The Correlation between Biochemical Indicators in COVID-19 Patients with and without Diabetes Mellitus in Basra, Iraq

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https://dx.doi.org/10.13005/bpj/2822

(Received: 01 September 2023; accepted: 04 October 2023)

The coronavirus disease (COVID-19) is an infectious viral illness that leads to the development of acute respiratory syndrome. It exhibits a high level of contagiousness. The aforementioned virus is accountable for an incidence of pneumonia that transpired in early December 2019 in Wuhan, situated in the People's Republic of China. The global pandemic declaration on March 11, 2020, marked a significant turning point in the world's demography, as the virus had tragically claimed the lives of over 5.3 million individuals worldwide. The emergence of the Coronavirus (COVID-19) pandemic has presented an unparalleled catastrophe, resulting in the loss of many lives via several channels including social, psychological, physical, and economic dimensions. The danger associated with the virus originates from its heightened transmissibility and extensive mutational variability, as well as its impact on several bodily systems including the circulatory, neurological, renal, hepatic, nervous, and endocrine systems. The pathogenesis of Coronavirus disease 2019 (COVID-19) is intricate, and its clinical presentation is diverse, exhibiting various imaging findings that vary based on the severity of the illness and its progression through time. A general statistical comparison was made for the biochemical markers in the patients infected with only Coronavirus and patients infected with Coronavirus and complications of diabetes mellitus compared to the control group according to gender, in order to monitor the role of different biomarkers in causing a disease, with an evaluation of the difference in their levels, and the study aimed to investigate biomarkers and study the relationship between these biomarkers for COVID-19 patients with and without Diabetes Mellitus, to provide a dynamic approach to understanding the disease to diagnosis and follow-up, so as to improve the development of patients' treatment. The study performed a representative sample of (238) participants between the ages (25-80) year, of whom (81) were in a healthy control group, (78) were infected only with Coronavirus, (79) were infected with Coronavirus and had complications of diabetes mellitus, who visited Al-Basra Teaching Hospital and Allmwanei Hospital in Al-Basra province between October 2021 and February 2022. The age average for the study population was (25-80) years. Serum and blood levels of human CBC, ESR, CRP, Ferritin, D-Dimer, IL 6, Albumin, FBS, HbA1c, Troponin, Cholesterol, Triglyceride, HDL, LDL, VLDL, Creatinine, Urea, Uric acid and GFR were measured. The results show a highly significant increase in WBcs, ESR, CRP, Ferritin, D-Dimer, IL-6, Creatinine, Urea and Uric acid., and a highly significant decrease in lymphocyte, albumin, HDL and GFR for patients compared to the control group as a total number and the number of males and females separately, While the results of comparing biochemical markers in the patients infected with Coronavirus and who had a diabetic complication a higher significant increase than patients without diabetic complication. The study of these biomarkers provides a dynamic approach to understanding the disease to diagnosis and follow-up, so as to improve the development of patients' treatment and study the relationship between these biomarkers for COVID-19 patients with and without Diabetes Mellitus.

> Keywords: Biochemical indicators; Clinical Markers; COVID-19; Diabetes Mellitus; Inflammatory Markers.

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Coronavirus (COVID-19) will continue to be a major threat to public health. Understanding the pathophysiology and physiology of the organ function, that is targeted by the virus, was proven to be crucial for the rational creation of medications¹. COVID-19 disease has been characterized by a complex pathophysiology, and heterogeneous clinical presentation, with a wide range of imaging findings, depending on both disease severity and time course². The pathogenesis of Coronavirus disease 2019 (COVID-19) is intricate, and its clinical presentation varies widely. The imaging results associated with the disease exhibit considerable diversity, influenced by the severity of the illness and its progression through time².

The scientific community needs reliable biomarkers that indicate the development of The scientific community needs reliable biomarkers that indicate the development of coronavirus disease (COVID-19), these biomarkers are measurable biochemical that can be used to determine disease severity, these biomarkers can be physiological, anatomical, or biochemical, and can be objectively measured and evaluated. They also allow assessment of drug response and allow timely therapeutic intervention. Clinical symptoms can also be interpreted with greater confidence by using biochemical markers in order to classify patients at risk according to the speed and severity of disease progression. Also, These biomarkers are associated with an understanding of the mechanisms causing viral disease, as well as cellular damage, which are useful for clinical management and prevention of death risk³.

Biomedical markers in COVID-19 disease can be useful in several areas, including early detection of the disease, identifying and classifying the severity of the disease, the possibility of admission to the hospital and the formulation of standards for staying in the intensive care unit and determine the criteria for leaving the intensive care unit or hospital⁴.

Epidemiology, in fact, builds on clinical study, observation, and analysis, as well as screening and diagnosis. Changes in biochemical markers indicate changes in the composition of body fluids and tissues through which, it is possible to find a homogeneous classification of the disease and its associated risk factors. This in turn expands our basic information related to the early manifestations of the disease and up to the final stages of it^5 .

Numerous studies have demonstrated that diabetes mellitus could induce diverse complications, such as diabetes mellitus complications nephropathy, diabetes mellitus complications cardiovascular, diabetes mellitus complications neuropathy, and diabetes mellitus complications liver, and diabetes mellitus complications diabetic retinopathy which have been the major causes of its morbidity and mortality⁶.

Biochemical Indicators and Inflammatory markers of COVID-19

COVID-19 disease has been characterized by a complex pathophysiology, and heterogeneous clinical presentation, depending on both disease severity and time course. Accordingly, several factors which contribute to the early diagnosis of COVID-19 pneumonia have been identified, providing important information regarding the inflammatory process, organ damage, severity of the disease, the extent of stay in the stay in (ICU) and mortality, so in this research the evaluation of levels of different inflammatory and biochemical indicators in patients infected with Coronavirus with or without diabetes, such as:

- 1. Complete blood count (CBC) is a regular study for all patients that gives essential parameters that can help with clinical care, such as diagnosis, the presence of infection or inflammation, anaemia, therapy response, aetiology, and the stage of inflammatory disease. According to a study conducted in five nations throughout Asia, Africa, and the United States, (CBC) is the most widely used initial laboratory test⁷.
- 2. Erythrocytes Sediment Rate (ESR) is a laboratory indicator of inflammation that is typically only moderately increased in viral infections, studies have demonstrated that the host's inflammatory reaction to COVID-19 can be substantial. This heightened response may result in a cytokine storm, which can contribute to additional disease complications and dysfunction in multiple organs⁸.
- 3. C-reactive protein (CRP) is a hepatically synthesized protein that serves as an early biomarker for the presence of infection and inflammation, the normal concentration of (CRP) in the blood is less than 10 mg/l; nevertheless, it rises rapidly within 6-8 hours and peaks 48 hours after the commencement of the disease (Marnell *et al.*, 2005), and was identified as a key measure

that changes considerably in severe COVID-19 patients⁹.

- 4. Interleukin-6 (IL-6) is a multifunctional proinflammatory cytokine that promotes the proliferation of myeloid progenitor cells, facilitates the growth and activation of leukocytes, and induces fever along with the synthesis of acute phase proteins, including C-reactive protein (CRP). The cytokine storm associated with COVID-19 is primarily characterized by the overexpression of interleukin-6 (IL-6) which is a cytokine of significant importance that is produced in response to Toll-like receptor 7 (TLR-7) signalling, activated by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)¹⁰.
- 5. D-dimer which can specifically reflect secondary hyperfibrinolysis and a hypercoagulable condition in the body during coagulation function testing and serves as an index sensitive to reflecting thrombosis. Fibrinogen (FIB) levels can suggest a prethrombotic condition in the body^{11,12}.
- 6. Ferritin Hyperferritinemia, which is caused by infection-induced inflammation, is linked to Intensive care unit (ICU) admission and high mortality, and it serves as a warning sign to identify high-risk patients and direct therapeutic action to decrease inflammation¹³.
- 7. Cardiac troponin I (cTnI): It has been used as a crucial biomarker for non-specific cardiac conditions, such as myocardial infarction and acute coronary syndrome. This advancement enables broader screening capabilities, facilitating the early detection and subsequent intervention of cardiac injury¹⁴. In the context of COVID-19, the levels of cardiac troponin I (cTnI) were notably elevated in individuals with severe manifestations of the disease (Lippi et al., 2020). However, because the troponin readings did not appear to presage the disease's progression, it is impossible to say whether troponin is a 'predictive' sign for COVID-19 severe variants15.
- Fasting Blood Sugar (FBS) is a rapid screening tool, with patients at high risk being assessed for more precise mortality indicators. During an epidemic, this method could be useful for triaging patients and ensuring that they are properly managed¹⁶.
- 9. Glycosylated haemoglobin (HbA1c) is a reliable indicator of long-term glucose control that gives an average of the previous three months' values, it can be used to assess diabetes status and identify COVID-19 high-risk patients with low diabetes awareness¹⁷.

10. Renal functions test which include:

• Blood Urea: Higher urea production is related to any illness associated with tissue breakdown. Less than 10% of the urea generated by the liver is removed through perspiration and the digestive system, but the bulk is transported via the circulation to the kidneys, where it is expelled as urine¹⁸.

• Serum Creatinine: Plasma and/or serum creatinine are two of the chemicals that are most often analysed in clinical chemistry laboratories all around the world (Delanaye et al., 2014). Therefore, it has developed into an essential clinical tool for GFR measurement. In clinical settings, reduced GFR is measured by an increase in plasma and/or serum creatinine¹⁹.

- 11. Estimate Glomerular Filtration Rate (eGFR): The gold standard for evaluating kidney function is measured GFR (mGFR) utilizing urine or plasma clearance of exogenous filtration indicators, however, it is not commonly available due to the complexity of testing techniques. Serum creatinine is the most frequent indicator used to calculate GFR, and the MDRD Study equation is the gold standard for doing so²⁰.
- 12. Uric Acid: The majority of research found that inflammation can cause an increase in (uric acid), especially when the virus infects the respiratory system ⁽²¹⁾. Serum uric acid on the other hand, tends to drop with a central nervous system illness²².
- 13. Lipid Profile: The lipid disorders in COVID-19 patients have lower total cholesterol (TC), low-density cholesterol (LDL-C), and high-density cholesterol (HDL-C) levels. The relationship between COVID-19 and triglyceride (TG) levels isn't always clear according to some research (Feingold, 2000). Dyslipidaemia is linked to metabolic, vascular, and coagulation issues, thus this is important, COVID-19 sufferers may experience more severe symptoms as a result²³.
- Serum Albumin: Hypo-albuminemia is very frequently noticed in patients with conditions like diabetes, hypertension and chronic heart failure, and these patients are statistically most vulnerable to SARS-CoV-2 infection²⁴.

MATERIALS AND METHODS

Samples Collection

The study was conducted on (238) participants between the ages (25-80) years, of whom (81) were in a healthy control group,

(78) infected only with Coronavirus. and (79) infected with Coronavirus and had a complications of diabetes mellitus. Patients diagnosed with COVID-19 who also have diabetes and associated comorbidities were categorized according to the severity of their diseases and their hospitalization status. Patients classified as moderate-risk were sent to hospital wards, and those deemed severe were assigned to intensive care units. In intensive care units classified patients according to with or without Positive Airway Pressure (CPAP) therapy. Between November 2021 and May 2022, all participants of the study conducted visits to Al-Basra Teaching Hospital and Allmwanei Hospital, both located in the AL Basra province, ethical approval ID=815 issued by the Basra Health Department dated 10-11-2021. The mean age of the study population ranged from 25 to 80 years. All participants in this research were assessed by hospital experts. The practical component of the research was conducted in the Department of Medical Laboratory Technology at Southern Technical University in Basra.

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Blood samples were collected, extracting over 5 ml of blood from both the patients and controls. Subsequently, about 1.8 ml of the blood was transferred into anticoagulant tubes that contained sodium citrate. Subsequently, the specimen underwent centrifugation at a speed of 3000 revolutions per minute for a duration of 15 minutes. Following this, the plasma was extracted and preserved at a sub-zero temperature of -20 °C till its utilisation for analytical purposes. In addition, there are Erythrocyte Sedimentation Rate (ESR) test tubes and tubes containing EDTA as an anticoagulant that may be used. The plasma and serum of each patient were allocated into Eppendorf tubes and afterwards subjected to freezing. The laboratory examination will commence after the necessary quantity has been attained. A significant number of individuals were excluded from the study due to their failure to meet the specified inclusion criteria. These criteria encompassed patients with comorbid conditions, such as hypertension, as well as patients with hormonal imbalances. also, investigated verify the patient's information, age, gender, height, weight, vaccination or not, and the severity of the injury. **Statistical Analysis**

The Statistical Package for the Social Sciences (SPSS) version 22 was used in order to carry out the statistical analyses. For the purpose of data representation, means and standard deviations were used. The analysis of variance (ANOVA) was carried out in order to determine whether or not there was a statistically significant difference in the mean of normally distributed variables., P-values (Pd" 0.05) are significant.

RESULTS

The complete information is shown in table (1).

The results show by the statistical comparison between the biomarkers in the patients infected with Coronavirus and the control group a highly significant increase in WBCs, ESR, CRP, Ferritin, D-Dimer, IL-6, Creatinine & Urea and Uric acid for patients compared to the control group as a total number and as a (males and females) number, While, the results show a highly significant decrease in lymphocyte, albumin, HDL and Glomerular filtration rate (GFR) for patients compared to the control group as a total number

Study Groups/	_	Groups nu		Complication			
Age (year)	Ge	ender	Total	Sever	ity	Severe	= 35
	Male	Female	number	Moderate	Severe	With CPAP	Without CPAP
Control group (Healthy) Age = (30-80)	41	40	81	_		_	
Covid-19 patients without diabetes $Age = (30-80)$	40	38	78	_	_		
Covid-19 patients with diabetes Age = (38-80)	40	39	79	44	35 1	8 Aged (55-80) 17

 Table 1. Basic characteristics of the participants, according to the number and disease complications

Bio-Markers		Contract	Groups	Ċ	mitter betterder Of Firm			P-Value		
	Total = 81	Male = 41	Female = 40		Male = 40	щ	Total C	Male C	Female C	Male
	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD	vs Total	vs infected	vs infected	infected vs Female
							infected	Male	Female	infected
CBC Wbcs	8.00±4.16	7.29±3.55	8.83±4.73	10.33 ± 8.19	9.99 ± 5.69	10.67 ± 10.18	0.043	0.026	0.042	0.731
Lymp	2.51 ± 0.54	2.59±0.45	2.40±0.62	1.23 ± 1.04	1.06 ± 0.77	1.40 ± 1.24	0.0001	0.0001	0.0001	0.181
ESR	14.10 ± 9.62	12.04±6.24	16.52 ± 12.19	58.27 ± 31.98	52.43 ± 28.71	58.27 ± 31.98	0.0001	0.0001	0.0001	0.010
CRP	5.31±1.70	5.404±1.784	5.209±1.650	94.31 ± 73.91	106.04 ± 85.16	94.31 ± 73.91	0.0001	0.0001	0.0001	0.186
Ferr	98.71±73.70	100.50 ± 82.25	96.62 ± 64.00	133.90 ± 26.93	134.86 ± 28.19	133.90 ± 26.93	0.0001	0.0001	0.0001	0.701
D-Dimer	257.04±106.31	263.19 ± 98.18	249.83±116.96	1243.22± 1608.6	1702.7 ± 2175.1	1243.22± 1608.6	0.0001	0.0001	0.0001	0.018
L6	6.09 ± 3.37	6.25 ± 3.06	5.909±3.766	28.41 ± 10.30	29.01 ± 9.44	28.41 ± 10.30	0.0001	0.0001	0.0001	0.626
Albumin	3.84 ± 0.75	3.76 ± 0.75	3.923±.759	3.05 ± 0.61	2.90 ± 0.61	3.203 ± 0.61	0.0001	0.0001	0.0001	0.769
FBS	94.98 ± 9.31	97.70±8.77	91.78±9.07	130.90 ± 46.50	134.8 ± 28.1	132.90 ± 46.50	0.0001	0.0001	0.0001	0.584
HbAlc	4.73 ± 0.91	4.65 ± 0.91	4.81 ± 0.92	5.63 ± 0.61	5.59 ± 0.57	5.63 ± 0.61	0.0001	0.0001	0.0001	0.280
Trop	0.019 ± 0.007	0.019 ± 0.007	0.020 ± 0.007	0.03 ± 0.05	0.04 ± 0.07	0.014 ± 0.05	0.165	0.062	0.009	0.005
Cholesterol	132.2 ± 45.5	123.63 ± 34.11	142.5 ± 55.0	135.9 ± 46.4	131.5 ± 37.9	146.2 ± 49.5	0.864	0.388	0.787	0.048
ΓG	130.08 ± 45.5	128.270 ± 49.20	132.213 ± 48.78	140.94 ± 86.35	138.540 ± 59.11	154.357 ± 103.84	0.776	0.289	0.280	0.048
HDL	63.20 ± 10.94	62.51 ± 8.99	64.13 ± 13.02	30.027 ± 11.56	30.029 ± 13.47	30.026 ± 9.48	0.0001	0.0001	0.0001	0.999
DL	67.92 ± 38.42	60.704 ± 35.13	76.391 ± 41.03	75.39 ± 35.67	68.057 ± 30.44	82.729 ± 39.30	0.029	0.391	0.055	0.086
Creatinine	0.706 ± 0.129	0.795 ± 0.069	0.602 ± 0.501	0.983 ± 0.465	1.058 ± 0.472	0.907 ± 0.451	0.0001	0.002	0.0001	0.175
Urea	26.780 ± 10.71	25.926 ± 4.66	27.783 ± 15.103	47.424 ± 23.95	58.506 ± 25.64	36.343 ± 14.81	0.0001	0.0001	0.039	0.0001
Uric acid	4.258 ± 1.438	4.037 ± 1.49	4.517 ± 1.35	5.034 ± 2.38	5.365 ± 2.67	4.704 ± 2.04	0.043	0.016	0.678	0.249
aGED	110.740 ± 14.56	$100 148 \pm 10.88$	112600 ± 1804	00 257 ± 37 30	88 657 ± 31 35	00 157 ± 37 67	0.0001	0.001		0.001

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Bio-Markers		[cuttor]	Groups	C	- national protocologies (P-Value		
	Total = 81 Mean± SD	Control Male = 41 Mean≟ SD	Female = 40 Mean± SD	Total = 79 Mean≟ SD	covid meeted patents + Div Male = 40 Mean± SD	DM Female = 39 Mean± SD	C vs DM total	C vs DM male	C vs DM female	Male DM Vs female DM
CBC Wbcs	8.00±4.16	7.29±3.55	8.83±4.73	12.38±7.39	11.73±7.33	13.00±7.49	0.0001	0.029	0.0326	0.450
		2.59±0.45	2.40 ± 0.62	1.05 ± 0.59	0.99±0.47	1.11 ± 0.69	0.0001	0.0001	0.0001	0.395
ESR	14.10 ± 9.62	12.04 ± 6.24	16.52 ± 12.19	69.21 ± 30.17	64.24±29.32	74.06±32.73	0.0001	0.0001	0.0001	0.216
CRP	5.31 ± 1.70	5.404 ± 1.784	5.209 ± 1.650	196.2±74.30	282.9 ± 104.0	111.75 ± 88.56	0.0069	0.003	0.001	0.031
Ferr	98.71±73.70	100.50 ± 82.25	96.62 ± 64.00	613.86 ± 55.28	771.94 ± 62.40	459.73±54.45	0.0001	0.0001	0.006	0.011
D-Dimer	257.04 ± 106.31	263.19 ± 98.18	249.83 ± 116.9	11944.7 ± 1800.0	1854.2±1315.4	2423.0 ± 2678.0	0.0001	0.0001	0.0001	0.012
L 6	6.09±3.37	6.25 ± 3.06	5.909±3.766	30.48 ± 12.10	31.41±14.99	29.60 ± 8.160	0.0001	0.0001	0.0001	0.167
Albumin	3.84 ± 0.75	3.76 ± 0.75	3.923 ± 0.759	3.11 ± 0.53	3.14 ± 0.52	3.087 ± 0.549	0.0001	0.001	0.0001	0.660
FBS	94.98 ± 9.31	97.70±8.77	91.78±9.0	296.14±117.4	305.67±121.83	286.8 ± 113.8	0.0001	0.0001	0.0001	0.481
HbA1c	4.73 ± 0.91	4.65 ± 0.91	4.81 ± 0.92	8.59±2.22	8.17 ± 0.79	8.99±1.52	0.0001	0.0001	0.0001	0.101
Trop	0.019 ± 0.007	0.019 ± 0.007	0.020 ± 0.007	0.084 ± 0.062	0.125 ± 0.011	0.044 ± 0.051	0.038	0.029	0.052	0.182
Cholesterol	132.2 ± 45.5	123.63 ± 34.11	142.49 ± 55.06	150.17 ± 46.02	143.84 ± 33.65	156.5 ± 54.648	0.019	0.040	0.034	0.026
Tg	130.08 ± 48.5	128.27 ± 49.21	132.21 ± 48.78	163.2 ± 92.30	148.38 ± 61.10	177.7 ± 109.0	0.019	0.028	0.024	0.031
HDL	63.20 ± 10.94	62.51 ± 8.99	64.13 ± 13.02	30.99 ± 17.45	30.33 ± 17.58	31.640±17.521	0.0001	0.001	0.002	0.715
LDL	67.92±38.42	60.70 ± 35.15	76.39 ± 49.030	86.20±38.21	76.79±32.76	95.373±42.876	0.017	0.041	0.0368	0.068
Creatinine	0.706 ± 0.128	0.795 ± 0.068	0.602 ± 0.501	1.361 ± 0.715	1.422 ± 0.182	1.304 ± 0.701	0.0001	0.035	0.003	0.661
Urea	26.78 ± 10.72	25.926 ± 4.66	27.783 ± 15.103	77.78 ± 66.13	74.83±32.80	80.65±77.53	0.0001	0.0001	0.001	0.667
Uric acid	4.258 ± 1.438	4.037 ± 1.49	4.517 ± 1.35	6.65±3.68	6.54 ± 3.063	6.764±2.767	0.0001	0.011	0.006	0.790
GFR	110 74+14 56	$109\ 148 + 10\ 88$	117609 + 1804	73 39+34 25	77 49+30 04	69 40+35 34	0 000 1	0.0001	0.0001	7070

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and the number of males and females separately, as show in table (2)

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A general statistical comparison was made for the biochemical markers in the patients infected with Coronavirus and who had a diabetic complication compared to the control group according to gender and as a total number of (79) patients, the results showed that people with diabetes significantly increased biomarkers than patients without diabetes minutes, as shown in the statistical Table (3).

DISCUSSION

The study of these biomarkers provides a dynamic approach to understanding the disease to diagnosis and follow-up, so as to improve the development of patients' treatment. The results show a highly significant increase in WBcs, ESR, CRP, Ferritin, D-Dimer, IL-6, Creatinine & Urea and Uric acid. While, the results show a highly significant decrease in lymphocyte, albumin, HDL and Glomerular filtration rate (GFR) for COVID-19 patients compared to the control group as a total number and the number of males and females separately

This is consistent with what has been confirmed by another study²⁵.Also, other studies showed that death and disease severity in COVID-19 were associated with a higher WBC count accompanied by lower lymphocyte levels. The resistance against infectious diseases is activated through the immune system, Studies have found that angiotensin-converting enzyme (ACE) is an effector and plays a strong role in recruiting inflammatory cells to tissues^{26, 27}. Circulating lymphocytes throughout the body produce proteins and antibodies to fight off pathogens and help the immune system fight infection. B cells attack viruses while T cells produce cytokines and destroy virus-damaged cells. Lymphocytes take in the virus as they contain about 1000 molecules of ACE2 which leads to a decrease in these cells through programmed death as a result of infection with the virus⁽²⁸⁾, and this confirms our study.

Other studies that align with the findings of our research, in one study that targeted the diagnostic and warning role of (CRP) in COVID-19 patients, which included 85 patients, it was found that the (CRP) levels were much higher than the normal rate. Where the increase in (CRP) levels of more than 53 mg / L is associated with a 10 times higher risk for disease progression. Increasing serum ferritin levels is an important marker in the acute phase of viral infections, including COVID-19. Hyperferritin contributes to the severity of COVID-19, through inflammation, hyperproteinemia, hypercoagulability, and immune dysfunction²⁹, it was found that there is a strong significant correlation between ferritin level with the severity of the injury in the clinical results obtained³⁰. In a cross-sectional study of a large number of COVID-19 patients, D-dimer was elevated, and its levels were associated with disease severity. Thus, it can be considered a reliable predictive biomarker for the mortality of patients in hospitals³¹. The measurement of D-Dimer levels along with coagulation parameters is very useful in controlling and managing the disease in the early stage³². And that align with the findings of our research, this agrees with the results of our study.

Regarding IL-6 other studies agree with the results of our study, as across-sectional study, IL-6 levels were estimated for COVID-19 patients in intensive care units and acute respiratory distress syndrome (ARDS). It was found an increase in (IL-6) levels compared to the healthy group. This proves the sensitivity of this inflammatory marker as an indicator in infection control and diagnosis. In the same study, it was found that the value (20.92 pg/ml) is an indicator of long-term injury³³. In another clinical study correlating (COVID-19 with IL-6), (366) patients were included as moderate cases, (411) as serious cases and (124) as critical cases. Clinical data reported a higher level of (IL-6) for patients compared to the control group, with a high statistically significant relationship. The study also revealed that (IL-6) remained high in critical patients even after the recovery stage, and its value was (37.65 pg/ml), and this predicts the possibility of death inside the hospital³⁴.

Studies indicated hypoalbuminemia was common in patients with (COVID-19), and that its levels are associated with the severity of the disease, which is consistent with our study. Therefore, dynamic monitoring of albumin levels is necessary and should be followed up during the treatment of patients and used as a tool for evaluation and diagnosis of infection³⁵, It was found that low albumin levels could predict the outcome of disease on admission to patients independently of other biochemical indicators^{36,37}. This is consistent with previous studies reporting lower blood albumin, which is associated with acute kidney injury and the severity of respiratory distress syndrome. In another study, it was found that 17.7% of COVID-19 patients had hypoalbuminemia during the analysis of 3 consecutive time points during one week³⁸. In a large statistical study in which (2623) COVID patients were hospitalized with hypoalbuminemia as follows: (38.2%) of them were in non-critical condition and (71.2%) suffered from serious diseases. The hypoalbuminemia was related to cytokine release, which was also associated with age, comorbidities, length of hospitalization and death³⁵.

With regard to blood sugar indicators, studies confirmed consistent with the results of our research, in one of these studies there were nine cross-sectional studies, involving approximately (40) million participants worldwide. The results indicated that the incidence of diabetes was (15.53) per (1000) person after recovery. Also, the relative risk of contracting diabetes after the end of infection increased by (1.7), and there was a high positive significant association between infection with corona and the risk of developing type 2 diabetes for all ages and genders after recovery³⁹. COVID-19 is sometimes associated with the inflammation of the pancreas. The virus can be found in the pancreas cells that are responsible for producing insulin. This raised some concerns about COVID-19 causing diabetes. Where Miao et al. reported pancreatitis in some patients with COVID-19 without respiratory symptoms⁴⁰.

COVID-19 infection was associated with a mild elevation in cardiac indices⁴¹. Elevated levels of cardiac troponin (26.9%) were found. These levels were significantly associated with disease severity and mortality. Thus, early measurement of cardiac troponin is useful in risk classification in COVID-19⁴². Coronavirus infection causes an increase in inflammatory cytokines, and this may lead to alter the lipid profile of patients. Recent research indicates that low levels of high-density lipoprotein cholesterol are associated with mortality and the severity of disease, as it plays a role in controlling infectious diseases and modulating the immune system through its association with pathogenic fats⁴³. A similar study included 75 cases, (50) of them were infected with coronavirus and(25) were healthy people, the statistical results showed, lower levels of high-density lipoprotein cholesterol compared to healthy subjects⁴⁴, that is agrees with the results of our study.

Regarding renal function indicators, it was found in a study conducted on (59) patients infected with COVID-19 that (27%) of them had elevated levels of urea nitrogen with a high level of creatinine in the blood⁴⁵. Another study also conducted on (710) patients with (COVID-19) showed that (26.9%) had simple hematuria, (44%) had proteinuria, (14.1%) had elevated levels of urea nitrogen and (5.5%) had elevated serum creatinine⁴⁶. Kidneys act as filters that filter out toxins and body waste, so small clots formed in the bloodstream can block the small blood vessels of people with COVID-19, impairing kidney function⁴⁷. And that aligns with the findings of our research.

In one study it agrees with the results of our study, include (1800) patients aged (73-86) years, of whom 55% were males, were included. The estimated glomerular filtration rate was in the range (45-59). Thus, the death rate for (28) days was (42.3%). It is concluded from this, that the eGFR rate upon hospital admission is an independent predictor of mortality in elderly patients infected with COVID-19⁴⁸. Most evidence indicates a negative impact of COVID-19 on a decreased glomerular filtration rate, with an increased risk of patients being admitted to the intensive care unit (ICU) and dying^{49,50}.

Regarding about comparison made for the biochemical markers in the patients infected with Coronavirus and who have a diabetic complication compared to the control group, the results showed that people with diabetes significantly increased biomarkers than patients without diabetes minutes likely to suffer serious complications when infected with COVID-19. In general, people with diabetes are more susceptible to complications and more severe when infected with any virus⁵¹. Diabetes is considered a risk factor for the severity of COVID-19. Coronavirus usually triggers the body to produce cytokines, which are inflammatory factors that make insulin resistance worse and, as a consequence raise blood sugar. When blood sugar is high, the ability of the white blood cells of the

body to fight infection is reduced, which again, puts a diabetic at greater risk⁵².

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Studies confirmed that the Coronavirus caused a greater decrease in the number of lymphocytes in patients with diabetes^{53, 54}, the number of white blood cells is significantly associated with death in patients with COVID-19. Therefore, higher (WBC) levels should be given more attention in the treatment of COVID-19²⁵. In a study that included (63) patients with coronavirus, of whom (16) had diabetes and (47) did not, it was found that the diabetic group had a lower number of lymphocytes and reached the minimum level. In summary, diabetics with COVID-19 have fewer lymphocytes with a longer hospital stay⁵⁵. These studies agree with the results of our research.

In a series of articles (29) that included (15,282) patients, of whom (4,733) had diabetes and (10,549) did not have diabetes. The pooled result of these studies showed that serum (CRP and D-dimer) was significantly higher in patients with COVID-19 diabetes and significantly higher than in non-diabetic patients⁽⁵⁶⁾. Recent studies found a strong correlation between serum ferritin and blood glucose levels in patients with diabetes (type 2). In a study that included (172) patients, (84) of them had type-2 diabetes and (88) formed a control group. Serum ferritin, (HbA1c), (CRP) and uric acid levels were compared between groups. The results showed increased levels of ferritin for diabetes patients with significantly increased levels of (HbA1c) and a positive correlation was found between them in the blood. This indicates the possibility of using (CRP) and serum ferritin levels as a screening tool for the early diagnosis of diabetes⁵⁷. It was found that the severity of COVID-19 disease depends primarily on cytokine storm syndrome. Consequently, people with diabetes show elevated levels of ferritin in the blood and face the possibility of developing serious complications58. and all these studies agree with our research.

Regarding IL-6 In one study which agrees with our research, that included (59) patients with COVID-19, Interleukin-6 and D-dimer levels were assessed, and their levels were significantly higher in the diabetic group than in the normal group (P < 0.001). Although all patients received standard treatment for COVID-19 infection, (D-dimer and IL-6) levels were higher in patients with diabetes⁵⁹. Interleukin-6 is a multifunctional pro-inflammatory cytokine that stimulates the development of inflammation, insulin resistance and the pathogenesis of diabetes type-2⁶⁰. About albumin the results show a highly significant decrease in albumin for diabetes patients infected with COVID-19 compared to the control group. A study was conducted to analyze hypoalbuminemia as an indicator of mortality in patients with COVID-19, and the results of the study indicated that checking serum albumin upon admission of Corona patients to the hospital may help in identifying patients at risk of infection, which determines life and death⁶¹.

For kidney biomarkers, the results show a highly significant increase in (creatinine, urea, and uric acid), with a significant decrease in (eGFR), for diabetes patients infected with COVID-19. In one study that investigated (819) patients with COVID-19 who were admitted to the hospital, the results of clinical analyses revealed patients with high sugar and blood pressure, in addition to kidney disease. The high level of creatinine in the blood was one of the most important factors associated with deaths, which underscores the importance of renal function for COVID-19 patients and the importance of careful management of these patients⁶², and that aligns with the findings of our research.

Also, confirmed the results of our research through many studies regarding COVID-19 patients who had diabetes Mellitus, such as, in a study of (193) patients with severe symptoms of COVID-19 disease, (48) had diabetes. The results showed that diabetic patients had higher levels of white blood cell count, (CRP), ferritin, D-dimer, and interleukin (IL-6). The non-surviving patients were reported to have a severe inflammatory response, thrombosis, and (hepatic & renal) impairment. In short, diabetes may contribute to an increased risk of death63. In a study conducted on (466) patients who were hospitalized with severe symptoms of COVID-19 disease. Most of them had diabetes. In this study, (168) of the patients who survived had a heart attack. The results showed that myocardial injury is a common outcome in patients with COVID-19, and an elevated troponin level was an independent predictor of mortality⁶⁴. In a large observational study involving (51, 919) COVID-positive participants and two uninfected

groups. They found an increase in total cholesterol, triglycerides, and (LDL) cholesterol with a decrease in (HDL) cholesterol. The results also confirmed that the degree of dyslipidaemia was greater for those with infection who needed intensive care admission. Dyslipidaemia was attributed to behavioural factors during the recovery period, such as decreased physical activity after the virus, or binge eating after the return of taste⁶⁵.

CONCLUSION

Diabetes is responsible for the slow destruction of the immune response and is responsible for the severity of the infection with COVID-19. So, a statistical study for chemical biomarkers in patients with type 2 diabetes mullets, according to the complication of infection severity, and evaluating of the levels of different biochemical markers in patients infected with Coronavirus with or without diabetes, such as (CBC, ESR, CRP, Ferritin, Albumin, D-Dimer, IL-6, FBS, HbA1C, eGFR, uric acid, urea v creatinine and lipid profile). Where, the clinical symptoms associated with the severity of the infection and diabetes complication are illustrated, through the elevated levels of the inflammatory biochemical markers. The results showed all biomarkers tend to have high sensitivity and specificity for COVID-19 with Diabetes Mellitus patients. Here, we find that the blood characteristics of those infected with COVID-19 changed, which led to the activation of inflammatory reactions, cytokine storms, and the stimulation of hypercoagulation. This, in turn, gave a more accurate interpretation of the severity of the disease and risk classification to distinguish moderate and severe cases.

ACKNOWLEDGMENTS

The authors express their gratitude to M.Sc. Muntadher A Hassan and M.Sc. Zeina M Mubarak for their valuable support and exceptional technical assistance.

Conflict of Interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Funding source

The funding is of a personal nature.

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