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Association of diabetes with severity and outcome of COVID - 19 positive patients: a retrospective cohort study in King Abdullah Medical Complex, Jeddah, Saudi Arabia

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Abstract

Introduction: The Corona Virus Disease 19 (COVID-19) is a pandemic infectious disease caused by the novel coronavirus Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2). Almost 8 million instances of the illness were confirmed, and there were over 450,000 fatalities. We aim to explore diabetes as a risk factor associated with the severity and outcome of hospital-admitted COVID-19 positive cases.

Method: It is a hospital-based retrospective cohort study of hospital admitted RT-PCR COVID positive cases from March to June 2020. Data were outlined using mean and standard deviation (SD) for quantitative variables; categorical sociodemographic data were compared by disease severity and outcome by Pearson's Chi-square test ***(X^2).*** Univariate and multivariate logistic regression analyses were used to estimate the risk factor associated with disease severity and outcome of the patients.

Result: Of the 224 diagnosed COVID positive patients, 74 (33.04%) have diabetes. Among these 74 COVID-positive cases with diabetes, 52 (43.70%) cases have severe to critical conditions. Both univariate (OR: 2.87, 95% C.I, 1.58 – 5.20; p = 0.00) and multivariate (aOR: 2.76, 95% C.I, 1.34 – 8.42; p = 0.00) analysis show diabetes has a significant association with severity of COVID infection. Regarding the outcome of hospital admitted COVID patients with diabetes, 52 (28.26%) were discharged alive after recovery from COVID infection. In the univariable (OR: 3.16, 95% C.I, 1.57 – 6.38; p = 0.00) and multivariable (aOR: 3.12, 95% C.I, 1.15 – 8.42; p = 0.02) analysis, diabetes has been significantly associated with the outcome of hospital admitted COVID cases.

Conclusion: Our study identified diabetes as a risk factor for increased severity of COVID positive cases. Risk factors like older age and obesity also significantly predict COVID-19 disease progression.

Keywords: SARS-CoV-2; Diabetes; Risk factors; COVID-19; Disease severity

1. Introduction

In the twenty-first century, diabetes has elevated to a substantial global public health issue. The prevalence of diabetes is rising quickly across all age groups. Also, this is to blame for the load on socioeconomic advancement [1,2]. According to the International Diabetes Federation's 2019 Diabetes Atlas, there are currently an estimated 463 million diabetics worldwide, and by 2045, that number is expected to rise to 700 million cases. The IDF Diabetes Atlas also predicts that nearly 232 million were oblivious of their diabetic condition. Atlas IDF diabetes DM is considered one of the top 10 causes of death in 2019. The IDF predicted that diabetes alone would be responsible for 4.2 million deaths worldwide [3]. Diabetic patients had 2-3 times increase in all-cause mortality [2]. Diabetes patients are more likely to contract certain infections [1,2,4]. Also, it is generally known that diabetes mellitus increases the risk of infection [4].

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In December 2019 in Wuhan, China, the first case of atypical pneumonia with severe acute respiratory syndrome coronavirus 2 was discovered. Due to the coronavirus disease's (COVID – 19) swift global expansion in 2019, The World Health Organization (WHO) classified COVID - 19 as a pandemic on March 11th, 2020. COVID-19 has killed 4 699 359 people and infected 229 415 774 people worldwide, with a case fatality rate of 2.5 percent [5]. According to WHO Coronavirus Dashboard for COVID -19 prognosis, around 80% of cases have mild illnesses, 14% have severe illnesses, and 5% have critical illnesses. Studies and reviews done on COVID -19 have outlined the clinical features of this disease [6].

Regarding the most noticeable symptoms, the factors linked with greater susceptibility to infection and the severity of the disease are also linked. The presence of comorbidities does not appear to affect the core symptoms, and the mild clinical presentation of patients was consistent across age groups and geographical regions. Despite this, studies have revealed that those with chronic illnesses, such as diabetes mellitus (DM), hypertension, or cardiovascular disease, have a worse prognosis [7,8]. The probability of a more severe course of COVID cases and an increase in mortality are both increased by diabetes and other related comorbidities [9-13].

It is known that people with diabetes have a higher risk of infection, which is partially attributable to immunological dysfunction caused by hyperglycemia or elevated blood sugar levels [14-18]. On the other hand, severe SARS-Co-2 infection and the hyperinflammation that goes along with it cause hyperglycemia by adversely influencing insulin target tissues indirectly and maybe directly on the pancreatic beta cell [19]. It can result in hyperglycemia and worsen COVID positive patients' prognosis [20-22].

This study investigates the association between diabetes and the severity (mild to moderate and severe to critical) of COVID – 19 positive patients. Also, explore the association between diabetes and outcome (Patient discharge from hospital alive or not) of the COVID positive patients admitted to the hospital.

2. Material and methods

2.1. Study Design

This retrospective cohort was conducted by retrospective electronic medical record review. Data collected from the RT-PCR patient confirmed COVID positive cases (through nasal or pharyngeal swabs). This study included all the patients of the age of the patient ≥ 18 years old and admitted to the King Abdullah Medical Complex (KAMC) from March 2020 to June 2020 in Jeddah Region. Patients who were pregnant, with incomplete medical records, and those recodes in which patients were not reachable were all excluded from the study. We extracted 224 Ministry of Health allowed the ethical approval. To maintain patient privacy, all patient data was made anonymous.

2.2. Data collection

A modified standardized data collection form from the WHO/International Severe Acute Respiratory and Emerging Infection Consortium case record form for COVID-19 [23]. Data was collected by MOH Electronic Medical Review (EMR). The sociodemographic data of all RT- PCR positive COVID cases, including age, sex, height in cm, weight in kg, body mass index (BMI), and nationality, employment status was collected. The main risk factor, diabetes, is diagnosed based on a blood test (HbA1c). If the result of HbA1c is ≥ 6.5, the patient was considered to have diabetes in this study.

To diagnose whether the patient has mild to moderate or severe to critical COVID positive patient, data was collected on admission vital signs of the patient, including respiratory rate, blood oxygen saturation, PaO2/FiO2 ratio 50% of the lung field within 24- 48 hours. In addition, to diagnose severe to critical patient data of ARDS, Sepsis, altered consciousness, multi-organ failure, patient with cytokine release syndrome, Ferritin >300 ug/L (or surrogate) with doubling within 24 hours, Ferritin >600 ug/L at presentation and LDH >250, Elevated D-dimer (>1 mcg/mL) were collected.

2.3. Endpoint Definitions

The main result is the severity of the COVID-19 disease, which is categorized and characterized according to the MOH criteria for the disease into mild/moderate, severe, and critical MOH Publications - COVID-19 Guidelines [24].

- **Mild to Moderate COVID-19 cases** are defined as PCR-confirmed and are either asymptomatic or symptomatic (no O2 requirements/no evidence of pneumonia).
- **Severe and Critical COVID-19 Cases: Severe cases** are defined as PCR-confirmed and have symptoms of ≥ 1 of the following: Respiratory rate ≥30/min, Blood oxygen saturation ≤93%, PaO2/FiO2 ratio 50% of the lung field within 24 - 48 hours. ***Critical cases*** are defined as having symptoms of ≥ 1 of the following: ARDS, Sepsis, Altered consciousness, and multi-organ failure. Patient with cytokine release syndrome (Serum IL-6 ≥3x upper normal limit, Ferritin >300 ug/L (or surrogate) with doubling within 24 hours, Ferritin >600 ug/L at presentation, and LDH >250, Elevated D-dimer (>1 mcg/mL).

2.4. Statistical analysis

Data were outlined using mean and standard deviation (SD) for quantitative variables: age, height in cm, weight in kg, and BMI. Categorical sociodemographic data, including gender (male or female), nationality (Saudi or non-Saudi), BMI category (18.5 – <25, 25 - <30, >=30), and employment status (employed or not employed) were compared by disease severity and outcome by Pearson Chi-square test *(X)2.* Univariate and multivariate logistic regression analyses were used to estimate the risk factor associated with disease severity and outcome of the patients. Retrograde regression analysis was done to achieve the final model. The final model was adjusted for confounders (age and BMI). A two-sided α of less than 0.05 was considered statistically significant. All statistical analyses of this study were performed by using Stata version 17.0 (Stata Corp, College Station, Texas, USA)

3. Results

Table 1 Sociodemographic characteristics according to severity of the disease among hospital admitted COVID - 19 cases (on admission)

Sociodemographic data	Mild to moderate COVID positive patient (n = 105)	Severe to critical COVID positive patient (n = 119)	P value
	Mean ± S.D	**Mean ± S.D**	
Age	43.37 ± 15.2	53.21 ± 13.4	**0.00**
Height in cm	165.74 ± 1.24	165.51 ± 0.92	0.87
Weight in kg	76.84 ± 2.18	82.59 ± 1.59	**0.03**
Body Mass Index (BMI)	28.03 ± 0.81	30.14 ±0.62	**0.03**
	N (%)	**N (%)**	
Gender			
Male	78 (74.29%)	95 (79.83%)	0.32
Female	27 (25.71%)	24 (20.17%)	
BMI categories			
Normal weight	34 (32.38%)	27 (22.69%)	**0.04**
Overweight	42 (40.00%)	42 (35.29%)	
Obese	29 (27.62%)	50 (42.02%)	
Nationality			
Saudi	39 (37.14%)	40 (33.90%)	0.61
Non-Saudi	66 (62.86%)	78 (66.10%)	
Employment			
Employed	66/86 (76.74%)	50/82 (60.98%)	**0.03**
Not employed	20/86 (23.26%)	32/82 (39.02%)	

A total of 224 COVID – 19 positive patients were enlisted in this study. According to severity, out of 224 patients, 105 (46.88%) have mild to moderate, and 119 (53.13%) have severe to critical COVID infection. As shown in Table 1, among mild to moderate cases, the mean age is 43.37 ± 15.2 compared to the mean age of severe to critical cases is 53.21 ± 13.4. In both categories of severity, the major population is male COVID cases, 78 (74.29%) and 95 (79.83%) in mild to moderate and severe to critical cases, respectively. The non-Saudi population is more commonly affected by COVID than the Saudi population, with 66 (62.86%) in mild to moderate and 78 (66.10%) in severe to critical cases. Also, in the mild to moderate category, the majority is overweight cases, 42 (40.00%), and among the severe to critical category majority of the patient is obese, 50 (42.02%). (Table 1)

In table 2, According to the outcome of this study, we found 184 (82.14%) COVID patients discharged from the hospital alive. The mean age of the patients who were discharged from the hospital alive was 47.18 ± 1.11 compared to the patients who died; the mean age was 55.12 ± 2.14. The mean BMI is higher in those who died, 30.89 ± 1.02. COVID-positive cases from the Saudi population were higher in percentage in both categories of outcome; 116 (63.39%) cases left the hospital alive, and 28 (70.00%) cases died due to COVID infection.

Table 2 Sociodemographic characteristics according to outcome of the disease among hospital admitted COVID - 19 cases on admission

Sociodemographic data	**COVID positive patient discharged Alive (n = 184)**	**Death (n = 40)**	**P value**
	Mean ± S.D	**Mean ± S.D**	
Age	47.18 ± 13.11	55.12 ± 12.14	**0.01**
Height in cm	165.98 ±0.93	164.42 ± 1.05	0.36
Weight in kg	79.25 ± 1.56	82.80 ± 2.41	0.26
Body Mass Index (BMI)	28.67 ± 0.57	30.89 ± 1.02	**0.00**
	N (%)	**N (%)**	
Gender			
Male	144 (78.26%)	29 (72.50%)	0.43
Female	40 (21.74%)	11 (27.50%)	
BMI categories			
Normal weight	54 (29.35%)	7 (17.50%)	**0.03**
Overweight	69 (37.50%)	15 (37.50%)	
Obese	61 (33.15%)	18 (45.00%)	
Nationality			
Saudi	116 (63.39%)	28 (70.00%)	0.42
Non-Saudi	67 (36.61%)	12(30.00%)	
Employment			
Employed	105/145 (72.41)	11/23 (47.83)	**0.02**
Not employed	40/145 (27.59)	12/23 (52.95)	

Table 3 illustrates that out of 224 COVID cases, 74 (33.04%) are diabetic. Among these diabetic COVID positive cases, severe to critical COVID cases are 52 (43.70%). The association between diabetes and severity of COVID – 19 cases. In the univariable (OR: 2.87, 95% CI, 1.58 – 5.20) and multivariable (aOR: 2.76, 95% CI, 1.34 – 8.42) analysis diabetes was significantly associated with the severity of COVID cases.

Table 3 Association of DM (n = 74) with severity of COVID cases in King Abdullah Medical Complex (KAMC) from 2020 till 2020

Diabetes (n = 224)	Mild to moderate COVID positive patient (n = 105)	Severe to critical COVID positive patient (n = 119)	Univariate analysis		Multivariate analysis	
			OR (95% C.I)	P value	aOR** (95% C.I)	P value
Present (n = 74)	22 (20.95%)	52 (43.70%)	2.87 (1.58 – 5.20)	**0.00**	2.76 (1.34 – 5.68)	**0.00**
Absent (n = 150)	83 (79.05%)	67 (56.30%)				

**Adjusted for confounder (age)

Table 4 Association of DM (n = 74) with outcome of COVID cases in King Abdullah Medical Complex (KAMC) from 2020 till 2020

Diabetes (n = 224)	COVID positive patient discharged Alive (n = 184)	Death (n = 40)	Univariate analysis		Multivariate analysis	
			OR (95% C.I)	P value	aOR** (95% C.I)	P value
Present (n = 74)	52 (28.26%)	22 (55.00%)	3.16 (1.57 – 6.38)	**0.00**	3.12 (1.15 – 8.42)	**0.02**
Absent (n = 150)	132 (71.74%)	18 (45.00%)				

**Adjusted for confounder (age and BMI)

Table 4 displays the association between diabetes and the outcome of COVID – 19 cases. In the univariable (OR: 3.16, 95% CI, 1.57 – 6.38) and multivariable (aOR: 3.12, 95% CI, 1.15 – 8.42) analysis, diabetes was significantly associated with the outcome of hospital-admitted COVID cases. Each final model was adjusted for confounders (age and BMI).

4. Discussion

This retrospective cohort study included 224 COVID positive patients in KAMC, Jeddah., which revealed that being diabetic, the odds of having severe to critical COVID infection is 2.76 times higher than being nondiabetic. Our result is similar to other studies, including a study done by *Stuart J McGurnaghan et al.* in which the Odds (Odd ratio) of need for critical care unit treatment for COVID infection was 1.37 times in type 2 diabetic cases compared to nondiabetic cases (OR:1·369; C.I:1·276–1·468; p<0·0001) [25-27].

Also, our study demonstrates that death is 3.12 times more likely in diabetic patients than in nondiabetic COVID-positive patients. Our finding is similar to the findings of studies done by *Giuseppe Pugliese et al.* and *M.M.Lima-Martínez et al*. [26-28].

In tables 1 and 2, we observed that COVID infection is more severe with older age, and the outcome is unsatisfactory. The mean age of severe to critical COVID infection is 53.21 ± 1.23, whereas the mean age is only 43.37 ± 1.48 in mild to moderate cases. A population-based cohort study conducted in England (2020) reveals similar findings [13].

Our study reveals that the male population with COVID infection is comparatively higher than the female population. Among the severity and outcome of COVID cases, most of them are male. Our finding is not different from other previously conducted studies [13, 25].

A meta-analysis by *Romil Singh et al.* shows that obesity was associated with an increased risk of severe COVID infection (RR=1.52, 95% CI 1.41-1.63, p<0.001). Furthermore, mortality was higher in obese patients (RR=1.09, 95% CI 1.02-1.16, p=0.006) [29]. This result is similar to our findings in this study. (Tables 1 and 2)

There are a few restrictions on this study. A smaller sample size may have attenuated the relationship for some factors associated with COVID infection because this study is a retrospective review of the medical records of patients at KAMC who tested positive for COVID. Data were obtained from the electronic medical record and challenges with incomplete medical records were faced. Information bias could also result from it. Second, certain details like food practices, exercise routines, smoking, alcohol consumption, and lifestyle choices were not documented.

Despite its limitations, this is one of the few studies done in the Kingdom of Saudi Arabia to study diabetes as a risk factor for disease severity and the outcome of the COVID positive patients who were admitted to the hospital. This study includes a broad range of population, especially with the allowance of all residents to be treated in the Kingdom, and this leads to an increase in the generalizability.

5. Conclusion

Our study concludes the potential necessity for more thorough follow-up and therapy for COVID positive diabetic individuals. Moreover, efforts to manage diabetes positively impact the result of COVID significantly. New goals that are essential to a better treatment plan for diabetics with COVID infections might be the focus of policymakers. Further cohort studies on RT-PCR-positive confirmed COVID cases with a large population and dependable controls for possible confounding are advised.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have no conflicts of interest to disclosure.

Statement of informed consent

The patient's informed consent was not required as the study was limited to reviewing existing electronic medical records.

Author contributions

All authors contributed to data analysis, preparing, or revising the article, finalizing the version to be published, and agreeing to be held responsible for all facets of the work.

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