

A Retrospective Study to Characterize Cardiovascular Symptoms among COVID-19 Contracted Patients with Type 2 Diabetes Mellitus

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Submitted to: Asian/Pacific Island Nursing Journal
on: April 16, 2025

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Table of Contents

Original Manuscript.....	5
Supplementary Files.....	15

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A Retrospective Study to Characterize Cardiovascular Symptoms among COVID-19 Contracted Patients with Type 2 Diabetes Mellitus

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Abstract

Background: Type 2 diabetes mellitus is a well-established risk factor for severe complications and poor outcomes in patients with coronavirus disease-19. Patients with Type 2 Diabetes mellitus who contract Coronavirus disease-19 are at increased risk for hospitalization, intensive care unit admission, and mortality. Cardiovascular complications, including myocardial injury, arrhythmias, and thromboembolic events, have also been reported at higher rates in patients with Coronavirus disease-19. However, it remains unclear whether patients with Type 2 Diabetes mellitus who contract Coronavirus disease-19 present with distinct cardiovascular symptoms compared with non-diabetic patients. Understanding these differences may help guide early diagnosis and tailored management strategies for this high-risk population.

Objective: Considering the increased severity and mortality associated with COVID-19 infection in diabetes patients, we investigated whether the presence of diabetes affected the number and character of presenting symptoms.

Methods: This retrospective, observational study evaluated patients with acute COVID-19 infection who presented to the Emergency Department of one of the teaching hospital with cardiac symptoms, including chest pain/pressure, shortness of breath, palpitations, and left arm pain between 7/1/2021-12/31/2021. Patients with acute COVID-19 infection who presented to the ED with the ICD-10 codes of Chest Pain/Chest Pressure: R07.89, R07.9, R07.1, R07.81, R07.2, I25.119, I25.9, I20.9, I20.8, Shortness of Breath: R06.02, Palpitation: R00.2, R00.0, or Left arm pain: M79.602, M79.622 were included in our analysis. Demographic information - including age, gender, ethnicity – chief complaint at presentation, and ED disposition were extracted. Hemoglobin A1c was obtained for all patients. This study received approval from the Institutional Review Board.

Results: Baseline characteristics of the study population are listed in Table 1. A total of 5,574 patients presented to the UTSW ED in the setting of acute COVID-19 infection. 2077 patients (37%) had a history of T2DM, with a mean hemoglobin A1C of 7.04%. The mean patient age was 51; 43% of patients were male. There was an even distribution of white, non-Hispanic/ Latino, and Hispanic/Latino patients noted. In terms of presenting symptom/chief complaint, shortness of breath (48%) and chest pain (45.6%) were the most common presenting symptoms, with palpitations (3.2%) and arm pain (3.1%) noted less frequently. There was an increased incidence of presenting symptoms in those with T2DM compared with patients without a history of T2DM (odds ratio of 4.4, which was statistically significant [$p < 0.05$]). Of the patients admitted to the hospital for COVID-19 infection, 17% of them had T2DM. Ultimately, 161 patients died – 45 patients (28%) had T2DM, while 116 (72%) did not have T2DM.

Conclusions: Patients with Type 2 diabetes mellitus who contracted Coronavirus disease-19 were more likely to report cardiovascular symptoms than non-Type 2 diabetes mellitus patients, with the majority complaining of shortness of breath and chest pain. Additional studies would be helpful to verify this finding. The healthcare team should be aware of the difference in clinical presentation between Type 2 diabetes mellitus and non-Type 2 diabetes mellitus patients who contract Coronavirus disease-19 so that they may be triaged accordingly. Clinical Trial: none

(JMIR Preprints 16/04/2025:76104)

DOI: <https://doi.org/10.2196/preprints.76104>

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Original Manuscript

Title: A Retrospective Study to Characterize Cardiovascular Symptoms among COVID-19-Contracted Patients with Type 2 Diabetes Mellitus

Abstract

Background

Type 2 diabetes mellitus is a well-established risk factor for severe complications and poor outcomes in patients with coronavirus disease-19. Patients with Type 2 Diabetes mellitus who contract Coronavirus disease-19 are at increased risk for hospitalization, intensive care unit admission, and mortality. Cardiovascular complications, including myocardial injury, arrhythmias, and thromboembolic events, have also been reported at higher rates in patients with Coronavirus disease-19. However, it remains unclear whether patients with Type 2 Diabetes mellitus who contract Coronavirus disease-19 present with distinct cardiovascular symptoms compared with non-diabetic patients. Understanding these differences may help guide early diagnosis and tailored management strategies for this high-risk population.

Hypothesis

Patients with Type 2 diabetes mellitus who contract Coronavirus disease-19 have a higher incidence of cardiovascular symptoms compared to non-type 2 Diabetes mellitus patients with Coronavirus disease-19.

Methods

A retrospective, observational study was conducted to evaluate patients with acute Coronavirus disease-19 infection who presented to the Emergency Department with cardiovascular symptoms.

Findings

There was an increased incidence of presenting symptoms in those with Type 2 Diabetes mellitus compared with patients without a history of Type 2 diabetes mellitus (odds ratio of 4.4, which was statistically significant [$p < 0.05$]). Of the patients admitted to the hospital for Coronavirus disease-19 infection, 17% of them had Type 2 diabetes mellitus. Ultimately, 161 patients died – 45 patients (28%) had Type 2 diabetes mellitus, while 116 (72%) did not have Type 2 Diabetes mellitus.

Discussion

Our study shows a significantly higher incidence of cardiovascular symptoms in Type 2 diabetes mellitus patients with Coronavirus disease-19 compared to non-type 2 diabetes mellitus patients (odds ratio: 4.4, $p <$

0.05). This supports the known association between Type 2 diabetes mellitus and increased inflammation, endothelial dysfunction, and prothrombotic states, which may heighten cardiovascular vulnerability during Coronavirus disease-19. Seventeen percent of hospitalized Coronavirus disease-19 patients had Type 2 Diabetes mellitus, and 28% of deaths occurred in Type 2 diabetes patients, highlighting the clinical impact of diabetes on Coronavirus disease-19 outcomes. While most deaths occurred in non-type 2 diabetes mellitus patients (72%), the increased cardiovascular burden in Type 2 Diabetes mellitus patients remains significant.

Conclusion

Patients with Type 2 diabetes mellitus who contracted Coronavirus disease-19 were more likely to report cardiovascular symptoms than non-Type 2 diabetes mellitus patients, with the majority complaining of shortness of breath and chest pain. Additional studies would be helpful to verify this finding. The healthcare team should be aware of the difference in clinical presentation between Type 2 diabetes mellitus and non-Type 2 diabetes mellitus patients who contract Coronavirus disease-19 so that they may be triaged accordingly.

Summary of relevance

Problem or Issue

The COVID-19 pandemic has significantly impacted individuals with pre-existing health conditions, especially those with Type 2 Diabetes Mellitus. Preliminary evidence suggests that patients with Type 2 diabetes mellitus who contract COVID-19 experience a higher incidence of cardiovascular symptoms compared to non-diabetic individuals with the virus. This elevated risk could be attributed to the interplay between the metabolic disturbances associated with Type 2 Diabetes mellitus and the inflammatory response triggered by COVID-19. Understanding this relationship is crucial for improving management strategies and mitigating cardiovascular risks in diabetic patients during the pandemic.

What is already known

It is well-established that individuals with Type 2 Diabetes Mellitus face higher risks of severe outcomes from COVID-19, including hospitalization and mortality, due to impaired immune responses and metabolic disturbances. Type 2 Diabetes mellitus is also linked to increased cardiovascular disease risk, with factors such as insulin resistance, dyslipidemia, and hypertension contributing to conditions like coronary

artery disease and heart failure. COVID-19 can exacerbate these risks by causing direct heart damage and inflammation, leading to complications like myocarditis and arrhythmias. Diabetic patients with COVID-19 appear to experience a higher incidence of cardiovascular symptoms, likely due to the interplay between the virus and existing metabolic dysregulation, although further research is needed to fully understand this relationship.

What this paper adds

This paper adds to the existing literature by exploring the heightened incidence of cardiovascular symptoms in patients with Type 2 Diabetes Mellitus who contract COVID-19. Additionally, the paper provides insights into how metabolic dysfunction in Type 2 diabetes mellitus may exacerbate the inflammatory response triggered by the virus, offering a deeper understanding of the interaction between Type 2 diabetes mellitus, COVID-19, and cardiovascular risk. This information can help guide clinical management and inform strategies to mitigate cardiovascular complications in diabetic patients.

Introduction

In January 2020, the World Health Organization (WHO) identified a novel pneumonia strain in China caused by the SARS-CoV-2 virus. Globally, as of 29 November 2023, there have been 772,166,517 confirmed cases of COVID-19 infection, including 6,981,263 deaths, reported to the WHO.¹

COVID-19 causes variable symptoms in infected hosts, ranging from asymptomatic infection or very mild upper respiratory symptoms to multi-organ failure and death. An increased risk of cardiovascular complications – including ischemic heart disease, dysrhythmias, and thromboembolic disease – has been identified following COVID-19 infection.²

Individuals with a history of type 2 diabetes mellitus (T2DM) have been shown to have a more severe course following COVID-19 infection.³ Longer lengths of stay and higher mortality have previously been demonstrated for COVID-19-contracted patients with diabetes or uncontrolled hyperglycemia.⁴ However, it is unclear whether patients with T2DM who are acutely infected with COVID-19 present with similar symptoms to people without T2DM, and whether the two groups are triaged differently. If diabetes patients are shown to have different symptoms than non-diabetes patients after contracting COVID-19, this could affect

management and potentially contribute to the differences in mortality seen between the two groups. The difference in presenting cardiovascular symptoms between diabetes and non-diabetes patients is therefore the focus of our retrospective study.

Background and Significance

Type 2 Diabetes mellitus has been identified as a dominant risk factor affecting the severity of COVID-19 infection.⁵ Multiple mechanisms have been implicated in the increased morbidity and mortality seen with acute COVID-19 infection in diabetes patients, including an increase in inflammatory mediators in the blood, increased reactive oxygen species production, modulation of natural killer cell activity, and an increase in clotting components⁶. These mechanisms have been implicated in the greater incidence of heart failure, thromboembolism, and severe respiratory symptoms during acute COVID-19 infection.⁷⁻⁹

A retrospective cohort study in Indonesia revealed that diabetes patients who contracted COVID-19 had more symptoms and greater mortality than patients without diabetes.¹⁰ A study in Iran similarly showed that diabetes patients with COVID-19 infection were more likely to be symptomatic than their non-diabetes counterparts; additionally, inflammatory markers such as C-reactive protein were considered as significant predictions for mortality.¹¹ A study conducted in Madurai, India, revealed that the risk of mortality among COVID-19 patients was three times greater in the presence of comorbidities such as diabetes, hypertension, or coronary artery disease, with the presence of all three comorbidities increasing the mortality risk the highest.¹²

Purpose

Considering the increased severity and mortality associated with COVID-19 infection in diabetes patients, we investigated whether the presence of diabetes affected the number and character of presenting symptoms.

Methods

Study Design

This retrospective, observational study evaluated patients with acute COVID-19 infection who

presented to the Emergency Department of one of the teaching hospital with cardiac symptoms, including chest pain/pressure, shortness of breath, palpitations, and left arm pain between 7/1/2021-12/31/2021. Patients with acute COVID-19 infection who presented to the ED with the ICD-10 codes of Chest Pain/Chest Pressure: R07.89, R07.9, R07.1, R07.81, R07.2, I25.119, I25.9, I20.9, I20.8, Shortness of Breath: R06.02, Palpitation: R00.2, R00.0, or Left arm pain: M79.602, M79.622 were included in our analysis. Demographic information - including age, gender, ethnicity – chief complaint at presentation, and ED disposition were extracted. Hemoglobin A1c was obtained for all patients. This study received approval from the Institutional Review Board.

Statistical Analysis:

Systematic data collection was conducted with the help of a database analyst. Data analysis was done using RStudio. Frequency and percentage for categorical variables, mean, standard deviation, and range for continuous variables were determined using descriptive statistics, while comparison between categorical variables was done using the chi-square test.

Results

Baseline characteristics of the study population are listed in **Table 1**. A total of 5,574 patients presented to the UTSW ED in the setting of acute COVID-19 infection. 2077 patients (37%) had a history of T2DM, with a mean hemoglobin A1C of 7.04%. The mean patient age was 51; 43% of patients were male. There was an even distribution of white, non-Hispanic/ Latino, and Hispanic/Latino patients noted. In terms of presenting symptom/chief complaint, shortness of breath (48%) and chest pain (45.6%) were the most common presenting symptoms, with palpitations (3.2%) and arm pain (3.1%) noted less frequently.

There was an increased incidence of presenting symptoms in those with T2DM compared with patients without a history of T2DM (odds ratio of 4.4, which was statistically significant [$p < 0.05$]). Of the patients admitted to the hospital for COVID-19 infection, 17% of them had T2DM. Ultimately, 161 patients died – 45 patients (28%) had T2DM, while 116 (72%) did not have T2DM.

Table 1. Baseline characteristics of the study population

Total patients		5574
Age (mean)		51
Gender		
	Male	2341 (43%)
	Female	3233 (57%)
T2DM		
	Yes	2009 (37%)
	No	3565 (63%)
Ethnicity		
	White	1730 (16.5%)
	Non-Hispanic/Latino	1718 (16.4%)
	Hispanic/Latino	1727 (16.5%)
	Declined to answer	1759 (16.8%)
	Unspecified	3536 (33.8%)
Presenting Symptom (Chief Complaint)		
	Shortness of Breath	2675 (48%)
	Chest Pain	2541 (45.6%)
	Palpitations	178 (3.2%)
	Arm pain	173 (3.1%)

Discussion

While individuals with Type 2 Diabetes mellitus have been shown to have a more severe course after contracting COVID-19, it has been unclear whether Type 2 diabetes mellitus patients with acute COVID-19 infection present with similar symptoms compared with non-Type 2 Diabetes mellitus patients. Given that diabetes patients are well known to have atypical symptoms in the context of cardiac ischemia¹³, we sought to determine if diabetes patients would also present with atypical symptoms in the setting of COVID-19 infection. We determined that there was a statistically significant increase in cardiovascular symptoms in Type 2 Diabetes mellitus patients who contract COVID-19 compared with patients without T2DM (odds ratio of 4.4). Additionally, shortness of breath (48%) and chest pain (45.6%) were the most common presenting symptoms in diabetes patients who contracted COVID-19.

Prior studies have examined the complex interplay between COVID-19, Type 2 Diabetes mellitus, and cardiovascular disease. Potential mechanisms for adverse cardiovascular outcomes in COVID-19 affected

patients include endothelial dysfunction¹⁴, coagulation abnormalities¹⁵, angiotensin-converting enzyme 2-mediated myocardial injury¹⁶, and dyslipidemia-mediated effects¹⁷. The added diagnosis of diabetes increases the risk of mortality in patients who contract COVID-19¹⁸, possibly through effects on immunity¹⁹ as well as inflammatory and prothrombotic factors²⁰. This heightens the need for prevention and treatment strategies in diabetes patients to reduce cardiovascular mortality. Strengths of our study include a heterogeneous patient population, with relatively even distribution in terms of patient demographics. Additionally, the large sample size of patients in our study helps to amplify differences between the diabetes and nondiabetic groups.

Limitations

Study limitations include the possibility that atypical presenting symptoms of some patients who contracted COVID-19 might not have been included, since presenting symptoms were identified by specific ICD-10 search criteria. Additionally, due to the retrospective design of the study, causality cannot be inferred, and increased cardiovascular symptoms among diabetes patients who contracted COVID-19 may be due to other factors besides diabetes.

Conclusion:

Patients with Type 2 Diabetes mellitus who contracted COVID-19 were more likely to report cardiovascular symptoms than non-Type 2 diabetes mellitus patients, with the majority complaining of shortness of breath and chest pain. Additional studies would be helpful to verify this finding. If similar results were noted, providers should be aware of the difference in clinical presentation between Type 2 Diabetes mellitus and non-Type 2 Diabetes mellitus patients who contract COVID-19 so that they may be triaged accordingly.

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Supplementary Files