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A Study of Some Biochemical Parameters in COVID-19 Patients with Diabetes Mellitus: Comparative Study

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Abstract

COVID-l9 is considered a global health emergency, this disease affects all individuals and its symptoms are similar to the common cold. The purpose of this study is to compare diabetic and non-diabetic patients in some biochemical tests of patients infected with COVID-l9. Of the l20 patients included in the study, 7l patients were males (59.l7%) and 49 were females (40.83%). The study showed that the highest percentage was in males with diabetes (63.33%), followed by non-diabetics (55.00%), without significant difference. As for the age group, most patients were over 50 years, and it was most common among non-diabetics in addition to diabetes. Mean glucose was significantly different between the diabetic group and the non-diabetic group. For the diabetic group, the mean blood sugar was 229.22 ± 82.25mg/dl, while the mean blood sugar in the non-diabetic group was l32.25 ± 44.08 mg/dl. In addition, there was a significant difference in mean HbA1c between the diabetic and non-diabetic groups $p < .001$. For the diabetic group, the mean HbA1c was 7.5l ± l.27 %, but in the non-diabetic group, the mean HbA1c was 5.41 ± 0.73%. While there was a significant difference between the two groups with and without diabetes in the mean ferritin ratio $p < .00l$. For the diabetic group, the mean serum ferritin was 638.78 ± 327.78 ng/ml, although in the non-diabetic group, the mean serum ferritin was 393.74 ± 330.83 ng/ml. There were no significant differences between the diabetic and non-diabetic group in the mean of D-dimer, urea, creatinine and uric acid, in the diabetic groups, the mean was 6.00 ± 5.80 ug/ml, 86.02 ± 64.27 mg/dl, 1.64+1.45mg/dl and 5.37 ± 3.11mg/dl, respectively. While in the non-diabetic group, the mean was 5.82 ± 5.76 ug/ml, 74.68 ± 68.27mg/dl, 1.88 ± 2.62 mg/dl, and 4.86 ± 2.62 mg/dl, respectively.

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Keywords: Type 2 diabetic mellitus; Non-diabetic mellitus; HbA1c; Uric acid; Creatinin; Ferritin; D-dimer.

1. Introduction

COVID-2019 is an emergent infectious disease with uncertain etiology take place in China the city of Wuhan, Hubei Province [1]. COVID-19 is a pandemic that created confusion and fright around the world, and consider originate from infected bats, and can be transmitted to humans and animals, as well as to humans [2] Impairment in renal function can result in obstruction of excretion of metabolites and toxicity in the body that effect on balance of acid-base in the human body. Furthermore, when severity damage in renal function, uremia will occur, which is hazardous on life [3]. Dynamic changes in renal function after infection with COVID-19 and its prognostic value for deprived prognosis of COVID-19 have not yet been reported [4]. The COVID-19 can damage the renal function via diverse mechanisms, and the more severe is the function damage. There has been slight discussion about early monitoring of kidney function to predict the changes condition in-patient, thus reducing mortality [5]. The D-dimer can specifically reflect secondary hyper fibrinolysis and a hypercoagulable state in the body and serves as an index sensitive to reflecting thrombosis [6]. Ferritin is a main mediator of immune dysregulation, particularly under extreme hyperferritinemia, by pro-inflammatory effects and direct immune-suppressive that contribute to the cytokine storm [7]. Ferritin is located in heart, liver, kidney, spleen, and intestinal mucosal cells but it is unclear whether serum ferritin reflects or causes inflammation, or whether it is involved in an inflammatory cycle [8]. The aim of this study was to compare between diabetic and non-diabetic patient in some biochemical test in-patient with COVID-19.

2. Material and Methods

In this prospective study, blood samples were collected from patients who tested positive for PCR of COVID-l9 admitted to Al-Shifa Medical Center in Baghdad's Capital, Al- Rusafa during the period from December 1, 2021 to February 28, 2022. Ethical approval for this study was acquired from the Iraqi Ministry of Health and Environment (No.2311in17/1/2022).

Nomenclature			
HbA1c	Hemoglobin A1c	c r	Creatinine
SARS- CoV	Severe acute respiratory syndrome corona virus 2	T2DM	Type 2 diabetes mellitus
PCR	Polymerase chain reaction test	FBS	Fasting blood sugar test

One hundred and twenty cases with complete clinical data were defined with sever COVID-19 patients divided into two groups the first group comprise of 60 patients with diabetics and the second group with 60 patients without diabetics. Biochemical test was carried out for renal function test (urea, creatinin and uric acid), ferritin and D-dimer test.

3. Results

3.1. Gender

Among the 120 patients included in the study 71 patients were males (59.17%) and 49 were females (40.83%). The most frequently observed category of gender was male (n = 71, 59.17%) as a whole and within the Non-diabetic group (n = 33, 55.00%) as well as the diabetic groups (n = 38, 63.33%) Table 1 and 2.

Table 1 Distribution of patient's groups according to gender

	Covid-l9 disease patients' groups	
gender	Non-Diabetic Group	Diabetic Group
Female	27 (45.00%)	22 (36.67%)
Male	33 (55.00%)	38 (63.33%)
Total	60 (l00.00%)	60 (l00.00%)

3.2. Age

More than 50 years age group was the most frequent age within the Non-Diabetic Covid-19 disease (n = 31, 51.67%) as well as the Diabetic Covid-19 disease, (n = 33, 55.00%). Frequencies and percentages are presented in Table 2.

Table 2 Distribution of subjects based on age

	Covid-19 disease patients' groups		
	Non-Diabetic (Mean ± SD)	Diabetic (Mean ± SD)	P value
Age (years)	51.22± 16.94	53.45±15.22	0.45
Age groups	n (%)	n (%)	
18- ≤30	7 (11.67%)	3 (5.00%)	ns
31- ≤40	12 (20.00%)	9 (15.00%)	ns
41- ≤50	10 (16.67%)	15 (25.00%)	ns
>50	31 (51.67%)	33 (55.00%)	ns
Total	60 (100.00%)	60 (100.00%)	

3.3. Glucose

The mean level of glucose was significantly different between the diabetic and Non-diabetic group, $t(90.31) = 8.05$, $p < .001$. For diabetic group, serum glucose had an average of 229.2 ± 81.56 mg/dl, (SE_M = 10.62, *Median* = 224.00). For Non-diabetic group, serum glucose had an average of 132.25 ± 43.71mg/dl (SEM = 5.69, *Median* = 123.00). The results are presented in Table 3. A box plot of the ranks is presented in Fig. 1-A.

3.4. HbA1c

The mean of HbA1c was significantly different between the diabetic group and Non-diabetic groups $t(118) = 11.13$, $p < .001$. For diabetic group, HbA1c had an average of 7.51 ± 1.26% (SE_M = 0.16, Median = 7.35). For Non-diabetic group, HbA1c had an average of 5.41 ± 0.72% (SEM = 0.09, Median = 5.50). The results are presented in Table 3. A box plot of the ranks is presented in Fig. 1-B.

3.5. Serum ferritin

The mean of ferritin was significantly different between the diabetic and Non-diabetic groups, $t(118) = 4.08$, $p < .001$. For diabetic group, serum ferritin had an average of 638.78 ± 325.04ng/ml (SE_M = 42.32, Median = 676.95). For Non-diabetic group, serum ferritin had an average of 393.74 ± 330.83 ng/ml (SEM = 42.71, Median = 292.30). The results are presented in Table 3 and Fig. 2-A.

3.6. Serum D-dimer

The mean of D-dimer was not significantly different between the diabetic and Non-diabetic group, $t(118) = 0.17$, $p = .865$. The for diabetic group, serum D-dimer had an average of 6.00 ± 5.75ug/ml (SE_M = 0.75, Median = 3.90). For Non-diabetic group, serum D_dimer had an average of 5.82 ± 5.71 ug/ml (SE_M = 0.74, Median = 2.34). The results are presented in Table 3 and Fig. 2-B.

3.7. Urea

The mean of Urea was not significantly different between the diabetic and Non-diabetic groups t(118) = 0.94, p = .351. For diabetic group, Urea had an average of 86.02 ± 63.73mg/dl (SE_M = 8.30, Median = 62.00). For Non-diabetic group, serum Urea had an average of 74.68 ± 67.70mg/dl (SE_M = 8.81, Median = 50.50). The results are presented in Table 3 and Fig. 2-C.

3.8. Serum creatinine

The mean of creatinine was not significantly different between the diabetic and non-diabetic groups. t(118) = 1.32, p = .189. For diabetic group, serum creatinine had an average of 1.64 ± 1.45mg/dl (SE_M = 0.19, Median = 1.05). For Non-diabetic group, serum creatinine had an average of 1.66 ± 1.96mg/dl (SE_M = 0.26, Median = 0.93). The results are presented in Table 3 and Fig. 2-D.

3.9. Serum uric acid

The mean of uric acid was not significantly different between the diabetic and non-diabetic group groups. t(118) = 0.97, p = .333. For diabetic group, serum uric acid had an average of 5.37 ± 3.08mg/dl (SE_M = 0.40, Median = 5.05). For Non-diabetic group, serum uric acid had an average of 4.86 ± 2.59mg/dl (SE_M = 0.34, Median = 4.50). The results are presented in Table 3.

Table 3 Summary Statistics for Diabetic groups and non-diabetic group to measurement Kidney function and other Biochemical Variables

variables	groups	Median (lst Q- 3rd Q)	Mean± SD	SEM	p-values
FBS	Diabetics	224.0 (l5l.75- 284.25)	229.2± 8l.56	l0.62	< 0.00l
	Non-diabetics	l23.0 (97.00- l54.75)	l32.25± 43.7l	5.69	
HbA1c	Diabetics	7.35 (6.80- 7.90)	7.5l± l.26	0.l6	< 0.00l
	Non-diabetics	5.50 (4.78- 5.89)	5.4l± 0.72	0.09	
Ferritin	Diabetics	676.95 (3l8.83- l000)	638.78± 325.04	42.32	< .00l
	Non-diabetics	292.30 (l57.40- 553.78)	393.74± 328.07	42.7l	
D-dimer	Diabetics	3.90 (0.88- 9.98)	6.00± 5.75	0.75	0.865
	Non-diabetics	2.34 (l.73- 9.75)	5.82± 5.7l	0.74	
Urea	Diabetics	62.00 (40.00- lll.0)	86.02± 63.73	8.30	0.35l
	Non-diabetics	50.50 (26.00- l04.0)	74.68± 67.70	8.8l	
Cr	Diabetics	l.05 (0.68- 2.03)	l.64± l.45	0.l9	0 .l89
	Non-diabetics	0.93 (0.6l- l.83)	l.66± l.96	0.26	
Uric acid	Diabetics	5.05 (2.78- 7.30)	5.37± 3.08	0.40	0 .333
	Non-diabetics	4.50 (3.00- 6.30)	4.86± 2.59	0.34	

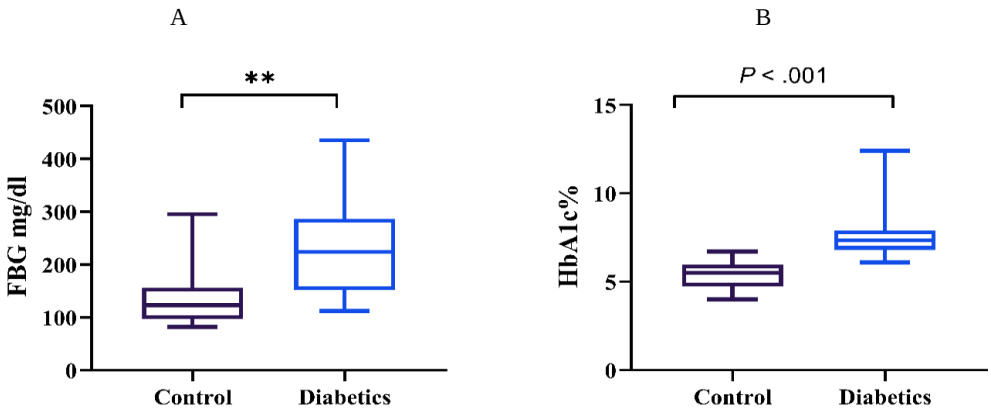

Fig 1. The rank values of FBS and Hblc % by levels of group with the error bars represent a 95% confidence interval of the means (± l.96 standard deviations)

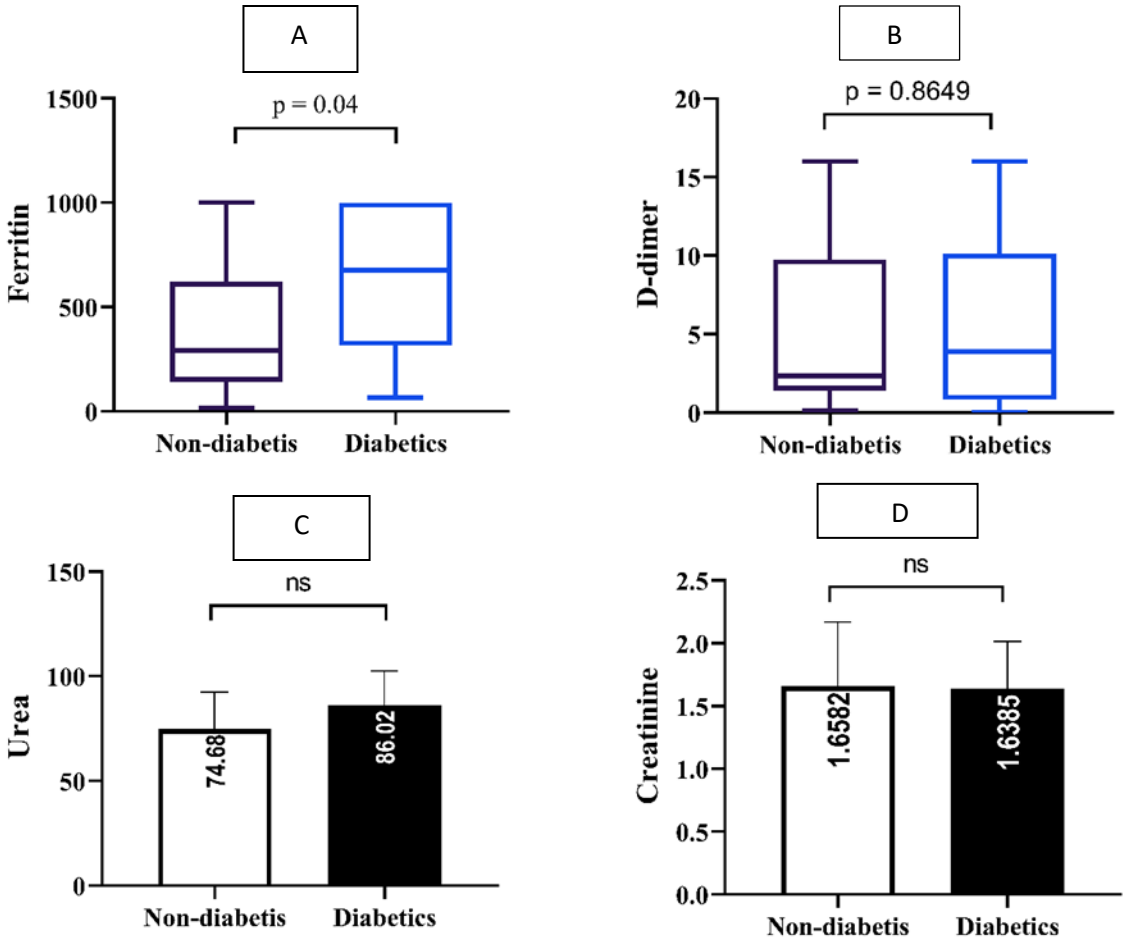

Fig 2. The rank values of Ferritin, D-dimer and the mean values of Urea and Creatinine by levels of group with the error bars represent a 95% confidence interval of the means (± l.96 standard deviations)

4. Discussions

COVID-19 is pandemic that creates confusion and fright around the world, consider originate from infected bats, and can be transmitted to humans and animals, as well as to humans [9]. In present prospective study performance in both diabetic and non-diabetic patients were of no significant difference and due to increase exposure to COVID 19 infection therefore a high male infected ratio was 59%, this is in agreement with Ad'hiah *et al.* [10]. Many countries such as Sweden Italy, , Switzerland, Scotland and Belgium have reported an elevation in percentage of cases among women according to Global Health 50/50 but other countries such as Costa Rica ,Greece, Iran , Pakistan , Thailand and Mexico that have the rates of infection among men appear to be much higher [2] .In the current study, the data showed that all ages are susceptible to infection with COVID-19 in both diabetic and non-diabetic patients and the range increase >50 years old with no significant association found. This study is in agreement with Mohammed *et al*. who revealed during a study there are non-significant values with a great percentage frequency of the age range about between 64-74 years were 25.9% owing to immune status, most infected persons with COVID- 19 were non- smokers with an incident of 59%, the percentage of contact's history with others who were infected with COVID- 19 was 44% of the total number, 56% of patients with COVID- 19 infections in this study who were suffering from the history of chronic diseases [11].

The major marker of blood glucose control is Glycated hemoglobin (HbA1c), which primarily reflects the level of blood glucose of patients in the previous two to three months and has become golden standard for indicating long-term blood glucose monitoring for diabetes [12].

In new study, that made the association of HbAlc levels with clinical outcome of COVID-19 patients, finding that significantly different between diabetic and non-diabetic in patients.Yuan *et al*.**,** who suggested that HbAlc might be a prognostic marker for evaluating the risk of death in COVID-19 patients. Besides, by using the criterion of HbA1c ≥ 6.5%, we observed further increase of mortality in patients with newly identified DM compared with pre-diagnosed DM. Moreover, in patients with pre-diagnosed DM, the mortality was decreased in patients treated with anti-hyperglycaemic drugs. Early identification of diabetes and initiation of appropriate treatment might be vital to improve clinical outcome in COVID-19 patients [13].

The D-dimer can specifically reflect secondary hyper fibrinolysis and a hypercoagulable state in the body and serves as an index sensitive to reflecting thrombosis. Previous studies suggested that monitoring coagulation function and HbA1c in patients with DM played a role in refereeing the progression of complications of the condition, particularly for microangiopathy [6]. In the present study, there were no significant differences in parameter of D-dimer between men and women in T2DM with COVID-19 patients who admission to the hospital this study is agreement with [12].Ferritin is a main mediator of immune dysregulation, particularly under extreme hyperferritinemia, by pro-inflammatory effects and direct immune-suppressive that contribute to the cytokine storm [7]. Ferritin is located in heart, liver, kidney, spleen, and intestinal mucosal cells but it is unclear whether serum ferritin reflects or causes inflammation, or whether it is involved in an

inflammatory cycle [8].The fatal outcomes by COVID-19 are accompanied by cytokine storm syndrome, thus the severity of disease dependent on the cytokine storm syndrome [3]. Several diabetes patients exhibit higher serum ferritin levels [14], and it is known that they face an elevated probability to experience serious complications from COVID-19[15]. Thus, levels of ferritin can be an essential factor i the severity of COVID-19[14]. The serum ferritin increase from damaged of the cells and is consequently a marker of cellular damage, Ferritin has no circadian rhythm and entirely taken up by liver [8].The current study appeared that significant and a higher serum ferritin level was independently associated with severe COVID-19, this study correspond with Mukesh et *al*., who found there significant increased levels of level serum ferritin as the level of HbA1c high in the cases. The high significant levels of serum ferritin were saw in poorly controlled diabetic COVID-19 cases in compare to well-controlled diabetic COVID-19 cases. Correlation analysis between cases of diabetic COVID-19 and non-diabetic COVID-19 controls indicates that serum ferritin level increases as the glucose level increases in the body [16].Diabetes and its associated with hyperferritinemia in the affected COVID-19 individuals will add to the problem. There are at least one underlying disorder (hypertension, diabetes, and chronic obstructive pulmonary disease) in severe cases compared to mild cases [17].Zhang *et al*., who shown that association of hyperglycemia without DM with a increase risk of critical care admission, mechanical ventilation, and death. Besides, the rate of mortality in COVID-19 was reported to be worse in patients with elevated in level of fasting blood glucose even when it is in the normal range [18].

Several mechanisms were assumed to explain the worst effect in COVID-19 patients with diabetic. First, this include higher in marker of inflammation like D-dimer is strongly associated with serious COVID-19 infection and mortality [19].Thus diabetic patients were found to have higher levels of this marker [18]that indicate their increase risk of serious presentation and worse outcome. Second, the infection with COVID-19 has been associated with risk of abnormal coagulation pattern and thrombosis [20]. Non-survivors have higher significant in D-dimer [20], the levels of fibrin degradation product, longer prothrombin and activated partial thromboplastin time [20].The diabetic's cause's thrombosis since it influences to prothrombotic state secondary to coagulative activation, endothelial dysfunction, and platelet hyper reactivity mediated by hyperglycemia, insulin resistance, inflammation and oxidative stress [21]. The SARS-CoV-2 can cause β cell damage, which could lead to a new onset diabetes or sustained in-hospital hyperglycemia [22]. Besides, it might be precipitate acute hyperglycemic disaster in the form of diabetic ketoacidosis or hyperglycemic hyperosmolar state [22]. Uric acid was considered a predictor of gout quality and a product of purine metabolism [23]. Hyper uric acid refers to a condition, which of UA concentration is higher in human serum than the upper limit of normal range under the condition of a normal purine diet, it more than 420 mmol/L in men and 360 mmol/L in women . The incidence rate of HUA due to changes in population, lifestyle, dietary habits and drug use, has been increasing worldwide. The occurrence of HUA was upper in T2DM patients [24]. There were several differences in laboratory results between the diabetes and the non-diabetes with COVID-19. Urea nitrogen (BUN), a marker of kidney function, was higher in the diabetes group .In our study, the result showed non-significant difference in all urea, creatinine and uric acid.

In previous study that conducted by Luo *et al*., who was appeared the outcomes in diabetes patients and non-diabetic with COVID-19 the Creatinine level (μmol/L) were 63.6 (53.3- 78.0) in non-diabetic and 63.0 (53.0-77.4) in diabetics with significant difference and the $P < 0.001$. While the uric acid level (μmol/L) in non-diabetics were 258 (204- 336) and in diabetics were 257 (205-336) with non-significant differences the $P= 0.499$ [25].

5. Conclusions

The level of HbA1c in the non-diabetic patients it was high than normal range , There are significant differences between the diabetic group and the non-diabetic group in mean of HbA1c, ferritin,The level of serum ferritin was higher in diabetic than non-diabetics in patients with COVID-l9.

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