Al-Azhar International Medical Journal

Volume 5 | Issue 1 Article 36

2024
Section: Internal Medicine

Characteristics of patients newly diagnosed with diabetes mellitus after Coronavirus disease-19 (COVID-19)

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How to Cite This Article

Mohamed Aly, Alboraie; Mohamed Rabie, Megahed; Ahmed Mohamed, Abohasan; Mahmoud Ezzat, Abdelraouf; and Gamal Aly, Badr (2024) "Characteristics of patients newly diagnosed with diabetes mellitus after Coronavirus disease-19 (COVID-19)," *Al-Azhar International Medical Journal*: Vol. 5: Iss. 1, Article 36.
DOI: https://doi.org/10.58675/2682-339X.2222

ORIGINAL ARTICLE

Characteristics of Patients Newly Diagnosed with Diabetes Mellitus After Coronavirus Disease 2019

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Abstract

Background: **At this moment, there is a greater than ever level of concern over the 2019 [coronavirus disease 2019 (COVID-19)] coronavirus illness pandemic and its related morbidities.**

Aim and objectives: **Case series with the systematic review of the frequency of newly diagnosed diabetes mellitus among COVID-19 patients, its varied symptoms, and glycemic control in diabetic patients.**

Patients and methodology: **Hundred patients altogether were split into two groups for this cross-sectional study. Every examination is done at the time of diagnosis and 2 months afterwards. They were evacuated from Al-Hussein University Hospital between January and July 2022.**

Results: **Our findings showed that the hemoglobin A1C levels 2 months after diagnosis and the hemoglobin A1C levels had statistically significant differences (at diagnosis). Fasting glucose, C-reactive protein, D-dimer, and random blood glucose measurements were higher upon diagnosis than 2 months after release. People who had steroid treatment had greater random blood glucose levels than those who did not.**

Conclusion: **Patients with more serious diseases were more likely to have newly diagnosed diabetes or have its symptoms during their illness, while COVID-19 patients were more likely to do so.**

Keywords: COVID-19, New-onset DM, Severe infection, Mortality

1. Introduction

There is an inverse association between coronavirus disease 2019 (COVID-19) and type 2 diabetes. However, severe COVID-19 development is more likely when hyperglycemia is present.[1]

These tough diabetic symptoms reveal a complex etiology for diabetes associated with COVID-19. The common flu coronavirus, COVID-19, which causes severe acute respiratory illness, attaches to ACE2 receptors in essential metabolic tissues and organs like the small intestine, adipose tissue, the kidneys, and pancreatic beta cells.[2]

COVID-19 illness, on the other hand, has been related to serious metabolic disorders, including hyperosmolarity and diabetic ketoacidosis, which need exceedingly high insulin dosages. SARS-potential CoV-2 can cause pleiotropic abnormalities in glucose metabolism, which may aggravate the pathophysiology of existing diabetes and give birth to new disease processes. Diabetes with a high risk of ketoacidosis has been induced by viruses in the past, and various coronaviruses are examples of these viruses. Fasting glycemia and acute hyperglycemia were more common in SARS coronavirus 1 pneumonia patients compared to those with other kinds of pneumonia.[3]

So, the aim of this study as a case series with the systematic review of the frequency of newly diagnosed diabetes mellitus (DM) among COVID-19 patients, its varied symptoms, and glycemic control in diabetic patients.

Accepted 2 September 2023.
Available online 8 April 2024

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https://doi.org/10.58675/2682-339X.2222

2. Patients and methods

Patients who tested positive for COVID-19 are included in this cross-sectional study. From January 2022 to July 2022, they were gathered at Al-Hussein University Hospital's clinics. Ethics Committee regulations established by Al-Azhar University must be adhered to at all times. Before any information is gathered or treatments are carried out, each patient must sign a permission form. Genuine diversity requires that people of both sexes feel welcome. Diabetic patients who statistically and clinically fulfill the COVID-19 profile are considered to have hyperglycemia. We excluded patients who had diabetes or who did not meet the COVID-19 criteria.

A thorough systemic evaluation is performed on each patient, including a review of their medical history and physical examination. The BMI is one statistic used in anthropology. Glycated hemoglobin, random glucose, fasting C-peptide, alanine aminotransferase, aspartate aminotransferase, albumin, total protein, amylase, serum creatinine, fibrinogen, and D-dimer are some signs that may be examined while a person is fasting. Low-density lipoprotein (bad) cholesterol, triglyceride, and total cholesterol values. At the time of diagnosis and again 2 months later, the patient's total blood count, C-reactive protein (CRP), and COVID-19 RNA were all examined. These included neutrophil–lymphocyte ratio, lymphocyte–monocyte ratio, white blood cell count, hemoglobin, red blood cells, platelets, and white blood cells.

All participants were subjected to the following battery of tests upon arrival: the absolute blood count of a patient is calculated using a Sysmex XN-2000 autoanalyzer (Siemens Diagnostic, Erlangen, Germany). Biochemical blood tests, including glucose, hemoglobin A1C (HbA1C), CRP, albumin, aminotransferases (alanine aminotransferase, aspartate aminotransferase), creatinine, and D-dimer were analyzed using Cobas c702/8000 (Roche Diagnostic, Mannheim, Germany) analyzers (Roche Diagnostic). Ferritin, fasting insulin, and C-peptide levels in the serum of people with diabetes were analyzed using a Cobas c602/8000 (Roche Diagnostic). Reverse transcription-PCR was used to test nasal and pharyngeal swabs to confirm the COVID-19 diagnosis.

Based on fasting plasma glucose readings of 126 or 200 mg/dl, random blood glucose, and HbA1C readings of 6.5% or HbA1C (6.5% alone), the American Diabetes Association divided patients into newly diagnosed (no history of DM) and previously undiagnosed groups.

3. Results

3.1. Statistical analysis

Social Science Statistical Software, version 24 was used to conduct the analyses (SPSS). Data were analyzed using Statistical Program for Social Science (SPSS) version 24 (Cairo, Egypt). Quantitative data were shown using mean ± SD. Quantitative information was represented by frequency and proportion. A group of discrete numbers' average value is the sum of their values divided by the total number of values in the group. The dispersion of a set of numbers is quantified by its SD. A small SD indicates that the values cluster close to the mean, whereas a large one indicates that they are spread across a wide range.

The following tests were done: use the Mann–Whitney *U* test to compare means (for abnormally distributed data). Probability levels below 0.05 were regarded to be meaningful. The significance level set with a *P* value of 0.001 was high. *P* values higher than 0.05 were deemed statistically insignificant.

Each patient under investigation's age and sex are included in Table 1. All of the patients that were looked into ranged in age from 24 to 96, with an average age of 53.3. The research included 65 male patients and 35 female patients regarding their sex. The overall study participants' average BMI was 29.8 kg/m^2, with a minimum and highest BMI of 20.4 and 42.3 kg/m^2, respectively.

Table 2 shows significant ($P = 0.026$) in the statistical sense. Two months after diagnosis, the HbA1C was higher than it had been at diagnosis (5.4 ± 0.5%) (5.6 ± 05%). At the time of diagnosis, fasting glucose was considerably higher than it had been 2 months before ($P = 0.001$) (117.5 ± 29.6).

A substantial ($P = 0.001$) increase in blood glucose levels was seen at the time of diagnosis (305.9 ± 74.5 mg/dl) and 2 months later (170.7 ± 62.0 mg/dl).

At the time of diagnosis or 2 months later, the difference between fasting C-peptide and fasting insulin was not statistically significant.

Table 1. Sex and age breakdown of all participants.

	Studied patients ($N = 100$)	
Sex		
Male	65	65%
Female	35	35%
Age (years)		
Mean ± SD	53.3 ± 16.4	
Minimum–maximum	24–96	
BMI (kg/m^2)		
Mean ± SD	29.8 ± 5.3	
Minimum–maximum	20.4–42.3	

Table 2. Comparison of blood glucose assessment at diagnosis and after 2 months in all studied patients.

	At diagnosis ($N = 100$)	After 2 months ($N = 91$)	MW	P value
HbA1C (%)				
Mean ± SD	5.4 ± 0.5	5.6 ± 0.5	3705.5	0.026 S
Fasting insulin				
Mean ± SD	11.3 ± 5.7	10.5 ± 5.5	4229	0.4
Fasting glucose				
Mean ± SD	168.4 ± 23.9	117.5 ± 29.6	885	<0.001 HS
Random blood glucose				
Mean ± SD	305.9 ± 74.5	170.7 ± 62.0	647	<0.001 HS
Fasting C-peptide				
Mean ± SD	2.6 ± 0.8	2.5 ± 0.8	4150	0.293

HbA1C, hemoglobin A1C; MW, Mann–Whitney U test.
P values under 0.05 are regarded as significant (S). P values below 0.001 are regarded as highly significant (HS); P values above 0.05 are regarded as nonsignificant (NS).

Table 3 tells us: very significant statistically ($P = 0.001$). When compared to red blood cells upon diagnosis (5.6 ± 0.5), red blood cells at 2 months were lower (4.9 ± 0.4).

When compared to white blood cells (at diagnosis) (4.4 ± 1.3), white blood cells increased at 2 months in a manner that was highly statistically significant ($P = 0.001$) (6.3 ± 1.5).

LMR, NLR, Hb, and platelets did not statistically alter between the two times of diagnosis ($P > 0.05$).

Table 4 shows: aspartate aminotransferase (after 2 months) was statistically significant ($P = 0.008$) compared to aspartate aminotransferase (at diagnosis) (38.8 ± 9.4). The difference was 42.5 ± 8.0.

There was no statistically significant change between alanine aminotransferase, albumin, total protein, and creatinine at diagnosis and after 2 months (P<(0.05.

Table 3. Comparison of complete blood count at diagnosis and after 2 months in all studied patients.

	At discharge ($N = 100$)	2 months after discharge ($N = 91$)	MW	P value
RBCs				
Mean ± SD	5.6 ± 0.5	4.9 ± 0.4	1327.5	<0.001 HS
WBCs				
Mean ± SD	4.4 ± 1.3	6.3 ± 1.5	1249	<0.001 HS
LMR				
Mean ± SD	2.9 ± 0.4	2.9 ± 0.4	4328	0.929 NS
NLR				
Mean ± SD	2.9 ± 1.4	2.9 ± 1.4	4502	0.9 NS
Hb				
Mean ± SD	11.8 ± 1.7	11.6 ± 1.7	3798.5	0.165 NS
PLTs				
Mean ± SD	245.3 ± 84.2	256.4 ± 84.5	4151	0.296 NS

Hb, hemoglobin; MW, Mann–Whitney U test; PLT, platelet; RBC, red blood cell; WBC, white blood cell.
P values under 0.05 are regarded as significant (S). P values below 0.001 are regarded as highly significant (HS). P values above 0.05 are regarded as nonsignificant (NS).

Table 4. Comparison of liver and kidney function tests at diagnosis and after 2 months in all studied patients.

	At diagnosis ($N = 100$)	After 2 months ($N = 91$)	MW	P value
AST				
Mean ± SD	38.8 ± 9.4	42.5 ± 8.0	3538	0.008 S
ALT				
Mean ± SD	8.8 ± 11.2	9.2 ± 11.2	4396.5	0.686 NS
ALB				
Mean ± SD	4.02 ± 0.50	4.04 ± 0.51	4463.5	0.820 NS
TP				
Mean ± SD	7.4 ± 0.6	7.3 ± 0.7	4437	0.767 NS
Creat				
Mean ± SD	0.96 ± 0.24	0.96 ± 0.23	4403.5	0.7 NS

ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Creat, creatinine; MW, Mann–Whitney U test; TP, total protein.
P value less than 0.05 is considered significant (S). P value less than 0.05 is considered nonsignificant (NS).

Table 5. Comparison of other studied laboratory data at diagnosis and after 2 months in all studied patients.

	At diagnosis ($N = 100$)	After 2 months ($N = 91$)	MW	P value
D-dimer				
Mean ± SD	1.1 ± 0.6	0.6 ± 0.4	2331.5	<0.001 HS
Fibrinogen				
Mean ± SD	259.8 ± 44.6	262.0 ± 45.1	4404.5	0.703 NS
Amylase				
Mean ± SD	53.5 ± 20.7	54.0 ± 20.9	4475	0.844 NS
CRP				
Mean ± SD	29.8 ± 18.7	12.5 ± 5.7	1611.5	<0.001 HS

CRP, C-reactive protein; MW, Mann–Whitney U test.
P value less than 0.001 is considered highly significant (HS). P value less than 0.05 is considered nonsignificant (NS).

Table 5 shows when compared to the D-dimer (at diagnosis), the difference between the 2-month D-dimer levels (0.6 ± 0.4) was highly statistically significant (1.1 ± 0.6; $P = 0.001$). When compared to

Table 6. Relation between steroid intake and blood glucose level assessment at after 2 months.

	Steroid intake		MW	P value
	No ($N = 29$)	Yes ($N = 62$)		
HbA1C (%)				
Mean ± SD	5.42 ± 0.46	5.61 ± 0.49	690	0.074 NS
Fasting insulin				
Mean ± SD	10.3 ± 5.6	10.6 ± 5.5	870.5	0.808 NS
Fasting glucose				
Mean ± SD	107.0 ± 11.1	122.5 ± 34.1	731	0.152 NS
Random blood glucose				
Mean ± SD	145.3 ± 18.5	182.5 ± 71.1	612	0.014 S

HbA1C, hemoglobin A1C; MW, Mann–Whitney U test.
A P value of 0.05 or less is regarded as insignificant (S). P values above 0.05 are regarded as nonsignificant (NS).

CRP (at diagnosis), CRP (after 2 months) (12.5 ± 5.7) shown a very statistically significant ($P = 0.001$) decline (29.8 ± 18.7).

There was no statistical difference between fibrinogen and amylase at the time of the diagnosis and 2 months later ($P > 0.05$; Table 6).

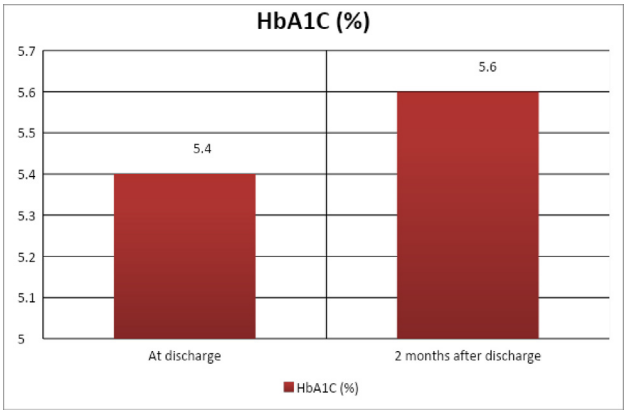

Fig. 1. Comparison of HbA1C at diagnosis and after 2 months in all studied patients. HbA1C, hemoglobin A1C.

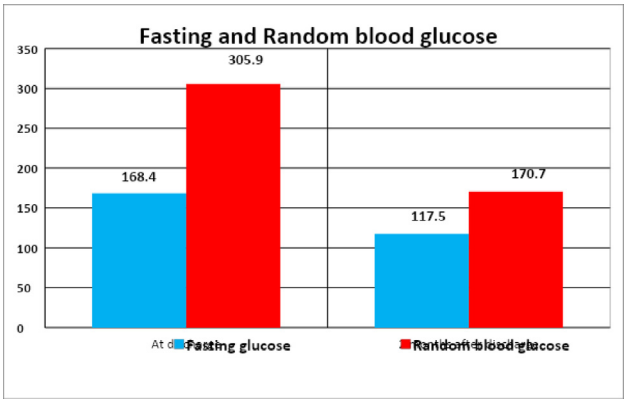

Fig. 2. Comparison of fasting ad random blood glucose at diagnosis and after 2 months in all studied patients.

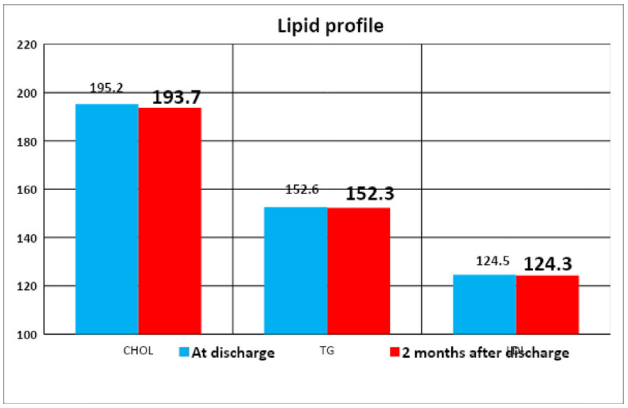

Fig. 3. Comparison of lipid profile at diagnosis and after 2 months in all studied patients.

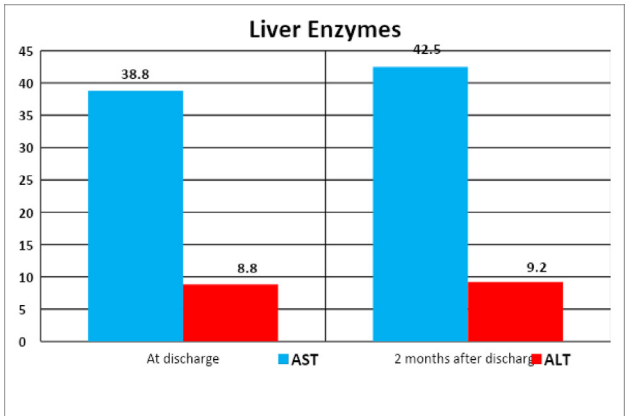

Fig. 4. Comparison of liver enzymes at diagnosis and after 2 months in all studied patients.

At 2 months after diagnosis: when compared to patients who did not get steroid medication, there was a statistically significant ($P = 0.014$) rise in RBS in the steroid therapy group (182.5 ± 71.1 vs. 145.3 ± 18.5).

There is no statistically significant link between steroid use and (HbA1C, fasting insulin, and fasting glucose; Figs. 1–4).

4. Discussion

It is possible that the link between diabetes and COVID-19 is because of the influence that SARS-CoV-2 infection has on organs that contribute to the development of diabetes. Direct targeting of angiotensin-converting enzyme 2 receptor-expressing pancreatic cells, stress hyperglycemia is brought on by a cytokine storm, and alterations to glucose metabolism are brought on by infection, and progression from prediabetes to diabetes are all possible mechanisms by which COVID-19 increases the risk of developing diabetes.[4]

Type 1 or type 2 diabetes accounted for the vast majority of diabetes codes, with medication and chemical-induced diabetes accounting for 1.5–2.2%. Short-term increases in blood sugar have been associated with intravenous steroid treatment. Because both of severe COVID-19 illness and diabetes are caused by obesity, it is possible that the pandemic had a role in the surge in diabetes incidence. An unusual pathophysiological shift in glucose homeostasis makes COVID-19-induced diabetes challenging to treat (severe insulin deficiency and insulin resistance together).[5]

This cross-sectional study set out to settle on where and when COVID-19 infections were most common, how often people were being diagnosed with diabetes, and how well people with newly

diagnosed diabetes were able to keep their blood sugar levels in check. The use of C-peptide assays and fasting insulin helped us in differentiating between type 1 and type 2 diabetes. All newly diagnosed diabetics had their HbA1C tested to determine if their diabetes was new or had been present for some time. So far this year, 82 people have been diagnosed with type 2 diabetes, 12 with type 1 diabetes, and 6 with both. It is difficult to distinguish between newly diagnosed diabetes and undiagnosed diabetes since many studies did not evaluate the HbA1C readings of everyone.[6]

In the current investigation, four persons with a fresh diagnosis of type 1 diabetes presented with diabetic ketoacidosis upon hospital admission. This was consistent with result, which demonstrated that COVID-19 may expedite the development of DKA in patients with preexisting or newly diagnosed DM.[7]

Additionally, newly diagnosed DM patients reported increased levels of inflammatory markers such CRP, ESR, and D-dimer, and more harsh symptoms of infection like cough, fever, and dyspnea compared to nondiabetic adults. A recent diagnosis of diabetes and hyperglycemia is associated with more severe symptoms and higher levels of inflammatory markers, as we showed, supporting the results of a larger research.[8]

Positive D-dimer values in diabetic individuals increased their likelihood of diagnosis (1.1 ± 1.8 vs. 0.6 ± 0.2, $P = 0.001$) than to be diagnosed 2 months later. According to our study, 2 months after hospital discharge, the mortality rate for COVID-19 patients was higher than that for people who had just been diagnosed with diabetes. Researchers from the United States discovered that COVID-19 individuals with diabetes had a death rate that was significantly greater than the overall population (28.8 vs. 6.2%).[9]

Additionally, it was reported that those with COVID-19 who were newly diagnosed with DM had a higher chance of dying than people with preexisting diabetes and normal blood sugar levels. Reduced immunity caused by chronic hyperglycemia has been linked to an increased risk of getting lower respiratory tract infections, which may have serious consequences.[10]

Among COVID-19 patients, we discovered that the highest risk variables for a new diagnosis of DM were older age, higher ESR, CRP, and D-dimer values ($P = 0.001$). Death from COVID-19 was shown to be significantly predicted by elevated levels of D-dimer, hypertension, and ischemic heart disease. The greater death rate in the older COVID-19 patients was corroborated by Zhou et al.[11]

After 28 days in the critical care unit, patients with serious infections or sepsis had a higher chance of mortality. Additionally, it was discovered that people with a history of cardiac problems were more likely to die from COVID-19.

One hundred diabetic patients with COVID-19 problems had median survival times ranging from 1 to 25 days. After the first 2-month follow-up period, the remaining 91 patients were revisited. Twenty-three patients reached euglycemia and were no longer prescribed antidiabetic medication during recovery, whereas the other 77 patients.[12]

Seventy-seven percent still had hyperglycemia and were hyperglycemia as a result of stress, an adaptive immune-neurohormonal response to physical stress, was one piece of evidence showing they had it. Patients in the COVID-19 study who had just been diagnosed with DM underwent laboratory testing and follow-up to see whether their hyperglycemia persisted. In light of these results, it has been proposed that a large-scale worldwide research be carried out to evaluate how diabetes develops and is treated in COVID-19 patients. The key drawback of this research was the very short length of time it followed participants.

4.1. Conclusion

Patients with more serious diseases were more likely to have newly diagnosed diabetes or have its symptoms during their illness, while COVID-19 patients were more likely to do so.

Conflict of interest

None declared.

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