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ORIGINAL ARTICLE

Association of Diabetes Mellitus with Coronavirus Disease 2019 Severity: A Retrospective Study from a Center in South-Western Nigeria

Association du Diabète Sucré Avec la Gravité de la Maladie à Coronavirus 2019 : Une Étude Rétrospective d'un Centre du Sud-Ouest du Nigeria

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ABSTRACT

BACKGROUND AND OBJECTIVES: Coronavirus Disease 2019 (COVID-19) is a novel viral infection, now a pandemic, caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Diabetes mellitus (DM) has been associated with severe COVID-19 and poor glycaemic control is reportedly the link between these conditions. This study aimed to determine the association between DM and the severity of COVID-19.

METHODS: This was a retrospective study involving 86 patients with COVID-19 admitted to a tertiary hospital in South-Western Nigeria. Socio-demographic, clinical and laboratory data were extracted from their medical records. Ethical approval was obtained and descriptive and inferential statistics computed.

RESULTS: The mean age of the patients was 61 ± 16.1 years and 61.6% were males. Fever was noted in 67.4% of patients and, similarly, 67.4% of the patients had an SpO_2<94% in ambient air when admitted. Thirty-six percent (36%) of the study patients had DM. Amongst patients with DM and those without DM, 72.2% and 62%, respectively, had severe or critical COVID-19 (p=0.323). Patients with DM were older than those without DM (65.8 years vs 57.3 years; p=0.015). The frequency of oxygen desaturation, respiratory failure, acute kidney injury (AKI) and multi-organ failure were significantly higher in COVID-19 patients with DM (p=0.037, 0.043, 0.004 and 0.016, respectively). Mortality was higher in COVID-19 patients with DM but this was not statistically significant (p=0.214). The odds of a patient with diabetes and COVID-19 developing respiratory failure and acute kidney injury were 1.395 (95%CI 1.154–6.913) and 1.125 (95%CI 1.025–1.621), respectively.

CONCLUSION: Diabetes mellitus was recorded in older patients with COVID-19 and associated with suboptimal oxygen saturation at presentation, respiratory failure, and acute kidney injury. There was no association found between DM and COVID-19 severity and mortality. **WAJM 2022; 39(10): 1007–1012.**

Keywords: COVID-19; Diabetes Mellitus; SARS- CoV-2.

RÉSUMÉ

CONTEXTE ET OBJECTIFS: La maladie de coronavirus 2019 (COVID-19) est une nouvelle infection virale, aujourd'hui pandémique, causée par le coronavirus-2 du syndrome respiratoire aigu sévère (SARS-CoV-2). Le diabète sucré (DM) a été associé à une COVID-19 sévère et un mauvais contrôle glycémique serait le lien entre ces deux pathologies. Cette étude vise à déterminer l'association entre le DM et la sévérité du COVID-19.

MÉTHODES: Il s'agit d'une étude rétrospective portant sur 86 patients atteints de COVID-19 admis dans un hôpital tertiaire du sud-ouest du Nigeria. Les données sociodémographiques, cliniques et de laboratoire ont été extraites de leurs dossiers médicaux. Une approbation éthique a été obtenue et des statistiques descriptives et inférentielles ont été calculées.

RÉSULTATS: L'âge moyen des patients était de 61 ± 16,1 ans et 61,6% étaient des hommes. De la fièvre a été notée chez 67,4 % des patients et de même, 67,4 % des patients avaient une SpO2<94 % à l'air ambiant lors de leur admission. Trente-six pour cent (36 %) des patients de l'étude étaient atteints de diabète. Parmi les patients atteints de DM et ceux qui ne l'étaient pas, 72,2 % et 62 % respectivement présentaient un COVID-19 sévère ou critique (p=0,323). Les patients atteints de DM étaient plus âgés que ceux sans DM (65,8 vs 57,3 ; p=0,015). La fréquence de la désaturation en oxygène, de l'insuffisance respiratoire, de l'insuffisance rénale aiguë (IRA) et de la défaillance multi-organique était significativement plus élevée chez les patients atteints de diabète de type 1 (p=0,037, 0,043, 0,004 et 0,016 respectivement). La mortalité était plus élevée chez les patients diabétiques de COVID-19, mais cela n'était pas statistiquement significatif (p=0,214). Les probabilités qu'un patient diabétique et COVID-19 développe une insuffisance respiratoire et une lésion rénale aiguë étaient de 1,395 (95%CI 1,154-6,913) et 1,125 (95%CI 1,025-1,621).

CONCLUSION: Le diabète sucré a été enregistré chez les patients âgés atteints de COVID-19 et associé à une saturation en oxygène sous-optimale à la présentation, à une insuffisance respiratoire et à des lésions rénales aiguës. Aucune association n'a été trouvée entre le DM et la sévérité du COVID-19 et la mortalité. **WAJM 2022; 39(10): 1007–1012.**

Mots clés: COVID-19 ; Diabète Mellitus ; SRAS- CoV-2.

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INTRODUCTION

COVID-19 is a viral infection caused by the RNA virus SARS-CoV-2.[1] COVID-19 was first reported from Wuhan in Hubei Province, China.[2,3] SARS-CoV-2 was named by the International Committee on the Taxonomy of Viruses while the World Health Organization (WHO) gave the name COVID-19 to the disease it causes.[4] In March 2020, WHO declared COVID-19 a pandemic and it has been reported from all the continents.[5,6] COVID-19 can present clinically in diverse ways but the common clinical features are fever, dry cough, sore throat, breathlessness, abdominal symptoms and generalized body aches.[7] A study done in Nigeria reported that 16% of hospitalized COVID-19 cases were asymptomatic and 75% presented with mild to moderate illness.[8] At the time of writing this article, approximately 255 000 individuals in Nigeria had been diagnosed with COVID-19 with the highest incidence in the south-west region of the country.[9] Another study from northern Nigeria quoted an in-hospital mortality rate of 16%.[10]

It is important to assess the severity of COVID-19 because it determines therapeutic and proactive measures at individual level; it enables efficient planning at health-facility level, and it shapes policy at the government level.[11] There are some factors that have been documented to be associated with severe COVID-19. These factors include advancing age, male gender and the presence of co-morbidities such as diabetes, hypertension, obesity, immunosuppressive illnesses and cardiovascular disease.[12] Some of the laboratory markers of severe COVID-19 include leukocytosis, lymphopenia, elevated C-reactive protein (CRP), raised serum ferritin levels, elevated D-dimer and procalcitonin.[13]

DM is a heterogeneous group of metabolic disorders characterized by chronic hyperglycaemia due to a defect in insulin secretion, action or a variable mixture of both.[14] Just like COVID-19, diabetes has also been declared as a pandemic.[15] Over 400 million people are living with diabetes worldwide and the number keeps increasing.[16] The estimated prevalence of diabetes in Nigeria in 2018 was 5.8%.[17]

Generally, poorly controlled DM is associated with increased occurrence and severity of infectious diseases.[18] This is as a result of impaired neutrophil function, reduced T lymphocyte response, disordered B lymphocyte function and impaired complement action.[18] The infectious processes can affect any organ or system in the body. Interestingly, infectious diseases can also precipitate metabolic complications in patients with diabetes or may be the pointer to the presence of previously undiagnosed diabetes.

Several studies, done in different parts of the world have reported the deleterious effect of DM on COVID-19 prognosis.[19–22] Poor glycaemic control among patients with DM has been associated with an increased risk of contracting COVID-19 and having worse outcomes.[23,24] The presence of DM in patients with COVID-19 is associated with poor prognostic markers such as lymphopenia, elevated D-dimer, lactate dehydrogenase and alanine transaminase as well as ICU admission and development of AKI.[22] Managing patients with both DM and COVID-19 is a major challenge in low resource settings like Nigeria.[25]

Primary Objectives

To determine the association between diabetes mellitus and COVID-19 among patients seen at a tertiary hospital in South-western Nigeria.

Secondary Objectives of the Study

1. To determine the frequency of diabetes mellitus among patients with severe and critical COVID-19 seen at a tertiary hospital in South-western Nigeria.
2. To assess the association between the presence of diabetes and markers of severity in COVID-19 patients.

METHODS

Study Design

This was a retrospective study amongst patients with COVID-19 admitted at a single facility between March and November, 2020.

Study Subjects and Study Location

The study location was the University College Hospital (UCH), Ibadan, Nigeria. University College Hospital, Ibadan is a tertiary hospital and a major referral centre for patients within South-Western Nigeria and sometimes beyond. It has an infectious disease treatment centre with a capacity of 4 beds at the time this study was conducted where patients with confirmed COVID-19 were managed. It also has a ward for suspected COVID-19 cases with a capacity of 8 bed spaces where patients awaiting their COVID-19 results were managed.

All patients were screened for diabetes mellitus during admission and DM was diagnosed according to the WHO guideline for persons not previously known with DM: fasting plasma glucose $\geq$126mg/dl or random plasma glucose $\geq$200mg/dl.[26] Others already diagnosed with DM prior to the time of admission were also considered as having DM.

Inclusion Criteria

All suspected patients had naso-pharyngeal and/or oropharyngeal swabs taken following the standard protocols. SARS-CoV-2 was tested in each sample using the reverse transcription polymerase chain reaction (RT-PCR) at the government-designated standard laboratories following the Nigerian Center for Disease Control (NCDC) guidelines for testing. Those who tested positive for SARS-CoV-2 and were admitted for in-patient care were recruited into the study.

Exclusion Criteria

1. Patients who were screened negative for COVID-19 were excluded from the study.
2. Patients who were screened positive but did not require inpatient care.

Definition of Terms

Altered consciousness – Glasgow coma scale less than 15

Desaturation on ambient air – SpO_2 less than 94%

Fever – Axillary temperature above 37.5°C

Hypotension – Mean arterial Pressure <65mmHg.

Tachypnoea – Respiratory rate greater than 20 breaths per minute.

Poor glycaemic control – Glycated Haemoglobin (HbA1c) of 7% and above.

Acute kidney injury – Elevated urea and creatinine or reduction in urinary output.

Quick severe organ failure assessment (QSOFA) score – One point each is awarded for any of the following: GCS <15, heart rate >100 and respiratory rate >22. A score of 2 and above suggests greater morbidity.

Data Acquisition

Data were obtained from the medical records of 86 patients. All patients with available data were recruited for the study. Data were extracted from the case notes using a data collection form designed by the investigators. These included sociodemographic data, contact history, symptoms, background co-morbidities like diabetes, hypertension, drug history, vital signs on admission and oxygen saturation (SPO_2) using a pulse oximeter. Other data retrieved included laboratory investigation results, details of treatment and duration of stay. Details of complications such as respiratory failure, shock, acute kidney injury, liver failure, intracranial haemorrhage and multi-organ failure were also retrieved. Classification of COVID-19 severity was also extracted using the WHO classification for severe acute respiratory infection.[27] Quick sequential organ failure assessment (QSOFA) score was also computed. QSOFA score is a quick bed side tool used to identify critically ill patients with sepsis which has also been used in other diseases.

Data Analysis

Categorical variables were presented as frequencies and percentages. Continuous variables were presented as mean ± standard deviation if uniformly distributed or as median with interquartile range if not uniformly distributed. Descriptive and inferential statistics were done using the Statistical Package for the Social Sciences (SPSS) version 22.

Ethical Consideration

Ethical approval for the study was obtained from the joint University College Hospital and University of Ibadan Institutional Review Board (Approval number: UI/EC/20/410). All the data were coded anonymously and handled only by authorized individuals to respect the confidentiality of the patients.

RESULTS

The mean age was 60.9 ± 16.1 years with a higher number of men than women. The age range was 20 to 86 years. Majority of the recruited subjects resided in South-western Nigeria. Most of the participants were married and about 60% had tertiary education. The average HbA1c was 8.6% amongst persons with diabetes mellitus (not shown in table). Other socio-demographic data of the participants are shown in Table 1.

Figure 1 shows the frequency (%) of diabetes and other co-morbidities in patients with COVID-19 in this study. The frequency of diabetes was 36% and hypertension was the commonest (54%) background co-morbidity among COVID-19 patients in this study.

Table 2 shows the vital signs of the patients at presentation. Tachypnoea was found in almost all (96.5%) the patients while fever and desaturation on ambient air were each found in about two-thirds (67.4%) of the patients.

Severe or critical disease was found in 66.3% of patients and mortality was recorded in 47.7% of patients. Other markers of severity/outcomes are shown in Table 3.

Table 1: Sociodemographic Data

Variable (n=86)	Frequency (n=86)	Percentage (%)
Age (mean ± sd) = 60.9 ± 16.1 years		
Gender		
Male	53	61.6%
Female	33	38.4%
Marital Status		
Married	72	83.7%
Single	3	3.5%
Widowed	7	8.1%
Divorced	4	4.7%
Educational Status		
Secondary or less	32	32.7
Tertiary	54	67.8

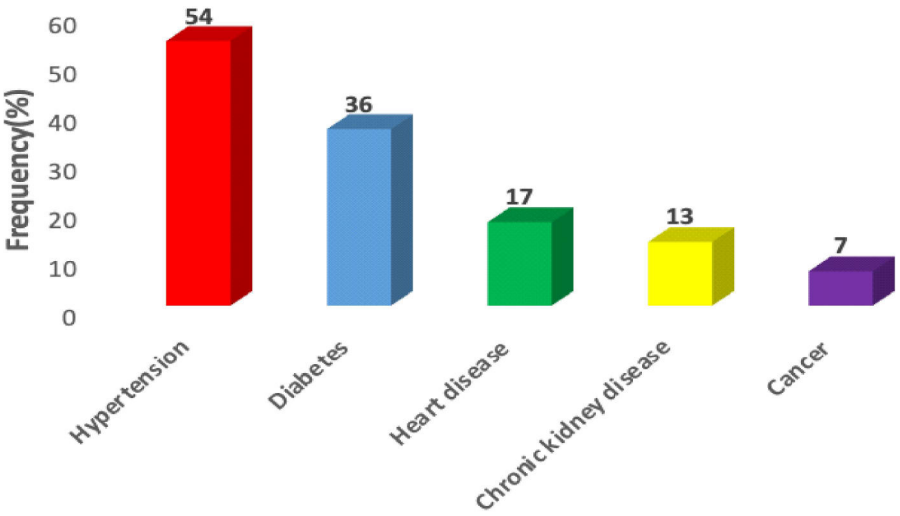

Fig. 1: Frequency of Diabetes and other Co-Morbidities

Table 2: Vital Signs at Time of Presentation

Variable	Frequency (n=86)	Percentage (%)
Tachypnoea	83	96.5
Fever	58	67.4
Desaturation in ambient air	58	67.4
Altered consciousness	23	26.7
Hypotension	8	9.3

Table 3: Markers of Severity/Outcome

Variable	Frequency (n=86)	Percentage (%)
WHO Classification of Severity		
Mild	6	7.0
Moderate	23	26.7
Severe	51	59.3
Critical	6	7.0
QSOFA* Score		
0	3	3.5
1	54	62.8
2	24	27.9
3	5	5.8
Respiratory Failure	26	30.2
Septic shock	7	8.1
Acute kidney injury	11	12.8
ICU admission	5	5.8
Multi-organ failure	4	4.7
Final Outcome		
Discharged	37	43.0
Dead	41	47.7
Transferred out	8	9.3

QSOFA, Quick Severe Organ Failure Assessment.

Table 4 below shows that patients with diabetes were significantly older than those without diabetes (65.8 years vs 57.3 years; p=0.015). Also, the frequency of oxygen desaturation at time of presentation, respiratory failure, acute kidney injury and multi-organ failure was significantly higher in COVID-19 patients with diabetes (p=0.037, 0.043, 0.004 and 0.016 respectively) compared with those without diabetes. Mortality was higher in COVID-19 patients with diabetes (55.6% vs 42%; p=0.214) compared with those without diabetes but this did not attain statistical significance. Severe or critical COVID-19 was reported in 72% of patients with diabetes compared with 62% in patients without diabetes (p=0.323).

Table 4: Impact of Diabetes on COVID-19

Variable		Diabetes		Test statistic	p-value
		Yes	No		
Mean age (years)		65.8	57.3	t= 2.48	0.015**
Gender	Male (%)	63.9	60.0	$\chi^2 = 0.134$	0.714
	Female (%)	36.1	40.0		
Tachypnoea at presentation (%)		97.2	96.0	$\chi^2 = 0.093$	0.761
Hypotension at presentation (%)		8.3	8.3	$\chi^2 = 0.000$	1.000
Fever at presentation (%)		68.6	66.0	$\chi^2 = 0.062$	0.804
Desaturation at presentation (%)		26.0	11.1	$\chi^2 = 2.925$	0.037**
Altered consciousness (%)		24.0	38.0	$\chi^2 = 1.264$	0.264
Severe and critical COVID-19 (%)		72.2	62	$\chi^2 = 0.979$	0.323
Respiratory failure (%)		41.7	22.0	$\chi^2 = 3.838$	0.043*
Septic shock (%)		11.1	6.0	$\chi^2 = 0.731$	0.392
Acute kidney injury (%)		25.0	4.0	$\chi^2 = 8.275$	0.004*
Multi-organ failure (%)		11.1	1.1	$\chi^2 = 5.287$	0.016*
ICU admission (%)		3.8	8.0	$\chi^2 = 1.042$	0.307
Mortality (%)		55.6	42.0	$\chi^2 = 1.542$	0.214

**, Statistically significant*

DISCUSSION

The average age of the patients in this study was about 61 years. Several studies on COVID-19 have also documented similar age profile in their cohorts.[28–30] It has been documented that advancing age is an independent risk factor for contracting the virus causing COVID-19 and developing a severe illness.[7] Moreover, comorbid conditions that predispose to severe COVID-19 increase in prevalence as age advances.[31] More males presented with COVID-19 in this study than females and other studies have also reported similar gender disparity in their cohorts.[8,29,32] The proposed reasons for this male preponderance include increased frequency of risk factors for COVID-19 such as diabetes and hypertension among men and the likelihood that men have lifestyle and social habits that could predispose them to acquiring the infection.[33] Also, the finding of higher tissue Angiotensin Converting Enzyme 2 (ACE 2) receptor (to which COVID-19 binds) expression and higher plasma levels of ACE 2 in men than women has been alluded to as a reason for the male preponderance of the disease.[34] Hormonal differences as well as differences between the sexes in immune responses to infection have also been postulated.[34]

The frequency of diabetes in COVID-19 patients in this study was 36%. A study done in China quoted 32% as

the frequency of diabetes among COVID-19 patients in the study, which is similar to the finding of this present study.[35] Poor glycaemic control has been reported to be the main link between diabetes and increased susceptibility and severity of COVID-19.[23,32] Findings from our study are in keeping with this hypothesis; we found an average glycated haemoglobin of 8.6% among patients with diabetes which suggests background poor glycaemic control. The patients with diabetes were significantly older (mean age 66 years) compared with those without diabetes (mean age 57 years). Generally, the incidence of type 2 diabetes increases with age and this may explain this disparity.[16] A case report on diabetes and COVID-19 from Northern Nigeria also highlighted undiagnosed diabetes in persons with COVID-19.[24]

Our study found that patients with COVID-19 and diabetes were more likely to present with oxygen desaturation (using pulse oximetry) compared with those without diabetes. Similar findings have been reported by other researchers.[19,20] Similarly, COVID-19 patients with diabetes were found to have a significantly higher incidence of respiratory failure compared with those without diabetes, in the present study. This is in keeping with what other researchers have reported.[19,20] It has been reported that there is a high concentration of aberrantly glycated angiotensin converting enzyme (ACE) in the lung parenchyma of patients with poorly controlled diabetes which is unable to bind to ACE receptors in the lungs.[33] Coincidentally, the virus, SARS-CoV-2, also requires ACE receptors to gain entry into the cells. Therefore, given the lack of binding by the aberrantly glycated ACE, the ACE receptors are available to the virus to bind and enter the cells causing inflammation in the lungs which may progress to respiratory failure.

In addition, there was a significantly higher frequency of acute kidney injury (AKI) among COVID-19 patients with diabetes compared with those without diabetes. Abdi, *et al* also reported a higher frequency of AKI among COVID-19 patients with diabetes compared with those without diabetes.[36] Hyper-glycaemia has been documented to cause glomerular endothelial dysfunction which is thought to be responsible for the increased incidence of AKI among hospitalized patients with diabetes.[37]

Moreover, diabetes was also associated with a significantly higher frequency of multi-organ failure among COVID-19 patients when compared with patients without diabetes. Similar findings have been reported by previous researchers on COVID-19.[19,20] Mortality was also observed to be higher in COVID-19 with diabetes compared with those who did not have diabetes, although the difference did not attain statistical significance. Poor glycaemic control, which was also documented in this study, might be responsible in part for these observations among COVID-19 patients with diabetes.[22,32]

Limitations

Our study had some limitations. It was a single center study which may affect the generalizability of the findings. A larger sample size may be needed to show statistical significance for some associations. The retrospective nature of data collection might have had some effect on the quality of the available data given that records are kept in paper form rather than electronically. There were also missing data given non-standardized methods of clinical documentation in paper records.

CONCLUSION

COVID-19 patients with diabetes mellitus hospitalized at a tertiary health facility in South-Western Nigeria had poor glycaemic control and prominent markers of severity such as desaturation on ambient air at presentation, respiratory failure and acute kidney injury. However, diabetes mellitus was not found to be significantly associated with presence of severe or critical COVID-19 or mortality.

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Duality of Interest

All authors hereby state that they have no conflict of interest to declare.

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