A Dissertation on

PROGNOSTIC INDICATORS OF MORBIDITY AND MORTALITY IN NON DIABETIC SOFT TISSUE INFECTIONS

Dissertation submitted to

THE TAMIL NADU Dr.M.G.R.MEDICAL UNIVERSITY CHENNAI.

With partial fulfilment of the regulations

For the Award of the degree of

M.S. GENERAL SURGERY

Branch – I

MADRAS MEDICAL COLLEGE

THE TAMIL NADU Dr.M.G.R.MEDICAL UNIVERSITY CHENNAI

CHENNAI.

APRIL - 2014

BONAFIDE CERTIFICATE

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ACKNOWLEDGEMENT

I would like to express my sincere thanks to the Dean of the Madras medical College **Prof. Dr. V.KANAGASABAI, M.D.,** for permitting me to conduct the study in Madras Medical College & Government General Hospital.

With deep sense of gratitude and respect, I take this opportunity to thank my teacher and professor **Dr.R. G. SANTHASEELAN** M.S., for his constant inspiration, able guidance and kind help which he rendered in preparing this dissertation and in pursuit of my post graduate studies.

I also thank the Registrar of Department of Surgery **DR. A.MUTHURAJA M.S.,** who helped me to progress through this study with great interest.

I am very grateful to all the Assistant Professors of my unit **DR.G.GAJENDRARAJ M.S., DR. P. RAMADOSS M.S., DR. A. SAGAYA INBA SEKAR M.S.,** for the constant support and guidance through my study.

Last but not the least my heartfelt gratitude to the patients for their kind understanding and cooperation.

CONTENTS

PROGNOSTIC INDICATORS OF MORBIDITY AND MORTALITY IN NON DIABETIC SOFT TISSUE INFECTIONS

Introduction

Soft tissue skin infections (SSTI's) were first described in the Hippocratic era. The principles of management, including early diagnosis with prompt and repeated surgical debridement, aggressive resuscitation and physiological support, broad spectrum antimicrobial drugs, and nutritional support, have been well documented. Despite this well accepted management approach, the mortality rate remains between 16 – 34% in most major published series. Due to the lack of defined criteria to determine the type of treatment that has to be given for patients at the time of admission, most patients undergo multiple surgical procedures which increases the morbidity and mortality.

Aim of the study

The primary objective of this analysis is to create a simple clinical score to aid in the prediction of morbidity defined by the number of days of hospital stay or limb loss and mortality in patients with SSTIs at the time of first assessment. The scoring system may further be used to predict limb loss at first assessment, thereby reducing multiple surgeries for the same patient.

Methods

A retrospective review of 200 consecutive patients with necrotizing soft tissue infections, treated at Rajiv Gandhi Government General Hospital during a 1-year period, was conducted. Using a model for logistic regression analysis, characteristics of each patient and his/her clinical course were tested for impact on outcome. The variables which were found to independently alter the outcome were

used to establish a scoring system. This was then applied to a prospective pool of 50 patients admitted over 6 months in the same hospital.

Results

The scoring system decreased the number of surgeries undergone by each patient significantly. The scoring system also reduced the number of days of hospital stay per patients, though not significantly. The use of the scoring system did not alter the mortality in any way.

Conclusion

Skin and soft tissue infections of the limbs have a high mortality and morbidity especially if necrosis is present. The morbidity is in the form of prolonged hospital stay and limb loss. Further detailed studies are required to produce repeated significant results, which is essential for the scoring system to be applied as an established protocol.

INTRODUCTION

Soft tissue skin infections (SSTI's) were first described in the Hippocratic era. In time various surgeons described the disease process in details. The most well documented among these is the work of Joseph Jones a confederate army surgeon, who reported 2,642 cases of "hospital gangrene" with a mortality rate of 46%. Since then, multiple reports and classification systems have been published in an attempt to define this disease better and achieve lower mortality rates with better outcomes. The principles of management, including early diagnosis with prompt and repeated surgical debridement, aggressive resuscitation and physiological support, broad spectrum antimicrobial drugs, and nutritional support, have been well documented. Despite this well accepted management approach, the mortality rate remains between 16 – 34% in most major published series. Over the last decade, there has been an interest in understanding SSTIs better. Some investigators have focused on methods that aid in early diagnosis so that surgical debridement can be accomplished promptly, whereas other researchers have focused on identifying patients at higher risk of death. Although several predictors of death have been identified, differences in patients across series limit their broad applicability.

Due to the lack of defined criteria to determine the type of treatment that has to be given for patients at the time of admission, most patients undergo multiple surgical procedures which increases the morbidity and mortality. The primary objective of this analysis is to create a simple clinical score to aid in the prediction of morbidity defined by the number of days of hospital stay or limb loss and mortality in patients with SSTIs at the time of first assessment. The scoring system may further be used to predict limb loss at first assessment, thereby reducing multiple surgeries for the same patient.

AIMS OF THE STUDY

The aims of the study is,

1) To establish a scoring system to predict the outcome of a patient with non diabetic soft tissue limb infection at the time of admission.

2) To determine the factors which increase the morbidity of a patient with non diabetic soft tissue limb infection as determined by no. Of days of hospital stay or limb loss or death of the patient.

REVIEW OF LITERATURE

HISTORY

Skin and soft tissue infections have been described since 5th century BC. The first clear reference to necrotizing fasciitis (NF) dates back to the 5th century BC, with Hippocrates' description of a fatal infection, "Many were attacked by the erysipelas all over the body when the exciting cause was a trivial accident. The erysipelas would quickly spread widely in all directions. Flesh, sinews and bones fell away in large quantities…Fever was sometimes present and sometimes absent…There were many deaths. The course of the disease was the same to whatever part of the body it spread."[1]

From the 18th and 19th century the British naval surgeons referred to the necrotizing fasciitis (NF) as "hospital gangrene." Indeed the first modern report that describes a detailed case of "hospital gangrene" was reported by Joseph Jones, a Confederate Army Surgeon during the American Civil War. He was the first person to describe this disorder in a large group of patients. He reported 2,642 cases and found a mortality rate of 46%. [2]. Jean Alfred Fournier (1883) described a similar necrotizing soft tissue infection of the perineum in five male

patients.[3] The condition that bears his name is now described in both male and female patients.

A major advance took place in 1924 when Meleney and Breuer isolated streptococcal infection as the prime cause of lethal NF[4]. Before the advent of the antibiotics, NF was treated successfully with "bear-claw scratch debridement" and tubes irrigating the tissues with Dakin's solution of chlorinated sofa[5]. In 1924, a Beijing missionary surgeon reported similar conditions among the opium addicts.

Over the years, many terms have been developed and used such as flesh-eating bacteria syndrome, suppurative fasciitis, and streptococcal gangrene."Meleney's gangrene" is commonly used for abdominal fasciitis, but strictly speaking should be streptococcal dermal gangrene on any part of body. The term "necrotizing fasciitis" was coined by Wilson in 1952, to delineate the histological appearance of the disease, that is, an invasive necrotizing infection involving deep fascia and soft tissue. [6]

From 1987 to 1990, scattered outbreaks of NF were reported in both the USA and Scandinavia, while significant media attention focused on a close cluster of NF cases in West Gloucestershire in 1994[7]. In 1995 a small number of cases were reported in Canada and California. [8] Nowak suggests

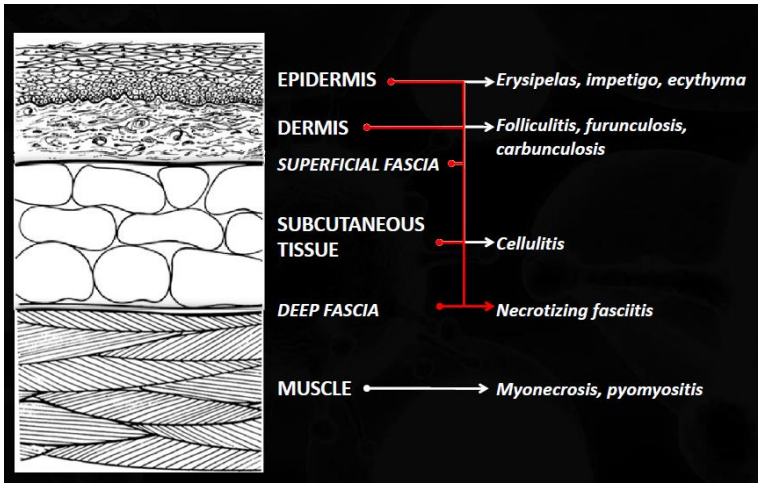
there has been an increase in the incidence of severe streptococcal infection throughout the 20th century, resulting in more cases of NF being identified and treated.[9] While most Westernised countries are said to have an incident rate of around one in every 100,000 people, the latest Indian statistics suggests an incidence of 4 in every 100,000 people.[10]

Recently, the term necrotizing soft tissue infection has been adopted.[11]

DEFINITION

Skin and soft tissue infections (SSTI) are classified into complicated and uncomplicated infections.[11] Uncomplicated SSTI's include cellulitis, erysipelas, simple abscesses,impetigo, ecythyma, follicilitis, furunculosis and carbuncles. They are superficial infections and have a low mortality and morbidity (limb loss). They can be treated by antibiotic therapy and drainage procedures.

Complicated SSTI's includes necrotizing soft tissue infections, complicated abscesses, infected burn wound, infected ulcers, infections with significant underlying disease states that complicates response to treatment (e.g. DM). These are usually deeper infections with higher mortality and morbidity, (i.e.) a higher chance of limb loss.[12]



Necrotizing soft tissue infections by definition include the presence of necrotic or devitalized tissue as part of the pathophysiology[13].Necrotic tissue provides a growth medium for bacteria and precludes delivery of host defence mechanisms and antimicrobial agents[13]. Necrotizing soft tissue infections includes, necrotizing cellulitis (involvement of dermal and subcutaneous layers), necrotizing fasciitis (involvement of deep fascia) and pyomyositis or myonecrosis or a combination of any of the above.[14]

PATHOPHYSIOLOGY

Necrotizing fasciitis is characterized by widespread necrosis of the subcutaneous tissue and the fascia. Although the pathogenesis of necrotizing fasciitis is still open to speculation, the rapid and destructive clinical course of necrotizing fasciitis is thought to be due to multibacterial symbiosis and synergy.[15]Historically, group A beta-haemolytic Streptococcus (GABS) has been identified as a major cause of this infection. This monomicrobial

infection is usually associated with an underlying cause, such as diabetes,[16] atherosclerotic vascular disease, or venous insufficiency with oedema. GABS usually affects the extremities; approximately two thirds of the GABS infections are located in the lower extremities.[17]

During the last 2 decades, researchers have found that necrotizing fasciitis is usually polymicrobial rather than monomicrobial.[18, 19, 20] Anaerobic bacteria are present in most necrotizing soft-tissue infections, usually in combination with aerobic gram-negative organisms. Anaerobic organisms proliferate in an environment of local tissue hypoxia in those patients with trauma, recent surgery, or medical compromise. Facultative aerobic organisms grow because polymorphonuclear neutrophils (PMNs) exhibit decreased function under hypoxic wound conditions. This growth further lowers the oxidation/reduction potential, enabling more anaerobic proliferation and, thus, accelerating the disease process. Carbon dioxide and water are the end products of aerobic metabolism. Hydrogen, nitrogen, hydrogen sulphide, and methane are produced from the combination of aerobic and anaerobic bacteria in a soft tissue infection. These gases, except carbon dioxide, accumulate in tissues because of reduced water solubility. In

necrotizing fasciitis, group A haemolytic streptococci and Staphylococcus aureus, alone or in synergism, are frequently the initiating infecting bacteria.

However, other aerobic and anaerobic pathogens may be present, including the following:

- Bacteroides
- Clostridium
- Peptostreptococcus
- Enterobacteriaceae
- Coliforms (eg, Escherichia coli)
- Proteus
- Pseudomonas
- Klebsiella

Bacteroides fragilis is usually noted as part of a mixed flora in combination with E coli. B fragilis does not directly cause these infections, but it does play a part in reducing interferon production and the phagocytic capacity of macrophages and PMNs.

A variant synergistic necrotizing cellulitis is considered to be a form of necrotizing fasciitis, but some authorities feel that it is actually a nonclostridial myonecrosis. This condition begins in the same manner as

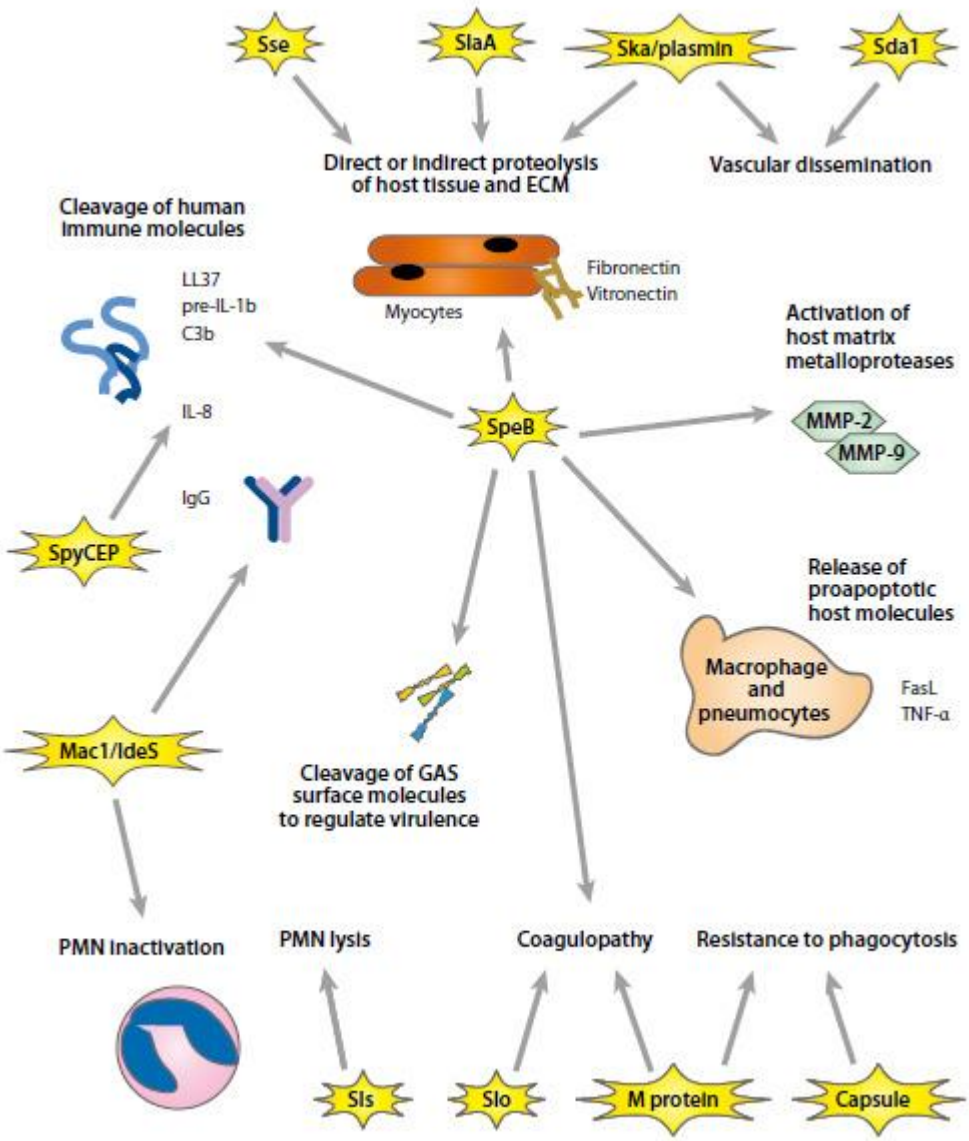
necrotizing fasciitis, but it progresses rapidly to involve wide areas of deeper tissue and muscle at an earlier stage than might be expected. Severe systemic toxicity occurs.

Anaerobic streptococci, occasionally seen in intravenous drug users, cause many forms of nonclostridial myonecrosis. Some cases of necrotizing fasciitis can be caused by Vibrio vulnificus. This organism is seen more often in patients with chronic liver dysfunction, and it often follows the consumption of raw seafood. V vulnificus may cause subcutaneous bleeding.[23,24]

Organisms spread from the subcutaneous tissue along the superficial and deep fascial planes, presumably facilitated by bacterial enzymes and toxins. This deep infection causes vascular occlusion, ischemia, and tissue necrosis. Superficial nerves are damaged, producing the characteristic localized anaesthesia. Septicaemia ensues with systemic toxicity.

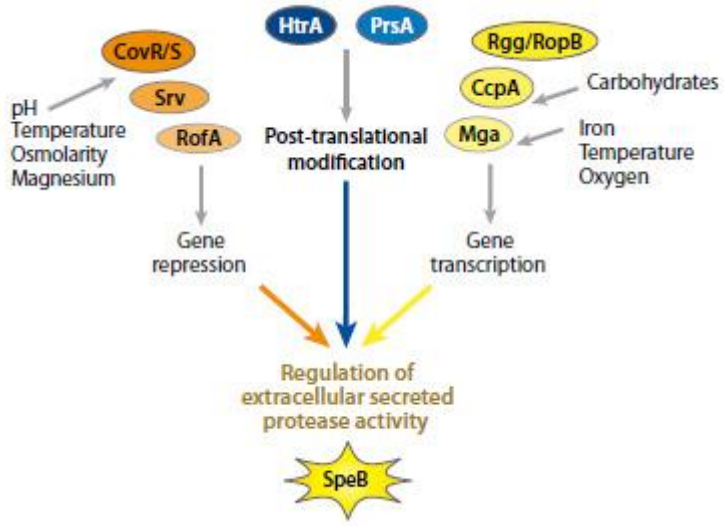
A subset of virulence factors, for instance, SpeB and Ska/ Plasmin directly damage the host tissues, degrade the extracellular matrix proteins, and induce vascular dissemination via their enzymatic pathway[26]. Other virulence factors such as SpyCEP and Mac1/IdeS indirectly damage the host tissue by cleaving immune molecules, inactivate PMN and stimulate release

of proapoptotic molecules. Host matrix metalloproteninases (MMPs) and coagulopathy are also implicated.



Important bacterial factors include surface protein expression and toxin production. M-1 and M-3 surface proteins, which increase the adherence of the streptococci to the tissues, also protect the bacteria against phagocytosis by neutrophils.

Organisms undergo a very complex molecular transition during the progression from a localized to an invasive infection. SpeB, a broad-spectrum cysteine protease virulence factor, is regulated by multiple intersecting and collateral pathways that respond to different environmental stimuli. SpeB is repressed, activated and regulated by multiple regulatory pathways. The combined effects result an in vivo temporal-spatial expression pattern of SpeB.



Streptococcal pyrogenic exotoxins[27] (SPEs) A, B, and C are directly toxic and tend to be produced by strains causing necrotizing fasciitis. These pyrogenic exotoxins, together with streptococcal superantigen (SSA), lead to the release of cytokines and produce clinical signs such as hypotension. The etiological agent may also be a Staphylococcus aureus isolate harbouring the

enterotoxin gene cluster seg, sei, sem, sen, and seo, but lacking all common toxin genes, including Panton-Valentine leukocidin.[28]

The poor prognosis associated with necrotizing fasciitis has been linked to infection with certain streptococcal strains. Community-acquired methicillin-resistant S aureus (MRSA) has also been associated with necrotizing fasciitis.[29]

Single-nucleotide changes are the most common cause of natural genetic variation among members of the same species. They may alter bacterial virulence; a single-nucleotide mutation in the group A Streptococcus genome was identified that is epidemiologically associated with decreased human necrotizing fasciitis.[30]

It was found that wild-type mtsR function is required for group A Streptococcus to cause necrotizing fasciitis in mice and nonhuman primates. It was speculated that a naturally occurring single-nucleotide mutation dramatically alters virulence by dysregulating a multiple gene virulence axis.

Severe myositis accompanying septic necrotizing fasciitis may be caused by a Panton-Valentine leukocidin–positive S

aureus strain.[31] Immunostaining may document strong binding of the Panton-Valentine leukocidin toxin to necrotic muscle tissues.

Although necrotizing fasciitis most frequently develops after trauma that compromises skin integrity, it may rarely develop in a healthy person after minor trauma such as an isolated shoulder sprain that occurred without a break in skin barrier.[32]

ETIOLOGY

Surgical procedures may cause local tissue injury and bacterial invasion, resulting in necrotizing fasciitis. These procedures include surgery for intraperitoneal infections and drainage of ischiorectal and perianal abscesses. Intramuscular injections and intravenous infusions may lead to necrotizing fasciitis.

Minor insect bites may set the stage for necrotizing infections. Streptococci introduced into the wounds may be prominent initially, but the bacteriologic pattern changes with hypoxia-induced proliferation of anaerobes.

Local ischemia and hypoxia can occur in patients with systemic illnesses (eg, diabetes). Host defences can be compromised by underlying

systemic diseases favouring the development of these infections. Illnesses such as diabetes or cancer have been described in over 90% of cases of progressive bacterial gangrene.

Of patients with necrotizing fasciitis, 20-40% are diabetic. As many as 80% of Fournier gangrene cases occur in people with diabetes. In some series, as many as 35% of patients were alcoholics. However, approximately one half of the cases of streptococcal necrotizing fasciitis occur in young and previously healthy people.

Studies have shown a possible relationship between the use of nonsteroidal anti-inflammatory agents (NSAIDs), such as ibuprofen, and the development of necrotizing fasciitis during varicella infections. Additional studies are needed to establish whether ibuprofen use has a causal role in the development of necrotizing fasciitis and its complications during varicella infections. This has not previously been described.

Group A beta-haemolytic streptococci have historically been noted as a cause of necrotizing fasciitis, but Haemophilus aphrophilus and S aureus are also associated with the condition, and some patients have mixed infections involving multiple species of bacteria, including mycobacteria, as well as fungi.[33, 34]

A synergistic infection with a facultative anaerobic bacterium may be significant. In 1 patient, Phycomycetes appeared to be responsible for necrotizing fasciitis.

Streptococcus pneumoniae is a rare cause of necrotizing fasciitis.[33] In one patient, S pneumoniae serotype 5 was also isolated. This serotype 5 antigen is included in the polysaccharide 23-valent pneumococcal vaccine, highlighting the value of pneumococcal immunization.

In type I necrotizing fasciitis[21], anaerobic and facultative bacteria work synergistically to cause what may initially be mistaken for a simple wound cellulitis. A variant of type I necrotizing fasciitis is saltwater necrotizing fasciitis in which an apparently minor skin wound is contaminated with saltwater containing a Vibrio species.

In type II necrotizing fasciitis,[22] varicella infection and the use of nonsteroidal anti-inflammatory drugs may be predisposing factors.

Type III necrotizing fasciitis is usually caused by Clostridium perfringens[25]. When type III necrotizing fasciitis occurs spontaneously, C septicum is more likely to be the etiologic agent; these cases usually occur in association with colon cancer or leukaemia.

Unusual causes include injection anthrax.[35] Rapidly progressive necrotizing fasciitis following a stonefish sting has been described in 2 patients.[36]

PREDISPOSING OR RISK FACTORS FOR NECROTIZING FASCIITIS[37,38]

- Immunosuppression
- Diabetes mellitus
- Alcoholism
- Malignancy
- Severe malnutrition
- Severe peripheral vascular disease
- Intravenous drug use
- Renal failure
- Radiotherapy
- Obesity

PROGNOSIS

The reported mortality in patients with necrotizing fasciitis has ranged from 20% to as high as 80%.[25, 27, 39] Pathogens, patient characteristics, infection site, and speed of treatment are among the variables that affect survival.

Poor prognosis in necrotizing fasciitis has been linked to infection with certain streptococcal strains. However, McHenry et al found that monomicrobial infection with S pyogenes was not associated with an increased mortality.[27]

A retrospective study by Hsiao et al found that Aeromonas infection, Vibrio infection, cancer, hypotension, and band form WBC count greater than 10% were independent positive predictors of mortality in patients with necrotizing fasciitis, while streptococcal and staphylococcal infections were not identified as predictors of mortality. Hemorrhagic bullae appeared to be an independent negative predictor of mortality. However, accuracy of these factors needs to be verified.[40]

In another study, pre-existing chronic liver dysfunction, chronic renal failure, thrombocytopenia, hypoalbuminemia, and postoperative dependence on mechanical ventilation represented poor prognostic factors in monomicrobial necrotizing fasciitis. In addition, patients with gram-negative monobacterial necrotizing fasciitis had more fulminant sepsis.[41]

The mean age of survivors is 35 years. The mean age of non survivors is 49 years.

A retrospective review by Cheng et al showed that upper extremity necrotizing fasciitis has a high mortality rate. In their review, about 35% of patients died. A state of altered consciousness and respiratory distress at initial presentation were found to be statistically significant factors for eventual mortality. Early diagnosis and referral for aggressive surgical treatment prior to the development of systemic toxic signs are essential for survival.[42]

In a retrospective review of craniocervical necrotizing fasciitis, Mao et al reported a survival rate of 60% for patients with thoracic extension (6 of 10) compared with 100% for those without thoracic extension. Lower overall survival for the patients in the thoracic extension group was attributed to older patient age, greater co morbidity, need for more extensive surgical debridement, and increased postoperative complications.

Better survival of the patients without thoracic extension was attributed to aggressive wound care and surgical debridement, broad-spectrum intravenous antibiotics, and care in the surgical intensive care unit.[43]

In a study by Rouse et al, the overall mortality rate was 73% (20 of 27 patients). They indicated that prompt recognition and treatment of

necrotizing fasciitis was essential: Of 12 patients whose treatment was delayed for more than 12 hours, 11 patients died.[25]

Similarly, McHenry et al reported that the average time from admission to operation was 90 hours in nonsurvivors of necrotizing soft-tissue infections; in survivors, this average time was 25 hours.[27] Early debridement of the infection was obviously associated with a significant decrease in mortality.

Necrotizing fasciitis survivors may have a shorter life span than population controls, owing to infectious causes such as pneumonia, cholecystitis, urinary tract infections, and sepsis.[44]

COMMON SITES OF INFECTION

While any area of the body can succumb to NF, the most common sites are the extremities, the abdominal wall, the perianal and groin area and post-operative wounds.

CLINICAL PRESENTATION

Diagnosis of necrotizing fasciitis can be difficult and requires a high degree of suspicion. In many cases of necrotizing fasciitis, antecedent trauma or surgery can be identified. Surprisingly, the initial lesion is often

trivial, such as an insect bite, minor abrasion, boil, or injection site. Idiopathic cases are not uncommon, however.

Olafsson et al indicate that the hallmark symptom of necrotizing fasciitis is intense pain and tenderness over the involved skin and underlying muscle.[45] The intensity of the pain often causes suspicion of a torn or ruptured muscle. This severe pain is frequently present before the patient develops fever, malaise, and myalgias.

In some cases, the symptoms may begin at a site distant from the initial traumatic insult. Pain may be out of proportion to physical findings. Over the next several hours to days, the local pain progresses to anaesthesia.

Other indicative findings include oedema extending beyond the area of erythema, skin vesicles, and crepitus. McHenry et al and others have noted that the subcutaneous tissue demonstrates a wooden, hardened feel in cases of necrotizing fasciitis.[26] The fascial planes and muscle groups cannot be detected by palpation.

A history of co morbid factors, including diabetes mellitus, should be sought in all cases of suspected necrotizing fasciitis.

Physical findings may not be commensurate with the degree of patient discomfort. Early in the disease course, the patient may look deceptively well; unfortunately, this may interfere with early detection, which is key to a favourable outcome. Soon, however, the patient will usually begin to appear moderately to severely toxic.

Typically, the infection begins with an area of erythema that quickly spreads over a course of hours to days. The redness quickly spreads, and its margins move out into normal skin without being raised or sharply demarcated. As the infection progresses, the skin near the site of insult develops a dusky or purplish discoloration. Multiple identical patches expand to produce a large area of gangrenous skin, as the erythema continues to spread.

Iwata et al reported that 2 of 3 patients who lacked inflammatory signs such as redness and heat experienced fulminant progression of necrotizing fasciitis and death.[46]

The initial necrosis appears as a massive undermining of the skin and subcutaneous layer. If the skin is open, gloved fingers can pass easily between the 2 layers and may reveal yellowish-green necrotic fascia. If the skin is unbroken, a scalpel incision will reveal it.

The normal skin and subcutaneous tissue become loosened from the rapidly spreading deeper necrotic fascia that is a great distance from the initiating wound. Fascial necrosis is typically more advanced than the appearance suggests.

Anaesthesia in the involved region may be detected, and it usually is caused by thrombosis of the subcutaneous blood vessels, leading to necrosis of nerve fibres. Without treatment, secondary involvement of deeper muscle layers may occur, resulting in myositis or myonecrosis. Normally, however, the muscular layer remains healthy red with normal bleeding muscle under the yellowish-green fascia.

Usually, the most important signs are tissue necrosis, putrid discharge, bullae, severe pain, gas production, rapid burrowing through fascial planes, and lack of classical tissue inflammatory signs.

Usually, some degree of intravascular volume loss is detectable on clinical examination. Other general signs, such as fever and severe systemic reactions, may be present. Local crepitation can occur in more than one half of patients. This is an infrequent finding, specific but not sensitive, particularly in cases of nonclostridial necrotizing fasciitis.

At this point the patient is grossly unwell, experiencing shock, reduced perfusion, fluid and electrolyte disturbances and an altered mental state. Death from disseminated intravascular coagulation and multi-organ system failure can occur in at least 30 per cent of cases.[1,8,47,48]

PHYSICAL FINDINGS OF CLINICAL FEATURES[49]

FINDINGS	PERCENTAGE
PAIN	100
ERYTHEMA	95
OEDEMA	82
CELLULITIS	75
FEVER	70
DISCOLOURATION	49
CREPITATION	25
VESICLES	16

Fournier gangrene in males begins with local tenderness, itching, oedema, and erythema of the scrotal skin. This progresses to necrosis of the scrotal fascia. The scrotum enlarges to several times its normal diameter. If the process continues beyond the penile-scrotal region to the abdomen or the upper legs, the normal picture of necrotizing fasciitis can be seen.

In males, the scrotal subcutaneous layer is so thin that most patients present after the skin is already exhibiting signs of necrosis. In 2-7 days, the skin becomes necrotic, and a characteristic black spot can be seen. Early on,

this infection may resemble acute orchitis, epididymitis, torsion, or even a strangulated hernia.

In women, Fournier gangrene acts more like necrotizing fasciitis because of the thicker subcutaneous layers involving the labia majora and the perineum.

Complications may include the following:

- Renal failure
- Septic shock with cardiovascular collapse
- Scarring with cosmetic deformity
- Limb loss
- Sepsis
- Toxic shock syndrome

Metastatic cutaneous plaques may occur in necrotizing fasciitis. Septicaemia is typical and leads to severe systemic toxicity and rapid death unless appropriately treated.

CLINICAL STAGES OF NECROTIZING FASCIITIS[55]

STAGE	FEATURES
1- EARLY	Tenderness beyond skin involvement Erythema Swelling Calor
2- INTERMEDIATE	Blisters or bullae formation
3- LATE	Crepitus Skin anaesthesia Skin necrosis

INVESTIGATIONS

Laboratory tests, along with appropriate imaging studies, may facilitate the diagnosis of necrotizing fasciitis.[50] Laboratory evaluation should include the following:

- Complete blood count with differential
- Serum chemistry studies
- Arterial blood gas measurement
- Urinalysis
- Blood and tissue cultures

Skin and superficial tissue cultures may be inaccurate because samples may not contain the infected tissue. Deeper tissue samples, obtained at the time of surgical debridement, are needed to obtain proper cultures for microorganisms. New techniques include rapid streptococcal diagnostic kits and a polymerase chain reaction (PCR) assay for tissue specimens that tests for the genes for streptococcal pyrogenic exotoxin (SPE; eg, SPE-B) produced by group A streptococci. B-mode and possibly colour Doppler ultrasonography, contrast-enhanced computed tomography (CT) scanning, or magnetic resonance imaging (MRI) can promote early diagnosis of necrotizing infections.[51] In addition, these studies permit visualization of the location of the rapidly spreading infection. More importantly, MRI or CT scan delineation of the extent of necrotizing fasciitis may be useful in directing rapid surgical debridement. However, when the patient is seriously ill, necrotizing fasciitis is a surgical emergency with high mortality. Therefore, laboratory tests and imaging studies should not delay surgical intervention.[52]

Most fluid collections in the tissue, especially in the musculoskeletal system, can be localized and aspirated under ultrasonographic guidance. Whether fluid is infected cannot be determined on the basis of its

ultrasonographic characteristics; however, laboratory analysis of the aspirated fluid can help in identifying the pathogen.[53]

In a study of 13 patients with thoracic and abdominal wall infections, Sharif et al reported that CT and MRI were superior to sonography, scintigraphy, and plain radiography in providing useful information about the nature and extent of infections.[54] Furthermore, they point out that while CT compares favourably with MRI in accurate diagnosis of soft tissue infection, multiplanar MRI images can be obtained without ionizing radiation and the use of intravenous contrast agents.

Although the laboratory results may vary in a given clinical setting, the following may be associated with necrotizing fasciitis:

- Elevated white blood cell (WBC count), possibly to more than 14,000/µL
- Elevated blood urea nitrogen (BUN) level, possibly to greater than 15 mg/mL
- Reduced serum sodium level, possibly to less than 135 mmol/L

SCORING SYSTEMS

A numerical score sheet, called the laboratory risk indicator for necrotizing fasciitis (LRINEC), was devised from lab parameters as a possible indicating tool for detection of necrotizing fasciitis. Score of ≥6

has a positive predictive value of 92% and a negative predictive value of 96%. [56]

Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score

Variable	Score
C-reactive protein (mg/l)	
<150	0
≥150	4
Total white cell count (per mm^3)	
<15	0
15-25	1
>25	2
Hemoglobin (g/dl)	
>13.5	0
11-13.5	1
<11	2
Sodium (mmol/l)	
≥135	0
<135	2
Creatinine (µmol/l)	
≤141	0
>41	2
Glucose (mmol/l)	
≤10	0
>10	1

IMAGING STUDIES

Radiographs

Plain radiographs, often obtained to detect soft-tissue gas that is sometimes present in polymicrobial or clostridial necrotizing fasciitis, are of no value in the diagnosis of necrotizing infections.[57] Indeed, nondiagnostic plain radiographs may even hinder the diagnosis of necrotizing infection.[51] In their study of 29 patients with necrotizing soft tissue infections, Lille et al reported that nondiagnostic radiographs correlate with a

delay in operative intervention and consequent increased morbidity and mortality.[58]

The presence of subcutaneous gas in a radiograph does not necessarily indicate a clostridial infection, as Escherichia coli, Peptostreptococcus species, and Bacteroides species may produce gas under appropriate conditions. Misleading subcutaneous gas can also result from the undermining of tissue planes during surgical debridement. Perforations of the oesophagus, the respiratory tract, or the GI tract related to endoscopy or chest tube insertion can result in the radiographic appearance of gas.

Ultrasonography

Bedside ultrasonography may be useful in patients with necrotizing fasciitis, as well as other soft-tissue infections including cellulitis, cutaneous abscess, and peritonsillar abscess. It may be superior to clinical judgment alone in determining the presence or the absence of occult abscess formation.[59]

Sonography may reveal subcutaneous emphysema spreading along the deep fascia, swelling, and increased echogenicity of the overlying fatty

tissue with interlacing fluid collections, allowing for early surgical debridement and parenteral antibiotics.[60]

Parenti et al retrospectively reviewed the ultrasonographic appearances of 32 pathologically proven cases of necrotizing fasciitis.[51] Ultrasonography revealed changes in the subcutaneous fat (28 of 32 patients), investing fascia (18 of 32 patients), and muscle (15 of 32 patients), which correlated well with histological findings. However, in some cases, ultrasonography missed histologically apparent inflammation in the subcutaneous tissues (3 of 32 patients) or muscle (8 of 32 patients).[61]

CT and MRI

CT scanning can pinpoint the anatomic site of involvement by demonstrating necrosis with asymmetric fascial thickening and the presence of gas in the tissues. However, note that early on, CT findings may be minimal.

While no published, well-controlled, clinical trial has compared the efficacy of various diagnostic imaging modalities in the diagnosis of necrotizing infections, MRI is the preferred technique to detect soft tissue infection because of its unsurpassed soft-tissue contrast and sensitivity in

detecting soft-tissue fluid, its spatial resolution, and its multiplanar capabilities.[62, 63]

The usefulness of MRI in the diagnosis of necrotizing fasciitis has been supported in a study by Rahmouni et al, who were able to differentiate nonnecrotizing cellulitis that would respond to medical treatment from severe necrotizing infections that required rapid life-saving surgery.[64] In necrotizing fasciitis, MRI can provide dramatic evidence of an inflammatory process infiltrating the fascial planes.[51]

Craig notes that the combined use of MRI and aspiration under ultrasonographic guidance is very useful in complicated infections (eg, septic arthritis and osteomyelitis) and that its role in the diagnosis of necrotizing fasciitis should be considered.[65] Early muscle necrosis may be apparent.

Absence of gadolinium contrast enhancement in T1 images reliably detects fascial necrosis in those requiring operative debridement. Combined with clinical assessment, MRI can determine the presence of necrosis and the need for surgical debridement. T2-weighted MRI may show well-defined regions of high signal intensity in the deep tissues. However, the sensitivity of MRI exceeds its specificity.[66]

OTHER TESTS

Finger Test and Biopsy

The finger test should be used in the diagnosis of patients who present with necrotizing fasciitis.[67, 68] The area of suspected involvement is first infiltrated with local. A 2-cm incision is made in the skin down to the deep fascia. Lack of bleeding is a sign of necrotizing fasciitis. On some occasions, a dishwater-colored fluid is noticed seeping from the wound.

A gentle, probing manoeuvre with the index finger covered by a sterile powder-free surgical double glove puncture indication system is then performed at the level of the deep fascia. If the tissues dissect with minimal resistance, the finger test is positive.

Tissue biopsies are then sent for frozen section analysis. The characteristic histologic findings are obliterative vasculitis of the subcutaneous vessels, acute inflammation, and subcutaneous tissue necrosis. If either the finger test or rapid frozen section analysis is positive, or if the patient has progressive clinical findings consistent with necrotizing fascia, immediate operative treatment must be initiated.

Excisional deep skin biopsy

Excisional deep skin biopsy may be helpful in diagnosing and identifying the causative organisms.[69] Specimens can be taken from the spreading periphery of the necrotizing infection or the deeper tissues, reached only in surgical debridement, to obtain proper cultures for microorganisms.

This procedure is not done from the actual necrosis or granulating centre, as many bacteria that neither cause nor add to the infection would be detected.

ASPIRATION AND GRAM STAIN

Uman et al recommended percutaneous needle aspiration followed by prompt Gram staining and culture for a rapid bacteriologic diagnosis in soft-tissue infections.[70] A needle aspirate should be taken on the advancing edge of the infection, where group A beta-haemolytic Streptococcus (GABS) is plentiful.[71]

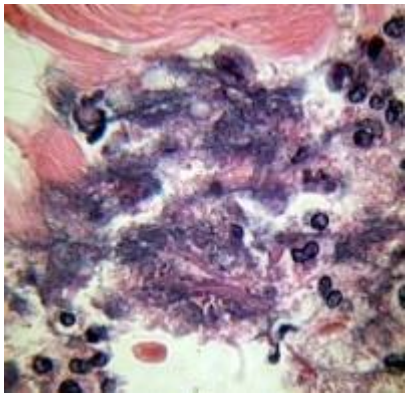
The Gram stain usually shows a polymicrobial flora with aerobic gram-negative rods and positive cocci when polymicrobial infection is present. However, in many cases, a single organism (eg, GABS, methicillin-

resistant Staphylococcus aureus[MRSA], Clostridium) may be causing the infection, while cultures, including blood cultures, may spuriously reveal a polymicrobial infection. The presence of plentiful cocci on the Gram stain is characteristic of necrotizing infection, whereas cocci are rarely identified in erysipelas.[71]

Polymicrobial infections are often associated with previous surgical procedures, pressure ulcers, penetrating trauma, perianal abscesses, and intravenous drug use. In the study by Andreasen et al, 71% of their patients had polymicrobial infections.[19]

Histologic Findings

Sections from necrotizing fasciitis tissue show superficial fascial necrosis with blood vessels occluded by thrombi. A dense infiltration of neutrophils may be observed in deeper parts of the subcutaneous tissue and fascia. Subcutaneous fat necrosis and vasculitis are also evident. Eccrine glands and ducts may be necrotic. Alcian blue or periodic acid-Schiff staining with diastase may show clusters of bacteria and fungi (see the image below).



TREATMENT AND MANAGEMENT

Approach Considerations

Once the diagnosis of necrotizing fasciitis is confirmed, treatment should be initiated without delay. Because of the complexity of this disease, a team approach is best. Hemodynamic parameters should be closely monitored, and aggressive resuscitation initiated immediately if needed to maintain hemodynamic stability.

Because necrotizing fasciitis is a surgical emergency, the patient should be admitted immediately to a surgical intensive care unit in a setting such as a regional burn centre or trauma centre, where the surgical staff is skilled in performing extensive debridement and reconstructive surgery. Such regional burn centres are ideal for the care of these patients because they also have hyperbaric oxygen facilities.

A regimen of surgical debridement is continued until tissue necrosis ceases and the growth of fresh viable tissue is observed. If a limb or organ is involved, amputation may be necessary because of irreversible necrosis and gangrene or because of overwhelming toxicity, which occasionally occurs. Prompt surgery ensures a higher likelihood of survival.

Antibiotic therapy is a key consideration. Possible regimens include a combination of penicillin G and an amino glycoside (if renal function permits), as well as clindamycin (to cover streptococci, staphylococci, gram-negative bacilli, and anaerobes).

While the literature appears to support the use of hyperbaric oxygen as an adjunctive treatment measure in patients with necrotizing fasciitis. However, transfer to a hospital equipped with a hyperbaric oxygen chamber should not delay emergency surgical intervention.

Surgical Debridement

Surgery is the primary treatment for necrotizing fasciitis. .Surgeons must be consulted early in the care of these patients, as early and aggressive surgical debridement of necrotic tissue can be life-saving.[4, 58, 72, 73, 74] In

addition, early surgical treatment may minimize tissue loss, eliminating the need for amputation of the infected extremity.[75,76]

It is recommended to do a wide, extensive debridement of all tissues that can be easily elevated off the fascia with gentle pressure. Wide debridement of all necrotic and poorly perfused tissues is associated with more rapid clinical improvement.

Controversy exists regarding how much tissue should be initially excised because the skin may often appear normal. Andreasen et al examined the normal-appearing tissues microscopically and reported that the tissues had extensive early vascular thrombosis as well as vasculitis.[19] Their findings indicate that these tissues, though they have a normal appearance, have a high potential for full-thickness loss.

After the initial debridement, the wound must be carefully examined. Hemodynamic instability is usually present after surgery, and it may cause progressive skin necrosis. After debridement, the patient may return as often as necessary for further surgical debridement. The anaesthesiologist is an important member of the operative team because continued resuscitative efforts are undertaken during the operative procedure.

The surgical regimen can be summarized as follows:

- Surgical incisions should be deep and extend beyond the areas of necrosis until viable tissue is reached
- The entire necrotic area should be excised
- The wound should be well irrigated
- Haemostasis should be maintained, and the wound should be kept open
- Surgical debridement and evaluations should be repeated almost on a daily basis
- The wound should be inspected in the operating room

Dressings

Following each debridement of the necrotic tissue, daily antibiotic dressings are recommended.[77] Silver sulfadiazine (Silvadene) remains the most popular antimicrobial cream. This agent has broad-spectrum antibacterial activity and is associated with relatively few complications in these wounds.

The current formulation of silver sulfadiazine contains a lipid-soluble carrier, polypropylene glycol, which has certain disadvantages, including pseudoeschar formation. When this antibacterial agent is formulated with poloxamer 188, the silver sulfadiazine can be washed easily from the wound

because of its water solubility, making dressing changes considerably more comfortable.

If the patient is allergic to sulpha, alternative agents include Polysporin, Bacitracin, and Bactroban. While these agents are relatively inexpensive, they may induce allergies.

Mafenide is an alternate agent that penetrates eschar more effectively than silver sulfadiazine. Consequently, it is frequently used on infected wounds that do not respond to silver sulfadiazine. Use mafenide with caution because it can induce metabolic acidosis.

Barrier dressings provide the beneficial antimicrobial properties of the silver ion by coating the dressing material with a thin, soluble silver film. This dressing appears to maintain antibacterial levels of silver ions in the wound for up to 5 days. Because these can remain on the wound for up to 5 days, the patient is spared the pain and expense associated with the dressing changes. Additional studies are now under way to determine the ultimate benefit of this product.

Soft-tissue reconstruction

Once all of the affected tissues have been debrided, soft tissue reconstruction can be considered. According to literature, this may take at least 2 debridements. When the debridement involves relatively small (< 25%) body surface areas, skin grafts and flaps can provide coverage. When donor-site availability is limited, alternatives to standard skin graft construction must be considered, including Integra artificial skin (Integra Life Sciences, Plainsboro, NJ) and AlloDerm (LifeCell Corporation, Blanchburg, NJ).[78, 79]

Antimicrobial Therapy

Empiric antibiotics should be started immediately. Initial antimicrobial therapy should be broad-based, to cover aerobic gram-positive and gram-negative organisms and anaerobes. A foul smell in the lesion strongly suggests the presence of anaerobic organisms. The maximum doses of the antibiotics should be used, with consideration of the patient's weight and liver and renal status.

Antibiotic therapy is a key consideration. Possible regimens include a combination of penicillin G and an amino glycoside (if renal function

permits), as well as clindamycin (to cover streptococci, staphylococci, gram-negative bacilli, and anaerobes).

A more specifically targeted antibiotic regimen may be begun after the results of initial gram-stained smear, culture, and sensitivities are available.

Although some necrotizing infections may still be susceptible to penicillin, clindamycin is the treatment of choice for necrotizing infections, for the following reasons[57] :

- Unlike penicillin, the efficacy of clindamycin is not affected by the inoculum size or stage of bacterial growth[80,81]
- Clindamycin is a potent suppressor of bacterial toxin synthesis[82, 83]
- Sub inhibitory concentrations of clindamycin facilitate the phagocytosis of GABS[51]
- Clindamycin reduces the synthesis of penicillin-binding protein, which, in addition to being a target for penicillin, is also an enzyme involved in cell wall synthesis and degradation[81]
- Clindamycin has a longer post antibiotic effect than β-lactams such as penicillin[83]
- Clindamycin suppresses lipopolysaccharide-induced mononuclear synthesis of tumour necrosis factor-α (TNF-α)[84]

Consequently, the success of clindamycin also may be related to its ability to modulate the immune response.[85]

Broad-spectrum beta-lactam drugs such as imipenem cover aerobes, including Pseudomonas species. Ampicillin sulbactam also has broad-spectrum coverage, but it does not cover Pseudomonas species; however, necrotizing fasciitis caused by Pseudomonas aeruginosa is unusual.[86]

If staphylococci or gram-negative rods are involved, vancomycin and other antibiotics to treat gram-negative organisms other than amino glycosides may be required. The use of vancomycin to treat methicillin-resistant Staphylococcus aureus (MRSA) may depend on the clinical situation. For example, use may depend on whether a nasocranial infection is present, or it may need to be avoided in patients who are likely to be carriers of MRSA (eg, those with diabetes, those who use illicit drugs, those undergoing haemodialysis).

Fluid, Nutritional Support, IVIG

Because of persistent hypotension and diffuse capillary leak, massive amounts of intravenous fluids may be necessary after the patient is admitted to the hospital. Nutritional support is also an integral part of treatment for

patients with necrotizing fasciitis. This supplementation should be initiated as soon as hemodynamic stability is achieved. Enteral feeding should be established as soon as possible to offset the catabolism associated with large open wounds.

Successful use of intravenous immunoglobulin (IVIG) has been reported in the treatment of streptococcal toxic shock syndrome (STSS).[87, 88] In a multicenter, randomized, double-blind, placebo-controlled trial of the efficacy and safety of high-dose polyspecific IVIG as adjunctive therapy in 21 patients with soft-tissue STSS, mortality at 28 days was 3.6-fold higher in the placebo group.[89]

Norrby-Teglund et al successfully used high-dose polyspecific IVIG, along with antimicrobials and a conservative surgical approach, in 7 patients with severe group A streptococcal soft tissue infections.[90] However, Sarani et al indicate that this therapy has not been approved by the FDA for the treatment of necrotizing fasciitis.[91]

Hyperbaric Oxygen Therapy

Once other modalities, including surgical debridement and antibiotic administration, have been used, hyperbaric oxygen therapy (HBOT) may be

considered, if available.[92, 40, 93] The literature suggests that HBOT can reduce mortality when used as part of an aggressive treatment regimen for necrotizing fasciitis.[94, 45, 95, 49, 96]

Well-controlled, randomized, clinical trials demonstrating a statistically significant benefit of HBOT are lacking, however, and consequently its use as an adjunctive therapy for necrotizing fasciitis remains controversial.[97, 98, 99] Transfer to a hospital equipped with HBOT should not delay emergency surgical intervention.

RECENT CONTROVERSIES

In the modern era, SSTIs were the focus of one of the first published clinical studies of an antibacterial agent[100], as well as one of the first active-controlled studies demonstrating the superiority of an antibacterial agent versus background medical therapy[101]. Given such a venerable and well-documented history, perhaps it is surprising that SSTIs have become such a dynamic—even contentious—contemporary topic.

Just in the last decade, the remarkable spread of methicillin-resistant Staphylococcus aureus (MRSA) as a cause of community-acquired infections has resulted in substantial changes in the epidemiology and treatment of SSTIs[102-106]. As a result, the frequency of health care visits and

antibacterial prescriptions for such infections has markedly increased[107]. Meanwhile, considerable controversy has arisen regarding the need to treat skin abscesses (including those caused by MRSA) with adjunctive antibacterial therapy, in addition to incision and drainage[108,109]. Such controversy has been exacerbated by the fact that most investigations exploring this issue have been highly underpowered and yet have still often shown trends toward a benefit of antibacterial therapy[109]. Furthermore, patients with complicated abscesses (eg, those accompanied by systemic signs of illness) have been excluded from such studies.

Another recent controversy has developed regarding the precise magnitude of the therapeutic benefit of antibacterial therapy for other forms of SSTIs, such as cellulitis and wound/ulcer infections[110,111] . This new controversy has resulted in a complete rethink of regulatory standards governing the conduct of clinical trials of new antibacterial agents for the treatment of complicated SSTIs. In the face of such dramatically changing clinical, scientific, and regulatory landscapes, new research in SSTIs is clearly needed to guide clinical practice, resolve scientific controversies, and create a framework for rational regulatory standards.

It is in this context that the importance of the study by Jenkins et al[112] that appears in this issue of Clinical Infectious Diseases should be appreciated. They systematically described the presentation, treatment, and outcomes of 322 cases of SSTIs at a comprehensive urban health care system in the United States during the year 2007. The high frequency of SSTIs seen during the year of study underscores the magnitude of the global societal problem. Furthermore, the authors described a general overuse of radiographic procedures (x-rays, computerized tomography, and magnetic resonance imaging scans) and laboratory testing (erythrocyte sedimentation rate and C-reactive protein) in patients with SSTIs. These tests resulted in very low diagnostic yields and thus likely substantially contributed to unnecessary health care expenditures related to SSTIs.

Another factor affecting health care resources was selection of antimicrobial therapy. Appropriately, empiric treatment against MRSA was administered to most patients. Of great concern, however, is that a high percentage of patients received treatment with broad-spectrum antibacterial agents that had activity against gram-negative bacilli and anaerobes. Such patients also often received combinations of 3 or more antibacterial agents. The vast majority of intact-skin SSTIs (including cellulitis and abscess) are

caused by streptococci and staphylococci[112,113]. Treatment of infections caused by such a narrow spectrum of etiologic microbes with combinations of multiple agents, including those with broad activity against gram-negative bacilli and anaerobes, is antithetical to critically needed antibacterial stewardship. Hence, there is much work to be done to improve antibacterial prescribing behaviours for SSTIs.

In previous years, cellulitis was considered by US Food and Drug Administration guidance to be indicative of an uncomplicated skin infection[114]. However, analysis of historical data has demonstrated that the mortality rate of cellulitis (or erysipelas as it was called before the 1950s) was ~11% in the preantibiotic era, underscoring that cellulitis is a complicated infection that is made relatively benign only in the context of effective antibacterial therapy[109]. Furthermore, while historical data do demonstrate a substantial effect of antibacterial therapy for wound infections and carbuncles/major abscesses, much of the available data are from historically controlled studies or a systematic review of single-armed cohort studies[109]. Therefore, the US Food and Drug Administration will likely allow only patients with cellulitis to be considered evaluable for primary efficacy analysis in future antibacterial clinical trials of complicated SSTIs,

and patients with complicated abscesses or wound/ulcer infections, in the absence of concomitant cellulitis of 5 cm in diameter, are likely to be excluded from such studies[110]. However, Jenkins and colleagues classified only 20% of SSTIs as cellulitis. Some additional cases of cellulitis were probably classified as SSTIs with additional complicating factors because of the presence of other cofactors, such as health care contact, bacteraemia, and significant co morbidities. Nevertheless, the overall proportion of SSTIs identified as cellulitis was low, and the majority of patients seen had other skin infections. Therefore, insistence that only patients with cellulitis be enrolled in future clinical trials of SSTIs will make completion of enrolment of such studies very difficult and will leave clinicians in the unacceptable position of not knowing the efficacy of new antibacterial agents for complicated abscesses and wound and ulcer infections—regulatory thinking on this matter should be readdressed.

The severity of the infections seen was also of crucial importance. For example, nearly 10% (10/103) of patients with abscesses as their SSTI manifestation were bacteraemia. This finding puts into sharp relief the debate regarding whether patients with cutaneous abscesses require adjunctive antibacterial therapy in addition to incision and drainage.

Adjunctive antibacterial therapy must not be withheld from patients who are potentially bacteraemia. Furthermore, the high rate of concomitant bacteraemia in patients with abscesses in the study by Jenkins and colleagues and the 6% mortality rate for complex abscesses in the preantibiotic era (which was largely due to sequelae from concomitant bacteraemia)[109] underscore that these infections indeed can be "complicated." Finally, the lack of mortality seen in the antibiotic era, including in the study by Jenkins and colleagues, underscores that antibacterial therapy is very effective in the treatment of complicated abscesses and that patients with these infections should be included in noninferiority studies of antibacterial therapy for SSTIs[109].

Limitations to the study by Jenkins and colleagues include the retrospective design, the lack of data capture on wound infections (resulting from the search criteria used), the commingling of severe SSTIs of several types within the broad category of SSTI with additional complicating factors, and the exclusion of paediatric data collection. Important information might have been gleaned by separately capturing data on cellulitis, wounds, ulcers, and abscesses and by analyzing these categories stratified by disease severity. Further study of SSTIs, including in children,

is greatly needed to advance clinical care, improve antibacterial stewardship, help reduce overuse of imaging and laboratory medical resources, and establish critical parameters in support of conduct of antibacterial clinical trials for these infections. Foci of study necessary to facilitate future antibacterial clinical trials include the following: quantification of the efficacy of active versus inactive antibacterial therapy for SSTI subtypes, establishment of a severity of illness scoring system for SSTIs, and identification of appropriate clinical end points for efficacy analysis.

Skin infections have been around ever since the invention of skin, have been written about by Homo sapiens for >2500 years, and have been studied in the context of antibacterial therapy since the discovery of antibacterial therapy. But these infections are ever evolving, and our understanding must evolve with them to facilitate optimal clinical care and rational investigation and use of antibacterial therapy for SSTIs.

PATIENTS AND METHODS

My study was conducted in the Department of general surgery, Rajiv Gandhi Government General hospital, Chennai for a period of 18 months from April 2012 to October 2013.

My study was to establish a scoring system to predict the outcome of a patient with non diabetic soft tissue infection of the lower limbs at admission using a multivariate analysis. My study also aims to determine the factors which increase the morbidity of a patient with a non diabetic soft tissue infection as determined by the no. Of days of hospital stay or limb loss or death of the patient.

Two hundred cases of non diabetic soft tissue infections of the lower limb were studied retrospectively and analysed statistically to determine the factors that altered the outcome. This analysis was then used to establish a scoring system which was then applied on fifty cases of non diabetic patients with soft tissue infections of lower limb at the time of their hospital admission to determine the mode of management.

SELECTION OF SUBJECT

All patients with soft tissue infections of the lower limbs including cellulitis, abscesses, necrotising fasciitis who were admitted to Rajiv Gandhi Govt. General Hospital during the study period were included.

EXCLUSION CRITERIA

Patients who were diabetics, either known cases or newly diagnosed were excluded from the study. Patients whose X-rays showed osteomyelitic changes were also excluded from the study. Patients who had prior surgeries for the same problem elsewhere were also excluded from the study.

DESIGN OF STUDY

Retrospective analysis on consecutive patients admitted and treated for non diabetic soft tissue infections of lower limbs, followed by a prospective analysis on consecutive patients admitted for non diabetic soft tissue infections.

STUDY POPULATION

Retrospective analysis included 200 patients who were admitted in Department of general surgery, Rajiv Gandhi Govt. General hospital during a period between April 2012 and April 2013. The prospective analysis

included 50 patients admitted with non diabetic soft tissue infection of lower limbs between May 2013 and October 2013.

METHODS

The following materials were evaluated in each patient included in the retrospective study

1. Clinical data
2. Laboratory data

The following variables were evaluated and compared between survivors and non survivors and also between those who underwent a limb salvaging procedure or an amputation.

1. Age in years
2. Gender of the patient
3. Duration of symptoms prior to admission in days
4. Co morbid conditions
5. Glasgow coma scale at admission
6. Presence of sepsis as determined by the presence of two or more of the following - fever/ hypothermia, raise/fall of total leukocyte count, tachycardia and tachypnoea
7. Requirement of ventilator support at admission

8. Requirement of ionotropic support at admission
9. Urea and creatinine at admission
10. Erythrocyte sedimentation rate at admission
11. Total bilirubin at admission
12. Surface area of body involved
13. Haemoglobin in gm% at admission
14. Depth of involvement

Because of the large number of potentially interdependent parameters examined in this retrospective analysis, it was believed that a more suitable test for significance would reside in a multivariate analysis, using a model of logistic regression analysis. From the large pool of univariately significant variables ($p < 0.05$), a smaller and more manageable group of 10 clinically relevant variables were selected for inclusion in the first step of the stepwise regression model. The selected parameters were age in years, duration of symptoms prior to admission in days, co morbid conditions, glasgow coma scale at admission, presence of sepsis as determined by the presence of two or more of the following - fever/ hypothermia, raise/fall of total leukocyte count, tachycardia and tachypnoea , requirement of ventilator support at

admission, requirement of ionotropic support at admission, surface area of body involved, haemoglobin in gm% at admission, depth of involvement.

The variables found on logistic regression analysis to significantly increase the risk of death or limb loss were used to form a scoring system. This score was then re applied to the retrospective study to analyze the actual outcome with the expected outcome. After taking the difference between the expected and actual outcomes into account, cut offs for the scoring system were established. This scoring system was then applied to a group of 50 patients and these patients were treated according to the score protocol. The results of this prospective study were then statistically analyzed.

DATA ANALYSIS:

To assess possible risk factors for morbidity and mortality, univariate analyses were completed initially to aid in determining the variables that should be included in a stepwise logistic regression model. Comparisons of proportions were made using Pearson's chi square statistic to identify univariate differences among defined variables with respect to mortality. Fisher's exact test for 2 X 2 tables was used in the small-sample case. For measured variables, the F statistic was used to compare means between survivors and non survivors. Clinically relevant variables were selected from

the large pool of variables with uni variate p values less than 0.05 for inclusion in the initial step of the logistic regression analysis. A p value of 0.05 also was chosen as the criterion by which to judge the entry and removal of variables at each step of the regression procedure. Results of the logistic regression analysis were expressed using beta coefficient values, odds ratios (defined as exp[coefficient]), and 90% confidence limits for the odds ratios. Statistical analysis was performed using SPSS software version 12.

RESULTS

A total of 200 cases which satisfied the inclusion criteria, admitted during a period of April 2012 to April 2013 were analysed retrospectively.

SAMPLE SIZE = 200 (n)

The following are the individual parameters studied

Age:

Age group – 14 years to 91 years

Mean Age of the Sample – 52.5 years

FIGURE (1)

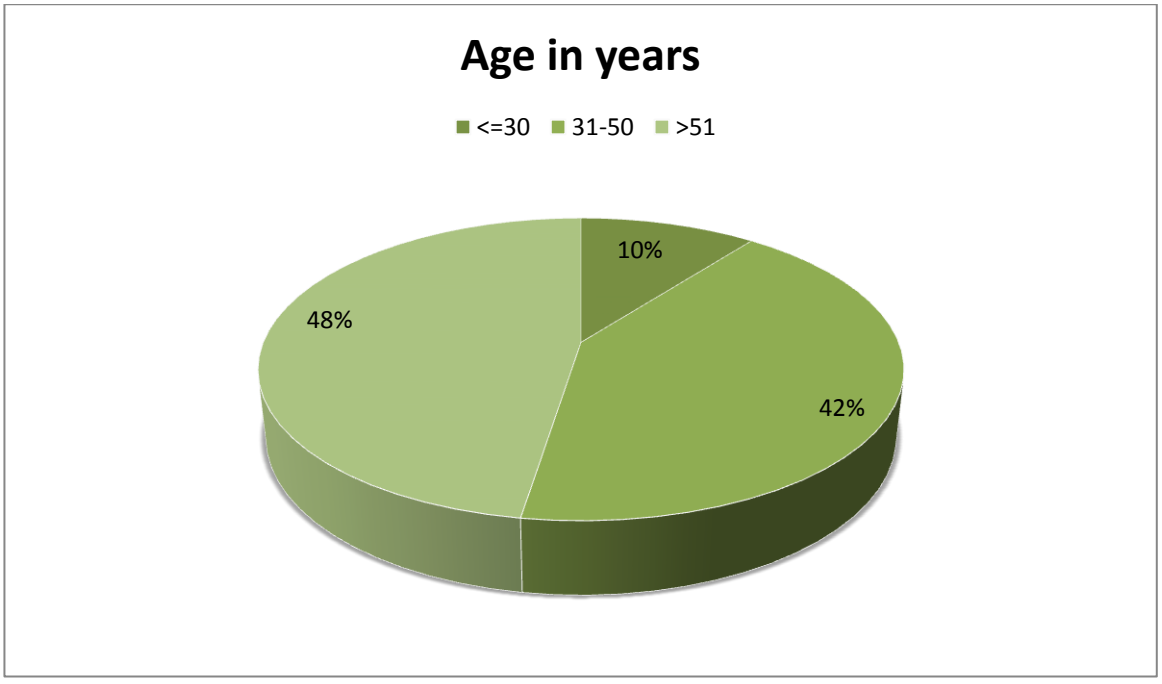
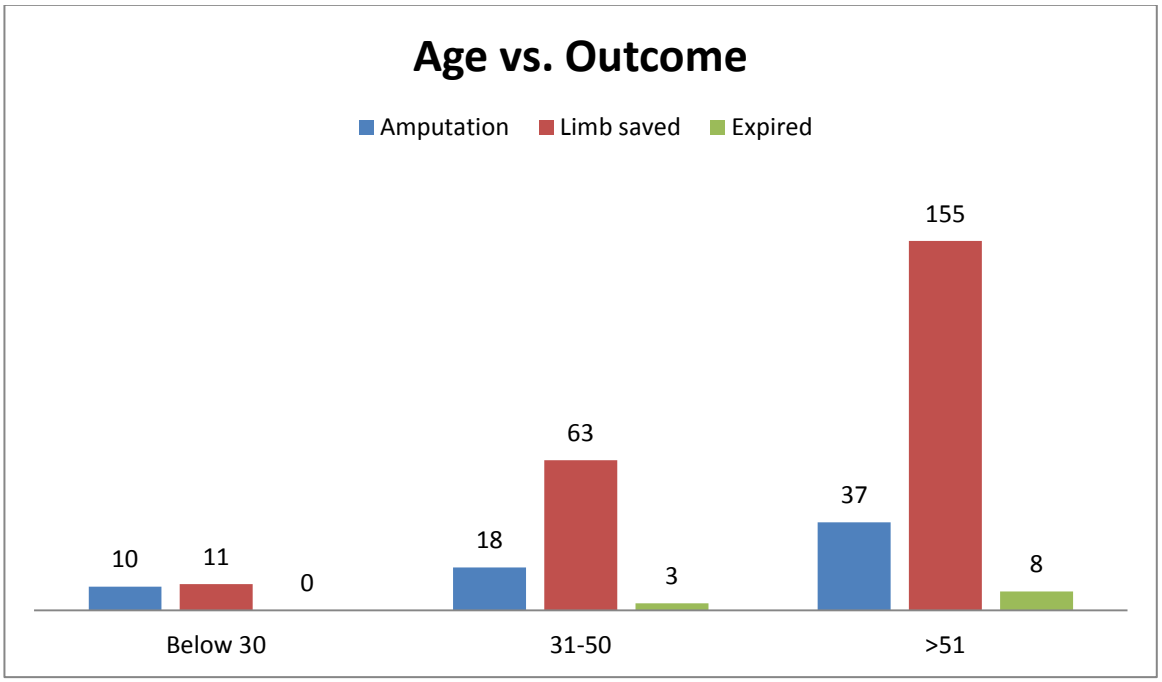


TABLE (1) Age grouping vs. outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
Age Group in years	Below 30	Count	10	11	0	21
		% within Age Group in years	47.6%	52.4%	.0%	100.0%
		% within Outcome	27.0%	7.1%	.0%	10.5%
	31-50	Count	18	63	3	84
		% within Age Group in years	21.4%	75.0%	3.6%	100.0%
		% within Outcome	48.6%	40.6%	37.5%	42.0%
	Above 50	Count	9	81	5	95
		% within Age Group in years	9.5%	85.3%	5.3%	100.0%
		% within Outcome	24.3%	52.3%	62.5%	47.5%
Total		Count	37	155	8	200
		% within Age Group in years	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation applied for age versus outcome of patient. P value found to be 0.001 (significant). Age grouping was done according to statistical significance, into three groups – less than 30 years, 31 – 50 years and more than 51 years.

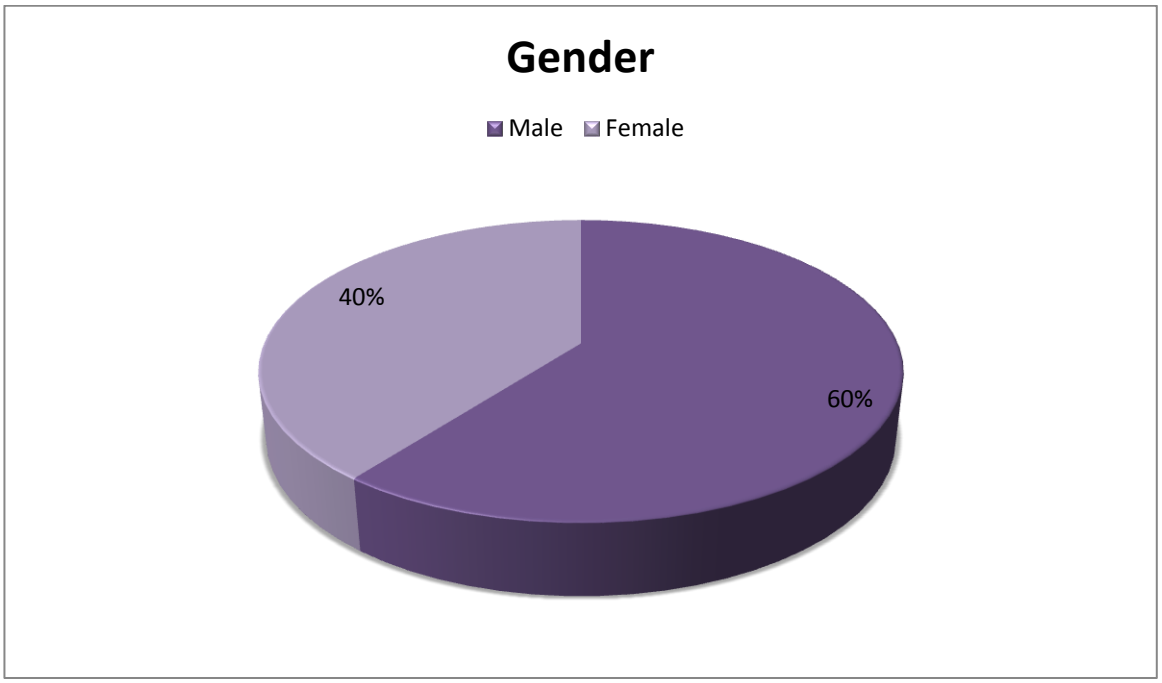
FIGURE (2)



Gender:

No. of male patients – 121, No. of female patients – 79

FIGURE (3)



Cross tabulation applied for sex versus outcome of patient. P value found to be 0.527 (not significant).

Distribution of duration of disease prior to hospital admission

Range – 1 day to 30 days

FIGURE (4)

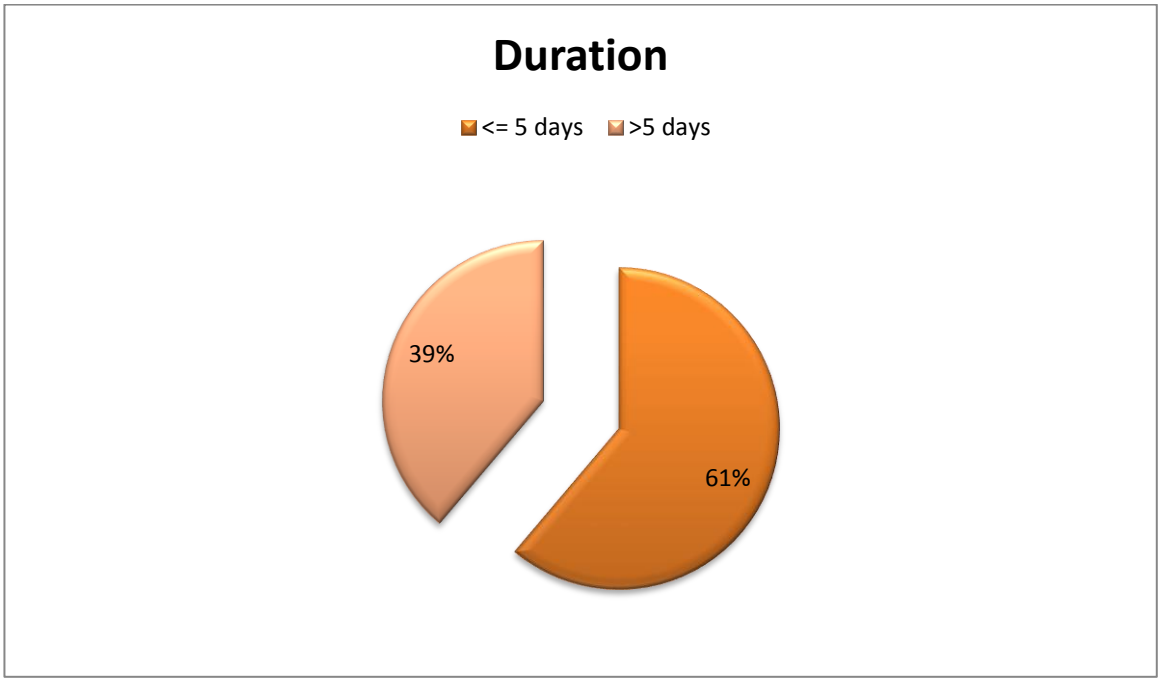
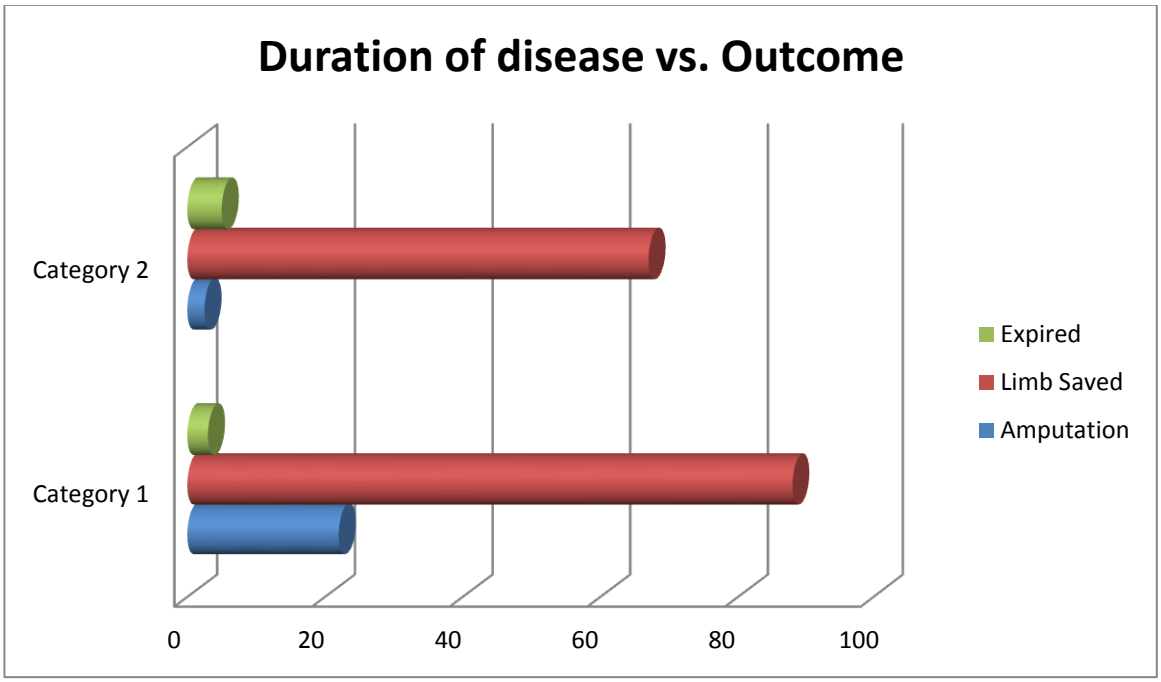


TABLE (2) Duration of disease vs. Outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
Duration in days	<= 5	Count	22	88	3	113
		% within Duration in days	19.5%	77.9%	2.7%	100.0%
		% within Outcome	59.5%	56.8%	37.5%	56.5%
	> 5	Count	15	67	5	87
		% within Duration in days	17.2%	77.0%	5.7%	100.0%
		% within Outcome	40.5%	43.2%	62.5%	43.5%
Total		Count	37	155	8	200
		% within Duration in days	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulations were done between duration of disease prior to admission and outcome. P value was found to be significant (<0.001). Duration grouping was done into two statistically significant groups of less than or equal to 5 days and more than 5 days.

FIGURE (5)



Distribution based on Glasgow Coma Scale (GCS)

GCS grouping was done according to statistical significance into three groups, less than or equal to 8, between 9 and 12 and greater than 13.

FIGURE (6)

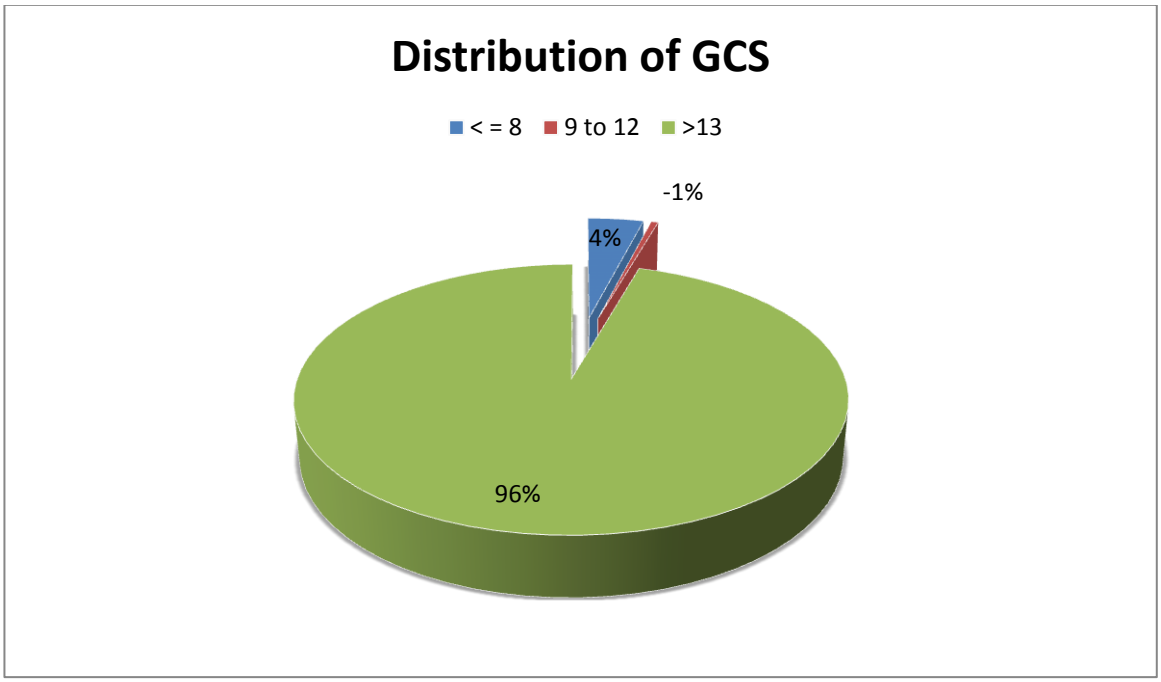
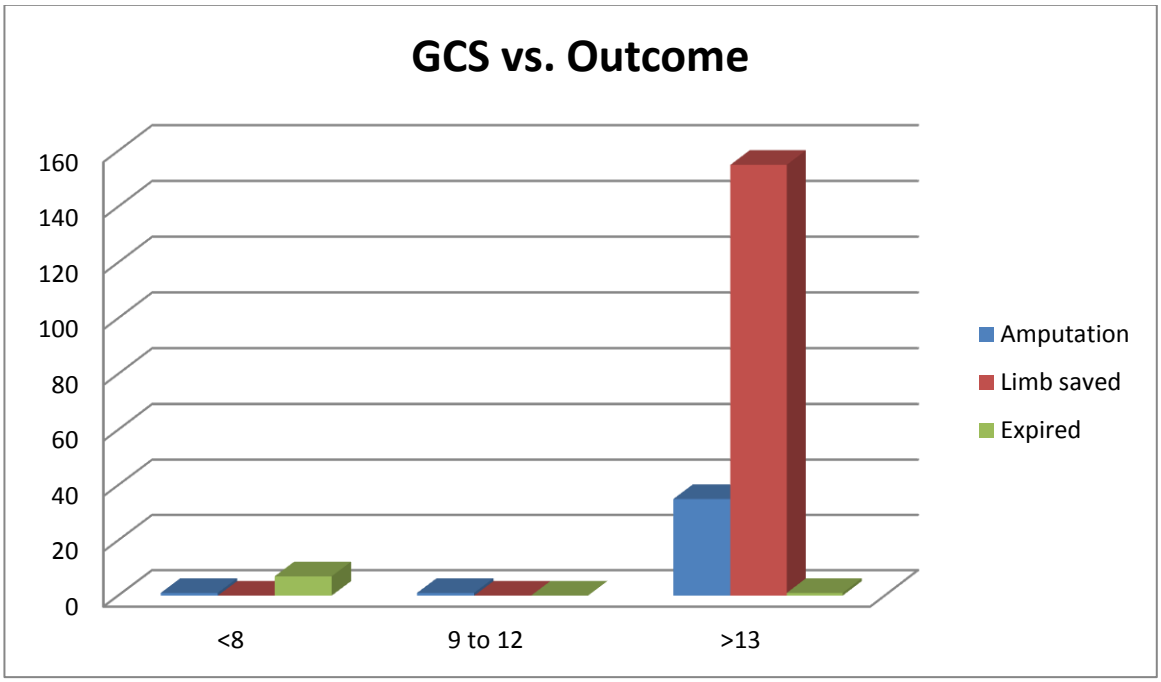


TABLE (3) GCS vs. Outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
GCS	<= 8	Count	1	0	7	8
		% within GCS	12.5%	.0%	87.5%	100.0%
		% within Outcome	2.7%	.0%	87.5%	4.0%
	9-12	Count	1	0	0	1
		% within GCS	100.0%	.0%	.0%	100.0%
		% within Outcome	2.7%	.0%	.0%	.5%
	> 12	Count	35	155	1	191
		% within GCS	18.3%	81.2%	.5%	100.0%
		% within Outcome	94.6%	100.0%	12.5%	95.5%
Total		Count	37	155	8	200
		% within GCS	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation applied for GCS vs. Outcome. P value found to be significant in all three groups (<0.001).

FIGURE (7)



Distribution of sepsis

The presence of sepsis was defined by the presence of two or more of

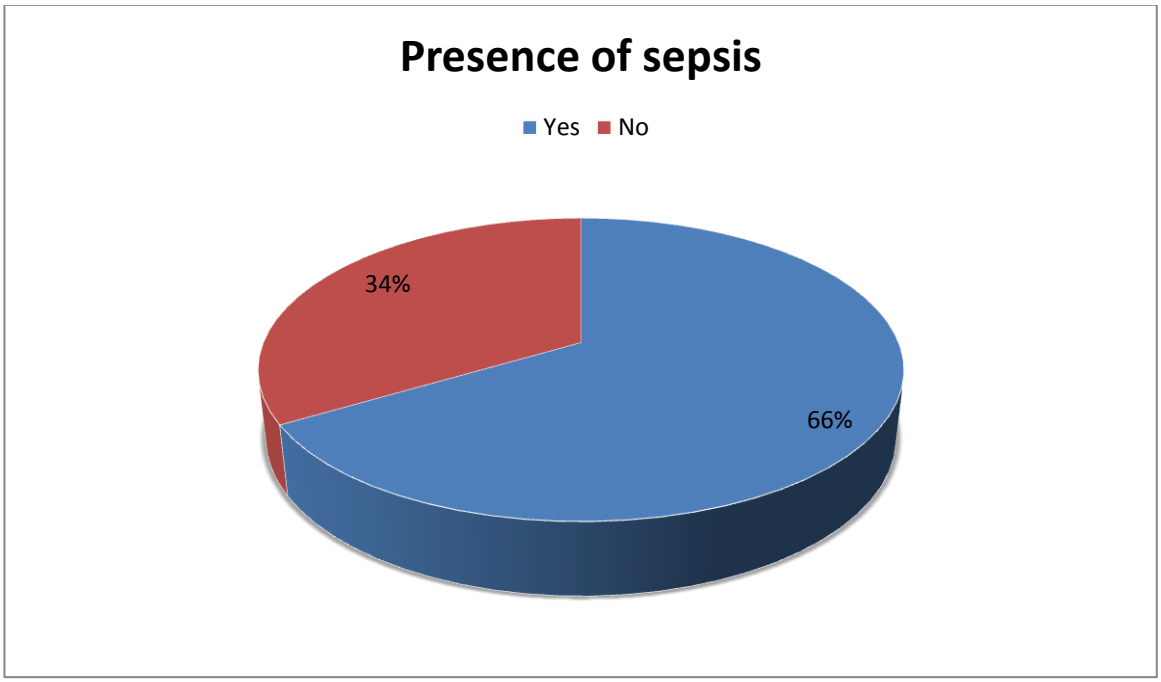
1) Temperature >38 or < 36 degree Celsius

2) Tachycardia

3) Tachypnoea

4) Leukocyte count >15,000/cumm or < 5,000/cumm

FIGURE (8)



Chi squared test showed a p value of 0.004 (significant).

Requirement of Ionotropic support

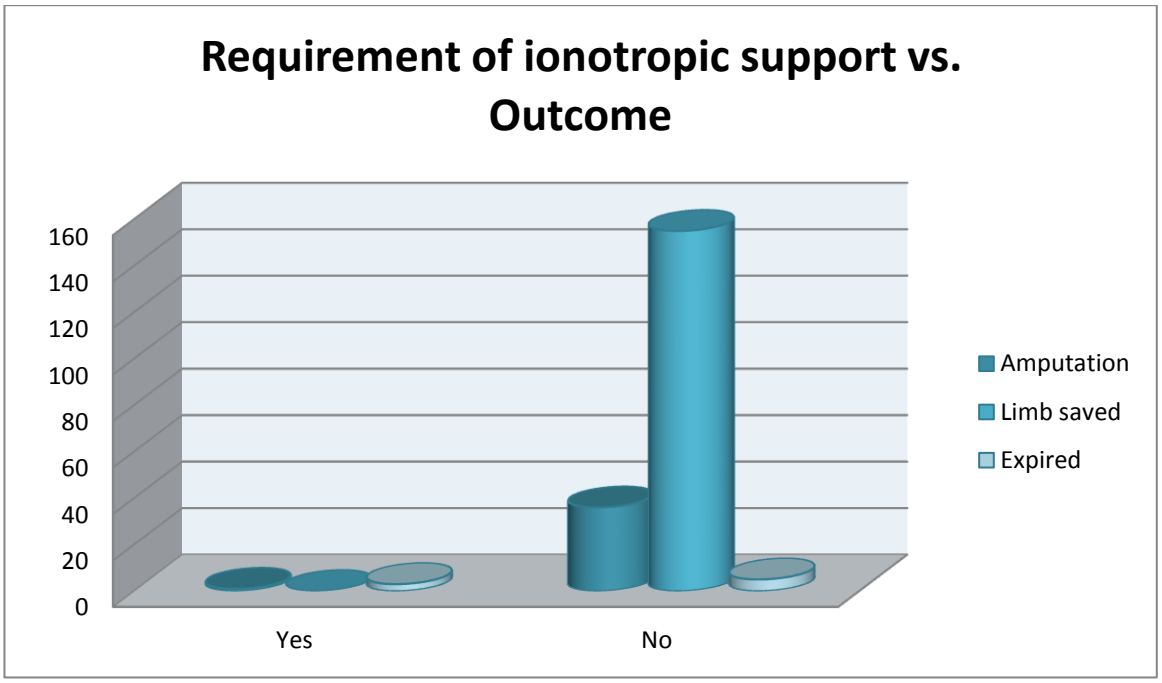
No. of patients who required ionotropic support – 4 (2%).

TABLE (4) Requirement of Ionotropic support vs. Outcome

			Outcome			Total
			Amputation	Limb Saved	Expired	
ION Support	Yes	Count	1	0	3	4
		% within ION Support	25.0%	.0%	75.0%	100.0%
		% within Outcome	2.7%	.0%	37.5%	2.0%
	No	Count	36	155	5	196
		% within ION Support	18.4%	79.1%	2.6%	100.0%
		% within Outcome	97.3%	100.0%	62.5%	98.0%
Total		Count	37	155	8	200
		% within ION Support	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulations between requirement of ionotropic support vs. Outcome was done. P value was <0.001 (significant).

FIGURE (9)



Requirement of ventilator support

No. of patients requiring ventilator support – 6 (3%).

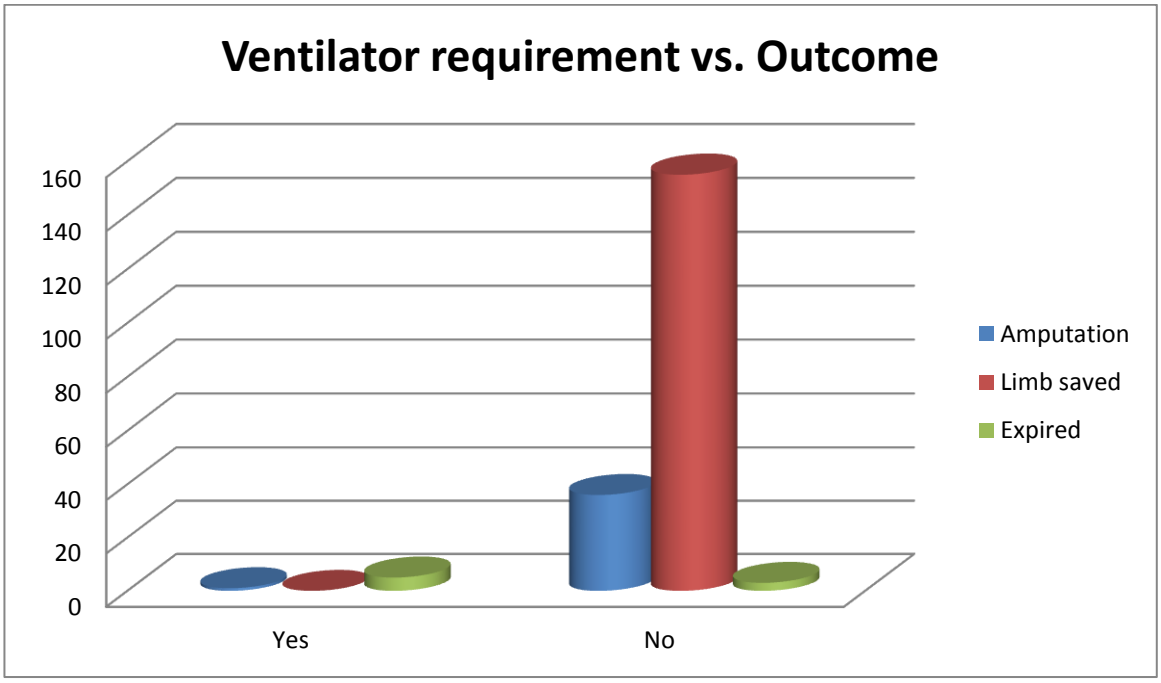
TABLE (5) Requirement of ventilator vs. Outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
Ventilator	Yes	Count	1	0	5	6
		% within Ventilator	16.7%	.0%	83.3%	100.0%
		% within Outcome	2.7%	.0%	62.5%	3.0%
	No	Count	36	155	3	194
		% within Ventilator	18.6%	79.9%	1.5%	100.0%
		% within Outcome	97.3%	100.0%	37.5%	97.0%
Total		Count	37	155	8	200
		% within Ventilator	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation between ventilator requirement and outcome was done.

P value was found to be <0.001(significant).

FIGURE (10)



Distribution of surface area involved

Body surface area (BSA) involved was assessed clinically using Wallace rule of nines (as for burns).

According to statistical significance surface area grouping was done into three - <10% of BSA, 10 – 30% of BSA and >30% of BSA involved.

FIGURE (11)

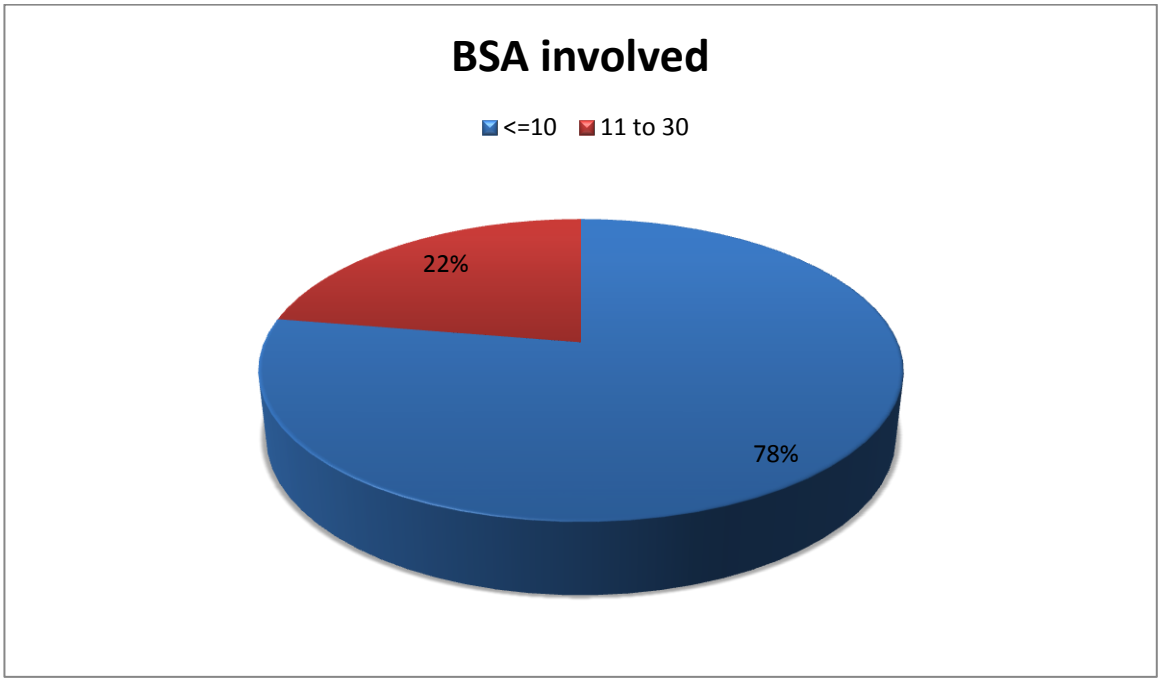
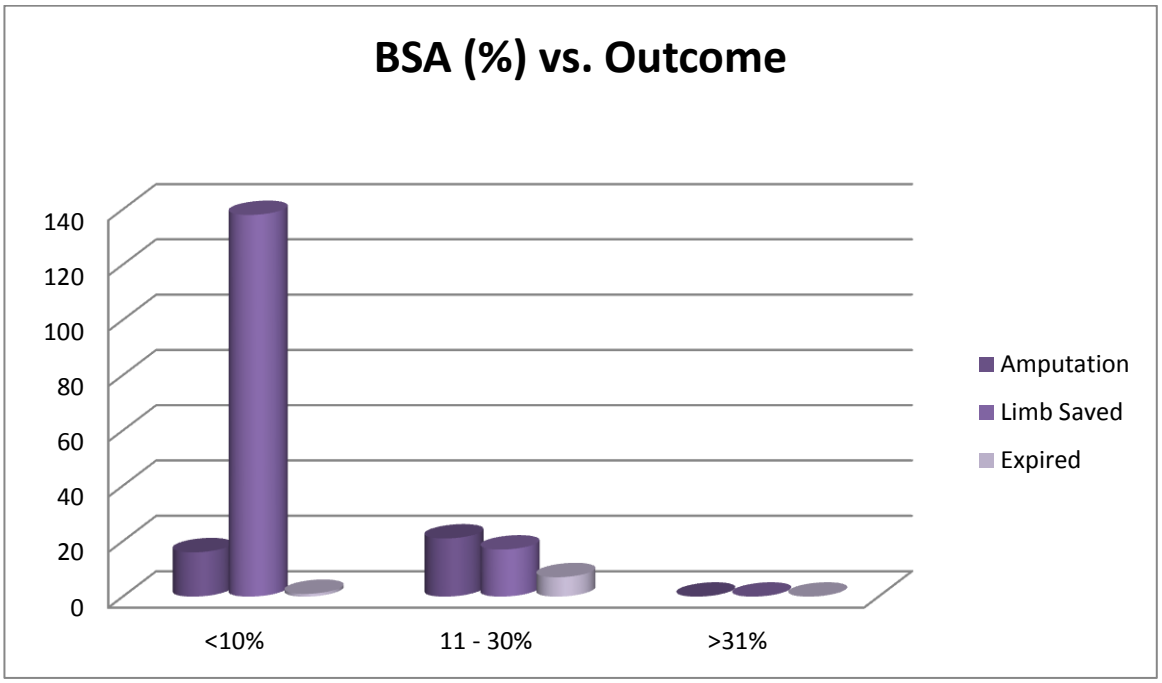


TABLE (6) BSA involved vs. Outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
SA%	<= 10	Count	16	138	1	155
		% within SA%	10.3%	89.0%	.6%	100.0%
		% within Outcome	43.2%	89.0%	12.5%	77.5%
	11-30	Count	21	17	7	45
		% within SA%	46.7%	37.8%	15.6%	100.0%
		% within Outcome	56.8%	11.0%	87.5%	22.5%
Total		Count	37	155	8	200
		% within SA%	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation was done between percentage of BSA involved and outcome. P value was found to be <0.001 (significant).

FIGURE (12)



Distribution of depth of involvement

No. of cases of cellulitis (skin) – 100 (50%)

No. of cases of necrotising fasciitis (sub cutaneous) – 95 (47.5%)

No. of cases of pyomyonecrosis (muscle) – 5 (2.5%)

FIGURE (13)

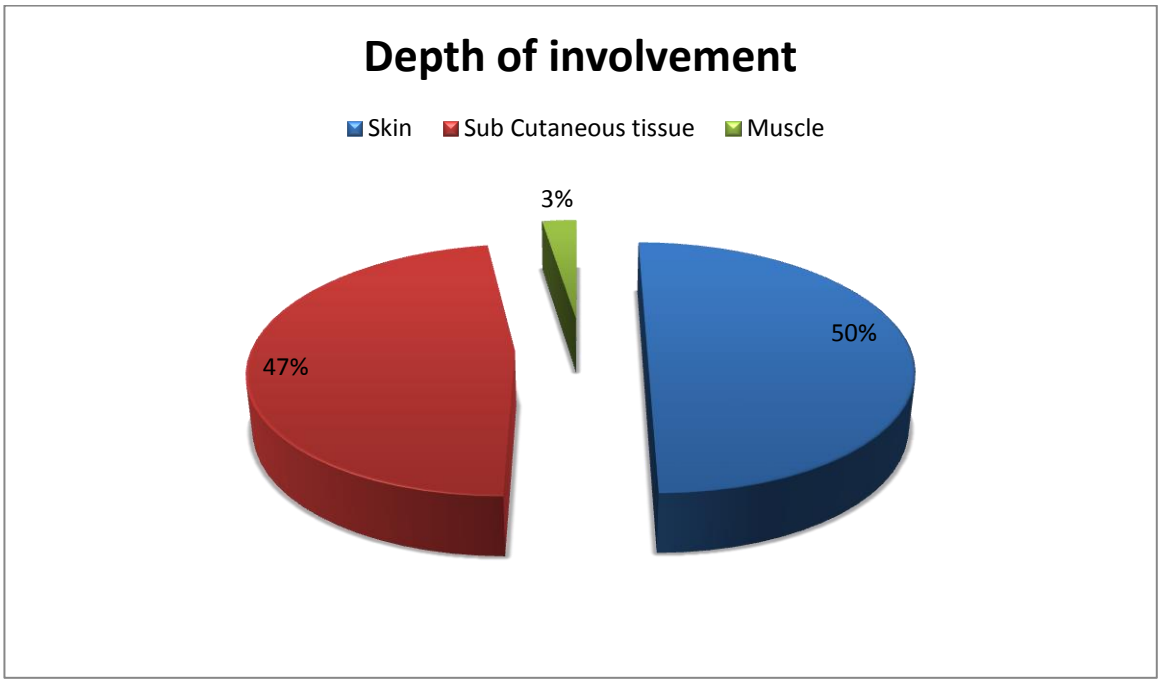
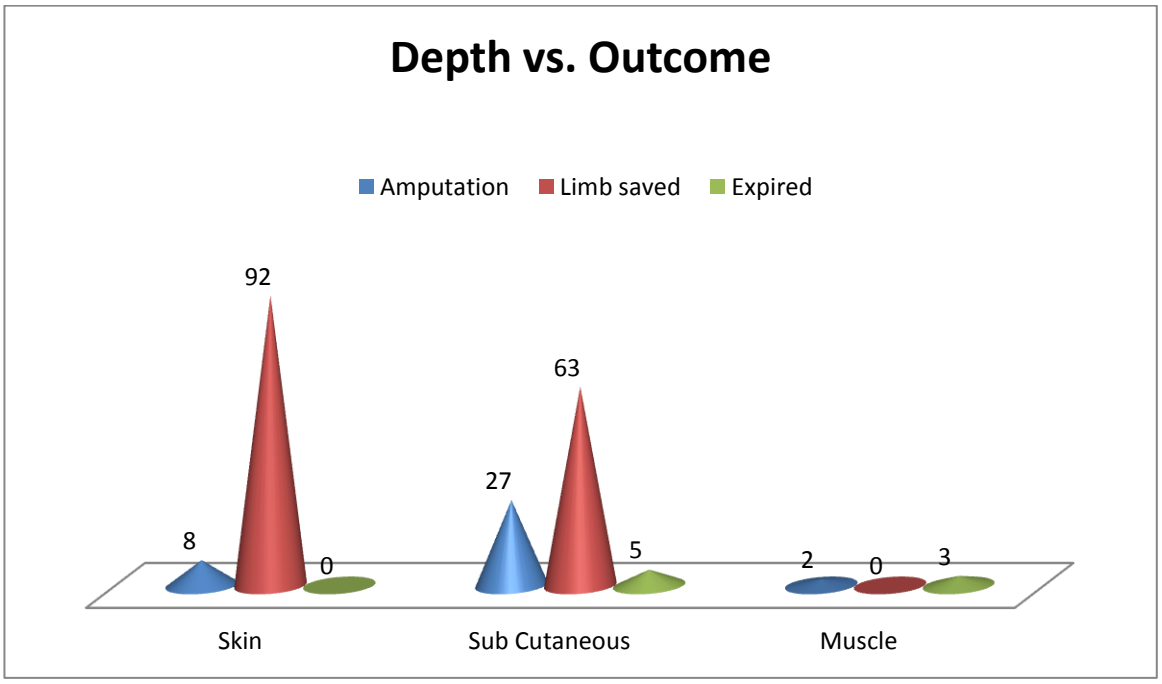


TABLE (7) Depth of involvement vs. Outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
Depth	Skin	Count	8	92	0	100
		% within Depth	8.0%	92.0%	.0%	100.0%
		% within Outcome	21.6%	59.4%	.0%	50.0%
	Sub cut	Count	27	63	5	95
		% within Depth	28.4%	66.3%	5.3%	100.0%
		% within Outcome	73.0%	40.6%	62.5%	47.5%
	Muscle	Count	2	0	3	5
		% within Depth	40.0%	.0%	60.0%	100.0%
		% within Outcome	5.4%	.0%	37.5%	2.5%
Total		Count	37	155	8	200
		% within Depth	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation between various depths of involvement and outcome was done. P value was found to be <0.001 (significant).

FIGURE (14)



Distribution of Co morbidities

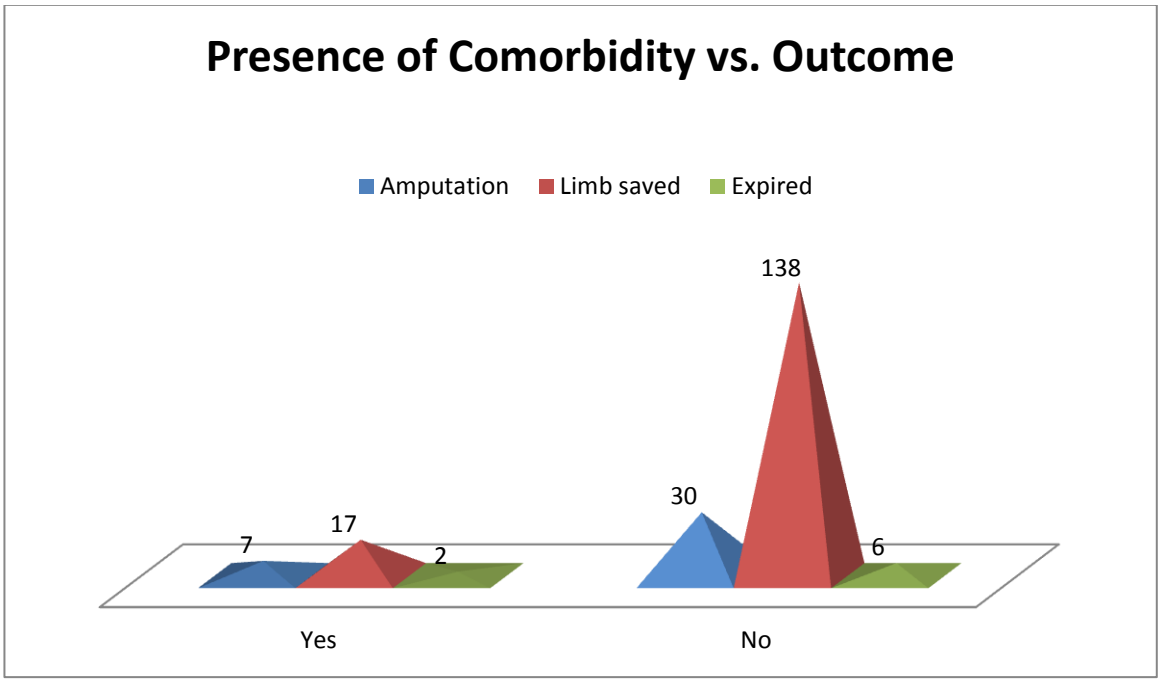
Presence of co morbidities other than diabetes mellitus was taken into consideration. Presence of more than one co morbidity statistically altered the outcome.

TABLE (8) Presence of do morbidity vs. Outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
Co-morbidity	Yes	Count	7	17	2	26
		% within Co-morbidity	26.9%	65.4%	7.7%	100.0%
		% within Outcome	18.9%	11.0%	25.0%	13.0%
	No	Count	30	138	6	174
		% within Co-morbidity	17.2%	79.3%	3.4%	100.0%
		% within Outcome	81.1%	89.0%	75.0%	87.0%
Total		Count	37	155	8	200
		% within Co-morbidity	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation done between presence of co morbidity and outcome done. P value found to be 0.025 (significant).

FIGURE (15)



Distribution on Haemoglobin

Patients grouped based on haemoglobin into two groups - <=8 and >8

FIGURE (16)

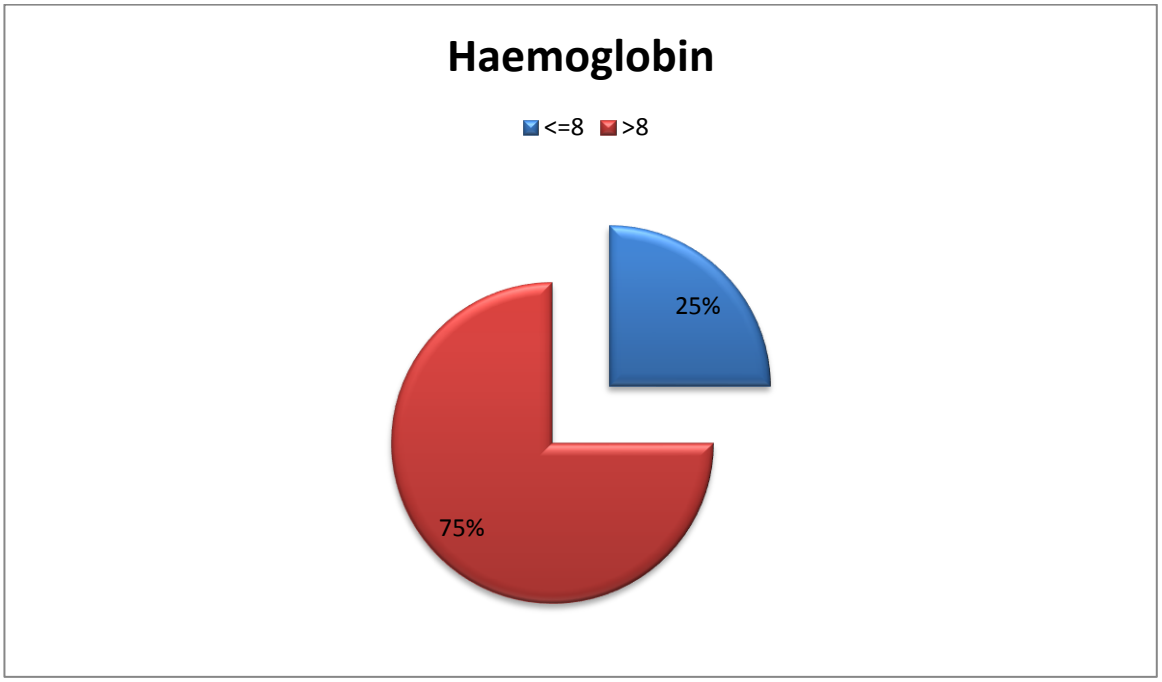
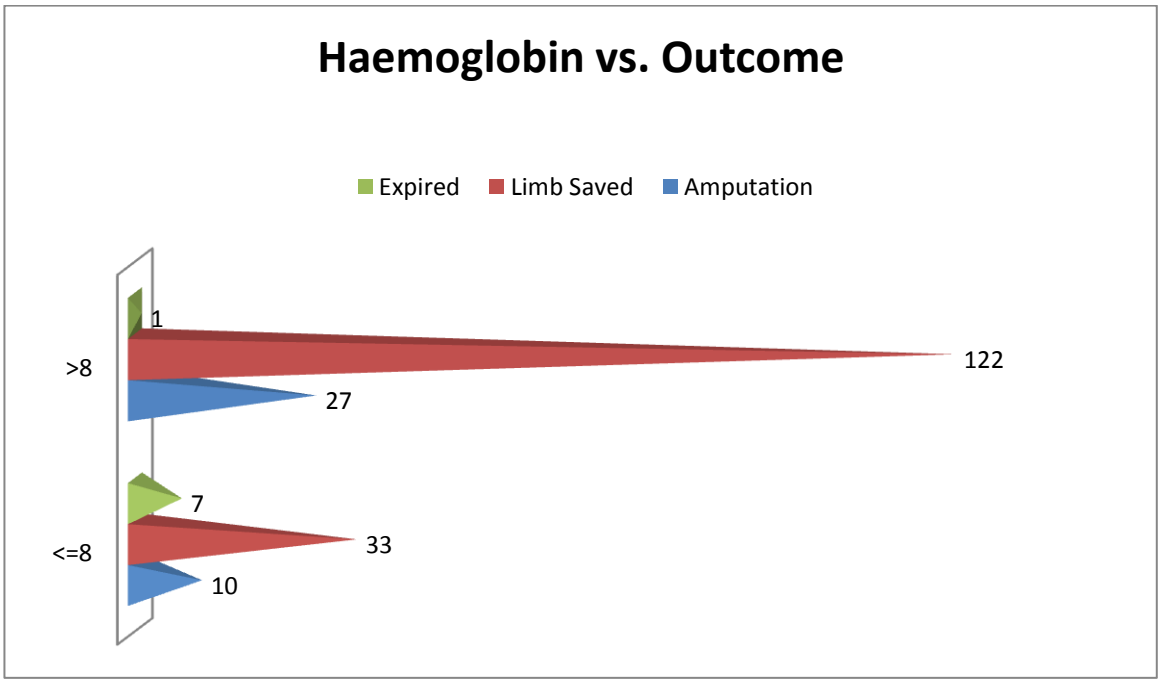


TABLE (9) Haemoglobin vs. Outcome

			Outcome			Total
			Amputation	Limb Saved	Expired	
Hb	<= 8	Count	10	33	7	50
		% within Hb	20.0%	66.0%	14.0%	100.0%
		% within Outcome	27.0%	21.3%	87.5%	25.0%
	> 8	Count	27	122	1	150
		% within Hb	18.0%	81.3%	.7%	100.0%
		% within Outcome	73.0%	78.7%	12.5%	75.0%
Total		Count	37	155	8	200
		% within Hb	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation showed the p value was <0.001(significant)

FIGURE (17)



Distribution of Erythrocyte Sedimentation Rate (ESR)

Distribution of ESR among the study population was not found to statistically alter the outcome of the patient. P value was found to be 0.255, statistically not significant.

Distribution of Urea/ Creatinine

Distribution of urea and creatinine among study population was not found to statistically alter the outcome of the patient. P value was found to be 0.576, statistically not significant.

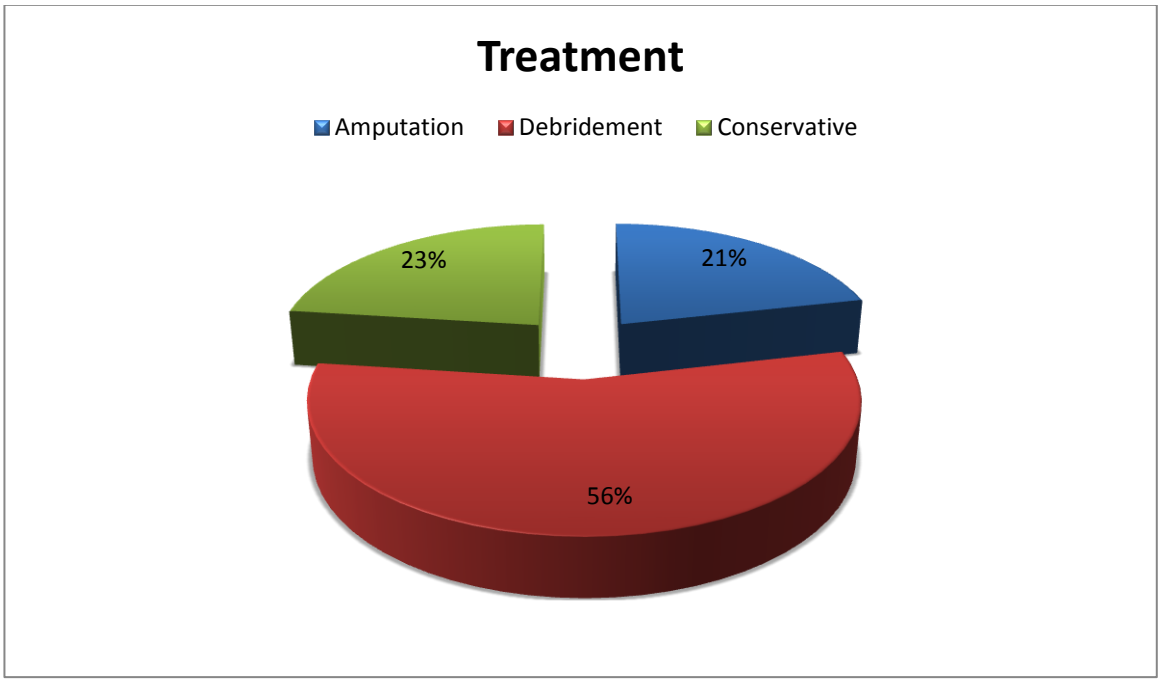
Distribution of Total Bilirubin

Distribution of total bilirubin among the study population was not found to statistically alter the outcome of the patient. P value was found to be 0.764, statistically not significant.

Treatment

All 200 patients in the study were treated either conservatively (46) or by debridement (111) or by amputation (43).

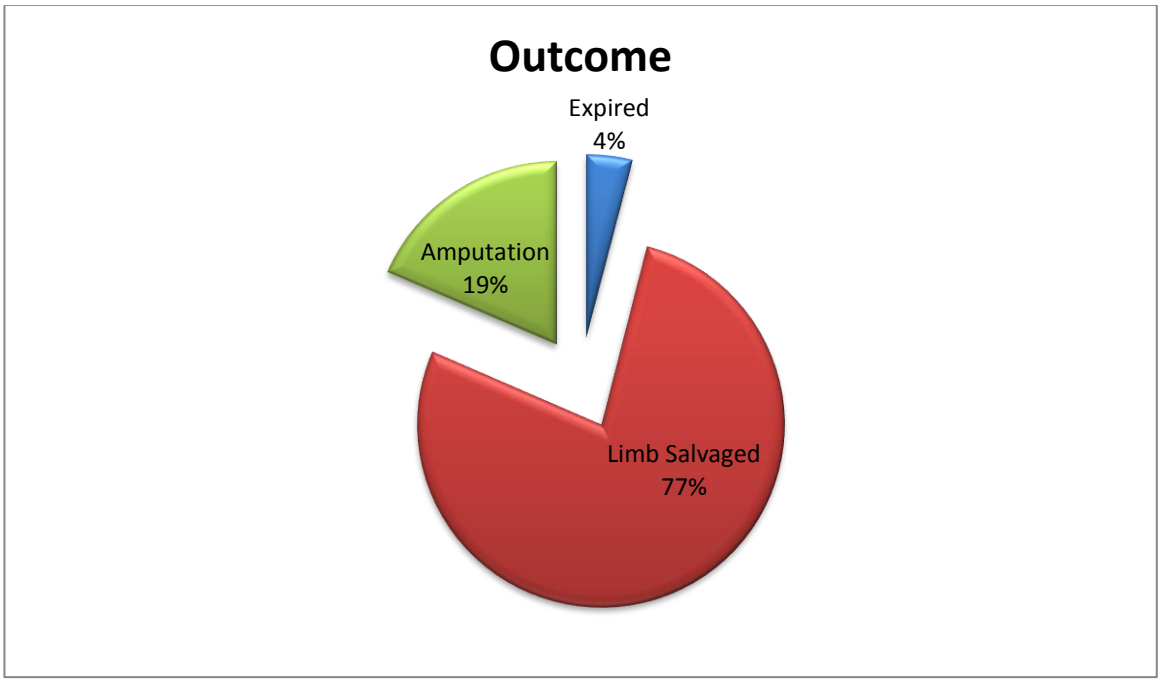
FIGURE (18)



Outcome

The outcome of the 200 patients was analysed and defined by the mortality or the morbidity (amputation/ duration of hospital stay).

FIGURE (19)

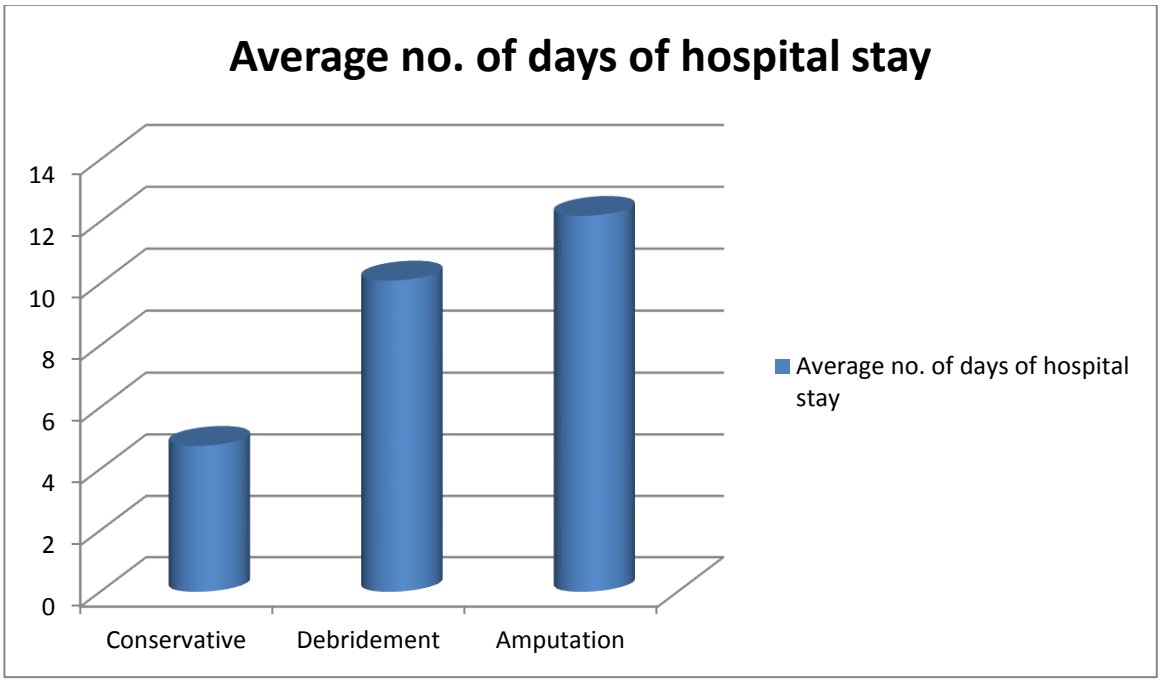


Outcome vs. Hospital stay

The average hospital stay required per patient varied according to the outcome. Patients treated by conservative treatment had an average hospital stay of 4.76 days. Patients treated by debridement had an average hospital stay of 10.1 days. Patients treated by amputation had an average hospital stay of 12.19 days.

Overall average number of days of hospital stay – 8.01 days.

FIGURE (20)



Outcome vs. No. of surgeries

The average no. of surgeries required per patients also varied according to the outcome. Patients who underwent debridement required an average of 2.27 surgeries per person. Patients who underwent an amputation required an average of 2.67 surgeries per patient with one patient requiring 4 surgeries (three debridements followed by amputation).

TABLE (10) No. of surgeries vs. Outcome

			Outcome			
			Amputation	Limb Saved	Expired	Total
No. of Surgeries	Nil	Count	0	46	0	46
		% within No. of Surgeries	.0%	100.0%	.0%	100.0%
		% within Outcome	.0%	29.7%	.0%	23.0%
	1	Count	19	82	4	105
		% within No. of Surgeries	18.1%	78.1%	3.8%	100.0%
		% within Outcome	51.4%	52.9%	50.0%	52.5%
	2	Count	15	26	4	45
		% within No. of Surgeries	33.3%	57.8%	8.9%	100.0%
		% within Outcome	40.5%	16.8%	50.0%	22.5%
	3	Count	2	1	0	3
		% within No. of Surgeries	66.7%	33.3%	.0%	100.0%
		% within Outcome	5.4%	.6%	.0%	1.5%
	4	Count	1	0	0	1
		% within No. of Surgeries	100.0%	.0%	.0%	100.0%
		% within Outcome	2.7%	.0%	.0%	.5%
Total		Count	37	155	8	200
		% within No. of Surgeries	18.5%	77.5%	4.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation showed that the p value was <0.001 (significant).

A total of 200 patients' records were thus analysed.

MULTIVARIATE ANALYSIS

Logistic regression analysis demonstrated that the following factors were independent predictors of outcome in non diabetic patients with soft tissue infections.

TABLE (11)

SL NO.	FACTOR	P VALUE
1.	AGE (YEARS)	<0.001
2.	DURATION OF DISEASE (DAYS)	<0.001
3.	PRESENCE OF CO MORBID CONDITIONS	0.025
4.	GCS	<0.001
5.	PRESENCE OF SEPSIS(as defined above)	0.004
6.	REQUIREMENT OF VENTILATOR	<0.001
7.	REQUIREMENT OF IONOTROPIC SUPPORT	<0.001
8.	BODY SURFACE AREA INVOLVED (%)	<0.001
9.	HAEMOGLOBIN (gm %)	<0.001
10.	DEPTH OF INVOLVEMENT	<0.001

Based on these parameters a scoring system was devised using the above ten mentioned parameters and scores were allotted according to the statistical groupings done earlier. The following was the proposed scoring system.

TABLE (12)

SL NO.	CRITERION	1	2	3
1.	AGE (YEARS)	<30	30-50	>50
2.	DURATION OF SYMPTOMSPRIOR TO ADMISSION(DAYS)	<5	>5	
3.	COMORBIDITIES	1	2	>2
4.	GCS	15	9-14	<9
5.	PRESENCE OF SEPSIS		YES	
6.	VENTILATORY SUPPORT		YES	
7.	IONOTROPIC SUPPORT		YES	
8.	BODY SURFACE AREA	<10%	10-20%	>20%
9.	HB (gm %)	>8	</=8	
10.	DEPTH OF INVOLVEMENT	CELLULTIS	EVOLVING NF	NF/MYONECROSIS

This scoring system was re applied to the 200 patients in the retrospective study and the outcomes were analysed.

The following were the results:

Conservative treatment:

No. of patients - 46

Among the 46 patients, 44 had a score of less than 13 and only 2 patients had a score of 14. The average no. of days of hospital stay in this group was 4.76 days.

Patients who underwent debridement:

No. of patients – 111

Among the 111, the least score was 12 (2 patients), and the maximum score was 19 (17 patients). Majority of patients had a score of 17 and 18 (42 each). Average no. of surgeries undergone per patient was 2.27. Average no. of days of hospital stay in this group was 10.1 days. Among this group 2 patients expired and both had a score of 19.

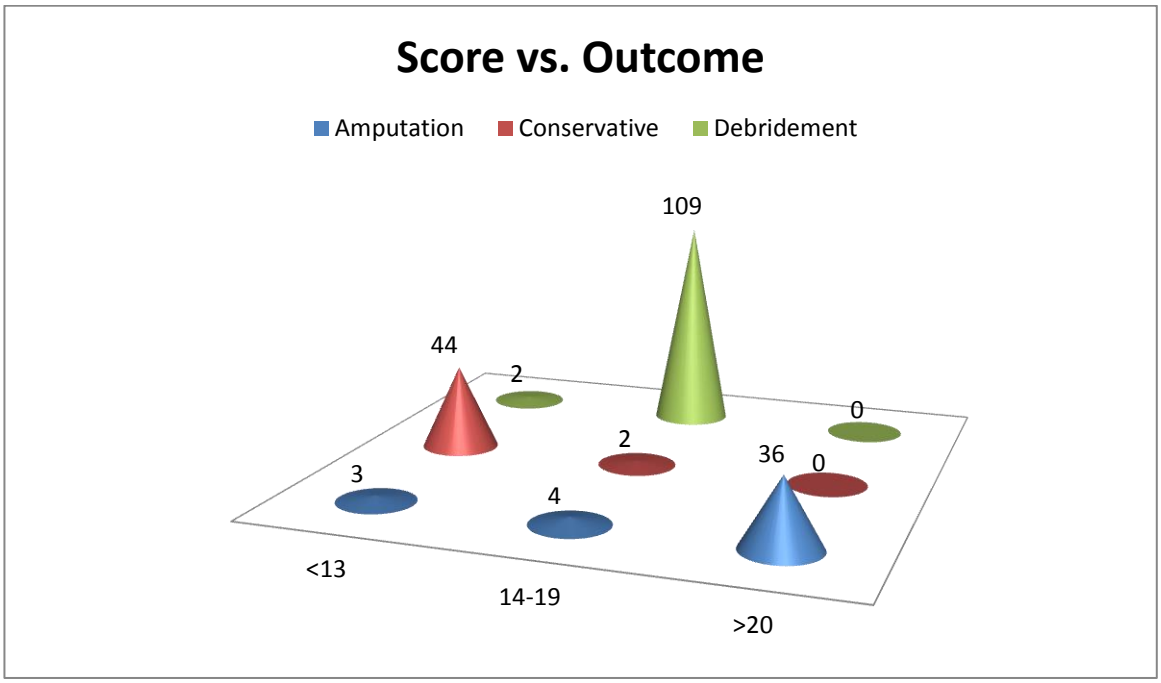
Patients who underwent amputation:

No. of patients – 43

Among the 43 patients, the minimum score was 13 (3 patients) and maximum score was 24 (6 patients). Majority of patients had a score of 21

(22 patients). Average no. of surgeries per patient was 2.67 and average no. of days of hospital stay was 12.19 days. Among this group 6 patients expired, one with a score of 24 and 5 with a score of 22.

FIGURE (21)



Based on this evaluation cut offs were established for the scoring system. Any patient with a score less than or equal to 13 would be treated conservatively. Any patient with a score between 14 and 19 would be treated with extensive debridement and any patient with a score greater than or equal to 20 would undergo an amputation.

This scoring system was then applied prospectively on a group of 50 patients who were admitted to the hospital from May 2013 to October 2013. The following were the results.

Score vs. Outcome

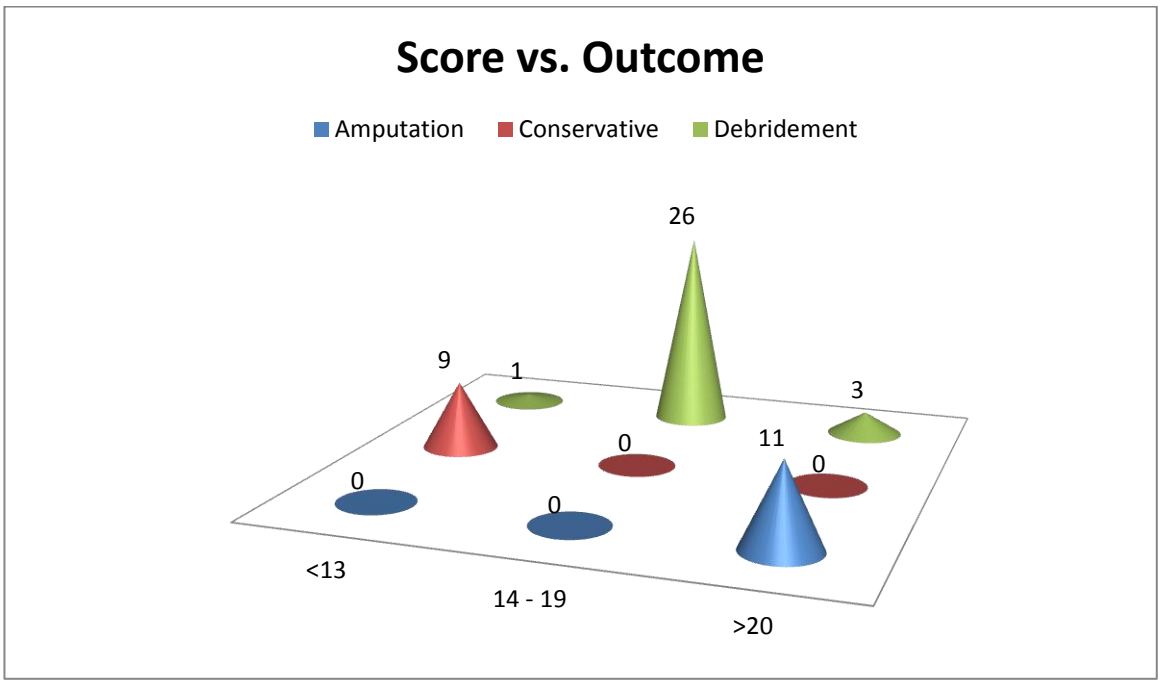
The scores of 50 patients was cross tabulated with the outcomes.

TABLE (13) Score vs. Outcome

			Outcome			
			Amputation	Conservative	Debridement	Total
Score	<= 13	Count	0	9	1	10
		% within Score	.0%	90.0%	10.0%	100.0%
		% within Outcome	.0%	100.0%	3.3%	20.0%
	14-19	Count	0	0	26	26
		% within Score	.0%	.0%	100.0%	100.0%
		% within Outcome	.0%	.0%	86.7%	52.0%
	> 19	Count	11	0	3	14
		% within Score	78.6%	.0%	21.4%	100.0%
		% within Outcome	100.0%	.0%	10.0%	28.0%
Total		Count	11	9	30	50
		% within Score	22.0%	18.0%	60.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation showed a p value of <0.001, which was statistically significant.

FIGURE (22)



Outcome vs. No. of surgeries

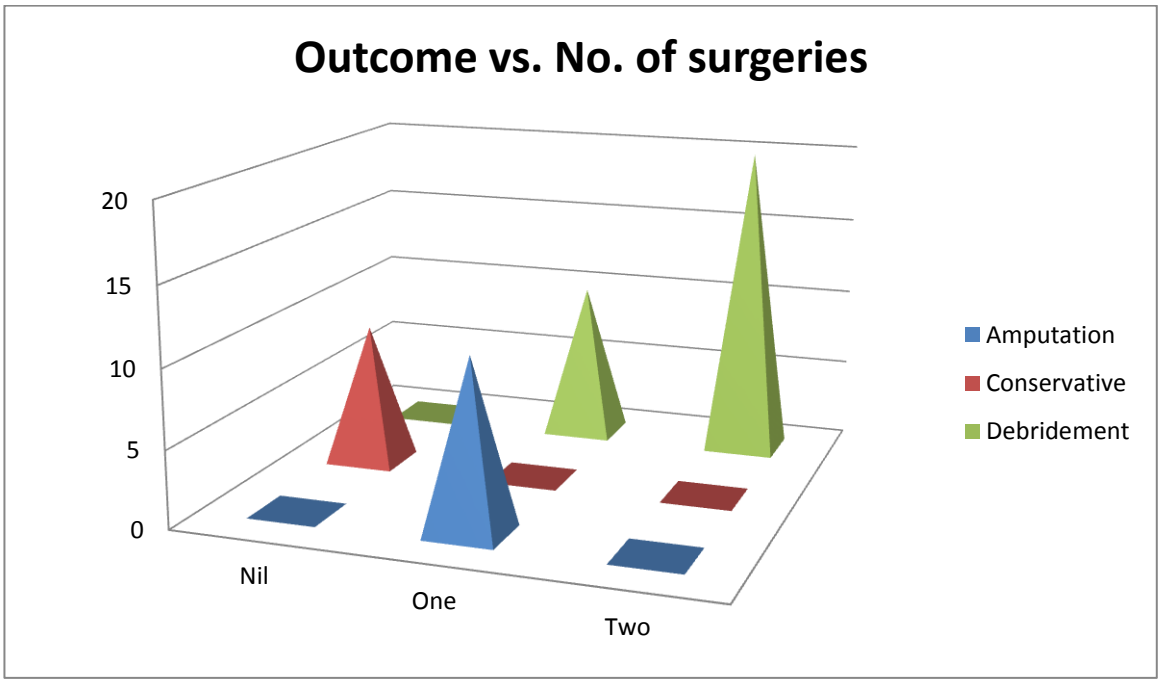
The no. of surgeries required per patient was cross tabulated with the outcome. No patient underwent more than 2 procedures.

TABLE (14) Outcome vs. No. of surgeries

			Outcome			
			Amputation	Conservative	Debridement	Total
No. of Surgeries	Nil	Count	0	9	0	9
		% within No. of Surgeries	.0%	100.0%	.0%	100.0%
		% within Outcome	.0%	100.0%	.0%	18.0%
	1	Count	11	0	10	21
		% within No. of Surgeries	52.4%	.0%	47.6%	100.0%
		% within Outcome	100.0%	.0%	33.3%	42.0%
	2	Count	0	0	20	20
		% within No. of Surgeries	.0%	.0%	100.0%	100.0%
		% within Outcome	.0%	.0%	66.7%	40.0%
Total		Count	11	9	30	50
		% within No. of Surgeries	22.0%	18.0%	60.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulations showed the p value was <0.001 which was statistically significant.

FIGURE (23)



Average no. of surgeries per person in patients undergoing debridement was found to be 1.67.

Average no. of surgeries per person in patients undergoing amputation was found to be 1.0.

Study of outcome vs. Hospital stay

TABLE (15) Oneway test – Descriptive

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Amputation	8	9.00	1.512	.535	7.74	10.26	7	12
Conservative	5	5.00	.707	.316	4.12	5.88	4	6
Debridement	23	11.35	2.308	.481	10.35	12.35	7	15
Total	36	9.94	2.976	.496	8.94	10.95	4	15

The test showed that the average no. of days of hospital stay in a patient undergoing conservative treatment was 5 days, undergoing debridement was 11.35 days, and undergoing amputation was 9 days.

TABLE (16) ANOVA - Hospital stay

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	174.671	2	87.336	21.314	<0.001
Within Groups	135.217	33	4.097		
Total	309.889	35			

The ANOVA test showed that procedure undergone by the patient determined the hospital stay of the patient.

TABLE (17) Post Hoc Tests - Multiple Comparisons

Dependent Variable: Hospital Stay

(I) Outcome	(J) Outcome	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Amputation	Conservative	4.00(*)	1.154	.004	1.17	6.83
	Debridement	-2.35(*)	.831	.021	-4.39	-.31
Conservative	Amputation	-4.00(*)	1.154	.004	-6.83	-1.17
	Debridement	-6.35(*)	.999	.000	-8.80	-3.90
Debridement	Amputation	2.35(*)	.831	.021	.31	4.39
	Conservative	6.35(*)	.999	.000	3.90	8.80

Multiple comparisons through post hoc test showed that inter group comparisons were statistically significant. (all p values <0.05).

Mortality vs. Procedure done

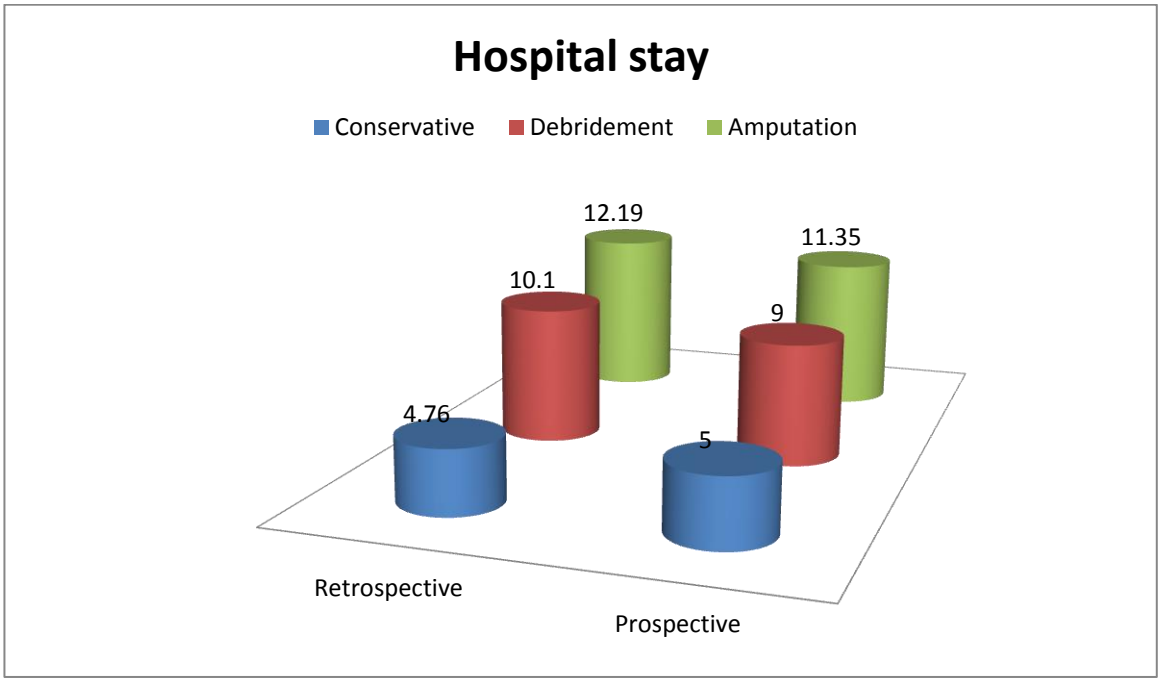
TABLE (19) Procedure done vs. Mortality

			Outcome			Total
			Amputation	Conservative	Debridement	
Mortality	Yes	Count	3	0	7	10
		% within Mortality	30.0%	.0%	70.0%	100.0%
		% within Outcome	27.3%	.0%	23.3%	20.0%
	No	Count	8	9	23	40
		% within Mortality	20.0%	22.5%	57.5%	100.0%
		% within Outcome	72.7%	100.0%	76.7%	80.0%
Total		Count	11	9	30	50
		% within Mortality	22.0%	18.0%	60.0%	100.0%
		% within Outcome	100.0%	100.0%	100.0%	100.0%

Cross tabulation was done and p value was found to be 0.244 (not significant). Therefore the procedure per se is not directly responsible for the mortality of the patient, but preoperative condition of the patient is the determining factor. The mortality was found to be 20%.

Comparison of hospital stay in the retrospective and prospective study:

FIGURE (24)



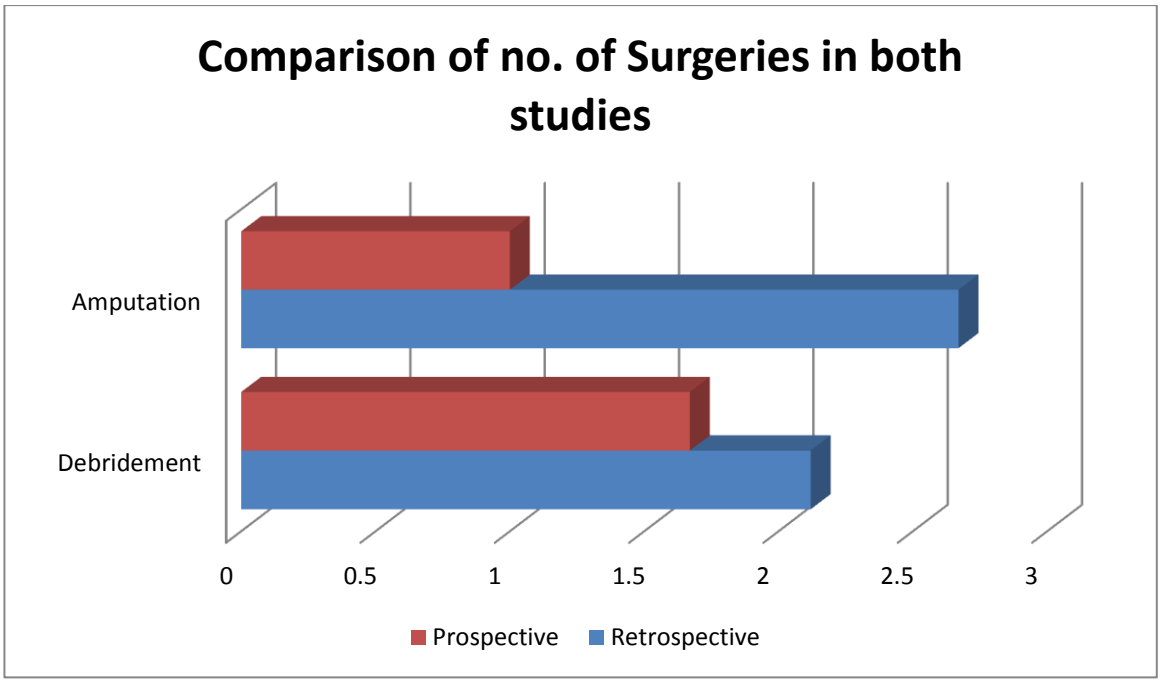
Cross tabulation done between no. of days of hospital stay in each group in the retrospective study to the prospective study. P value in all cases was not statistically significant.

TABLE (20)

	RETROSPECTIVE STUDY	PROSPECTIVE STUDY	P VALUE
CONSERVATIVE	**4.76**	**5**	**0.472 (not significant)**
DEBRIDEMENT	**10.1**	**9**	**0.142(not significant)**
AMPUTATION	**12.19**	**11.35**	**0.576(not significant)**

Comparison of no. of surgeries undergone per person in retrospective and prospective study:

FIGURE (25)



Cross tabulation done between the no. of surgeries in retrospective and prospective studies and the outcome.

TABLE (21)

Treatment				Study		
				Retrospective study	Prospective study	Total
Amputation	No. of Surgeries	1	Count	23	11	34
			% within No. of Surgeries	67.6%	32.4%	100.0%
			% within Study	53.5%	100.0%	63.0%
		2	Count	17	0	17
			% within No. of Surgeries	100.0%	.0%	100.0%
			% within Study	39.5%	.0%	31.5%
		3	Count	2	0	2
			% within No. of Surgeries	100.0%	.0%	100.0%
			% within Study	4.7%	.0%	3.7%
		4	Count	1	0	1
			% within No. of Surgeries	100.0%	.0%	100.0%
			% within Study	2.3%	.0%	1.9%
	Total		Count	43	11	54
			% within No. of Surgeries	79.6%	20.4%	100.0%
			% within Study	100.0%	100.0%	100.0%
Debridement	No. of Surgeries	1	Count	82	10	92
			% within No. of Surgeries	89.1%	10.9%	100.0%
			% within Study	73.9%	33.3%	65.2%
		2	Count	28	20	48
			% within No. of Surgeries	58.3%	41.7%	100.0%
			% within Study	25.2%	66.7%	34.0%
		3	Count	1	0	1
			% within No. of Surgeries	100.0%	.0%	100.0%
			% within Study	.9%	.0%	.7%
	Total		Count	111	30	141
			% within No. of Surgeries	78.7%	21.3%	100.0%
			% within Study	100.0%	100.0%	100.0%

P value for the first group (amputation) was 0.043 and for the second group (debridement) was <0.001. The comparison was statistically significant

showing that there is a statistically significant decrease in the no. of surgeries undergone by each patient in both the groups.

DISCUSSION

Necrotizing soft tissue infections of the skin have been reported to have a high morbidity and mortality. In 1924, Meleney[115] noted a mortality rate of 20% out of 20 patients. The mortality rate of 20% in the present series is slightly lower than the cumulative mortality of 34% as reported in the Mchenry et al. study[116]. Wong et al.[117], in their series of 89 patients, 70% involving lower limbs, have a mortality rate of 21.3%. Singh et al.,[118] in their series of 55 patients (31 involving lower limbs) reported a mortality of 27.2%. Tang et al.,[119] with 24 patients with necrotizing fasciitis of the limbs, in which 12 involved the lower limbs, reported a mortality of 33.3%. As we know necrotizing fasciitis of the lower limbs are more amenable for local control as amputation can be performed to control the local effect of the disease, whereas necrotizing fasciitis that involves trunk and genitourinary systems is more difficult to control since wound debridement hindered and not as thorough because it involves vital organs. Thus, lower limb involvement gives a more favourable outcome and a lower mortality rate.

In the current study, we studied various parameters which are considered risk factors for morbidity and mortality by various authors.

Several authors[56][20][19] reported that patients above the age of 60 were associated with higher mortality. Our study showed that an age above 51 years increased the morbidity and mortality of the patients. Other confounding factors must be taken into consideration as elderly patients are predisposed to illnesses such as diabetes mellitus and renal failure and their immunological status is generally poorer, all of which may contribute to the higher mortality rate. According to our study gender of the individual did not contribute to morbidity or mortality, contrary to results reported by Elliot *et al.* [120]. Initial presentation of necrotizing fasciitis is easily confused with other milder soft tissue infections such as cellulitis which require only a conservative treatment approach. Unfortunately, this can delay definitive treatment of debridement or amputation. According to our study a duration of greater than five days duration between initial symptoms and surgical procedure is associated with a higher rate of morbidity and mortality similar to the results of Eckmann *et al.* [121], who that noted those with a duration of initial symptoms to surgical treatment of more than 5 days were associated with a higher mortality rate. Although little can be done to influence the time between a patient development of symptoms and receipt of medical attention except to increase public awareness through education, measures can be

taken to hasten the diagnosis and early operative debridement. Wong *et al.* [117] developed a screening system for necrotizing fasciitis with a high predictive value that is helpful in making an early diagnosis, leading to situations where definitive treatment can be carried out as early as possible.

The presence of sepsis at the time of admission was defined by the presence of two or more of the following, increase or decrease of body temperature, increase or decrease of total leukocyte count, tachycardia and tachypnoea. There was significant effect of temperature on admission on morbidity and mortality in the present study, similar to results published by Bosshardt *et al.* [122] in which high admission temperature was identified as a risk factor of mortality. We did not find that admission blood pressure affected mortality, contrary to reports by Bosshart et al. and Fustes-Morales *et al.* who identified low blood pressure as a determinant for mortality [122][123]. The presence of co morbid condition apart from Diabetes mellitus was found to significantly contribute to the morbidity and mortality as was seen in the study by Brand *et al.* and Elliot *et al.* [121][116]. The consciousness of the patient as assessed by the Glasgow coma scale at the time of admission showed that a GCS of less than 13 affected the morbidity and mortality adversely, more so if the GCS was less than 8. This was similar to the results

of Darke *et al.*[124] who showed that a GCS of less than 7 significantly affected the mortality. The surgical literature has been divided regarding the impact of extent of infection on survival; in this study, patients with less extensive infection, expressed in terms of body surface area involved (much as for burns), had a definite survival advantage, whereas such an association was not borne out in the study of 57 patients with Fournier's gangrene by Clayton et al.[125]. Similarly depth of infection adversely affected the mortality in our study. But there are no similar results in any of the published studies. In many other published reports, no instances of myonecrosis were even reported; in others, it was rare.[122][124] . Among the lab parameters that were studied, haemoglobin was found to adversely affect the morbidity and mortality if it was less than 8. This was similar to the results published by Patino et al.[126]. According to our study blood urea, serum creatinine, erythrocyte sedimentation rate or total bilirubin values at the time of admission were not significant contributory factors to morbidity and mortality.

The scoring system established by our study did not affect mortality. The usage of the scoring system in the prospective study showed a significant reduction in the number of procedures required by a patient. Even

though the usage of the scoring system showed a decrease in the number of days of hospital stay, the decrease was not statistically significant.

CONCLUSION

Skin and soft tissue infections of the limbs have a high mortality and morbidity especially if necrosis is present. The morbidity is in the form of prolonged hospital stay and limb loss. Our study does not show any change in the percentage of people undergoing an amputation, but it does show a decrease in hospital stay for the same patients, even though it is not statistically significant. Since our sample size is small, this aspect of the study might require more evaluation with a larger sample size to get statistically significant results. Further the retrospective study showed that patients underwent multiple procedures and sometimes required an amputation after said procedures. Our prospective study showed a statistically significant decrease in the number of procedures undergone per patient. Therefore the scoring system may be used to decrease the number of procedures undergone by a patient and thereby decrease psychological stress to the patient and help in saving unnecessary hospital expenditure. Although our study has showed a statistical significance in decreasing the number of procedures required by a patient at admission, it requires further detailed studies to produce repeated significant results. This is essential for the scoring system to be applied as an established protocol. Our current study is also limited by the small sample size of the prospective pool. Diabetes

mellitus has been identified as co-morbidity in most large studies conducted. Since our study excludes this co morbidity, further evaluation will be needed to maybe modify the scoring system including Diabetes as one of the variables.

Our study also does not take into account the delay between admission and surgery which according to certain studies[122] alters the morbidity and mortality. We did not have data in our retrospective study which described the adequateness of debridement and therefore we have not described the criteria which would signify an adequate debridement in our prospective study. Establishing fixed criteria for the same might help decrease the number of procedures further. This requires further study with large sample sizes.

The biggest short coming would perhaps be the fact that we did not include microbiology of the infection in our study as the same was not available in all the cases studied retrospectively, and according to Wong et al.[122] this variable significantly alters the outcome. In conclusion, if validated, this prediction system may improve patient outcomes by reducing unnecessary procedures and unnecessary wastage of hospital revenue and man power. Except for those patients with overwhelming risk factors for

dying at the time of admission (e.g., more than 4 organ systems in failure combined with profound metabolic acidosis), aggressive resuscitation, surgical debridement, and intensive care results in survival for three fourths of the patients presenting with necrotizing soft tissue infections.

PROFORMA

NAME: AGE: IP NO.

D.O.A: D.O.D:

HISTORY:

COMPLAINTS:

DURATION OF SYMPTOMS PRIOR TO ADMISSION:

H/S/O SEPSIS:

COMORBID CONDITIONS:

TREATMENT HISTORY:

EXAMINATION:

GCS: PR: BP:

TEMP.: ICTERUS:

SYSTEMS: CVS: P/A:

RS: CNS:

LOCAL EXAMINATION:

SURFACE AREA INVOLVED:

DEPTH OF INVOLVEMENT:

INVESTIGATIONS:

CBC: RFT:

HB: BLOOD SUGAR:

HCT: BLOOD UREA:

TLC: SERUM CREATININE:

DC: SODIUM:

ESR: POTASSIUM:

LFT:

TOTAL BILIRUBIN: X RAY FINDING:

DIRECT BILIRUBIN:

AST:

ALT: PUS C/S:

ALP:

TOTAL PROTEINS:

SERUM ALBUMIN:

WHETHER PATIENT IS IN SEPSIS: YES/ NO

DIAGNOSIS: CELLULITIS/ABCESS/NECROTISING FASCIITIS

TREATMENT: ANTIBIOTICS/LIMBSALVAGE/AMPUTATION

IONOTROPIC SUPPORT: YES/NO

VENTILATORY SUPPORT: YES/NO

NO. OF DAYS OF HOSPITAL STAY:

FINAL OUTCOME:

CONVALESCING

REQUIRED AMPUTATION

EXPIRED

SCORE:

SL NO.	CRITERION	1	2	3
1.	AGE (YEARS)	<30	30-50	>50
2.	DURATION OF SYMPTOMSPRIOR TO ADMISSION(DAYS)	<5	>5	
3.	COMORBIDITIES	1	2	>2
4.	GCS	15	9-14	<9
5.	PRESENCE OF SEPSIS		YES	
6.	VENTILATORY SUPPORT		YES	
7.	IONOTROPIC SUPPORT		YES	
8.	BODY SURFACE AREA	<10%	10-20%	>20%
9.	HB (gm%)	>8	</=8	
10.	DEPTH OF INVOLVEMENT	CELLULTIS	EVOLVING NF	NF

TOTAL SCORE:

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