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Original Research Article

Clinicopathology study of necrotizing fasciitis with special reference to Fournier's gangrene

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ABSTRACT

Background: Necrotizing fasciitis including Fournier's gangrene is an uncommon, critically serious infection of the subcutaneous tissue and fascia with relative sparing of the skin and muscle. Despite modern supportive measures, the reported mortality rate still is high and this is due to part to the aggressive nature of the infection. The present study was performed upon 50 patients to study clinicopathology of necrotizing fasciitis with special reference to Fournier's gangrene.
Methods: This cross-sectional study was conducted in Surgery ward of SGRD Hospital, for a period of 1 year (1st January 2015 to 31st December 2015). The performa filled for patients with necrotizing fasciitis was designed on the basis of NICE guidelines and details like history, examination, general survey, local examination, systemic examination and investigations, statistical analysis of data done.
Results: Necrotizing fasciitis, though it is found at any age but is a disease of middle and old aged adults in this part of the world, being commonest in the 4th, 5th, 6th decades of life and is more common in males. The disease is more common in people with low socio-economic groups with poor personal hygiene, diabetes mellitus and history of drug addiction. Trauma is the most common predisposing factor for the necrotizing fasciitis as a whole whereas idiopathic cause is the most common cause in cases of Fournier's gangrene. Polymicrobial infection is the most common variety, where in *E. coli*, *Streptococcus*, *Bacteroids* are most commonly isolated. Regarding monobacterial infection *streptococcus* being the most common.
Conclusion: Current study showed increased frequency of necrotizing fasciitis in people aged above 40 years. Diabetes mellitus and other premorbid conditions increase the risk of mortality. Polymicrobial infection in combination of *Escherichia coli*, *Streptococcus*, *Pseudomonas*, *Bacteroids* and *Staphylococcus* were the most commonly found. Early debridement, parenteral combined antibiotic and supportive measure formed the basis of treatment. Septicemia was a common complication which was often cause death.

Keywords: Fournier's gangrene, Necrotizing fasciitis

INTRODUCTION

Necrotizing fasciitis including Fournier's gangrene is an uncommon, critically serious infection of the subcutaneous tissue and fascia with relative sparing of the skin and muscles. The term necrotizing fasciitis was first used in 1952 by Wilson, and describes the most consistent feature of the infection, fascial necrosis.[1] Jean Alfred Fournier, a Parisian dermatologist and venereologist in 1883 was the first to be associated with this condition in a specific region of the body, namely scrotum.[2] The ratio of men to women is 1.4:1 but the reason for this difference is not explained. Peripheral vascular disease, diabetes, and a compromised immune

system are significant risk factors for necrotizing fasciitis. Diabetes is present in 18% to 60% of cases; in addition, 19% to 77% of patients use intravenous drugs. Other significant predisposing factors include alcohol abuse (9-31%), obesity and malnutrition. Pathogenic agents can be introduced as a result of minor trauma, insect bites, or surgical incisions. The disease is no longer restricted to young population but may affect a wide age range from neonates to the very elderly. Fifty-five cases have been reported in the paediatric literature, two-thirds of who were younger than 3 months. Though this disease process is more common in males, there are also several reports of genital gangrene occurring in women.[4]

Necrotizing fasciitis is caused by either polymicrobial (mixed anaerobic, aerobic, and facultative bacteria (e.g. *E. coli* and *Bacteroides*) or monomicrobial (Streptococcus or *Staphylococcus*) infections. *Streptococcus*, is associated with history of blunt trauma, varicella, intravenous drug use, penetrating injury and possibly with non-steroidal anti-inflammatory drugs.[5]

Clinical consideration

Necrotizing fasciitis is often acute, but can follow a subacute progressive course.[5] Initial signs are erythematous, exquisitely tender, swollen, warm area of cellulitis. As the disease process progresses, the skin darkens to a dusky blue, as early as thirty-six hours after onset. Within three to five days, blisters and bullae develop which may eventually become hemorrhagic. By this time, the involved areas are no longer painful, having become anesthetized secondary to destruction of superficial nerves and thrombosis of small blood vessels. Fascial necrosis is present with widespread undermining of the skin.

Patients usually appear toxic, with tachycardia, hypotension, and tachypnea. Once gangrene is established, pain often diminishes. Shock, intestinal ileus and delirium are common and progression to single or multi-organ failure may occur and is the usual cause of death in patients who succumb.[6]

Diagnostic consideration

The diagnosis of this condition is mainly based on clinical signs and symptoms. In doubtful cases, additional bedside techniques (finger test and rapid frozen section biopsy) or other investigations can be used.[6] Plain radiographs can show the characteristic marked swelling of the scrotal tissues and air density within the involved tissues as necrotizing fasciitis involving other sites.[7] Ultrasound is a useful diagnostic tool as it has the capacity to distinguish Fournier's gangrene from intra-scrotal pathology that also commonly produces scrotal pain, erythema and swelling.[8] CT can be of value in defining the cause and depicting the extent of necrosis accurately and a pre-operative scan though not essential may be helpful if the source of infection is a retroperitoneal or intra-abdominal process.[9]

Outcome

The reported mortality rate for NSTI varies from 6% to 33%.[10] Elliott et al, demonstrated that a combination of factors is more predictive of outcome than any individual factor. In their study, diabetes mellitus did not predict outcome, but when combined with peripheral vascular disease, renal failure, and age greater than 60, it was associated with a significant increase in mortality.[11] The major factor that physicians can control is the extent of debridement, and this appears to be the most important determinant of survival. Inadequate surgical debridement at the initial operative procedure results in adverse outcomes, with disease progression.[12]

Fournier's gangrene

Mortality rates are 3-40%.[13] Despite modern supportive measures, the reported mortality rate still is high and this is due to aggressive nature of the infection and due to the underlying co-morbid diseases.

METHODS

This cross-sectional study was conducted in Surgery ward of SGRD Hospital, Amritsar for a period of 1 year (1st January 2015 to 31st December 2015). A written informed consent was taken from the patients for participation in the study after screening for with history of necrotizing fasciitis involving any part of the body. The performa filled for patients with necrotizing fasciitis was designed on the basis of NICE guidelines and the form also included details like history, examination, general survey, local examination, systemic examination and investigations

Statistical analysis

The data collected was recorded in a performa and was analysed using descriptive statistics.

RESULTS

Over the period of this one year, 50 cases of necrotizing fasciitis including Fournier's gangrene have been studied. Of these 50 cases, 12 cases presented in the emergency and 38 had been admitted in the Department of General Surgery. 38 patients were males and the remaining 12 were females, giving a male: female ratio of 3.17:1.

82% of cases found in people with poor socio-economic status where as 10% and 8% come from patient with good and medium economic status respectively.

Low personal hygiene comprising 84% of cases of necrotizing fasciitis where as 16% cases come from the persons with good personal hygiene.

Table 1: Gender and age distribution in various age groups.

Age group	Male	Female	Male: Female
0-9	-	-	-
10-19	-	-	-
20-29	1	-	-
30-39	10	-	-
40-49	20	5	4:1
50-59	7	4	1.75:1
60-69	-	2	-
70-79	-	1	-
80 and above	-	-	-
Total	38	12	3.17:1

Table 2: Socio-economic status.

Socio-economic status	No. of cases	Percentage (%)
Poor	41	82
Medium	04	08
Good	05	10
High	00	00

Table 3: Personal hygiene.

Personal hygiene	No. of cases	Percentage (%)
Low	42	84
Good	08	16

Diabetes mellitus the most common pre-existing medical conditions in association with necrotizing fasciitis comprising 42% (total 21 cases) of which diabetes with peripheral vascular disease, diabetes with renal failure and diabetes with tuberculosis is accounts for 2% (1 case) for each respectively. Total number of tuberculosis is found in this study are 4% (2).

Table 4: Co-morbid conditions for developing necrotizing fasciitis.

Co- morbid condition	No. of cases	Percentage (%)
Diabetes	17	34
Diabetes and obesity	1	2
Diabetes and peripheral vascular disease	1	2
Diabetes and renal failure	1	2
Diabetes and tuberculosis	1	2
Tuberculosis	1	2
Leprosy	1	2
HIV	1	2

Between 21 cases of diabetes mellitus 16 are male (32%) and 5 are female accounting for 10%.

Alcoholism is the most common type of addiction. It has been found to account for 34% (17 cases) in the patient with necrotizing fasciitis and intravenous drug abuse is found 12% cases (6 in number).

Table 5: Addiction history.

Type of addiction	No. of cases	Percentage (%)
Alcoholism	17	34
Intravenous drug abuse	6	12

But in case of Fournier's gangrene alcoholism accounted for 22% (11 in number) a case where as there is no intravenous drug abuse is found.

Predisposing factors

Idiopathic factor is the most common predisposing factor and is account for 48% (24). Trauma was the next common whereas perianal abscess third predisposing factor for necrotizing fasciitis was. One case following strangulated femoral hernia operation, one case following intra-muscular analgesic injection and one case was found following unknown bite during sleep.

Table 6: Predisposing factors.

Predisposing factors	Number	Number
Idiopathic	12	46.15
Trauma	9	34.62
Perianal abscess	3	11.54
Scald	1	3.85
Insect bite	1	3.85

Table 7: Clinical features of necrotizing fasciitis.

Clinical features	Number	Percentage (%)
Pain	29	58
Local erythema and swelling	50	100
Pyrexia	31	62
Hypotension	13	26
Bullous lesion	16	32
Crepitation	4	8
Altered sensorium	9	18
Renal failure	2	4
Tachycardia	27	54
Shock	6	12

Local erythema and swelling was the commonest symptoms, being present in 50 (100%).

Pyrexia (>100.5ºF) was next common symptoms, with unexplained soft tissue pain being closed third. Tachycardia, bullous skin lesions, hypotension (systolic BP <100 mm of Hg) and altered sensorium were others clinical features.

Table 8: Tissue culture result.

Culture result	Number	Percentage (%)
Polymicrobial	39	78
Monomicrobial	4	8
No growth	7	14

The most the patients were taking three combined antibiotics with ampicillin/second or third generation cephalosporine + metronidazole/clindamycin + aminoglycoside according to culture sensitivity results.

Overall the most common of operation for definite surgery was mobilization of healthy tissue and apposition by suturing (24 cases) and split skin grafting were done in 21 cases. 5 patients were died before any definitive surgery.

Table 9: Tissue culture result.

Monomicrobial			Polymicrobial		
Name	**No.**	**Percentage (%)**	**Name**	**No.**	**Percentage (%)**
Streptococcus	4	8	*Escherishia coli*	26	52
			Streptococcus	18	36
			Staphylococcus	7	14
			Pseudomonas	9	18
			Proteus	7	14
			Enterobacter	2	4
			Klebsiella	2	4
			Bacteroids	9	18

Table 10: Antibiotic therapy.

Name of combined antibiotic	Percentage(%)	Number
Ceftriaxone, Metronidazole and Amikacin	46	23
Cefuroxime, Clindamycin and Amikacin	8	4
Ampicillin, Metronidazole and Gentamycin	18	9
Ampicillin and Clindadmycin	2	1
Ceftazidime, Clindamycin and Amikacin	2	1
Ceftriaxone, Clindamycin and Amikacin	18	9
Ampicillin, Clindamycin and Gentamycin	4	2
Ampicillin, Ceftriaxone and Metronidazole	2	1
Imipenem	2	1

Table 11: Type of operation.

Type of operations	Number	Percentage (%)
Mobilisation and suturing	24	48
Split skin graft	21	42
No operation	5	10

5 patients died out of 50, accounting mortality rate was 10% of which 4 were male (80%). 60% of dead patient having age equal or more than 50 years. Mortality was more common in Fournier's gangrene and necrotizing fasciitis involving lower extremities (both of which 2 in number). Diabetes mellitus was found in 3 cases two of associated with other comorbidities like renal failure and peripheral vascular disease. In this study, mortality was higher in polybacterial infections (3cases) than in monobacterial infections. *Streptococcus* was the most commonly isolated from dead patients (4 cases) followed by *E. coli* and *Pseudomonas* (each account for 2). Other organism was *Bacteroides* accounting 10% cases (1 in number). In 80% of mortality, first debridement was done after 24 hours of admission where as it was 20% when it was done within 24 hours of admission.

Table 12: outcome.

Outcome	Number	Percentage (%)
Survived	45	90
Died	5	10

DISCUSSION

The present study has been conducted in SGRD Medical College Hospital on 50 patients of necrotizing fasciitis involving various parts of body including scrotum and perineum (Fournier's gangrene) admitted to this hospital over the period of one year from 1st January 2015 to 31st December 2015.

Age

Hsieh WS and associate has asserted that NSTI can occur at any age, including infancy. In various separated study by Bosshordt TI, Mchenry CR, Lille St and associate, it was found that the youngest age was 9 years and the oldest one 90, while mean age varied from 32 years to 57.[14]

In the present study, youngest one was 22 years while the oldest one was 71 and mean age was 44.62 and 72% cases were arise from the patients aged between 40 to 59 years.

Gender

In the study of Bosshordt TI, Mchenry CR, Lille St and associate,Elliot DC male and female ratio was 1.4:1. In Rangaswamy M study also male-female ratio was 4:3.[15]

All of the above studies slightly differ with present study where male-female ratio was 3.17:1. Instead the findings of this study are closer to Maynor M study where male to female ratio was 2-3:1.

Socio-economic status

It is apparent from this study that the majority of the patients had come from a poor socioeconomic background, this bias may only be a reflection of the economy of the people attending the hospital and not a true indicator of the incidence of the disease in the various socio-economic strata. Though a report from Europe stated that the disease is not so frequent in the civilized world, Fournier's gangrene does occur in affluent as well as poor communities, as evidenced by many reports from affluent regions of the USA and Europe. It has been speculated, without proof, that there may be a strong resistance to infection in the Negro race or that the organisms involved in Africa lack sufficient virulence for more severe sepsis.[17]

Personal-hygiene

Majority of patients had poor personal hygiene in this study.

Comorbidity

The study has found that diabetes mellitus is the most common associated pre-existing medical conditions and which account for 42%. This finding tally with that of the work by Sudarsky LA, McHenry CR, Rubinstien E, Elliot DC and Bosshordt.[18] Four cases having more than one co-morbid condition in the combination of diabetes mellitus with obesity, renal failure, peripheral vascular disease and pulmonary tuberculosis. 8% patients had chronic ill health and are immunocompromised due to pre-existing tubercular lesion, lepromatous leprosy and having HIV infection.

Addiction

Alcoholism and intravenous drug abuse are found 34 % and 12% cases respectively. So thus, this study supports that of work by Bosshordt, McHenry CR, Lille St, Elliot DC and Sudersky LA.[19]

In case of Fournier's gangrene alcoholism is account for 22% of cases which is slightly below than that of Smith study. This lower percentage may due to lower intake of alcohol consumption in our study population or may due to false history given by patient himself.

Predisposing factors

26 (52%) patients having definite predisposing factor of which the commonest one was trauma (46%) in various form like direct minor blunt or penetrating trauma, insect bite, operative trauma, subcutaneous injections of insulin or illicit drugs or burn injury.

But in 48% cases no definite aetiology was found. These findings were near closure to the study of Bosshordt, Lille St, Sudarsky LA, Rubinstien E and Rangaswami M.[20]

In Fournier's gangrene, the single most common cause was idiopathic (46.15%) followed by trauma.

Clinical features

Distinguishing NSTI from other less severe infections is difficult but crucial since NSTI is surgical emergency. A majority of NSTI patients present with an erythematous, tender, swollen area (100%) resembling cellulitis with fever (62%) and disproportionately severe pain (50%) at the site of involvement. Certain findings like crepitus which was found in 8% cases in this study once believed to be classic are not as common as previously thought. As the infectious process progresses, the skin characteristically becomes more erythematous, painful and swollen, with indistinct borders.

The skin develops a violaceous hue, may become necrotic with bullae formation (32%) and eventually appears hemorrhagic and gangrenous. There may be involvement of more than one area, separated by islands of normal skin. Involvement of the muscle and/or nerves may lead to weakness and loss of sensory innervation.

Symptoms of NSTI are often present for several days before the patient presents. As a result of this delay, signs of advanced infection may be present. Hypotension (26% of cases), tachycardia (54%), mental obtundation (18%), acute renal failure (4%) and shock were encountered

Clinical finding mentioned above are well comparable with study of Bosshordt TI, Mchenry CR, Lille St, Elliot DC, Majeski JA, Sudarsky LA, Rubinstien E.[21]

Tissue culture

Targeted tissue culture identified that in 78% cases (39 in number) aetiological agents were poly-bacterial of which in 38 cases had two and one case had three organisms. Four patients had mono-bacterial aetiology on culture sensitivity. Sterile culture was found in 14 %cases (7 in number).

This is comparable with study of Stephenson et al who published a series of 29 cases of necrotizing fasciitis and found that in 23 patients there was more than one organism and in 16 patients had three or more organisms.[22]

Regarding sterile culture sensitivity which is found in 7 cases may due to prior antibiotic therapy or faulty technique or prolong preservation. Among the polybacterial aetiology *E. coli* was the most common organism (26 in number), *Streptococcus* is the second most common (18 in number), *Pseudomonas* and *Bacteroides* were jointly third (both of each 9 in number), *Staphylococcus* and *Proteus* were found in 7 cases each and *Klebsiella* and *Enterobacter* were found in 2 cases.

This is not comparable of study of Elliott DC and Bosshardt TL where overall the most common organism is *Streptococcus* but here is *E. coli* followed by *Streptococcus*.[23]

The increased incidence of *E. coli* infection in this study could be explained by the fact that the commonest site of infection was scrotum and perineum (Laro E).

Among the nonbacterial infection, *Streptococcus* was only organism that had been isolated and all were from the lower extremity. This is also tallies with study of Chelsom J and Wang KC.

In case of Fournier's gangrene, aetiological agents were multibacterial, *E. coli* being the most common (16 in number) followed by *Bacteroides* in 8 cases and *Proteus* in 5 cases. *Streptococcus* was not found even in single case. This finding tally with the work of Paty R series though where *streptococcus* is the second most organisms that has been isolated.

Antibiotic therapy

The most the patients were treated three combined antibiotics with ampicillin/second or third generation cephalosporine + metronidazole/clindamycin + aminoglycoside according to culture sensitivity results.

Type of operation

Present approach was to cover soft tissues with split-thickness skin grafts or by mobilization of healthy skin and apposition by suturing once the infection has been eradicated. No extensive procedures are employed in the acute setting. Prompt closure of wounds is important to eliminate a portal of entry for continued bacterial infection, to prevent ongoing serum loss, and to allow for early rehabilitation.

Overall the most common of operation for definite treatment was mobilization of healthy skin and apposition by suturing (24 cases) and split skin grafting were done in 21 cases. 5 patients died before any definitive surgery.

In case of Fournier's gangrene, mobilization of healthy skin and suturing was the most common definitive procedure, had been performed in 23 cases out of 26 of Fournier's gangrene. Split skin graft was done only one case. Split skin grafting was most commonly performed in the necrotizing fasciitis involving lower extremity and anterior abdominal wall.

Outcome

Five patients died out of 50, accounting mortality rate was 10%. In most of study like Bosshordt TI, Mchenry CR, Lille St and associate, Elliot DC, Majeski JA and associate, Sudarsky LA and Rubinstien E shows mortality rate varies from 6% to 33%.[24]

Diabetes mellitus has a direct effect in the outcome of the patients, Elliot et al mentioned that DM was the most common pre-existing medical condition which presents in 65.4% of admitted patients; however, the presence of diabetes did not affect mortality, unless it occurred in conjunction with certain other diseases.

Here out of 21 diabetic patients 3 died of which 2 have associated other co-morbidity like PVD and renal failure. So, diabetes comprises 60% of death, 40% of which have associated other co-morbidities.

So, this study is correlated with that of Elliot work but not with Rea and Wyrick who presented 44 cases of NF among them 8 patients was diabetic; 5 out of 8 died (63%).[25]

Mortality was more common in Fournier's gangrene and necrotizing fasciitis involving lower extremities (both of which 2 in number).

In this study, mortality was higher in polybacterial infections (3 cases) than in monobacterial infections. *Streptococcus* was the most commonly isolated from dead patients (4 cases) followed by *E. coli* and *Pseudomonas* (each account for 2). Other organisms were *Bacteroides* accounting 10% cases (1 in number). In 80% of mortality, first debridement was done after 24 hours of admission where as it was 20% when it was done within 24 hours of admission.

The relation to socio-economic status could not be assessed properly on an account of the fact that the hospital in which the study was conducted is attended by

the poor people mainly. The incidence of this disease in the population could not be assessed, as the study deals with hospital admission only. A detailed study could not be undertaken to establish any epidemiological trend, because of lack of time and available facilities. Long time follow up could not be possible because of lack of time.

CONCLUSION

Current study showed increased frequency of necrotizing fasciitis in people aged above 40 years. Diabetes mellitus other premorbid conditions increase the risk of mortality. The presence of erythema, swelling, bullous lesion and disproportional pain to local signs raised the suspicion of necrotizing fasciitis. Findings at surgical exploration and skin biopsy were the only reliable means of diagnosis. Polymicrobial infection in combination of *Escherichia coli*, *Streptococcus*, *Pseudomonus*, *Bacteroids* and *Staphylococcus* were most commonly found. Early debridement, parenteral combined antibiotic and supportive measure formed the basis of treatment. Septicemia was a common complication which often caused death.

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