


The severity and clinical characteristics of COVID-19 among patients with type 2 diabetes mellitus in Jazan, Saudi Arabia

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Abstract

Background: The objectives of the current study were to assess the severity and clinical characteristics of coronavirus disease 2019 (COVID-19) among Saudi adults with type 2 diabetes mellitus (T2DM) in Jazan region, Saudi Arabia.

Methods: This retrospective cohort study included 412 patients with COVID-19 selected randomly from the Health Electronic Surveillance Network system, which contains the primary data on COVID-19 infections in Jazan.

Results: COVID-19 disease duration was significantly longer in patients with T2DM (mean = 10.7 days) compared with those without T2DM (mean = 8.3 days) ($P = .01$). Six (7%) patients experienced an increase in blood glucose concentrations and had to escalate their total daily insulin dose accordingly. Median fasting and random blood glucose levels increased after infection with COVID-19 (pre-COVID median = 119 and 172 mg/dL, respectively; post-COVID median = 148 and 216 mg/dL, respectively) ($P = .02$). The total insulin dose pre-COVID (median = 42 units/d) increased after infection with COVID-19 (median = 58 units/d) ($P = .01$). Most patients with T2DM had clinical COVID-19 symptoms (91%) and the remainder (9%) were asymptomatic. A large proportion (80%) of T2DM patients with mild COVID-19 symptoms self-isolated at home. COVID-19 patients with T2DM (11%) who had an oxygen saturation of $\leq 90\%$ and admitted to the intensive care unit were higher than those without T2DM (5%) ($P < .001$). COVID-19 patients with T2DM (9%) had higher mortality rate than COVID-19 patients without T2DM (1%) ($P < .001$).

Conclusion: COVID-19 patients with T2DM were associated with a higher risk of admission to the intensive care unit and mortality than COVID-19 patients without T2DM.

Abbreviations: A1C = glycated hemoglobin A1C, BMI = body mass index, COVID-19 = coronavirus disease 2019, ICU = intensive care unit, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, T2DM = type 2 diabetes mellitus.

Keywords: Covid-19, SARS-CoV-2, type 2 diabetes mellitus

1. Introduction

The novel coronavirus disease-2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has dramatically spread worldwide.^[1] It has infected over 30,000,000 people causing over 950,000 deaths until September 20, 2020.^[1] In Saudi Arabia, the Ministry of Health reported approximately over 11,000 confirmed cases with COVID-19 infection on September 20, 2020 in Jazan region, which is located in the southwestern Saudi Arabia.^[2] COVID-19 is characterized clinically by the presence of fever, cough, shortness of breath or difficulty breathing, fatigue, headache,

loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, and diarrhea.^[3] These symptoms may become severe in patients with comorbidities. Diabetes is one of the major comorbidities in patients with COVID-19,^[4] exhibiting approximately a 19% prevalence rate and a 31% case-fatality rate.^[5] Evidence demonstrates that patients with diabetes are susceptible to COVID-19 infection, with poor prognosis and clinical outcomes.^[5,6] In the USA, the prevalence of hospitalization of COVID-19 patients with diabetes is 28.3%.^[7] A meta-analysis indicated that diabetes doubles the risk of admission to the Intensive Care Unit (ICU) and more than

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triples the risk of death compared with other conditions.^[8] In Saudi Arabia, type 2 diabetes mellitus (T2DM) is prevalent,^[9] therefore, the risk of getting COVID-19 among T2DM is increased. Therefore, assessing the clinical outcomes and severity of COVID-19 is necessary to elaborate the differences between those with diabetes and those without, especially in populations with high prevalence of T2DM. To our knowledge, very few published papers have attempted to draw a conclusion about clinical outcomes of COVID-19 and its effects on T2DM. The aim of this study is to assess the severity and clinical characteristics of COVID-19 in Saudi patients with T2DM.

2. Method

Jazan Region is located in the south–west corner of Saudi Arabia; it comprises a predominantly homogenous population with similar ethnic and socioeconomic characteristics.^[10–13] Jazan region includes 16 cities with approximately 1,600,000 estimated population, most of them (80%) are Arab ethnicity “Saudi.” A retrospective cohort design was applied in the current study on Saudi adults in Jazan Region aged at least 18 years and infected with COVID-19. All infected COVID-19 patients are registered in the Health Electronic Surveillance Network system, the country’s official central epidemiological surveillance program, and is considered the main source of data for patients infected with COVID-19 in Jazan. Thus, we extract and sort all infected Saudi patients with COVID-19 between July 1 and 31, 2020 from the Health Electronic Surveillance Network system database and listed them in the excel program as a sampling frame (Total number was 1457). Then we ordered them by serial numbers from 1 to 1457 and we entered those numbers in the Stata software^[14] which selected 434 participants randomly (Fig. 1). After exclusion criteria, total of 412 patients with COVID-19 were included; 86 (21%) had T2DM and 326 (79%) were nondiabetic. T2DM was diagnosed based on glycated hemoglobin. A glycated hemoglobin level of 6.5% or higher on 2 separate testes indicates diabetes according to American diabetes Association guidelines. The Jazan Health Institutional Review Board (Reference number: H-10-Z-073) granted ethical

approval (No. 2030) for the study to be conducted, and the research complied with the Declaration of Helenski.

2.1. Data collection and statistical analysis

Data collection included the participants’ demographic characteristics (i.e., age, sex, marital status, education level, and smoking history) and clinical features (i.e., history of T2DM, clinical history of COVID-19, date of contact with a known patient with COVID-19, date of COVID-19 clinical symptom onset, home-based isolation or hospital admission with intubation, date of recovery from COVID-19, and date of death). In addition, the anthropometric and laboratory measurements, including body mass index (BMI) and fasting and random blood glucose levels monitoring at home, were recorded during the COVID-19 course.

The clinical symptoms of COVID-19 included fever, cough, shortness of breath (difficulty breathing), loss of taste and smell (anosmia), chest pain, sore throat, congestion, a runny nose, fatigue, headache, diarrhea, and vomiting. The diagnosis of COVID-19 infection was confirmed by the identification of viral ribonucleic acid in a nasopharyngeal swab sample using real-time reverse transcription–polymerase chain reaction (LightCycler 480 Instrument II, Roche). Disease severity was categorized according to the World Health Organization guidelines.^[15] Severe cases were defined as those with oxygen saturation of $\leq 90\%$, a respiratory rate of ≥ 30 breaths per minute, and signs of severe respiratory distress. The incubation period was calculated in days and constituted the period between exposure to SARS-CoV-2 and the manifestation of clinical symptoms. Disease duration was calculated in days and was considered to be the period between the manifestation of clinical symptoms of COVID-19 and the date of recovery. The criteria for recovery were based on the guidelines of the Ministry of Health, Saudi Arabia; recovery was considered to have occurred when at least 3 days had passed after the resolution of fever and respiratory symptoms and after obtaining 2 negative polymerase chain reaction samples results taken ≥ 24 hours apart; alternatively, at least 10 days had to have passed since symptom onset.^[16] In keeping with the World Health Organization guidelines,^[17] BMI was calculated as weight in kilograms

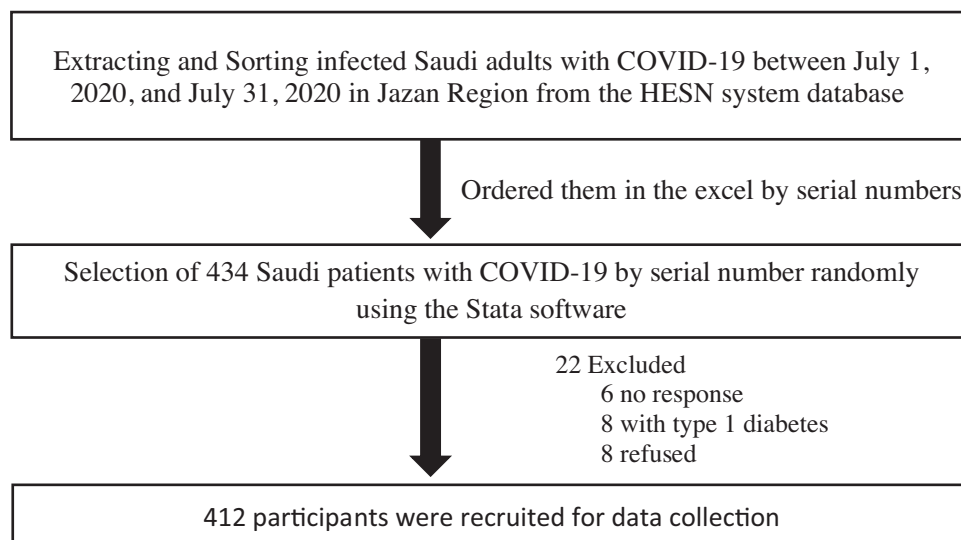


Figure 1. Patient enrolment and the sampling technique in the current study.

divided by the square of the person's height in meters. A BMI score of ≥ 30 was categorized as obese. Blood glucose levels measured at home were considered uncontrolled at levels >130 (mg/dL) before meals and >180 (mg/dL) 2 hours after meals.^[18]

Data entry and analysis were performed using Statistical Package for the Social Sciences software.^[19] The data were coded with anonymous identification numbers to ensure the privacy of the participants. The continuous variables were described as means \pm standard deviation, and the categorical variables were presented as percentages and frequencies. The chi-square and Fisher exact tests were used to assess any significant associations between the categorical variables. Wilcoxon signed-rank tests were performed to determine mean differences between small groups. Analysis of covariance "ANCOVA" and logistic regression were applied for adjusting covariates in the analysis. A *P* value of $<.050$ was considered to be statistically significant.

3. Results

Four hundred twelve patients were recruited in the current study. The participants' sociodemographic characteristics and health risks are depicted in Table 1. COVID-19 patients with T2DM were significantly older than those without T2DM.

3.1. Clinical symptoms of COVID-19 in relation to T2DM

The distribution of the clinical symptoms of COVID-19 in the study population including patients with T2DM is shown in Table 2. Most COVID-19 patients with T2DM had clinical symptoms (90.7%) and the remainder (9.3%) were asymptomatic. No difference in COVID-19 symptoms was observed between patients with and without T2DM (Table 2).

Table 1
Sociodemographic characteristics and health risks of the study population.

Factor	Overall (n = 412)	Without T2DM (n = 326)	With T2DM (n = 86)	<i>P</i>
Age				
18–44	281 (68.2%)	255 (78.2%)	24 (27.9%)	$<.001^*$
45–64	95 (23.1%)	52 (16.0%)	44 (51.2%)	
65–81	36 (8.7%)	19 (5.8%)	18 (20.9%)	
Sex				
Male	257 (62.4%)	200 (61.3%)	56 (65.1%)	.56
Female	155 (37.6%)	126 (38.7%)	30 (34.9%)	
Marital status				
Single	99 (24.0%)	90 (27.6%)	7 (8.1%)	.007*
Married	290 (70.4%)	222 (68.1%)	70 (81.4%)	
Widowed	7 (1.6%)	4 (1.2%)	3 (3.5%)	
Divorced	16 (4.0%)	10 (3.1%)	6 (7.0%)	
Education level				
Illiterate	34 (8.3%)	23 (7.1%)	13 (15.1%)	.02*
Primary	61 (14.8%)	41 (12.6%)	20 (23.3%)	
Secondary	134 (32.5%)	108 (33.1%)	25 (29.1%)	
University	183 (44.4%)	154 (47.2%)	28 (32.5%)	
Smoking				
No	351 (85.2%)	275 (84.4%)	74 (86.0%)	.43
Yes	61 (14.8%)	51 (15.6%)	12 (14.0%)	
BMI				
Not obese	315 (76.5%)	260 (79.8%)	54 (62.8%)	.004*
Obese	97 (23.5%)	66 (20.2%)	32 (37.2%)	

*Significant results (*P* value $<.05$).

3.2. Incubation period and disease duration

The mean incubation period and disease duration were (5.1) and (8.3) days, respectively (respective ranges of 2–15 and 5–43 days). After adjusting for age and BMI, Table 3 shows disease duration of COVID-19 was significantly longer in patients with T2DM compared with those without T2DM (*P* = .01).

3.3. COVID-19 effects in relation to blood glucose levels and total insulin doses

Of COVID-19 patients with T2DM, 6 (7%) patients experienced increased fasting and random blood glucose levels and they increased their insulin doses during the disease course (Table 4).

3.4. COVID-19 severity in relation to T2DM

COVID-19 patients in the studied population who had mild clinical symptoms were self-isolated at home while severe cases who had oxygen saturation of $\leq 90\%$ were admitted to ICU. COVID-19 patients with T2DM were more severely ill and had a

Table 2
COVID-19 clinical symptoms distribution in patients with and without T2DM.

Clinical symptoms	Overall (n = 412)	Without T2DM (n = 326)	With T2DM (n = 86)	<i>P</i>
Presence of symptoms				
Asymptomatic	47 (11.4%)	38 (11.7%)	8 (9.3%)	.65
Symptomatic	365 (88.6%)	288 (88.3%)	78 (90.7%)	
Fever				
No	184 (44.7%)	153 (46.9%)	31 (36.0%)	.13
Yes	228 (55.3%)	173 (53.1%)	55 (64.0%)	
Cough				
No	268 (65.0%)	220 (67.5%)	46 (53.5%)	.05
Yes	144 (35.0%)	106 (32.5%)	40 (46.5%)	
Shortness of breath				
No	311 (75.5%)	247 (75.8%)	63 (73.3%)	.74
Yes	101 (24.5%)	79 (24.2%)	23 (26.7%)	
Anosmia				
No	210 (51.0%)	164 (50.3%)	46 (53.5%)	.60
Yes	202 (49.0%)	162 (49.7%)	40 (46.5%)	
Chest pain				
No	336 (81.6%)	266 (81.6%)	69 (80.2%)	.79
Yes	76 (18.4%)	60 (18.4%)	17 (19.8%)	
Sore throat				
No	305 (74.0%)	238 (73.0%)	67 (77.9%)	.36
Yes	107 (26.0%)	88 (27.0%)	19 (22.1%)	
Congestion and runny nose				
No	338 (82.0%)	265 (81.3%)	73 (84.9%)	.48
Yes	74 (18.0%)	61 (18.7%)	13 (15.1%)	
Fatigue				
No	241 (58.5%)	195 (59.8%)	45 (52.3%)	.29
Yes	171 (41.5%)	131 (40.2%)	41 (47.7%)	
Headache				
No	202 (49.0%)	155 (47.5%)	46 (53.5%)	.36
Yes	210 (51.0%)	171 (52.5%)	40 (46.5%)	
Diarrhea				
No	304 (73.8%)	241 (73.9%)	64 (74.4%)	.99
Yes	108 (26.2%)	85 (26.1%)	22 (25.6%)	
Vomiting				
No	387 (94.0%)	308 (94.5%)	79 (91.9%)	.44
Yes	25 (6.0%)	18 (5.5%)	7 (8.1%)	

Table 3**Incubation period and disease duration means by analysis of covariance (adjusted for age and BMI).**

Variables	Mean (SD) [†]		P
	Without T2DM (n = 326)	With T2DM (n = 86)	
Incubation period mean	5.1 ± 2.8	5.7 ± 3.5	.58
Disease duration mean	8.3 ± 5.5	10.7 ± 8.4	.01*

* Significant results (*P* value < .05)[†] SD (standard deviation).

higher mortality (Table 5). The association between COVID-19 severity and T2DM was statistically significant after adjustment for age and BMI (Table 5). This indicates that COVID-19 patients with T2DM had more risk of ICU admission and death compared with those without T2DM.

Logistic regression was also performed to assess the association between disease severity and the T2DM when after adjusting for risk factors covariates, including age, BMI, and smoking (Table 6). A statistically significant difference was not found between the groups with respect to age, BMI, and smoking, with the exception of T2DM (*P* = < .010, odds ratio of 2.4); COVID-19 patients with T2DM were at greater risk (2 times higher) of severe illness compared with others.

4. Discussion

People with diabetes are highly susceptible to infection, with dire outcomes and poor prognosis.^[5] However, COVID-19 is a novel disease, and little is known about its clinical features in patients with comorbid diabetes. To our knowledge, the current study is the first study to assess the severity and clinical characteristics of COVID-19 in Saudi patients with T2DM in Jazan. In the present study population of individuals from Jazan, Saudi Arabia, the percentage of Covid-19 patients having T2DM is 20.8%, which is approximately similar to the percentage reported in other study among Chinese people (19%).^[51]

We found that men and people aged 45 to 64 years, who had T2DM were more likely to be infected with COVID-19. The relatively high infection of men and adults with middle age could be explained by the fact that they are more mobile and thus are at increased risk of infection. The majority of the participants with T2DM displayed clinical symptoms of COVID-19, but the differences between patients with T2DM and those without T2DM in this regard were not statistically significant. Similar results were reported in a previous study.^[20]

Underlying T2DM and illness severity could contribute to hyperglycemic and high glucose variability.^[21] Hyperglycemia

Table 4**Blood glucose levels and total insulin doses using Wilcoxon signed rank test.**

Variables	Median		P
	Pre-COVID-19 (n = 6)	Post-COVID-19 (n = 6)	
Fasting blood glucose levels	119	148	.02*
Random blood glucose levels	172	216	.02*
Total daily insulin doses	42	58	.01*

* Significant results (*P* value < .05).**Table 5****Severity of COVID-19 in T2DM using chi-square test.**

Severity	Overall (n = 412)	Without T2DM (n = 326)	With T2DM (n = 86)	P
Mild symptoms	381 (92.5%)	306 (93.9%)	69 (80.2%)	.001*
ICU [†] admission	19 (4.6%)	16 (4.9%)	9 (10.5%)	
Mortality	12 (2.9%)	4 (1.2%)	8 (9.3%)	

* Significant results (*P* value < .05)[†] Intensive care unit.

has been proven to be associated with stress and infection.^[22] In our study, we also noticed that blood glucose levels increased in patients with T2DM, especially among insulin users, which requires these patients to increase their insulin doses. These results were similar to results from a previous study that found diabetic patients with COVID-19 who were receiving insulin faced poor prognosis.^[20] One hypothesis suggested that SARS-CoV-2 may cause acute impairment of insulin secretion or destruction of β-cells, resulting in hyperglycemia.^[23] In addition, insulin resistance and altered glucose homeostasis in patients with T2DM was associated with over-inflammation.^[24] Thus, poor glycemic control worsens outcomes for patients with COVID-19.

Patients with T2DM experienced a higher proportion of hospital admissions compared with patients without T2DM, consistent with results found in recent publications.^[19,20] In China, a nationwide analysis reported that the most prevalent comorbidity in COVID-19 patients was diabetes (8.2%) and the simultaneous presence of these 2 chronic diseases was associated with adverse outcomes.^[25] In our study, 37.2% of patients with T2DM suffer from obesity, which may worsen outcomes of COVID-19.^[26] Obesity is associated with immune dysregulation and chronic inflammation, both of which can influence progression toward organ failure in severely ill COVID-19 patients.^[27] Respiratory dysfunction and the risk of invasive mechanical ventilation in obese patients with COVID-19 was high among those admitted to an ICU.^[28] Furthermore, pro-inflammatory pathways, such as those involving interleukin 6, could worsen the severity of lung diseases in patients with T2DM and COVID-19.^[29] The findings of our study suggest that COVID-19 patients with T2DM have worse outcomes than patients without T2DM. The odds of hospital admission increased in patients with T2DM and COVID-19. T2DM was independently associated with severe illness and hospital admission. Furthermore, in the present study, COVID-19 patients with T2DM had higher mortality rate than those without T2DM. Similar results were reported in a previous study.^[30]

Table 6**Predictors of COVID-19 severity using logistic regression.**

Predictor	P value	OR	(CI 95%)
Age	.53	1.0	(0.98–1.05)
Sex	.27	1.7	(0.65–4.71)
T2DM	<.01*	2.5	(0.90–7.71)
Smoking	.72	1.6	(0.15–3.60)
BMI	.25	1.05	(0.97–1.13)

* Significant results (*P* value < .05).

5. Conclusion

COVID-19 patients with T2DM had more severe clinical outcomes than COVID-19 patients without T2DM. COVID-19 patients with T2DM were associated with a higher risk of admission to the ICU and mortality than COVID-19 patients without T2DM. The need for early monitoring and supportive care should be addressed in these high-risk patients.

Author contributions

All authors contributed to the research steps: study design, data collection, statistical analysis, writing, and revising the manuscript.

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