Research Article

Evaluation of Fibrinogen level and Platelets Parameters in Patients with Covid-19 Infection in Atbara Town

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Abstract:

Background: COVID-19 can cause various conditions, including respiratory, enteric, and neurological diseases, and led to the pandemic that has affected millions worldwide. ***Methods***: This is a cross-sectional descriptive prospective study conducted at Atbara Teaching Hospital, which is located in Atbara town in Sudan, to determine the fibrinogen level and platelet count and platelet indices in patients with COVID-19 infection during the period between June and December 2021. A total of 100 patients who were diagnosed with the COVID-19 infection were enrolled in this study as test groups, with 50 healthy volunteers serving as a control group. Venous blood samples were collected from the test and control groups and transferred into Tri sodium citrate for measurement of fibrinogen levels and EDTA anticoagulant for analysis of platelet parameters. ***Results*:** The means of fibrinogen level, platelet count, PDW, and MPV in the test group were 147.63 md/dl, 274.90 x 109 /l, 14.587 FL, and 9.214 FL) respectively. The means of fibrinogen level, platelet count, PDW, and MPV in the control group were (163.86 md/dl, 332.46 x 109 /l, 15.426 FL, and 7.982 FL) respectively. Also, statistical analysis showed that there was significant variation in fibrinogen level, PDW, and MPV in a patient with COVID-19 when compared with healthy individuals. Low fibrinogen levels in COVID-19 patients may be due to an increased risk of thrombosis, so a greater degree of fibrinogen consumption occurs in COVID-19. ***Conclusions***: This study concludes that COVID-19 patients are at high risk of thrombosis because their blood tests reveal low fibrinogen levels. This study also concludes that there was thrombocytopenia in COVID-19 patients when their results showed a decrease in platelet distribution width and an increase in mean platelet volume.

Keywords: COVID-19, fibrinogen, platelet parameters, SARS-CoV-2, Atbara, Sudan.

Introduction:

Since December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-caused coronavirus disease-2019 (COVID-19) has infected about 30 million individuals globally and killed almost 1 million people. The sickness is very contagious and spreads through contact and aerosols. **[1].** since the initial diagnosis of COVID-19 in December 2019, SARS-CoV-2 has been quickly dispersing over the world. It has resulted in 209839 infection cases as of March 19, with 8778 fatalities. **[2].** 80% of patients infected by SARS-CoV-2 may be asymptomatic or only mildly symptomatic, but around 10% develop severe respiratory symptoms that evolve to acute respiratory distress syndrome (ARDS) **[3].** SARS-CoV-2 causes lung inflammation, which progresses to a cytokine storm in the most severe cases. The lungs of patients with COVID-19 show extensive alveolar and interstitial inflammation **[4].** COVID-19 causes a spectrum of diseases with frequent involvement of the hemostatic system **[5, 6].** Covid-19 vaccine is an immunization method used to reduce coronavirus incidence but lately caused life-threatening events such as thrombosis with thrombocytopenia syndrome **[7].** Severe pulmonary inflammation causes activation and damage to the pulmonary vasculature and may trigger pulmonary thrombosis early in the disease course **[8].** According to the Chinese Center for Disease Control and Prevention's preliminary figures, close to 20% of the patients were severe to critical, and their case-facility rate was significantly greater than that of the entire patient population. **[9].** Some individuals who were severely ill to critically ill saw the disease advance quite quickly. Therefore, it's critical to identify COVID-19 individuals at high risk as soon as possible to improve clinical procedures and results. The world Health Organization (WHO) **[10]** declared a pandemic on March 11th, 2020, after the identification of > 118.000 novel 2019 coronavirus disease (COVID-19) cases in 114 countries. As of May, 7 2020, a total of 3,825,028 cases had been identified in 187 countries, and unfortunately, 267,996 patients had died **[11].** The clinical spectrum of COVID-19 appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, severe viral pneumonia with respiratory failure, and even death **[12].** The common laboratory findings of viral infections are lymphopenia, leukopenia, and thrombocytopenia **[13,14].** In particular, COVID-19 has been shown to exert significant effects on the hematopoietic system and hemostasis **[15].** Studies have emphasized that patients diagnosed with COVID-19 are susceptible to hypercoagulation and thrombotic events **[16].** Microvascular thrombosis has been observed in autopsies performed on patients **[16].** Numerous viruses interact with platelets and megakaryocytes, the precursor cells of platelets, increasing the production of type I interferon genes, platelet-

mediated transport, and activation of proteases. Endothelial damage brought on by SARS-CoV-2 entry is known to occur, and this endothelial damage may draw platelets to the infection sites. The following platelet activation and degranulation could accelerate the progression of the disorders. **[17].** Additionally impacted are the mean platelet volume (MPV) and platelet distribution width (PDW). Megakaryocytes in the bone marrow express immunological molecules differently than those in the lung. This could be a result of the virus infecting these cells, which could lead to the generation of virus-containing platelets in the lungs. This could then change the pattern of transcription to increase the production of inflammatory cytokines. **[17].** Mean platelet volume (MPV) describes the average size of the circulating platelets and is a possible indicator of platelet function and activation **[18].** Inflammatory cytokines are known to induce the release of large platelets from the bone marrow by stimulating thrombopoiesis **[19].** It has been established that MPV is a key factor associated with mortality in many diseases **[20, 21].**

Materials and methods:

Study Design:

This is a cross-sectional descriptive study aimed to determine the fibrinogen level and platelet count and indices in Covid-19 patients.

Study Area:

The study was conducted in Atbara town which is located 315Km north of the capital Khartoum, the southern part of River Nile state and covering an area of about 200Km2.

Study Population:

A total of 100 patients with covid-19 were enrolled in this study with different ages from both sexes.

Inclusion Criteria:

Patients diagnosed with the covid-19 infection.

Exclusion Criteria:

COVID-19 patients suffering from other conditions like thrombosis, bleeding diseases, and pregnancy.

Specimen collection:

5.0ml of venous blood was taken from the patient and transferred 2.5 ml into an EDTA container for analysis. Platelets count and indices were done by an automated method. And 2.5 ml of blood was added to the anticoagulant at a ratio of 2.5ml to 0.5ml of citrate (3.2% (0.109M) buffered sodium citrate and gently mixed. The sample was centrifuged at 1300 rpm for 15min to obtain platelet-poor plasma (PPP). The PPP was placed into a plastic tube for analysis of the fibrinogen level by the Clauss method.

Method of platelets count and platelets indices Platelets count and indices will do by using Mindray Haematology Analyzer (Mindraybc3000):

Blood cells can be broadly divided into three categories. red blood cells, White blood cells, and platelets. The analyzer measures the number of cells and distinguishes between their types according to size using sheath flow DC detection. Electrical current is passed through a

solution; this method measures the changes in electrical resistance that occurs when blood cells pass through the detection aperture. This instrument performs hematology analyses according to the RF/DC detection method, Hydro Dynamic Focusing (DC Detection), and sodium lauryl sulfate (SLS) hemoglobin method. The radio frequencies and direct current (RF/DC detection method) detect the volume of blood cells by changes in direct-current resistance **[22]**. Platelet counts and indices were measured by using an automatic blood cell counter (Mindray-3000 analyzers).

Method of fibrinogen:

Fibrinogen level was measured by using an automatic coagulation device (Coatron M1). Coatron M1 coagulation analyzer measures the most important clotting-based coagulation tests using a low volume of reagents, the Coatron M1 directly converts the measured result from seconds. The Coatron M1 is a new coagulation device with an optic channel and LC-Display. The tests can be selected after switching them on. The dialog language is user-friendly and available in English and other languages for inquiry. The start of the measurement will be manually triggered by pressing the “optic” Key during the addition of the reagent. On the ready RS232 interface, a serial thermal printer can be connected at any time.

Data collection tools:

A questionnaire was used to obtain the primary information.

Data analysis and presentation:

Data collected in this study were analyzed using SPSS version 22, Chi-squire test will be used to assess the enter group's significance.

Ethical considerations:

Patients undergoing the test were given explanations of the venous blood sample process. All participants were informed about the research objectives and procedures during the interview period. Written valid consent was obtained from all participants. All result was with high privacy and confidentiality.

Results:

Coronavirus disease 2019 (COVID-19) causes a spectrum of diseases; some patients develop a severe proinflammatory state which can be associated with a unique coagulopathy and procoagulant endothelial phenotype. In this study, a total of (100) blood samples were collected from COVID-19 patients and (50) samples were collected as control from healthy individuals. Regarding sex (53%) of the study, the population was male, while (47%) was female as noted in **(Table1).** Also, regarding the age of the study population, the results showed that about (3%) with age less than (30 years), while the remaining (97%) with age more than (30 years) as demonstrated in **(Table2).** The results of this study revealed that the mean Fibrinogen level in the test group was (147.63mg/dl), while in the control group was (163.86 mg/dl) as shown in **(Table3).** Also, the results of this study showed that the mean of Platelet count, PDW, and M PV, in the test group, were (274.90 x10 9/l, 14.587%, 9.214 fl),

respectively, while in the control group were (332.46 x10 9/l, 15.426%, 7.982 fl), respectively as demonstrated in **(Table4).** Regarding The sex of the study population, the results revealed that the mean Fibrinogen level in the male group was (129.6 mg/dl), while in the female group was (167.9 mg/dl), as noted in **(Table5).** Also, the results of this study revealed that the mean of Platelet count, PDW, and M PV, in the male group, was (251.4 x10 9/l, 14.2%, 9.5fl), respectively, while in the female group was (301.4 x109/l, 15.0%, 8.8fl), respectively as showed in **(Table6).** According to age the results of this study revealed that the mean fibrinogen level in the age group less than (30) years was (136.0mg/dl), while in the age group more than (30) years was (147.9 mg/dl) as shown in **(Table7).** Also, the results of this study showed that the mean platelet count, PDW, and M PV, in the age group less than (30) years was (189.3 x10 9/l, 14.5%, 9.9 fl), respectively, while in the age group more than (30) years was (277.5 x109/l, 14.6%,9.2 fl), respectively as observed in **(Table8).**

Table-1: Distribution of study population according to sex.

Characteristic		***Frequency***	***Percent %***
Study groups	Case	100	66.7%
	Control	50	33.3%
Sex	Male	53	53%
	Female	47	47%

Table-2: Distribution of study population according to age:

Characteristic		***Frequency***	***Percent %***
Study groups	Test	100	66.7%
	Control	50	33.3%
Age	*Less than* 30 years	3	3.0%
	More than 30 years	97	97%

Table-3: The mean of fibrinogen level in test and control groups:

Test	**Groups**	**No**	**Mean**	**SD**	***P. value***
Fibrinogen mg/dl	Test	100	147.63	46.689	0.001
	Control	50	163.86	9.480	

Table-4: The mean of Platelet count, PDW, MPV in test and control group:

Test	***Groups***	***No***	***Mean***	***SD***	***P.value***
Platelet $x10^9$	Test	100	274.90	160.564	0.146
	Control	50	332.46	322.110	
PDW %	Test	100	14.587	2.5384	0.002
	Control	50	15.426	.2968	
MPV fl	Test	100	9.214	1.3962	0.000
	Control	50	7.982	.6853	

Table-5: The mean of fibrinogen level in COVID-19 patients according to sex:

Test	Groups	No	Mean	SD	*P. value*
Fibrinogen/ mg/dl	*Male*	53	129.6	51.5	0.000
	Female	47	167.9	29.8	

Table-6: The mean of Platelet count, PDW, MPV in COVID-19 patients according to sex:

Test	Groups	No	Mean	SD	*P. value*
Platelet $x10^9$	*Male*	53	251.4	152.0	0.121
	Female	47	301.4	167.3	
PDW %	*Male*	53	14.2	3.0	0.109
	Female	47	15.0	1.8	
MPV fl	*Male*	53	9.5	1.5	0.008
	Female	47	8.8	1.0	

Table-7: The mean of fibrinogen level in COVID-19 patients according to age

Test	Groups	No	Mean	SD	*P. value*
Fibrinogen mg/dl	*Less than* 30 years	3	136.0	21.6	0.664
	More than 30 years	97	147.9	47.3	

Table-8: The mean of platelet count, PDW, MPV in COVID-19 patients according to age:

Test	Groups	No	Mean	SD	*P. value*
Platelet $x10^9$	*Less than* 30 years	3	189.3	93.6	0.351
	More than 30 years	97	277.5	161.7	
PDW %	*Less than* 30yesrs	3	14.5	3.5	0.971
	More than 30years	97	14.6	2.5	
MPV fl	*Less than* 30yesrs	3	9.9	0.7	0.390
	More than 30years	97	9.2	1.4	

Discussion:

COVID-19 is a new type of pneumonia caused by infection with SARS-CoV-2, which is a member of β-coronaviruses; coronavirus family. No standardized laboratory tests exist to identify SARS-CoV-2**[23,24].** the presentation of COVID-19 includes chills, respiratory symptoms, and diarrhea in the early stage, while multiple organ dysfunction syndromes (MODS), septic shock, and coagulation dysfunction characterize the serious stage **[25]**. According to statistical analysis, the results of this study confirmed a decrease in the mean fibrinogen level in the test group, compared to the control group. So there was a strong significant variation with a *P. value* of (0.001). This Result agreed with the results of the study done by Oxford academic, national science review in America **[26].** And disagrees with the results of the study done by the University of Alabama at Birmingham, Birmingham in the United States **[27].** Low fibrinogen levels in COVID-19 patients may be due to an increased risk of thrombosis, so a greater degree of fibrinogen consumption occurs in COVID-19 patients. Also, statistical analysis of this study revealed a decrease in the mean of PDW in the test group, compared with the control group, led to a strong significant variation with *a P. value* of (0.002). This result was similar to the results of a study done by the International Journal of Medical science and Discovery in London. **[28]**, and disagree with the results of a study done by Erzurum Bolge Education and Research Hospital in Turkey **[29]**. Low PDW in covid-19 patients may be due to thrombocytosis and acute phase reactants, that is, the inflammatory response. Also, statistical analysis showed that there was an increase in the mean of MPV in the test group, compared to the control. This reveals a strong significant variation with a *P.value* of (0.000). This Result agreed with the results of a study done by Erzurum Bolge Education and Research Hospital in Turkey **[29]**. And with the results of a study done by Jining Medical University, Jiningin China. **[30, 31].** An increase in MPV in covid-19 patients may be due to an increase in the circulating of young platelets as a result of the body's response to thrombocytopenia in many study participants. Also, due to increased risk for thrombotic complications in acute coronary syndrome. Also, statistical analysis revealed a normal value in the mean platelet count in the test group, compared to the control group. There was no significant s difference observed among the study population with a P .value of (0.146). This result disagreed with the results of the study done by Erzurum Bolge Education and Research Hospital in Turkey **[29]**. This study found that there is a decrease in platelet count (thrombocytopenia)in many patients it may be due to infection of the bone marrow as in other coronaviruses, platelet destruction by the immune system and platelet consumption due to aggregation in the lungs. Also, statistical analysis of this study revealed a decrease in the mean fibrinogen level in the male group of covid-19 patients. So, there was a

strong significant variation with a *P. value* of (0.00). Also, statistical analysis revealed no significant variation in fibrinogen levels between different age groups with *a P. value* of (0.664). Also, statistical analysis of this study revealed an increase in the mean of MPV in the male group. So, there was a strong significant variation with a *P. value* of (0.008). Also, statistical analysis showed that there was no significant variation in MPV between different age groups with *a P. value* of (0.390). Also, statistical analysis of this study revealed no significant variation in the mean of platelet count and PDW regarding sex, with P. *values* of (0.121) and (0.109) respectively. Also, statistical analysis of this study revealed no significant variation in the mean of platelet count and PDW between different age groups, with *P. values* of (0.351) and (0.971) respectively.

Conclusion:

1. This study concludes that COVID-19 patients at high risk of thrombosis as revealed low fibrinogen level.
2. This study also concludes that there was thrombocytopenia in COVID-19 patients when their result shows a decrease in platelet distribution width and an increase in mean platelet volume.

Recommendations:

1. Fibrinogen level, Platelet distribution Width and Mean Platelet Volume should be checked regularly in Covid-19 patients.
2. Health education and avoid of overcrowded to achieve good control Covid-19 patients.
3. More investigations should be done for Covid-19 patients, to determine which risk factors and thrombotic markers are important predictor's thrombotic risk among Covid-19 patients.
4. Further studies should be carried out in this field with increasing sample size and use additional blood test like D.dimer, PT and PTT to obtain accurate results.

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Conflict of Interest:

The author has affirmed that there are no conflicting interests.

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