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Necrotizing Fasciitis: A Comprehensive Review Of Etiology, Pathophysiology, Diagnostic Approaches, And Management Strategies.

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Abstract:-

Necrotizing fasciitis (NF) is a rare, rapidly progressive, and potentially life-threatening soft tissue infection characterized by extensive necrosis of the fascia and surrounding subcutaneous tissues. It is commonly caused by polymicrobial organisms or Group A *Streptococcus* and is associated with high morbidity and mortality if not diagnosed and treated promptly. Clinical manifestations typically include severe pain disproportionate to physical findings, erythema, edema, fever, and systemic toxicity. Early diagnosis remains challenging because initial symptoms may resemble less severe skin and soft tissue infections. Diagnostic evaluation is primarily based on clinical assessment and may be supported by laboratory investigations, imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI), and scoring systems including the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC). Prompt surgical debridement, aggressive supportive care, and broad-spectrum intravenous antibiotic therapy constitute the mainstay of management. Delayed intervention significantly increases the risk of septic shock, multiorgan failure, limb loss, and mortality. This review summarizes the epidemiology, etiology, pathophysiology, clinical presentation, diagnostic approaches, and current management strategies of necrotizing fasciitis, with emphasis on the importance of early recognition and multidisciplinary treatment for improving patient outcomes.

Keywords:- Necrotizing fasciitis; Soft tissue infection; Group A *Streptococcus*; Surgical debridement; LRINEC score.

Abbreviations:- HBO = Hyperbaric Oxygen Therapy; NSAIDs = Non-Steroidal Anti-Inflammatory Drugs

Introduction :-

Necrotizing fasciitis (NF) is a relatively uncommon but potentially life-threatening soft tissue infection that rapidly spreads along the fascial planes, leading to extensive tissue destruction at a rate of approximately 2–3 cm per hour. The disease is commonly associated with polymicrobial infections and synergistic bacterial activity that frequently co-exist. NF may involve the perineum, genital region (Fournier's gangrene), upper or lower extremities, or the abdominal wall (2). A wide variety of aerobic and anaerobic microorganisms, including Clostridium, Peptostreptococcus, Enterobacteriaceae, Proteus, Pseudomonas, Klebsiella, and Bacteroides species, may be involved in NF. However, Staphylococcus aureus and Group A β-hemolytic *Streptococcus* are the most common causative organisms, either alone or in combination(3). Most cases involve anaerobic bacteria that proliferate in hypoxic environments and produce gas, which accumulates within soft tissues and produces the characteristic radiological appearance of gas gangrene on plain radiographs and computed tomography (CT) scans (4). Over the past 30 years, despite considerable progress in medical care and our understanding of the condition, the mortality rate associated with NSTI has stayed steady at 25% to 35%. Mortality and time to intervention are clearly correlated (5). The first description of "modern" NF was given by military surgeon Joseph Jones of the Confederate States of America. In 1871, he recorded 2,642 cases of gas gangrene treated in hospitals during the American Civil War, with a death rate of about 46%. Fournier's gangrene was first identified in 1883 when Jean Alfred Fournier reported perineal necrosis in five people (6). Initially, differentiating NF from cellulitis and other superficial skin infections may be difficult In fact, studies show that between 15% and 34% of NF patients are correctly diagnosed at the time of admission. Only early diagnosis and strong surgical therapy can reduce mortality and morbidity. Family doctors are often the first point of contact for patients because there are few early symptoms, and they need a high index of suspicion. This article aims to review NF, especially as it relates to early diagnostic signs. We also provide a scenario that illustrates the difficulty of early disease diagnosis. We chose a case with subacute NF to illustrate how its symptoms might be mild; we think family physicians should be aware of this illness (7). Because it is a clinical entity with a varied bacteriology and pathogenesis, it has certainly been identified in the past under names such acute streptococcal gangrene, gangrenous erysipelas, necrotizing erysipelas, and hospital gangrene.The term "necrotizing fasciitis" is used when the infection's most prominent symptom is widespread necrosis of the superficial fascia, which results in broad tissue undermining and severe systemic toxicity, regardless of the exact bacterial origin. A research and reevaluation of this extremely hazardous virus was spurred by 44 patients at Parkland Memorial Hospital in Dallas, Texas over the past 15 years (8). NF and STSS can sometimes coexist in 40% of NF patients and 6% of other people ($p<0.001$). Sometimes, NF and STSS can coexist. It is notoriously challenging but crucial to differentiate NF from other soft tissue infections since it is a surgical emergency that must be treated as a serious alarm needing quick and aggressive surgical debridement. Thus, illness puts a doctor's diagnosis and surgical skills to the test. In this paper, we provide a broad summary of the clinical characteristics of NF, covering everything from epidermis to general care (9).

Epidemiology:-

An estimated 500–1000 cases of NF occur annually, with an incidence of 0.40 cases per 100,000 individuals worldwide, according to reports. It has been demonstrated to favor men with a male-to-female ratio of 3:1; this ratio is mainly linked to the higher incidence of Fournier's gangrene in men. Although the sickness affects people of all ages, middle-aged and older patients (those over 50) are more vulnerable to infection. After evaluating the literature, the median mortality ratio for NF was determined to be 21.5%,

which is a controversial topic. However, it ranges greatly between 8.7 and 76% in the literature. Compared to infections of the belly and perineum, the mortality rate for NF of the extremities is slightly lower. Patients cwith Fournier's gangrene that has not spread to the abdominal wall typically have a better prognosis. In the absence of therapy, the death rate is typically nearly 100%. The lower extremities account for 57.8% of NF infections, with the abdomen and perineum following closely behind. NF of the upper limbs is less prevalent than NF of the lower limbs.

Etiology:-

Fournier's gangrene is often caused by pressure sores, surgical incisions, and skin abscess drainage. It may also appear as a consequence of anorectal infections, ischiorectal abscesses, or colon perforations. Other causes include injuries from an indwelling Foley catheter and a possible urethral stricture. It has often been linked to Bartholin abscesses in women or vulval skin infections. In Asia, eating raw or undercooked seafood or being injured by fish fins can cause NF. Usually referred to as "marine bacteria," bacteria such as Vibrio spp., Aeromonas spp., and Shewanella spp. are commonly linked to this group of illnesses (10).

Classification:-

Categories I through IV include NF (Table 1). The polymicrobial variety, or variety I, accounts for 70–90% of all NF cases. For pathogenic bacteria to fall under this NF group, they must consist of at least two microorganisms. In contrast, beta-hemolytic Streptococcus A (GAS or S. pyogenes) is often associated with the monomicrobial illness known as type II NF. Staphylococcus aureus (S. aureus), particularly methicillin-resistant S. aureus (MRSA), which occurs 10% to 30% of the time, is the causative pathogen. MRSA's increasing complexity and capacity to produce toxic shock syndrome may have greater detrimental effects.

Table 01: Classification of Necrotizing Fasciitis Based on Microbial Etiology, Clinical Profile, and Vulnerable Populations

Type	Common Locations	Infectious Profile	Common Microorganisms	Vulnerable Populations	Important Nuances
Type I (most common)	Perineum, trunk, groin, abdominal wall	Polymicrobial	=1 anaerobic (non typable streptococci and Enterobacteriaceae) + aerobic (Gram + or Gram -)	Mostly immunocompromised Patients Newborns (a complication of omphalitis)	Chronic illnesses/immunosuppression (diabetes mellitus, peripheral vascular disease, chronic renal failure, HIV, chronic cardiac/pulmonary disease) Recreational drug use (I.V. drug misuse, alcohol abuse) trauma (blunt/penetrating trauma, surgery, burns) Nutritional issues (obesity, malnutrition)
Type II (less common)	Extremities, head & neck	Monomicrobial	β-hemolytic group-A streptococcus *Staphylococcus aureus* Other streptococci	Mostly immunocompetent individuals with a history of recent trauma/operation	Toxic shock syndrome (30% of cases)
Type III (uncommon)	Extremities, trunk, perineum	Monomicrobial	*Vibrio* species (*Vibrio vulnificus* *Vibrio damsela* *Vibrio parahaemolyticus*) *Clostridium* species Gram-negative bacteria *Aeromonas hydrophila*	*Vibrio*: following minor injuries exposed to salt water *Clostridium*: Injury/Surgical wounds, drug addicts *Aeromonas*: Seafood consumption	Fulminant course Multiorgan failure, if untreated
Type IV (very rare)	Extremities, trunk, perineum	Fungal	*Candida species* *Zygomycetes*	*Mostly after trauma/burns in immunocompetent individuals severely immunocompromised individuals*	Aggressive especially in immunocompro

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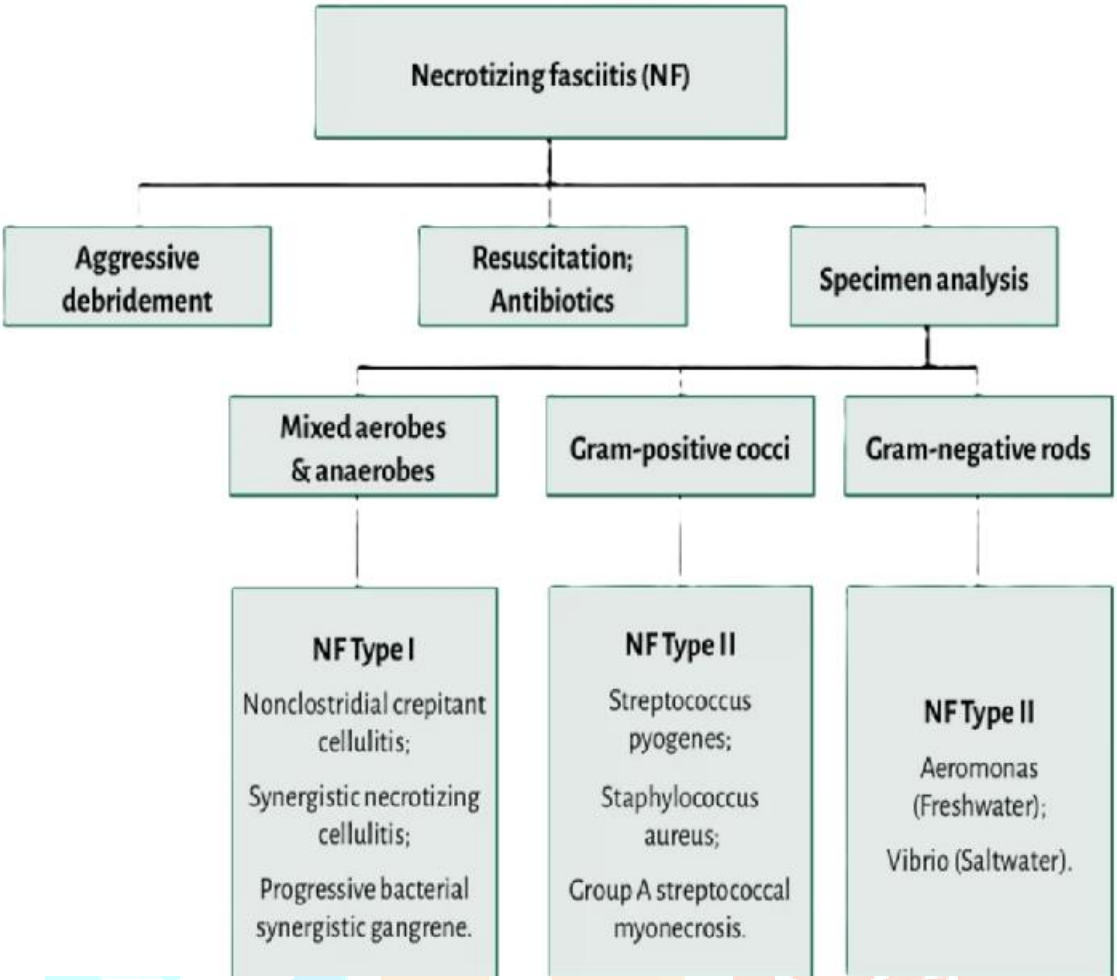

Figure No. 1: Classification of Necrotizing Fasciitis Based on Microbial Etiology

Pathophysiology:-

After external trauma, surgery, wounds, or direct bacterial dissemination via a perforated viscus, microorganisms can infiltrate the skin and subcutaneous tissues, resulting in necrotizing soft tissue infections (NSTIs). These serious infections are caused by a variety of bacteria and patient-related risk factors. The skin and subcutaneous tissue spaces experience extended vasoconstriction due to endotoxins and exotoxins generated by microorganisms within the dermal capillary network. These poisons cause multiple organ dysfunction syndrome (MODS) and systemic inflammatory response syndrome (SIRS), which can lead to septic shock and eventually death. Thrombosis of the perforating arteries supplying the skin and subcutaneous tissues is one of the main pathological characteristics of NSTIs. Early identification is challenging, particularly for inexperienced surgeons, because the severity and spread of infection beneath the skin sometimes do not correlate with obvious skin changes. If fulminant necrotizing fasciitis (NF) is not promptly identified and treated with rigorous surgical debridement, intensive care resuscitation, and adequate broad-spectrum antibiotic therapy, MODS can develop within the first 24 hours. Instead of being a Type II monomicrobial infection, NF is more frequently a Type I polymicrobial infection in clinical settings. Group A Streptococcus was found to be one of the most frequent causal organisms during a 15-year follow-up investigation. Anaerobic beta-hemolytic Streptococcus pyogenes, Peptostreptococcus, Clostridium, Bacteroides species, hospital-acquired Staphylococcus aureus, including MRSA, Acinetobacter, Serratia, Pseudomonas, Enterococcus, group B Streptococcus, and Pneumococcus species were among the other pathogens.Polymicrobial infections were prevalent, with an average of several bacterial species recovered from initial wound cultures, according to a retrospective analysis of 198 patients with confirmed NSTIs. Staphylococci, aerobic streptococci, Bacteroides species, Enterococci, and Escherichia coli were the most commonly found organisms. Clostridial organisms were frequently isolated, but unless they were linked to pure clostridial myonecrosis, their presence did not considerably raise mortality. The infecting organisms had an impact on mortality, bacteremia, delayed or

insufficient surgical intervention, and the severity of MODS at admission. Monomicrobial cases usually afflicted the limbs of young, otherwise healthy, immunocompetent people and were caused by either Staphylococcus aureus or Streptococcus pyogenes. Over 71% of the patients in the Anderson research were caused by polymicrobial illnesses(12).

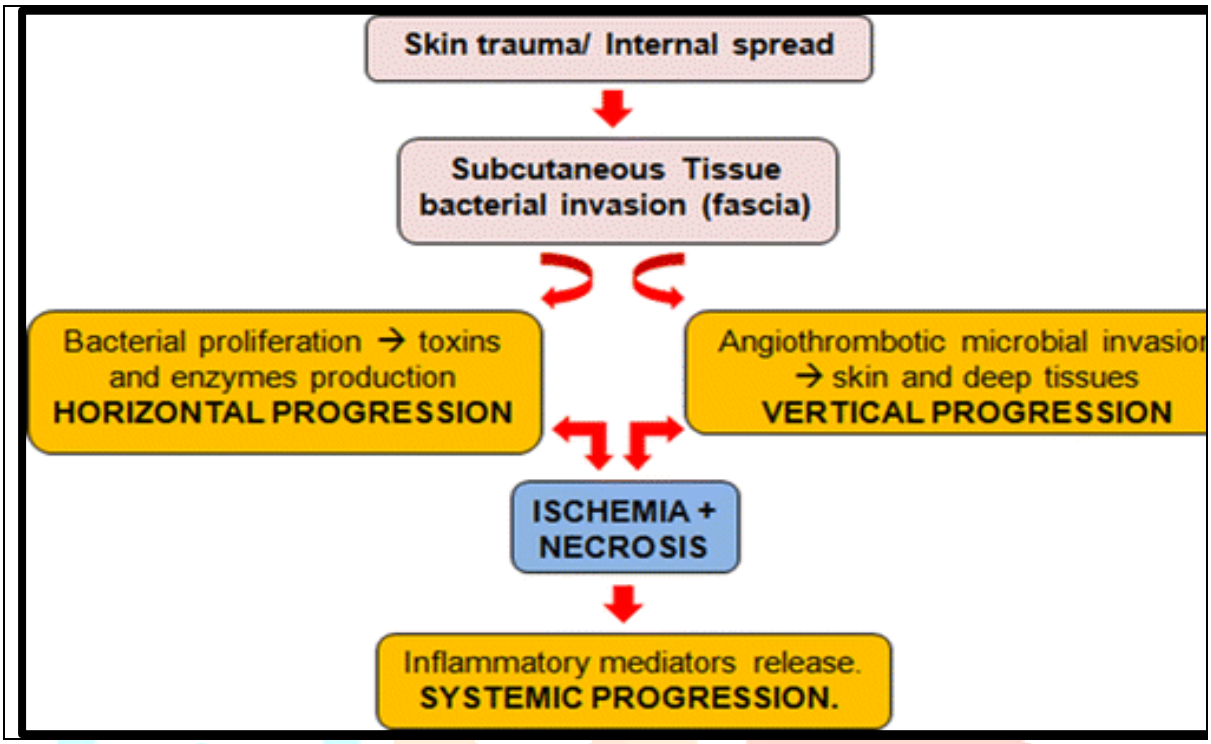

Figure No. 2-: Pathophysiology and Progression of Necrotizing Fasciitis

Imaging Studies:-

Since numerous false-negative results can occur with established NF, radiologic tests are only recommended as additional measures for instances that are questionable and cannot be used to rule out NF. Furthermore, physical observations are the only means to assess the degree of debridement during surgery. Even though one study indicated that 7 out of 22 (32%) NF patients had gas on a plain X-ray, compared to 6 out of 224 (3%) non-NF patients, a simple radiograph is typically ineffective. A tiny fraction of NF patients may have soft tissue air on CT or MRI, which can help assess the degree of tissue involvement.MRI can be especially sensitive because it cannot distinguish between cellulitis and NF and overestimates deep tissue involvement.One factor to bear in mind is that persons with impaired diseases, like diabetes, may display milder clinical signs than the real tissue damage depicted in photos(13).

Laboratory Investigations:-

Table 2: Summary of Laboratory Diagnostic Indices and Risk Assessment Criteria for Necrotizing Fasciitis.

Laboratory Index	Summary of Included Parameters	Parameters	Criteria
LRINEC	Six common serum parameters at the time of presentation	CRP total WBC count Heamoglobin serum Na Creatinine glucose	≥6 = higher risk of NF
MLRINEC	Six common serum parameters + liver disease at the time of presentation	CRP total WBC count Heamoglobin serum Na Creatinine glucose Lactate liver disease	≥12 = higher risk of NF
FGSI	Three vital signs + six serum markers	Temperature heart rate Respiration rate serum Na Serum K creatinine Hematocrit total WBC count Serum bicarbonate	9 = cut-off value for NF >9 = mortality likelihood of 75% ≤9 = survival likelihood of 78%
SIARI	Four comorbidities + three serum markers	Site of infection outside the lower limb History of immunosuppression Age ≤ 60 Creatinine Inflammatory markers (total WBC count CRP)	3 = cut-off value for NF 6–7 = moderate risk of NF ≥8 = high risk for NF
LARINF	Three comorbidities + three serum markers	Heart, liver, or renal insufficiency Immunosuppression (does not include diabetes) Obesity Procalcitonin CRP Hemoglobin	≥5 = higher risk of NF

Severe sepsis-induced increased serum creatine kinase (CK), coagulopathy, and liver and renal problems can all be indicators of multiple organ dysfunction . Leukocytosis is more common (84%) in patients with WBC >20×109 /L (OR 3.7; 95% CI 1.6-8.5), blood urea nitrogen >18 mg/dL (OR 6.8; 95% CI 2.9-16.3), and serum creatinine 1.2 mg/dL (OR 4.5; 95% CI 1.1-19.5) than in patients with NSTI (11, 29). WBC >15,400/mm3 and serum Na 16 mg/dL or CK >600 IU/L, according to one study, may cause physicians to rule out a diagnosis of group A streptococcus (GAS) NF and conduct a more thorough diagnostic examination .Notably, because liver cirrhosis impairs the liver's ability to produce proteins for the inflammatory response, WBC and CRP may not be helpful in these patients. In an attempt to provide diagnostic hints for NF at an early stage of its development, the Laboratory Risk Indicator for NF (LRINEC) score was created WBC >25,000/mm3, blood heamoglobin 141 µ mol/L (2 points each), blood glucose >10 mmol/L (1 point), and an increased CRP >150 mg/L (4 points) are all included in this score. A retrospective investigation found that a score of 6 was highly diagnostic of NF, with a 92% positive predictive value and a 96% negative predictive value, out of a possible total score of 13 .For patients with equivocal clinical symptoms but a moderate or high risk for NF based on the LRINEC score (>5), frozen section biopsy, computed tomography (CT), magnetic resonance imaging (MRI), or a bedside finger test should be taken into consideration. This score may be useful for assigning diagnostic resources, classifying patients into NF risk groups, and eventually assisting in the early detection of NF. Regardless

of the score, urgent debridement must be carried out in instances that are very likely to be NF since clinical acumen is still crucial(14).

Table 3.Summary of Laboratory Indices Used to Facilitate Diagnosis of NF

Sr.No	Index	Main Parameters	Cut-off / Interpretation
1	LRINEC	CRP, WBC, Hemoglobin, Sodium, Creatinine, Glucose	≥ 6 = High risk of NF
2	MLRINEC	LRINEC + Lactate + Liver disease	≥ 12 = High risk
3	FGSI	Vital signs + Serum markers	> 9 = Higher mortality
4	SIARI	Comorbidities + Inflammatory markers	≥ 8 = High risk
5	LARINF	Organ insufficiency + CRP + Hemoglobin	≥ 5 = High risk

Approximately 76.5% of wound cultures and 35.2% of blood cultures were reported positive in various studies. Some studies reported a predominance of monomicrobial infections, whereas others demonstrated a higher incidence of polymicrobial infections. Commonly isolated organisms included *Staphylococcus* species, *Streptococcus* species, *Bacteroides*, and *Escherichia coli*. There are sizable coastline regions in both of these nations. In warm coastal waters with temperatures ranging from 9°C to 21°C, marine organisms frequently harbor Vibrio spp. and other bacteria, including Aeromonas SPP (16).

Diagnosis:-

Clinical Signs and Symptoms-

Early diagnosis of NF can be difficult because the condition typically manifests as the traditional trifecta of vague symptoms: erythema, acute pain, and swelling. However, because the infection spreads more quickly through fascia, NF is commonly associated with considerable discomfort that is out of proportion to physical findings and extends beyond the affected skin. and frequently have multiple organ dysfunction syndrome, septic shock, altered mental status, and widespread soft tissue necrosis. Crepitus and bullae are examples of more sophisticated discoveries. With an incidence of 36% to 55%, NF most frequently affects the extremities, however it can affect any area of the body (Fig. 1). Additionally, it commonly affects the perineum (up to 36%) and trunk (18%–64%)(17).

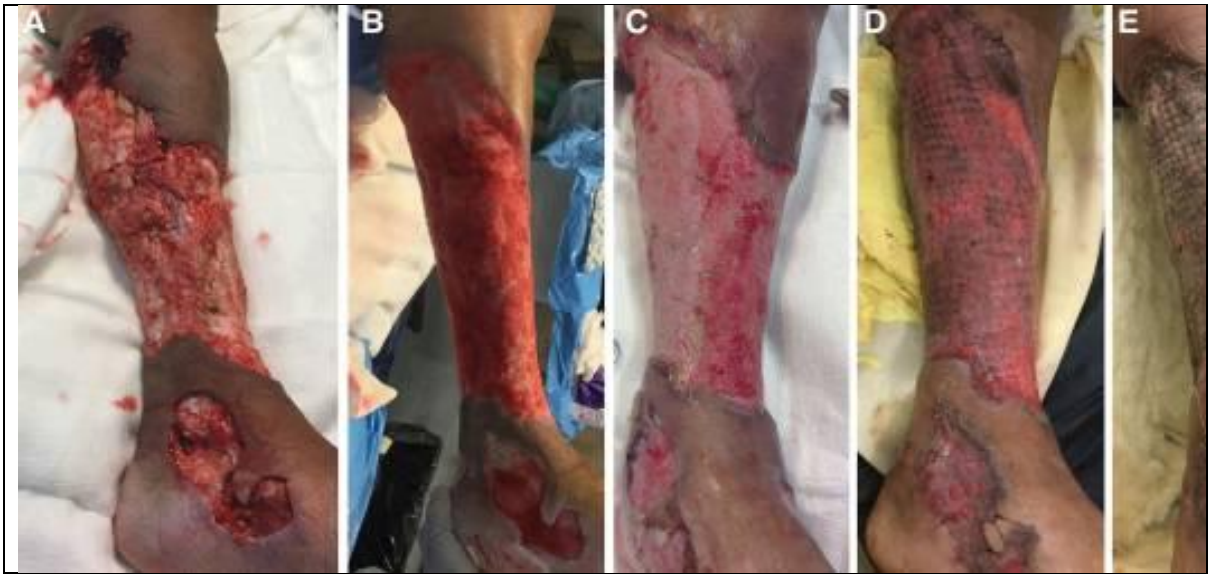

Figure No. 3: Clinical Presentation and Surgical Debridement in Necrotizing Fasciitis

NF of the leg and foot ,The wound before and after debridement ,respectively .C-E, Stages A-E healing after skin grafting.

Treatment and Management:-

1. Medical Management -

Broad-spectrum antibiotics that cover the usually suspected pathogens should be used empirically and promptly to treat patients with suspected NF. The NF first-line antimicrobial drugs are listed in Table 2. The antibiotic course of treatment for a type 1 infection should be decided by the patient's history, Gram stain, and culture. Ampicillin or ampicillin-sulbactam in combination with metronidazole or clindamycin is the recommended first line of treatment . Type 1 sickness requires a thorough understanding of anaerobes. For anaerobic bacteria, metronidazole or clindamycin, beta-lactams plus beta-lactamase inhibitors, or carbapenems are suitable options.. Broader gram-negative coverage should be required as an initial empirical therapy if patients have a history of previous hospitalization or antibiotic exposure. The potential agents in this situation include carbapenems, higher generation cephalosporins, ticarcillinclavulanate, ampicillin-sulbactam, and piperacillin-tazobactum. The causal agent of type 2 disease is primarily GAS, while MSSA/MRSA can also occasionally be found. Vancomycin or first-generation cephalosporins (such cefazolin) can be used in place of ampicillin/penicillin to cover methicillin-resistant Staphylococcus aureus (MRSA) or methicillin-sensitive Staphylococcus aureus (MSSA), respectively. Since clindamycin inhibits bacterial protein synthesis and is immune to the inoculum effect of numerous slow-growing organisms with reduced expression of penicillin-binding proteins, several authors contend that it is superior to penicillin in treating severe streptococcal infections .Additionally, a different study suggested that when NF or myositis is present, doctors should think about using clindamycin in the beta-lactam antibiotic treatment. However, it is noteworthy that Streptococcus pyogenes's developing clindamycin resistance may have significant ramifications for treating severe S. pyogenes infections .Based on the results of initial blood, wound, and tissue cultures, antimicrobials should be selected, but they should be used for at least 48 hours after the temperature and WBC have stabilized or until the infection is under control. If Vibrio infection is suspected, early administration of third-generation cephalosporins and tetracyclines (including doxycycline and minocycline) is essential because this significantly lowers the death rate .Given that NF is a deep-seated illness, an antibiotic treatment course of four to six weeks is typically advised. The use of intravenous immunoglobulin (IVIG) to neutralize streptococcal toxins is both desirable and reasonable. According to several publications, severe GAS infections may benefit from high doses of IVIG. It is worth taking into consideration as a potential treatment in severe situations, even if these studies only analyzed a limited number of individuals

and so require more research. Hyperbaric therapy as an adjuvant treatment has not yet been shown. The Infectious Diseases Society of America (IDSA) has guidelines for managing NF(18).

2. Surgical Management:-

Emergency surgical debridement of the diseased tissue is the cornerstone of treatment for NF. With a 70% mortality rate, surgical therapy is particularly recommended for NF patients who have multiorgan failure or systemic inflammatory response syndrome. Furthermore, if a patient has blisters, bullae, ecchymosis, or significant discomfort, surgery is required. By preventing the spread along the fascial planes, surgery lowers bioburden. Initially, incisions are performed parallel to the Langer lines to reduce the possibility of scarring and encourage improved wound healing. Unless there is involvement of the abdominal wall or retroperitoneal area, incisions perpendicular with Langer lines can be performed to maintain the wound open and permit more drainage and excision of necrotic tissue. It is necessary to closely monitor surgical incisions and tissue viability for the next 24 hours. As a "second-look operation," repeat surgical debridement may be helpful in complicated instances. The removal of all nonviable or necrotic tissue is essential, as the timing and scope of the initial debridement are the most crucial determinants in reducing the death rate. Delays of more than 12 hours in surgical debridement, necro sectomy, and fasciotomy may lead to fulminant NF and increased mortality. Ecker et al. discovered, for instance, that the death rate increased ninefold when surgery was postponed by 24 hours(19).

Risk Factors of Necrotizing Fasciitis (NF):-

1. Diabetes Mellitus-

Diabetes weakens the immune system and reduces blood circulation, especially to the extremities. High blood glucose levels also promote bacterial growth and delay wound healing, increasing susceptibility to severe soft-tissue infections.

2. Chronic Diseases-

Chronic illnesses such as liver disease, heart disease, and chronic lung disorders reduce the body’s ability to fight infections and recover from tissue damage.

3. Immunosuppressive Drugs (e.g., Prednisolone)-

Long-term use of corticosteroids or other immunosuppressive medications suppresses immune responses, making patients more vulnerable to aggressive bacterial infections.

4. Malnutrition-

Poor nutritional status weakens immune defense mechanisms and impairs tissue repair, increasing the risk of rapid infection spread.

5. Advanced Age (>50 years)-

Older individuals are more prone to NF because of decreased immunity, slower wound healing, and the presence of multiple comorbid conditions.

6. Intravenous Drug Misuse-

Injection drug use can introduce bacteria directly into soft tissues through contaminated needles or poor injection practices, leading to severe infections.

7. Peripheral Vascular Disease-

Reduced blood supply to tissues causes poor oxygen delivery and delayed healing, creating favorable conditions for tissue necrosis and bacterial growth.

8. Renal Failure-

Kidney dysfunction weakens immune responses and causes metabolic disturbances, increasing the severity and progression of infections.

9. Underlying Malignancy-

Cancer patients often have weakened immunity due to the disease itself or chemotherapy/radiotherapy, increasing the risk of opportunistic infections.

10. Obesity-

Obesity is associated with impaired circulation, chronic inflammation, and delayed wound healing, all of which contribute to a higher risk of NF.

Conclusion:-.

Necrotizing fasciitis is a rare but severe soft tissue infection associated with rapid progression, high morbidity, and significant mortality. Improving patient outcomes and lowering complications requires early clinical detection, prompt diagnosis, and prompt action. Systemic toxicity, fast tissue death, and severe discomfort that is out of proportion to physical findings are significant symptoms that call for immediate medical intervention. Prompt surgical exploration and debridement continue to be the cornerstone of care, even though diagnostic tools including imaging techniques and laboratory studies may complement clinical evaluation. In order to lower mortality and avoid limb loss, interdisciplinary treatment techniques, intense supportive care, and broad-spectrum antibiotics are crucial. For patients with necrotizing fasciitis to have a better prognosis and survive, early aggressive management and increased awareness among medical personnel are essential..

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