



Research Article

## Biochemical changes in type 2 diabetic patients comorbid with COVID-19



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### Abstract

**Background:** Uncontrolled Type 2 Diabetes Mellitus (T2DM) has been shown to be associated with an increased severity of COVID-19, it represents an important risk factor for adverse outcomes. Altered glucose metabolism was the basis of the viral infection, leading to a fatal inflammatory reaction, The relationship between COVID-19 and diabetes mellitus is complicated and bidirectional. Diabetes mellitus is considered one of the most important risk factors for a severe course of COVID-19. At the same time, severe COVID-19 infection, and its treatment with steroids, may have negative impact and side effects on diabetes itself, leading to worsening of hyperglycemia through increased insulin resistance and reduced  $\beta$ -cell secretory function. The aim of the study is to evaluate biochemical abnormalities in infected type 2 diabetic patients comorbid with COVID 19. **Methods:** The current study is a case control study was conducted on 89 persons, 35 males and 54 females of the same age group (40:75 years) were selected from outpatient clinic of diabetes, Diabetes and Endocrinology unit, and Intensive care unit of Department of internal medicine at Minia University Hospital from December 2021 to May 2022. **Results:** D-Dimer levels significantly higher in diabetic with COVID-19 group than diabetic group with p value ( $>0.001$ ). Serum cholesterol levels significantly higher in diabetic with COVID-19 group than diabetic group with p value (0.01). **Conclusion,** D-dimer is a good prognostic biomarker for outcome of type 2 diabetic patients infected with COVID-19.

**Key words:** Diabetes mellitus, COVID-19, Total cholesterol, D-dimer.

### Introduction

The world is struggling in lockdown for months since December of 2019 due to novel coronavirus disease (COVID-19) outbreak, a pandemic declared by the World Health Organization<sup>(1)</sup>. Research evidence is growing on the role of several symptoms, comorbidities, inflammation and hypercoagulability markers in relation to

disease progression and deaths in COVID-19 patients. Diabetes mellitus (DM) and obesity are an independent risk factors associated with severity of Coronavirus disease 2019 (COVID-19)<sup>(2)</sup>

The high incidence of diabetes is one of the leading causes of morbidity, and is associated with disease progression in

COVID-19<sup>(3)</sup>. Different pathophysiological mechanisms were suggested to explain the worse clinical outcome, including hyperglycemia, old age, and the presence of other comorbidities<sup>(4)</sup>.

Hypercoagulable state along with impaired immune response and heightened inflammatory response are hypothesized as the underlying mechanism of the unfavorable outcomes in patients with those comorbidities<sup>(5)</sup>.

COVID-19 patients with DM are at high incidence rate to be complicated with thrombo-embolism which is affected by poor glycemic control<sup>(6)</sup>. This is owing to diabetic patients are associated with a pro-thrombotic status and elevated D-dimer levels<sup>(7)</sup>.

#### **Aim of work:**

Evaluate biochemical abnormalities in infected type 2 diabetic patients comorbid with COVID

#### **Material and Methods**

The current study is a case control study was conducted on 89 persons, 35 males and 54 females of the same age group (40:75 years) were selected from outpatient clinic of diabetes, Diabetes and Endocrinology unit, and Intensive care unit of Department of internal medicine at Minia University Hospital from December 2021 to May 2022.

In current study: 89 subjects divided into three main groups:

First group: 25 of infected type 2 diabetic patients with COVID 19.

Second group: 25 of type 2 diabetic patients.

Third group: 35 of apparently healthy individuals.

The studied groups diagnosed according to American diabetes Association (ADA) 2022, WHO 2022, Centers for Disease Control and Prevention (CDC) 2022 and

guidelines of Egyptian ministry of Health 2022.

Exclusion criteria: the following patients were excluded from our study:

1. ITP patients.
2. Hematological malignancy.
3. Previous history of thromboembolism.
4. HTN or IHD or stroke patients.
5. Patients took any medications affecting coagulation profile or platelet's function.

All included patients were subjected to the following:

Complete history taking, Careful Clinical examination, laboratory investigations: D-dimer, Total cholesterol.

#### **Results**

Demographic and anthropometric data of the studied groups Shown in Table (1) as regard age was ranged in all groups from 40 to 75 yrs., The age was ranged in diabetics with COVID-19 from (54-75) years with mean  $\pm$  SD (65.3 $\pm$ 6.8), diabetics without COVID-19 from (40-70) years with mean  $\pm$  SD (55.3 $\pm$ 8.6) and control group from (40-70) years with mean  $\pm$  SD (47.6 $\pm$ 6.4) Females were more precipitated in this study 17 (68%) for diabetics with COVID19, 16(55%) for diabetics without COVID-19 and 21 (60%) for controls, There was no significant difference between the 3 groups as regards smoking.

Cholesterol levels significantly higher in diabetic with COVID-19 group than diabetic group with p value (0.01), (Table 2).

D-Dimer levels was significantly higher in diabetic with COVID-19 group than diabetic group and control group with p value (>0.001), (Table 3).

**Figure (1):** shows that the rate of mortality in Diabetic with COVID-19 patients was significantly directly proportional with D-Dimer level with p value (<0.001).

**Table (1): Demographic and clinical data of studied participants:**

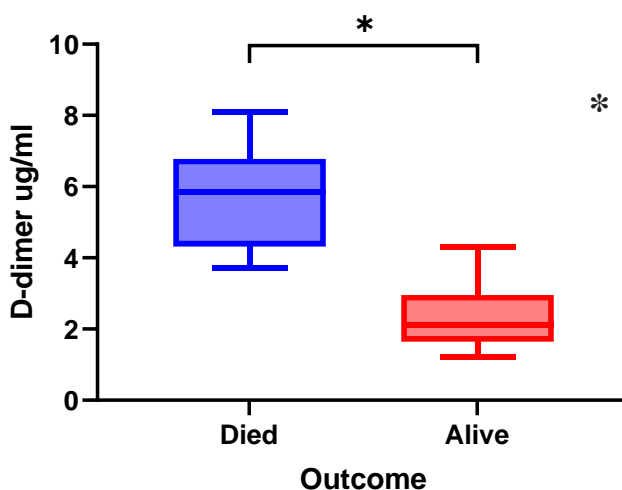
	Diabetic with COVID-19 (I)	Diabetic without COVID-19 (II)	Healthy control (III)	p value		
	(N=25)	(N=29)	(N=35)			
<b>Age (y)</b> <b>Mean±SD</b> <b>(Range)</b>	65.3±6.8 (54-75)	55.3±8.6 (40-70)	47.6±6.4 (40-70)	<0.001*		
				<i>I vs II</i>	<i>I vs III</i>	<i>II vs III</i>
				<0.001*	<0.001*	<0.001*
<b>Sex</b>				0.626		
<b>Male</b>	8 (32%)	13 (44.8%)	14 (40%)			
<b>Female</b>	17 (68%)	16 (55.2%)	21 (60%)			
<b>Smoking</b>				0.856		
<b>Non-smoker</b>	20 (80%)	24 (82.8%)	27 (77.1%)			
<b>Smoker</b>	5 (20%)	5 (17.2%)	8 (22.9%)			

**Table 2: Comparison between serum cholesterol in the studied groups:**

	Diabetic with COVID-19 (I)	Diabetic without COVID-19 (II)	Healthy control (III)	p value		
	(N=25)	(N=29)	(N=35)			
<b>Cholesterol</b> <b>Mean±SD<sup>(1)</sup></b> <b>(Range)</b>	154.5±36.2 (110-280)	185.2±46.8 (100-260)	148.7±20.9 (110-190)	<0.001*		
				<i>I vs II</i>	<i>I vs III</i>	<i>II vs III</i>
				0.01*	>0.99	<0.001*

**Table 3: Comparison between D-dimer in the studied groups:**

	Diabetic with COVID-19 (I)	Diabetic without COVID-19 (II)	Healthy Control (III)	p value
	(N=25)	(N=29)	(N=35)	
<b>D-DIMER ug/ml</b> <b>Mean±SD</b> <b>(Range)</b>	4±2.1 (1.2-8.1)	0.2±0.1 (0.1-0.5)	0.2±0.1 (0-0.4)	<0.001*



**Figure (1):** This figure shows that the rate of mortality in Diabetic with COVID-19 patients was significantly directly proportional with D-Dimer level with p value (<0.001).

## Discussion

In late 2019, a novel coronavirus was discovered in Wuhan, China, which was later named COVID-19. COVID-19 spread rapidly around the globe and was declared a pandemic on 11 March 2020. At 8 April 2022, there was 494,587,638 cases confirmed with COVID-19 and 6,170,283 deaths worldwide<sup>(8)</sup>.

As COVID-19 is not a localized respiratory infection but it is considered a multisystem disease, studies have been reported that various inflammatory, hepatic, coagulation and cardiac biomarkers are correlated with COVID-19 disease severity and mortality. Specifically, elevated levels of CRP, procalcitonin, and interleukin-6 have been associated with increased mortality<sup>(9)</sup>.

The current study is a case-controlled study was conducted on 89 persons, 35 males (40%) and 54 females (60%) of the same age group (40:75 years).

Our study revealed that the serum cholesterol levels significantly higher in diabetic with COVID-19 group than diabetic group with *p* value (0.01).

Matching with us Rezaei et al., 2021 who showed that lipid metabolism is altered in patients with COVID-19 through direct cellular infection as well as systemic inflammatory response. These alterations mainly result in a decrease in Total Cholesterol, LDL-C, and

HDL-C levels and increased TG levels among these patients. Lower HDL-C levels appear to have a significant prognostic role in predicting poor clinical outcomes<sup>(10)</sup>.

Contrarily Wei et al., 2020 said that LDL-c and TC levels were significantly lower in COVID-19 patients as compared with normal subjects ( $p < 0.001$ ), LDL-c and TC levels inversely correlated with C-reactive protein and interleukin-6, and positively correlated with the number of lymphocytes in patients<sup>(11)</sup>.

Yang et al., 2022 found that elevated non-traditional lipid parameters were significantly associated with pre-DM and T2DM in CHD patients, especially TG/HDL-C. High TG/HDL-C was the risk factor with a strong correlation with the risk of pre-DM and T2DM, and this is consistent with our study<sup>(12)</sup>.

Also, our study demonstrated that D-dimer levels are significantly higher in diabetic with COVID-19 group than diabetic and control groups with *p* value (0.001).

Debi et al., 2022 concluded that serum CRP and D-Dimer concentration that was used to diagnose the lung lesion and the existence of a prothrombotic condition was remarkably higher in COVID-19 diabetic patients. The severity of COVID-19 might be detected by early serum CRP and D-Dimer and provide cause for physicians to begin early initiation of treatment, and this is consistent with our results<sup>(13)</sup>.

Similarly, Castro & Frishman, 2021 found that COVID-19 has been widely associated with thromboembolic events such as pulmonary embolism, deep-vein thrombosis (DVT), ischemic stroke and myocardial infarction, which represent a predominant cause of death in patients with severe COVID-19. Similar to the proinflammatory state, diabetes mellitus is also associated with a hypercoagulable state. Patients with diabetes in general have an increased risk of thromboembolic events so infection with COVID-19 can add a higher risk of death<sup>(14)</sup>.

## Conclusion and Recommendations

T2DM patients infected with COVID-19 have distinguishing clinical features and biochemical changes during infection. It is necessary to develop a different clinical severity scoring system for patients with T2D who become infected with COVID-19. This may provide helpful clues for the assessment and management of COVID-19 in such patients. We hope this may provide

reference materials for more efficient supportive care and management of T2DM patients infected with COVID-19.

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