

ORIGINAL RESEARCH

Factors Related to Mortality in Patients with Fournier's Gangrene or Necrotising Fasciitis; a 10-year Cross-Sectional Study

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Abstract: **Introduction:** Fournier's gangrene (FG) is a life-threatening disease, even with early diagnosis and administration of vigorous treatment, its mortality rate is high. This study aimed to evaluate the factors relate to mortality in patients with FG or necrotising fasciitis managed in a referral center. **Methods:** This retrospective cross-sectional study was conducted on patients managed in a tertiary referral center, Tehran, Iran, from March 2009 to March 2019, with diagnosis of FG or necrotising fasciitis. The correlation between different demographic and clinical parameters with mortality was analysed and reported. **Results:** 73 cases with the mean age of 59.1 ± 15.8 (range: 25 – 88) years were studied (87.7% male). 21 (28.8%) patients died. *Escherichia coli* (26 cases, 35.6%) was the most frequent microorganism in cultures. Non-survived cases had higher mean age ($p = 0.01$), higher frequency of hyperlipidaemia ($p = 0.02$), immunosuppression ($p < 0.001$), longer hospital stay ($p=0.02$), lower blood pressure ($p=0.01$), and lower platelet count ($p<0.001$). Based on multivariate analysis, age ($p = 0.015$; Odds: 0.88 (0.79-0.97)), haematocrit level ($p = 0.01$; Odds: 1.27 (1.04-1.55)), platelet count ($p = 0.03$; Odds: 10.11 (1.14-89.35)), and immunosuppression ($p = 0.01$; Odds: 0.01 (0.0-0.54)) were independent related factors of mortality. **Conclusion:** The rate of mortality due to FG and necrotizing fasciitis was 28.8%. Based on multivariate analysis, the independent related factors of mortality were older age, lower haematocrit level and platelet count, and presence of immunosuppression.

Keywords: Fournier's Gangrene; Fournier's Gangrene Severity Index; Mortality; Thrombocytopenia

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1. Introduction

Fournier's gangrene (FG) is a rapidly progressive, life-threatening necrotising infection of soft tissues, which typically involves the external genitalia and perineal area, but

can also affect the abdominal wall and thighs (1).

The disease mortality rate remains high despite early surgical interventions and advances in intensive care and medical treatment, due to its rapidly progressive nature (2-4). In recent decades, several studies published in the medical literature have examined the diverse scoring systems used to predict the risk of mortality in these patients (5, 6). One of these scores is Fournier's Gangrene Severity Index Score (FGSI). FGSI incorporates nine clinical and para-clinical parameters, including temperature, heart rate, respiratory rate, serum sodium, serum potassium, serum creatinine, leuko-

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cyte count, haematocrit and arterial blood level of bicarbonate (7). Some studies confirmed the efficacy of FGSI (8) and Lin et al. introduced simplified FGSI including creatinine, hematocrit and serum potassium (9). In contrast, some studies concluded that this score cannot predict the mortality rate (10). Moreover, it seems that other parameters and laboratory data are also capable of effectively predicting the prognosis in such septic patients (11). The medical literature has also reported several other clinical factors related to the increased mortality risk in patients with FG. Some of these factors include primary anorectal cancer, immunosuppression, senectitude, delay in treatment initiation, and hepatic dysfunction (12, 13).

The aim of this study was to evaluate the factors related to mortality in patients with FG or necrotising fasciitis managed in a referral Urology Center, over the past ten years.

2. Methods

2.1. Study design and setting

This retrospective cross-sectional study was conducted on patients managed in a tertiary referral center, Tehran, Iran, from March 2009 to March 2019, with diagnosis of Fournier's gangrene or necrotising fasciitis. The correlation between different demographic and clinical parameters with mortality was analysed and reported. The ethical committee of the hospital approved this study and permitted us to review patients' medical data (IR.SBMU.RETECH.REC.1398.476). The patients' health records were anonymised.

2.2. Data gathering

The source of data was the medical profile of patients, which was searched using terms such as Fournier's gangrene, soft tissue infection, and necrotising fasciitis. The collected medical data included sex, age, co-morbidities (diabetes mellitus, cerebrovascular accidents, malignancies, urinary incontinence, bed ridden), laboratory findings, duration of hospital stay, antibiotics used in the treatment, immune system status and the final outcome. Disease diagnosis was based on the symptoms of pain, erythema, ulcers, swelling, crepitus, necrosis, purulent discharge and later confirmation by tissue inspection in the operating room. Also, vital signs (pulse rate, respiratory rate, blood pressure and temperature) were assessed for signs of systemic inflammatory response syndrome. In addition, Fournier's Gangrene Severity Index (FGSI), which incorporates nine variables (temperature, heart rate, respiratory rate, serum sodium, serum potassium, serum creatinine, haematocrit, white blood cell count, and serum bicarbonate), was calculated for all patients (3). The patients were classified, according to the extent of FG, in to the following groups: 1) patients with gangrene confined to the scrotum, 2) patients with penile and scrotal gangrene,

3) patient with scrotal gangrene extending to the perineum, 4) patient with scrotal gangrene extending to the abdominal wall or thighs.

Patients with solitary abscess as well as those with soft tissue infection without perineal or scrotal involvement were excluded from the study. Patients with incomplete data were also omitted.

Mortality was described as disease-related death during the hospital stay.

Two urology residents read the records and gathered the data and finally, the corresponding author verified the data.

2.3. Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences version 26. First, the normality of data was checked and independent t-test and Mann-Whitney test were used according to the type of hypothesis. Quantitative outcomes were shown using descriptive statistics (mean \pm standard deviation) and qualitative variables were reported as frequency (%). Regression analysis was performed to determine the association of risk factors and mortality of FG. A P-value less than 0.05 was considered statistically significant.

3. Results

106 patients with FG or necrotising fasciitis were admitted to the studied hospital during the study period. 33 cases were excluded because of insufficient data. 73 cases with the mean age of 59.1 ± 15.8 (range: 25 – 88) years were studied (87.7% male). 21 (28.8%) patients died.

The most commonly involved area was perineum. All cases were treated with surgical debridement of necrotic tissues, in 21 (28.8%) of whom debridement was extensive enough to necessitate additional tissue reconstruction (flap (3 cases), tissue graft (6 cases), and secondary suturing (12 cases)).

The results of wound culture were available for 52 patients and *Escherichia coli* (26 cases, 35.6%) was the most frequent microorganism. All four patients whose wound cultures were positive for *Klebsiella*, *Proteus*, *Pseudomonas* and *Acinetobacter* died. Non-survived cases had higher mean age ($p = 0.01$), higher frequency of hyperlipidaemia ($p = 0.02$), immunosuppression ($p < 0.001$), longer hospital stay ($p=0.02$), lower blood pressure ($p=0.01$), and lower platelet count ($p<0.001$). Seven patients had platelet counts of $<50000/\text{mm}^3$, six of whom died.

Regarding FGSI variables, non-survived patients had lower serum Haematocrit ($p=0.0$), lower serum bicarbonate ($p=0.0$), and higher respiratory rate ($p=0.03$).

The mean FGSI score was 8.7 ± 3.5 in dead and 3.5 ± 2.9 in survived cases ($p < 0.0001$). 50 (96.2%) survived cases and 11 (42.4%) dead cases had $\text{FGSI} \leq 9$. 10 (47.6%) non-survived cases had $\text{FGSI} > 9$. Table 1 compares the baseline charac-

teristics of participants between survived and non-survived cases.

Table 2 shows the factors related to mortality based on the multivariate analysis. Based on this analysis, age, haematocrit level, platelet count, and immunosuppression were independent factors related to mortality.

4. Discussion

This study investigated 73 cases of FG or necrotising fasciitis who were hospitalised in our center over a 10-year period. The rate of mortality amongst our FG patients was 28.8%. Based on multivariate analysis, the independent related factors of mortality were older age, lower haematocrit level and platelet count, and presence of immunosuppression.

The mean age of survivors and deceased patients was significantly different; also, in multivariate analysis, we showed that age had a direct effect on mortality of the patients. Some published studies show similar results (7), whilst the result of others is contradictory to ours (4, 14).

Tuncel et al. reported a correlation between diabetes mellitus (DM) and poor prognosis in FG patients (10), but Corcoran et al. found no similar association in their research (8). In this study, there was no significant difference between the frequency of DM amongst survivors and patients who died. The frequency of hyperlipidaemia and immunosuppression, was significantly different between survived and non-survived cases ($p = 0.02$ and $p < 0.001$, respectively).

E. coli, *Streptococcus*, *Staphylococcus*, *Enterococcus* and *Bacteroides* genera were the most common bacteriological microorganisms that had been isolated from FG patients in previous studies (15, 16). In this study, the bacteriological agents most frequently detected in the wound cultures corresponded to those reported in medical literature and included *E. coli*, as well as *Streptococcus*, *Staphylococcus*. In rare cases, *Enterococcus* and *Pseudomonas* species were isolated. In contrast, the results of wound culture were negative, with no causative agent detected, in 21 (28.8%) cases. This is probably due to an anaerobic microbial growth that could not be isolated using our culture conditions.

No clear consensus exists on the most reliable clinical parameters for prediction of poor prognosis in FG patients (15). FGSI has been developed to facilitate the prediction of FG outcomes in affected patients. Laor et al. found that an FGSI score of >9 corresponded to 75% probability of a lethal outcome, while a score of ≤ 9 correlated with 78% survival probability (3). This threshold for the prediction of patient mortality was also confirmed in other studies (14, 17). In this study, the mean FGSI score in deceased cases was significantly higher, which was consistent with other studies (7, 8, 18). Notwithstanding the significantly higher mean FGSI score in the deceased patient group, only 47.6% of patients

who died had FGSI >9 .

Yeniylol et al. found that deceased patients had elevated serum levels of urea, creatinine, alkaline phosphatase, and lactate dehydrogenase, and high leukocyte counts, while their levels of sodium, potassium, HCO_3 , haematocrit, total protein, and albumin were lower than the survivors' (14). Clayton et al. found that amongst various variables, a blood urea nitrogen level of higher than 50 mg/dl was the most significant factor in predicting FG mortality (19). In the study conducted by Tsung-Yen Lin, only serum creatinine, potassium and haematocrit levels showed notable association with the risk of patient mortality (9). In our study, respiratory rate, haematocrit, and HCO_3 level were found to be significantly different between survivors and deceased patients.

Thrombocytopenia increased bleeding tendency and susceptibility to infection (20) and multiple studies pointed to the relationship between thrombocytopenia and likelihood of death in sepsis (21, 22). Mean platelet counts of survivors and deceased patients was in a normal range but deceased patients had significantly lower mean platelet counts ($135400 \pm 77600/\text{mm}^3$ vs. $256700 \pm 136800/\text{mm}^3$, $p = 0.0001$). Platelet counts of seven patients were $<50000/\text{mm}^3$, six of whom died.

According to our findings, some of the nine parameters incorporated in FGSI were not significantly different between deceased and survived FG patients. However, some other factors including age, thrombocytopenia, and especially platelet counts $<50000/\text{mm}^3$ were found to be predictive of mortality risk in these patients. Therefore, more studies using larger sample sizes are required to further evaluate these parameters in order to facilitate the development of a more efficacious FG scoring model.

5. Limitations

One of the limitations of our study is that due to incomplete files and the retrospective fashion of the study, we had to exclude many cases before data analysis, so it reduced our sample size. Nevertheless, this sample size is one of the largest sample sizes for this rare disease.

6. Conclusion

The rate of mortality of FG and necrotizing fasciitis was 28.8% in this study. Based on multivariate analysis, the independent factors related to mortality were older age, lower haematocrit level and platelet count, and presence of immunosuppression.



Table 1: Comparing the baseline characteristics between survived and non-survived patients with Fournier's gangrene or necrotising fasciitis

Variables	Died (n = 21)	Survived (n = 52)	P value
Sex			
Male	16 (76.2)	48(92.4)	0.07
Female	5 (23.8)	4(7.6)	
Age (years)			
Mean \pm SD	66.2 \pm 11.1	56.1 \pm 16.5	0.01
Medical history			
Diabetes mellitus	11(52.3)	23(44.2)	0.35
Hyperlipidaemia	4(19.0)	1(1.9)	0.02
Immunosuppression	11(52.3)	7(13.4)	<0.001
Colorectal or urological surgeries	4(19.0)	16(30.7)	0.38
Presenting vital sign			
Temperature ($^{\circ}$ C)	37.4 \pm 0.7	37.3 \pm 0.8	0.90
Respiratory Rate (/minute)	19.2 \pm 4.8	16.8 \pm 1.8	0.03
Pulse Rate (beats/minute)	89.2 \pm 16.87	83.8 \pm 10.9	0.10
Systolic blood pressure	114.2 \pm 16.3	124.9 \pm 17	0.01
Laboratory findings			
Serum Creatinine (mg/dl)	2.8 \pm 1.8	1.7 \pm 2.9	0.06
Serum Sodium (mM)	134.5 \pm 7.3	137 \pm 4.8	0.10
Serum Potassium(mM)	4 \pm 0.6	4 \pm 0.4	0.70
Haematocrit (%)	27.1 \pm 5.1	33.5 \pm 5.5	< 0.001
White blood cells ($10^3/\mu$ L)	16.1 \pm 8.8	15.1 \pm 6.7	0.6
Serum HCO ₃ (mM)	17.2 \pm 6.2	23 \pm 6.1	< 0.001
Platelet (/mm ³)	135400 \pm 77600	256700 \pm 136800	< 0.001
Site of involvement			
Scrotum	1(4.7)	15(28.8)	0.30
Penis	0(0.0)	4(7.6)	
Perineum	7(33.3)	13(25.0)	
Perianal	9(42.8)	9(17.3)	
Abdomen	4(19)	11(21.1)	
Hospital stay (days)			
Mean \pm SD	18.0 \pm 22.6	10.1 \pm 7.1	0.02

Data are presented as mean \pm standard deviation or frequency (%).

Table 2: Independent factors related to mortality in patients with Fournier's Gangrene or Necrotising Fasciitis

Independent factors	P-value	Odds ratio (95% CI)*
Age	0.015	0.88 (0.79-0.97)
Haematocrit	0.01	1.27 (1.04-1.55)
Immunosuppression	0.03	10.11(1.14-89.35)
Platelet > 50000	0.02	0.01 (0.0-0.54)

*CI: confidence interval.

7. Declarations

7.1. Author contribution

AAD: Conception and design, Critical revision of the manuscript for important intellectual content, Supervision

AR: Analysis and Interpretation of data, Statistical analysis

BJ: Administrative, technical or material support, Supervision

SM: Drafting of the manuscript

VS: Acquisition of data, Analysis and Interpretation of data

SAH: Acquisition of data

SG: Drafting of the manuscript

RH: Drafting of the manuscript, Supervision

JK: Conception and design, Critical revision of the manuscript for important intellectual content, Administrative, technical or material

7.2. support Supervision

All authors have read and approved the manuscript.



7.3. Data availability

Authors guarantee that data of the study are available and will be provided if anyone needs them.

7.4. Conflict of interests

None.

7.5. Funding

None.

7.6. Acknowledgements

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