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The Impact of Severe COVID-19 Infection on Renal and Liver Markers (Urea, Creatinine, GOT, GPT) in Diabetic Patients

Marwah S. Yones[1] *MSc*, **Estabraq A. Alwasiti**[2] *PhD,* **Abdul Hameed A. Al-Qaseer**[3] *FICMS,* **Anees K. Nile**[4] *FIBMS*

[1]Clinical Laboratory Science Dept., College of Pharmacy, Al-Mustansiriyah University, Baghdad, Iraq, [2]Dept. of Chemistry and Biochemistry, College of Medicine, Al-Nahrain University, Baghdad, Iraq, [3]Dept. of Medicine, College of Medicine, Al-Mustansyria University, [4]Dept. of Surgery, College of Medicine, Al-Nahrain University

Abstract

Background Coronavirus disease 2019 (COVID-19), an epidemic illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), affecting the lower respiratory tract. It may impact renal and hepatic function by causing a cytokine storm and inflammation. Although numerous studies on the effects of COVID-19 on people with diabetes Mellitus (DM) have been conducted across the globe, their conclusions have varied due to differences in study populations' demographics, racial and ethnic composition, and geographic locations.

Objective To comprehend the effects of a severe COVID-19 infection on renal and hepatic function in patients with diabetes mellitus.

Methods This study was carried out at the Chemistry and Biochemistry Department of Al-Nahrain University in Baghdad, Iraq. A total of 100 participants with a severe case of COVID-19 were included in the study between February and April 2022. There was a total of 100 hospital admissions due to COVID-19; 50 of these patients had diabetes, while the other 50 did not. In both groups, serum urea, creatinine, glutamic-oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT) were mustered using appropriate methods.

Results The median concentration of the DM patients' group had significantly lower concentration of urea, creatinine, GOT and GPT than non-DM patient's group. While all these parameters were significantly higher in COVID-19 patients than in controls.

Conclusion Diabetes (COVID-19 patients) exhibited lower levels of biochemical markers as compared to non-diabetic people. Patients with diabetes in COVID-19 take a range of drugs, including insulin injections. In severe circumstances, this medicine may disrupt biochemical markers in addition to the effects it has on renal and hepatic function from COVID-19.

Keywords COVID-19, diabetes Mellitus, urea, creatinine, GOT, and GPT.

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List of abbreviations: ACE2 = Angiotensin converting enzyme 2, ACEi = Angiotensin converting enzyme inhibitors, Ang (1-7) = Angiotensin (1-7), Ang-I = Angiotensin-I, Ang-II = Angiotensin-II, ARBs = Angiotensin-receptor blockers, AT1R = Angiotensin-II type 1 receptor, AUC = Area under curve, COVID-19 = Coronavirus disease 2019, DM = Diabetes mellitus, GOT = Glutamic-oxaloacetic transaminase, GPT = Glutamic-pyruvic transaminase, PCR = Polymerase chain reaction, SARS-CoV-2 = Severe acute respiratory syndrome Coronavirus 2

Introduction

Diabetes mellitus (DM) is an endocrine condition characterized by hyperglycemia, polyuria, polydipsia, and weight loss and caused by a failure in insulin secretion and/or action. When there is a viral infection, DM is frequently linked to

metabolic, macrovascular, and microvascular problems that raise morbidity and mortality [1].
Chronic kidney failure can be caused by diabetic nephropathy, and diabetes mellitus is the leading cause of renal morbidity and mortality. It is widely established to evaluate renal function using blood urea and creatinine [2]. Controlling blood sugar levels well is crucial for preventing further kidney damage. As there is a significant association between blood sugar and urea level, it can be necessary to monitor both of these parameters [3].
A worldwide pandemic has been brought on by the coronavirus disease 2019 (COVID-19) [4,5], an infection brought on by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that is an enclosed virus with a single-stranded RNA genome. Due to a lowered immune response, people with diabetes have an increased risk of nosocomial bacteremia, lung infections, and infectious diseases [6,7].
SARS-CoV-2 infects the host (lung, heart, gut, and endothelial cells) using the membrane-bound peptidase angiotensin converting enzyme 2 (ACE-2), which is more prevalent in the kidney than other organs [8]. Angiotensin I (Ang I) is transformed into angiotensin II (Ang II) by ACE, whereas Ang II is degraded to angiotensin 1-7 (Ang-(1-7)) by ACE2. Vasoconstriction and adrenergic stimulation are influenced by Ang II, which binds to type 1 Ang II receptors (AT1) [9].
While Ang-(1-7) blocks the Ang II-AT1 axis through vasodilatation, anti-inflammatory, and antifibrotic effects, primarily through boosting nitric oxide production. SARS-CoV2 causes a change in the overproduction of Ang II and an increase in ACE activity by downregulating ACE2 [10]. As a result, the kidneys enter a pro-fibrotic and pro-inflammatory state (including complement activation). Figure 1 summarizes the processes of renal damage caused by SARS-CoV-2. Renal damage may result from both primary, directly linked to the virus processes, and secondary, associated with the hemodynamic and immunological response to the infection [11].
This study aimed to comprehend the effects of a severe COVID-19 infection on renal and hepatic function in patients with DM.

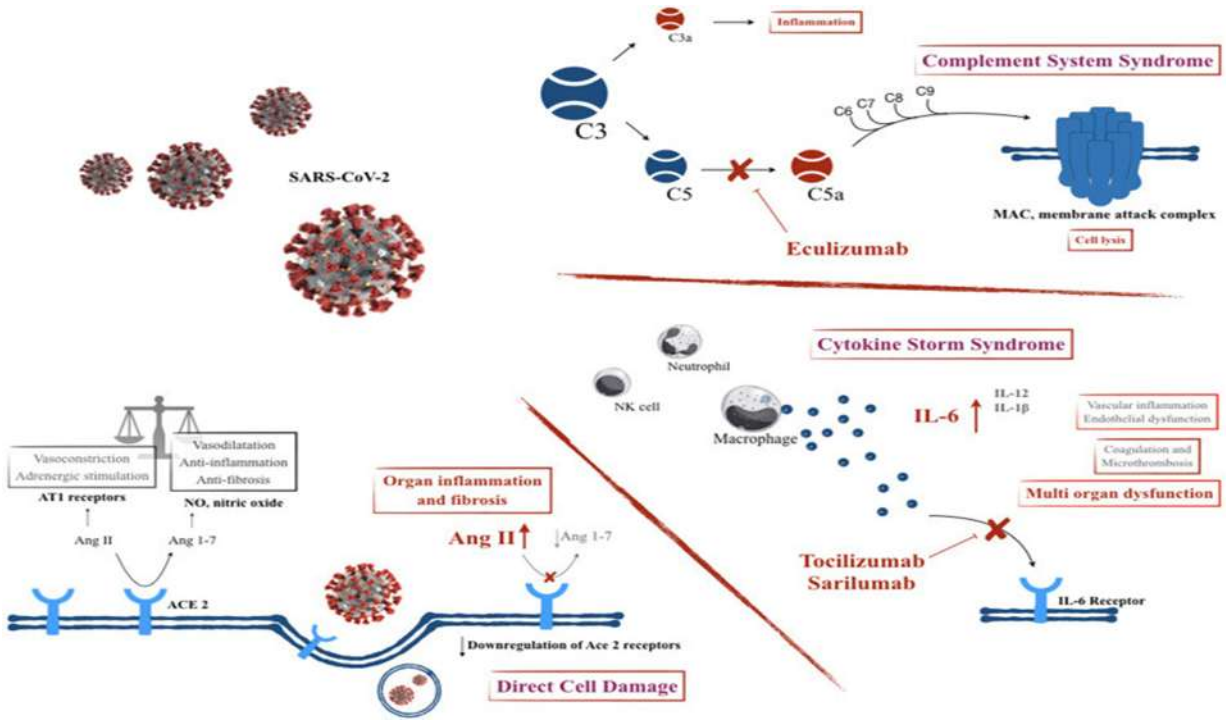

Figure 1. The Pathogenesis of SARS-CoV-2

Methods

Materials

About 5 ml of venous blood samples were obtained from all participants. The blood was clotted at room temperature for 15 minutes. Serum was isolated after coagulation by centrifugation at 3000 rpm for 10 minutes. Measurements of serum urea, creatinine, glutamic-oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT) were done using appropriate methods.

Instrumentation

The instruments that were used in this study and their companies include Centrifuge (U.S.A.), Cobas C311 analyzer, Dimension EXL 200 Siemens for biochemistry, and a fully automatic biochemistry analyzer, all from Germany.

Procedure

A case-control study was conducted at the Department of Chemistry and Biochemistry in the College of Medicine at Al-Nahrain University between February 3rd and April 4th, 2022. The study protocol was approved by the Ethical Committee of the College of Medicine at Al-Nahrain University. One hundred Iraqi patients at Al-Yarmouk Hospital and Dar Al Salam Field Hospital with severe COVID-19 infection confirmed by polymerase chain reaction (PCR) of a nasopharyngeal swab participated in the study.

Blood samples were drawn from all patients after their agreement, and the data of the patients was obtained depending on a questionnaire. The tests were done in Al-Yarmouk Hospital and Dar Al Salam Field Hospital.

These patients were divided into two groups:

1. Group I: n= 50 COVID-19 patients with diabetes mellitus admitted to the hospital.
2. Group II: n= 50 COVID-19 patients without diabetes mellitus admitted to the hospital.

All participants in these groups, who range in age from 50 to 80, were evenly divided by gender and age. The disease severity is based on clinical WHO criteria, in which the patients are presented with:

- SpO_2 oxygen saturation level: 93%
- A respiration rate of more than 30 breaths per minute
- A CT scan that reveals a pneumonic shadow covering more than 50% of the lung field.

(The control group) includes 100 healthy and sex-matched subjects (age 50-80 years) collected from relatives under the supervision of the second supervisor.

Inclusion criteria

1. Age of patients: 50-80 years
2. Apparently, health is good (physically and mentally).
3. Severity of COVID-19 patients.

Exclusion criteria

Subjects who have had carcinoma anywhere, malignant disease and/or chemotherapy, autoimmune disease, or organ failure.

Statistical analysis

Microsoft Office 2019 with version 25.0 of the statistical package for social sciences (SPSS) was used to analyze the data. The variables were described as median and range and compared by Mann Whitney test. When the p values <0.05, the results were considered statistically significant.

Results

The concentrations of the biochemical parameters, urea, creatinine, GOT, and GPT were found to be non-normally distributed. Thus, they were presented as median and range. The median urea level of the patient groups was 62 mg/dl, range (33.1-280), which was significantly higher than the control group (30 mg/dl), range (16-40). Furthermore, the patients' group had a higher concentration of creatinine (median = 0.8, range 0.2-3.4) than

the control group (median = 0.75, range 0.50-1.31), As GPT concentrations were also higher in patients than control group, the differences were non-significant for creatinine and GPT but its highly significant for GOT (Table 1).

Table 1. Comparison of biochemical parameters between controls and patients with severe COVID-19

Variables	Control (n=100) Median (Range)	COVID-19 Patients (n=100) Median (Range)	P-value
Urea (mg/dl)	30 (16-40)	62 (33.1-280)	<0.001
Creatinine (mg/dl)	0.75 (0.5-1.31)	0.8 (0.2-3.4)	0.341
GOT (U/l)	23.5 (5-41)	29.2 (12.3-240)	<0.001
GPT (U/l)	29 (6-50)	29.9 (7.6-99)	0.240

The concentration of biochemical parameters between DM and non-DM groups with COVID-19 shown in table 2. In this table, the median urea level of DM patients' groups was 52.0 (mg/dl), range (33.1–261.20), which was non-significantly lower than non-DM patients' groups 67.7 (mg/dl), range (34.8-280). Furthermore, the DM patients' group had a significantly lower concentration of creatinine (median = 0.7 mg/dl, range 0.2-2.2) than the non-DM patients' group (median = 0.95 mg/dl, range 0.2-3.4), with a significant difference. Regarding GOT and GPT concentrations, there is a reduction in DM patients than non-DM patient's group, the differences were significant.

Table 2. Comparison of biochemical parameters between DM and non-DM severe COVID-19 patients

Variables	COVID-19 with DM (n= 50) Median (Range)	COVID-19 without DM (n=500) Median (Range)	P-value
Urea (mg/dl)	52.0 (33.1-261.2)	67.7 (34.8-280)	<0.001**
Creatinine (mg/dl)	0.7 (0.2-2.2)	0.95 (0.2-3.4)	<0.001
GOT (U/l)	26.55 (12.3-64)	29.8 (12.4-240)	<0.001
GPT (U/l)	26 (7.6-79)	35 (9.7-99)	0.005

Discriminative values of biochemical markers

The area under curve (AUC) for urea was 0.972, 95% CI = 0.955-0.990, P value 0.001. The test had 100% sensitivity and 87.71% specificity at the cutoff values of urea = 41 mg/dl.

The AUC for creatinine was 0.52, 95% CI = 0.54-0.61. The test had 81.25% sensitivity and 61.36% specificity at the cutoff values of creatinine = 0.95 mg/dl (Figure 3).

The AUC for GOT was 0.68, 95% CI = 0.603-0.758. The test had 100% sensitivity and 58.06% specificity at the cutoff values of GOT = 41.6 U/l (Figure 4).

The AUC for GPT was 0.49,95% CI = 0.41-0.58. The test had 80.9% sensitivity and 54.08% specificity at the cutoff values of GPT = 16.8 U/l (Figure 5).

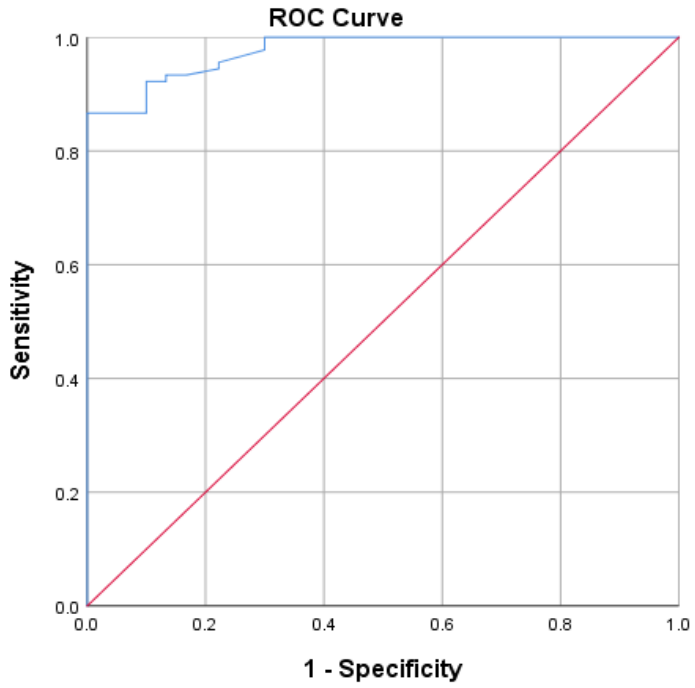

Figure 2. Receiver operating characteristic curve for urea between patients and controls

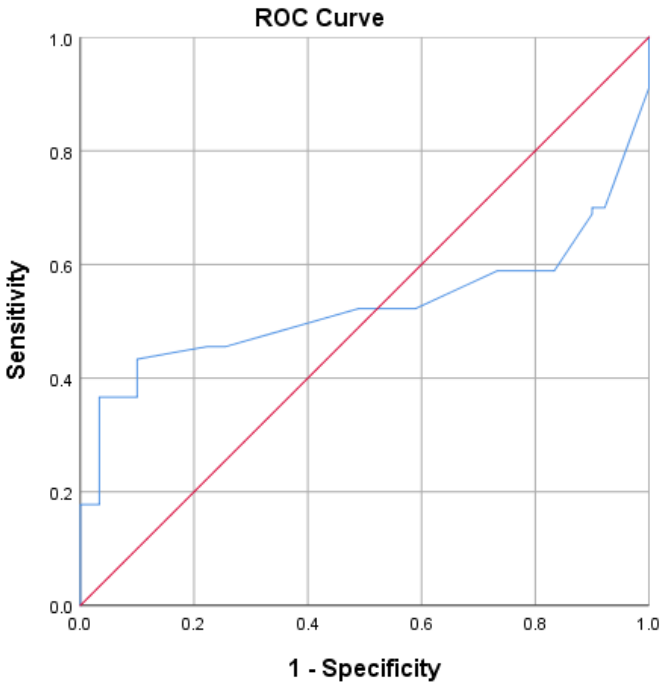

Figure 3. Receiver operating characteristic curve for creatinine between patients and controls

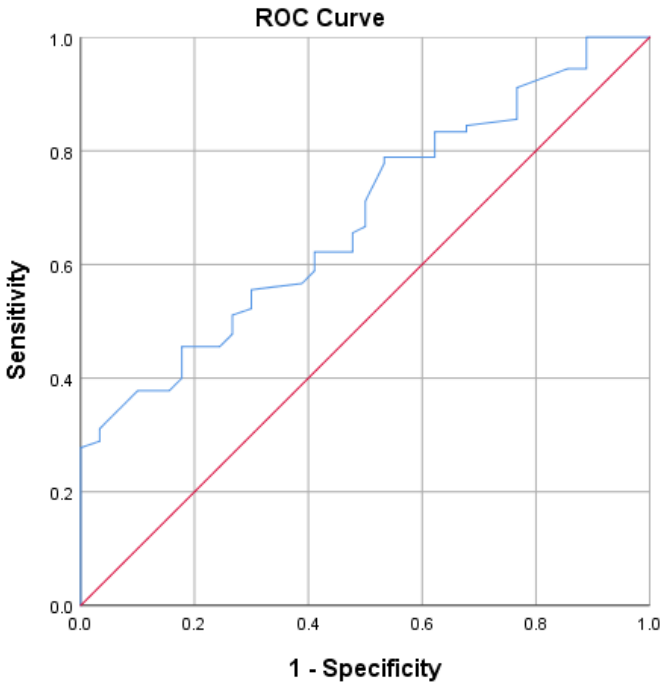

Figure 4. Receiver operating characteristic curve for GOT between patients and controls

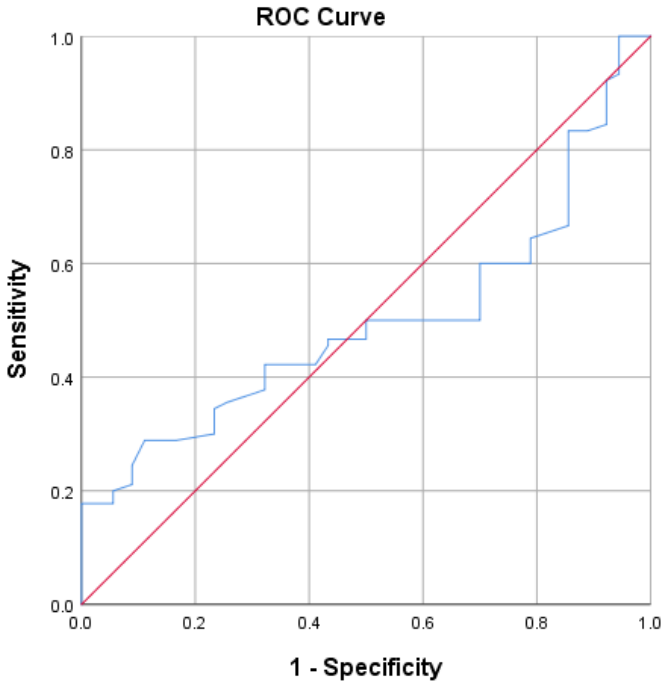

Figure 5. Receiver operating characteristic curve for GPT between patients and controls

Discussion

When insulin is administered, the release of both glucose and urea will be immediately partially inhibited, in proportions that suggested reduced gluconeogenesis [12].

Significant decreases in albuminuria and eGFR decline have been documented when comparing these types of glucose-lowering pharmaceuticals to placebo and other glucose-lowering medications [13].

In this study, there was discernible difference in urea levels between DM and non-DM groups, and there were significant disparities in the normal laboratory results (creatinine, GOT, and GPT) of individuals with COVID-19 who were severely affected, regardless of diabetes status. This may be caused by cytokine-related inflammation and overactivity, which are pathological characteristics of COVID-19. It highlights the need for quick and proper corticosteroid administration in severe cases in order to avert a cytokine storm. This type of treatment raises the level of gluconeogenesis, inhibits glycolysis, and suppresses insulin levels [14,15]. Patients with T2DM are frequently treated with ACEIs and/or ARBs, which could both result in increased production of ACE-2 in tissues, enhance viral absorption, and raise the severity of infection risk in T2DM patients. T2DM may be associated with the renin-angiotensin system being activated [16-18].

COVID-19 patients who were critically ill were found to have lower insulin sensitivity than the control group, indicating that COVID-19 may promote insulin resistance [19].

Hepatic abnormalities are more common following COVID-19 infection and during the course of the illness, which may be a marker of the liver-damaging effects of SARS-CoV-2 or pharmaceutical side effects in patients. Additionally, another study revealed steatosis and liver damage in a COVID-19 patient's liver biopsy. Acute renal injury following COVID-19 has also been recorded more frequently than liver injury in certain articles, which may be related to the presence of SARS-CoV-2, the inflammation caused by the illness, or a combined effect of the two on kidneys [20].

In conclusion, diabetic (COVID-19 patients exhibited lower levels of biochemical markers as compared to non-diabetic people. Patients with diabetes in COVID-19 take a range of drugs, including insulin injections. In severe circumstances, this medicine may disrupt biochemical markers in addition to the effects it has on renal and hepatic function from COVID-19.

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Author contribution

All authors participated in concept and design, acquisition, analysis, interpretation of data, statistical analysis, administrative, technical, and material support, and critical revision of the manuscript.

Conflict of interest

None.

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Correspondence to Marwah S. Yones
E-mail: chem.marwasabbah@gmail.com
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