Al-Nahrain Journal of Science
ANJS, Vol.25 (4), December, 2022, pp. 16-20

Coronavirus Causes Diabetes in People who Did Not Have Diabetes Before They Contracted COVID-19

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Article's Information

Received:
20.07.2022
Accepted:
28.11.2022
Published:
31.12.2022

Keywords:
COVID-19
Glucose level
HbA1C
Acute parameters

Abstract

Coronavirus disease infects the respiratory system through binding to the receptor of angiotensin-converting enzyme2 (ACE2), Symptoms of the disease develop within 5-6 days after infection, accompanied by mild to moderate symptoms in the initial stage of the disease, and continue for 10-15 days.

But it has the potential to develop into severe acute respiratory distress syndrome (ARDS), which leads to the destruction of multiple organs in the body, including the beta cells in the islets of Langerhans in the pancreas, causing type 1 or type 2 diabetes and high blood sugar. The aim of the study is to detect diabetes mellitus in people with COVID-19 who did not have diabetes and did not have a family history of the disease before they were exposed to the virus. COVID-19 was diagnosed by nasal swab through PCR Real-time. The detection of diabetes was through blood tests such as blood sugar, and glycated hemoglobin (HbA1C), and the acute stage of the infection was detected through Dimer, LDH, Ferritin, and C - reactive protein (CRP) tests. From the results that obtained during the research, it was found that the patient percentage with diabetes due to the virus is 20% of type I, while 80% diabetes of type II.

DOI: 10.22401/ANJS.25.4.03
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1. Introduction

Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus (SARS)2 (SARS-CoV-2), has a wide range of complications and clinical manifestations starting from symptoms of Acute respiratory injury to the kidneys, liver, heart, pancreas and other organs and even death [1,18]. The virus enters the lungs through its binding to Angiotensin Converting Enzyme-2, (ACE2), causing a defect in the performance and function of the respiratory system, and this, in turn, leads to the occurrence of an immune response where a cytokine and chemokine are produced and it is called a cytokine storm which can be fatal [2,19].

Shuibing Chen, a stem cell biologist at Weill Cornell Medicine in New York City, was able to use two small lungs in a dish, it was discovered that some cells died after being infected with the virus [3]. Entry of the virus through the ACE2 enzyme and due to the presence of receptors for this virus in the cells of the pancreas, small intestine, liver, and some tissues, It was found that the virus can spread from the lungs to other organs including the kidneys, gut, heart, liver, pancreas, and others. Which causes damage to these organs [4].

The virus can also damage the beta cells in the pancreas that are responsible for regulating blood sugar levels, causing type 1 or type 2 diabetes [2,5].

There are several explanations for the development of diabetes after exposure to the Coronavirus in people who have no history of diabetes or problems Control of blood sugar, including:

1. The first possibility is the production of immune cells such as cytokines and chemokines, which destroy beta cells in the pancreas, causing a lack of insulin secretion [6].
2. The second possibility is that the virus itself attacks the cells of the pancreas, causing the cells to die and the pancreas to lose its main functions [3,5].
3. The third possibility is that the virus causes inflammation in the pancreas, which leads to a slowdown in the work of the pancreas in producing insulin [7].
4. In the case of type 2 diabetes, stress may be a factor in insulin resistance and raising blood sugar levels [8].
5. Some medicines that are given to patients in hospital wards, such as glucocorticoid hormone, which is one of the types of steroid hormones that affect high blood sugar [9].
6. Obesity, unhealthy eating, and inactivity also play a role in diabetes and insulin resistance, as complicate the metabolism process [10,11].

In this work has been proven that the Coronavirus causes diabetes type 1 or type 2 in people who do not suffer from diabetes and do not have a family history of diabetes.

2. Materials and Methods

2.1 Patient information:

Patient information including age, gender, weight, history of illness and recovery, possible complications from diabetes, blood pressure, kidney, liver, respiratory system, the appearance of some symptoms such as cough, fever, muscle and joint pain, shortness of breath, stomach pain, vomiting, and information about medical treatment such as antivirals, corticoids, and insulin.

2.2 Sample collection:

Samples were collected from patients in private laboratories and Yarmouk Teaching Hospital in Baghdad in the year 2021-2022, and included 50 (control group) and 200 patients, 100 males, and 100 females, in the age group 15-75 years. Two samples were collected from the patient, including a nasal swab for the PCR test for positive or negative infection, and the blood sample for laboratory analyses such as glucose, glycated hemoglobin (HbA1c), lactate dehydrogenase (LDH), D-Dimer, C-reactive protein (CRP) and ferritin to know the complications of corona such as diabetes. These tests were performed by the automated SIEMENS ATELLICA system.

2.3 Inclusion and exclusion criteria:

- Blood samples for corona patients were collected from people without diabetes before exposure to the virus and without a family history of the disease.
- The collection of blood samples for corona patients from people with diabetes before exposure to the virus was excluded.
- Blood samples of corona patients were excluded from people who did not have diabetes before exposure to the virus but had a family history of the disease.

2.4 Statistical analysis:

Data was expressed as mean ± SD and percentage. The men ($\bar{X}$)) and the standard deviation (SD) were calculated by using the following equation:

$$SD=\sqrt{\frac{\sum(X-\bar{X})^2}{N-1}}$$

3. Results

Two groups of people were worked on, which included 50 of the control group and 200 of the affected group, which included 50% of men and 50% of women in the age group from 15 to 75. Corona cases were detected by nasal swabs using a real-time PCR machine and using the zybio kit, the negative and positive result was inferred by the control threshold value (CT-value), which determines whether a person is positive or not from:

Positive: when CT-value for (FAM, ROX, VIC) < 35.

Negative: when (FAM, ROX) fluorescence channels are not detected and CT-value for (VIC) < 35, as shown in the Figures 1 and 2.

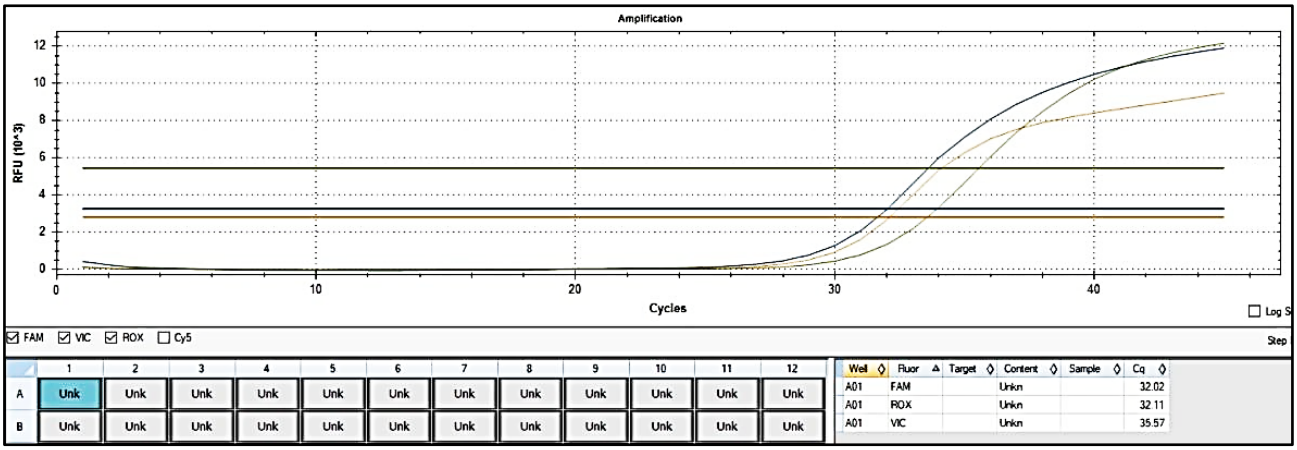

Figure 1. Shows the fluorescence curves of the three dyes (FAM,ROX,VIC) to the positive result in PCR-real time CT < 35.
VIC: green dye indicates internal
FAM: blue dye indicates N gene.
ROX: orange dye indicates RdRP gene.
CT value: the cycle threshold value in real-time PCR.

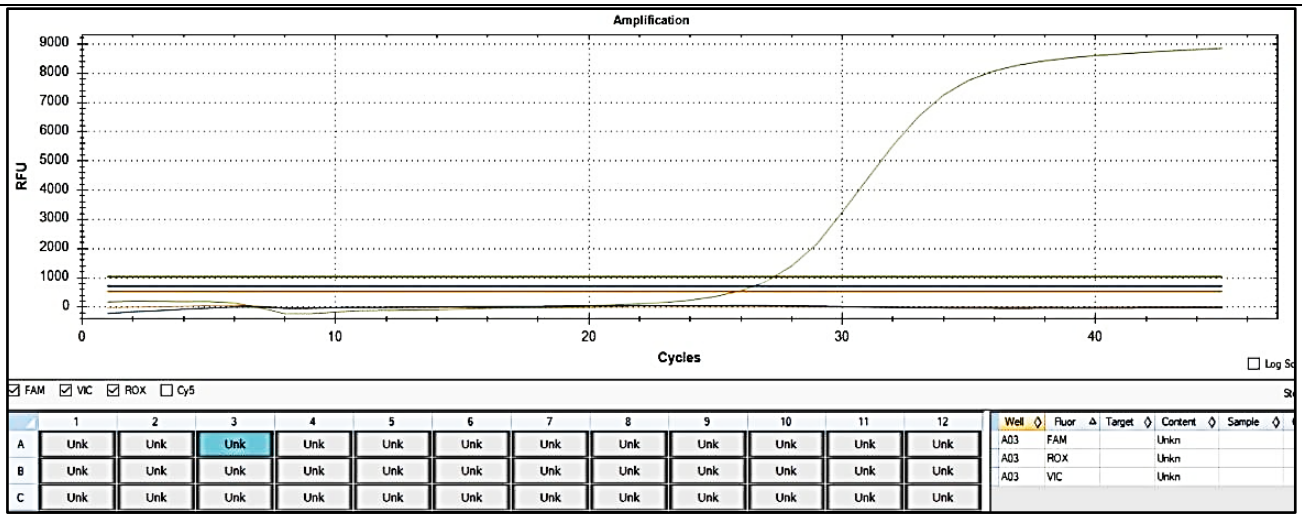

Figure 2. Shows the fluorescence curve of VIC dye for a negative result in PCR-REAL TIME CT < 35.
VIC: green dye indicates internal; CT value: the cycle threshold value in real-time PCR.

Diagnosis of the Coronavirus by examining the PCR and knowing the severity of the disease through the value of the CT for (FAM, ROX, VIC), where the acute cases were CT-value < 25, while the moderate cases were CT-value (25-35) as shown in Table 1.

Table 1. Shows the relationship between disease severity and CT-value in the PCR-real-time.

Fluorescence Dyes	CT value (1-40)		
	Healthy	Mild	Sever
VIC	25 ± 10	25 ± 10	25 ± 10
FAM	Not detected	29.7 ± 5.8	21.1 ± 4.9
ROX	Not detected	29.4 ± 4.7	20.6 ± 4.4

As for the detection of corona complications, a blood sample was taken and the following tests were performed: glucose, glycated hemoglobin (HbA1c), LDH, D-Dimer, CRP, and ferritin.

The levels of glucose, HbA1c, LDH, D-Dimer, CRP, and ferritin were within normal levels for each assay, and the PCR test result was negative for the control group as shown in Table 2.

Table 2. Shows the result of the PCR value and chemical parameters with the severity of the virus infection.

Parameters	Healthy (50)	Infected (200)	
		Mild	Sever
Age	45 ± 30	35 ± 20	55 ± 20
Male	25%	74%	26%
female	25%	82%	18%
PCR Real-time Fluorescence CT value for (FAM& ROX dyes)	Not detected	CT (25-35)	CT < 25
Blood fasting sugar(mg/dl)	74 ± 4.2	129 ± 3.3	145 ± 80
HbA1c (%)	4.80 ± 0.70	5.80 ± 0.95	6.20 ± 1.80
LDH (U/L)	135 ± 78	390 ± 240	446 ± 183
Ferritin(ng/ml)	125 ± 100	200 ± 175	470 ± 280
CRP (mg/L)	2.2 ± 1.5	50 ± 31	105 ± 48
D-Dimer (ng/dl)	220 ± 65	600 ± 240	900 ± 200

Where the normal range for each examination is as follows:

- Glucose (70-110) mg/dl.
- HbA1c (4.5-6.5) %.
- LDH (135-214) U/L.
- Ferritin (10-290) ng/ml.
- CRP (0.00-5.00) mg/L.
- D-Dimer (< 500) ng/ml.

While the affected group was divided into two categories, acute cases, and moderate cases, the results were as shown in Table 2 as follows:

The age group of moderate cases was (35 ± 20), while acute cases (55 ± 20) and this indicates that the elderly are more vulnerable to acute cases than other age groups, and the proportion of men in acute cases (was 26%), while the proportion of women (18%), meaning that men are more susceptible to acute cases than women.

The result of the CT-value for PCR examination was (25-35) for moderate cases, while (CT-value was < 25) for severe cases. As for the blood test. The comparison between acute and moderate cases was as follows the fasting blood sugar was (129 ± 3.3) for moderate cases, while(145 ± 80) higher for severe cases, an HbA1c examination was (5.80 ± 0.95) for moderate cases while (6.20 ± 1.80) higher for severe cases, Ferritin was (200 ± 175) for moderate cases while(470 ± 280) higher for severe cases, LDH was (390 ± 240) for moderate cases while (446 ± 183) higher for severe cases, D-Dimer was (600 ± 240) for a moderate while (900 ± 200) higher for severe cases and CRP was(50 ± 31) for a moderate while(105 ± 48) higher for severe cases.

People with type 1 diabetes were detected within severe cases with CT-value < 25 and with a rate of 20%, including 12% of men and 8% of women, while type 2 diabetes patients were moderate cases with CT-value (25-35) and at a rate of 80% included 50% men, 30% women As in Table 3.

Table 3. Shows the relationship between the type of diabetes and the severity of the disease.

Types	Male	Female	Total	CT-value	Severity
Type1	12%	8%	20%	< 25	acute
Type2	50%	30%	80%	25-35	moderate

The patients with type 2 diabetes were followed up after recovery, and their percentage ranged 80%, and the results were as shown in Table 4.

Table 4. Shows the change in sugar levels over 10 months.

Months	The Second Month	The Fourth Month	The Sixth Month	The Eighth Month	The Tenth Month
FBS (mg/dl)	130.3 ± 1.8	129.1 ± 0.8	129.4 ± 0.5	125 ± 0.8	121 ± 1.7
PPBS (mg/dl)	180.5 ± 5.1	175.2 ± 3.5	162.6 ± 8.2	157.8 ± 0.7	140.9 ± 2.5
HbA1c%	5.2 ± 0.8	6.4 ± 0.4	6.7 ± 0.9	6.0 ± 0.4	5.8 ± 0.9

It was found from Table 4 that the blood sugar concentration (mg/dl) after two months of infection was (130.3 ± 1.8), in the fourth month it was (129.1 ± 0.8), in the sixth month it was (129.4 ± 0.5), in the eighth month it was (125 ± 0.8) and in the tenth month (121 ± 1.7). This means that the levels of sugar higher than normal values and the patient is still suffering from high blood sugar.

Postprandial blood sugar (PPBS) (mg/dl) measurement after two months of infection was (180.5 ± 5.1), in the fourth month it was (175.2 ± 3.5), in the sixth month it was (162.6 ± 8.2), in the eighth month it was (157.8 ± 0.7) and in the tenth month (140.9 ± 2.5) This means that the levels of sugar higher than normal values and The patient is still suffering from (hyperglycemia).

The HbA1C measurement after two months of infection was (5.2 ± 0.8) still a normal measurement because HbA1C is the average glucose concentration for three months, in the fourth month it was (6.4 ± 0.4) and in the sixth month (6.7 ± 0.9) it was higher than the normal range, In the eighth months (6.0 ± 0.4) and the tenth month (5.8 ± 0.9), the sugar levels had returned to the upper limit of normal values and the patient still suffers from (high blood sugar).

4. Discussion

through performing the sugar tests and HbA1c shown in Table 1 one of the several complications of Corona was reached, which is that people who do not have diabetes and do not have a family history of the disease develop hyperglycemia, type 1 and type 2 after exposure to the Coronavirus, as Paul Zimt said, who studying metabolic disease at Monash University in Melbourne, Australia. "Not only does having diabetes increase the risk of contracting the virus, but the virus also causes diabetes [12].

They were followed up for ten months after recovery, and it was found that the disease was not cured, and the patient is still receiving diabetes treatment, as shown in Table (4). Where the percentage of people with type 1 diabetes was 20%, including 12% were men, while 8% were women, while the percentage of people with type 2 diabetes was 80%, including 50% men and 30% women, This is due to the infection and damage of the beta cells in the pancreas with the Coronavirus and their inability to produce insulin [13]. As shown in Table 3.

It was also found that type 1 diabetes was associated with disease severity, with CT-value < 25, while type 2 diabetes was associated with the moderate disease within CT-value (25-35) as shown in Table 3. The severity of the disease was also monitored through chemical parameters such as the LDH test, where it was higher in severe cases than in moderate ones because LDH is an iso-enzyme that converts pyruvate to lactate, It is present in the form of ISO-enzyme in many tissues, such as the lung and pancreas, and due to the lack of oxygenation in the affected organ, the proportion of lactate increases [14]. As well as examining

the ferritin, which is higher in severe cases than in the moderate, because the ferritin increases in the acute phase [15]. The d-dimer test was also measured, which increases in severe cases than in moderate ones, due to the cytokine storm (immunity system) [16,20], and the CRP test, which was higher in severe cases than in moderate ones, its increase reflects the severity of the disease [17,21].

5. Conclusions

In this research, it was found that the Coronavirus causes diabetes type 1 or 2 in people who do not suffer from diabetes and do not have a family history of diabetes, in similar studies Rubino et al. and Hamilton-Shield et al.; and that diabetes continues for a year now, even after recovering from the virus and that patients are still undergoing diabetes treatment.

According to the results obtained after studying 200 infected patients, it has been proven that the incidence of the type1 was related with the severity of the disease, while the incidence of the type2 was related to the moderate incidence of the disease.

The percentage of those with type I was 20%, while the highest percentage of those with type II was 80%, this means that the incidence of diabetes due to the coronavirus is type 2 about five times more than type 1.

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