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# All-Cause Mortality in Type 2 Diabetes Patients Hospitalized for COVID-19 and Treated with Corticosteroids: A Single Center Cross-Sectional Study

## ABSTRACT

**Objective: This study aims to compare all-cause mortality and other hospital outcomes of hospitalized coronavirus disease of 2019 patients using corticosteroids.**

**Materials and methods: A comparative cross-sectional study was performed over three months by collecting data from patients' medical charts.**

**Results: The sample included 129 patients with type 2 diabetes (T2D) and 293 patients without diabetes, with more men than women in both groups. Patients with T2D were older, namely, those aged more than 70 years (54.3%) with the majority having abnormal glucose levels on admission (76.1%) and at discharge (76.9%). As a primary outcome, higher all-cause mortality was reported among patients without diabetes having more than two comorbidities (38.2%) compared to those with two or single comorbidities (21.0% and 13.9% respectively; $p = 0.009$). It significantly increased if patients without diabetes had abnormal glucose levels at admission (51.7%; $p < 0.001$) and discharge (44.7%; $p < 0.001$) compared to those with normal levels. Critical cases had higher all-cause mortality compared to less severe cases in patients with T2D (58.8%; $p < 0.001$) and without diabetes (61.0%; $p < 0.001$). Among secondary outcomes, a higher length of stay in the hospital was noted among patients with T2D (8.4 vs. 7.3 days; $p = 0.015$), in addition to a significantly higher number of ventilator-free days (2.7 vs. 1.6 days; $p = 0.039$).**

**Conclusions: Although the treatment with corticosteroids was comparable between patients with and without T2D, hospital outcomes varied between the groups. Findings from this study can help provide additional clinical support for patients with T2D to allow better in-hospital management of COVID-19 cases.**

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**Keywords: patients with type 2 diabetes, corticosteroids, all-cause mortality, COVID-19, hospital outcomes**

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## Introduction

The coronavirus disease of 2019 (COVID-19) pandemic imposed new challenges on the management and treatment of diabetes and other non-communicable diseases [1]. Reports revealed prioritization of COVID-19 patients [2] and delays in the screening and controlling of other patients [3]. Among others, diabetes mellitus affects over 422 million people worldwide [4], and its prevalence is predicted to double by 2030 [5]. It predisposes patients to higher odds of respiratory infections and an increased risk of hospitalization [6].

The severity of COVID-19 infections was shown to be accentuated among patients with type 2 diabetes (T2D) [7] who required special clinical considerations during the pandemic [8]. Furthermore, patients with T2D had a higher COVID-19 mortality risk due to pulmonary and cardiac outcomes [9]. Research reported that patients with T2D had 44% lower odds of surviving the infection during hospitalization than patients without diabetes [10]. A meta-analysis found that patients with T2D had a two-fold increased risk of mortality caused by COVID-19 compared to other patients [11]. Uncontrolled diabetes and abnormal glycemic control were significantly associated with in-hospital mortality [12]. The 28-day all-cause mortality among COVID-19 patients was 3.6 times higher among patients with T2D compared to those without diabetes [13]. Moreover, reports found a more extended hospital stay [14], higher odds of use of mechanical ventilation [15], and an increased likelihood of side effects among patients with T2D [16]. In Lebanon, the prevalence of T2D is high (21%) and seems to be increasing over time [17, 18], placing a substantial proportion of the population at risk of severe infections. Moreover, the quality of life and mental health of patients with T2D was negatively affected during the pandemic highlighting the need for community and individual support together with therapeutical follow-up [19].

The World Health Organization guidance recommends refraining from using corticosteroids in managing COVID-19 patients unless prescribed for other reasons [20]. Despite these recommendations, corticosteroids were frequently used among hospitalized COVID-19 patients to reduce the inflammation of the lungs [21]. Nevertheless, they can worsen hyperglycemia, management of new patients with T2D, and the corresponding complications [22]. Recent research reported bidirectional causal associations between T2D and COVID-19 [23], which highlights the importance to assess outcomes among patients with T2D. Knowledge gaps exist in exploiting the differences in the outcomes among patients with T2D, particularly those suffering from COVID-19 and taking corticosteroids. This study aims to assess the outcomes of patients hospitalized for COVID-19 taking corticosteroids and compare these outcomes between those with and without diabetes. The primary studied outcome was all-cause mortality. The secondary outcomes were the time of initiation of corticosteroids, length of hospital stay, days till death, ventilator-free days, the need and duration of mechanical ventilation, the length of intensive care unit (ICU) stay, and the use of antibiotics, remdesivir, ivermectin and plasma from recovered donors.

## Materials and methods

### Study design

A comparative cross-sectional study was performed over three months (May–July 2021) in which data were collected from the patient's medical chart. Hospitalized COVID-19 patients taking corticosteroids were grouped into patients with T2D and without diabetes.

### Study population and population size calculation

Adults patients admitted to the hospital after a confirmed COVID-19 infection and receiving corticosteroids, irrespective of the stage and severity of the disease, were included in the study. Data were collected from the patients' medical charts during the study period. They were classified as patients with T2D if they were previously diagnosed (cases) and patients without diabetes (controls). Those diagnosed during their hospital stay or after initiation of the therapy were included as cases. WinPepi software was used to generate the sample size needed to test the difference between proportions in a comparative study with a power of 80% and a significance level of 5%. To allow the detection of the outcomes of interest, a minimum number of 128 patients with T2D and 256 controls was required. In the present study, 422 patients were included (129 in the T2D group and 293 in the group without diabetes).

### Data collection

Data were collected by two clinical pharmacists using a uniform data collection form (supplementary material) developed after an extensive literature review and taking into account an expert opinion. The initial data completion took an average of 15 minutes per patient and was updated based on the status of the patients.

### General information about the patients

The sex, age, height, weight, and smoking status of the patients were collected in this part. Age was then classified (18–60, 61–70, >70), and the body mass index (BMI) was calculated. Furthermore, the admission floor (internal medicine or intensive care unit) was registered in addition to the glucose level on admission and at discharge (categorized based on the criteria of the American Diabetes Association [24]. Information about whether or not the patient did a real-time Polymerase Chain Reaction (PCR) test and if it was done before or during the admission process was also registered. Patients were then classified as critical (septic shock, sepsis, mechanical ventilation, or vasopressor therapy), severe (oxygen saturation ≤ 90%, respiratory rate > 30

breaths/min or the existence of signs of severe respiratory distress), and non-severe cases (absence of any signs of severe or critical COVID-19) [25].

### Medical history of the patients

The number of comorbidities (none, one, two, or more than two) and their types (hypertension, coronary artery disease, dyslipidemia, heart failure, chronic kidney disease, chronic obstructive pulmonary disease (COPD), asthma, and cancer) were collected in this part (multiple answers were allowed).

### Treatment characteristics

Three corticosteroids were mainly used: dexamethasone (intravenous), methylprednisolone (intravenous), and oral prednisone. The number of drugs provided was noted, and the dosage of each type of corticosteroid was classified (as low, moderate, or high) based on the recommendations of the American Society of Health-System Pharmacists in the assessment of evidence for COVID-related treatments [26]. The duration of treatment was categorized into 7 days or less or more than 7 days based on a meta-analysis performed in 2021 [27]. Hyperglycemia and superinfection occurrence were also recorded in addition to using antibiotics, remdesivir, ivermectin, and plasma from recovered donors. The need for mechanical ventilation, its duration (if needed), and the length of ICU stay (if applicable) were registered.

### Ethical considerations

The research protocol and data collection tool were reviewed and approved by the institutional review board of Ain Wazein Medical Village. Data were completely anonymous and non-identifiable. Data collectors assigned an ID for every patient and another researcher performed the analysis. The storage of data followed the Lebanese university general data protection regulation guidelines.

### Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS Inc, Chicago, Illinois) Version 27. The age of the patients, height, weight, BMI, length of hospital stay, and ICU stay, together with the duration of treatment with corticosteroids, are presented using means and standard deviations, while categorical variables are presented using frequencies and percentages. Bivariate analyses were conducted by taking all-cause mortality as the dependent variable and (i) the general information about the patients, (ii) the medical history, and (iii) the corticosteroid regimen characteristics as independent variables. Chi-square/Fisher exact tests were used to compare percentages between associate categorical variables. A p-value $< 0.05$ was considered statistically significant. Univariate and multivariable (adjusted for age, sex and with comorbidities that differed between the groups: hypertension, coronary artery disease and diabetes) Cox proportional hazards models were run, with associations expressed as hazard ratios (HR) and 95% confidence intervals (CI).

## Results

### Baseline characteristics of the patients

Table 1 represents the distribution of the baseline characteristics of the patients. The sample included more men than women in both patients with T2D (57.4% vs. 42.6%) and patients without diabetes (59.7% vs. 40.3%) ($p = 0.649$). The group with T2D had significantly older patients, namely those aged more than 70 years (54.3% vs. 33.4% in the group without diabetes) ($p < 0.001$). No significant differences were noted regarding the patients' height, weight, and BMI in both groups ($p > 0.05$). The glucose level on admission and at discharge was significantly higher ($\geq 126$ mg/dL) among around 75% of patients with T2D ($p < 0.001$). Most patients in both groups were admitted to the internal medicine floor, while a third of those with T2D and 27.3% of patients without diabetes were admitted to the intensive care unit ($p = 0.209$). Almost 20% of patients with T2D were smokers compared to only 10.7% of the group without diabetes ($p = 0.020$). Most patients in both groups did a PCR test during their hospital admission ($p = 0.190$). Around 40% of patients in both groups were classified as non-severe cases and 26% were classified as critical cases with no significant differences ($p = 0.901$). Around 33% of patients without diabetes had no previous comorbidities. The number of comorbidities significantly varied between the groups, with 51.3% of patients without diabetes having only one compared to 11.9% of patients with T2D. Nevertheless, 45.2% of patients with T2D had more than two comorbidities in comparison to only 17.3% in the group without diabetes ($p < 0.001$). Hypertension, coronary artery diseases, and chronic kidney disease were the most common comorbidities, particularly among patients with T2D. No significant differences were noted between the groups regarding the regimen of corticosteroids adopted with dexamethasone as the primary prescribed type. More than a third of patients took a high dosage of corticosteroids (37.2% and 34.5% respectively, in the group with T2D and the group without diabetes). Twenty patients with T2D (18.5%) encountered side effects from corticosteroids out of which 80% had hyperglycemia and 35.0% had a superinfection with no significance between groups.

**Table 1. Distribution of the Baseline Characteristics of the Patients**

| | Patients with T2D (N = 129) Frequency (%) | Patients without diabetes (N = 293) Frequency (%) | p-value |
|---|---|---|---|
| Sex | | | |
| Men | 74 (57.4%) | 175 (59.7%) | 0.649 |
| Women | 55 (42.6%) | 118 (40.3%) | |
| Age [years] | | | |
| Mean ± SD | 68.5 ± 11.3 | 61.3 ± 16.7 | < 0.001 |
| 18–60 | 30 (23.3%) | 142 (48.5%) | |
| 61–70 | 29 (22.5%) | 53 (18.1%) | <0.001 |
| More than 70 | 70 (54.3%) | 98 (33.4%) | |
| BMI [kg/m$^2$] | | | |
| Mean ± SD | 28.1 ± 3.7 | 27.9 ± 5.2 | 0.901 |
| The glucose level on admission | | | |
| < 126 mg/dL | 17 (23.9%) | 110 (65.5%) | < 0.001 |
| ≥ 126 mg/dL | 54 (76.1%) | 58 (34.5%) | |
| The glucose level at discharge | | | |
| < 126 mg/dL | 18 (23.1%) | 117 (60.6%) | < 0.001 |
| ≥ 126 mg/dL | 60 (76.9%) | 76 (39.4%) | |
| Admission floor | | | |
| Internal medicine | 86 (66.7%) | 213 (72.7%) | 0.209 |
| Intensive care unit | 43 (33.3%) | 80 (27.3%) | |
| Smoking status | | | |
| Non-smoker | 101 (80.8%) | 258 (89.3%) | 0.020 |
| Smoker | 24 (19.2%) | 31 (10.7%) | |
| PCR test available | | | |
| Yes | 124 (96.1%) | 275 (93.9%) | 0.345 |
| No | 5 (3.9%) | 18 (6.1%) | |
| If yes, time done | | | |
| Before admission | 36 (29.0%) | 63 (22.9%) | 0.190 |
| During admission | 88 (71.0%) | 212 (77.1%) | |
| Severity of cases | | | |
| Non-severe | 51 (39.5%) | 122 (41.6%) | |
| Severe | 44 (34.1%) | 94 (32.1%) | 0.901 |
| Critical | 34 (26.4%) | 77 (26.3%) | |
| **Medical history** | **Frequency (%)** | **Frequency (%)** | **p-value** |
| Comorbidities | | | |
| None | — | | 96 (32.8%) |
| One | 15 (11.9%) | 101 (51.3%) | |
| Two | 54 (42.9%) | 62 (31.5%) | <0.001 |
| More than two | 57 (45.2%) | 34 (17.3%) | |
| Hypertension | 106 (82.2%) | 140 (47.8%) | <0.001 |
| Coronary artery disease | 39 (30.2%) | 53 (18.1%) | 0.005 |
| Dyslipidemia | 15 (11.6%) | 20 (6.8%) | 0.099 |
| Heart failure | 7 (5.4%) | 16 (5.5%) | 0.989 |
| Chronic kidney disease | 11 (8.5%) | 10 (3.4%) | 0.026 |
| COPD | 4 (3.1%) | 15 (5.1%) | 0.357 |
| Asthma | 1 (0.8%) | 17 (5.8%) | 0.017 |
| Cancer | 4 (3.1%) | 10 (3.4%) | 0.566 |

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**Table 1 (cont.). Distribution of the Baseline Characteristics of the Patients**

| Corticosteroid regimens | Patients with T2D (N = 129) Frequency (%) | Patients without diabetes (N = 293) Frequency (%) | p-value |
|---|---|---|---|
| Number of corticosteroids used | | | |
| One | 114 (88.4%) | 245 (83.6%) | 0.207 |
| Two | 15 (11.6%) | 48 (16.4%) | |
| Type of corticosteroids | | | |
| Dexamethasone | 78 (60.9%) | 181 (62.2%) | 0.958 |
| Methylprednisolone | 46 (35.9%) | 102 (35.1%) | |
| Prednisone | 4 (3.1%) | 8 (2.7%) | |
| Dosage | | | |
| High | 48 (37.2%) | 101 (34.5%) | 0.358 |
| Moderate | 48 (37.2%) | 130 (44.4%) | |
| Low | 33 (25.6%) | 62 (21.1%) | |
| Duration of treatment | | | |
| Mean ± SD | 5.8 ± 4.2 | 5.7 ± 3.5 | 0.785 |
| ≤ 7 days | 108 (83.7%) | 244 (83.3%) | 0.910 |
| > 7 days | 21 (16.3%) | 49 (16.7%) | |
| Side effects | | | |
| Yes | 20 (18.5%) | 66 (25.9%) | 0.131 |
| No | 88 (81.5%) | 189 (74.1%) | |
| Hyperglycemia | 16 (14.6%) | 51 (20.6%) | 0.196 |
| Superinfection | 7 (35.0%) | 25 (37.9%) | 0.816 |

Results are given in terms of frequency (percentage) or mean ± standard deviation
BMI — body mass index; COPD — chronic obstructive pulmonary disease; PCR — polymerase chain reaction; SD — standard deviation; T2D — type 2 diabetes

## All-cause mortality among hospitalized COVID-19 patients with T2D and without diabetes

Overall, 92 patients died (26 (20.2%) in the group with T2D vs. 66 (22.5%) in the group without diabetes). The reported causes of death were heart failure (23 patients; 25%), septic shock (21 patients; 22.8%), respiratory failure (20 patients; 21.7%), pulmonary embolism (17 patients, 18.5%) and 11 patients (12.0%) had an unknown cause of death. Table 2 compares the association between all-cause mortality and the characteristics of the patients in each of the groups. Among patients without diabetes, higher all-cause mortality was associated with a glucose level at admission or discharge ≥ 126 mg/dL ($p < 0.001$). All deceased patients with T2D were non-smokers ($p = 0.004$) and the more severe the case, the significantly more patients died in both with ($p < 0.001$) and without ($p < 0.001$) diabetes groups. All-cause mortality increased per increase in the number of comorbidities among patients without diabetes ($p = 0.009$). When associating all-cause mortality with corticosteroid regimen characteristics, significantly more patients without diabetes died if they were treated for 7 days or less (24.6%) compared to those treated for more than 7 days (12.2%; $p = 0.050$). Furthermore, most patients with diabetes having superinfections (85.7%) died during their hospitalization.

Age 70 years or older (HR, 0.81; 95% CI, 0.53 to 1.22; log-rank test 0.294), women (HR, 1.01; 95% CI, 0.67 to 1.53; log-rank test 0.956), hypertension (HR, 0.67; 95% CI, 0.45 to 1.01; log-rank test 0.051), and coronary artery disease (HR, 1.19; 95% CI, 0.74 to 1.93; log-rank test 0.456) were not associated with mortality in univariate analysis (Fig. 1 and Tab. 3). After adjusting for covariates, diabetes was not shown to be a significant risk factor associated with death (HR, 0.80; 95% CI, 0.49 to 1.29; $p = 0.366$). Nevertheless, patients with hypertension had a lower mortality risk (HR, 0.61; 95% CI, 0.38 to 0.96; $p = 0.034$).

## Comparison of secondary hospital outcomes between patients with T2D and those without diabetes

Table 4 compares the observed secondary outcomes between the groups. No significant differences were noted between groups as regards the time of corticosteroid initiation, days till death, the need and duration of mechanical ventilation, and the use of antibiotics, remdesivir, or ivermectin ($p > 0.050$). Nev-

**Table 2. Association between All-Cause Mortality and the General Characteristics of the Patients, Medical History, and Corticosteroid Regimen Characteristics**

| General characteristics of the patients | Dead cases (N = 26) Frequency (%) | Survived cases (N = 103) Frequency (%) | Dead controls (N = 66) Frequency (%) | Survived controls (N = 227) Frequency (%) |
|---|---|---|---|---|
| Sex | | | | |
| Men | 11 (14.9%) | 63 (85.1%) | 43 (24.6%) | 132 (75.4%) |
| Women | 15 (27.3%) | 40 (72.7%) | 23 (19.5%) | 95 (80.5%) |
| p-value | 0.082 | | 0.307 | |
| Age [years] | | | | |
| 18-60 | 5 (16.7%) | 25 (83.3%) | 24 (16.9%) | 118 (83.1%) |
| 61-70 | 5 (17.2%) | 24 (82.8%) | 15 (28.3%) | 38 (71.7%) |
| More than 70 | 16 (22.9%) | 54 (77.1%) | 27 (27.6%) | 71 (72.4%) |
| p-value | 0.706 | | 0.082 | |
| The glucose level on admission | | | | |
| < 126 mg/dL | 6 (35.3%) | 11 (64.7%) | 17 (15.5%) | 93 (84.5%) |
| ≥ 126 mg/dL | 15 (27.8%) | 39 (72.2%) | 30 (51.7%) | 28 (48.3%) |
| p-value | 0.554 | | **< 0.001** | |
| The glucose level at discharge (last test) | | | | |
| < 126 mg/dL | 3 (16.7%) | 15 (83.3%) | 18 (15.4%) | 99 (84.6%) |
| ≥ 126 mg/dL | 21 (35.0%) | 39 (65.0%) | 34 (44.7%) | 42 (55.3%) |
| p-value | 0.139 | | **< 0.001** | |
| Admission floor | | | | |
| Internal medicine | 19 (22.1%) | 67 (77.9%) | 48 (22.5%) | 165 (77.5%) |
| Intensive care unit | 7 (16.3%) | 36 (83.7%) | 18 (22.5%) | 62 (77.5%) |
| p-value | 0.438 | | 0.995 | |
| Smoking status | | | | |
| Non-smoker | 26 (25.7%) | 75 (74.3%) | 58 (22.5%) | 200 (77.5%) |
| Smoker | — | 24 (100%) | 6 (19.4%) | 25 (80.6%) |
| p-value | **0.004** | | 0.692 | |
| Severity of cases | | | | |
| Non-severe | 1 (2.0%) | 50 (98.0%) | 3 (2.5%) | 119 (97.5%) |
| Severe | 5 (11.4%) | 39 (88.6%) | 16 (17.0%) | 78 (83.0%) |
| Critical | 20 (58.8%) | 14 (41.2%) | 47 (61.0%) | 30 (39.0%) |
| p-value | **< 0.001** | | **< 0.001** | |
| **Medical history** | **Frequency (%)** | **Frequency (%)** | **Frequency (%)** | **Frequency (%)** |
| Number of comorbidities | | | | |
| One | 5 (33.3%) | 10 (66.7%) | 14 (13.9%) | 87 (86.1%) |
| Two | 7 (13.0%) | 47 (87.0%) | 13 (21.0%) | 49 (79.0%) |
| More than two | 13 (22.8%) | 44 (77.2%) | 13 (38.2%) | 21 (61.8%) |
| p-value | 0.162 | | **0.009** | |
| Hypertension | 19 (17.9%) | 87 (82.1%) | 27 (19.3%) | 113 (80.7%) |
| p-value | 0.175 | | 0.204 | |
| Coronary artery disease | 6 (15.3%) | 33 (84.6%) | 16 (30.2%) | 37 (69.8%) |
| p-value | 0.374 | | 0.140 | |
| Dyslipidemia | 4 (26.7%) | 11 (73.3%) | 7 (35.0%) | 13 (65.0%) |
| p-value | 0.502 | | 0.167 | |
| Heart failure | 1 (14.3%) | 6 (85.7%) | 5 (31.3%) | 11 (68.8%) |
| p-value | 0.691 | | 0.390 | |
| Chronic kidney disease | 2 (7.7%) | 9 (81.8%) | 1 (10.0%) | 9 (90.0%) |
| p-value | 0.865 | | 0.466 | |

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**Table 2 (cont.). Association between All-Cause Mortality and the General Characteristics of the Patients, Medical History, and Corticosteroid Regimen Characteristics**

| Corticosteroid regimens | Dead cases (N = 26) Frequency (%) | Survived cases (N = 103) Frequency (%) | Dead controls (N = 66) Frequency (%) | Survived controls (N = 227) Frequency (%) |
|---|---|---|---|---|
| Number of corticosteroids used | | | | |
| One | 21 (18.4%) | 93 (81.6%) | 54 (22.0%) | 191 (78.0%) |
| Two | 5 (33.3%) | 10 (66.7%) | 12 (25.0%) | 36 (75.0%) |
| p-value | 0.176 | | 0.654 | |
| Dosage | | | | |
| High | 7 (14.6%) | 41 (85.4%) | 22 (21.8%) | 79 (78.2%) |
| Moderate | 14 (29.2%) | 34 (70.8%) | 32 (24.6%) | 98 (75.4%) |
| Low | 5 (15.2%) | 28 (84.8%) | 12 (19.4%) | 50 (80.6%) |
| p-value | 0.145 | | 0.700 | |
| Duration of treatment | | | | |
| ≤ 7 days | 25 (23.1%) | 83 (76.9%) | 60 (24.6%) | 184 (75.4%) |
| > 7 days | 1 (4.8%) | 20 (95.2%) | 6 (12.2%) | 43 (87.8%) |
| p-value | 0.073 | | **0.050** | |
| Side effects | | | | |
| Hyperglycemia | 6 (37.5%) | 10 (62.5%) | 12 (23.5%) | 39 (76.5%) |
| p-value | 0.178 | | **0.027** | |
| Superinfection | 6 (85.7%) | 1 (14.3%) | 11 (44.0%) | 14 (56.0%) |
| p-value | **0.007** | | **0.050** | |

ertheless, a higher length of stay in the hospital was noted among patients with T2D (p = 0.015) in addition to a significantly higher number of days without ventilation (p = 0.039).

## Discussion

The present study aimed to compare the outcomes between patients with T2D and patients without diabetes hospitalized for COVID-19 and taking corticosteroids. The study sample included more men than women in both groups. No significant differences were noted between groups regarding the characteristics of corticosteroid regimens. Among patients without diabetes, all-cause mortality significantly increased per increase in the number of comorbidities and if patients had abnormal glucose levels at admission or discharge. All deceased patients with T2D were non-smokers. The increase in the severity of cases and being treated by corticosteroid for 7 days or less induced a higher all-cause mortality risk in both groups. Patients with T2D spent significantly more days in the hospital and had higher ventilator-free days than patients without diabetes.

Most patients with T2D admitted to the hospital were older than 70 years. Previous research reported a combined risk of getting infected and hospitalized for COVID-19 for older patients with diabetes [28]. The group above had significantly more patients with abnormal blood glucose during admission and discharge, possibly related to the higher secretion of inflammatory cytokines during acutely stressful events resulting in an increase in insulin resistance and a decrease in the insulin-stimulated glucose uptake in peripheral tissues [29]. Similar percentages of patients from both groups were admitted to the ICU, contrasting findings from the literature that reported a higher risk for patients with T2D [30]. Smoking was shown to adversely impact the severity of cases and hospital outcomes [31] and could have had an additional effect in this study since smokers were more frequent in the group of patients with T2D. Most patients tested positive for COVID-19 during admission, which might have influenced the severity of the cases due to late diagnosis. Nevertheless, no significance was noted between groups in terms of the severity of the infection, even though diabetes itself was reported to be an essential driver [32]. Moreover, recent research emphasized the need to adapt glucose-lowering therapy based on the severity of COVID-19 cases [33], which could have influenced hospital outcomes in this study. The number of comorbidities was significantly higher among patients with T2D. The co-existence of other chronic diseases is

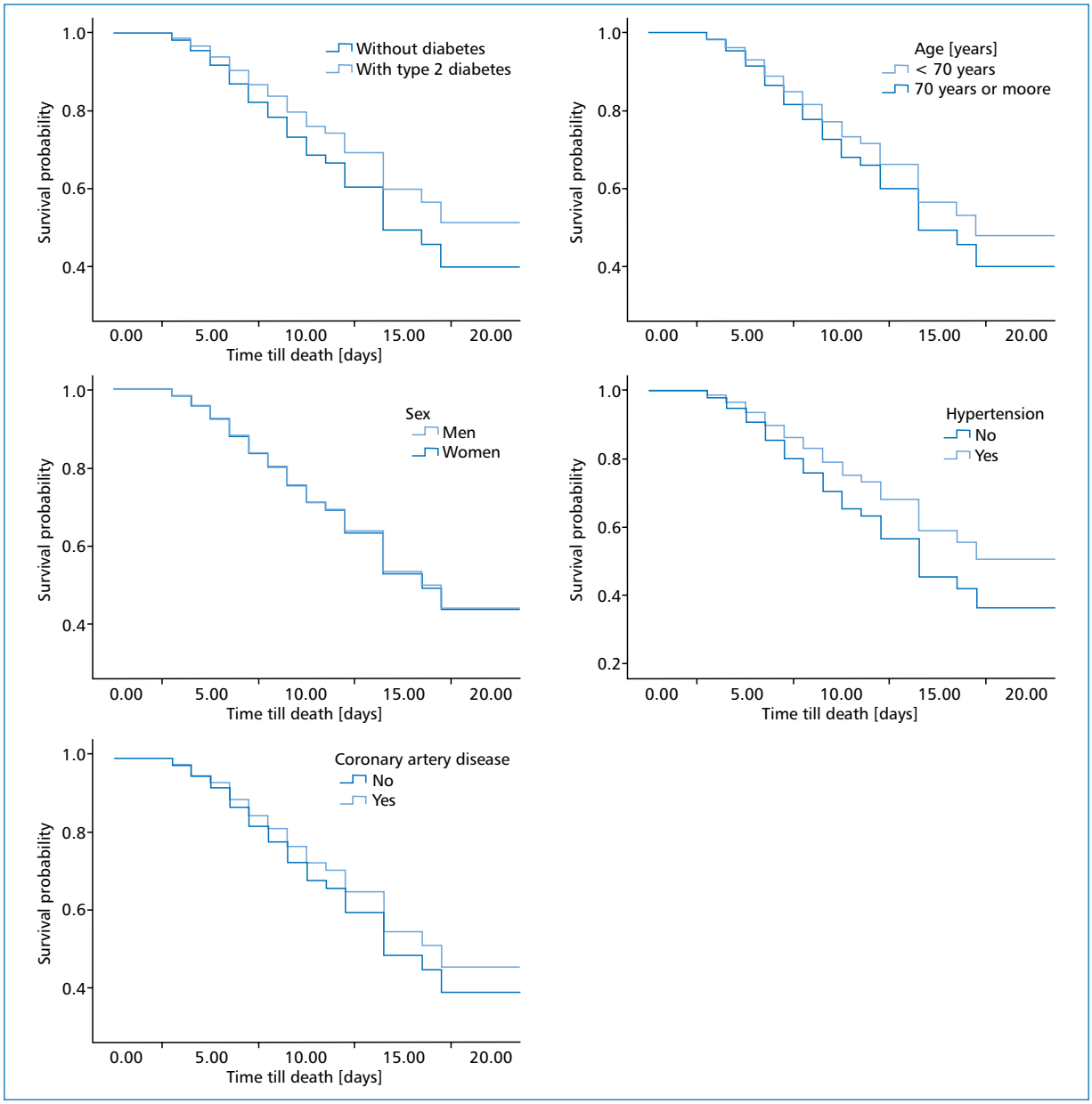


**Figure 1.** Kaplan-Meier Curves for In-Hospital Mortality by Demographic and Clinical Data

**Table 3. Risk Factors for Mortality in COVID-19 Patients Taking Corticosteroids**

| | Unadjusted model HR [95% CI] | Adjusted model HR [95% CI] |
|---|---|---|
| Diabetes (No as a reference) | 0.73 [0.46–1.15] | 0.80 [0.49–1.29] |
| Sex (men as reference) | 1.01 [0.67–1.53] | 1.01 [0.66–1.54] |
| Age (< 70 as a reference) | 0.81 [0.53–1.22] | 1.40 [0.89–2.19] |
| Hypertension (No as a reference) | 0.67 [0.45–1.01] | 0.61 [0.38–0.96] |
| Coronary artery disease (No as a reference) | 1.19 [0.74–1.93] | 1.33 [0.79–2.24] |

CI — confidence interval; HR — hazard ratio

common since diabetes was shown to be associated with comorbidities [34], particularly among hospitalized COVID-19 patients [35].

The primary outcome exploited in this study was all-cause mortality, which was found to be higher among patients without diabetes having abnormal glucose

**Table 4. Comparison of the Secondary Outcomes between Patients with T2D and Patients without Diabetes**

| | Patients with T2D (N = 129) Frequency (%) | Patients without diabetes (N = 293 Frequency (%) | p-value |
|---|---|---|---|
| Time of corticosteroid initiation < 72 hours | 122 (94.6%) | 286 (97.6%) | 0.108 |
| ≥ 72 hours | 7 (5.4%) | 7 (2.4%) | |
| Length of hospital stay | | | |
| Mean ± SD | 8.4 ± 4.5 | 7.3 ± 3.4 | 0.015 |
| Days till death | | | |
| Mean ± SD | 8.2 ± 6.0 | 9.2 ± 8.4 | 0.577 |
| Ventilator-free days | | | |
| Mean ± SD | 2.7 ± 4.2 | 1.6 ± 2.2 | 0.039 |
| Mechanical ventilation | | | |
| Yes | 44 34.1%) | 94 (32.1%) | 0.683 |
| No | 85 (65.9%) | 199 (67.9%) | |
| Duration of the mechanical ventilation | | | |
| Mean ± SD | 4.3 ± 3.6 | 5.1 ± 2.8 | 0.177 |
| Length of ICU stay | | | |
| Mean ± SD | 6.7 ± 3.8 | 5.9 ± 3.4 | 0.157 |
| Use of antibiotics | 122 (94.6%) | 279 (95.2%) | 0.778 |
| Use of remdesivir | 50 (38.8%) | 124 (42.5%) | 0.477 |
| Use of ivermectin | 8 (6.2%) | 14 (4.8%) | 0.550 |
| Need for plasma | 1 (0.4%) | 6 (2.1%) | 0.184 |

Results are given in terms of frequency (percentage) or mean ± standard deviation
ICU — intensive care unit; SD — standard deviation; T2D — type 2 diabetes

levels at admission or discharge. This finding suggests that some might be undiagnosed or untreated patients with T2D, making them prone to other comorbidities and resulting in a higher mortality risk [36, 37]. All deceased patients with T2D were non-smokers. Although some research reported similar findings [38], a meta-analysis performed in 2021 revealed higher all-cause mortality associated with COVID-19 among smokers [39]. Patients with only one comorbidity (diabetes) had higher all-cause mortality. In contrast, the increase in the number of comorbidities induced mortality among the group without diabetes. A recent study reported a high prevalence of undiagnosed comorbidities among hospitalized COVID-19 patients [40], which might have affected their management. Although the corticosteroid regimen was similar in both groups, those treated for 7 days or less were more likely to die in agreement with the literature [41]. Kaplan Meier curves showed no significant differences in the risk of mortality between patients. After adjusting for covariates, diabetes remained a non-significant all-cause mortality factor. However, those with hypertension had a significantly lower risk, in agreement with a recent research showing a protective effect of antihypertensive drugs on mortality among COVID-19 patients [42]. In contrast, a study published in 2023 showed that hypertension was a driver for increased severity of cases among patients with T2D [43].

Among the secondary outcomes assessed, an extended duration of hospitalization was observed in patients with T2D. Similarly, in other studies, COVID-19 patients with diabetes and/or uncontrolled hyperglycemia had a more extended hospitalization than other patients [44, 45]. In addition, a significantly higher number of days without ventilation was observed among patients with T2D. Despite the fact that these patients are more susceptible to mechanical ventilation [46], the limited number of ventilators in the hospital could have impacted the prioritization of that need.

This study has limitations. Data were collected from the patients' medical charts, which may not cover all patients' information, such as side effects and reported causes of mortality. It only included patients from one hospital, which might affect the generalizability of the results to other settings. However, the use of a uniform data collection form by trained pharmacists allowed better comparison of results; in addition that a different researcher performed data coding and analysis. The

present study is the first one comparing the outcomes between patients with T2D and patients without diabetes in the region and can therefore provide additional information for managing this sensitive group. A longitudinal multi-center study is recommended to allow better external validity and representativeness of Lebanon and other similar settings.

## Conclusions

Although the treatment with corticosteroids was comparable between patients with T2D and those without diabetes, hospital outcomes varied between the groups. Higher all-cause mortality was noted among patients without diabetes having high glucose levels on admission and at discharge. Patients with T2D having superinfections in the hospital had a higher risk of death. Patients with T2D had also longer hospital stays and ventilator-free days compared to those without diabetes. Findings from this study highlight the need for special therapeutic and clinical management of both patients in both groups having certain characteristics.

## Ethics approval and consent to participate

The study protocol, questionnaire, and consent form were reviewed and approved by the institutional review board of Ain Wazein Medical Village on October 13th, 2021 (reference: CRU329).

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## Conflict of interests

None declared.

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