucose metabolic reprogramming of immune cells contributed to the release of proinflammatory mediators and accumulation of lactate. The study also found that the elevated levels of serum LDH are correlated with higher mortality. [12]

Study	Result
Jhu lu et al	Surviours group group ldh value 200-350 lu/l in 131 patients Non surviours group >450 iu/l in 62 patients
Our study	250-450 all of them recovered 450-700 ampuated >700 death

When gender wise distribution of serum albumin was done it was found that serum albumin was slightly more in female in comparison to male and results were found to be statistically insignificant. Inflammation reduces levels of some proteins such as albumin, which are called negative acute phase proteins (because their levels decrease with the inflammatory process). Albumin values tend to fall in the presence of an active-phase reaction such as sepsis and trauma, with a mean decrease ranging from 10-15 g / L in the first week. There are several causes for the occurrence of hypoalbuminemia in septic patients, namely, decreased albumin synthesis in the liver, reduced intake of amino acids, increased fluid transfer to the interstitial (plasma leakage), and increased tissue catabolism The peak of the decrease in albumin levels occurs at 2-4 days post-inflammation and will decrease along with the resolution of the inflammatory

process on days 4 to 7. So, it is ideal to look at acute phase protein levels as a diagnostic tool for the sepsis process. [13] In a previous study by Mei Yin et al [14]. in 2016, 116 patients were included in the study, the overall 28-day mortality was 26.7%. Compared with the survivor group, non-survivor patients had lower serum albumin values. The ROC curve data showed that albumin level was a strong predictor of 28-day. mortality, with the optimal cut-off value being 2.92 g / dl. Through multivariate regression analysis, low serum albumin levels (<2.92 g / dl) were identified as an independent risk factor for mortality. Patients with lower serum albumin had a lower 28-day survival rate than patients with serum albumin > 2.92 g / dl.9 Another study found albumin levels <2.6g / dl were associated with the 30-day mortality of septic patients. [15]

Study	Results
Mei Yin et al	26.4% mortality in patients with albumin <2.9
Our study	Recovered patients having s.albumin>2.9 Amputated & Death patients has s.albumin <2.9

In this study extremities were more frequently affected sites, which was around 85%, of which lower limb happened to be the most common site which was involved in 83% of the patients. Increased frequency of lower limb infection corresponds to the fact that most of the patients were diabetics who were predisposed to lower limb infections. High blood sugar levels and low oxygen tension favours bacterial growth [16].

Hence the comorbidities present in the study population was analysed, it was found that diabetes in 37(40.2%) subjects, IHD in 3(3.3%) subjects , ischemic stroke , anaemia and HIV in 1(1.1%), 1(1.1%) and 1(1.1%) subjects, and patients without any comorbidities in 49(53.3%) subjects, And on comparing gender wise distribution of Comorbidities it was insignificant .In the present study when the site was compared it was found that, Among the subjects , 62(100%) were males in which 39(60%), 18(27.7%), 2(3.1%)and 6(9.2%) subjects were diagnosed of right lower limb nf, left lower limb NF, right upper limb NF and left upper limb NF in males. , 27(100%) were females in which 8(29.6%), 15(55.6%), 3(11.1%) and 1(3.7%) subjects were diagnosed of right lower limb NF, left lower limb , right upper limb and left upper limb in females. Results were found to be statistically significant when comparing diagnosis with gender. It was clear in graph less subjects were diagnosed with right upper limb in males and less subjects were diagnosed with left upper limb in females. This is in accordance with the previous studies.

A study done by Sigh G et al, [16] showed that most common sites were lower extremities. Very rarely it affects the different regions of the body.

Study	Results
Sigh et al	70.8% patients lower extremities were involved
Our study	83% patients effected region was lower extremities

When analysis was done on microbial flora, 8(100%) were staphylococcus aureus in which 1(12.5%) subjects were death, 5(62.5%) subjects were recovered and 2(25%) subjects were amputated. 10(100%) were klebsiella pneumonia in which 1(10%) subjects were death, 9(90%) subjects were recovered and none subjects were amputated. 2(100%) were citrobacter frenudii in which none subjects were death, 1(50%) subjects were recovered and 1(50%) subjects were amputated. 13(100%) were pseudomonas aeruginosa in which none subjects were death, 12(92.3%) subjects were recovered and 1(7.7%) subjects were amputated. 4(100%) were acinetobacter in which 1(25%) subjects were death, 3(75%) subjects were recovered and none subjects were amputated. 2(100%) were proteus mirabalis in which none subjects were death, 2(100%) subjects were recovered and none subjects were amputated. 6(100%) were

streptococcus in which 1(16.7%) subjects were death, 4(66.4%) subjects were recovered and 1(16.7%) subjects were amputated. 5(100%) were E.coli in which 1(20%) subjects were death, 4(80%) subjects were recovered and none subjects were amputated. Results were found to be statistically insignificant when comparing microbial flora with outcome.

When hospital stay was compared the results were significant Among the subjects , death of 11(100%) subjects occurred who stay hospital only 1-5 days, 3(4%) , 61(81.3%) and 11(14.7%) subjects recovered who stay in hospital around 6-21 days, 22-41 days >;41 days. 5(83.3%) and 1(16.7%) subjects were having amputation who stay in hospital around 6-21 days and 22-41 days. Results were found to be statistically significant when comparing hospital stay without come.

Study	Results
Madhumitha et al	33.8+/- 8 days
Our study	34+/- 7 days

Some of the studies had reported significant rise in the incidence of monomicrobial infections. [17] Ming- Jong Bair et al in a study had described that two third of infections were of monomicrobial aetiology. 18Yaug-Meng Liu et al 19 has also showed 67.8% of monomicrobial agents as primary cause of

Necrotising Fasciitis. D. Yadhav et al [20] had retrospectively studied 45 patients with necrotising fasciitis documented to be of monomicrobial aetiology.

Yao-Hung Tsai et al [21] in a retrospective study had reported higher incidence (70.6%) of monomicrobial infection. The documentation of higher number of monomicrobial aetiological agent in this study is comparable with the other Asian studies. Yuang-Meng Liu et al [19] in their study has depicted that Enterobactriaceae were the frequent pathogens, with K. pneumoniae being the most common organism isolated. Though type I polymicrobial necrotising fasciitis has been the cause of 80% of cases as shown by several of the studies, there has been a substantial increase in incidence of monomicrobial necrotising fasciitis evident from recent studies. [22] Klebsiella pneumonia, E.coli, Vibrio vulnificus, Aeromonas hydrophila were reported to be the most common isolates in Asia. Fazal et al [23] in their case series had reported 50.3% of Klebsiella spp infections. Mixed aerobic and anaerobic infection constituted about 50% of the polymicrobial infections. [24] Mathew et al in their study had isolated 11.1% of mixed aerobic and anaerobic bacteria. Kreig et al [26] retrospectively analysed patients with necrotising fasciitis between the year 1996 and 2005 and had reported that the cultures of 30.8% of the patients with type I polymicrobial infection also had anaerobes as synergistic pathogens.

Anerobic infections in the present study had been documented in clinical infections. The virulence factors of these anaerobes had been documented in

clinical infections. Several hypothesis had been proposed to substantiate such microbial synergy. 27

The synergy of bacteria may be explained by the following mechanisms;

(a)Due to mutual protection from phagocytosis and intracellular killing,

(b) Production of essential growth factors,

(c) Reduction of oxidation-reduction potential in host tissues, 27-29

Type II diabetes was found to be the most frequent co-morbid condition associated with necrotising fasciitis accounting for 40.2% of the study population. Patients with hypertension constituted to 3.3%. 1% had ischemic stroke, 1% had anemia and 1% had HIV infection affected in the present study.

Out of the total 92 patients, most of the patients had trauma as the main predisposing factor for NF and 10% had hypertension alone as co-morbidity. Several of the studies had analysed that Type II DM as the most common comorbid condition 30. Madhumita et al 31 in a prospective study had reported Type II diabetes as the commonest co-morbidity. Yeung et al in their retrospective study had documented Type II DM as the frequent Comorbidity.

The above quoted studies had documented results that are comparable to this study. Type II DM has been documented as co-morbidity in 59%, (n=59%) of study population. P- Value calculated using one sample Z test was 0.0001, hence the association of type II DM and NF is statistically significant. 31

STUDY	RESULTS
Madhumita et al	T2DM was comorbiditiy in 40%
Yeung et al	T2DM was comorbidity in 64.7%
Our study	T2DM was comorbidity in 59%

Trauma had been documented as a predisposing factor in 36.25% of the patients by Mathew et al. 25 Nissar shaikh in his retrospective study had documented trauma as a predisposing Condition in 10% of the patients. 4% of patients had trauma as predisposing factor in this study. 32

Several of the patients serially underwent two to three debridement during their hospital stay. Duration of hospitalization of patients happened to be around thirty to forty-five days in average. Out of the five patients four were diabetics and one other patient was a non- diabetic. Other patients improved during the course of their hospital stay.

All the patients received intravenous fluids and broad-spectrum intravenous antibiotics. The antibiotics administered, included Piperacillin- Tazobactam, Metronidazole, Imipenem. Clindamycin, Imipenem and combination of Penicillin and β-lactamase inhibitor target against anaerobic organisms. Imipenem, Piperacillin- Tazobactam combination also provides coverage for Enterobacteriaceae family members, and Staphylococcus aureus. 33-38

Conclusion:

Necrotizing fasciitis is a lethal soft-tissue infection mostly affecting males in middle-age group. Major predisposing factors include poor personal hygiene, age more than 50 years, and diabetes mellitus. Lower extremity is the most common site affected. Most infections are polymicrobial, including gram positive and gram-negative organisms. Staph aureus, streptococcus, e, coli, being the most common bacteria isolated. Procalcitonin is the major diagnostic factor. The present study proved that the procalcitonin helps to predict the severity and the prognosis of the infection. LDH is a proinflammatory marker which helps to access the severity of the infection. Serum albumin values of the patients always changes during the mortality and the initial stage of the infection. The values of serum albumin lower as infection increases. Sepsis and the septic shock is the major cause of death. Amputation is the replace mental therapy. Early and aggressive debridement's, often at repeated sittings, are the mainstay in the treatment of necrotizing fasciitis, supplemented by adequate antibiotics and supportive measures are important in the treatment of the necrotising fasciitis. Thus to conclude S.PCT, S.LDH, S.Albumin are the important diagnostic markers for diagnosing the severity and prognosis of the patient with necrotizing fasciitis.

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ANNEXURES

SAMPLE INFORMED CONSENT FORM:

TITLE OF THE PROJECT : **A STUDY OF CLINICAL PRESENTATIONS, BIO-CHEMICAL MARKERS AND MICROBIAL FLORA IN OUTCOME OF NECROTIZING FASCIITIS**

PG GUIDE : **DR. ARAVIND V PATIL**

M.S. (GENERAL SURGERY)

PROFESSOR OF SURGERY

DEPARTMENT OF SURGERY

PRINCIPAL INVESTIGATOR : **DR.M. JAGADISH CHAITANYA**

PURPOSE OF RESEARCH:

I have been informed that the purpose of the study is too early diagnosis of necrotizing fasciitis and outcome after the treatment

PROCEDURE:

I am aware that in addition to routine care received I will be asked a series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or my treatment.

BENEFITS:

I understand that my participation in the study will help in prompt diagnosis and to predict the morbidity and mortality of the patients with necrotizing fasciitis.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to confidentiality. Information on sensitive personal nature will not be part of the medical record but will be stored in the investigations research file.

If the data are used for publication in the medical literature or teaching purposes, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study to **Dr.M.**

Jagadish Chaitanyain the Department of General Surgery who will be available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that **Dr. M. Jagadish Chaitanya** may terminate my participation in the study after he has explained the reasons for doing so

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study if such injury were reported promptly, the appropriate treatment would be available to me. But, no further compensation would be provided by the hospital. I understand that my agreement to participate in this study and not waiving any of my legal rights.

I have explained to _____ the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr. M. Jagadish Chaitanya Date

(Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr**.** M. Jagadish Chaitanya explained to me the purpose of the research, the study procedure, that I will undergo, and the possible discomforts as well as benefits that I may experience in my language. I have been explained all the above in detail in my language and I understand the same. Therefore I agree to give consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to signature) Date

APPENDIX – IX

PROFORMA FOR CASE TAKING

SL NO

Name

AGE OP NO /IP NO

Sex UNIT

Religion DOC/DOA

Occupation DOD

Address:

Mobile No:

Associated Co-morbidities (if any):

HISTORY OF PRESENT ILLNESS:

PERSONAL HISTORY:

GENERAL PHYSICAL EXAMINATION:

Built: Well/Moderate/Poor

Nourishment: Well/Moderate/Poor

Temperature: Pulse: SPO2:

B.P: Respiratory Rate:

LOCAL EXAMINATION:

SYSTEMIC EXAMINATION:

Per Abdomen

Respiratory System

Cardio Vascular System

Central Nervous System

LABORATORY TESTS

Haemoglobin% :

Total Count :

Platelets :

Differential Count

Neutrophil :

Lymphocytes :

Eosinophils :

Basophils :

Monocytes :

Blood Urea :

Serum Creatinine :

Serum LDH :

Serum procalcitonin :

SERUM ALBUMIN :

Culture and sensitivity :

OTHERS:

DIAGNOSIS:

Follow up:

1week:

3weeks:

6 weeks:

ETHICAL CLEARANCE CERTIFICATE:

B.L.D.E. (DEEMED TO BE UNIVERSITY) IEC/NO-09/2021 Date-22/01/2021

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated: 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A study of clinical presentations, biochemical markers microbial flora and outcome in necrotizing fasciitis

Name of PG student: Dr M Jagadish Chaitanya, Department of Surgery

Name of Guide/Co-investigator: Dr A.V.Patil, Professor
Department of Surgery

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

PLAGIARISM CERTIFICATE

Document Information

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SA	**Necrotizing fascitis - full thesis.docx** Document Necrotizing fascitis - full thesis.docx (D123687801)	1
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SA	**Dr_Balamurugan Thesis_1_12_22.docx** Document Dr_Balamurugan Thesis_1_12_22.docx (D152053316)	1

MASTER CHART:

	A	B	C	D	E	F	G	H	I	J
1	AGE	SEX	COMORBIDTIES	DIAGNOSIS	S.PROCALCITONIN	S.LDH	S.ALBUMIN	CULTURE AND SENSITIVITY	OUTCOME	HOPITAL STAY
2	60	M	DIABETES	RIGHT LOWERLIMB NF	48.92	682	2.5	STERILE	DEATH	4 DAYS
3	65	M	NIL	RIGHT LOWERLIMB NF	0.263	238	2.6	STERILE	RECOVERED	30 DAYS
4	55	F	NIL	LEFT LOWERLIMB NF	8.06	495	2.5	STAPHYLOCOCUS AUREUS	AMPUTATION	20 DAYS
5	59	F	DIABETES	RIGHT UPPERLIMB NF	2.321	242	2.1	STERILE	RECOVERED	40 DAYS
6	35	M	NIL	RIGHT LOWERLIMB NF	0.169	267	1.8	KLEBSIELLA PNEUMONIA	RECOVERED	25 DAYS
7	62	M	NIL	RIGHT LOWERLIMB NF	1.321	113	1.9	STERILE	RECOVERED	32 DAYS
8	54	M	HIV	RIGHT LOWERLIMB NF	1.029	382	2	STERILE	RECOVERED	28 DAYS
9	65	F	NIL	LEFT LOWERLIMB NF	1.231	148	2.8	CITROBACTER FRENUDII	RECOVERED	34 DAYS
10	48	M	NIL	RIGHT LOWERLIMB NF	1.328	246	2.4	STERILE	RECOVERED	21 DAYS
11	49	F	IHD	LEFT LOWERLIMB NF	98.82	546	2.1	STERILE	RECOVERED	>42 DAYS
12	60	M	DIABETES	LEFT LOWERLIMB NF	2.361	963	2.4	PSEUDOMONAS AERUGINOSA	RECOVERED	38 DAYS
13	45	M	ANEMIA	RIGHT LOWERLIMB NF	1.321	421	2.8	STERILE	RECOVERED	28 DAYS
14	68	M	IHD	RIGHT LOWERLIMB NF	32.08	514	1.9	ACINETOBACTER	DEATH	5 DAYS
15	62	M	NIL	LEFT LOWERLIMB NF	1.341	436	2.4	STERILE	RECOVERED	31 DAYS
16	65	F	NIL	RIGHT LOWERLIMB NF	0.688	256	2.8	PROTEUS MIRABILIS	RECOVERED	26 DAYS
17	70	F	NIL	RIGHT UPPERLIMB NF	15.92	795	2	STREPTOCOCUS	DEATH	5 DAYS
18	60	F	DIABETES	LEFT LOWERLIMB NF	0.282	245	2.9	STERILE	RECOVERED	21 DAYS
19	60	M	NIL	RIGHT LOWERLIMB NF	1.213	367	2.8	PSEUDOMONAS AERUGINOSA	RECOVERED	36 DAYS
20	58	M	NIL	LEFT LOWERLIMB NF	0.623	234	3.2	ACINETOBACTER	RECOVERED	24 DAYS
21	60	M	DIABETES	LEFT LOWERLIMB NF	8.925	567	2.2	STERILE	AMPUTATION	22 DAYS
22	55	M	NIL	RIGHT LOWERLIMB NF	0.234	235	3.1	STAPHYLOCOCUS AUREUS	RECOVERED	28 DAYS
23	64	M	NIL	LEFT LOWERLIMB NF	1.292	434	2.8	PSEUDOMONAS AERUGINOSA	RECOVERED	30 DAYS
24	65	M	DIABETES	LEFT LOWERLIMB NF	0.836	287	3	KLEBSIELLA PNEUMONIA	RECOVERED	29 DAYS
25	58	M	NIL	RIGHT LOWERLIMB NF	2.345	303	2.9	STERILE	RECOVERED	34 DAYS
26	65	M	DIABETES	LEFT LOWERLIMB NF	0.839	187	3.2	STERILE	RECOVERED	26 DAYS
27	70	M	DIABETES	RIGHT LOWERLIMB NF	28.04	894	2	STERILE	DEATH	4 DAYS
28	65	M	NIL	RIGHT LOWERLIMB NF	1.238	237	3.1	STAPHYLOCOCUS AUREUS	RECOVERED	31 DAYS
29	55	F	NIL	LEFT LOWERLIMB NF	0.187	264	2.9	STERILE	RECOVERED	24 DAYS
30	52	F	NIL	RIGHT LOWERLIMB NF	1.902	289	2.8	STERILE	RECOVERED	36 DAYS
31	48	M	DIABETES	LEFT LOWERLIMB NF	2.345	307	3	STERILE	RECOVERED	40 DAYS
32	65	M	DIABETES	RIGHT LOWERLIMB NF	0.573	204	3.1	STERILE	RECOVERED	24 DAYS
33	65	M	ISCHEMIC STROKE	LEFT LOWERLIMB NF	12.245	984	2.1	STAPHYLOCOCUS AUREUS	AMPUTATION	21 DAYS
34	29	M	NIL	RIGHT LOWERLIMB NF	3.568	349	3.6	PSEUDOMONAS AERUGINOSA	RECOVERED	>42 DAYS
35	31	M	NIL	RIGHT LOWERLIMB NF	2.978	271	3.4	STERILE	RECOVERED	40 DAYS
36	70	F	DIABETES	RIGHT LOWERLIMB NF	4.786	279	2.6	KLEBSIELLA PNEUMONIA	RECOVERED	>42 DAYS
37	60	F	NIL	LEFT LOWERLIMB NF	98.82	945	1.9	E.COLI	DEATH	4 DAYS
38	45	M	NIL	LEFT LOWERLIMB NF	3.981	207	2.9	KLEBSIELLA PNEUMONIA	RECOVERED	>42 DAYS
39	56	F	NIL	RIGHT LOWERLIMB NF	0.147	349	2.8	STERILE	RECOVERED	29 DAYS
40	52	M	DIABETES	RIGHT LOWERLIMB NF	5.367	492	2.2	PSEUDOMONAS AERUGINOSA	RECOVERED	>42 DAYS
41	57	F	NIL	LEFT LOWERLIMB NF	0.187	240	2.8	E.COLI	RECOVERED	28 DAYS
42	65	M	DIABETES	RIGHT LOWERLIMB NF	2.156	168	2.9	STERILE	RECOVERED	42 DAYS
43	50	M	DIABETES	RIGHT LOWERLIMB NF	47.946	948	2	STREPTOCOCUS	DEATH	4 DAYS
44	70	M	DIABETES	RIGHT LOWERLIMB NF	38.935	995	1.8	STERILE	DEATH	4 DAYS
45	60	M	IHD	LEFT UPPER LIMB NF	32.378	890	2.2	STERILE	DEATH	4 DAYS
46	42	M	NIL	RIGHT UPPERLIMB NF	78.932	1026	3.1	STAPHYLOCOCUS AUREUS	DEATH	4 DAYS
47	45	F	NIL	LEFT LOWERLIMB NF	0.167	218	2.9	KLEBSIELLA PNEUMONIA	RECOVERED	24 DAYS
48	60	F	NIL	LEFT UPPER LIMB NF	0.134	214	2.8	KLEBSIELLA PNEUMONIA	RECOVERED	24 DAYS
49	70	M	DIABETES	RIGHT LOWERLIMB NF	12.458	689	2.8	PSEUDOMONAS AERUGINOSA	AMPUTATION	21 DAYS
50	67	F	DIABETES	LEFT LOWERLIMB NF	0.483	247	2.8	STERILE	RECOVERED	28 DAYS
51	62	M	NIL	RIGHT LOWERLIMB NF	1.596	315	2.7	PSEUDOMONAS AERUGINOSA	RECOVERED	36 DAYS
52	65	M	NIL	RIGHT LOWERLIMB NF	0.864	207	3	STERILE	RECOVERED	29 DAYS
53	30	M	NIL	LEFT UPPER LIMB NF	0.367	265	3.4	STERILE	RECOVERED	21 DAYS
54	70	M	DIABETES	RIGHT LOWERLIMB NF	0.957	289	2.8	STAPHYLOCOCUS AUREUS	RECOVERED	30 DAYS
55	62	M	DIABETES	LEFT UPPER LIMB NF	1.472	129	2.9	STERILE	RECOVERED	35 DAYS
56	65	M	DIABETES	RIGHT LOWERLIMB NF	1.845	137	2.9	KLEBSIELLA PNEUMONIA	RECOVERED	38 DAYS
57	58	M	NIL	RIGHT LOWERLIMB NF	0.689	168	2.8	STERILE	RECOVERED	27 DAYS
58	65	M	DIABETES	LEFT UPPER LIMB NF	28.063	954	2.1	STERILE	DEATH	4 DAYS
59	70	F	DIABETES	LEFT LOWERLIMB NF	10.256	728	1.8	CITROBACTER FRENUDII	AMPUTATION	21 DAYS
60	70	M	DIABETES	RIGHT LOWERLIMB NF	0.789	183	2.8	STERILE	RECOVERED	28 DAYS
61	68	M	DIABETES	RIGHT LOWERLIMB NF	35.087	976	2	STERILE	DEATH	4 DAYS
62	35	M	NIL	RIGHT LOWERLIMB NF	2.087	482	2.1	PSEUDOMONAS AERUGINOSA	RECOVERED	40 DAYS
63	70	M	DIABETES	LEFT LOWERLIMB NF	0.394	247	2.8	STERILE	RECOVERED	24 DAYS
64	25	F	NIL	LEFT LOWERLIMB NF	1.247	206	3.6	ACINETOBACTER	RECOVERED	31 DAYS
65	50	M	NIL	RIGHT LOWERLIMB NF	3.543	307	3.1	STERILE	RECOVERED	>42 DAYS
66	20	M	NIL	RIGHT LOWERLIMB NF	2.654	267	3.8	PROTEUS MIRABILIS	RECOVERED	40 DAYS
67	60	M	NIL	LEFT LOWERLIMB NF	1.223	183	2.9	STREPTOCOCUS	RECOVERED	38 DAYS
68	35	M	NIL	LEFT LOWERLIMB NF	0.476	219	3.2	STERILE	RECOVERED	27 DAYS
69	65	M	DIABETES	RIGHT LOWERLIMB NF	0.376	286	2.7	PSEUDOMONAS AERUGINOSA	RECOVERED	24 DAYS
70	64	M	NIL	LEFT LOWERLIMB NF	0.629	264	2.8	ACINETOBACTER	RECOVERED	30 DAYS
71	35	M	NIL	RIGHT UPPERLIMB NF	4.978	382	2.9	STREPTOCOCUS	RECOVERED	>42 DAYS
72	68	M	DIABETES	LEFT UPPER LIMB NF	4.356	359	1.8	STAPHYLOCOCUS AUREUS	RECOVERED	>42 DAYS
73	65	M	NIL	RIGHT LOWERLIMB NF	2.359	298	2.8	PSEUDOMONAS AERUGINOSA	RECOVERED	38 DAYS
74	70	M	DIABETES	LEFT LOWERLIMB NF	18.278	991	1.8	KLEBSIELLA PNEUMONIA	DEATH	4 DAYS
75	70	F	DIABETES	RIGHT LOWERLIMB NF	0.584	156	2.9	STERILE	RECOVERED	29 DAYS
76	70	F	NIL	RIGHT LOWERLIMB NF	1.783	273	2.7	E.COLI	RECOVERED	32 DAYS

77	65	F	NIL	RIGHT LOWERLIMB NF	0.749	206	2.8	STERILE	RECOVERED	29 DAYS
78	65	F	NIL	LEFT LOWERLIMB NF	0.278	261	2.9	STERILE	RECOVERED	24 DAYS
79	54	F	DIABETES	LEFT LOWERLIMB NF	2.356	384	3.1	STREPTOCOCUS	RECOVERED	34 DAYS
80	62	M	DIABETES	RIGHT LOWERLIMB NF	0.178	270	3.2	STERILE	RECOVERED	24 DAYS
81	64	F	NIL	RIGHT UPPERLIMB NF	2.109	216	2.9	PSEUDOMONAS AERUGINOSA	RECOVERED	38 DAYS
82	35	M	DIABETES	LEFT UPPER LIMB NF	3.134	381	3.2	STERILE	RECOVERED	>42 DAYS
83	68	M	NIL	RIGHT LOWERLIMB NF	2.908	294	2.9	STAPHYLOCOCUS AUREUS	RECOVERED	40 DAYS
84	65	M	NIL	LEFT LOWERLIMB NF	1.245	167	2.9	PSEUDOMONAS AERUGINOSA	RECOVERED	38 DAYS
85	70	M	DIABETES	RIGHT LOWERLIMB NF	0.269	195	2.5	STERILE	RECOVERED	27 DAYS
86	70	M	DIABETES	RIGHT LOWERLIMB NF	1.267	438	2.7	KLEBSIELLA PNEUMONIA	RECOVERED	32 DAYS
87	70	M	DIABETES	RIGHT LOWERLIMB NF	1.984	297	2.9	E.COLI	RECOVERED	34 DAYS
88	65	M	NIL	LEFT LOWERLIMB NF	2.036	338	2.6	KLEBSIELLA PNEUMONIA	RECOVERED	38 DAYS
89	65	M	NIL	LEFT LOWERLIMB NF	1.79	298	2.8	STERILE	RECOVERED	32 DAYS
90	54	F	DIABETES	RIGHT LOWERLIMB NF	2.345	358	3.1	PSEUDOMONAS AERUGINOSA	RECOVERED	40 DAYS
91	62	F	NIL	LEFT LOWERLIMB NF	0.335	172	2.9	E.COLI	RECOVERED	24 DAYS
92	70	F	NIL	LEFT LOWERLIMB NF	3.098	389	2.6	STERILE	RECOVERED	>42 DAYS
93	48	M	DIABETES	RIGHT LOWERLIMB NF	0.735	248	3.1	STREPTOCOCUS	RECOVERED	29 DAYS
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