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The correlation between diabetes mellitus and COVID-19 severity in Babylon Province

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ABSTRACT

Compared to other pandemic diseases, COVID-19 had the highest transmission rate and high fatality risk. Diabetes is the hand was also one of the most frequent diseases among individuals. This study aimed to evaluate the relationship between diabetic patients infected by COVID-19 and some hematological parameters associated with diabetes and COVID-19. Patients with COVID-19 were diagnosed by PCR and/or chest computer topography (CT) scan, eight parameters were detected by AFIAS-6. The results of eight parameters for patients with diabetes mellitus infected with COVID-19 and patients with COVID-19 only showed that the Mean of Fasting Blood Glucose (FBG), glycated haemoglobin HbA1c, Insulin Sensitivity (INS) and ferritin show significant differences at (0.000, 0.000, 0.017, 0.000) respectively for the two groups, while insulin resistance (INR), insulin (IN), C-reactive protein (CRP) and D-dimer don't show any significant differences for two groups, the statistical analysis performed at P-value ≤ 0.01 and 0.05. Infection duration results showed that the mean Insulin level (IN) and D-dimer show significant differences at (0.033 and 0.011) respectively for all infection duration categories, while FBG, HbA1c, INR, INS, CRP, and ferritin don't show any significant differences for all day's category. The Correlation Coefficients Between diabetes mellitus patients infected with COVID-19 and blood parameters highly correlated between FBG with INR at (0.647), HbA1c with IN at (0.078), INR with IN at (0.791), INS with CT-Scan at (0.058), CRP with D-dimer at (0.287), D-dimer with ferritin at (0.331), Ferritin with infection duration at (0.098). In conclusion, we find that the diabetes mellitus patients infected with COVID-19 suffer from a high increase of inflammatory proteins and parameters associated with diabetes compared to other patients infected with COVID-19 only, making them more susceptible to disease and more deaths compared to other people.

INTRODUCTION

COVID-19 disease caused by coronavirus, SARS-COV-2 shows a highly variable clinical presentation, ranging from mild to severe infection likely led to death [1]. There are many symptoms such as COVID-19 patients, including fever, headache, fatigue, myalgia, cough, loss of smell and taste, and muscle pain, these symptoms may be mild or severe depending on the patient's immunity but sometimes the infection leads to hypercoagulation and septic shock.

Failure of multi organs and acute respiratory distress syndrome (ARDS) finally, led to death [2, 3]. COVID-19 symptoms ranged from mild at 5%, moderate at 40%, and severe at 80%, many other factors may associate with the severity of COVID-19 disease, including age, gender, sex, immunodeficiency, and chronic diseases such as cardiovascular disease and diabetes, which are serious factors that lead to increased rates of morbidity and mortality [4], In addition to an increase in some factors associated with diabetes patients infected COVID-19 such as increasing of concentration of fasting to blood sugar, insulin resistance and sensitivity that is increasing the severity of the disease, which requires making many early serological

tests to the disease progresses [5]. Diabetes mellitus has two main types: insulin resistance in the blood and a deficiency of the hormone insulin-releasing hormone in the blood [6]. Diabetes is a chronic disease resulting from a large metabolic derangement in the body, which leads to the formation of advanced glycation end products and leads to the glucotoxicity of body tissues, and it leads to many chronic diseases in the heart, blood vessels, and kidneys [7, 8].

Diabetes mellitus is a chronic disease that affects the body's immunity and is the cause of many bacterial and viral infections, including the production of mitochondrial reactive oxygen species and activation of hypoxia-inducible factor 1α, which leads to an increase of COVID-19 spreading in the body [9]. One of the most important effects of the Coronavirus on diabetic patients is an increase in insulin sensitivity and its effect on insulin-producing beta cells in the pancreas, which leads to high blood sugar as a result of the pathological effect of the virus [10], in addition to this the complications from the virus and the cytokine storm make diabetic patients infected COVID-19 more likely to die from the others [11]. Diabetes leads to an increase in the concentration of inflammatory proteins in the body such as C-reactive proteins, IL-6, plasminogen activator inhibitor-1, tumor necrosis factor-alpha, leptin and adiponectin, in addition, the Coronavirus also leads to an increase in these proteins as well, which increases its effect on the body, and thus monitoring its effect and its concentration in the blood gives a good vision about of the disease progression [12]. COVID-19 severity was associated with many factors, including age, sex, severe obesity, and diabetes, which are well-established risk factors for increased morbidity and mortality, in addition, the contribution of fasting blood sugar, sensitivity and insulin resistance to the severity of the disease Not very well known which should be evaluated for its predictive value [13]. The aim of this study was to diagnose the severity of COVID-19 in diabetes patients by measuring the concentration of many blood markers related to diabetes including fasting blood sugar, insulin, insulin sensitivity and insulin resistance and inflammatory protein related to COVID-19 including C-reactive protein (CRP), D-dimer, ferritin, and computerized tomography scan (CT-Scan) test

MATERIALS AND METHODS

Sample collection

About five milliliters of venous blood were collected from each patient and control subject in the study. and the number reached 92 samples. 31 samples were healthy people, 30 samples were infected with COVID, and 31 samples were infected with diabetes + COVID where the healthy group matched with the group of patients. The blood was collected into (EDTA, gel, sodium citrate) tubes put 2 ml of blood in the EDTA tube was used to measure Hba1c levels and for DNA extraction stored at - 20˚C (deep freeze). 2 ml of blood into disposal serum gel tubes containing separating gel, then centrifuged at 2000 rpm for 10 minutes. Then continued to haematological parameters measurements, adding 1 ml of sodium citrate to serum for D-dimer measurement.

Ethical statement

Every volunteer has given written informed permission. This research received ethical approval (DSM/HO-15314) for scientific research from the Ministry of Health MOH and

Ministry of Higher Education and Scientific Research MOHESR ethics committees in Iraq.

Biochemical analysis

This cross-sectional study was done at Marjan Teaching Hospital and Al-Turki Hospital, in the private department of patients with COVID-19 diagnosed by PCR and/or chest Computer Topography (CT) scan in Babylon state, Iraq. From October to December 2021included males and females' individuals. Samples were divided into three groups, Control, COVID-19 and COVID with Diabetic Mellitus (DM), then divided into another three groups according to their infection levels into mild, moderate, and severe in Intensive Care Units (ICU).

There were Eight physiological parameters which were as follows: fasting blood glucose (FBG), glycated haemoglobin (HbA1C), insulin level (IN), insulin resistance (IR), insulin sensitivity (IS), C-reactive protein (CRP), and ferritin and D-dimer.

FBG, IN, IR and IS measurements were collected from their clinical files at the time of admission to the hospital from 5 October to 12 December 2021 (the test period), while (HbA1C) was measured according to the leaflet of human hemoglobin A1c (HbA1c) Assay Kit (Crystal Chem. Co. USA), for both of CRP, Ferritin and D-dimer were measured by AFIAS-6 (automated immunoassay analyzer with the all-in-one cartridge system, Korea).

Statistical analysis

All data were analyzed using SPSS software version 16 (Spss I., Chicago, Illinois, USA) for one-way ANOVA, explore, Duncan's, correlation, and means were compared using the L.S.D test. The levels of significance were as follows: P<0.01 and P<0.05 [14].

RESULTS

Association between COVID-19 patients and patients with diabetes mellitus infected COVID-19 according to some blood parameters

Table 1 showed the association between the COVID-19 patients with diabetes and patients with COVID-19 only for each mild, moderate and severe infection levels according to our markers candidate for this study, where the Mean of FBG, HbA1c, INS and ferritin show significant differences at (0.000, 0.000, 0.017, 0.000) respectively for the two groups, while INR, IN, CRP and D-dimer don't show any significant differences for two groups, the statistical analysis performed at P-value ≤ 0.01 and 0.05.

Table 1. Association between patients with COVID-19 only and COVID-19 with diabetes.

parameters	COVID+DM			COVID			Sig.
	Mild	Moderate	Sever	Mild	moderate	Sever	
FBG	265.23±10.6*	223.54±15.3	273.36±16.4	114.95±9.7*	108.81±10.2	154.25±11.2	0.000**
HbA1c	9.06±1.9*	9.07±2.3**	9.57±1.9**	5.37±0.8*	5.30±0.4**	5.46±0.2**	0.000**
INR	22.52±1.5	14.69±2.4	7.11±1.6	8.08±0.7	11.22±1.4	3.44±0.6	0.371
INS	0.29±0.03	0.28±0.04	0.38±0.04	0.31±0.04	0.29±0.04	0.35±0.07	0.017*
IN	28.00±5.9	26.91±2.3	11.27±1.5	30.98±7.8	40.28±9.1	7.70±1.8	0.532
CRP	71.48±7.2	55.71±6.5	39.19±2.6	39.78±4.9	38.97±1.5	70.16±9.1	0.392
D-dimer	1573.75±22.4	961.91±18. 3	994.62±24.5	1523.36±212.2	704.00±86.2	3903.13±12.9	0.438
Ferritin	392.79±46.3	819.13±70.5**	720.04±28.5	220.58±14.5	120.93±20.0**	1083.03±137.8	0.000**

*Significant at P-value ≤ 0.05, **Significant at P-value ≤ 0.01

The association between diabetic patients with COVID-19 and infection duration

Table 2 showed the association between patients with diabetes mellitus infected with COVID-19 and infection duration at >7,7-14 and <14 days according to the parameters under study. Where the Mean of INR, INS, IN, CRP, D-dimer and ferritin show significant differences for all categories of days at (0.046, 0.041,0.023,0.030, 0.031 and 0.034) respectively, while the FBG and HbA1c don't show any significant differences for all categories, the statistical analysis was made at p-value (≤ 0.05). Diabetic patients showed many changes in metabolism and blood vessels that weaken defenses of the body and prevent the immune system from making correct responses against viral and bacterial infection, in addition, many diseases occur in the innate immune system that increases the risk of pneumonia and influenza [15].

Our results showed an increase in the mean of insulin (IN) and insulin resistance (INR) in the first 7 days of infection at (28.00±2.7 a & 22.52±3.8 a) respectively which was explained by Muniyappa and Gubbi [16] that patients suffering from both diabetes type 1 and type 2 had an ACE-2 production increased due to treatment with ACE-2 inhibitors and angiotensin II type 1 receptor blocker (ARB), which had nephroprotective and antihypertensive effects. Treatment with ACE-2 and angiotensin-receptor blocker inhibitors increases ACE-2 production, which facilitates COVID-19 infection [17].

Table 2. The association between patients with diabetes mellitus with COVID-19 and infection duration.

Parameters	COVID+DM (Infection duration)			Sig.
	>7 days	7-14	<14	
FBG	265.23±17.2	223.54±15.3	273.36±58.5	0.707
HbA1c	9.06±1.9 a	9.07±2.3 a	9.57±1.9a	0.885
INR	22.52±3.8 a	14.69±2.2 a	7.11±1.1b	0.046*
INS	0.29±0.03 a	0.28±0.04a	0.38±0.10b	0.041*
IN	28.00±2.7 a	26.91±2.2 a	11.27±1.2b	0.023*
CRP	71.48±57.12 a	55.71±45.65 a	39.19±28.60b	0.030*
D-dimer	1573.75±202.4 a	961.91±10.9b	994.62±96.5b	0.031*
Ferritin	392.79±46.3 a	819.13±70.5 b	720.04±178.5 b	0.034*

*Significant at P-value ⩽ 0.05 level by Duncan test

The association between only COVID-19 patients and infection duration

Table 3 showed the association between COVID-19 patients and infection duration at >7,7-14 and <14 days according to the parameters under study. Where the mean of INR, IN, D-dimer and ferritin show significant differences for all categories of days at (0.039, 0.026,0.022 and 0.000) respectively, while the FBG, HbA1c, INS, and CRP don't show any significant differences for all categories, the statistical analysis was made at P-value ≤ 0.01 and ≤ 0.05.

Table 3. The association between COVID-19 patients and infection duration.

Parameters	COVID only			Sig.
	>7 days	7-14	<14	
FBG	114.95±8.6 a	108.81±10.02 a	154.25±5.4 a	0.220
HbA1c	5.37±0.8 a	5.30±0.4 a	5.46±0.2 a	0.961
INR	8.08±1.7 a	11.22±1.4 a	3.44±1.4b	0.039*
INS	0.31±0.04 a	0.29±0.04 a	0.35±0.07 a	0.182
IN	30.98±7.3 a	40.28±3.4 a	7.70±1.7b	0.026*
CRP	39.78±4.9 a	38.97±7.5 a	70.16±9.7 a	0.471
D-dimer	1523.36±252.27 a	704.00±86.2b	3903.13±41.9c	0.022*
Ferritin	220.58±33.5a	120.93±24.0b	1083.03±137.8c	0.000**

*Significant at P-value ⩽ 0.05, ** significant at P-value ⩽ 0.01

Association between COVID-19 patients and diabetic patients with COVID-19 according to infection level

Table 4 showed the association between the patients with diabetes mellitus infected with COVID-19 and patients with COVID-19 only according to infection duration at >7,7-14 and <14 days according to parameters understudy

Where the Mean of IN and D-dimer shows significant differences at (0.033 and 0.011) respectively for all infection duration categories, while FBG, HbA1c, INR, INS, CRP, and ferritin don't show any significant differences for all day's category, the statistical analysis was made at p-value (≤ 0.01 & ≤ 0.05).

We found highly significant differences in INR at (22.52±8.0) in >7 days of infection because the infection by SARS-CoV-2 in pancreatic beta cells can generate insulin resistance and decreased insulin secretion, worsening hyperglycemia in the acute phase of infection, whereas, in the chronic phase, it may trigger autoimmunity of these pancreatic cells in predisposed patients.

Table 4. Association between COVID-19 patients and diabetic patients with COVID-19 according to infection duration.

Parameters	COVID+DM			COVID only			Sig.
	>7 days	7-14	<14	>7 days	7-14	<14	
FBG	265.23±17.0	223.54±18.3	273.36±58.5	114.95±14.6	108.81±10.0	154.25±5.4	0.707
HbA1c	9.06±1.9	9.07±2.3	9.57±1.9	5.37±0.8	5.30±0.4	5.46±0.2	0.885
INR	22.52±8.0	14.69±2.2	7.11±1.0	8.08±1.7	11.22±1.4	3.44±0.4	0.546
INS	0.29±0.03	0.28±0.042	0.38±0.10	0.31±0.04	0.29±0.04	0.35±0.07	0.061
IN	28.00±2.3	26.91±4. 3	11.27±1.4	30.98±7.8	40.28±7.9	7.70±1.8	0.033*
CRP	71.48±7. 2	55.71±4.6	39.19±8.6	39.78±4.1	38.97±7.5	70.16±9.1	0.430
D-dimer	1573.75±202.4	961.91±98.0	994.62±46.5	1523.36±252.2	704.00±86. 3	3903.13±112. 5	0.011*
Ferritin	392.79±46.3	819.13±70.5	720.04±27.3	220.58±34.5	120.93±14. 3	1083.03±137.8	0.114

*Significant at P-value ≤ 0.05, ** significant at P-value ≤ 0.01

The correlation coefficients between COVID-19 patients and blood parameters

Table 5 showed the correlation between COVID-19 patients and infection duration at (1-14 days) according to the parameters under study. Where the correlation coefficient (r) of FBG with HbA1c, CRP and ferritin shows significant differences at (0.503, 0.495, and 0.693) respectively, while with INR, INS, IN, D-dimer and infection duration didn't show any significant differences. HbA1c with CRP and d-dimer shows significant differences at (0.699, and 0.458) respectively. while INR, INS, IN, ferritin and infection duration don't show any significant differences.

INR with INS and IN showed significant differences at (0.762 and 0.956) respectively, while CRP, D-dimer, ferritin, and infection duration didn't show any significant differences. INS with IN showed significant differences at (0.737), while with CRP, D-dimer, ferritin, and infection duration didn't show any significant differences. IN doesn't show any significant differences with any markers. CRP with D-dimer and ferritin showed significant differences at (0.719 and 0.601) respectively, while infection duration didn't show any significant differences.

D-dimer and ferritin show significant differences at (0.566), while infection duration doesn't show any significant differences. Ferritin with infection duration shows significant differences at (0.587). the statistical analysis was made at a p-value (≤ 0.01 & ≤ 0.05).

Table 5. The correlation coefficients between COVID-19 patients and blood parameters.

Parameters		HBA1c	INR	INS	IN	CRP	D-dimer	Ferritin	CT-Scan	Covid duration
FBG	r	0.503**	0.057	0.121	0.191	0.495**	0.136	0.693**	0.703**	0.346
	p	0.005	0.765	0.522	0.312	0.005	0.473	0.000	0.000	0.061
HbA1c	r	1	0.105	0.039	0.027	0.699**	0.458*	0.345	0.478**	0.026
	p		0.580	0.839	0.888	0.000	0.011	0.062	0.007	0.891
INR	r		1	0.762**	0.956**	0.165	0.228	0.117	0.182	0.025
	p			0.000	0.000	0.383	0.225	0.537	0.335	0.897
INS	r			1	0.737**	0.190	0.347	0.210	0.211	0.050
	p				0.000	0.314	0.060	0.265	0.263	0.793
IN	r				1	0.265	0.230	0.260	0.322	0.093
	p					0.158	0.222	0.166	0.083	0.626
CRP	r					1	0.719**	0.601**	0.774**	0.079
	p						0.000	0.000	0.000	0.679
D-dimer	r						1	0.566**	0.530**	0.147
	p							0.001	0.003	0.438
Ferritin	r							1	0.898**	0.587**
	p								0.000	0.001
CT-Scan	r								1	0.454*
	P									0.012

*Significant at the 0.05 level (2-tailed), **Significant at the 0.01 level (2-tailed).

The correlation coefficient between diabetic patients with COVID-19 and blood parameters

Table 6 showed the correlation coefficient between mellitus infected COVID-19 patients and infection duration at (1-14 days) according to the parameters under study. Where the correlation coefficient (r) of FBG with INR shows significant differences at (0.647), while with HbA1c, INS, IN, CRP, D-dimer, ferritin, and infection duration don't show any significant differences. HbA1c doesn't show any significant differences from other markers.

INR with INS and IN shows significant differences at (0.394 and 0.791) respectively, while with CRP, D-dimer, ferritin and infection duration don't show any significant differences. INS with IN and infection duration shows significant differences at (0.592 & 0.369) respectively, while CRP, D-dimer, and ferritin don't show any significant differences. IN, CRP, D-dimer and ferritin don't show any significant differences with any markers. the statistical analysis was made at a p-value (≤ 0.01 & ≤ 0.05).

Table 6. The correlation coefficient between diabetic patients with COVID-19 and blood parameters.

Parameters		HbA1c	INR	INS	IN	CRP	D-dimer	Ferritin	CT-Scan	Covid duration
FBG	r	0.323	0.647**	-0.200	0.250	0.127	0.029	0.077	0.147	0.072
	p	0.076	0.000	0.280	0.175	0.497	0.875	0.680	0.430	0.699
HbA1c	r	1	0.169	-0.040	0.078	0.027	0.025	0.007	-0.168-	-0.027-
	p		0.364	0.830	0.675	0.885	0.892	0.971	0.365	0.887
INR	r		1	-0.394*	0.791**	-0.025-	-0.030	-0.102-	-0.100-	-0.177-
	p			0.028	0.000	0.894	0.871	0.585	0.594	0.341
INS	r			1	-0.592**	0.024	-0.120	-0.126-	0.058	0.369*
	p				.000	0.900	0.519	0.499	0.757	0.041
IN	r				1	-0.020	-0.096	-0.111-	-0.085-	-0.219-
	p					.913	0.606	0.551	0.648	0.237
CRP	r					1	0.287	0.206	0.272	-0.271-
	p						0.117	0.265	0.139	0.141

D-dimer	r	1	0.331	0.328	-0.154-
	p		0.069	0.072	0.408
Ferritin	r		1	0.576**	0.098
	p			0.001	0.598
CT-Scan	r			1	0.586**
	P				0.001

* Significant at the 0.05 level (2-tailed), ** Significant at the 0.01 level (2-tailed).

DISCUSSION

A broad spectrum of COVID-19 severity ranged from mild to severe often to death, and that influenced by many factors' outcomes including sex, age, infection level, duration of infection and preexisting chronic diseases like hypertension and diabetes [18].

Generally, this study found that patients with diabetes mellitus individuals with severe COVID-19 infection levels show high significant value differences from the patients without diabetes as listed in table 1. Our results agreed with the finding obtained from a Chinese study, in which COVID-19 patients with uncontrolled diabetes had a high risk of mortality [16]. Moreover, a British cohort showed that COVID-19 patients with diabetes had a 7.3% rate of motility [5]. In the current study, we find a significantly high level of blood parameters in all COVID-19 patients with diabetes than in patients with COVID-19 only (Table 1). Previous studies by Chen et al [15] showed Al found an increase in many blood markers, including haemoglobin, CRP, dimer, ferritin, and other factors, and this is consistent with the results we obtained, which showed an increase in these parameters for diabetic patients with COVID-19 compared to non-diabetics. The reason for such differences in COVID-19 severity with diabetes is likely due to multifactorial syndromes of diabetes, we found that diabetic patients had a higher percentage of FBG, HBA1c, and INR as 273.36± 16.4,9.57± 1.9 and 22.52± 1.5 respectively compared to non-diabetic patients as 154.25± 11.2, 5.46± 0.2, and 11.22± 1.4, respectively.

Many studies have mentioned that there was a significant association between diabetes and increased morbidity of COVID-19, there was evidence that people with diabetes show an increased risk of severe infection levels by COVID-19, some findings showed that the prevalence of diabetes among 16% of infected patients with mild infection level of COVID-19 infection [19], these results agreed with this study's finding that the percentage of inflammatory parameters as FBG and Insulin sensitivity increased significantly for diabetic patients infected with COVID-19 (Table 2).

The research mentioned that COVID-19 disease may cause damage to B cells in the pancreas through the direct cellular effect of the virus, which in turn leads to high blood sugar as a result of a decrease in the concentration of insulin in the blood and an increase in some hematological parameters with the increase in the period of infection [20], that it was consistent with the current results that showed a high level of HbA1c at (9.57±1.9).

One of the most important reasons that lead to an increase in the pathological effect of the Coronavirus on diabetic patients is the increase in the period of infection and the increase in the recovery period [21], as the above table showed the association between infection duration of COVID-19 and diabetes patients, Therefore, by studying the effect of the period of infection, we were able to focus light on the characteristics of such new cases.

Viral studies in which culture has been performed and where viral replication can be elicited are also better data for inferring the infectious period, relative to viral load

estimates alone [22]. Therefore, our data included mean periods of 7-14 days after symptoms, where some research indicates that the duration of detection of the virus can be during this period [23].

In the current study, we found the mean of parameters increased with the infection duration except for CRP, D-dimer and ferritin elevated in the first 7 days then decreased after that, this is due to the effect of these inflammatory markers being higher than blood parameters at the beginning of the disease. After having assessed the association between infection duration with the severity of COVID-19, Wu et al [23, 24] indicated that the rate of infection with the COVID-19 becomes more severe as the incubation period increases, and thus the proportions of some parameters in the blood such as HbA1c, clotting factor (INR) and fasting blood sugar levels rise (Table 3).

In the current study, we found highly significant differences in our parameters in diabetes patients infected with COVID-19 in contrast to the COVID-19 patients only, where its high levels in the blood can be explained by the high association between, diabetes and SARS-CoV-2 infection can follow a two-way model as SARS-CoV-2 worsening pre-existing diabetes or predisposing non-diabetic people to diabetes. The mechanism that allows the entry of the virus into the cell involves ACE-2, which is highly expressed in the liver and pancreas, especially beta cells that produce insulin hormones [25].

Hyperglycemia and insulin resistance, as a result of diabetes, induce increased synthesis of advanced glycation end products and pro-inflammatory cytokines like CRP that generate oxidative stress [15], which is consistent with our findings when we found an increase in the percentage of CRP, ferritin, D-dimer.

It is necessary to measure some blood and immunological parameters to assess the severity of COVID-19, so we can easily assess patient severity and infection by monitoring these indicators In our findings, we analyzed some haematological parameters of COVID-19 patients and among these parameters, we found a decrease in the level of HbA1c and increased levels of CRP, ferritin, and d-dimers, these results are consistent with Rahman et al [26], who find Hematological parameters are associated with COVID-19 severity, Also, some other studies supported the present findings describing the evidence of the correlation between CRP, D-dimer and ferritin levels in Covid -19 patients [27, 28]. Lippi et al make four different studies about the blood parameters in covid -19 patients where it has been showing that there is a high correlation between HbA1c level and COVID that contributed to the good diagnosis of disease, especially the role of coronavirus in clot blood formation [27].

Our results showed that the correlation coefficient between ferritin and COVID-19 in the blood increased significantly since ferritin is a protein that can store iron, Therefore, the elevated concentration can induce cytokine storms and severity in COVID-19 patients [29, 30]. Thus, ferritin levels can serve as a factor for monitoring COVID-19 severity [31].

In the current study, we noticed highly significant differences between inflammatory proteins and COVID-19 such as CRP, d-dimer and ferritin which were consistent with a previous study that showed that COVID-19 patients had significantly increased levels of serum inflammation-related biomarkers, represented by interleukin-6, D-dimer and C-reactive protein, as well as biomarkers related to disease prognosis [17, 32].

Individuals with diabetes are more prone to SARS-CoV-2 infection, and the severity of the disease is on the rise. Pathogenic links between DM and COVID-19 include raising

fasting blood sugar and the release of inflammatory proteins that lead to the cytokine storm [33].

The severity of COVID 19 is highly correlated with glycemic such as insulin, insulin resistance, insulin sensitivity, and fasting blood sugar, because of the ability of the Coronavirus to ACE 2 receptors of Beta cells in the pancreas, liver cells and other organs [34]. Table 6 showed highly significant differences between these parameters in diabetic patients infected with COVID-19.

Previous studies showed that diabetes was a risk factor for multiple viral infections and deaths, including 2009 A (H1N1) influenza, MERS-CoV and SARS-CoV [35], so the correlation coefficient was tested between these two parameters. Besides the current results, we also analyzed the Ct-Scan data and found that diabetic patients had a higher incidence of COVID-19 than non-diabetics, as these results indicate that diabetic patients with COVID-19 have severe inflammatory responses and lung infiltration, which was the main cause of elevated inflammatory protein and other haematological parameters [22].

In the current study, we found that the concentration of serum D-dimer of diabetic patients was significantly higher than that of nondiabetic patients indicating that COVID-19 patients with diabetes are more likely to develop a hypercoagulable prothrombotic state, These results are consistent with what was mentioned by the researcher Le et al [16], who mentioned that the D-dimer is one of the main markers of coagulation activity and the higher concentration in serum is closely related to a variety of thrombotic diseases, including myocardial infarction, cerebral infarction, pulmonary embolism, and venous thrombosis.

CONCLUSION

We concluded that the diabetes mellitus patients infected with COVID-19 suffer from a high increase of inflammatory proteins and parameters associated with diabetes compared to other patients infected COVID-19 only, making them more susceptible to disease and more deaths compared to other people.

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AUTHOR CONTRIBUTIONS

Conception and design of the study: Maryam A. Hussain and Ali H. Al-Saadi. Drafting the manuscript: Ali H. Al-Saadi. Analysis and/or interpretation of data: Maryam A. Hussain.

CONFLICTS OF INTEREST

There is no conflict of interest among the authors.

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