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Diabetes Mellitus and COVID-19: Prevalence, Severity, Management, and Mortality: A Secondary Study

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Abstract

Objective: This study aimed to conduct a systematic review about diabetes mellitus and COVID-19 severity, management, and mortality.
Materials and Methods: Thirteen studies were included in this review, comprising a total of 1155 COVID-19 patients with diabetes mellitus as a significant comorbidity. Data regarding patient demographics and the prevalence of comorbidities, including smoking, hypertension, cardiovascular disease, chronic kidney disease, and chronic liver disease, were collected.
Results: Among COVID-19 patients with diabetes mellitus, the majority were male (57.1%) compared to females (42.9%). The prevalence of comorbidities in COVID-19 are varied, with smokers accounting for 1-12.6%, hypertension ranging from 8-41.6%, diabetes mellitus ranging from 7.4-70.8%, cardiovascular disease ranging from 1.6-23.0%, chronic kidney disease ranging from 0.7-2.9%, and chronic liver disease ranging from 0.5-4.6%. In comparison to COVID-19 patients without diabetes, a higher proportion of patients with diabetes mellitus were admitted to the intensive care unit (36.8%). Among COVID-19 patients with diabetes mellitus, the survival rate was significantly higher at 62.2% compared to a lower rate of 13.4% observed among non-survivors with diabetes mellitus.
Conclusion: This systematic review emphasizes the significance of diabetes mellitus as a comorbidity in COVID-19 patients, increasing the risk of ICU admission. These findings emphasize the importance of identifying and effectively managing diabetes mellitus as a comorbidity in COVID-19 patients to enhance overall outcomes.
Keywords: COVID-19, Diabetes mellitus, Diabetes complications, SARS-CoV-2

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Introduction

Coronaviruses are a family of viruses with a protective envelope and RNA as their genetic material. They can cause respiratory and gastrointestinal infections in both humans and animals and have been associated with outbreaks of diseases such as the common cold, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS). In 2019, a new coronavirus called SARS-CoV-2 was identified as the cause of a respiratory illness outbreak in Wuhan, China, which later spread globally. This outbreak resulted in the disease known as coronavirus disease 2019 (COVID-19), which presents a varying range of symptoms and clinical manifestations, from mild flu-like symptoms to severe pneumonia and acute respiratory distress syndrome. Due to the rapid transmission of SARS-CoV-2 and the severity of COVID-19, the World Health Organization (WHO) declared it a global pandemic in March 2020. In response to this crisis, various public health organizations, including the U.S. Centers for Disease Control and Prevention (CDC) and the WHO, have closely monitored the situation and guided prevention and treatment strategies. Combining the development of effective vaccines and therapeutics with ongoing public health measures like social distancing, mask-wearing, and COVID-19 PCR testing has become crucial in controlling the spread of the virus and reducing the impact of the COVID-19 pandemic (1).

Diabetes mellitus

Diabetes mellitus encompasses a set of metabolic disorders characterized by elevated blood glucose levels caused by deficiencies in insulin secretion, insulin action, or both. The persistent high blood glucose levels in diabetes mellitus lead to lasting harm, impairment, and potential organ failure, particularly affecting the eyes, kidneys, nerves, heart, and blood vessels. This condition impairs the body's capacity to efficiently utilize glucose, which is essential for facilitating energy production in the cells responsible for muscle, tissue, and brain development. The root causes of diabetes mellitus vary depending on the type of diabetes. There are two main types of chronic diabetes: type 1 and type 2 diabetes. Furthermore, there are types of diabetes that have the potential to be reversed, such as prediabetes and gestational diabetes. Prediabetes is characterized by elevated blood sugar levels that have not reached the diagnostic criteria for diabetes. Without appropriate management, prediabetes can advance to type 2 diabetes. On the other hand, gestational diabetes occurs specifically during pregnancy and typically resolves after childbirth.

Material and methods

This study aims to provide a comprehensive analysis of common medical conditions (comorbidities) frequently observed in COVID-19 patients and investigate potential factors associated with severe COVID-19 outcomes. Additionally, it delves into the management of diabetes mellitus in the context of COVID-19, specifically emphasizing the evaluation of disease severity. This evaluation includes a comparative analysis of ICU admission rates and mortality between survivors and non-survivors among COVID-19 patients with diabetes.

Data source and search plan

Following established guidelines for systematic reviews, we comprehensively searched relevant literature in the PubMed and Google Scholar databases. Our search strategy included a combination of medical subject headings and keywords specific to patients with both diabetes and COVID-19. We applied the standard filter for randomized clinical trials across all databases to ensure consistency. The search was restricted to articles published in the English language. To augment our investigation, we reviewed related articles and references cited by identified studies. Following the initial screening of titles and abstracts, we accessed the full text of potentially relevant articles to determine their eligibility for inclusion in our analysis. Furthermore, we examined the bibliographies of included studies for additional relevant sources.

Study selection

Four independent reviewers conducted a screening process based on predefined inclusion and exclusion criteria to retrieve potentially relevant studies and determine study eligibility. The article selection process spanned three years, from 2019 to 2021.

Inclusion criteria

The study enrolled patients of all ages who had received a confirmed diagnosis of COVID-19. However, only patients hospitalized for at least 15 days were included in the analysis.

Exclusion criteria

The study excluded pregnant and lactating women, as well as patients who did not have a confirmed diagnosis of COVID-19. Furthermore, full-text articles lacking sufficient data, non-English full texts, and studies focusing exclusively on the Western population were also excluded from the analysis.

Data extraction

In this study, we gathered data from various sources, including details about the study design (such as sample size and date of the study), patient characteristics, and the research methodology (including eligibility criteria, blinding, and randomization method). We also collected information on the interventions used and the main results obtained. To gather the data, we conducted a systematic literature search in well-known databases like PubMed, Google Scholar, and Elsevier, covering the period from the inception of these databases up until August 31, 2021. The search utilized keywords like "COVID-19," "SARS CoV-2," and "Diabetes" to identify relevant articles. We collected and analyzed data related to patient characteristics, comorbidities, previous or current history of COVID-19, the severity of COVID-19, and the time interval between COVID-19 and diabetes diagnosis. We examined different endpoints and outcomes to draw meaningful conclusions. To ensure the data's accuracy, we entered it into Microsoft Excel and carefully reviewed the entries. During this process, we excluded articles that lacked sufficient data, were not available in English, or focused solely on Western populations. Pregnant and lactating women, as well as patients without a confirmed COVID-19 diagnosis, were also excluded from the study.

The extracted data were organized into specific tabular columns to facilitate analysis and presentation.

Search strategy in databases

COVID-19 OR SARS-CoV-2 OR coronavirus disease OR diabetes mellitus OR hyperglycemia blood glucose OR hypoglycemic agents OR insulin therapy OR mortality rate OR hbA1c OR antiviral therapy OR antibiotic therapy OR glucocorticoid therapy OR invasive mechanical ventilation OR non-invasive mechanical ventilation OR smokers OR nonsmokers

Ethical considerations

Vijaya Institute of Biomedical and Health Research, Chennai approved this study, and the ethical code was registered (IEC-VBMHR/LTR/2020/010). The analysis was performed by the principles of the Declaration of Helsinki.

Results

The research began by conducting an electronic search using PubMed and Google Scholar, which yielded 48 articles. After carefully reviewing the titles and abstracts and evaluating the full-text articles for eligibility, 30 articles were chosen for further analysis.

Among them, 17 articles were excluded because they lacked sufficient data, had non-English full text, or focused on Western populations. Ultimately, the systematic review included 13 studies meeting the criteria (Figure 1).

Gender-wise classification

Out of the 5,297 confirmed COVID-19 patients included in the study, 1,155 had diabetes mellitus as a significant comorbidity and met the inclusion and exclusion criteria of the 13 studies. Of these 1,155 patients, 660 (57.1%) were male, and 495 were female (42.9%). It was observed that a higher proportion of male patients had diabetes mellitus as a significant comorbidity in COVID-19 compared to females (Figure 2).

Prevalence of comorbidities in COVID-19

Out of the 5,297 subjects, the percentage of comorbidities varied between different studies. The rate of smokers ranged from 1% to 12.6%, hypertension from 8% to 41.6%, diabetes mellitus from 7.4% to 70.8%, cardiovascular disease from 1.6% to 23.0%, and chronic kidney disease from 0.7% to 2.9%. These variations suggest that the prevalence of comorbidities among COVID-19 patients varies depending on the study population. However, it is noteworthy that diabetes mellitus was consistently reported as a significant comorbidity associated with COVID-19 disease across all studies (Table 1, Figure 2).

Based on COVID-19 severity

Only four included studies compared ICU admission rates between COVID-19 patients with and without diabetes. The data from these studies indicate that patients with diabetes had a higher risk of ICU admission (36.8%) than those without diabetes (15.8%). Figure 3 visually represents the severity of ICU admission in COVID-19 patients with and without diabetes (Table 2).

Discussion

In response to the imperative demand for evidence-based therapeutic methodologies, multiple empirical inquiries have been undertaken to evaluate and juxtapose the effectiveness of diverse medical interventions for patients afflicted by COVID-19.

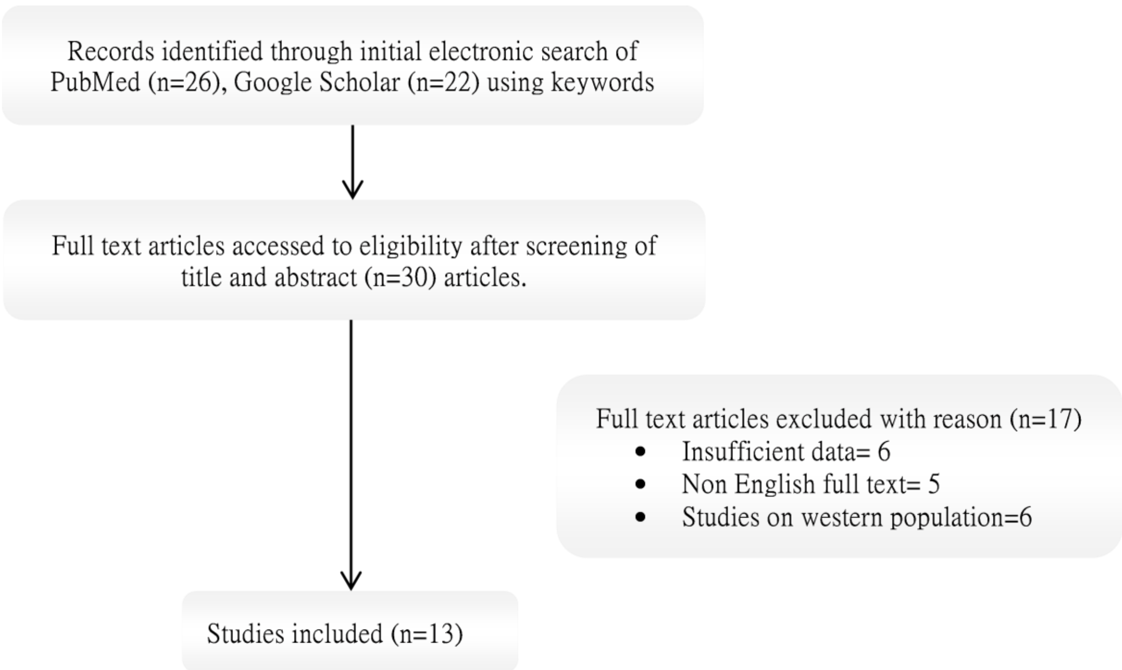

Figure 1. Flow chart of the literature search strategy

Table 1. Prevalence of comorbidities in COVID-19 patients in studies

First Author	Year	Total patients	Smokers (%)	HTN (%)	D.M. (%)	CVD (%)	CKD (%)	CLD (%)
Shi	2020	1561	1	8	9.8	3	0.7	0.5
Gue	2021	241	NR	14.9	7.8%	3.7*	NR	4.6
Li	2020	453	NR	33.1	70.8	9.7*	1.7	2.6
Hue	2020	845	NR	41.6	50.1	13.3*	NR	NR
Yang	2020	52	4.0	NR	17.0	23.0	NR	NR
Zou	2020	191	6.0	30	19.0	8.0*	1.0	NR
Wu	2020	201	NR	19.4	10.9	4.0	1.0	3.5
Chen	2020	274	7.0	34.0	17.0	8.0	1.0	NR
Guan	2020	1099	12.6	15.0	7.4	3.8	0.7	NR
Liu	2020	61	6.6	19.7	8.2	1.6	NR	NR
Yang	2020	138	NR	31.2	10.1	19.6	2.9	2.9
Lee	2020	140	NR	30	12.1	8.6	1.4	NR
Huang	2020	41	7.3	14.6	19.5	15.0	NR	2.4

(*reported coronary heart disease only, N.R. – Not reported)

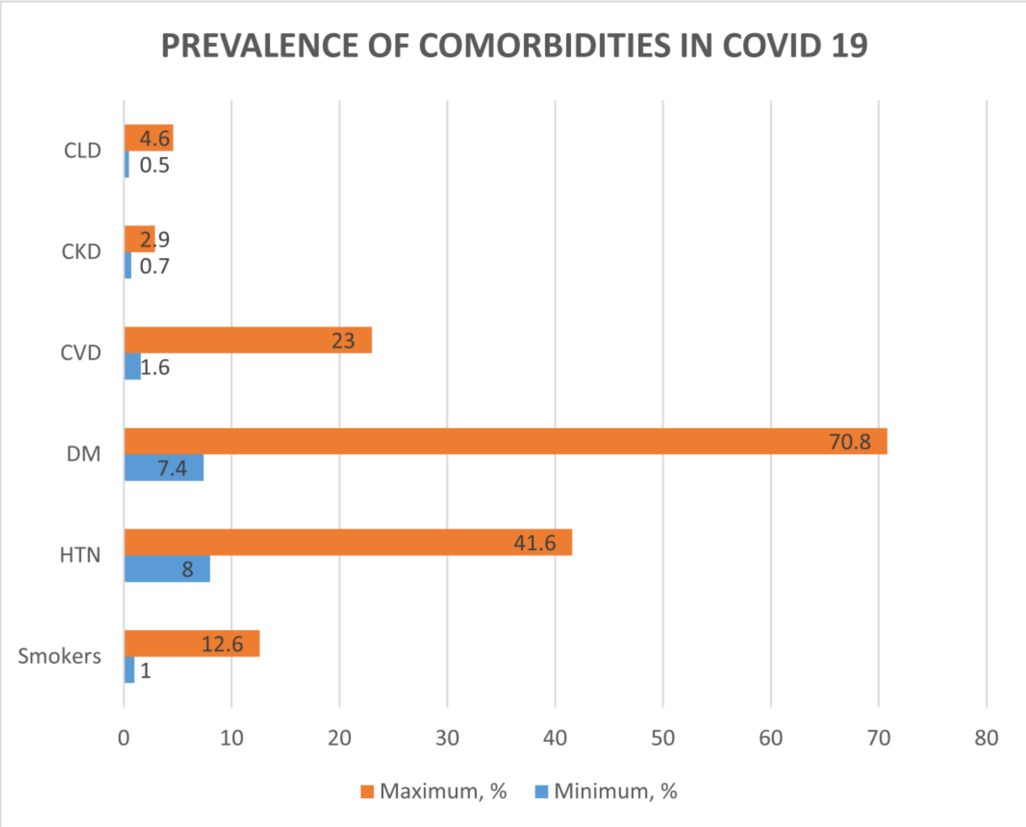

Figure 2. Prevalence of comorbidities in COVID-19

Table 2. COVID-19 severity in ICU patients with and without diabetes mellitus

Total patients (n)	Diabetes patients (%)	ICU admission in non-diabetes patients (%*)	ICU admission in diabetes patients (%*)	REF. No.
1561	9.8	7.8	17.6	38
241	7.8	15.8	36.8	39
453	70.8	1.5	7.1	40
845	50.1	14.0	18.9	41

(%* is calculated from total population having either ICU admission in COVID-19 infection with diabetes or ICU admission in COVID-19 infection without diabetes)

A particular emphasis has been placed on scrutinizing these interventions in the context of patients with and without comorbid diabetes. These rigorous investigations have systematically examined a broad spectrum of treatment modalities encompassing antiviral therapy, antibiotic therapy, glucocorticoid therapy, oxygen supplementation, mechanical ventilation, and renal replacement therapy, among others. Employing a stratification approach based on patients' diabetic status, the primary objective of these endeavors has been to elucidate potential disparities in treatment requirements and clinical outcomes.

This stratified analysis serves as a foundation for healthcare professionals to customize therapeutic regimens, optimizing patient care. As the battle against COVID-19 endures, the wealth of knowledge derived from these studies is poised to inform the development of evidence-based treatment guidelines, offering critical guidance to healthcare practitioners in their relentless pursuit of ameliorating the pandemic's impact.

It is pertinent to acknowledge the existence of multiple studies exploring these themes, each offering nuanced insights into treatment approaches. However, to maintain conciseness and focus on the broader context, this discussion does not provide an exhaustive examination of each individual study.

Patients were categorized into two distinct groups, namely those with diabetes mellitus and those without, in order to evaluate treatment disparities. It is imperative to underscore that these studies possess inherent limitations, necessitating further investigations to validate and refine the treatment strategies under scrutiny (2).

One such investigation conducted by Gue et al. offered a complementary perspective, specifically investigating the medical interventions administered to patients diagnosed with diabetes mellitus. This encompassed a comprehensive spectrum of treatments, encompassing antiviral agents, antibiotics, corticosteroids, immunoglobulins, insulin therapy, nasal cannula oxygen delivery, and high-flow nasal cannula administration (3).

Another notable study employed a more granular approach, segregating patients into four distinct categories based on their glycemic status: normal glucose, hyperglycemia, newly diagnosed diabetes, and known diabetes. The therapeutic strategies for each of these categories were carefully delineated (4).

Furthermore, it is noteworthy that COVID-19 patients with comorbid diabetes frequently exhibited other underlying health conditions, most notably hypertension and renal disorders. Upon admission, a substantial proportion relied solely on oral hypoglycemic agents, with metformin as the predominant treatment modality. However, as their hospitalization progressed, the treatment landscape evolved, necessitating a combination of oral hypoglycemic agents and insulin. Moreover, a significant proportion of both diabetic and non-diabetic patients necessitated steroid therapy during their hospital stay (5).

In a separate investigation, patients were categorized as survivors and non-survivors, with treatment regimens tailored accordingly. The therapeutic interventions spanned a spectrum that included high-flow nasal cannula therapy, mechanical ventilation, prone position ventilation, extracorporeal membrane oxygenation, renal replacement therapy, vasoconstrictive agents, antiviral agents, antibacterial agents, glucocorticoids, and immunoglobulins (6).

In a similar vein, another study stratified patients into survivor and non-survivor cohorts, implementing a diverse range of treatment modalities, including antiviral therapy, glucocorticoid therapy, antibiotics, IV immunoglobulin therapy, interferon inhalation, high-flow nasal cannula administration, mechanical ventilation, noninvasive ventilation, continuous renal replacement therapy, and extracorporeal membrane oxygenation (7).

Yet another investigation illuminated that a significant proportion of patients underwent intravenous antibiotic therapy, while others received oseltamivir therapy. Oxygen therapy and mechanical ventilation were also common interventions, with systemic glucocorticoids and antifungal medications administered selectively. Notably, the utilization rates of extracorporeal membrane oxygenation, continuous renal replacement therapy, and intravenous immunoglobulin varied among patients (8).

In a parallel endeavor, treatment patterns were assessed among patients, with a focus on antiviral therapy, antibiotic treatment, corticosteroids, oxygen supplementation, noninvasive ventilation, nasal cannula administration, invasive mechanical ventilation, and nebulization inhalation therapy, including recombinant human interferon alpha2b and acetylcysteine (9).

A comprehensive analysis revealed that a majority of patients received antiviral therapy, with antibacterial therapy administered in various forms. Additionally, glucocorticoid therapy, continuous kidney replacement therapy, oxygen support through nasal cannula, noninvasive ventilation, invasive mechanical ventilation, and extracorporeal membrane oxygenation were among the treatment modalities employed (10).

Similarly, an investigation highlighted the administration of antiviral treatment, antibiotics, corticosteroids, and continuous renal replacement therapy. Oxygen support methods, including nasal cannula, noninvasive ventilation, invasive mechanical ventilation, and extracorporeal membrane oxygenation, were also outlined (11).

Notably, despite being a recognized risk factor for severe COVID-19, patients with diabetes mellitus were generally subjected to comparable treatment interventions as their non-diabetic counterparts. Nevertheless, discernible differences were observed in treatment patterns, with diabetic patients more frequently necessitating insulin therapy and continuous renal replacement therapy. It remains paramount to acknowledge that these investigations possess inherent limitations, underscoring the imperative need for further research to corroborate and optimize treatment strategies. In summation, the collective findings derived from these studies significantly enrich our comprehension of the multifaceted medical interventions deployed against COVID-19 and underscore the imperative of ongoing research endeavors aimed at refining treatment paradigms across diverse patient populations. By adhering to a paradigm of perpetual assessment and adaptation rooted in scientific evidence, healthcare providers stand poised to elevate patient outcomes and mitigate the protracted impact of the COVID-19 pandemic.

Based on mortality

The primary objective of this study was to investigate the prevalence, severity, treatment, and mortality of diabetes in COVID-19 patients. The data presented in Figure 3 were analyzed to depict the prevalence of survivors versus non-survivors among COVID-19 patients with diabetes. The findings revealed that non-survivors had a mortality rate ranging from 2% to 13.4%, while survivors had a rate ranging from 3.9% to 62.2%. These results suggest that COVID-19 patients with diabetes face a higher mortality risk. It is worth noting that there is a scarcity of similar studies on this topic, highlighting the novelty of our research. However, to validate our findings, further investigation is warranted.

Conclusions

Preliminary investigations suggest that male patients exhibit a higher incidence of diabetes mellitus as a significant comorbidity in COVID-19 compared to their female counterparts. The existing literature on the prevalence of comorbidities in COVID-19 highlights a significantly high frequency of diabetes mellitus, thus identifying it as a prominent comorbidity in patients affected by COVID-19. Additionally, research comparing COVID-19 patients with diabetes mellitus and those without diabetes revealed a greater likelihood of ICU admission in the former group. Furthermore, a comparison of the prevalence of survivors and non-survivors indicated a lower mortality rate among COVID-19 patients with comorbid diabetes

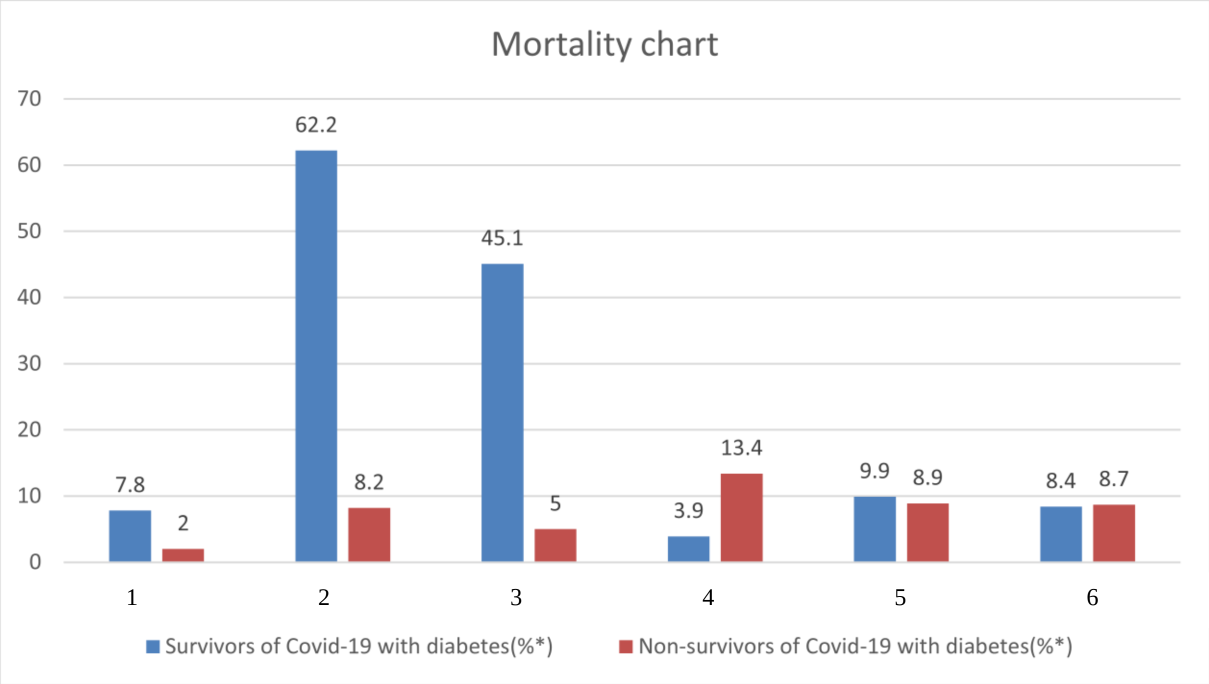

Figure 3. Prevalence of survivors versus non-survivors in COVID-19 patients with diabetes

mellitus. It should be noted that additional research is required to examine the hypotheses above.

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Conflict of Interest

The authors declare no conflict of interest

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