

# COVID-19 could trigger diabetes in healthy individuals and worsen symptoms in pre-diagnosed DM patients

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## ABSTRACT

COVID-19 is novel diseases started at the sea food Wuhan market and continue to spread to evolve to be a global pandemic. Our data have shown a significant increase  $P=****$  in sugar level for patients (COV-I-DM) have contracted COVID-19, as compared to the other group of patients (COV-NS) that have shown normal levels of blood sugar. Similar significant results have been seen as we compare their A1C levels, which further support our assumption that COVID-19 can induce diabetes in almost 18% of patients. 80% of Males and females' patients were in the 50-65 age groups, while only 20% were in the 35-50 years old group. Moreover, significant correlation  $P=****$  has been detected when we compare the sugar level of patients (COV-DM) contracted COVID-19, with their tests before the infection. Their A1C levels have shown similar significant difference before and after the infection, which strongly support our hypothesis that COVID-19 negatively affect endocrine health. Finally, we have not detected any significant correlation between COV-DM patients and smoking criteria. However, we believe that increasing the number of data might detect this kind of correlation. In conclusion, we are in a fair position than many other Middle East countries to react to the pandemic. However, an advanced approach needs to be used with diabetic patients who might hit hard by COVID-19.

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## 1. INTRODUCTION

On March 17, 2020, the Iraqi Government ordered quarantine and restrict autos and pedestrian's movement to reduce COVID-19 viral spread. These rules intended to minimize the chances of meeting the infected individuals with the uninfected ones.

COVID-19 is initiated by a virus having a single stranded RNA genome circulated by a positive-stranded bilayer lipid [5]. The virus can enter the body via angiotensin-converting enzyme 2 (ACE2), that is expressed in various cells, but highly expressed in lung alveolar cells [25].

Data from epidemiological notes in zones critically affected by SARS-CoV-2 and documents from the United States of America Centers for Disease Control and Prevention (CDC) and other worldwide countries health centers and hospitals revealed that the danger of a deadly consequence from COVID-19 is up to 50% established in patients with diabetes than in those who do not have diabetes [1].

People with DM hit so hard with COVID-19 as it compared with healthy individuals, and tens of papers have documented that patients with diabetes mellitus might predispose to possible lethal outcomes [23].

There are two key types of diabetes. Type 1, formed by the body's own immune system fighting the islet cells in the pancreas that create insulin, a so-called autoimmune sickness. Ultimately, there are no islets left and henceforward no insulin can be primed to govern serum glucose ranks. We don't distinguish what triggers this autoimmunity, but viral infections have been mentioned as a feasible trigger.

Type 2 diabetes happens when the islet cells have to generate enormous amounts of insulin as the central target organs (liver, muscle, fat) do not respond as well as they should to insulin's letter. Finally, the islet cells established, exhausted and might die.

### ***1.1 Can COVID-19 initiate diabetes?***

One of the key insights from organoids is what SARS-CoV-2 does to cells in the respiratory system. Kazuo Takayama, a stem cell biologist at Kyoto University, Japan, and his colleagues have created bronchial organoids with four distinct cell types, prepared from frozen cells from the outer bronchial layer, or epithelium. After SARS-CoV-2 infected the organoids, they found that the virus principally targets stem cells that fill epithelial basal cells, but hardly entered protective, secretory 'club cells [24].

The shared comorbidities were chronic cardiac disease (29%), simple diabetes (19%), non-asthmatic chronic pulmonary disease (19%) and asthma (14%); 47% had not documented comorbidity [22].

Diabetes mellitus is caused by either absolute insulin lack in type 1 diabetes or insulin resistance in type 2 diabetes. Chronic hyperglycemia is the main metabolic imbalance in diabetes and gives rise to glucotoxicity to body tissues with the formation of progressive glycation end products [4].

The virus can also destroy cells that control blood sugar in pancreatic organoids which add to rising evidence that the virus can trigger diabetes in some people than others.

## **2. Material and methods**

**Patients:** The study had started March 15, 2020 to July 15 and included 5000 patients, we focused on 500 patients that meet our requirements. We divided them into two groups, first group (COV-DM) is represented the 100 patients that have diabetes and contracted COVID-19. Second group has included 400 patients and we separated them into (COV-I-DM) is represented the 72 patients that predispose to diabetes after they got infected by COVID-19. The second group includes 328 patients (COV-NS) represented patients got infected with COVID-19 and manage to control their blood sugar in normal levels.

**Age:** men and women in various age groups have been included in our study. To organize the data, we segregated the males and females' patients into two age groups (35-50) year or (50-65) year.

**Specimens:** Blood has been taken from patients in our Thi Qar Specialized Diabetes, Endocrine and Metabolism Center, Nassiriya, Thi-Qar, Iraq.

## 2.1 Lab tests

BS-120 chemistry analyzer has been used to measure the level of plasma and serum sugar levels. Hemoglobin HbA1C1 measurements have been recorded using HPLC.

### 2.1.1 Random Blood Sugar Test

We have measured patients' blood sugar at the time they're present to the clinic with no need to be fasted first. We considered the patient is diabetic if the blood sugar level is 200 mg/dL or higher.

### 2.2 A1C Test

It measures the patients average blood sugar level via the past 2 or 3 months. An A1C below 5.7% is normal, between 5.7 and 6.4% indicates the patient have prediabetes, and 6.5% or higher indicates the patient has diabetes.

### 2.3 Polymerase chain reaction PCR

Biorad PCR machine has been used to detect corona virus RNA. Syber green and commercial forwards and reversal primers have been used [1], [2].

### 2.4 Statistical analysis

GraphPad prism version 8 software for Windows, La Jolla California USA, www.graphpad.com, was used to average and plot the data groups in this study with Standard deviation. In addition to performing student t-test between two groups, prism was used ANOVA to analyze three or more groups followed by multiple comparison using Tukey's test. Chi-square analysis was employed to compare the mouse survival Percentages compared to the expected results. Significant data denoted by star as the Following:  $0.01 \leq *p < 0.05$ ;  $0.001 \leq **p < 0.01$ ;  $***p < 0.001$ .

## 3. Results

Sugar levels have dramatically increased in patients have COV-DM as it compared to the other group of patients who managed to keep their sugar in normal level. The highest sugar is 486 and A1C 13.3, while the minimum is 13.3 and 6 for sugar and A1C, respectively. On the other hand, the highest sugar and A1C for COV-NS is 136,6.3, respectively. While, the lowest level is 63, 4 for sugar and A1C, respectively table (1).

Table (1): Statistical analysis of 3 groups of patients	COV-DM		COV-I-DM		COV-NS	
	Random Sugar	A1C	Random Sugar	A1C	Random Sugar	A1C
Average	317.3125	10.83333	218.125	8.175	94.875	4.510417
Median	253	10.4	189	8	99	4
Mode	140	7	323	9	130	4
Max	663	16.4	486	13.3	136	6.3

Min	134	6.4	120	6	63	4
STDEV.S	137.8303	2.76933	96.39715	1.534322	20.6816	0.693531
STDEV.P	136.0517	2.733596	95.15326	1.514523	20.41473	0.684582
Var.s	18997.18	7.66919	9292.41	2.354143	427.7287	0.480985
Var.p	18510.08	7.472544	9054.143	2.29378	416.7613	0.468652

**3.1 COVID-19 can induce DM in group of patients**

We compare the sugar level of COV-DM and COV-NS patients and we detected dramatic differences, figure (1).

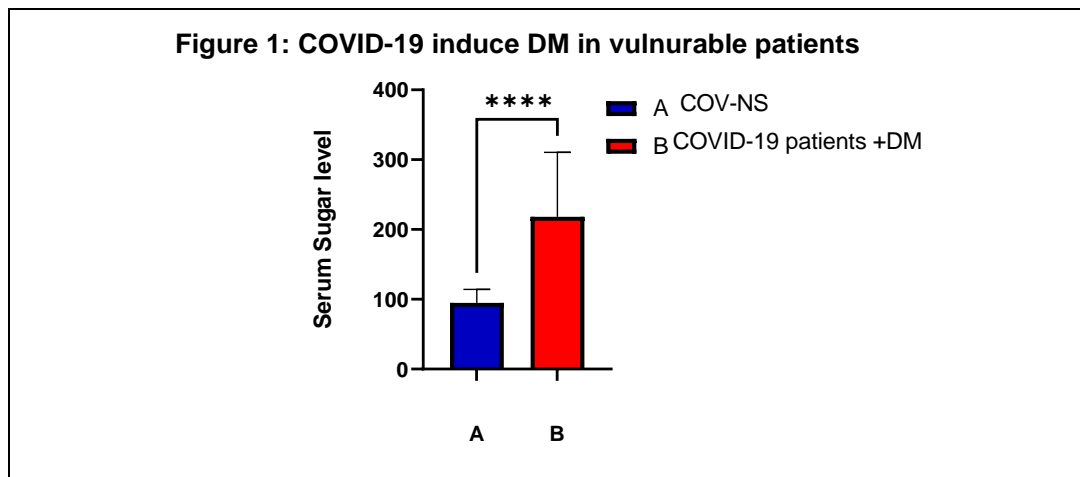
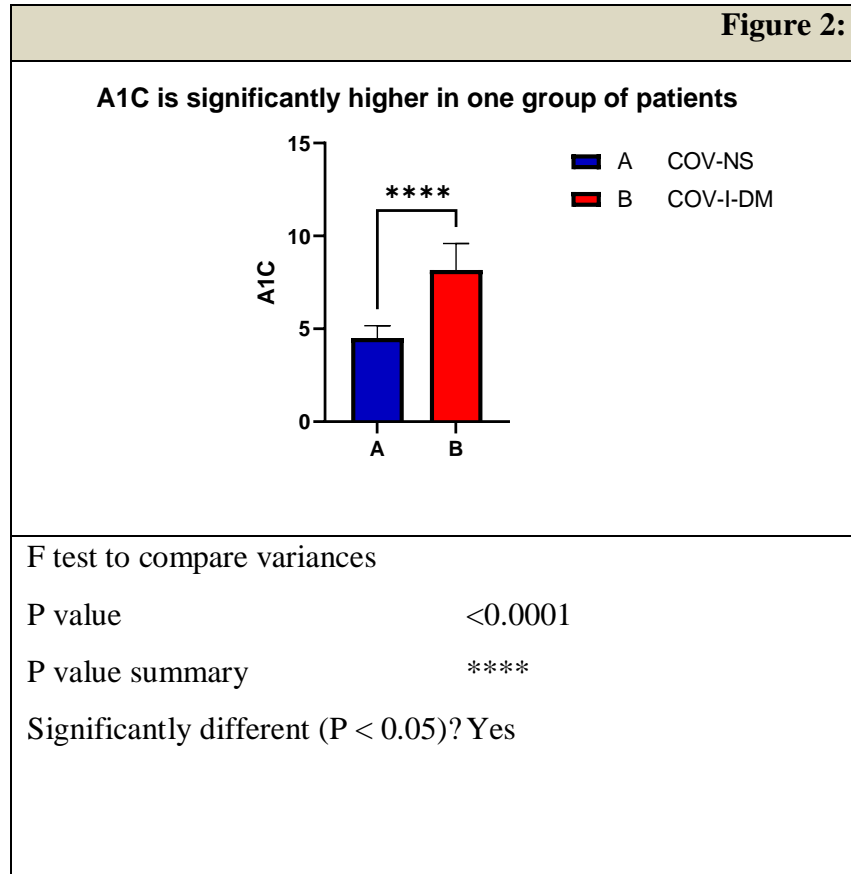


Table Analyzed	Data 4
Column B	COVID-19 induce diabetes
vs.	vs.
Column A	COVID-19 patients with normal Sugar level
Unpaired t test with Welch's correction	
P value	<0.0001
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
F test to compare variances	
P value	<0.0001

P value summary	****
Significantly different (P < 0.05)?	Yes

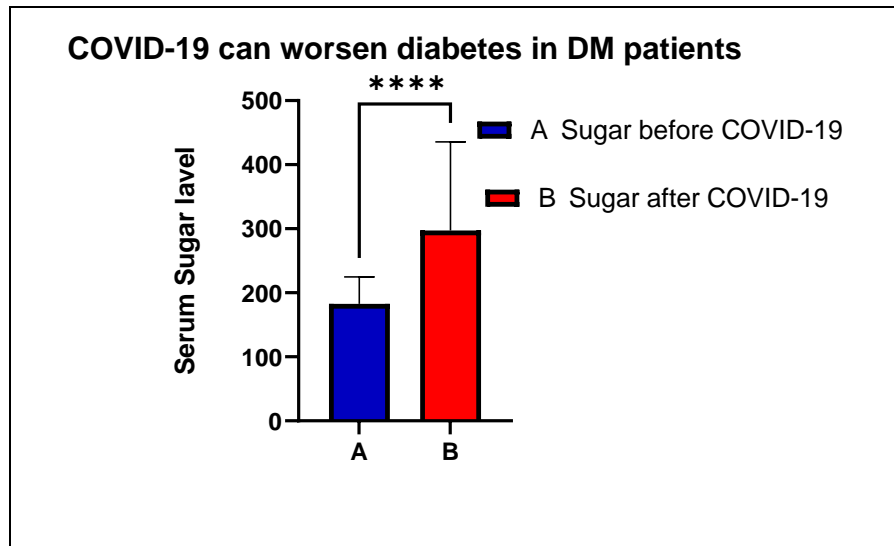
### 3.2 A1C levels

The A1C levels were dramatically increased in one group of patients that develop diabetes as compared to the other group who showed normal sugar and A1C level, figure (2).

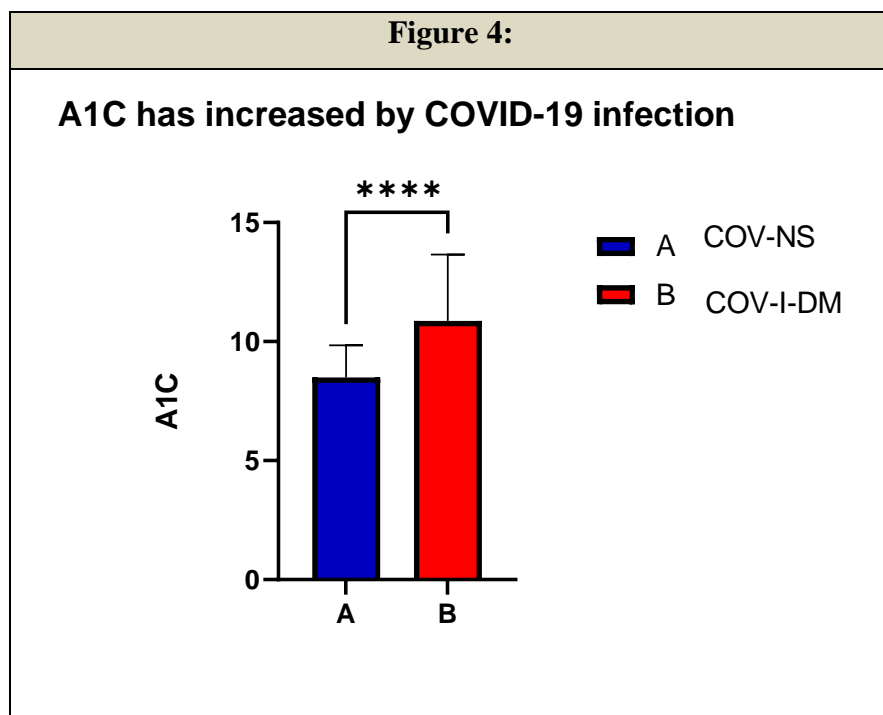


COVID-19 is correlated with hyperglycemia in patients with type-2 diabetes:

**Figure 3:**



A1C for the same group of patients has been measured before and after the COVID-19 infection. We detect significant differences, which further support our assumption that COVID-19 exacerbates diabetes in patients.



### 3.3 Smoking

Our study was unable to detect significant correlation between the smoking condition and COVID-19 induce diabetes. However, we think the limited number of patients was the reason behind these results.

### 4. Discussion

There are numerous hypotheses to elucidate the amplified rate and severity of COVID-19 infection in individuals with diabetes. In general, folks with any type of diabetes are at increased risk of infection because of defects in innate immunity weaken phagocytosis, neutrophil chemotaxis, and cell-mediated immunity; though, the high occurrence of diabetes in serious cases of COVID-19 could probably mirror the higher occurrence of type 2 diabetes in older persons. Besides, diabetes in older age is related with cardiovascular

disease, which in itself could help to reveal the bond with terminal outcomes of COVID-19.

In general viruses can reduce immunity and decreased body functions [2].

<b>Table (2): List of abbreviation</b>	
COV-DM	Diabetic patients got COVID-19
COV-I-DM	Covid-19 induce diabetes in patients
COV-N-DM	Covid-19 patients No Diabetes
ACE2	angiotensin-converting enzyme 2
DM	Diabetes mellitus type 1
HPLC	High performance liquid chromatography

## 5. Conclusion

Our data suggest that small proportion of patients around 72 (18%) of the whole number of patients 400 included in the study has developed DM due to COVID-19 infection.

## 6. Recommendation

We recommend performing screen test for COVID-19 patients infected or cured patients that included a larger group of patients.

We recommend perform study to monitor if COVID-19 can worsen other disease such as cancer [3].

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