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Original Article

The Relationship between Diabetes Mellitus and The Prognosis of COVID-19

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ABSTRACT

Background: Coronavirus disease 2019 [COVID-19] was first reported in Wuhan, China. It then rapidly spread and became a global epidemic due to infection by severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]. COVID-19 is highly transmissible with a high risk of mortality. Patients with diabetes mellitus [DM] are more susceptible to infectious agents like SARS-CoV-2.

Aim of the work: The aim of the study was to evaluate the relationship between DM and COVID-19 infection regarding severity, mortality, admission rate, complications, and prognosis.

Patients and Methods: A cross-sectional study was performed between April 2021 and September 2021. It included 75 patients divided into three groups: Group A [COVID-19 patients with diabetes, n=25], Group B [COVID-19 patients who developed diabetes, n=25] and Group C [COVID-19 patients without diabetes, n=25]. Demographic, clinical, laboratory, radiologic, management, complication, and clinical outcome data were collected and compared between the groups.

Results: Patients with diabetes had a higher rate of complications like respiratory failure and acute cardiac injury. Respiratory failure was not significantly different between groups [20%, 28% and 12% in groups A, B and C respectively, P=0.368]. However, acute cardiac injury was significantly higher in groups A than B and in A and B than C [[44%, 20% and 8% respectively, P=0.01]. The mortality rate was also significantly higher among groups A and B than C [56%, 40% vs 8%, P=0.001].

Conclusion: Diabetes is an independent risk factor for COVID-19 prognosis. Diabetic patients should be closely monitored during treatment, especially those requiring insulin therapy.

Keywords: COVID-19; Diabetes; SARS-CoV-2; Respiratory Failure; Acute Cardiac Injury.

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INTRODUCTION

The coronaviruses are responsible for many viral infections. The severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] was responsible for the emergence of a coronavirus diseases at the end of the year 2019 [COVID-19] [1]. The crown-like projections on the surface [detected by electron microscopy] of the single-stranded, enveloped RNA, virus give the family its name. It belongs to the subfamily of Coronviridae family called coronavirinae. It shares the clinical manifestations as the severe acute respiratory syndrome [SARS] and the Middle East Respiratory syndrome [MERS] [2]. All the three viruses share many characteristics in their structure, biochemical contents and their clinical picture. The infection is manifested by fever, cough, difficult respiration, myalgia, gastrointestinal [GIT] manifestations and others. COVID-19 started in Wuhan district, China and defined as a zoonotic infectious epidemic [3].

COVID-19 is associated with a low mortality, that was reported in the critically ill patients. However, the mild to moderate infection is responsible for about 80% of reported cases. The number of deaths progressively increased from the start of disease onwards, till the development of its vaccine or herd immunity [4].

Compared to influenza, COVID-19 is highly transmissible with greater risk of fatality. The majority of COVID-19 patients were expected to have a favorable outcome. However, older patients with underlying disease or those critically ill, have a poor outcome [5].

Diabetes mellitus [DM] is a common disease of older people and is associated with a greater morbidity worldwide. Patients with DM are more susceptible to different infectious agents [e.g., staphylococcus aureus, streptococcus pneumoniae and mycobacterium tuberculosis, among others] [6].

Studies from Wuhan linked the DM to bad prognosis of COVID-19 and suggested that patients with DM may be more prone to SARS-CoV-2 and might have a bad prognosis [7-9].

In addition, DM was associated with severe course and high mortality in patients with symptomatic COVID-19 patients. It may be associated with a higher need for mechanical ventilation [MV] and mortality. In addition, the worse prognosis associated with DM had been described with MERS and SARS-CoV-1 [10]. However, the available literature is not conclusive about this association.

This study aimed to assess the potential relationship between DM and COVID-19 infection regarding severity, rate of admission, complications, mortality and prognosis.

PATIENTS AND METHODS

This was a cross-sectional analytical study, which was carried out between April 2021 to September 2021. The study subjects were recruited from Suez General Hospital and Al-Azhar university hospital. Patients were divided, after through history, meticulous clinical examination and full investigations, into the following groups: 1] Group A: COVID-19 patients with known diabetes mellitus [n=25]; 2] Group B: COVID-19 patients who developed diabetes mellitus at onset of infection [n=25]; 3] Group C: COVID-19 patients without diabetes mellitus [n=25].

Inclusion and Exclusion Criteria: All patients with positively tested with COVID-19 PCR and aged > 18 years old were eligible. However, patients under 18 years of age or pregnant females were excluded from the study.

Ethical Considerations: Before conducting the field work, the research proposal was reviewed and accepted by the Research Ethics Committee of Al-Azhar University's Faculty of Medicine. In addition, all patients signed an informed written consent. The study was completed and data was reported according to the ethical codes of Helsinki declaration.

All participants underwent a detailed assessment composed of full medical history, clinical examination and laboratory investigations by available kits and according to manufactures' recommendations.

The diagnosis of DM was set by meeting one of the following findings: 1] fasting blood sugar [FBS] ≥ 126 mg/dl, 2] Post-prandial Plasma glucose levels ≥ 200 mg/dl, two hours after a 75 mg of oral glucose load [oral glucose tolerance test], 3] Plasma glucose level > 200 mg/dl; 4] Glycated hemoglobin [HbA1c] ≥ 6.4% [10]. Fever was recognized when axillary temperature was > 37.3 °C.

The severe disease [Critical illness] was recognized by satisfaction of at least one of the following criteria: 1] respiratory failure [RF] mandating MV; 2] shock performance; 3] multiple organ failure needing ICU monitoring. However, the RF was defined as an arterial partial oxygen pressure [PaO2] lower than 60 mm Hg [10].

COVID-19 infection was confirmed by the assessment of throat swabs. The swabs were collected from the upper respiratory tract and samples were examined for the virus using the reverse transcription polymerase chain reaction [PCR].

Statistical Analysis: The collected data were transformed to anonymous data and fed to personal computer. The arithmetic mean ± SD [standard deviation] was used as the measures to express the continuous numerical, normally distributed data. The three groups [means] were tested for variability using one-way analysis of variance [ANOVA]. On the other side, Chi square or Fisher exact test was used to test association between categorical variables, which was represented by their frequency and percentages. P value < 0.05 was considered significant. All calculations were performed by the statistical package for social science [SPSS] version 15 for windows [SPSS Inc., Chicago, IL, 2001].

RESULTS

Table [1] showing the baseline characteristics of the studied groups. Among the studied patients, 32 [42.6%] were females; while 43 [57.4%] were males. There was no significant difference between the included groups regarding their sex. However, there was a significant difference in terms of age, as patients with diabetes tended to be older [p < 0.001]. The most common sign among all groups was Fever. There was no significant difference between different groups regarding their symptoms and signs. Moreover, there was no significant difference between different groups regarding the presence of CVS. However, there was significant difference between them in terms of hypertension [P < 0.001].

Most of the included patients did not have a critical case when admitted. Moreover, there was no significant difference between the two groups regarding the severity at the time of admission [P = 0.654]. Patients with diabetes had a higher proportion of complications, including respiratory failure difference [20%, 28% vs 12%, P = 0.368] but without significant and acute cardiac injury [44%, 20% vs 8%, P= .01] with a significant difference [Table 2].

Table [3] showing the management of the included patients. Of the 75 patients, 32 [44%] received antiviral treatment, 24 [32%] received an antibiotic, 14 [18.6%] received corticosteroid, and 5 patients [6.5%] were admitted to the ICU.

Table [4] showing the prognosis and mortality rate among the included patients. Of the 75 patients, 26 [34.5%] died. The mortality rate was significantly higher among the diabetic group [56%, 40% vs. 8%; P=0.001].

Table [1]: Clinical and Demographic characteristics of the studied groups

Variables		Non-Diabetic	Diabetic	Developed DM	P-Value
Age [years]	< 65 > 65	20 [80%] 5 [20%]	4 [16%] 21 [84%]	3 [12%] 22 [88%]	< 0.001
Sex, n [%]	Females Males	11 [44%] 14 [56%]	9 [63%] 16 [37%]	12 [48%] 13 [52%]	0.683
Symptoms and Signs, n [%]	Fever Cough Fatigue Anorexia	12 [48%] 4 [16%] 6 [24%] 3 [12%]	15 [60%] 3 [12%] 3 [12%] 4 [16%]	11 [44%] 6 [24%] 2 [8%] 6 [24%]	0.518
Comorbidities, n [%]	Hypertension Cardiovascular diseases Renal diseases Liver diseases	2 [8%] 4 [16%] 1 [4%] 1 [4%]	14 [56%] 11 [44%] 1 [4%] 0 [0%]	15 [60%] 10 [40%] 0 [0%] 1 [4%]	< 0.001

Table [2]: Severity and complications of the patients' condition at admission

Variables		Non-Diabetic	Diabetic	Developed DM	P-Value
Complications, n [%]	Respiratory failure Acute cardiac injury	3 [12%] 2 [8%]	5 [20%] 11 [44%]	7 [28%] 5 [20%]	0.368 0.01
Severity at admission, n [%]	Critical Noncritical	6 [24%] 19 [76%]	8 [32%] 17 [68%]	9 [36%] 16 [64%]	0.645

Table [3]: Management of the included groups

Variables	Non-Diabetic	Diabetic	Developed DM	P-Value
Antiviral therapy	10 [40%]	11 [44%]	11 [44%]	0.976
Antibiotics	7 [28%]	9 [36%]	8 [32%]	
Corticosteroids	3 [12%]	5 [20%]	6 [24%]	
ICU Admission	1 [4%]	2 [8%]	2 [8%]	

Table [4]: Prognosis of the included groups

Variables	Non-Diabetic	Diabetic	Developed DM	P-Value
Death	2 [8%]	14 [56%]	10 [40%]	0.001
Alive	23 [92%]	11 [44%]	15 [60%]	

DISCUSSION

DM is a chronic inflammatory condition. Multiple micro- and macro-vascular abnormalities were the main pathological features of the condition. These abnormalities change the normal response to infectious agents. Viral Infections [e.g., influenza and pneumonia] are more common in older patients with DM. In addition, DM was considered as a risk factor for morbidity and mortality associated with different viral infections [e.g., 2009 influenza A [H1N1], MERS-CoV, and SARS- CoV]. However, the association between diabetes and the prognosis of COVID-19 is not adequately addressed [10, 11].

In the current work, we 75 patients with COVID-19 [25 with pre-existing diabetes, 25 developed diabetes after COVID-19 infection and 25 patients free of DM]. The results indicated that, patients with DM were significantly older than non-diabetics. The high incidence of diabetes among elderly is a well-known fact. In addition, older age is well-recognized as a bad indicator for COVID-19 prognosis. Thus, the higher incidence of older subjects in diabetic groups may lead to a poor prognosis [12]. Furthermore, the clinical symptoms were recorded and patients with DM had an increased incidence of fever, fatigue and anorexia. This might lead to a poor nutritional status. However, the differences between groups were statistically non-significant. This agrees with **Shang *et al.*** [13] who found a non-significant difference in symptoms frequency between the two groups.

Another aspect that needs to be considered is the presence of coexistent comorbid conditions with diabetes in patients with COVID-19. For example, hypertension have been considered as risk factor for the COVID-19 severity. When hypertension coexists with diabetes, more harmful effects can be anticipated. In the current work, coexistent comorbid conditions were associated with a significant increase in mortality. This agreed with the previous study done by **Shang *et al.*** [13] who found that hypertension was more prevalent among the diabetics. On the other hand, **Guo *et al.*** [14] did not find any difference between the two groups regarding the comorbidities.

In this work, there were more critically ill patients [Severe disease] in the diabetes groups at the time of admission. This agreed with the results of previous studies reported that the diabetic groups had more severe illness than non-diabetics. They suggesting that diabetic patients are more likely to progress to a severe form after the COVID-19 infection [12-14].

In the current research, the acute cardiac injury was significantly higher in the diabetes than non-diabetes groups. This is in line with **Shang *et al.*** [13] These results indicated that more attention must be paid to respiratory support and protection of the heart in COVID-19 patients with diabetes. Currently, there was no clear sound evidence to show that antiviral treatment is associated with a significant improvement of COVID-19 prognosis. The available treatment of COVID-19 did not include antiviral therapy as a part of routine therapy. Otherwise, they only received oxygen, fluid management, and respiratory support. Some received antibiotics, corticosteroids, and antiviral drugs [15].

Critically ill subjects are usually needing monitoring in the ICU MV. In the current study, patients with DM were more likely to receive corticosteroids than patients without DM. This indicated that patients with DM usually had a more severe disease with progression and needed more advanced therapeutic intervention. However, mortality is still higher among patients with DM irrespective of the use of advanced treatment. This agrees with the previously conducted study done by **Huang *et al.*** [12].

Our cohort demonstrates that COVID-19 with diabetes is associated with a significant increase in mortality rate. This agrees with previous the study of **Barron *et al.*** [16] They showed that diabetes [either type 1 or type 2] was associated with increased odds of in-hospital mortality in COVID-19 patients when compared to COVID-19 patients without DM. Moreover, patients with DM had more severe pneumonia with a severe course of illness. These patients had a significant reduction of O2 saturation with higher respiratory rate on admission than the control group [13].

Our study agrees to the previous literature, considered DM and uncontrolled blood glucose levels as an independent risk factor for fatality in COVID-19 [12, 17]. However, these results should be treated carefully due to heterogeneity in patients and small sample size. Consisting with the results of the current work, two studies from England with large scale population

showed that, patients with DM and COVID-19 were shown to be at increased risk for higher mortality [11, 16].

Finally, **Al-shaibany *et al.*** [18] reported an interesting case report of 51- years old male, who had COVID-19 pneumonia, manifested clinically by fever, difficult respiratory, lethargy and dizziness, with a positive history of bronchial asthma. His electrocardiogram revealed a third-degree heart block that need pacing of the heart with favorable outcome. This reflected the cardiovascular comorbid conditions associated with COVID-19, as in the current work.

This study had some limitations: 1] A multicentric studies with a greater sample size is needed to support our findings, 2] A longer follow-up is required to determine the long-term complications, 3] Further prospective trials are required to develop and verify our results.

In conclusion, DM could be considered as an independent risk factor and predictor for the prognosis of COVID-19. Patients with DM be strongly monitored during treatment.

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Conflicts of interest: None.

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