

A CLINICOPATHOLOGICAL STUDY OF NECROTISING FASCIITIS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Necrotising fasciitis lesions are entities not frequently seen in daily surgical practice. These infections are marked by absence of clear local boundaries or palpable limits, which is responsible both for their severity and the frequent delay in recognizing their surgical nature. Necrotising fasciitis continues to challenge the practicing surgeon.

MATERIALS AND METHODS

50 patients of necrotising fasciitis were treated during the study period from August 2016 up to one year. Age, sex, associated co-morbid conditions, site of involvement, predisposing factors, addictions, clinical parameters like pyrexia, duration of symptoms, presence of hypotension are studied and compared.

RESULTS

50 patients of necrotising fasciitis are treated during the study period. The age ranged from 22 to 71 years, the mean age being 44.5 ± 8.36 years. There were 38 males and 12 females. Male: female ratio is 3.17:1. Among 38 males, 6 patients died. This constitutes about 15.7%. Among 12 number of females 4 died. This constitutes about 33.3% mortality.

CONCLUSION

Necrotising fasciitis is more common in middle aged males. Diabetes mellitus is the most common co-morbid condition associated with necrotising fasciitis. Type I infection is more common. The presence of multiple co-morbid conditions reduces the survival. Early diagnosis and aggressive surgical debridement reduces mortality.

KEYWORDS

Necrotising Fasciitis, Diabetic Vascular Disease, Future Therapies.

HOW TO CITE THIS ARTICLE: Adeppa P, Sarada B, Kiran Kumar A. A clinicopathological study of necrotising fasciitis in a tertiary care hospital. J. Evid. Based Med. Healthc. 2018; 5(52), 3567-3574. DOI: 10.18410/jebmh/2018/727

BACKGROUND

Necrotising Fasciitis is characterized by rapidly progressing inflammation and necrosis, ranging from necrosis of the skin to life threatening infection involving the fascia and muscle when it is called as "Necrotising Myositis."¹

"Streptococcus Pyogenes", occasionally by Staphylococcus aureus, Clostridium Perfringens, Clostridium septicum, Pseudomonas Aeruginosa, Vibrio species and some fungi cause the commonest and most serious infections. Rarely it may be as a result of non-group-A streptococci, Streptococcus Pneumoniae or Haemophilus Influenza type-B infections. Sometimes bacteria that are Anaerobic and Aerobic or facultative act together to cause tissue necrosis.

There are several recognized risk factors. Patients who have compromised immunity such as patients with Diabetes mellitus, Cancer, Peripheral Vascular Disease, Intravenous drug users, those who have recently undergone surgery, receiving Steroids or other immunosuppressive treatments alcoholism especially patients with malnutrition like anaemia, hypoproteinaemia^{2,3,4} are all predisposed.

Healthy children in particular with recent varicella Zoster infection, and also whose skin is breached by minor trauma or skin infection are affected. Some investigators have found that the use of Non - steroidal Anti-inflammatory drugs in these children increase the risk of Necrotising Fasciitis.

Main Features of Necrotising Fasciitis-

1. Erythema
2. Pain or tenderness beyond margins of erythema
3. Swelling
4. Crepitus or Skin Necrosis
5. Induration
6. Bullae
7. Fluctuance
8. Fever
9. Hypotension

Financial or Other, Competing Interest: None.
Submission 28-11-2018, Peer Review 06-12-2018,
Acceptance 14-12-2018, Published 19-12-2018.

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DOI: 10.18410/jebmh/2018/727



It can occur anywhere in the body, but perineum, Abdominal area and extremities are the commonly affected organs. Patients with a rectal focus of infection had a greater number of bacteria and required longer hospitalization and more operative procedures than patients with dermal or urethral foci.

Infection causes the activation of interleukins, Tumour necrosis factor alpha, and Gamma-interferon through a triggering mechanism. This results in capillary thrombosis with necrosis of the fascia, cutis, and sub cutis.

In a fulminant necrotising fasciitis, the development of sepsis with consecutive multi-organ dysfunction mainly determines the course of the disease.

In well-vascularised lower extremities, an occasional soft tissue infection gains access to the perifascial space. Active infection within this perifascial space portends grave consequences for the patient. The perifascial space contains loose areolar tissue that even under normal permits the surgeon to dissect the subcutaneous fat off the fascia with gentle digital pressure. Infection in this plane can disseminate rapidly.

Furthermore, the perifascial spaces are relatively avascular, which means most responsiveness to infection in this plane is poor even with normally vascularised extremities. Vertical invasion of soft tissue infection into the perifascial plane occurs more frequently in the ischemic extremity. Host response to the infection is poor. The result is rapidly dissecting infection known in the current parlance as "Necrotising Fasciitis".

Necrotising Fasciitis in many of these cases dissects in the perifascial space above the fascia and does not result in fascial necrosis.

Perforating arterial vessels arise from arterial trunks deep to the fascia and enter into the lower-extremity subcutaneous tissue by penetrating through the fascia.

The dissecting infection thromboses the perforating vascular blood supply to the skin and subcutaneous tissue, but the fascia may maintain its viability unless the muscular plane beneath the fascia is involved.

The muscular tissues are involved in these infections only when the initial injury has penetrated the fascia or when usually virulent or neglected infections have extensive fascial necrosis and secondary muscle involvement. The clostridia infections involving muscle is known as Clostridia Myonecrosis⁵ or Gas gangrene.

Diabetic patient with long-standing disease have the combined effects of large-vessel atherosclerosis, micro vascular disease of diabetes and diabetic neuropathy.

Vasculopathy and neuropathy are synergistic and predispose this patient of foot ulceration, followed by local contamination and invasive infection into the deep compartments, necrosis and suppuration of skin, subcutaneous tissue, interosseous space yields a complex infectious process. The neuropathy of diabetes results in the loss of sensation, degeneration of motor fibres and loss of autonomic neuron control in the foot.

Loss of sensation results in pressure ulceration. Loss of vasomotor control also leads to inadequate cutaneous blood

supply. The net effect of these neuropathic changes is that the diabetics are prone to ulceration with secondary invasive infection. After infection, the lesion enters into the deep spaces of the leg, true limb-threatening circumstance exists.

The diagnosis of NECROTISING FASCIITIS is obvious in these cases, but some are subtler than in others. In that a bad wound is not confirmation, that deep compartment infection is present.

Necrotising Fasciitis of the head and neck are rare, probably owing to the robust regional blood supply.

Aims and Objectives

1. To identify the factors responsible for mortality & morbidity in Necrotising Fasciitis.
2. Study of factors like Age, sex, smoking, Cardiac Disease, cancer patients, Peripheral vascular disease, Recent surgery, whether Patients on immune suppressants, steroids; chronic alcoholics, diabetes.
3. To evaluate the various socio demographic factors influencing mortality & morbidity.

MATERIALS AND METHODS

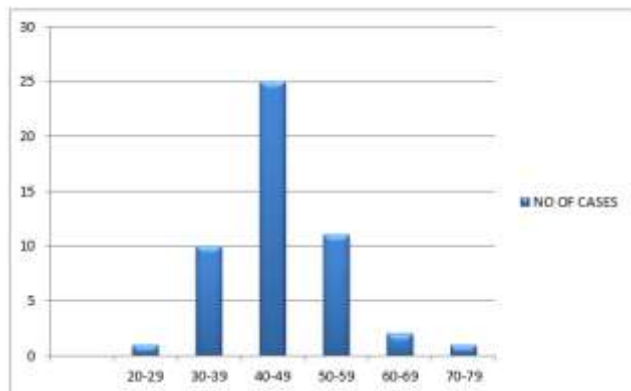
This prospective study is conducted in Department of General Surgery at S.V.R.R.G.G. Hospital from August 2016 to November 2017 on patients attending surgical OPD and admitted in General Surgical wards. Data is collected for each patient. Data includes Age, sex, associated co-morbid conditions, site of involvement, predisposing factors, addictions. Clinical parameters like pyrexia, duration of symptoms, presence of hypotension. Laboratory parameters like Haemoglobin, Total leucocyte count, Random blood sugar, serum proteins, serum creatinine, bacteriology, HPE, duration of hospital stay and final outcome. The diagnosis of Necrotising fasciitis is based on clinical findings e.g., pain, oedema, the presence of changes of the involved area in the form of bullae besides the presence of fever and toxemia. Necrotic superficial fascia and subcutaneous tissue with serosanguinous fluid and microscopic demonstration of Polymorphonuclear cell infiltration and underlying fascia with obliterative thrombosis of arteries and veins. Histopathologic evidence of Necrotising fasciitis included the presence of necrosis of superficial fascia (with or without polymorphonuclear infiltrates) or bacteria and oedema of the reticular dermis, subcutaneous fat, and superficial fascia. In the absence of findings of pathologic examination of resected tissue, the diagnosis required characteristic surgical findings that included the presence of grey necrotic fascia with lack of resistance to blunt dissection, absence of bleeding during surgical dissection, and presence of foul-smelling "dishwater" pus.

RESULTS

50 patients of Necrotising Fasciitis are treated during the study period. The Age ranged from 22 to 71 years, the mean age being 44.5 ± 8.36 years. Maximum (50%) cases were between 40-49 years. Patients aged between 30-59 years comprised of 92% of the total. There were 38 males and 12 females. Male: female ratio is 3.17:1.

Age Group (Yrs.)	No. of Cases
20-29	1
30-39	10
40-49	25
50-59	11
60-69	2
70-79	1

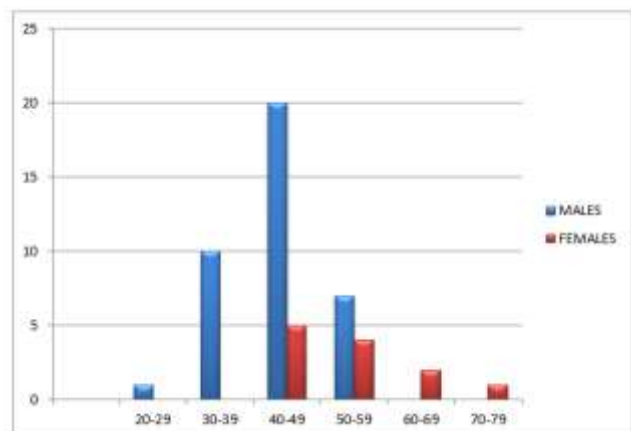
Table 1. Showing Age Distribution of Necrotising Fasciitis



Graph 1. Showing Age Distribution

Males	Females	M:F Ratio	Age Group (yrs.)
1	0		20-29
10	0		30-39
20	5	04:01	40-49
7	5	1.4:1	50-59
0	1		60-69
0	1		70-79

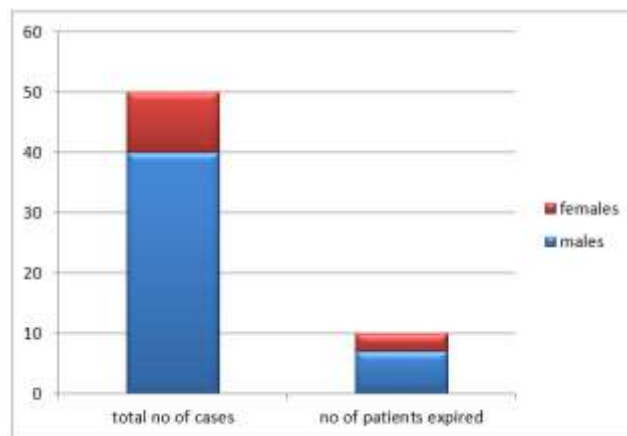
Table 2. Showing Male and Female Distribution



Graph 2. Showing Age and Sex Distribution

	Total No. of Cases	No. of Patients Expired
Males	38	6(15.7%)
Females	12	4(33.3%)

Table 3. Showing Mortality in Both Sexes



Graph 3. Showing Mortality in Both Sexes

Among 38 males, 6 patients were dead. This constitutes about 15.7%. Among 12 number of females 4 were found dead. This constitutes about 33.3% mortality.

Age Group	Total No. of Cases	Mortality (%)
20-29	1	0
30-39	10	0
40-49	25	4(56%)
50-59	11	4(36.3%)
60-69	2	2(100%)
70-79	1	0

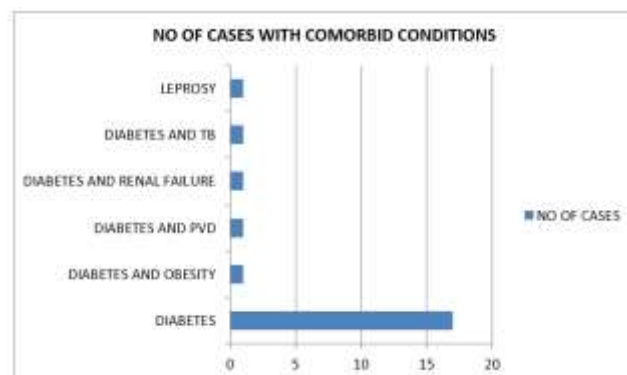
Table 4. Showing Mortality in Various Age Groups

Comorbid Conditions- Mortality

Diabetes Mellitus was the most common associated comorbid condition comprising of 21 patients (42%).

Comorbid Condition	No. of Cases	Percentage (%)
Diabetes	17	34
Diabetes and Obesity	1	2
Diabetes and PVD	1	2
Diabetes and Renal Failure	1	2
Diabetes and TB	1	2
Leprosy	1	2

Table 5. Showing the Associated Comorbid Conditions



Graph 4. Showing the Associated Comorbid Conditions

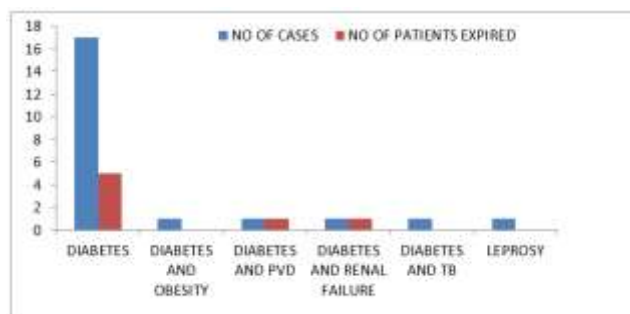
The Associated Comorbid Conditions-

- Diabetes,
- Diabetes & Obesity,
- Diabetes & Peripheral vascular disease,
- Diabetes & Renal failure,
- Diabetes & Tuberculosis,
- Tuberculosis,
- Leprosy,

Comorbid Condition	No. of Cases	No. of Patients Expired	Mortality (%)
Diabetes	17	5	5.80%
Diabetes and Obesity	1	0	0
Diabetes and PVD	1	1	4.76%
Diabetes and Renal Failure	1	1	4.76%
Diabetes and TB	1	0	0
Leprosy	1	0	0

Table 6. Showing the Mortality Associated with Various Comorbid Factors

Among the diabetics constituting about 21 members (42%), the mortality rate constitutes 14.28%.



Graph 5. Showing Mortality Associated with Various Comorbid Factors

In 17 patients Diabetes alone is the associated comorbid factor. Of which 5 patients expired constituting 29.4% of mortality. Among the rest of the expired patients, 2 patients has diabetes in association with other comorbidities like peripheral vascular disease and renal failure. Mortality is 4.76% in these patients.

Site of Involvement- Mortality

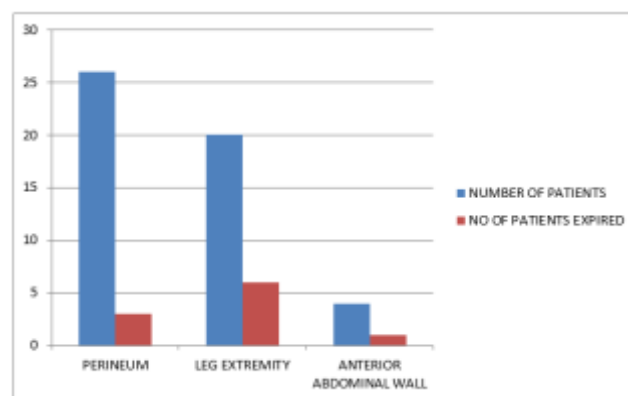
The perineum was the most common site involved in 26 (52%) patients followed by the lower extremity in 20 (40%) patients and anterior abdominal wall in 4 (8%) patients. In the lower extremity, only the thigh was involved in 6 (12%) patients, the leg & foot were involved in 12 (24%) patients and the whole extremity was involved in 1 patient (2%).

	No. of Patients	Percentage (%)
Perineum	26	52
LEG Extremity	20	40
Anterior Abdominal Wall	4	8

Table 7. Showing the Site of Involvement and Percentage

Site of Involvement	No. of Patients	Percentage (%)	No. of Patients Expired (%)
Perineum	26	52	3(11.5%)
Leg extremity	20	40	6(30%)
Anterior Abdominal Wall	4	8	1(25%)

Table 8. Showing Site of Involvement and Associated Mortality



Graph 6. Showing Site of Involvement and Associated Mortality

Perineum was involved in about 26 patients. Among them 3 patients expired constituting about 11.5% mortality. Anterior abdominal wall was involved in 4 patients. 1 patient expired constituting 25% of mortality.

Leg extremity was involved in 20 patients. 6 patients expired constituting 30% mortality.

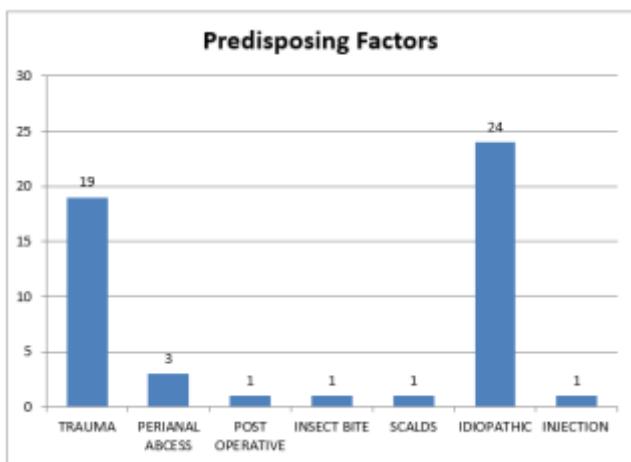
Pessa and Howard et al⁶ demonstrated a mortality rate of 18% in extremity infection compared with 44 and 33% in abdominal and perineal infections, respectively.

Predisposing Factors- Mortality

Trauma is the most common predisposing factor found in 19 (38%). No predisposing factors were found in 24 (48%) patients.

Predisposing Factors	Number	Percentage (%)
Trauma	19	38
Perianal Abscess	3	6
Post-operative	1	2
Insect bite	1	2
Scalds	1	2
Idiopathic	24	48
Injection	1	2

Table 9. Showing Predisposing Factors for Necrotising Fasciitis

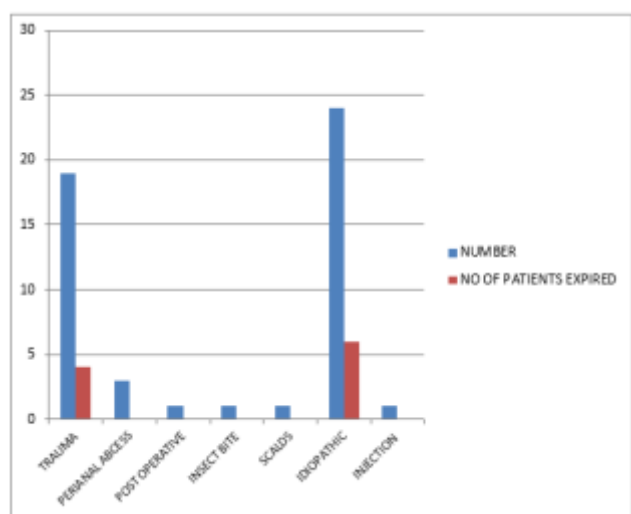


Graph 7. Showing Predisposing Factors for Necrotising Fasciitis

Predisposing Factors	Number	No. of Patients Expired (%)
Trauma	19	4(21.05%)
Perianal Abscess	3	0
Post-operative	1	0
Insect bite	1	0
Scalds	1	0
Idiopathic	24	6(25%)
Injection	1	0

Table 10. Showing Predisposing Factors and Associated Mortality

Trauma was the most common predisposing factor seen in 19 patients. Among them 4 patients expired constituting 21.05%. In majority of the cases it is Idiopathic. This includes 24 patients. Among them 6 patients expired constituting 25% mortality.

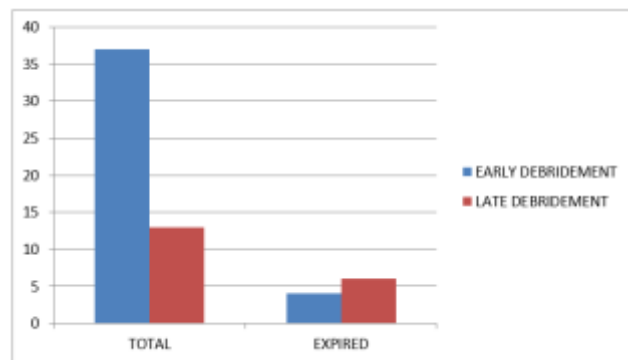


Graph 8. Showing Predisposing Factors and Associated Mortality

Mortality Based on Early and Late Debridement-

	Total No. of Cases	No. of Patients Expired
Early Debridement < 24 hrs	37	4 (10.8%)
Late Debridement > 24 hrs	13	6(46.1%)

Table 11. Showing Timing of Debridement and Associated Mortality



Graph 9. Showing Timing of Debridement and Associated Mortality

Early debridement (within 24 hrs of admission) had a better prognosis. 37 patients undergone early debridement. 13 patients had their first debridement later than 24 hrs after admission.

Parameter	Total No. of Patients	No. of Patients Expired	Mortality
Leucocytosis >14000/cumm	13	6	46.10%
Blood Sugar >180 mg/dL	6	3	50%
Serum Creatinine > 1.5 mg%	6	1	16.67%

Table 12. Showing Parameters and Associated Mortality

Among 50 patients, 13 of them has leucocytosis >14,000/cu mm. of them 6 patients expired. This constitutes about 46.10% mortality.

6 of them had blood sugar > 180 mg/dL, of them 3 patients expired. This constitutes about 50% mortality.

6 of them had serum creatinine > 1.5 mg%, of them 1 patient expired. This constitutes about 16.67% mortality.

Mortality based on Bacteria Isolated

The commonest bacteria isolated was E.coli in 26 (52%) patients followed by group A streptococcus in 18 (36%) patients. The culture was polymicrobial in 39 (78%) patients, monomicrobial in 11 (22%) patients and. In case of monomicrobial aetiology, all were streptococcus involving only the lower extremity.

Commonly Identified Bacteria					
Monomicrobial			Polymicrobial		
Name	No.	(%)	Name	No.	(%)
Streptococcus (involving lower extremity)	4	8	Escherichia coli	26	52
			Streptococcus	18	36
			Staphylococcus	7	14
			Pseudomonas	9	18
			Proteus	7	14
			Enterobacter	2	4
			Klebsiella	2	4
			Bacteroides	9	18

Table 13. Showing Commonly Identified Bacteria

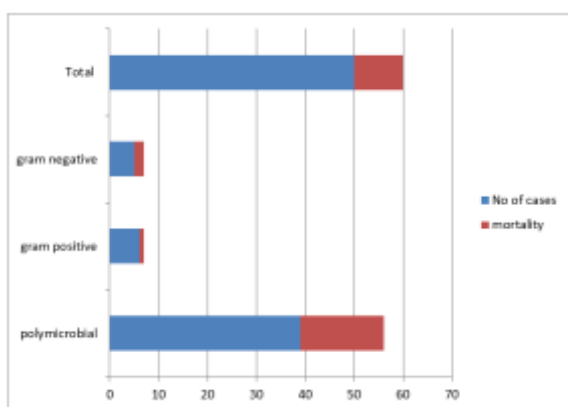
The culture and sensitivity tests from the exudate are summarized in the table.

Sl. No.	Organisms	Antibiotic Sensitivity
1.	Proteus Species	Gentamycin, Amikacin
2.	Klebsiella, E.coli	Ciprofloxacin, Amikacin, Cephalosporin.
3.	Staphylococcus Aureus, E.coli	Cephalexin, Amikacin
4.	Proteus, Klebsiella	Amoxycillin, Cefuroxime, Cephalothin
5.	Staphylococcus Aureus	Cephalexin, Gentamycin
6.	Klebsiella	Ciprofloxacin
7.	Pseudomonas	Ceftriaxone
8.	E.coli, Pseudomonas	Gentamycin, Cefuroxime.

Table 14. Showing Organisms and Culture Sensitivity

	Total No. of Cases	Mortality
Polymicrobial	39	7(17.9%)
Gram Positive alone	6	1(16.6%)
Gram negative alone	5	2 (40%)
Total	50	10(20%)

Table 15. Showing the Mortality Based on Bacteriology



Graph 10. Showing Associated Mortality and Various Bacteria

Polymicrobial infection (most commonly isolating Bacteroides, klebsiella, proteus, streptococcus, staphylococcus)⁷ was found in 39 number of cases. 7 of patients were found dead. This constitutes about 17.9% mortality.

Among gram positive and gram negative the following mortality rates were observed.

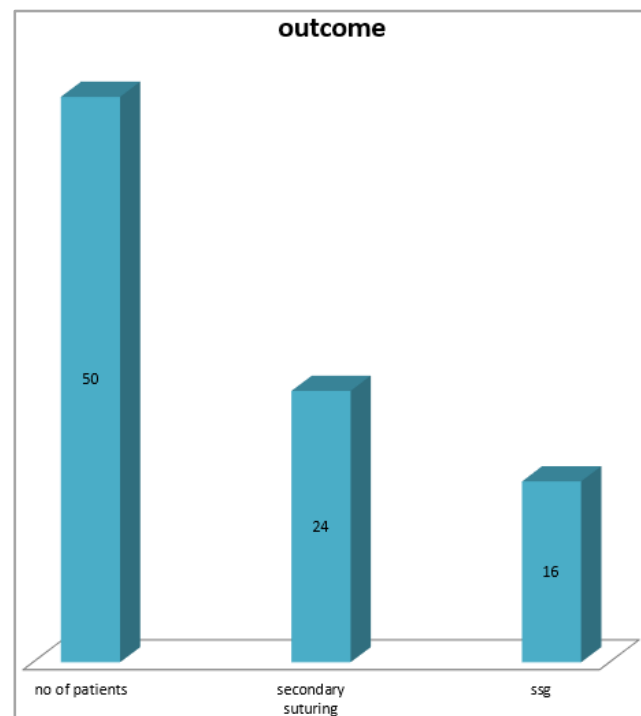
	Bacteria	No. of Cases	Mortality
Gram Positive	Streptococcus	18	7(25.7%)
	Staphylococcus	0	0
Gram Negative	E.coli	26	3(11.5%)
	Pseudomonas	1	0
	Proteus	2	0
	Enterobacter	3	0

Table 16. Showing Association of Bacteriology and Mortality

Among the gram positive bacteria, streptococcus was the most common organism isolated from the dead patients. Total number cases from which streptococcus isolated include 18. Out of which 7 were dead. This constitutes about 25.7% mortality.

Among the gram negative bacteria E.coli was being isolated in 26 number of cases. Among these 3 were found dead. This constitutes about 11.5%.

Secondary surgical procedures included mobilization and suturing 24 Patients (48%) and skin grafting 16 (32%).



Graph 11. Showing Outcome of the Patients

DISCUSSION

50 patients of Necrotising Fasciitis were treated during the study period from August 2016 up to one year.

To our observation and to that of others,^{8,9,10} differentiating between such entities as streptococcal Necrotising cellulitis, Fournier's gangrene, Meleney's synergistic gangrene, Necrotising fasciitis, clostridial cellulitis, and others serves no purpose other than to confuse the issue. The diagnostic and treatment regimens are the same for all.^{11,12}

Based on the widely varying levels of soft tissue affected by the infection and the variety of microflora, only two types of Necrotising soft tissue infections need to be delineated:

- i. Pure clostridial myonecrosis (because of the homogeneity of its invasion of muscle and its vastly higher mortality rate) and
- ii. Other Necrotising soft tissue infections (NSTI).

The patients with NSTI included in this study, as well as those described in other reports^{1,2,8} had a great number of premorbid medical problems, especially diabetes mellitus and peripheral vascular disease.

In the present study, all the study individuals are in range of 25-71 years with mean age of 44.5 years. The associated mortality is comparable and similar to the other studies like Madhumitha Mukhopadhyay et al and Mc Henry CR et al.

In the present study 50% of the patients were between 40-49 years. Necrotising fasciitis is commonly seen in middle age males Diabetes mellitus was the most common co-morbid condition in our study (42%) which is correlated with that in other literature.^{13,14}

Future Therapies-

As a life-threatening condition, NF demands new management strategies. Unfortunately, there is no single new therapy that can manage NF; they all seem to play an assistive role. Undoubtedly, the use of Vacuum Assisted Closure (VAC) has many benefits in wound healing, and it will be adopted by more physicians in the future.

A study by Anaya et al.¹³ highlighted the role of Intra Venous Immunoglobulins (IVIG) in the treatment of NSTI, especially if NSTI is associated with group A streptococcal infection.

The authors concluded that the use of IVIG seemed rational in patients with group A streptococcal infection who developed streptococcal toxic shock syndrome and in those with a high mortality risk (advanced age, hypotension, and bacteraemia). However, relevant studies investigating its use are contentious and difficult to compare because of the small number of patients and the different methodologies used.

An interesting study by Lu et al.¹⁴ showed that kallistatin, originally found to be a tissue kallikrein-binding protein, can increase the survival of group A streptococcus infected mice. The researchers concluded that kallistatin significantly increased the survival rate of GAS-infected

mice, and also reduced local skin damage and bacterial counts.

Moreover, its use improved infiltrating cell viability in the local infection site, as well as bacterial clearance activity of immune cells.¹⁵ The efficiency of intracellular bacterial killing in neutrophils was directly enhanced by kallistatin administration. Several inflammatory cytokines, including tumour necrosis factor alpha, interleukin 1 β , and interleukin 6, in local infection sites were reduced by kallistatin.

Furthermore, kallistatin treatment was reported to reduce vessel leakage, bacteraemia, and liver pathology after local infection. However, further studies are warranted before safe conclusions can be drawn concerning its use in gas-forming infections, such as Necrotising Fasciitis.¹⁶

CONCLUSION

Necrotising fasciitis is more common in middle aged males. Diabetes mellitus is the most common co-morbid condition associated with necrotising fasciitis. Type I infection is more common. The presence of bullae and blistering and discolouration of the skin should raise the suspicion of necrotising fasciitis. Findings at surgical exploration and skin biopsy are reliable methods of diagnosis. The presence of multiple co-morbid conditions reduces the survival. Early diagnosis and aggressive surgical debridement reduces mortality.

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