ORIGINAL ARTICLE

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The Relationship Between Diabetes Mellitus and Fournier's Gangrene

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Abstract

Objective: Fournier's gangrene is necrotizing fasciitis with polymicrobial infection involving the scrotum, perineum and perianal region, sometimes spreading to the abdomen and chest with a high mortality. The purpose of the present study was to examine whether diabetes mellitus (DM) has an effect on Fournier's gangrene mortality, length of hospital stay and laboratory values.

Methods: The patient files with a history of hospitalization in University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital were used in the study. The epicrisis of 250 patients who were diagnosed with necrotizing fasciitis and gangrene between January 2014 and July 2021 were read and 50 patients who had Fournier's gangrene were identified from epicrisis. Demographic analyzes, physical examination and laboratory findings of the identified patients, and the drugs they used were reviewed retrospectively.

Results: DM was detected in 28 (56%) of 50 patients hospitalized with the diagnosis of Fournier's gangrene in the study. The patients were divided into 2 groups as those with and without diabetes mellitus. No statistically significant differences were detected between the discharge and death distributions of the diabetic and non-diabetic groups (p=0.371). The length of hospital stay was statistically significantly higher in the diabetic group than in the non-diabetic group (p=0.017).

Conclusion: Diabates mellitus has an important place among the risk factors for Fournier's gangrene disease and it was detected in more than half of the patients in the present study. It was found that diabetes prolonged the hospitalization period of patients who had Fournier's gangrene, but had no effect on mortality.

Keywords: Diabetes mellitus, Fournier's gangrene, SGLT-2 inhibitors, necrotizing fasciitis

INTRODUCTION

Fournier's gangrene (FG) is a necrotizing fasciitis that develops because of the synergistic polymicrobial infection of the perineal, genital, or perianal regions (1). Despite all treatments, it has a high mortality rate (20-40%) (2). The most common causes are gastrointestinal system with 30-50%, genitourinary system with 20-40%, and cutaneous causes with 20% (3). There are many risk factors that prepare the ground for the formation of the disease and facilitate its spread. Diabetes mellitus (DM) is one of these risk factors and is found in 32-66% of all FG patients (4). FG was also reported in patients using Sodium Glucose Co-Transporter 2 (SGLT-2) inhibitors, which are among the oral antidiabetic drugs used in the treatment of DM (5). In the present study, the purpose was to investigate the relationship between FG and DM.

METHODS

The study was planned retrospectively. Patients with FG were determined by reading the epicrisis of patients diagnosed with A48.0 gas gangrene, R02 gangrene, and M72.5 fasciitis among the patients who were hospitalized in the University of Health Sciences Turkey Prof. Dr. Cemil Taşcıoğlu City Hospital between January 2014 and July 2021. The patients' history, additional diseases, demographic characteristics, hospitalization physical examination findings, standard biochemistry analyses, treatments

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(oral antidiabetic drugs, insulin), mortality, and hospitalization times of patients diagnosed with FG were evaluated. Patients who were diagnosed with FG were divided into 2 groups as those with and without DM. The clinical, laboratory, and endpoints were also compared. Study University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital It was examined in the meeting of University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital Clinical Research Ethics Committee dated 07/06/2021 and was found to be ethically appropriate according to the decision numbered 225. Ethics committee approval decision/protocol number: E-48670771-514.10. Our study is retrospective; therefore, there is no need for a patient consent form. In the power analysis of our study performed with the G*power 3.1 program, the effect size for the presence of DM in the study group was found to be 0.40 (FG: Review of 120 patients and predictors of mortality) (alpha error probability =0.05); In the sample size analysis performed by taking the power value of 0.80, the total number of samples required to be taken in total was found to be 50.

Statistical Analysis

In this study, statistical analyses were performed with Number Cruncher Statistical System 2007 Statistical Software (Utah, USA) package program. In the evaluation of the data, in addition to descriptive statistical methods (mean, standard deviation, median, interquartil range), the distribution of the variables was examined with the Shapiro-Wilk normality test, the independent t-test for the comparison of the paired groups of the variables with normal distribution, and the Mann-Whitney U test for the comparison of the pairwise groups of the non-normally distributed variables. The chi-square test was used to compare the qualitative data. The results were evaluated at the significance level of $p<0.05$.

RESULTS

A total of 50 patients who had FG diagnosed because of retrospective screening were included in the study. All 50patients were receiving antibiotic therapy and had a post-surgical intensive care history. DM was diagnosed in 28 of the 50 patients (56%), and hypertension was accompanied by 48%, cardiovascular disease in 28%, chronic kidney failure in 10%, and malignancy in 8% after diabetes. Among the 50 patients, 27 (54%) were male and 23 (46%) were female. The patients were divided into 2 groups: those with and without diabetes mellitus. No statistically significant differences were detected between the gender distributions of the diabetic and non-diabetic groups (p=0.226). In the diabetic group, 11 (39.2%) patients were using only oral antidiabetic, 9 (32.1%) patients were using only insulin therapy, 6 (21.4%) were using both oral antidiabetic and insulin therapy. One patient was using an SGLT-2 inhibitor (empagliflozin) and 2 patients (7.1%) were not using medication, although they had diabetes. The mean age of the diabetic group was 56.39 found to be 56.39±13.44 years, and the mean age of the non-diabetic group was 59.36±13.82 years. No statistically significant differences were detected between the mean age of the diabetic and non-diabetic groups (p=0.447) (Table 1).

When the clinical characteristics of the groups with and without FG diabetes during hospitalization were examined, no significant differences were detected in terms of fever (p=0.156) and pulse (p=0.063) values (Table 2).

When the laboratory values were evaluated, no significant differences were detected in leukocytes (p=0.557), hemoglobin (p=0.367), creatinine (p=0.277), potassium [p=0.247, alanin aminotransferaz (ALT) (p=0.710), C-reaktive protein (CRP) (p=0.257), and bicarbonate (HCO_3) levels (p=0.364)]. The mean sodium levels of the group with diabetes were found to be lower than those of the non-diabetic group at a statistically significant level (p=0.001). The mean fasting glucose value of the diabetic group was found to be 201 mg/dL, and the mean glucose level of the non-diabetic group was 93 mg/dL (Table 2).

Discharge and mortality were excluded from the statistics because 1 out of 50 patients who had FG left the hospital by

Table 1. Demographic and clinical characteristics of the patient group

	DM (-) (n=22)		DM (+) (n=28)		p
Age mean ± SD	59.36±13.82		56.39±13.44		0.447
Male	14	63.64%	13	46.43%	0.226
Female	8	36.36%	15	53.57%	0.226
HT	5	22.73%	19	67.86%	**0.002**
CVD	4	18.18%	10	35.71%	0.171
CRF	3	13.64%	2	7.14%	0.447
Malignancy	2	9.09%	2	7.14%	0.801

HT: Hypertension, CVD: Cardiovascular disease, CRF: Chronic kidney failure, DM: Diabetes mellitus, SD: Standard deviation, Statistically significant p values are indicated in bold

signing a treatment refusal, and 1 patient was transferred to the intensive care unit. In the remaining 48 patients, the mortality rate was 31.25%. No statistically significant differences were detected between the distribution of discharge and death rates between the groups with and without diabetes (p=0.371) (Table 3).

The mean hospital stay was 52 days in the group with diabetes and 29 days in the non-diabetic group. The length of stay in the group with diabetes was found to be higher than that in the non-diabetic group at a statistically significant level (p=0.017) (Table 3).

No statistically significant differences were detected between the mean Fournier gangrene severity index (FGSI) of the diabetic and non-diabetic groups (p=0.480).

DISCUSSION

DM was detected in 56% of the 50 patients who had FG. When divided into diabetic and non-diabetic groups, the hospitalization time of the diabetic group was found to be higher than -the non-diabetic group at a statistically significant level. No statistically significant differences were detected when the mortality of the diabetic and non-diabetic groups was compared.

FG is a necrotizing fasciitis that develops because of a polymicrobial infection that affects the scrotum, perineum, and perianal regions and sometimes spreads to the abdomen and chest (1).

There are many risk factors that prepare the ground for the formation of the disease and facilitate its spread. DM is among these risk factors (4).

The common characteristic of all risk factors in FG is that they reduce cellular immunity and impairs immune resistance (3). Diabetics have many bacteria on their skin, making the risk of skin infection easier. Immune functions, such as chemotaxis and phagocytosis, are impaired in diabetes. As a result of this, the spread of the bacteria increases. Diabetic angiopathy impairs blood circulation in the disease area, facilitating anaerobic infection (6). Impaired blood flow causes tissue ischemia in small vessels. Diabetic neuropathy increases the risk of urinary infection in patients with urethral obstruction and prepared the ground for FG (7). Diabetic neuropathy also delays the clinical course of FG (8).

Table 2. The comparison of the clinical and laboratory characteristics of the patient groups

		DM (-) (n=22)	DM(+) (n=28)	p
Pulse	**Mean ± SD**	86.32±8.94	93.36±15.44	0.063
Temperature	**Mean ± SD**	36.5±0.47	36.73±0.62	0.156
WBC	**Mean ± SD**	18758.64±8299.26	20313.21±9894.96	0.557
Hemoglobin	**Mean ± SD**	11.15±2.44	11.85±2.27	0.367
Creatinine	**Mean ± SD**	1.87±2.07	1.12±0.7	0.277
	Median (IQR)	1.05 (0.78-2.05)	0.85 (0.63-1.38)	
Na	**Mean ± SD**	136.91±4.26	132.14±4.96	**0.001**
K	**Mean ± SD**	4.06±0.71	4.30±0.69	0.247
ALT	**Mean ± SD**	29.73±37.67	22.75±15.37	0.710
	Median (IQR	16 (8.75-36)	17 (11.25-33.75)	
CRP	**Mean ± SD**	212.5±111.13	260.86±144.65	0.257
	Median (IQR)	185 138.75-263.5)	222.5 (158.5-374.5)	
HCO_3	**Mean ± SD**	19.38±5.01	21.5±7.07	0.364
Glucose	**Mean ± SD**	93.64±20.91	201±106.67	**0.0001**

WBC: White blood cell, Na: Sodium, K: Potassium, ALT: Alanine aminotransaminase, CRP: C-reactive protein, HCO_3: Bicarbonate, DM: Diabetes mellitus, SD: Standard deviation, Statistically significant p values are indicated in bold

Table 3. The comparison of the types of discharge (death and discharge with recovery) and length of stay of the patient groups

	DM (-) (n=22)	DM (+) (n=28)	p
Discharge-death	15-5	18-10	0.371
Hospitalization period	29.05±21.89	52.57±51.07	**0.017**

DM: Diabetes mellitus

It was reported that 32-66% of patients with FG also have DM (4). In a previous study that examined 1,726 patients who had FG, 20% of patients who had diabetes were identified (3). In another study that was conducted with 41 patients who had FG in our country, 41.4% of diabetic patients were detected (9). Also, in a study conducted with 120 patients who had FG in our country, the rate of patients who had diabetes was found to be 57.5% (10). In this study, DM was detected in 56% of 50 patients who had FG, similar to the literature data. As reported in many studies, DM was found to be an important risk factor for patients with FG in our study.

Despite all treatments, it has a high mortality rate (20-40%) (2). In a study that was conducted with 1,641 patients who had FG, its mortality was found to be 16% (3). In another study conducted in our country, mortality was found to be 20.8% (10). Mortality was found to be 31.25% in our study.

In some previous studies, it was reported that DM has no effect on mortality in patients with FG (4,11-13). However, DM was found to have a higher mortality rate in a 17-year systematic review and meta-analysis (14). In our study, although mortality was higher in the group with DM, no statistically significant difference was detected compared to those without DM (p=0.371).

Also, there are different results in studies conducted on length of hospital stay. In a study, DM did not affect the length of hospital stay (4). In another study that was conducted in our country, it was found that the length of hospital stay was longer in patients who had DM FG (15). In our study, the average length of hospital stay in the diabetic group was 52 days, and it was 29 days less in the non-diabetic group. The length of hospital stay was statistically and significantly higher in the diabetic group than in the non-diabetic group (p=0.017). There are multiple levels of dysfunction in the immune system in diabetes. Cytokine signals are affected in innate and adaptive immunity. Diabetes suppresses many cytokines. Neuropathy increases susceptibility to lesion in the skin barrier, which is the first defense system. Diabetes does not develop an appropriate immune response because of poor vascular flow at sites of infection and predisposes to secondary infections, making recovery more difficult. It was considered that making efforts to regulate blood sugar in patients with DM may affect the length of hospital stay.

Leukocytes (p=0.557), hemoglobin (p=0.367), creatinine (p=0.277), potassium (p=0.247), ALT (p=0.710), CRP (p=0.257) and HCO_3 (p=0.364) values were not significantly different in the diabetic group compared to the non-diabetic group. Sodium was significantly lower in the diabetic group. The reason for this is that glucose is high in the diabetic group (mean fasting glucose is 93 mg/dL in the non-diabetic group, 201 mg/dL in the diabetic group).

FGSI, which is a scoring system, was developed by Laor et al. (16) by using vital signs and some laboratory data to determine the severity of infection and prognosis in cases of FG. Temperature, pulse, respiratory rate, hematocrit, leukocytes, creatinine, serum sodium and potassium, and HCO_3 are used in this scoring system. In their study, Laor et al. (16) found the mortality risk to be 75% if the FGSI was >9 and the survival rate to be 78% if it was ≤9%. No statistically significant differences were found in our study between the FGSI of the groups with and without diabetes (p=0.480).

Cases of FG were reported in the treatment of SGLT-2 inhibitors. The FDA defined 55 cases of FG in patients who were receiving SGLT2 inhibitors between March 1, 2013 and January 31,2019 (5). In the present study, one of 28 diabetic patients was using an SGLT-2 inhibitor.

The study was conducted in a single center and had a retrospective design limited to a relatively low number of patients.

CONCLUSION

DM has an important place among the risk factors for FG disease. It prolonged the hospital stay but had no effect on mortality. In addition, no effects were detected on the laboratory values and the FGSI, which is considered to show the severity of the disease, in patients who had diabetes FG. It is considered that SGLT-2 inhibitors that are used in the treatment of DM are not related to FG.

Ethics

Ethics Committee Approval: Study University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital. It was examined in the meeting of University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital Clinical Research Ethics Committee dated 07/06/2021 and was found to be ethically appropriate according to the decision numbered 225. Ethics committee approval decision/protocol number: E-48670771-514.10.

Informed Consent: Our study is retrospective; therefore, there is no need for a patient consent form.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: S.S., A.B., M.A., Design: S.S., M.A., Data Collection or Processing: S.S., A.B., Analysis or Interpretation: S.S., M.A., Literature Search: S.S., A.B., Writing: S.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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