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RESEARCH ARTICLE

FOURNIER'S GANGRENE: OUR EXPERIENCE WITH 50 PATIENTS AND ANALYSIS OF FACTORS AFFECTING MORTALITY

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ABSTRACT

Fournier's gangrene (FG) is a rare, rapidly progressive, fulminant form of necrotizing fasciitis of the genital, perianal and perineal regions, which may extend up to the abdominal wall between the fascial planes. Early diagnosis, aggressive resuscitation of the patient, administration of broad-spectrum antibiotics and aggressive radical surgical debridement(s), are the key of successful treatment. In this study, we aimed to investigate patients with FG and to identify risk factors that affect mortality. In this study the treatment records of 50 patients admitted to Patna medical college, General Surgery Department, with a diagnosis of Fournier's gangrene during the 1 year period between May 2015 to April 2016 were reviewed. Of the 50 patients studied, 12 died and 38 survived; the overall mortality rate was 24%. The most frequent bacterial organisms cultured from the wound sites were **Escherichia coli** (85.6%) and Klebsiella (40.5%). Patients had a median hospital stay of 21 (range, 4–66) days. The median hospitalization time (MHT) for the surviving patients was 26.00 days compared to 8.00 days for the non-survivors.

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INTRODUCTION

Fournier's gangrene (FG) is a rare, rapidly progressive, fulminant form of necrotizing fasciitis of the genital, perianal and perineal regions, which may extend up to the abdominal wall between the fascial planes (Corman *et al*., 1999). It is secondary to polymicrobial infection by aerobic and anaerobic bacteria with a synergistic action (Morpurgo and Galandiuk, 2002; Yanar *et al*., 2006; Paty and Smith, 1992). The cause of infection is identifiable in 95% of cases, mainly arising from anorectal, genito-urinary and cutaneous sources (Jeong *et al*., 2005). Predisposing factors such as diabetes and Immunosuppression lead to vascular disease and suppressed immunity that increase susceptibility to polymicrobial Infection. Diagnosis is based on clinical signs and physical examination. Radiological methods may help to delineate the extent of the disease but false negatives may happen. Dissemination of the disease was found to be a major determinant of patients' outcomes in previous reports (Yilmazlar *et al*., 2007; Roghmann *et al*., 2012). It may reflect the aggressiveness of the involved infectious agents or reflects the degree of patients' immunosuppression. Several reports tried to evaluate the usefulness of diverse scoring systems.

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Fournier's Gangrene Severity Index (FGSI) has become a standard for researchers, being routinely published in FG literature and is considered as a good predicting tool (Verma *et al*., 2012; Morua *et al*., 2009). The mortality rate for FG is still high, at 20–50% in most contemporary series (Sorensen *et al*., 2009; Ugwumba *et al*., 1998). However, the incidence is rising, most likely due to an increase in the mean age of the population, as well as increased numbers of patients on immunosuppressive therapy or suffering from human immunodeficiency virus (HIV) infection, especially in Africa (Fournier, 1883; Unalp *et al*., 2008). Early diagnosis, aggressive resuscitation of the patient, administration of broad-spectrum antibiotics and aggressive radical surgical debridement(s), are the key of successful treatment. In this study, we aimed to investigate patients with FG and to identify risk factors that affect mortality.

MATERIALS AND METHODS

In this study the treatment records of 50 patients admitted to Patna medical college, General Surgery Department, with a diagnosis of Fournier's gangrene during the 1 year period between May 2015 to April 2016 were reviewed. The inclusion criteria included patients undergoing wide surgical excision of scrotal and/or perineal necrosis along with other involved areas

with a postoperative diagnosis of Fournier's gangrene. Excluded were patients who had a local superficial inflammation of the perianal or urogenital regions as they were treated in Urology Department. Mortality was defined as disease-related death during the hospital stay and survival was measured in days. The prognostic variables used in the outcome analysis were the patient's age, female gender, history of diabetes, the interval between the onset of symptoms and the initial debridement, renal failure, need for postoperative mechanical ventilation and occurrence of septic shock. Mortality was accepted as disease-related death during the hospitalization period.

RESULTS

Of the 50 patients studied, 12 died and 38 survived; the overall mortality rate was 24%. There were 44 men and 6 women with a mean age of 48 ± 16.81 years (range 18–85 years). The survivors (mean age 44.36 + 16.05 years) were significantly younger than the non-survivors (mean age 57.5 + 19.24 years) ($p < 0.001$). Sex was not a factor affecting mortality, even if the mortality among women was slightly higher (33.33%) compared to men (22.72%), but it did not reach statistical significance ($p = 0.14$).

Table 1.

Male	44
Female	6
Died	12
Survived	38
Diabetic	17

The source of infection was identified in 72 percent of the patients. The commonest source of sepsis was the urinary. Twenty one patients had at least one comorbidity. Diabetes mellitus (DM) was the most common comorbidity associated with FG and was present in 17 patients (34%) at the time of admission. In 29 patients (58%), predisposing factors could not be identified. Diabetes mellitus was an important factor affecting mortality as the mortality rate among non-diabetic patients was lower (15.5%) than patient with DM (41%) ($p = 0.3$). Furthermore DM influenced hospital stay or number of debridments.

Table 2. Factors affecting mortality & morbidity

Mortality among Diabetic	7 (41%)
Mortality among non diabetic	5 (15.5%)
Mortality among Males	10 (22.72%)
Mortality among Females	2 (33.33%)
Mean Hospital stay (diabetic)	45.62 days
Mean Hospital stay (non-diabetic)	32.90 days

The most common symptoms at the time of admission were deterioration of the general state (44%), perineal necrosis (92%), fever (60%), perineal or genital pain (76%), septic shock (22%). the average time of symptoms prior to referral to treatment was 11 days, ranging from 4 to 25 days. Regarding the exams performed on admission, complete blood count showed the presence of a hyperleukocytosis (> 10.000/mm3) in 39 patients (78%). The degree of anemia was severe necessitating blood transfusion in 9 patients (18%). Renal failure on admission (blood urea >0.5 g/l) was higher among the patients who died when compared to the survival group ($p < 0.001$). As for the location and extent of the injury, it was observed that FG was confined to the perineal area in 5 patients (10%), affecting the scrotum in 35 (70%) individuals. The gangrene extended to the abdominal wall in 9 patients (18%) and thorax in 1 patient (2%). It was found that the extension of the infection to the abdominal wall was a predictor of mortality ($p < 0.003$) (50% in the non survivors compared to 7% in the survivors).

Table 3. Site of Fournier's gangrene

Site of FG	No. of patients (%)
Perineal	5 (10%)
scrotal	35 (70%)
abdominal	9 (18%)
thoracic	1 (2%)

The most frequent bacterial organisms cultured from the wound sites were Escherichia coli (85.6%) and Klebsiella (40.5%). Before surgery, all patients underwent aggressive fluid resuscitation and were treated mostly with parenteral broad-spectrum triple antimicrobial agents, using a third-generation cephalosporin, an amino glycoside and metronidazole and received hemodynamic support when required. Mechanical ventilation, continuous monitoring, and inotropic support were applied when necessary in patients with cardiopulmonary failure due to sepsis. All patients underwent radical surgical debridement, ranging from 1 to 10 procedures, with an average of 2.5. Debridement consisted of excision of all necrotic tissue, cleansing with hydrogen peroxide, then saline and drainage. Along with the initial radical debridement, 5 patients (10%) underwent fecal diversion, with loop colostomy. Orchidectomy was carried out unilaterally for gangrenous testes in one patient (2%). It's interesting to notice that mortality rate was 52.63% in the single-debridement group and 66.66% in repeated debridement; however, these rates were not significantly different ($p = 0.08$). Mechanical ventilation, due to sepsis was applied in 11 patients (22%).

Table 4. Additional treatments required in Fournier's gangrene

Additional treatment required	No of patients
Mechanical ventillation	11 (22%)
Faecal diversion	5 (10%)
Orchidectomy	1(2%)

It was significantly higher in non survivor patients (91.6%) comparing to the survivors (0%) ($p < 0.001$). Patients had a median hospital stay of 21 (range, 4–66) days. The median hospitalization time (MHT) for the surviving patients was 26.00 days compared to 8.00 days for the non-survivors However the female gender, interval between the symptoms and surgical intervention and repeated debridements did not appear as predictors of mortality. In the subsequent multivariate analysis, none of above studied variables was identified as independent predictors of mortality.

DISCUSSION

Fournier's gangrene, caused by synergistic aerobic and anaerobic organisms, is a life-threatening disorder in which infection of the perineum and scrotum spreads along fascial planes, leading to soft-tissue necrosis. This infectious was initially described by Baurienne in 1764 (Tuncel *et al*., 2006). Before in 1883 Jean Alfred Fournier, French dermatologist described a syndrome of unexplained sudden onset and rapidly progressing gangrene in the penis and scrotum of 5 young men with no other pathology basis of sudden onset and rapid progression (Czymek *et al*., 2010). In its early reports Fournier's gangrene was described as an idiopathic entity, but in most cases a perianal infection, urinary tract and local trauma or skin condition at that level can be identified (Fournier, 1883). The mortality rate for FG is still high, (20–50%) in most contemporary series (Sorensen *et al*., 2009; Ugwumba *et al*., 1998), despite an increased knowledge of the etiology, diagnosis and treatment, and intensive-care techniques. The high mortality reflects both the aggressive nature of the infection and the destructive effects of accompanying predisposing factors. Several factors affecting the mortality were studied such as increasing age, primary anorectal infections, existence of diabetes, delay in treatment, evidence of systemic sepsis at presentation, extent and depth of involvement, a low haematocrit, a high leukocytosis and blood urea nitrogen, a high alkaline phosphatase and serum albumin, and many others (Verma *et al*., 2012; Morua *et al*., 2009; Sorensen *et al*., 2009; Ugwumba *et al*., 1998; Fournier, 1883; Unalp *et al*., 2008; Malik *et al*., 2010; Sallami *et al*., 2012; Yilmazlar *et al*., 2010; Ruiz-Tovar *et al*., 2012). These and other studied variables that influence the outcome of patients with FG, in large part, remains controversial. In this purpose, the FGSI was developed to help clinicians predict the outcome of patients with FG and remains an objective and simple method to quantify the extent of metabolic aberration at presentation in patients with FG. It has been validated in several reported studies (Verma *et al*., 2012; Morua *et al*., 2009; Ugwumba *et al*., 1998; Sallami *et al*., 2012). The average age of the patients was 47.5 years, in most published series from 40.9 to 61.7 years (Sorensen *et al*., 2009; Fournier, 1883). In a population based study of 1641 patients, Sorensen *et al*. found that an increasing patient age was the strongest independent predictor of mortality ($p < 0.0001$) (Fournier, 1883). Our results are in keeping with the study of Sorensen *et al*. as the survivors were significantly younger than the non-survivors in our series. With regard to gender, the male predominance is reported in 96%, so the female was present only in 4% (Sorensen *et al*., 2009; Fournier, 1883). Czymek *et al*., compared mortality between male and female in a series of 38 patients (26 M vs 12 F). Authors found that mortality is significantly higher among female (50% F vs 7.7% M, $p = 0.0011$) (Yilmazlar *et al*., 2010). We could not confirm this result, as female gender did not appear as predictor factor of mortality in our study (Table 2). Numerous factors have been implicated at the onset of FG, in particular, those involving the immune system (Ruiz-Tovar *et al*., 2012; García *et al*., 2011; Jarboui *et al*., 2008; Dahm *et al*., 2000). Diabetes mellitus was the most reported co-morbid disease associated with this pathology. Some authors estimate the prevalence of DM among FG patients between 50 and 70 percent (Nisbet and Thompson, 2002; Laor *et al*., 1995; Martinschek *et al*., 2012). Despite of being a risk factor for FG and associated with a more progressive and fatal outcome (decreased phagocytic and intracellular bactericidal activity and neutrophil dysfunction), most reported studies have failed to demonstrate the influence of DM on outcomes in FG (Ersoz *et al*., 2012; Clayton *et al*., 1990; Erol *et al*., 2010). It is also suggested that renal failure on admission might be a noticeable factor for the prediction of the mortality rate (Verma *et al*., 2000; Olsofka *et al*., 1999). Among many laboratory parameters studied in FG, Clayton *et al*., reported that only a level of blood urea >0.5 g/l on admission was statistically significant for mortality (Spirnak *et al*., 1984). In our study we also found that renal failure on admission is significantly higher in non survivors. Few articles have highlighted the poor prognosis of FG in patients with a delay between time of presentation and treatment. This factor has been reported in a study by Jeong *et al*., as a predictor of mortality (Yilmazlar *et al*., 2007). Along with other studies, we did not find delay this to be a major predictor of mortality (Aridogan *et al*., 2012; Yeniyol *et al*., 2004). The extension of the disease and the mortality rate are controversial themes in the literature. Some studies have reported that the spread of the disease is related to a higher death rate, while other studies report that the extension of the gangrene does not relate to a poorer prognosis (Spirnak *et al*., 1984; Sugihara *et al*., 2012). In this field, extent to abdominal wall has been reported to be directly related to mortality (Dahm *et al*., 2000), which was confirmed in our series. Ultimately, occurrence of septic shock and need for postoperative mechanical ventilation, have been demonstrated as a powerful (even late) factors of mortality (Verma *et al*., 2000; Morua *et al*., 2009; Laor *et al*., 1995). Furthermore, Yanar *et al*. found that the presence of sepsis was as the only significant independent risk factor for mortality in FG (Yanar *et al*., 2006). Our results join those reported in literature, although in multivariate analysis, these parameters have been not identified as independent predictors of mortality. Finally we acknowledge that our study has important limitations. Data collection was retrospective, the patient cohort is small, we focused on some variables but surely dismiss others not less important, we did not have access to important clinical and laboratory data so that we could not use and evaluate the performance of the Fournier's Gangrene Severity Index.

Conclusion

Fournier's gangrene is still a very severe disease with a high mortality rate. The advanced age, renal failure on admission, extension of infection to the abdominal wall, occurrence of septic shock and need for postoperative mechanical ventilation are the main prognostic factors of mortality. Early recognition of infection associated with invasive and aggressive treatment is essential for attempting to reduce these prognostic indices.

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