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## D-dimer levels in COVID-19 out-hospitalized patients in Egypt

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### ABSTRACT

**Background:** The D-dimer is formed by the activation of the plasmin enzyme, and elevated levels indicate that there is a hypercoagulable state and secondary fibrinolysis in the body, which is extremely useful for the diagnosis of thrombotic diseases. Patients with COVID-19 were reported to have a hypercoagulable state. **Patients and methods:** This study included 231 out hospitalized patients with confirmed COVID-19 infection in Alexandria, Egypt, these study subjects were randomly selected irrespective of the age group and both genders were included. **Results:** The present study included patients aged from 14 years to 75 years mean age was  $44.5 \pm 30.5$  who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, This study reveals high plasma D-dimer levels in 84 patients (36.4%), which was a significant biomarker for COVID-19 diagnosis in out-hospitalized patients (Outpatients and patients under home observation), with a p-value is 0.00001 which less than 0.05. **Conclusion and Recommendations:** False data about D-dimer was caused more deaths in Egypt for patients and physicians, they thought Anticoagulation therapy was only for hospitalized patients and not for out-hospitalized patients with moderate infection, they thought the D-dimer test is not important for out-hospitalized patients, but this study showed a high level of D-dimer 36.4% in out- hospitalized patients with COVID-19, so 36.4% of outpatients and patients under home observation need Anticoagulation therapy to decrease the complications of COVID-19 infection, Many individuals with diabetes and immunosuppressive diseases it is known that they face a higher probability to experience serious complications from COVID-19 infection so Anticoagulation therapy is suggested before the elevation of D-dimer level to avoid serious complications.

**Keywords:** D-dimer, COVID-19, out-hospitalized patients, biomarker

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## 1. Introduction:

The D-dimer is formed by the activation of the plasmin enzyme. This indicates the presence of a demolished fibrin in the bloodstream. The Fibrinolytic system breaks down the fibrin mesh after the formation of the clot. D-dimer represents the activation of coagulation and fibrinolysis systems<sup>(1)</sup>. The D-dimer test is usually used in clinical practice to exclude a diagnosis of deep vein thrombosis (DVT) and pulmonary embolism (PE) and confirm the diagnosis of disseminated intravascular coagulation (DIC)<sup>(2)</sup>. The D-dimer levels rise almost in all patients with severe VTE. In physiological conditions such as pregnancy and pathological conditions such as cancer, inflammation, and surgery the elevated level of D-dimer can be seen<sup>(3)</sup>.

On 29 December 2019, a patient with symptoms of pneumonia was diagnosed by Chinese doctors, who reported to the World Health Organization (WHO) on 31 December 2019<sup>(4)</sup>. In the early phase of COVID-19 infection, leukopenia, lymphocytopenia, high level of CRP, high D-dimer, prolonged PT, and high levels of fibrinogen

have been reported<sup>(5,6)</sup>. It has been reported that Covid-19 was associated with hemostatic abnormalities, and markedly elevated D-dimer levels were observed in those non-survivors<sup>(5)</sup>. D-dimer elevations were seen in 3.75–68.0% of the COVID-19 patients<sup>(7,8)</sup>. Anticoagulation therapy was associated with lower mortality in COVID-19 and this was especially true for patients with high D-dimers<sup>(9)</sup>.

False data about D.dimer was caused more deaths in Egypt for patients and physicians, they thought Anticoagulation therapy was only for hospitalized patients who have high D-dimer levels and not for out-hospitalized patients with moderate infection, they thought the D-dimer test is not important for out-hospitalized patients, so this study aimed to evaluate D-Dimer levels in patients with COVID-19, Outpatients

and patients under home observation are included in this study, while hospitalized patients are not included.

## 2. Patients and methods

### 2.1. Study population Patients

This study included 231 out-hospitalized patients with confirmed COVID-19 infection, these study subjects were randomly selected irrespective of the age group and both genders were included.

It was performed following the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All the studied population was informed about the purpose of sample collection and their consents were obtained. Patients were free to refuse sample collection.

### 2.2. Data collection

In this cross-sectional study, we obtained data regarding 231 out- hospitalized patients and patients under home observation with confirmed COVID-19 via real-time reverse transcription-polymerase chain reaction (PCR), they came to Alyameny laboratory in Alexandria, Egypt for biomarkers and complete blood count investigations, We reviewed the medical records and compiled data between August 12 and December 30, 2020.

### 2.3. Collection and processing of blood samples:

Plasma prepared from whole blood anticoagulated with sodium citrate was collected for performing D-dimer test (BioMedica Diagnostic inc. Canada DIMERTEST latex assay for semi-quantitative evaluation) on 231 Positive COVID-19 patients for individuals matching in age and gender.

### 2.4. Assay procedure as manufactory instructions:

Reagents of BioMedica Diagnostic inc. Canada kit human D-dimer test and samples allowed to be at room temperature before testing, (plasma was separated from a citrated blood sample by centrifugation), considered normal plasma D-dimer level less than 0.20 mg/l (200 ng/ml) U/L.

**2.5. Statistical analysis**

Data were analyzed using SPSS statistical software, version 20.0 (SPSS, Chicago, Illinois, USA). All continuous data are presented as means and standard deviations, while categorical data are presented as numbers and percentages. A chi-square test was used to compare categorical variables. Multivariate regression analysis was performed to analyze relationships between COVID-19 infected patients and plasma D-dimer level, this model was generated using independent variables achieving a p-value of 0.10 during bivariate analysis. Then, the best-fit model was generated without interaction variables. For all calculations, a p-value of less than 0.05 was considered statistically significant.

**3. Results:**

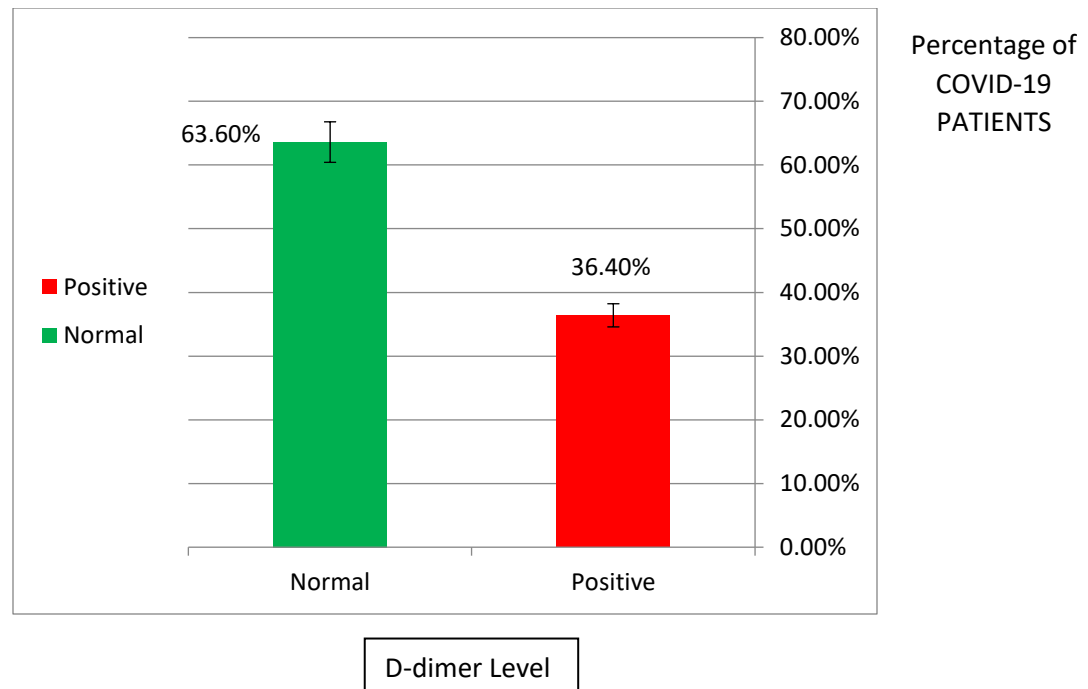
Table (1): shows The percentage of COVID-19 out-hospitalized Patients relation to the plasma D-dimer level, The present study included patients aged from 14 years to 75 years mean age was  $44.5 \pm 30.5$  who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, female gender was more frequent (n=119, 51.5%) than Male gender (n=112, 48.5%). This study reveals high plasma D-dimer levels in 84 patients (36.4%), which was a significant biomarker for COVID-19 diagnosis in non-hospitalized patients (Outpatients and patients under home observation), with a p-value is 0.00001 which is less than 0.05.

**Table (1):** The percentage of COVID-19 out-hospitalized Patients and plasma D-dimer level.

| COVID-19 POSITIVE Patients | Plasma D-dimer level |      |            |    | Total |      |
|----------------------------|----------------------|------|------------|----|-------|------|
|                            | *Normal              |      | **Positive |    |       |      |
|                            | No.                  | %    | No.        | %  | No.   | %    |
| Male                       | 91                   | 61.9 | 21         | 25 | 112   | 48.5 |
| Female                     | 56                   | 38.1 | 63         | 75 | 119   | 51.5 |
| Total                      | 147                  |      | 84         |    | 231   |      |

The chi-square statistic is 29.148. The p-value is < 0.00001. Significant at  $p < .05$ .

The chi-square statistic with Yates correction is 27.6892. The p-value is < 0.00001. Significant at  $p < .05$ .

**Figure (1): Plasma D-dimer level with the percentage of COVID-19 PATIENTS**

#### 4. Discussion:

D-dimer is the product of fibrinolytic degradation of fibrin, and elevated levels indicate that there is a hypercoagulable state and secondary fibrinolysis in the body, which is extremely useful for the diagnosis of thrombotic diseases. Patients with COVID-19 were reported to have a hypercoagulable state<sup>(10)</sup>, with 71% of patients who died from COVID-19 were found to have met the DIC standard, this ratio among surviving patients was only 0.6%<sup>(5)</sup>. In addition, the incidence of venous thromboembolism (VTE) in patients with severe COVID-19 was 25%, and 30% of COVID-19 patients were diagnosed with pulmonary embolism<sup>(6,11)</sup>. The results of this study showed that there were 84 (36.4%) patients with abnormal D-dimer from 231 Outpatients with mild symptoms and patients under

home observation were included in this study, which has a significant p-value. The present study included patients aged from 14 years to 75 years mean age was  $44.5 \pm 30.5$  who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction (PCR).

Increased ferritin levels could cause a cytokine storm by exerting direct immunosuppressive and pro-inflammatory effects, It has been reported that fatal outcomes by COVID-19 are accompanied by cytokine storm syndrome and ferritin level was significant in COVID-19 home observation patients<sup>(12)</sup>, many studies were conducted on severe and very severe COVID-19 hospitalized patients, Coagulopathy and overt disseminated intravascular coagulation appear to be associated with high mortality rates. Among the

coagulation parameters, D-dimer elevation was the strongest independent predictor of mortality from 191 cases 91 non-survivors have a high level of D-dimer<sup>(8)</sup>, Non-survivors have shown significantly higher levels of plasma D-dimers and fibrin degradation products, increased prothrombin times, and activated partial thromboplastin times compared to survivors the study was on 183 cases, 21 non-survivors<sup>(5)</sup>, Han et al., reported increasing of D-dimer level compared with control in 94 cases<sup>(13)</sup>, Wu et al., reported increasing of D-dimer level in ARDS cases<sup>(14)</sup>, Zhang et al., a study Of 140 cases showed elevation of D-dimer in severe cases<sup>(15)</sup>, a study by Gao et al., on 43 cases (28 mild and 15 severe cases) showed a high level of D-dimer in severe cases<sup>(16)</sup>, Liu et al., showed elevation of D-dimer level in 17% of cases and the study was conducted on 30 cases<sup>(17)</sup>, but Mo et al., reported normal D-dimer level in 70 mild cases and slightly higher in 85 severe cases<sup>(18)</sup>.

### Conflict of interest

There are no conflicts of interest.

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