Estimation of D-Dimer Level among Sudanese Patients with COVID-19 Infection-Khartoum State 2022

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INTRODUCTION:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) has rapidly evolved from an epidemic outbreak in Wuhan, China, into a pandemic infecting more than one million individuals all over the world, where as billions of citizens are affected by measures of social distancing and the socioeconomic impact of the pandemic. COVID-19 has been reported as the primary cause of death in critically ill patients. Furthermore, its potential role in predicting mortality in septic critically-ill patients has recently been reported. VTE is one of the severe complications identified in critical COVID-19 patients and coagulopathy resulting in VTE and DIC has been reported to be the primary cause of death in critical patients. Numerous hemostatic cellular and plasmatic elements interact to trigger inflammatory and immune cascade leading to VTE in the presence of sepsis and acute respiratory distress syndrome (ARDS). Our aim was to describe effect of COVID 19 over coagulation tests. This study was designed to measure the D-dimer level among Sudanese patients with COVID-19 infection.

MATERIAL AND METHODS:
This was case control study conducted at COVID-19 quarantine hospitals in Khartoum state during the period from May to July 2022. For the measurement of D-dimer level among Sudanese covid 19 patients. One hundred participants were selected as cases and apparently fifty participants were selected as control group. 28 ml of venous blood samples were collected in Tri Sodium Citrate anticoagulant The D-dimer was performed using BS5protein analyzer.

RESULTS: When compared the D-dimer results between case and control there was highly significant difference with p value 0.000. In addition the D-dimer in cases compared with the other study variables which revealed; significant differences with the chronic disease and the severity of the disease, in significant differences with the age, gender and smoking status.

CONCLUSION: This study concluded that D-dimer was significantly increase in COVID-19 patients, and it had significant differences with the chronic disease and the severity of the disease, insignificant differences with the age, gender and smoking status.

Keywords: COVID-19, SARS-CoV-2, D-dimer, chronic disease and BS5protein analyzer.
without history of bleeding thrombi or under anticoagulant drugs were selected as control group. 2.8 ml of blood samples were gathered in trisodium citrate anticoagulant container for D-dimer measurement. The participants were interviewed with questionnaires; the questions were about demographic data and clinical information along with other data required in the study. Permission to carry out the study was obtaining from ethical committee of collage of medical laboratory science, West Nile Collegeand verbal consent was taken from each participant.

**Principle of the test:**

Is based upon an immunometric flow through principle. The plasma sample is applied to the test well of the device. When the sample has soaked in to the device D-dimer molecules are trapped on a membrane carrying D-dimer specific monoclonal antibodies.

The conjugate solution then was added contains D-dimer specific monoclonal antibody conjugated with ultra-small gold particles. The D-dimer on the membrane was bind the gold-antibody conjugated in a sandwich-type reaction. The excess conjugate is removed from the membrane by the washing solution.

In the presence of D-dimer levels above 0.1 mg/L in the sample the membrane appears reddish with color intensity proportional to the D-dimer concentration. The color intensity is evaluated using B50 protein analyzer.

**Test Procedure**

Prewashing; apply 50 ml of washing solution to the test device. Avoid touching the membrane with the pipette. Sample; apply 50 ml undiluted platelet-free citrated plasma or control to the test device. The sample was absorbed into the membrane in less than 50 second. Conjugate; apply 50 ml of conjugate to the test device. The conjugate was absorbed into the membrane in less than 50 second. Washing; apply 50 ml of washing solution to the test device. The positive was used to confirm the efficacy of the reagents and the correct performance of the test. The measured value within the acceptable limits stated on the vial label.

**RESULT**

**Socio-demographic data**

In the present study, one hundred participants were selected as cases and apparently fifty participants were selected as control group. In the case group about 60% were male and 40% were female, their mean of age was (57.6 ± 15.6) years. In addition to that about 22% were smoker and 78% were not smoker, for the history of chronic disease about 24% had a history of diabetes mellitus, 15% had history of hypertension and about 41% didn’t have a history of any chronic disease. (Table 1, 2) (Figure 1,2,3).

Regarding to the severity of COVID-19 among the case group, about 41% were a moderate cases, 34% severe cases, and 25% were mild cases. (Table 3) (Figure 4)

**Table 1: Sociodemographic data**

| Gender | Frequency | Percent |
|--------|-----------|---------|
| Case   |           |         |
| Male   | 60        | 60.0    |
| Female | 40        | 40.0    |
| Total  | 100       | 100.0   |
| Control|           |         |
| Male   | 37        | 74.0    |
| Female | 13        | 26.0    |
| Total  | 50        | 100.0   |

| Case ( Age ) | Minimum | Maximum | Mean  | Std. Deviation |
|--------------|---------|---------|-------|----------------|
|              | 26      | 95      | 57.6  | 15.6           |

| Control(Age) | Minimum | Maximum | Mean  | Std. Deviation |
|--------------|---------|---------|-------|----------------|
|              | 23      | 92      | 62.9  | 17.1           |

| Cases | Smokers | Frequency | Percent |
|-------|---------|-----------|---------|
|       | 22      | 22        |         |

| Cases | Non smokers | Frequency | Percent |
|-------|-------------|-----------|---------|
|       | 78          | 78        |         |

**Table 2: Distribution of Chronic disease in the case group**

| Chronic disease | Frequency | Percent |
|-----------------|-----------|---------|
| No              | 41        | 41.0    |
| Diabetic        | 24        | 24.0    |
| Hypertensive    | 15        | 15.0    |
| Asthma          | 4         | 4.0     |
| Cardiac disease | 9         | 9.0     |
| CRF             | 7         | 7.0     |
| Total           | 100       | 100.0   |
Table 3: Distribution of Severity of disease

| Severity of disease | Frequency | Percent |
|---------------------|-----------|---------|
| Mild                | 25        | 25.0    |
| Moderate            | 41        | 41.0    |
| Sever               | 34        | 34.0    |
| Total               | 100       | 100.0   |

3.1.2 Hematological Result:
The mean of D-dimer in the cases was (8.5± 5.4) while in the control group was (0.3±1) (table 4) (figure 5). When compared the D-dimer mean between case and control group there was highly significant differences (p. v= 0.000) (table 5).

Also the D-dimer in cases compared with the other study variables which revealed; significant differences with the chronic disease and the severity of the disease, in significant differences with the age, gender and smoking status. (Table 6, 7).

Table 4: Mean of D-Dimer in case and control

| Variables | N         | Minimum | Maximum | Mean | Std. Deviation |
|-----------|-----------|---------|---------|------|----------------|
| Case      | D-Dimer   | 100     | .85     | 21.10| 8.5            |
|           |           |         |         |      | 5.4            |
| Control   | D-Dimer   | 50      | .14     | .51  | 0.3            |
|           |           |         |         |      | 0.1            |
Table 5: Comparison of D-Dimer between case and control

| Study population | D-Dimer | P. value |
|------------------|---------|----------|
| Case (n=100)     | 8.5 ± 5.4 |          |
| Control (n=50)   | 0.33 ± 0.12 | 0.000*   |

Table 6: Comparison of D-Dimer according to study variables

| Variables              | D-Dimer Mean ± SD | P. value |
|------------------------|-------------------|----------|
| Gender                 |                   |          |
| Male (n=60)            | 8.7 ± 5.7         | 0.605    |
| Female (n=40)          | 8.1 ± 5.1         |          |
| Age                    |                   |          |
| ≤ 40 years (n=15)      | 7.0 ± 5.0         |          |
| 40 - 60 years (n=38)   | 8.3 ± 5.7         | 0.465    |
| > 60 years (n=47)      | 9.0 ± 5.4         |          |
| Smoking status         |                   |          |
| Non-smoker (n=78)      | 7.9 ± 4.9         | 0.089    |
| Smoker (n=22)          | 10.6 ± 6.7        |          |
| Chronic disease        |                   |          |
| No (n=41)              | 4.4 ± 2.5         |          |
| Diabetic (n=24)        | 8.9 ± 4.2         |          |
| Hypertensive (n=15)    | 12.2 ± 4.9        |          |
| Asthma (n=4)           | 11.5 ± 5.0        | 0.000*   |
| Cardiac disease (n=9)  | 15.3 ± 5.0        |          |
| CRF (n=7)              | 11.7 ± 6.3        |          |

Table 7: Comparisons of D-Dimer according to severity of disease

| Severity of disease (I) | Severity of disease (II) | D-Dimermean (I) | D-Dimermean (II) | P. value |
|-------------------------|--------------------------|-----------------|-----------------|---------|
| Mild                    | Moderate                 | 2.3 ± 0.9       | 6.7 ± 1.6       | 0.000*  |
|                         | Sever                     |                 | 15.0 ± 2.9      | 0.000*  |
| Moderate                | Sever                     | 6.7 ± 1.6       | 15.0 ± 2.9      | 0.000*  |

Figure 5: Mean of D-Dimer in case and control

DISCUSSION

A case control study was enrolled, one hundred and fifty individuals were included in our study, one hundred patients with COVID-19 as case group and fifty healthy individuals as control group. In patients with COVID-19 about 60% were male and 40% were female, their mean of age was (57.6 ± 15.6) years. That agree with Araya S et al study, 455 Covid-19 patients, among the study participants, 289 (63.5%) were males with a mean of 49.9±18.3 years. Also agree with BabakSayad and ZohrehRahimi; the most frequent patients were male (59.4%) with a mean age of 65.1±17.1 years. Also consistent with study conducted by C. Ibañez, et al; Nineteen
patients were included, 53% patients were males and 47% were females with a mean age of 61 years. [1,11,12,13]

This study revealed that most frequent chronic disease was diabetes mellitus. That conflict with C. Ibañez, et al, showed that most frequent comorbidity was hypertension (47%). [13]

In present study, regarding to the severity of COVID-19 among the case group; about 41% were a moderate cases, 34% severe cases, and 25% were mild cases. That agree with Araya S et al, from the total 455 study subjects, there were 297 mild cases, 90 severe cases, and 68 critical cases based on disease severity of COVID-19. [11]

In our study, the mean of D-dimer in the cases was (8.5± 5.4) while in the control group was (0.3±1) with highly significant differences (p = 0.000), that consistent with Babak Sayad and Zohreh Rahimi, 2020 which reported; The mean level of D-dimer was increased in patients with COVID-19 (5.1±7.3) (0.1-25) µg/ml. [12] Also agree with C. Ibañez, et al, 2020; D-dimer levels were 6.2 (4.8-7.6 g/L), 1000 (600-4200 ng/ml). [11]

That corresponding with Thiago Domingos Corrêa, et al, 2020, D-dimer plasma levels were higher than normal reference range. [14] Franklin L. Wright, et al, 2020, showed elevated in D-dimer level. [15] Also another study conducted by Islam Elljilany and Abdel-Naser Elzoubki, 2020, revealed D-dimer was elevated. [16] In another study conducted by Lili Luo, et al, 2020, D-dimer levels were significantly elevated in COVID19 patients. That agree with study of Guan et al, 2020, presented that D-dimer in the cases was (8.5± 5.4) µg/ml. [14] Also another study conducted by C. Ibañez, et al, 2020, that consistent with C. Ibañez, et al, 2020; D-dimer levels were significantly elevated in COVID-19 patients admitted to the ICU: An exploratory study. PLos One 2020 Dec 15; 15(12):e0243604. https://doi.org/10.1371/journal.pone.0243604.

CONCLUSION

This study concluded that D-dimer was significantly increase in COVID-19 patients, and it had significant differences with the chronic disease and the severity of the disease, insignificant differences with the age, gender and smoking status.

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