Original Article

Prospective evaluation of risk factors for mortality in patients of Fournier's gangrene: A single center experience

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ABSTRACT

Introduction: Fournier's gangrene is an aggressive disease with high morbidity and mortality. The aim of this study was to assess risk factors associated with mortality among patients of Fournier's gangrene.

Materials and Methods: Between May 2011 and September 2012, all patients of Fournier's gangrene treated at our center were included in the study. All patients underwent emergency surgical debridement and received broad spectrum intravenous antibiotics. Their baseline characteristics, treatment, and follow-up data were recorded and analyzed.

Results: A total of 30 patients were included in the study. Of these, six patients (20%) died during the treatment. Age >55 years, total leukocyte count >15000 cumm, extent of the area involved, septic shock at admission, visual analog scale (VAS) >7 at admission, and Fournier gangrene severity index (FGSI) score >8 at admission were significantly associated with increased mortality.

Conclusion: In patients of Fournier's gangrene, increased age, total leukocyte count, extent of the area involved, septic shock at admission, VAS score, and FGSI score at admission have a significant association with mortality.

Key words: Fournier's gangrene, Fournier gangrene severity index, mortality, surgical debridement

INTRODUCTION

Fournier's gangrene (FG) is a rapidly progressive necrotizing fasciitis of the genitalia, perineum and abdominal wall that primarily involves subcutaneous tissues.[1] It was first described in 1883 by the French Dermatologist Jean-Alfred Fournier as idiopathic gangrene of the penis and scrotum in five young men.[2] FG is a polymicrobial, synergistic aerobic and anaerobic infection from a colorectal, genitourinary or cutaneous infection from genitals, perineum or anus. The most common pathogens being *Escherichia coli*.[3,4] Predisposing factor for FG are impaired host defense (diabetes mellitus (DM), chronic alcoholism, malignancy, radiotherapy, chemotherapy, AIDS), local trauma, chronic renal failure (CRF), periurethral urine leak, perineal surgery, and paraphimosis among others.[5-8] The presentation of the disease is variable with classical presentation of pain, fever, edema, erythema, and crepitus is seen in 50-62% of cases.[9] FG continues to have high mortality despite advances in surgical technique, critical care and development of newer antibiotics. Most studies report mortality rates between 20% and 40% with a range of 4-88%.[10,11] We evaluated risk factors associated with mortality in our experience in the management of FG.

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MATERIALS AND METHODS

Between May 2011 and September 2012, all patients admitted with a diagnosis of FG at our institution were considered for inclusion in the study. Patients who refused to give consent and those who lost to follow-up earlier than 1 month after admission were excluded from the study.

On admission, patient's demographic data, detailed past and present illness history, physical examination findings and routine investigation data (hemoglobin, total leukocyte

count, serum creatinine, serum sodium, serum potassium, and blood sugar) were recorded. Pain score was recorded using 10 point visual analog scale (VAS). Fournier gangrene severity index (FGSI) score, associated co-morbidity and quality of life score using SF-12 questionnaire (physical component summary (PCS) and mental component summary (MCS)) were also calculated on admission.

All patients underwent extensive debridement of the necrotic tissue within 6 h of admission. Empirically, the combination of antibiotics (piperacillin + tazobactum and metronidazole) covering gram positive, gram negative, and anaerobe was started in all patients. Pus collected during surgery was sent for culture and sensitivity. Once culture and sensitivity report became available, the antibiotic was changed accordingly. In cases where necrotic tissue reappeared, repeat debridement was carried out. Patients were discharged when the wound was healthy and granulating and toxic symptoms resolved. In cases where the wound size was too large for healing by secondary intention, split thickness skin graft was placed over the wound. Patients were followed-up for a period of 1 month when their quality of life score using SF-12 questionnaire (PCS and MCS) were recorded.

Data were recorded on Microsoft Excel spreadsheet (Microsoft, Seattle, WA, USA) and analyzed by S.P.S.S software package version 12.0 (SPSS Inc., Chicago, IL). Fisher's exact test was used for categorical data and unpaired *t*-test was used for continuous data. Univariate and multivariate regression analysis was used to analyses factors associated with mortality. $P < 0.05$ was considered statistically significant.

RESULTS

During the study period, 35 patients were admitted with the diagnosis of FG, out of which 30 patients who fulfilled inclusion/exclusion criteria were included in the study. Of the five patients excluded, four lost to follow-up after discharge and one patient refused to give informed consent. Out of 30 patients included in the study, six (20%) died during the hospital admission (between 14 h and 78 h of admission). All 30 patients were male.

Baseline characteristic of the patients is summarized in Table 1. The mean age and total leukocyte count at admission was significantly higher in non-survivors. The mean serum sodium concentration was significantly lower among non-survivors. The incidence of septic shock at presentation was significantly higher among non-survivors. The mean VAS score, FGSI score, and PCS score was significantly worse among non-survivors. The mean length of hospital stay was 9.66 ± 2.29 days.

Table 1: Baseline characteristics

Routine investigation	Survivor (*n*=24)	Non-survivors (*n*=6)	*P* value*
Age (years)	35.70±9.45	55±9.46	0.0001 (S)
Duration between start of symptom and presentation (days)	4.43±1.52	4.89±0.89	0.14 (NS)
Hematcrit (%)	35.25±3.39	38.16±4.70	0.09 (NS)
Total leukocyte count (cumm)	14570±2493.1	17928.33±2249.8	0.005 (S)
Serum creatinine (mg/dl)	1.91±0.75	2.11±0.14	0.52 (NS)
Serum sodium (meq/l)	132.48±2.68	129.1±0.90	0.005 (S)
Blood sugar	202.62±99.28	231±40.47	0.50 (NS)
Septic shock at admission	0†	3†	0.01 (S)#
VAS (10 point analogue scale) at admission	6.87±0.74	9.33±0.81	<0.0001 (S)
FGSI score at admission	5.83±1.71	10±0.89	<0.0001 (S)
QOL score (SF-12 Questionnaire)			
PCS at admission	21.08±3.28	16.16±0.75	0.001 (S)
MCS at admission	29.20±7.34	23.83±5.19	0.10 (NS)
Comorbidity			
Diabetes mellitus	14†	5†	0.72 (NS)#
Cardiac disease	2†	1†	0.52 (NS)#
Hypertension	6†	3†	0.40 (NS)#
Area of involvement at presentation			
Scrotum	20†	2†	0.44 (NS)#
Scrotum and penis	3†	0†	
Anterior abdominal wall and thigh	1†	4†	0.01 (S)#

VAS=Visual analog scale, FGSI=Fournier gangrene severity index, QOL=Quality of life, MCS=Mental component summary, PCS=Physical component summary, S=Significant, NS=Not significant.*Unpaired *t*-test, #Fisher's exact test, †Data in number, Data in mean±SD

As far as the area of involvement at presentation is concerned, involvement of the abdominal wall and thigh was significantly higher in non-survivors. The average number of debridement was 2.08 ± 0.92 versus 2.66 ± 0.81 ($P = 0.17$) among the survivors and the non-survivors respectively. Among the associated co-morbidities, none was significantly different among survivors and non-survivors. The result of bacteriological culture and sensitivity are summarized in Table 2.

On univariate and multivariate regression analysis [Tables 3 and 4], age >55 years, TLC >15000 cumm at presentation, involvement of the abdominal wall and thigh, septic shock at presentation, VAS score >7 at presentation, and FGSI score >8 at presentation had a significant association with mortality.

A total of 24 patients completed 1 month follow-up and all of them were doing well (PCS score and MCS score 47.08 ± 4.74 and 48.45 ± 3.94 respectively). Two patients required split thickness skin graft and, in the rest of the patients, wounds healed by secondary intention or delayed closure.

DISCUSSION

FG is a specific type of necrotizing fasciitis, a potentially fatal infectious condition that affects primarily the skin and subcutaneous tissues of the external genitalia and perineum.[10] It is believed to be a polymicrobial infection that leads to obliterative endarteritis, ischemia, and consequently, necrosis of the skin, and adjacent tissues.[12,13] The mainstay of treatment is aggressive and repeated radical surgical debridement and intravenous antibiotic therapy and sometimes intensive care.[1] The need for colostomy diversion and multiple surgical debridement have a significant impact on survival.[14,15]

Various co-morbidities are known to be associated with FG, of which DM is the most common. Its association with increased mortality is controversial.[8,16-18] There is similar uncertainty about the association of age and mortality.[8,19-22] Ischemic heart disease and CRF, specially hemodialysis dependence, seem to be significantly associated with mortality.[1,8,20,23]

Janane *et al.*,[24] found that the extent of body surface area involved by the disease process has a significant impact on the mortality ($P = 0.001$). Other studies also found its significant association with mortality.[1,17] However, this association is not universal.[25,26] Kara *et al.*, found that the presence of septic shock at admission is significantly associated with mortality ($P < 0.05$). Altarac *et al.*,[1] found that severe sepsis at presentation, hypotension and high heart and respiratory rates had a significant impact on mortality. Abnormal laboratory parameters at admission such as greater leukocyte counts, urea, creatinine, creatine kinase, alkaline phosphatase, and lactate dehydrogenase levels and lower hematocrit, bicarbonate, sodium, potassium,

Table 2: Bacteriological culture and sensitivity

Bacteria	Number of patients (%)	Antibiotic sensitivity
Escherichia coli	10 (33.33)	Levofloxacin, amikacin, imipenum, piperacillin+tazobactum
Staphylococcus	3 (3.33)	Amoxicillin+clavulanic acid, vancomycin
Pseudomonas	4 (13.33)	Levofloxacin, amikacin, piperacillin+tazobactum, imipenum
Streptococcus	2 (13.33)	Amoxicillin+clavulanic acid, piperacillin+tazobactum
Anaerobes	5 (16.66)	Piperacillin+tazobactum, clindamycin, metronidazole
No organism	6 (20)	

Table 3: Univariate regression analysis: Correlation of various parameters with mortality

Variable	Number of pts (%)	Mortality (%)	*P* value
Age			
≤55 years	21	0	0.01 (S)
>55 years	9	66.66	
TLC			
≤15,000/cumm	22	0	0.02 (S)
>15,000/cumm	8	75	
Area Involved			
Scrotum	22	9.09	0.01 (S)
Scrotum and penis	3	0	
Ant abdominal wall and thigh	5	80	
Diabetes mellitus			
Yes	19	26.31	0.72 (NS)
No	11	9.09	
Cardiac disease			
Yes	3	33.33	0.31 (NS)
No	27	18.51	
Hypertension			
Yes	9	33.33	0.41 (NS)
No	21	14.28	
Septic shock at admission			
Yes	3	100	0.005 (S)
No	27	0	
VAS at admission			
≤7	21	0	<0.001 (S)
>7	9	66.66	
FGSI score at admission			
≤8	22	0	<0.001 (S)
>8	8	75	

S=Significant, NS=Not significant, TLC=Total leukocyte count, VAS=Visual analog scale, FGSI=Fournier's gangrene severity index

Table 4: Multivariate regression analysis: Correlation of various parameters with mortality

Outcome	Parameters	HR	95% CI	*P* value
Mortality	Diabetes mellitus	1.14	0.96-1.33	0.13 (NS)
	Cardiac disease	1.11	0.91-1.35	0.33 (NS)
	Hypertension	1.15	0.93-1.41	0.44 (NS)
	Septic shock at admission	1.23	1.1-2.49	<0.001 (S)
	Area of involvement	4.9	3.81-6.32	<0.001 (S)
	VAS at admission	1.41	1.03-1.93	0.03 (S)
	FGSI score at admission	1.83	1.03-3.26	0.04 (S)
	Age	1.63	1.2-2.24	0.003 (S)
	TLC count	1.71	1.2-2.12	0.03 (S)

S=Significant, NS=Not significant, TLC=Total leukocyte count, VAS=Visual analog scale, FGSI=Fournier's gangrene severity index, HR=Hazard ratio, CI=Confidence interval

calcium, total protein, and albumin levels had a significant impact on mortality.[21,25] Clayton *et al*.,[26] found blood urea nitrogen level more than 50 mg/dl to be significantly associated with mortality. Tuncel *et al*.,[22] found only serum albumin and alkaline phosphatase level among the admission laboratory parameters to be significantly associated with mortality. Ruiz-Tovar *et al*.,[27] in their study found that serum creatinine >1.4 mg/dl, hemoglobin <10 g/dl, and platelet count < 150×10^9/L are associated with higher mortality rates.

Laor *et al*.,[25] first introduced the FGSI score and concluded that a threshold parameter of 9 predicts survival. FGSI score >9 had 75% probability of death and ≤9 had 78% probability of survival. Since then, several studies were published regarding the validity of FGSI, but the results are still controversial. Kara *et al*.,[18] found that FGSI scores ≥7 were factors affecting mortality rates with statistical significance ($P < 0.05$). Altarac *et al*.,[1] found FGSI score to be significantly higher among non-survivors (11 vs. 6, $P < 0.0001$). On the other hand, Janane *et al*.,[24] found that median admission FGSI scores for survivors and non-survivors were not significantly different (2.1 ± 2.0 vs. 4.2 ± 3.8, $P = 0.331$). Tuncel *et al*.,[22] did not find a significant association of FGSI to mortality.

In our study, the mortality rate was 20%. Univariate and multivariate regression analysis revealed age >55years, total leukocyte count >15000 cumm, larger extent of the area involved, septic shock at admission, VAS score >7 at admission, FGSI score >8 at admission was significantly associated with the mortality rate.

CONCLUSION

In patients of Fournier's gangrene, increased age, total leukocyte count, extent of the area involved, septic shock at admission, VAS score, and FGSI score at admission are significantly associated with increased mortality.

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