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Infection of the Skin and Soft Tissue: Necrotizing Soft Tissue Infection (NSTI)

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Abstract:- Skin and soft tissue infections (SSTIs) are widespread infections of the epidermis, dermis, or subcutaneous tissue. Necrotizing soft tissue infections (NSTIs) are uncommon and possibly deadly bacterial infections that cause severe skin and subcutaneous tissue necrosis. This review aims to figure out an overview of Skin and soft tissue infection and management strategies for NSTI. A literature review was performed to determine the Antibiotics recommended for the empiric treatment of NSTIs. As soon as NSTI is detected, empiric therapy of broad-spectrum antibiotics should start. The selection of the initial antibiotic is crucial. It has been demonstrated that proper use of antibiotics is associated with improved clinical outcomes and decreased morbidity and death. Rapid surgical debridement of all contaminated tissues, broad spectrum antibiotic therapy, and intensive care unit treatment of related organ failures are the cornerstone of the first urgent management of NSTIs. As a result, clindamycin, vancomycin, and piperacillin-tazobactam are frequently used as the first treatment for NSTI. In comparison to vancomycin, studies have found that linezolid is more efficient in treating SSTIs caused by MRSA or Gram-positive bacteria.

Keywords:- *Skin and soft tissue infection, SSTI, Necrotizing soft tissue infection, NSTI, Rare bacterial infection.*

I. INTRODUCTION; SKIN AND SOFT-TISSUE INFECTION.

Skin and soft tissue infections (SSTIs) are a major reason why patients request treatment in both inpatient and outpatient settings, accounting for over 14 million outpatient visits annually[1] and almost 900000 hospital hospitalisations in the United States[2]. There are several aetiologies, clinical manifestations, and degrees of severity for SSTI[4]. The outcome can range from spontaneous remission without the need for antibiotics at one end of the spectrum to sepsis with a fatal outcome at the other[5]. Pathogen isolation in SSTIs is constrained by currently accessible diagnostics and affected by host and regional conditions, so choosing an empiric antibiotic treatment is challenging[2,3,6,7]. Widespread infections of the dermis, epidermis, or subcutaneous tissue are referred to as SSTIs. Their symptoms include warmth, erythema (redness), induration (hardening), discomfort, and soreness. They can range in severity from minor, self-limiting furunculosis (boils) to deadly necrotizing fasciitis[6]. SSTIs include Impetigo, Infections that cause necrosis in soft tissue and skin, Infections caused by human and animal bites, Infections in soft tissues as a result of animal interaction, Infections at the site of surgery, Infections that affect those whose immune systems are weak AND Treatment-related infections (i.e., iatrogenic), such as those that develop in surgical wounds[8].

II. CLASSIFICATION OF SSTI

The Food and Drug Administration classifies SSTIs as either "uncomplicated" or "complicated" (Table 1). Uncomplicated SSTIs include small abscesses, cellulitis, furuncles (boils), carbuncles, and impetigo lesions. They are also superficial infections and small surgical wounds that may be treated with antibiotics. Complicated SSTIs are characterised as infections that impact deeper tissues, including skeletal muscle, fascia, and subcutaneous tissue. Additionally, they can affect individuals with co-occurring medical disorders such as HIV, diabetes mellitus, or other immune-compromised conditions (FDA 1998)[5,8,9].

Table 1. FDA classification of Skin and soft-tissue infections.

Uncomplicated SSTI	Complicated SSTI
➢ Mainly Gram-positive	➢ Maybe Gram-positive or negative
➢ Superficial • Simple abscesses • Carbuncles • Impetigo lesions • Cellulitis • Furuncles • Erysipelas	➢ Deep soft tissue • Cellulitis • Necrotising fasciitis • Major abscesses • Infected ulcers • Infected burns

[source: Data Source from[9], Reproduced from the source][9]

A. Treatment of Uncomplicated and Complicated SSTI

While complicated SSTIs usually need hospitalisation, treatment with antibiotics via IV, and perhaps surgical intervention, uncomplicated SSTIs can be managed locally with or without antibiotics[10]. For patients with complex SSTIs, the choice of the first antibiotic is critical. It has been established that better clinical results are linked to the appropriate use of antibiotics. In patients who have an illness, it has been shown that proper antibiotic treatment is related to

decreased morbidity and death[11]. Beta-lactam antibiotics , vancomycin, linezolid and clindamycin are frequently used to treat SSTIs brought on by Gram-positive cocci[12]. Beta-lactam medicines are the cornerstone therapy for MSSA and suspected streptococcal infections. The use of benzylpenicillin is still suitable in conditions that have been demonstrated to be penicillin-sensitive[8].

B. Severe SSTI

Although there isn't a commonly accepted scale for grading the severity of a disease caused by SSTI, the degree of skin structure involvement has a loose correlation with sickness severity. We will define individuals with severe SSTI as having necrotizing fasciitis, toxic shock syndrome, or gas gangrene/myonecrosis. Additionally, individuals who have any SSTI and fulfill the requirements for severe septic shock or sepsis or who have a fast Sequential Organ Failure Assessment score of at least 2 are deemed to have a severe SSTI. Table 2 shows a few of the common organisms associated with severe SSTI, as well as their characteristics and suggested antibiotics.

Table 2: Common organisms associated with severe SSTI, as well as their characteristics and suggested antibiotics.

Pathogens	Characteristics	Antibiotic therapy
MRSA	TSS and purulent infections are possible associations. IVDU (intravenous drug use), past MRSA colonisation, and low socioeconomic position are more likely.	Vancomycin. If there is a possibility of TSS, add Clindamycin or use Linezolid. Ceftaroline and Daptomycin may be recommended in patients with renal impairment.
Streptococcuspyogenes	Cellulitis-causing agent, type II necrotizing fasciitis.	Clindamycin and penicillin, but not as empiric treatment. IVIG may be considered in refractory shock
Anaerobic bacteria	Perineal/ abdomen, head and neck, and lower extremities SSTI, including diabetes, are more prevalent.	Carbapenem, Piperacillin-Tazobactam, or Metronidazole
Clostridium spp.	Gas gangrene and myonecrosis are also conditions that can occur. Trauma,'skin popping,' neutropenia, delivery, and 'home' abortions are all risk factors.	Clindamycin and penicillin, but not as empiric treatment.
Gram-negative bacteria	Abdominal/ perineal SSTI is more frequent in the lower extremities. More common in immunocompromised patients, diabetics, care facility residents, and those who have recently used antibiotics.	Antipseudomonal Carbapenem, Cefepime, or Piperacillin-Tazobactam

[source: Data Source from[3], Reproduced from the source][3]

III. NSTI; AN OVERVIEW

Necrotizing soft tissue infections (NSTIs) are uncommon, possibly lethal bacterial infections characterised by extensive necrosis of the skin and subcutaneous tissues. The extremities, particularly the lower limbs, are most often affected by NSTIs, however, they can affect any portion of the body[13–16]. Prior comorbidities, such as diabetes, intravenous drug use, obesity, immunosuppression and cardiovascular disease are present in the majority of individuals who acquire STIs[1,17,18]. Non-penetrating soft tissue injuries, traumatic injuries, and tiny skin or mucosal breaks can result in the spread of infection[13] In the US, there are 500–1500 reported instances of necrotizing soft tissue infections (NSTIs) annually. Hospitalists should consult with surgeons and infectious disease specialists when NSTIs are suspected to ensure effective results[19]. Due to the potential for skin lesions that initially appear benign and the potential absence of hemodynamic instability, early illness diagnosis can be challenging. A high degree of suspicion is needed, and clinical signals are frequently used to make diagnoses. These clues may lead to further investigations, but their importance is limited, especially in patients who are severely sick. NSTI can spread quickly, causing substantial tissue damage that commonly requires reconstructive surgery, demands surgical source management, and frequently leaves patients permanently disabled[14]. Depending on how severe the patient was at the beginning, mortality can vary from 10 to 30 percent, and morbidity in survivors includes the possibility of amputation and a significant impact on the long-term health-related standard of life[20–22]. Rapid surgical debridement of contaminated tissues, broad-spectrum antibiotic therapy, and intensive care unit treatment of related organ failures are the cornerstone of the first urgent management of NSTIs[13].

A. NSTI; Epidemiology and risk factors

Necrotizing skin and soft-tissue infections are uncommon, with an average incidence rate of 4 per 100,000 people each year [23–27], and they only make up a small part of Intensive Care Unit admissions—an estimated 0.2% in the United Kingdome[28] or 1.2% of all critically ill patients hospitalized with sepsis in the Netherlands[29]. However, hospital admission to the intensive care unit (ICU) is frequently necessary due to the illness's severity, underlying co-morbidities, and the extent of postoperative wound care[26,27,30,31]. Over one-third of patients with NSTI show acute renal damage[32], and 25–50% of patients with NSTI have septic shock [27] or need mechanical ventilation[31,32]. The first 24 hours after admission are when organ failures usually get worse. ICU stays frequently last between 5 and 12 days[30]. Patients with NSTI typically

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range in age from 50 to 60[27],26,29,31e35,39e41], with a slight male preponderance[26,27,31,33]. The most prevalent clinical manifestation is necrotizing fasciitis of the extremities[22,27,30,33,34], followed by perineal NSTI, sometimes referred to as Fournier's gangrene[22,30,31,33,34]. Less frequently, the trunk or the head and neck are involved[22,30–32,34]. According to several studies[30–32], 4% to 12% of NSTI patients experience recurrent NSTI. Diabetes mellitus is a co-morbidity related to NSTI in 22%e59%[26,27,30–32,34], and obesity is a co-morbidity associated with NSTI in 17%e31%[31,33,34]. Other risk factors include immunosuppression (4% to 30%), cardiovascular disease (9% to 45%), peripheral vascular disease (3% to 19%), intravenous drug use (2% to 80%), and chronic alcohol abuse (6% to 27%). Remarkably, up to 25% of individuals with NSTI lack a clear predisposing factor[22]. Local trauma is detected at the portal of entry in 10% to 38% of NSTI patients; this might be anything from a simple skin abrasion or bug bite to operation damage or violent trauma. A persistent wound or dermatosis may also be the cause of NSTI[22,32]. Non-steroidal anti-inflammatory medication use is often observed in the weeks before admission, with the potential to conceal the clinical signs and symptoms of a developing NSTI[27,34]. A causative connection has not been demonstrated, though. Long-term functional deficits are severe in NSTI patients. Amputation will eventually be necessary for 10% to 20% of patients with limb NSTI, which is significant[32,34]. According to several studies, 20% to 30% of NSTI patients pass away while they are hospitalized[22,32], while mortality may be lower depending on the case mix. Mortality risk factors include disease severity, as measured by sickness severity ratings such as the APACHE II[33], hypotension, and/or the requirement for vasopressors. Studies indicated a 16%–18% increase in mortality risks per unit higher APACHE II score. The odds ratio for death is 28.4 (95% CI 1.35e77.8) if vasopressors are needed upon admission to the intensive care unit (ICU), compared to a patient who is hypotensive at the time of admission, where the mortality doubles[35]. Also identified to be a mortality risk factor was bacteremia at admission. Age[35,36] and gender[26,35], are additional non-modifiable prognostic variables. Diabetes is not always linked to a higher risk of mortality[25–27]. The prognosis is made worse by other comorbid conditions such as cardiovascular[35], peripheral vascular, chronic renal, or hepatic illness. The delay in surgical intervention, the surgeon's skill, and the hospital's case load are all potentially modifiable risk factors related with NSTI mortality[14,26].

B. NSTI; Classification and Microbiology

The causative organisms differ greatly depending on the site of infection, the underlying circumstances, as well as the different geographical regions of the world[13,16,37–40]. NSTI illnesses are frequently classified based on the organisms that cause them. Type I infections are polymicrobial, including bacteria that are facultatively anaerobic, aerobic, and anaerobic[14]. Type I is most frequently seen in diabetics and people with peripheral vascular disease, as well as following surgical procedures[41]. Type II infections, however, are monomicrobial and can affect any patient population. The most common infectious agent is Streptococcus pyogenes, which is followed by other b-hemolytic streptococci such as the newly discovered Streptococcus dysgalactiae. Nearly 50% of NSTI caused by GAS is related to streptococcal toxic shock syndrome (STSS), and because of this frequent association, myositis, necrotizing fasciitis, and gangrene are all included in the consensus definition[14].

MRSA, Vibrio vulnicifus, Clostridium species, and and other Gram-negative bacilli are uncommon causes of type II infection[42]. Even more so in immunocompromised individuals, a wide variety of bacterial species, including multidrug-resistant (MDR) Gram-negatives, may be developed from NSTI[43,44]. Secondary to gastrointestinal or genitourinary infections that finally migrate along tissue planes are anogenital and abdominal infections. These infections are type I in nature and involve pathogens with genitourinary and intra-abdominal infections. According to reports, multidrug-resistant organisms are spreading around the world[42], such as extended-spectrum lactamase-producing Escherichia coli or Klebsiella spp[14]. However, almost 1/3rd of NSTIs are monomicrobial (type II infections), with GAS and Staphylococcus aureus as the predominant players[16,22,45,46]. The prevalence of GAS can be reported in up to 40% of NSTIs overall, even though it is more common in monomicrobial and upper-extremity infections[13,47]. The microbiology of NSTI is depicted in Table 3.

Table 3: Microbiology of Necrotizing soft tissue infection (NSTI)

Class/ Species	Organism
Aerobic bacteria. Gram-positive bacteria.	Group A (beta-hemolytic)Streptococcus. Group B Streptococcus. Enterococcus. Coagulase-negative Staphylococcus. S. aureus Bacillus spp.
Gram-negative bacteria.	Enterobacter cloacae. Escherichia coli. Pseudomonas aeruginosa. Klebsiella spp. Acinetobacter calcoaceticus. Citrobacter freundii.

	Pasteurella multocida. Proteus spp. Serratia spp.
Anaerobic bacteria.	Bacteroides spp. Clostridium spp. Peptostreptococcus spp.
Marine Vibrio spp.	V. damsel. V. alginolyticus. V. vulnificus. V. parahaemolyticus..
Fungi.	Candida spp. Rhizopus. Aspergillus spp.

[source: Data Source from[41], Reproduced from the source][41]

C. NSTI; Pathophysiology

Pathogens proliferate in subcutaneous tissue along the superficial and deep fascial planes, leading to necrotizing infection[48]. This process involves bacterial enzymes and toxins[49]. Surface proteins and toxins produced by bacteria are thought to have a significant role in NSTI. Streptococci adhere to tissues more readily and are protected from neutrophil phagocytosis by the surface proteins M-1 and M-3. Cytokines are released as a result of streptococcal superantigen and pyrogenic exotoxins A, B, and C[50]. Toxic shock syndrome (in the case of Gram-positive bacteria), following organ failure, and death may result from exotoxins binding to T-cell receptors and inducing excessive production of TNFa, IL-1, and IL-6. The streptococcal infection has been firmly linked to necrotizing infection[51]. To determine the clinical presentation, it is crucial to comprehend the pathophysiology of NSTI. The superficial fascia is predominantly affected by the quick necrotizing process, but the bacteria then multiply and enter the subcutaneous tissue and deep fascia as well as release poisonous bacterial products. Due to the thrombosis of the perforating arteries to the skin, skin involvement may eventually occur. Extensive facial, skin, subcutaneous fat, and skeletal muscle gangrene develops as the illness worsens[52]. Toxin-induced, [53]platelet/neutrophil aggregate-mediated vascular occlusion causes the fast tissue death that distinguishes both streptococcal and clostridial myonecrosis. Local ischemia likely spreads regionally until a complete tissue bed is damaged as the infection worsens and more toxins are generated and absorbed. Microvascular occlusion may potentially play a role in the systemic shock and organ dysfunction brought on by these infections. Although platelet-neutrophil complex formation in group A streptococcal and clostridial NSTIs has the same outcome, their underlying processes differ. In the case of C. perfringens, the activation of gpIIb/Ia caused by phospholipase C is primarily responsible for the creation of massive platelet-neutrophil complexes. Large platelet/neutrophil aggregates are produced by this activation via both gpIIb/IIIa and P-selectin. Toxins do not significantly increase the number of big platelet/neutrophil aggregates in S. pyogenes, which shows that exotoxins do not directly activate gpIIb/IIIa. Additionally, functional overexpression of the neutrophil adhesion molecule complex CD11b/CD18 is probably boosted by such secondary gpIIb/Ia-mediated binding[41]

IV. NSTI MANAGEMENT

A. NSTI; Surgical Debridement

The cornerstone of treating NSTI is surgical debridement; without it, the death rate for NSTI is close to 100%. As a result, when NSTI has been identified, all necrotic tissue must be removed quickly and aggressively. The fascial planes should be investigated, and depending on the intraoperative results, the extent of the debridement may need amputation. Surgery aims to drain any fluid collections and debride frank necrosis back to normal bleeding tissue while preserving as much viable tissue as feasible. Hemostasis is carefully monitored. NSTIs often need many visits back to the operating room before the necrosis stops progressing. Wet-to-dry dressings are first used to maintain wound care; however, after the infection is visibly subsiding, negative pressure treatment may be used. Negative pressure treatment is then used to reduce the wound surface, remove wound exudate and cell debris, and induce granulation after debridement and after the wound is stabilized. Additionally, it makes wound care easier and improves patient comfort in the ICU. In Fournier's gangrene, a temporary diverting colostomy is beneficial to reduce fecal contamination and manage infection of extensive perianal lesions[54]. For secondary wound closure using plastic reconstructive procedures, adequate wound conditioning in NSTI is required[55]. To obtain surgical source control as early as feasible in the early stage of the therapy and to make reconstructive surgery easier later on strong collaboration between surgeons and intensivists is needed throughout(Peetermans et al. 2020).

B. NSTI; Antibiotic therapy

One of the most significant modifiable prognostic variables is the use of antibiotics and early surgical debridement in the treatment of NSTIs[56]. More than 50% of patients who arrive with septic shock should receive immediate and bactericidal intravenous antibiotics[6,13,57]. Even the location of infection is insufficient to direct empiric antibiotic therapy for NSTIs since they are frequently polymicrobial, even if several admission features have been connected with monomicrobial forms. Antimicrobial therapy

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for NSTI aims to achieve the following goals: (i) adequate activity against gram-positive bacteria and Enterobacteriaceae or other Gram-negative bacteria at risk for MDR; (ii) decreased toxin production in Streptococcus pyogenes or Clostridium perfringens infections; and (iii) anaerobic coverage essential in all polymicrobial infections[6,14]. As soon as NSTI is detected, empiric therapy of broad-spectrum antibiotics should start. Empiric therapy is directed at the most prevalent causal pathogens, including gram-negative and anaerobic bacteria, Streptococcus spp., Clostridium spp., and Staphylococcus spp. Patient mortality is decreased when given antibiotics that block protein synthesis and reduce the toxins generated by group A Streptococcus (GAS)[58,59]. In addition to providing coverage for gram-positive, enteric gram-negative, and anaerobic pathogens, antibiotics should also provide extra protection against MRSA. A broad-spectrum beta-lactam (such as piperacillin-tazobactam) is the cornerstone of empiric therapy, with added aminoglycosides in the event of septic shock. In cases of known or suspected group A streptococcus (GAS) infection (limb infection, streptococcal toxic shock features, absence of chronic skin lesions, absence of comorbidities, homelessness, injectable drug use, blunt trauma use of non-steroidal anti-inflammatory drug), clindamycin should be added. In addition to taking into account the local ecology, carbapenems should be used in cases where there are personal risk factors (hospital acquired infection, exposure to beta-lactam or quinolone within the last three months, history of extended-spectrum beta-lactamase (ESBL) carrying, germ colonization/infection, or travel to areas with high ESBL endemicity within the earlier three months). Similarly, if you have a chronic dialysis regimen, live in an assisted living facility, have permanent transcutaneous medical devices, have previously contracted or colonised methicillin-resistant Staphylococcus aureus (MRSA), or live in a local endemic condition, you should consider using anti-MRSA medications such as vancomycin, linezolid, or daptomycin. When possible, therapeutic drug monitoring should be employed to ensure that the pharmacokinetics (PK) and pharmacodynamics (PD) of compounds having time-dependent bactericidal action, such as beta-lactams, are optimized[13]. In the absence of evidence, de-escalation of the spectrum by the documentation is appropriate, and the indicated treatment duration is 48–72 hours following the last procedure in case of clinical improvement[6,57]. Table IV provides recommended antibiotic therapy in the empiric treatment of NSTIs[13].

Table IV: Antibiotics recommended for the empiric treatment of NSTIs

Antibiotic	**Route**	**Antimicrobial Spectrum/Anti-Toxinic Activity and Other Specific Aspects**	**The volume of distribution (Vd)**	**Protein Binding**	**Dosing Regimen***
Piperacillin + tazobactam	IV.	Methicillin- susceptible *S. aureus, S. pyogenes, Entero bacteriaceae*, nonfermenting bacilli, anaerobic bacteria	Hydrophilic (0.24 L/kg)	Low (16%)	4 g q6h IV Consider prolonged (4 h) or continuous infusion with a loading dose
Cefotaxime	IM/IV.	Methicillin- susceptible *S. aureus, S. pyogenes, Enterobacteriaceae*	Hydrophilic (0.28 L/kg)	Low (30-51%)	2 g q6–8h IV
Meropenem	IV.	Methicillin- susceptible *S. aureus, S. pyogenes, Enterobacteriaceae*, nonfermenting bacilli anaerobic bacteria activity on multi-drug resistant gram-negative bacilli	Hydrophilic (0.25 L/kg)	Very low (2%)	1–2 g q8h IV Consider prolonged infusion 3 h
Gentamycin	IM/IV.	*S. aureus, S. pyogenes, Enterobacteriaceae,* nonfermenting bacilli Rapid bactericidal action Should be added in cases of septic shock	Hydrophilic (0.26 L/kg)	Very low (0–3%)	5–8 mg/kg over 30 min, q24h
Amikacin	IM/IV.	*S. aureus, S. pyogenes, Enterobacteriaceae,* nonfermenting bacilli Rapid bactericidal action should be added in cases of septic shock	Hydrophilic (0.26 L/kg)	Very low (< 10%)	25–30 m/kg over 30 min, q24h
Metronidazole	IV.	Anaerobic bacteria	Lipophilic (0.65 L/kg)	Very low (< 10%)	500 mg q8h IV

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Vancomycin	IV.	Methicillin-resistant *S. aureus*	Hydrophilic (0.70 L/kg)	Medium (55%)	Consider continuous infusion of 30 mg/kg/24 h with a loading dose of 30 mg/kg and TDM
Daptomycin	IV.	Methicillin-resistant *S. aureus*	Hydrophilic (0.10 L/kg)	High (92%)	8–12 mg/kg q24h
Linezolid	IV., oral	Methicillin-resistant *S. aureus* In vitro evidence ofanti-toxinic action	Lipophilic (0.65 L/kg)	Low (31%)	600 mg q12h IV (higher doses might be needed in obese patients)
Clindamycin	IV., oral	*S. aureus*, *S. pyogenes* Anaerobic bacteria (but with a high proportion of resistant strains), High evidence of in vivo and in vitro anti-toxic action	Lipophilic (1.1 L/kg)	High (90%)	600–900 mg q8h IV

* These doses are established for a standard-weight adult without hepatic or renal impairment. When necessary, the dosage modification guidelines should be followed. AUC: Area under curve. Cmax: Maximal concentration. fT: fraction of time. IV: Intravenous. IM: Intramuscular. MIC: Minimal inhibitory concentration. NSTI: Necrotizing soft tissue infection. The selection of molecules is contingent upon the indigenous ecology and personal susceptibilities to harbour resistant bacteria, such as MRSA and ESBL. If there are recognised risk factors for MRSA infections, vancomycin, linezolid, or daptomycin should be added to a beta-lactam regimen. Owing to its potent anti-toxic properties, clindamycin need to be considered in cases of limb NSTI; nonetheless, it must not be utilised as an empirical monotherapy. In the event of septic shock, aminoglycosides ought to be administered. When gram-negative bacteria have risk factors for becoming drug-resistant, carbapenems should be added. [source: Data Source from,[13] Reproduced from the source][13]

C. Safety and Effectiveness of Clindamycin, Vancomycin, and Linezolid

As a result, clindamycin, vancomycin, and piperacillin-tazobactam are frequently used as the first treatment for NSTI. Despite this, rates of clindamycin resistance in Streptococcus spp. have been continuously rising across the United States. In addition, therapy with vancomycin is linked to acute kidney damage (AKI), and treatment with clindamycin is linked to an increased risk of Clostridioides difficile infection (CDI) in comparison to other antibiotic options[60]. Considering all of these factors, it is becoming more and more important to find novel therapeutic approaches that can cure NSTIs while being safe and efficient[61]. Linezolid, a protein synthesis inhibitor, reduces toxin generation by preventing the expression of exotoxin[60]. When compared to clindamycin, it also shows greater in vitro susceptibility rates against typical gram-positive bacteria[60,62]. Linezolid has good bioavailability and can also be used orally. Given these qualities, linezolid could be an appropriate substitute for both clindamycin and vancomycin for treating NSTIs, leading to a lower incidence of CDI, AKI, and general antibiotic exposure[59,63].

Many studies have shown that linezolid is more successful than vancomycin in treating SSTIs brought on by MRSA or other Gram-positive bacteria[64–66]. Another comprehensive study's findings[8,67] indicate that there is no statistically significant difference between linezolid and vancomycin. Another review claims that linezolid is a better treatment for SSTIs than vancomycin. Higher rates of clinical cure (RR 1.09, 95% CI 1.03 to 1.16) and microbiological cure (RR 1.08, 95% CI 1.01 to 1.16) were associated with linezolid treatment. There was no statistically significant difference in mortality between linezolid and vancomycin (RR 1.44, 95% CI 0.75 to 2.80). Compared to the vancomycin group, the linezolid group experienced fewer cases of rash (RR 0.27, 95% CI 0.12 to 0.58), pruritus (RR 0.36, 95% CI 0.17 to 0.75), and Red Man Syndrome (RR 0.04, 95% CI 0.01 to 0.29). Nevertheless, thrombocytopenia (RR 13.06, 95% CI 1.72 to 99.22) and nausea (RR 2.45, 95% CI 1.52 to 3.94) were more common in the linezolid group. Using subgroup analysis, researchers discovered that linezolid was superior to vancomycin in curing MRSA infections both clinically (RR 1.09, 95% CI 1.03 to 1.17) and microbiologically (RR 1.17, 95% CI 1.04 to 1.32). The linezolid group's hospital stays were shorter than those of the vancomycin group's patients. Oral linezolid was less expensive per day for outpatient treatment than intravenous vancomycin. Even though linezolid's inpatient therapy was more expensive per day than vancomycin's inpatient treatment, linezolid's median hospital stay was three days shorter. As a result, linezolid therapy costs less overall per patient than vancomycin treatment[8].

V. CONCLUSION

Skin and soft tissue infections are frequent infections of the epidermis, dermis, or subcutaneous tissue. Despite being rare, NSTIs are life-threatening conditions that physicians continue to find challenging to diagnose and treat. The prompt identification and treatment of these severe cases should be given top priority, with surgery and the proper antibiotic medication playing a key role. Successful surgical debridement requires complete debridement. After the offending organisms have been identified, the first empirical antibiotic treatment should be wide to cover all probable causative agents and then targeted.

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