

## Assessment of D. Dimer in Sudanese Patients with COVID19 in Khartoum State 2021

Olla Albagir Abdeen<sup>1</sup>, Ehab Mohammed Elmadinah Mohammed Ahmed<sup>2</sup>, Albara Abdulfatah Mohammed Ahmed<sup>3</sup> and Sahar Elderdiri Gafar Osman<sup>3\*</sup>

<sup>1</sup>Medical Laboratory Science Department, National University, Sudan

<sup>2</sup>Faculty of Medical Laboratory Sciences, Dongola University, Sudan

<sup>3</sup>Medical Laboratory Science Department, Alfajr College for Science and Technology, Sudan

**\*Corresponding Author:** Sahar Elderdiri Gafar Osman, Medical Laboratory Science Department, Alfajr College for Science and Technology, Khartoum, Sudan.

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### Abstract

**Background:** D. dimer is an important prognostic tool, an elevated level of D-dimer in coronavirus disease (COVID19) patients has emerged as a critical characteristic of the disease, and the association between elevated D. dimer level and severe coronavirus disease19 have been reported by several studies.

**Objective:** This study was aimed to assess the D. dimer in Sudanese patients with COVID19.

**Methods:** This was a case-control study conducted at the Isolation Center of Jabra Emergency Hospital during the period January 2021 to May 2021. D. dimer was assessed in 198 Sudanese patients with COVID19 (case) confirmed with Real-Time Polymerase Chain Reaction (TR-PCR) and healthy individual negative TR-PCR (control) ninety-nine (99) in each arm.

**Results:** In the present study 122 (62%) were male, and 76 (38%) were female. The mean (STD) of age and D. dimer level was significantly higher in cases versus control group p. value (0.047 and < 0.001 respectively), also D. dimer significantly higher in cases admitted to Intensive Care Unit (ICU) versus cases not admitted to ICU with P. Value (< 0.001). The mean (STD) of D. dimer in cases with chronic disease was significantly higher than cases without chronic disease. In the case group with chronic disease, D. dimer level was significantly higher in Diabetes Mellitus (DM), hypertension, renal disease, thrombotic disease whereas no significant differences between Asthmatic and non-asthmatic patients with P. Value (< 0.001, < 0.001, < 0.001, 0.004, 0.915) respectively.

**Conclusion:** The assessment of D. dimer level can be used as a prognostic marker for the COVID19 disease severity, and outcomes.

**Keywords:** COVID19; D. Dimer Level; Sudanese Patients

### Introduction

The novel coronavirus pneumonia outbreak (coronavirus disease 2019) which was caused by severe acute respiratory syndrome coronavirus2 (SARS-CoV-2) was reported in Wuhan, China, in December 2019 [1]. The Chinese center for disease control and prevention

then detected the genomic sequence of beta-coronavirus new type in samples from a patient with pneumonia. The outbreak rapidly infected people across the world and became global a pandemic [2]. Globally, the cumulative number of confirmed COVID19 cases is about 183 million, and the number of confirmed deaths is about 4 million [3]. In Sudan according to last update for WHO there were 37.183 confirmed cases, 2.776 confirmed deaths, and the total number of vaccine doses have been administrated 819.035 [4]. The disease is transmitted from natural host (Bats) to human through an unknown intermediate host and from human to human, through close contact with COVID19 patients via respiratory tract droplets [5]. Several studies indicate that the digestive system may serve as an alternative mode of transmission through vomiting and fecal-oral transmission. The virus invades host human cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor. Angiotensin-converting enzyme2 receptor found in various human organs, particularly in colon higher than respiratory system [6]. Although COVID-19 is primarily manifested as a respiratory tract infection, increasing data suggest a multi-systemic disease including: gastrointestinal, cardiovascular, hematopoietic, neurological, and immune system [7]. The symptoms of COVID-19 are non-specific; the most common symptoms are fever and dry cough. Less common symptoms include fatigue, respiratory sputum production, loss of the sense of smell, loss of taste, shortness of breath, muscle and joint pain, sore throat, headache, chills, vomiting, coughing out blood, diarrhea, and rash [8]. The severity of the disease ranges from mild, moderate, severe, to critical disease according to clinical manifestations [2]. The primary outcome of COVID19 is twenty-eight days' death after ICU admission, and the secondary outcomes include: acute respiratory distress syndrome (ARDS) and mechanical ventilation required as main supportive treatment, shock, and acute renal injury [9]. The real-time polymerase chain reaction (RT-PCR) is considered as the gold standard for detection of SARS COV2 Nucleic Acid in lower and upper respiratory tract samples, also in the stool [10]. Chest imaging by computed tomography scan (CT) used as an alternative to diagnose the asymptomatic patient with negative PCR, also has a critical role in the detection of complications and prognosis of the disease [11]. Serological tests such as enzyme-linked immune-sorbent assay (ELISA), point of care test (POCT), and Chemiluminescence Immuno-assay help in screening and diagnosis of suspected patients with negative molecular test [12]. Because the diagnosis of COVID19 is primarily based on symptoms, which is nonspecific the assessment of D. dimer level is necessary as a primary auxiliary test for early diagnosis and prognosis [13]. D. dimer is fibrin degradation fragments that are produced when plasmin, an enzyme activated through the fibrinolytic pathway, cleaves fibrin to break down clots during normal hemostasis [14]. It consists of two covalently bonded fibrin D domains that were cross-linked by activated factor XIII when the clot was formed [15]. The formation of fibrin clots by the coagulation system in response to vascular injury is balanced by the breakdown of the clot by the fibrinolytic system. D-dimer levels are increased in all cases of acute venous thromboembolism (VTE). However, any process that increases fibrin production or breakdown also increases D-dimer levels such as: pregnancy, inflammation, cancer, Deep venous thrombosis (DVT), Disseminated intravascular coagulation (DIC), and surgery [16]. D-dimer levels in healthy individuals increase with age over 70 years [17]. Several studies reported that D. dimer antigen can use as a marker to predict those who are progressing to critical cases [2,18].

### Aim of the Study

The present study was aimed to assess the D. dimer in Sudanese patients with COVID19.

### Methods

#### Study design

This was a case-control study conducted at the Isolation Center of Jabra Emergency Hospital during the period January 2021 to May 2021 to assess D. Dimer in Sudanese patients with COVID19 in Khartoum state.

#### Participants

A total of one hundred ninety-eight (198) participants were enrolled in the study, ninety-nine (99) in each case group and control group. COVID19 patients confirmed by RT-PCR were cases and individuals with Negative RT-PCR, without chronic disease were controls.

Chronic diseases were defined according to WHO [19]. The demographics, clinical, and laboratory data were collected in a structured questionnaire. The data and specimens were collected by the trained working staff at the center of isolation.

**Test method**

Vacutainer citrate test tubes were used to collect venous blood samples and D. dimer level was measured by I Chroma™ analyzer. 10 µl of citrated venous blood samples were added to tubes containing detection buffered, samples were mixed gently 10 times, then 75 µl from sample mixture were dispensed into the well on the cartridge and the samples loaded cartridge was left at room temperature for 12 minutes. Finally, the samples loaded cartridge was inserted into cartridge holder in I Chroma™ analyzer and the displayed result on screen were recorded. D. dimer less than 500 ng/ml was considered as normal whereas D. dimer more than 500 ng/ml was considered as positive [20]. All participants were asked to assign a written consent form.

**Ethical consideration**

The study was approved by the Ethical Committee of Medical Laboratory Sciences College, National University (NU-REC/08-02/03).

**Analysis**

The statistical package of social sciences (SPSS) was used for the statistical analysis version (20). Descriptive statistics obtained from categorical variables and Chi-square (X<sup>2</sup> test) were used to test the significance of frequency. Descriptive statistics were obtained from continuous variables and a T-test was used to test the significance of mean (STD). Statistical significance was set at P < 0.05.

**Results**

In the present study 122 (62%) were male, and 76 (38%) were female. The mean (STD) of age and D. dimer level was significantly higher in cases versus control group P. value (0.047, and 0.001, respectively), also D. dimer significantly higher in cases admitted to Intensive Care Unit (ICU) versus cases were not admitted to ICU with P. Value (< 0.001) (Table 1). When the COVID19 case group was divided according to the presence of chronic disease, the mean (STD) of D. dimer in COVID19 cases with chronic disease were significantly higher than cases without chronic disease, whereas no significant differences between Asthmatic and non-asthmatic patients. In the COVID19 case group with chronic disease, D. dimer level was significantly higher in Chronic Lymphoid Leukemia, Renal disease, Diabetes mellitus, Hypertension, Thrombotic disease, Asthma, Liver disease in the ordered descending (Table 2).

Variables		Frequency	Mean (STD)	P. Value
Age Between (40 to 84)	Cases	99	60.25 (11.688)	0.047
	Controls	99	56.90 (11.960)	
D. dimer	Cases	99	4984 (4210.7)	< 0.001
	Controls	99	247.80 (131.15)	
D. dimer	Admitted to ICU	58	80117.60 (2513.0)	< 0.001
	Not Admitted to ICU	41	692.66 (617.1)	

**Table 1:** Mean (STD) of age and D. dimer levels ng/ml in the study population.

Disease Name		Frequency (%)	Mean (STD)	P. Value
Diabetes Mellitus	Yes	29 (29.3)	8743.00 (2001.4)	<0.001
	No	70 (70.7)	3426.76 (3753.9)	
Asthma	Yes	7 (7.1)	5145.43 (3949.8)	0.915
	No	92 (92.9)	4971.76 (4153.9)	
Hypertension	Yes	29 (29.3)	7663.62 (2850.2)	<0.001
	No	70 (70.7)	3873.93 (4068.3)	
Renal disease	Yes	10 (10.1)	9131.00 (1659.9)	<0.001
	No	89 (89.9)	4518.09 (4056.3)	
Thrombotic Disease	Yes	13 (13.1)	7981.85 (2378.7)	0.004
	No	86 (86.9)	4530.88 (4146.7)	
Chronic Lymphoid Leukemia	Yes	1 (1.01)	10000.00	-
	No	98 (98.99)	4932.86 (4110.0)	
Liver Disease	Yes	1 (1.01)	2872.00	-
	No	98 (98.99)	5005.59 (4136.2)	
Chronic disease	Yes	63 (63.4)	7542.43 (2916.9)	<0.001
	No	36 (36.6)	506.86 (266.8)	

**Table 2:** Mean (STD) of D-Dimer levels ng/ml among cases with chronic diseases.

## Discussion

The main finding of the present study is that the level of D. dimer was significantly higher in COVID19 patients compared to control. COVID19 is characterized by hypercoagulability, and patients with COVID19 were at risk to developed both venous and arterial thrombosis [21-23]. Although the mechanism is unclear, the previous studies suggested that the endothelial dysfunction and inflammatory responses induced by SARS-CoV-2 may play a critical role in hypercoagulability [24], so this may explain the reason for increased plasma D. dimer level in COVID19 patients. In a meta-analysis study conducted by Du., *et al.* (2021) [25], they found a significant relationship between D. dimer and coronavirus disease [19]. To exclude if the chronic diseases are the reason for increased D. dimer level, we divided patients with COVID19 (cases) into COVID19 with chronic disease, and without chronic disease group. In the present study, the level of D. dimer was significantly higher in COVID19 patients with the chronic disease compared to COVID19 patients without chronic disease, this finding may prove the impact of chronic disease on COVID19 progression. Also, when compared between the mean (SD) of COVID19 patients without chronic disease versus the control group the differences were found (506.86 (266.8) vs (247.80 (131.15)), respectively and this is consistent with the fact that COVID19 is characterized by hypercoagulability as mentioned above. Yao., *et al.* (2020) retrieved 248 consecutive COVID19 patients and excluded hematological malignancy, cancer, pregnancy, chronic liver disease, acute coronary syndrome, and surgery or trauma within 30 days. They demonstrated an elevated D. dimer level at hospital admission and associated with severity and mortality. In the current study D. dimer was significantly high in a patient with Chronic lymphoid leukemia, renal disease, thrombotic disease, and liver disease, and these results were agreed with Muntanola., *et al.* (2020) [26]; Navarrete., *et al.* (2021) [27]; Zhang., *et al.* (2020); Tsutsumi., *et al.* (2021) [28], respectively. D. dimer was significantly increased in COVID19 patients with diabetes mellitus (DM) versus COVID19 patients without DM, and this may be because increased blood glucose level (hyperglycemia) lead to endothelial dysfunction and inflammation, and the later lead to thrombus formation [9]. The level of D. dimer was significantly higher in COVID19 with hypertension and this result was consistent with Yang., *et al.* (2020). Although the role of hypertension in the progression

or outcomes of COVID19 is not clear, several studies suggested that activation of the Renin-Angiotensin System (RAS) plays a critical role in disease progression. Angiotensin-Converting Enzyme2 (ACE2) is the receptor of SARS-CoV-2 in the host cell, any drugs that lead to upregulation of (ACE2) will lead to an increase in the risk for infection and inversely outcomes in COVID19 [29]. In the present study, we divided the COVID19 patient cases group into cases needed for ICU admission (critical cases) and cases not needed for ICU admission (not critical cases). D. dimer level was found significantly higher in cases that needed admission to the Intensive Care Unit (ICU) compared to cases were not needed admission to the Intensive Care Unit (ICU). This finding is consistent with J. Zhang, *et al.* (2020) [30], they found that the level of D. dimer in COVID19 critical cases is significantly higher than COVID19 severe cases, and concluded that the monitoring of D. dimer level assists in the identification of critical cases at an early stage. Also, similar findings reported by He., *et al.* (2021) [31], they examined D. dimer level in patients with mild, moderate, severe, and critical cases to explore the value of D. dimer on the prognosis of COVID19. They found that D. dimer level was related to clinical classification and prognosis of outcomes.

### Conclusion

Dimer level was significantly higher in the COVID19 patients. The assessment of the D. dimer level can help physicians to predict clinical outcomes and monitoring of COVID19 severity.

### Conflict of Interest

There is no conflict of interest.

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