ijlpr 2022; doi 10.22376/ijpbs/lpr.2022.12.3.L14-20

International Journal of Life science and Pharma Research

ISSN 2250-0480

Research Article

Medical Science

The Increasing Prevalence of Diabetes Mellitus in COVID-19 Patients: Why?

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Abstract: Coronavirus infection disease 2019 (COVID-19) is caused by SARS COV-2 and it has been increasing continuously in a number of cases and mortalities. COVID-19 had caused more than 197 million infections and 4 million deaths. This study aimed to assess the prevalence, risk factors and outcome of Diabetes Meletus (DM) among COVID-19 patients. Prospective, cross-sectional, hospital-based study conducted in which 400 COVID-19 patients enrolled in COVID-19 isolation centers in North Sudan. In this study, we noticed that most of the participants were males and constituted 275 (68.9%) of the study participants, the majority of participants' ages ranged were between 40 to 60 years and was 150 (37.4%). The prevalence of DM was found to be 49.25% among the study participants. Diabetics were significantly more likely to have a respiratory rate higher than 30 (P=0.012), and oxygen saturation less than 93% (P<0.001), to develop shock (P=0.004), to require oxygen therapy (P<0.001), to be intubated (P<0.001), to develop respiratory failure and organ failure (P<0.001), and to have a poorer outcome (P<0.001). New-onset diabetes occurred in 20 (5%) participants and their mortality was higher compared to non-patients with diabetes (P=0.04). The total mortality of participants was 15.8%, factors associated with poorer outcomes were older age (P<0.001), and having type I diabetes (P=0.025). The prevalence of diabetes is very high among COVID-19 patients, and is associated with a more severe disease and a poorer outcome. New onset diabetes was associated with poorer outcomes compared to non-diabetics. More researches requested to discover more risk factors and complications associated with Covid-19.

Keywords: COVID-19; DM; Diabetogenicity; Isolation Centers; Sudan

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Received On 17 January 2022
Revised On 14 March 2022
Accepted On 23 March 2022
Published On 02 May 2022

Funding This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation Sufian Khalid, Khadeja Ismail Osman Farah, Awadalkareem AA.,Musa Kheir ,Hisham M. Abdelrahim, Motwakil Imam Awadelkareim, Ahmed ElSayed, Mohamed Osman Elamin, Ahmed A. Osman, Ali M. Alshehri, Hatim Abdullah Natto,Tassnim Sinky and Mohammed Salah , The Increasing Prevalence of Diabetes Mellitus in COVID-19 Patients: Why?.(2022).Int. J. Life Sci. Pharma Res.12(3), 14-20 http://dx.doi.org/ijlpr 2022; doi 10.22376/ijpbs/lpr.2022.12.3.L14-20

1. INTRODUCTION

Coronavirus infection disease 2019 (COVID-19) is caused by SARS COV-2 and it has been increasing continuously in a number of cases and mortalities. To date (August 2021), COVID-19 infection has affected more than 197 million persons and has been responsible for the deaths of more than 4 million[1]. Diabetes mellitus (DM) has a high prevalence among the general population; therefore, it is crucial to understand COVID-19 trends in patients with diabetes. DM in acute infections could increase the risk of morbidity and mortality due to patients' compromised immunity. Uncontrolled glucose level, linked to 60% of hospitalization and severity of pneumonia[2]. DM had increased the mortality and morbidity in past viral pandemics, and it was considered as an independent risk factor for mortality and morbidity of the SARS-COV-1 outbreak in 2002-2003[3]. With Influenza (H1N1) in 2009, DM increased the risk of hospitalization by three times and the risk of intensive care unit admission by fourfolds[4].Half of the affected population were found to have DM with the Middle East Respiratory Syndrome Coronavirus (MERS-COV) 2012 outbreak and the odds ratio for MERS-COV severity ranged between (7.2-15.7) in patients with diabetes compared to the general population. The odds ratio of patients admitted in intensive care was found to be 4.29 (95% CI 1.29–14.3) among patients having DM compared to patients without DM[5]. The mortality rate of patients with diabetes in COVID-19 was exceeded a third with the MERS outbreak[6]. In recent studies, DM, hypertension, and cardiovascular disease were considered risk factors for developing COVID-19 infection, despite the variability of prevalence in many studies from different countries. Many Chinese studies centered on COVID-19 found a high prevalence of hypertension, diabetes, and cardiovascular disease (CVD) in study patients. Patients with diabetes are more vulnerable to severe critical forms of disease ranging between 14-32% in severalstudies[7].Angiotensin-converting Enzyme 2 (ACE-2) receptors may play a major role in the effect of SARS COV-2 on the blood glucose level. Evidence of the presence of hyperglycemia even without being diabetic up to 3 years was noticed with SARS COV infection indicating transient damage to beta cells. Therefore, it is critical to monitor blood glucose, especially in acute presentations of the disease[8]. The relationship between COVID-19 and DM paid attention and was of great concern among public health stakeholders as there was a direct correlation in the increase in a number of cases of COVID-19 patients and new DM cases. To our knowledge, this research is the first study conducted in a multi-center in Sudan to identify this relationship. The study will shed light on the gap in the knowledge of the possible factors that contributed to the development of DM in patients having COVID-19. In this study, we aim to assess the prevalence, risk factors, and outcome of diabetes among COVID-19 patients.

2. METHODS

The present study was a prospective, cross-sectional, hospital-based study conducted in the COVID-19 Isolation Centers of North Sudan, namely: Dongola, Karema, Atbara, and Shandi cities. The study was conducted between September 2020 to November 2020. We included all adult patients having COVID-19 who were diagnosed via Polymerase Chain Reaction (PCR) tests in the isolation centers. The inclusion criteria of the patients were: being18 years of age and older, accepting to participate in the study, having a positive result of COVID-19 by PCR, and being admitted to one of the COVID-19 isolation centers involved in the study. We used the total coverage technique as the sampling method to collect data from the total number of included participants. Thus, the total number of included participants was 400 patients.

2.1 Data collection method & tool:

Data were collected using a structured interview questionnaire. The questionnaire was filled directly from the patients and from their medical files. For all the patients involved in the study a Random Blood Sugar (RBS), Fasting Blood Sugar (FBS), and 2 Hours Postprandial (2HPP) glucose measurements were done. In case of the abnormal elevated glucose level, we performed HbA1c.

2.2 The questionnaire involved data regarding

The questionnaire included items to measure socio-demographic characteristics (gender, age, residence, and marital status), comorbid conditions, diabetes-related data (random blood glucose at presentation, and discharge, symptoms, duration of symptoms, type of diabetes, and type of medication), COVID-19 related data (presenting symptom, place of receiving care, type of medication received, need for intubation, complications, and the final outcome), family history (diabetes, hypertension, and asthma), long term drugs, and social habits.

2.3 Ethical Consideration:

Ethical approval for this study was obtained from the Research Ethics Committee of Sudan Medical Specialization Board (SMSB) and the Ministries of Health in North Sudan (SMSB-E.C.66.2021), in inconsistency with Helinsky's declaration of the international conference on harmonization, regulations, and laws of Sudan. Informed consent was obtained from all individuals prior to their participation in the study; participants were informed that their participation in the study is voluntary and that they have the right to withdraw at any time. The dignity and confidentiality of the participants were preserved throughout the study.

3. STATISTICAL DATA ANALYSIS

Data was reviewed, ordered, and coded, and then Statistical Package for Social Sciences (SPSS) version 20 was used for data analysis. Descriptive statistics were used to analyze the participants' data. Mann-Whitney test was used to test for a significant difference in the mean arterial pressure of diabetic and non-diabetic COVID-19 patients. Chi-Square test and Fisher Exact test were used to test for a significant difference in the presentation of diabetic and non-diabetic COVID-19 patients, additionally; Chi-Square test was used to test for a significant difference between diabetic and non-diabetic COVID-19 patients in terms of type of management needed, complications, and outcome. Finally, the Chi-Square test was used to test a significant association between socio-demographic characteristics, social habits, and the type of diabetes to the outcome of the study participants.

4. RESULTS

A total of 400 COVID-19 patients were included in the study with 177 patients with diabetes and 223 non-diabetic (this later included 20 newly discovered). The prevalence of DM was 49.25% (197; 177 previously known diabetic, 20 newly discovered DM). More than two-thirds of the participants were males and more than one-third of them were in the age group of 40 to 60 years. Nearly two-thirds of them were from urban areas and the majority of them (75.6%) were married (Table 1).

Table 1 Demographic factor of the participants (N = 400).

Factor	N	%
Gender		
Male	275	68.9
Female	125	31.1
Age		
18 – 40	110	27.6
40 – 60	150	37.4
60 – 80	130	32.5
>80	10	2.6
Marital Status		
Married	302	75.6
Single	98	24.4
Residency		
Urban	251	63.3
Rural	149	36.7

Table.1 shows the demographic factors of 400 Covid-19 patients involved in the study, majority of cases were male (68.9%), while the age group 40-80 years was dominant among patients.

Table 2 Co morbidities, social habits and Medications of study participants (N = 400).

Factor	N	%
Chronic Illness		
DM	177	44.2
Heart disease	50	12.5
Stroke	6	1.5
Liver disease	4	1.0
Renal problem	19	4.8
Asthma	12	3.0
Malignancy	1	0.2
Family History		
DM	148	37.0
HTN	109	27.2
COVID-19	116	29.2
Social habits		
Smoking	77	19.2
Snuffing	34	8.5
Alcohol	11	2.8
Medications		
Yes	335	83.7
No	65	16.3

Table 2 shows that the most frequent comorbidity was DM (44.2%) and the least was malignancy (0.2%), a considerable portion of the participants had a family history of DM (37%), HTN (27.2%), and COVID-19 (29.2%). The most frequent social habits of participants in the study were smoking (19.2%), 16.3% of the study participants were taking long-term medications. (Table 2)

Table 3 Types, duration and medications of DM among study participants (N = 400).

Factor	N (177)	% (100)
Type of DM		
Type 1 (IDDM)	55	31.0
Type 2 (NIDDM)	122	69.0
Duration		
< 5 years	66	37.3
5 – 10 years	62	35.0
> 10 years	39	22.0
Medications		
OHA	61	34.4
Insulin	116	65.5

Table.3 clarified that the majority of the patients with diabetes (69%) had type 2 diabetes (Table 3). Duration of diabetes extended from 3 months to 30 years with a mean duration of 8.8 years (±6.4). 36.9% and 35% of the patients with diabetes in our study had diabetes for 1 -5 years and 5 - 10 years, respectively. Among the diabetics involved in the study, 65.7% were on insulin and 34.3% were on oral anti-diabetic medications.

Table 4 Presentations, Complications and Outcome of COVID-19 among study participants (N = 400).

Factor	N	%
Symptoms		
Fever	343	85.8
Cough	320	80.0
Diarrhea	110	27.5
Headache	84	21.0
Vomiting	31	7.8
RR > 30	101	25.2
SpO_2< 93%	96	24.0
PaO_2< 300	4	1.0
Shock	11	2.8
Treatment		
Antibiotics	385	96.2
Steroids	302	75.5
Oxygen	236	59.0
Intubation	126	31.5
Complications		
Respiratory Failure	79	19.8
Shock	26	6.5
Organ Failure	44	11.0
Outcome		
Recovery	337	84.3
Death	63	15.8

Table 4 shows that most of the patients in our study had a fever (85.8%) and cough (80%). On the other hand, the least frequent presentations were PaO2 less than 300 mmHg (1%), shock (2.8%), and vomiting (7.8%), Most of the participants received: antibiotics (96.2%), dexamethasone steroids (75.5%), Oxygen (59%), and (31.5%) of them were intubated. The most frequent complication among the study participants was a respiratory failure (19.8%), followed by organ failure in (11%) of the study participants, and shock in (6.5%). The Majority (84.3%) of the study candidates made a full recovery.

Table 5 Comparison of severity of COVID-19 between patients with diabetes and non-patients with diabetes (N = 400).

Factor	Diabetic (%)	Non diabetic (%)	P. value
Symptoms			
Fever	88.1	84.2	0.332
Cough	82.4	78.5	0.397
Diarrhea	24.9	29.6	0.347
Headache	19.8	22.0	0.680
Vomiting	7.9	7.6	0.915
RR > 30	31.6	20.0	0.012
SpO_2< 93%	33.9	16.1	< 0.001
PaO_2< 300	1.7	0.4	0.326
Shock	5.6	0.4	0.004
Treatment			
Antibiotics	94.4	97.8	0.129
Steroids	81.4	70.9	0.021
Oxygen	72.9	48.0	< 0.001
Intubation	46.3	19.7	< 0.001
Complications			
Respiratory Failure	33.9	8.5	< 0.001
Shock	12.4	1.8	< 0.001
Organ Failure	20.9	3.1	<0.001
Outcome			
Recovery	75.7	91.0	< 0.001
Death	24.3	9.0	< 0.001

Table 5 shows no significant difference in the clinical presentation of diabetic or non-diabetic patients, this was proved using the Chi-square test and Fisher exact test in most of the tested variables except in having a respiratory rate more than 30 (P=0.012), in Oxygen saturation less than 93% (P<0.001) and shock (P=0.004), in which a statistically significant difference was found, the frequency of these signs was more in diabetic than in non.Chi-square test revealed a statistically significant difference between diabetic and non-diabetic patients in receiving steroids which were received more by non-diabetics (P=0.021), oxygen was received more by patients with diabetes (P<0.001) and intubation, being more frequently done for diabetics (P<0.001). Chi-square tests showed a statistically significant difference in complications between diabetics and non-diabetics. All COVID-19 complications were present more frequently among diabetics (P<0.001). Respiratory failure was present in 33.9% among them compared to 8.5% only among non-diabetics. Shock was present in 12.4% of diabetics and 1.8% of non-diabetics. Finally, Organ failure was present in 20.9% of patients with diabetes compared to 3.1% among non-diabetics. Significant differences in the outcome were found between diabetic and non-diabetics(P<0.001), with a higher death rate among diabetics (24.3%).

Table 6 Risk factors for the outcome of COVID-19 in the study population (N = 400).

Factor	Recovery	Death	P. value
Age			
18-40 years	99.1	0.9	
40-60 years	84.8	15.2	
60-80 years	73.8	26.2	< 0.001
>80 years	40.0	60.0	
Gender			
Male	82.9	17.1	0.361
Female	87.1	12.9	
Residency			
Urban	84.5	15.5	0.973
Rural	83.8	16.2	
Marital status			
Married	80.5	19.5	< 0.001
Single	96.7	3.3	
Type of DM			
Type 1	64.2	35.8	0.025
Type 2	81.4	18.6	
Smoking	77.9	22.1	0.128
Snuffing	85.3	14.7	0.861
Alcohol	72.7	27.3	0.390

Table 6 shows that no difference was found in the outcome between those who smoke, take snuff or drink alcohol and those who do not. Chi-square test revealed a significant difference when comparing the outcome and the type of DM with higher mortality rates in patients with type 1 DM (35.8%) compared to those who have type 2 diabetes (18.6%) (P=0.025).

5. DISCUSSION

To the best of our knowledge, this is the first study about the prevalence of diabetes among patients of COVID 19 in Sudan. A total of 400 COVID-19 patients were recruited from COVID-19 centers in the Northern States of Sudan. The prevalence of diabetes was found to be 49.3% of the participants, most of them had type II diabetes (69%). This result is comparable to that of a study conducted in Saudi Arabia where they found 45.3% of COVID-19 patients had DM[9]and higher than studies conducted in Italy and China where they found the prevalence of diabetes was 35.5% and 20% respectively[10,11]. Results from systematic reviews also showed lower frequencies of diabetes among COVID-19 patients ranging between 9.7% and 14.5%[12-14]. According to the World Health Organization (WHO), the prevalence of diabetes is increasing in low- and middle-income countries, and this explains why a higher percentage of COVID-19 patients in our study and the Saudi Arabia study in comparison to international studies[9,15]. Patients with diabetes in this study had a more severe COVID-19 infection. Diabetics were significantly more likely to have a respiratory rate higher than 30, oxygen saturation less than 93%, and were more likely to develop shock. There was also a significant association between having diabetes and requiring oxygen and intubation, suggesting a more severe form of COVID-19 is present among patients with diabetes. Furthermore, the complications of COVID-19 (respiratory failure and organ failure) were significantly more common among diabetics than in non-patients with diabetes. On the other hand, the diabetic COVID-19 patients had significantly higher mortality (24.3%) compared to non-patients with diabetes (9%). This finding is consistent with the findings of the previously conducted studies, where they showed that diabetes is a risk factor for developing severe COVID-19 infection, a higher risk for complications, and a higher risk of death[10,12,14,16]. Additionally, there was a statistically significant association between the type of diabetes and the outcome, type 1 diabetic COVID-19 patients had higher mortality (35.8%) compared to type 2 patients with diabetes (18.6%). This finding contradicts the finding of a previous study, where type 2 diabetes was associated with a poorer COVID-19

outcome[17]. COVID-19 seems to have a diabetogenic effect, in this study out of the 223 non-patients with diabetes, 20 (5%) developed diabetes and this is double of what was revealed in a study conducted in North Sudan where the prevalence of undiagnosed diabetes was found to be 2.6%[18], and this may indicate that COVID 19 has an effect on the prevalence of diabetes. On the other hand, the prevalence of diabetes was found to be 18.7% and 19.1% in two separate studies conducted in north Sudan[19,20]. The prevalence of DM was far high than the study conducted in AT "the same hospital" about the pattern of disease in which they found that the prevalence of DM among admitted patients was 6% which may also reflect the diabetogenicity of COVID-19[21]. Interestingly our study revealed a very high prevalence of diabetes among COVID 19 patients in North Sudan, so from the previous studies and our study the prevalence of DM is increasing rapidly and this may indicate the diabetogenicity of COVID 19. Furthermore, those with newly diagnosed diabetes had significantly higher mortality (25%) compared to non-patients with diabetes (8.9%). This finding is similar to the finding of a previous study, where new-onset diabetes was found to be associated with a poorer COVID-19 prognosis, the latter study also suggested that when compared to patients with pre-existing diabetes, patients with newly onset diabetes also have a worse outcome[22]. In this study 337 (84.3%) achieved full recovery and 63 (15.8%) died. The mortality rate is higher than that reported in other countries, as the case-fatality rate in the United States is 1.8% and 2.9% in the United Kingdom. However, it is comparable to that of neighboring countries, as in Yemen the rate is 19.8% and 7.2% in Syria[23]. The discrepancy in the mortality rate could be explained by the difference in the medical facilities available in a developed country (the United States or the United Kingdom) and a developing country such as Sudan. This poor outcome among patients with diabetes who acquire COVID-19 or those who develop diabetes during the COVID-19 infection could be explained by the abnormal immunity of patients with diabetes, as studies showed that diabetics have an abnormal phagocyte function, impaired T-cell mediated immunity, ineffective microbial clearance, and abnormal cytokines production, all of which could aid in the formation of the "cytokines storm" responsible for COVID-19 related complications and subsequently death[10,24,25]. An additional finding of this study is that age was found to be significantly associated with poor outcomes and the mortality increased with increasing age confirming the fact that COVID-19 is more lethal among the elderly population[13, 16, 17].

6. CONCLUSION

The study concluded that the prevalence of diabetes among Sudanese COVID-19 patients was very high, this was associated with more severe disease and a poorer outcome. The new-onset diabetes was associated with poorer outcomes compared to non-diabetics, diabetic patients were significantly more likely to develop respiratory and organ failure (COVID-19) seems to have a diabetogenic effect on patients as 5% of non-diabetic patients in this study develop diabetes after being infected with COVID-19, the mortality was relatively high at 15.8%.

7. LIMITATIONS

This study has limitations, as this study was a hospital-based study with a relatively small sample size when compared to the prevalence of the disease as the cross-sectional design does not allow for the determination of the temporal relationship between risk factors and outcome. This study may not be truly representative of all patients of COVID-19 and involve patients from isolation centers and not from home isolation, despite this limitation this study is novel and reflects the prevalence and risk factors associated with diabetes among COVID-19 patients.

8. AUTHORS CONTRIBUTION STATEMENT

All authors contributed to the study's conception and design. Material preparation and data collection were performed by Sufian Khalid, Khadeja Farah, Awadal kareem AA., Musa Kheir, Hisham Abdelrahim, Motwakil Awadelkareim, Ahmed ElSayed, and Mohamed Elamin. The analysis and final draft were done by Ali Alshehri, Hatim Natto, Tassnym Sinky, and Mohammed Salah. The first draft of the manuscript was written by Ahmed Osman and Mohamed Elamin. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

9. ACKNOWLEDGMENT

We would like to thank all those who facilitate this study.

10. ABBREVIATIONS

ACE2 Angiotensin-Converting Enzyme 2, COVID-19 Coronavirus infection disease 2019, CVD Cardiovascular Disease, Diabetes Mellitus (DM), FBS Fasting Blood Sugar, H1N1 Influenza A, HbA1c Glycosylated Hemoglobin, HTN Hypertension, MERS-COV Middle East Respiratory Syndrome Coronavirus, PCR Polymerase Chain Reaction, RBS Random Blood Sugar, SARS-CoV-2, 2HPP 2 Hours Postprandial Glucose level.

11. CONFLICT OF INTEREST

The authors declared no conflict of interest.

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