

Coagulation Parameters Among Sudanese Individuals Vaccinated with Johnson and Johnson Vaccine at Khartoum State, 2022

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Abstract: *Background:* A COVID-19 vaccine is a vaccine intended to provide acquired immunity against severe acute respiratory syndrome corona virus 2. Ad26.COV2.S (Johnson & Johnson) vaccine is adenovirus vector-based vaccine that targets the spike protein of the SARS-CoV-2 virus, when it enters the body it stimulates the immune response. *Materials and methods:* This was a cross sectional study, health facility base, Conducted in Vaccine centre at Omer ben Alkhatib, Khartoum, Sudan during the period July to August, 2022 to estimate changes of coagulation parameters among Sudanese vaccinated with Johnson & Johnson vaccine. Sixty samples were collected from the Participants that took the first dose of Johnson & Johnson vaccine; thirty samples before the vaccination, and thirty after vaccination. The coagulation parameters were performing by different methods. *Results:* The means of parameters before the vaccination were; APTT was (36.2 ±3), PT was (15.8±2.4), INR (1.2 ±0.2), platelets (285.9 ±7.2), fibrinogen (243.4 ±4.6) and D-dimer (0.17±0.03). The means of parameters after the vaccination for the APTT, PT, INR, platelets count, fibrinogen and the D-dimer were; (35.2 ±2.9), (13.9±2.1), (1.21±0.3), (272.8±57.9), (284.2 ±53.3) and (0.37±0.8) respectively. When compared between the results of parameters per and post vaccination the results revealed that; there was significant decrease in the time for the APTT and PTT (p value ≤0.05), in significant differences with the INR and platelets count (p value ≥0.05), significant increase for the fibrinogen and D- dimer level (p value ≤0.05). While when compared the mean of the parameters with the age, genders, and symptoms there was insignificant differences (p value ≥0.05), except the D – dimer had a significant differences with the age and symptoms (p value ≤0.05). *Conclusion:* In the conclusion of this study there was significant decrease of the activated partial thromboplastin time (APTT), Prothrombin time (PT), and significant increase in fibrinogen and D-dimer level in the Sudanese individuals after the first dose of Johnson and Johnson Vaccine.

Keywords: COVID-19, Vaccine Johnson and Johnson Vaccine, Coagulation, Fibrinogen, D-dimer

1. Introduction

The Novell coronavirus aliment 2019 (COVID-19), became first diagnosed in Wuhan in December 2019, resulting from intense acute breathing syndrome corona virus 2 (SARSCoV-2). As of the stop of January 2022, about years had exceeded considering the fact that starting of the COVID-19 pandemic, with the quantity of inflamed human beings worldwide exceeding 3.5 billion and the quantity of deaths exceeding 550 million at that time, the COVID-19 is regularly complex by coagulopathy and thrombosis [1].

The most frequently appearing symptoms are cough, fatigue, and fever, which are mostly associated with much less common symptoms consisting of headache, dyspnea, skin rashes, sore throat, diarrhea, anosmia, and nausea, about 80% of COVID-19 sufferers do not need hospitalization, after infection by COVID-19 the coagulation and immune system is activated, However, the relationship between COVID-9 infection and activation of the coagulation system still requires elucidation [2]. To protect people from COVID-19 infection several vaccines have been developed and distributed worldwide by many countries to avoid the prevalence of the infection and reduce the riskiness of COVID-19 [1, 3].

Vaccine is a simple, safe, and effective way of protection against harmful disease, it uses the body natural defences to build resistance to specific infections and makes strong immune system Vaccine for SARS-CoV-2 from Pfizer-Biontech was the first vaccine to be approved by the Kingdom medicines and Health care Products regulatory agency (MHRA). As of July 26, 2021, 3.85 billion doses vaccine for SARS-CoV-2 were administered in 180 countries [4, 5].

Astraeneca vaccine commercial name weakened adenovirus (ChAdOx1-S; AD1222) developer by the university of Oxford/Astrazeneca, platform is deficient chimpanzee adenovirus, sero prevalence of vector used is very low, stable for at least 6 months at 2-8 temperature immunogenicity in humans is high (90%) [4].

Johnson and Johnson vaccine uses existing technology that includes a virus called adenovirus, the DNA in the adenovirus is modified in order that it can produce a key part of the SARS-CoV-2 virus particle to which the body then develops an immune response. The adenovirus that provides the SARS-CoV-2 DNA particle cannot multiply so it does not new no longer motive infection, because this device is primarily based totally on solid DNA molecules, it does not now no longer require ultracold storage, making it less difficult to distribute [6].

Vaccine-induced immune thrombocytopenia and thrombosis (VITT) is a brand new syndrome related to the ChAdOx1 nCoV-19 adenoviral vector vaccine against severe acute breathing syndrome coronavirus after SARS-Co-2 vaccination, VITT is rare appear. In many cases coagulation activation exceeds fibrinolytic activation and thrombosis appear, but in few cases, bleeding appears when fibrinolytic activation exceeds coagulation activation [1, 7].

In Sudan according to the published data, only 8.3 % of the populations were fully vaccinated, there is no clear

guideline's toward the vaccine program concerning the side effect that may occurs, also there is no published data regarding the present of this syndrome in Sudanese vaccinated people mainly Johnson & Johnson vaccinated, in result of that this study was designed to find out the changes of coagulation parameters that is related to VITT syndrome among Sudanese vaccinated with Johnson & Johnson vaccine in Khartoum state.

2. Material and Methods

This was a cross sectional study, health facility base, Conducted in Vaccine centre at Omer ben Alkhatab, Khartoum, Sudan during the period July to August, 2022 to estimate changes of coagulation parameters among Sudanese vaccinated with Johnson & Johnson vaccine. Apparently healthy Participants took the first dose of Johnson & Johnson vaccine; their ages between 18 and 60 were included. A Participants that had a history of bleeding, thrombi or under anticoagulant drugs or any one has been infected with corona virus before or took any corona vaccine were excluded. Organized Questionnaire was used to collect the data. Also this study was approved by the ethical committee of the Faculty of Medical Laboratory Sciences, University of Medical Science and Technology. A written clear informed consent was obtained from all participants and explains the purpose of the research before sample collection. From each participant two venous blood samples were collected, one in EDTA containers and one in tri sodium citrate containers, the samples were collected before and after vaccination; the first sample before Johnson & Johnson vaccine dose, and the second sample after 2-3 days of vaccination.

2.1. Platelets Counts

The platelets count was done by using Sysmex Automated Hematology Analyzer KX 21N series SN B 2010.

2.2. Prothrombin Time (PT) Test Principle

The coagulation tests (PT) were performed using semiautomatic device (coagulometer). The principle of the test consists of the use of calcium thromboplastin to measure the clotting time of patient's plasma. The test was measured as a whole. The activity of extrinsic coagulation factors: factor XI (prothrombin), factor V (proaccelerin), factor VII (proconvertin) and factor X (Stuart factor).

2.3. Activated Partial Thromboplastin Time (APTT) Test Principle

The test was involved the recalcification of plasma in the presence of a standardized amount of platelet substitute and a specific activator. This procedure minimizes test variables by standardized the contact activation and optimizes the concentration of platelet like phospholipids. The APTT explores the intrinsic coagulation pathway (factors XII, XI, IX, X, V, II, I). The coagulation tests (APTT) was performed using semiautomatic device (coagulometer).

2.4. Fibrinogen Test Principle

The test was done by BioMed-Fibrinogen kite, for quantitative determination of Fibrinogen in plasma. The principle of this kite is addition of thrombin coagulates fresh citrated plasma, the coagulation time is proportional to the fibrinogen concentration. This allows the estimation of plasma fibrinogen by functional clotting assay.

2.5. D-dimer Test Principle

Ichroma™ D-dimer is fluorescence Immunoassay (FIA) for the quantitative determination of D-dimer in human whole blood / plasma. The test will be used a sandwich immune detection method; the detector antibody in buffer binds to antigen in sample, forming antigen antibody complexes and migrates onto nitrocellulose matrix to be captured by the other immobilized-antibody on test strip. The more antigen in sample forms the more antigen-antibody complex and leads to stronger intensity of fluorescence signal on detector antibody, which is processed by instrument for ichroma™ tests to show D- dimer concentration in sample.

3. Result

In the present study 60 samples were collected from the Participants that took the first dose of Johnson & Johnson vaccin; 30 samples before the vaccination, and 30 after vaccination. The frequency of the gender and age in this study; 58.3% were male and 41.7% were female, 66.7 % their ages group from (20-30) years old, 26.7% their age group less than 20 years old and 6.7%. their age group more than years. (Figure 1, 2).

The frequency of the symptoms that occurred after vaccination; 50% had moderate symptoms, 30% had a mild symptoms, and only 10% had a severe symptoms. (Figure 3).

The means of coagulation parameters before the vaccination were; APTT was (36.2 ± 3), PT was (15.8 ± 2.4), INR (1.2 ± 0.2), platelets (285.9 ± 7.2), fibrinogen (243.4 ± 4.6) and D-dimer (0.17 ± 0.03). The means of coagulation parameters after the vaccination for the APTT, PT, INR, platelets count, fibrinogen and the D-dimer were; (35.2 ± 2.9), (13.9 ± 2.1), (1.21 ± 0.3), (272.8 ± 57.9), (284.2 ± 53.3) and (0.37 ± 0.8) respectively. (Figure 4- 9).

When compared between the results of parameters per and post vaccination the results revealed that; there was significant decrease in the time for the APTT and PTT (p value ≤ 0.05), in significant differences with the INR and platelets count (p value ≥ 0.05), significant increase in the fibrinogen and D- dimer level (p value ≤ 0.05). (Table 1) While when compared the mean of the parameters with the age, genders, and symptoms there was insignificant differences (p value ≥ 0.05), except the D – dimer had a significant differences with the age and symptoms (p value ≤ 0.05). (Table 2-4) Regarding the correlation test; there was a significant correlation for the APTT, PT, INR, platelets count, fibrinogen level post and pre vaccination (p value ≤ 0.05) and insignificant correlation with the D-dimer (p

value ≥ 0.05). (Tables 5-10).

Table 1. Comparison of coagulation parameter between pre-vaccine and post-vaccine.

Parameter	Pre-vaccine	Post-vaccine	P. value
D-dimer	0.17 ± 0.03	0.37 ± 0.08	0.011*
APTT	36.2 ± 3.0	35.2 ± 2.9	0.028*
PT	15.8 ± 2.4	13.9 ± 2.1	0.000*
INR	1.2 ± 0.2	1.1 ± 0.3	0.116
Platelet count	285.9 ± 73.3	272.8 ± 57.9	0.271
Fibrinogen level	243.4 ± 43.6	284.2 ± 53.3	0.000*

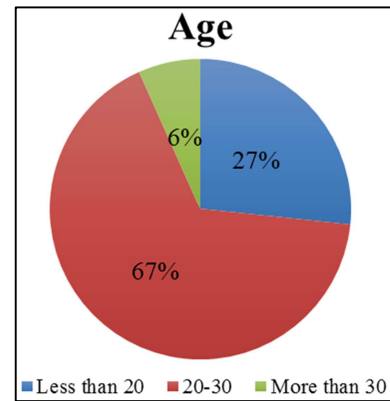


Figure 1. Distribution of age.

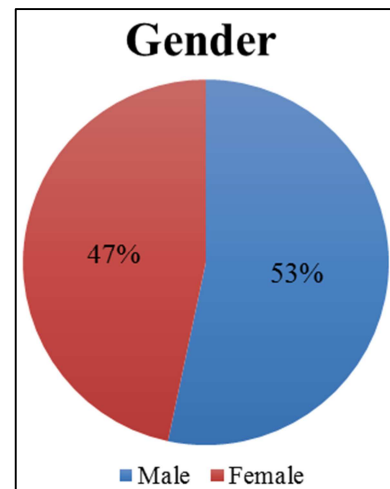


Figure 2. Distribution of gender.

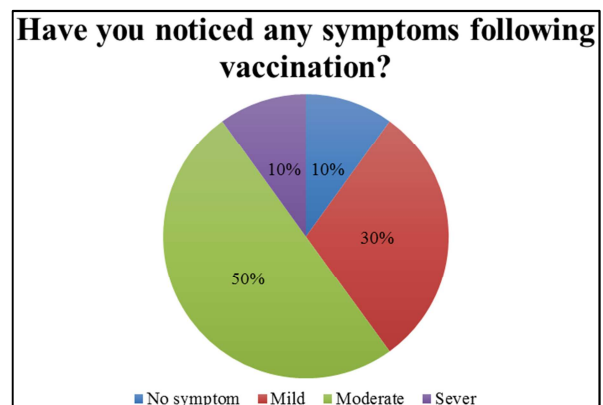


Figure 3. Distribution of symptoms.

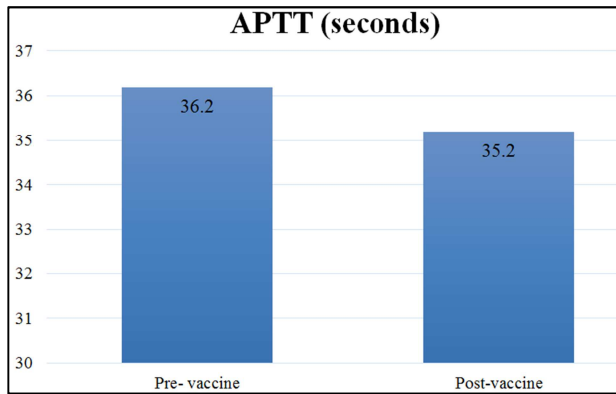


Figure 4. Mean of APTT pre-vaccine and post-vaccine.

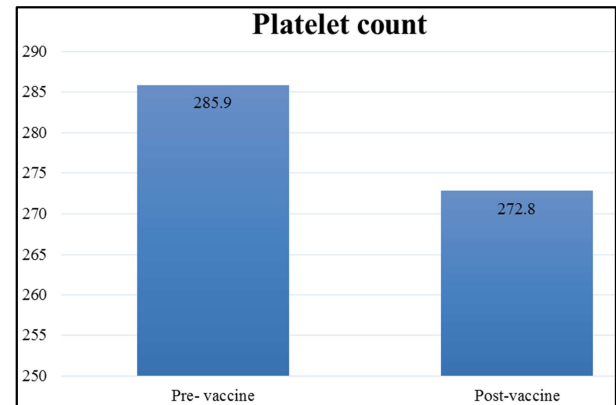


Figure 7. Mean of platelet count pre-vaccine and post-vaccine.

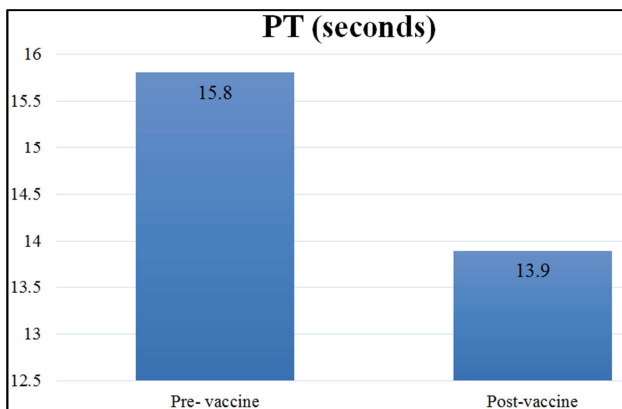


Figure 5. Mean of PT pre-vaccine and post-vaccine.

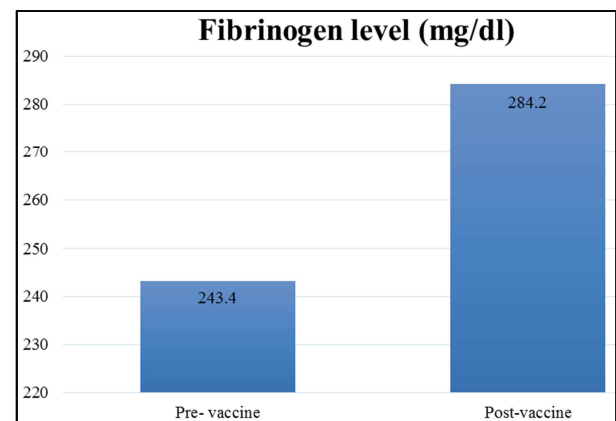


Figure 8. Mean of fibrinogen level pre-vaccine and post-vaccine.

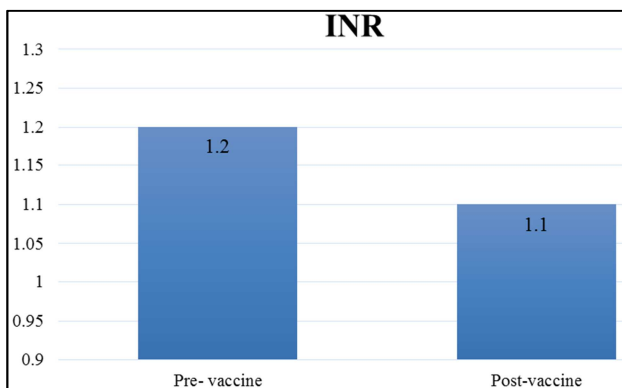


Figure 6. Mean of INR pre-vaccine and post-vaccine.

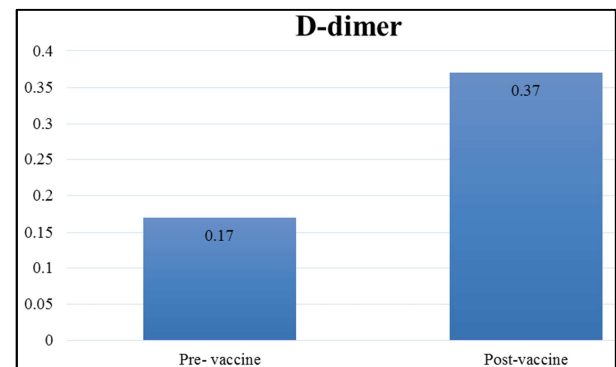


Figure 9. Mean of D-dimer pre-vaccine and post-vaccine.

Table 2. Comparison of coagulation parameters according to age.

Parameter		Age			P. value
		Less than 20 (n=8)	20-30 (n=20)	More than 30 (n=2)	
D-dimer	Pre- vaccine	0.15 ± 0.03	0.18 ± 0.04	0.12 ± 0.06	0.877
	Post-vaccine	0.29 ± 0.05	0.31 ± 0.05	1.3 ± 1.1	0.002*
APTT	Pre- vaccine	35.7 ± 3.4	36.7 ± 2.8	33.3 ± 2.5	0.264
	Post-vaccine	35.2 ± 2.0	35.2 ± 3.4	34.9 ± 0.4	0.994
PT	Pre- vaccine	15.6 ± 2.7	16.0 ± 2.5	15.2 ± 0.4	0.875
	Post-vaccine	14.4 ± 1.9	13.9 ± 2.3	12.7 ± 0.7	0.615
INR	Pre- vaccine	1.2 ± 0.2	1.1 ± 0.2	1.1 ± 0.02	0.850
	Post-vaccine	1.1 ± 0.1	1.1 ± 0.3	0.95 ± 0.1	0.638
Platelet count	Pre- vaccine	276.3 ± 96.6	297.1 ± 55.8	212.5 ± 130.8	0.280
	Post-vaccine	282.0 ± 87.7	271.4 ± 46.5	250.5 ± 27.6	0.787
Fibrinogen level	Pre- vaccine	237.0 ± 24.9	248.9 ± 50.1	214.0 ± 16.9	0.512
	Post-vaccine	279.9 ± 38.5	278.8 ± 53.9	355.5 ± 77.1	0.148

Table 3. Comparison of coagulation parameter according to gender.

Parameter		Gender		P. value
		Male (n=16)	Female (n=14)	
D-dimer	Pre- vaccine	0.15 ± 0.03	0.18 ± 0.06	0.615
	Post-vaccine	0.43 ± 0.1	0.30 ± 0.07	0.412
APTT	Pre- vaccine	36.5 ± 3.5	35.9 ± 2.5	0.651
	Post-vaccine	35.2 ± 3.7	35.2 ± 1.9	0.969
PT	Pre- vaccine	16.4 ± 2.3	15.2 ± 2.5	0.173
	Post-vaccine	14.3 ± 2.2	13.6 ± 1.9	0.342
INR	Pre- vaccine	1.2 ± 0.2	1.2 ± 0.2	0.994
	Post-vaccine	1.1 ± 0.07	1.1 ± 0.07	0.995
Platelet count	Pre- vaccine	257.2 ± 62.4	318.6 ± 72.8	0.019*
	Post-vaccine	258.8 ± 54.1	288.8 ± 59.9	0.161
Fibrinogen level	Pre- vaccine	244.9 ± 38.7	241.6 ± 50.0	0.840
	Post-vaccine	285.1 ± 56.1	283.2 ± 52.1	0.927

Table 4. Comparison of coagulation parameters according to present of symptoms.

Parameter		Present of symptoms				P. value
		No symptom (n=3)	Mild (n=9)	Moderate (n=15)	Sever (n=3)	
D-dimer	Pre- vaccine	0.24 ± 0.1	0.21 ± 0.1	0.14 ± 0.02	0.10 ± 0.5	0.548
	Post-vaccine	1.09 ± 0.7	0.38 ± 0.1	0.25 ± 0.03	0.27 ± 0.06	0.013*
APTT	Pre- vaccine	36.6 ± 4.8	35.4 ± 4.2	36.9 ± 1.9	34.9 ± 1.7	0.611
	Post-vaccine	34.1 ± 6.5	35.6 ± 3.2	35.6 ± 1.8	32.6 ± 2.6	0.375
PT	Pre- vaccine	17.1 ± 1.8	16.3 ± 2.6	15.2 ± 2.6	16.5 ± 1.7	0.545
	Post-vaccine	13.9 ± 4.2	14.6 ± 2.4	13.9 ± 1.6	12.4 ± 1.2	0.516
INR	Pre- vaccine	1.2 ± 0.1	1.1 ± 0.06	1.1 ± 0.05	1.2 ± 0.06	0.949
	Post-vaccine	1.0 ± 0.3	1.2 ± 0.3	1.0 ± 0.1	1.2 ± 0.5	0.372
Platelet count	Pre- vaccine	225.3 ± 93.6	303.6 ± 80.4	277.5 ± 66.9	335.3 ± 26.3	0.253
	Post-vaccine	251.0 ± 20.7	278.3 ± 79.4	273.7 ± 54.5	273.7 ± 37.0	0.925
Fibrinogen level	Pre- vaccine	271.3 ± 60.5	259.8 ± 54.9	228.6 ± 27.3	240.0 ± 50.3	0.238
	Post-vaccine	328.3 ± 108.7	293.7 ± 48.9	263.9 ± 41.3	313.3 ± 14.9	0.140

Table 5. Correlations APTT pre- vaccine and post-vaccine.

APTT pre-vaccine		
APTT post-vaccine	Pearson Correlation	.648*
	P. value	.000

Table 6. Correlations PT pre- vaccine and post-vaccine.

PT pre-vaccine		
PT post-vaccine	Pearson Correlation	.616*
	P. value	.000

Table 7. Correlations INR pre- vaccine and post-vaccine.

INR pre- vaccine		
INR post-vaccine	Pearson Correlation	.526*
	P. value	.003

Table 8. Correlations platelet count pre- vaccine and post-vaccine.

Platelet count pre- vaccine		
Platelet count post-vaccine	Pearson Correlation	.549*
	P. value	.002

Table 9. Correlations fibrinogen level pre- vaccine and post-vaccine.

Fibrinogen level pre- vaccine		
Fibrinogen level post-vaccine	Pearson Correlation	.467*
	P. value	.009

Table 10. Correlations D-dimer pre- vaccine and post-vaccine.

D-dimer pre- vaccine		
D-dimer post-vaccine	Pearson Correlation	.287
	P. value	.125

4. Discussion

The COVID-19 vaccine played vital role in combating the COVID-19 pandemic. The vaccine is less expensive and easier to store than other vaccines against severe acute respiratory syndrome corona virus (SARS-CoV-2). The safety of the COVID-19 vaccines has been a major concern to the public, resulting in vaccine hesitancy, especially those developed by the new mRNA technology. Several case series reported hematological abnormalities, including thrombocytopenia and immune thrombocytopenic purpura (ITP) after vaccination. [8-10]

This was a case control study health facility base, Conducted in Vaccine centre at Omer ben Alkhatib, Khartoum, Sudan during the period of July to august 2022 to estimate the changes of coagulation parameters among Sudanese vaccinated with Johnson & Johnson vaccine. In the present study 60 samples were collected from the Participants who took the first dose of Johnson & Johnson vaccine; 30 samples before the vaccination, and 30 after vaccination. Our

result showed that the frequency of the gender and age in this study; 53.3 % were male and 47.7% were female, 66.7 % their ages from (20-30) years, 26.7 % less than 20 years and 6.7% more than (30) years. The frequency of the symptoms that occurred after vaccination; 50% had moderate symptoms, 30% had a mild symptoms, and only 10% had a severe symptoms.

The means of parameters before the vaccination were; APTT was (36.2 ± 3), PT was (15.8 ± 2.4), INR (1.2 ± 0.2), platelets (285.9 ± 7.2), fibrinogen (243.4 ± 4.6) and D-dimer (0.17 ± 0.03). The means of parameters after the vaccination for the APTT, PT, INR, platelets count, fibrinogen and the D-dimer were; (35.2 ± 2.9), (13.9 ± 2.1), (1.21 ± 0.3), (272.8 ± 57.9), (284.2 ± 53.3) and (0.37 ± 0.8) respectively.

After compared the means of platelets count between pre and post vaccination there was a significant difference, however there was a clear decrease in the platelets count after vaccination, also there was insignificant difference when compared with the age, genders, and symptoms, although there was significant correlation for the platelets count pre and post vaccination.

This finding agreed with Maryam Sharifian- et al, which finding low in platelets count and increase of D-dimer serum levels after vaccination with adenovirus vector-based Covid-19 vaccine [11].

Also Luca Zazzeron et al reported; Patients who developed vaccine-induced immune thrombotic thrombocytopenia were more likely to be young women (age 20-50) who were given the Johnson & Johnson/Janssen or AstraZeneca. Laboratory findings showed; thrombocytopenia, low fibrinogen, and elevated d-dimer levels, while positive platelet factor 4 antibodies were always positive [12].

However, Arad Dotan et al mention; after the vaccination all patients had a decline in platelet counts at diagnosis, high levels of d-dimer and low levels of fibrinogen [13].

One of researches showed; the platelet count is $< 150 \times 10^9/L$ or falling in serial counts, D-dimer levels are elevated and the fibrinogen levels are reduced to $< 2 \text{ g/L}$. [14]. Isaac See et al also published a study containing low platelet count in patient with ages ranged from 18 to younger than 60 years [15].

Also Bruno Fattizzo et al reported; in VITT pathologic, anti-platelet factor 4 (PF4) antibodies leading to thrombocytopenia, and thrombosis in the absence of heparin exposure, a mechanism, similar to "autoimmune" heparin-induced thrombocytopenia (HIT). [16]

Greiner et al mention; the presence of EDTA in the vaccine possibly contributes to capillary leakage and dissemination of components in blood. These aggregates are recognized by the Immunoglobulin (Ig) G antibodies and the complement system leading to clustering of PF4 with resulting platelet activation. Cumulative reactions lead to the formation of neutrophil extracellular traps (NETs) with a pan cellular FcγIIa receptor activation akin to Heparin-induced thrombocytopenia (HIT). This culminates in a massive coagulation system activation, leading to consumptive coagulopathy with significantly elevated D Dimer levels and

hypofibrinogenemia. [17]

In the current study when compared between the means of PT, APTT and INR pre and post vaccination the results showed; there was significant decrease in the time for the PT and APTT ($p \text{ value} \leq 0.05$), and in significant difference with the INR ($p \text{ value} \geq 0.05$). In addition to that, when compared the mean of the parameters with the age, genders, and symptoms there was insignificant differences. This study results agree with study conducted by, Hisham Ali Waggiallah et al which found there was significant decreased in the time for the PT after vaccination [18], and agree with study carried out by the Sharun K, et al which revealed; the patient had received the Ad26.COV2.S (Janssen; Johnson & Johnson) vaccine; a Prothrombin time was 13.5 seconds and a partial thromboplastin time was 27.0 seconds. [19]

Also consist with Theodore E Warkentin et al which said; Testing of the Prothrombin time (PT) help assess the presence of disseminated intravascular coagulation (DIC) and may be used in estimating the likelihood of VITT. [20]

While the study finding was disagreed with Schultz NH et al which said; Individuals with VITT have a high frequency of overt, decompensate disseminated intravascular coagulation (DIC), which manifests the following abnormalities: Moderate to severe thrombocytopenia, or a significant decrease from the individual's baseline platelet count, Elevated D-dimer (often greatly elevated, $>10 \text{ mg/L}$ [$>10,000 \text{ ng/mL}$]), Decreased fibrinogen (approximately half have a fibrinogen level below the normal range; many of the remainder are in low-normal range) and Normal or mildly increased prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT). [21] However Amged Hussein et al results showed significant different between case and control in (PT, APTT and INR) and significant different between male and female in (PT, APTT) after vaccination [22] also disagreed with Warkentin et al results which reported; activated partial thromboplastin time (APTT) result was normal or mildly increased in the patients with VITT. [20]

In addition Abou-Ismael et al which reported that; Vaccine-induced thrombotic thrombocytopenia following Ad26.COV2.S vaccine presenting as acute venous thromboembolism, the result of activated partial thromboplastin time (APTT) was found to be prolonged in patients who took the vaccine [23].

On the other hand, a study by Stevens-Johnson et al; determined the activated partial thromboplastin time (APTT) it was normal and excluding intravascular coagulation disease by Vaxvetria (AZD1222) COVID-19 vaccine [24].

The fibrinogen level in this study, the results showed; When compared the fibrinogen levels between pre and post vaccination there was significant increase in the fibrinogen level however when compared with the age, genders, and symptoms there was insignificant differences. The correlation test revealed there was a significant correlation for the fibrinogen level post and pre vaccination.

this result was opposing with Luca Zazzeron et al which

found low levels of fibrinogen in the Patients who developed vaccine-induced immune thrombotic thrombocytopenia after given the AstraZeneca or Johnson & Johnson/Janssen vaccine. [12] also an Australian study which showed the same results. [14]

However Thomas Gattringer et al study showed; Laboratory investigations revealed moderate thrombocytopenia ($84 \times 10^9/L$) and significantly elevated D-dimer (14.2 mg/L; normal <0.5 mg/L). Fibrinogen and other routine parameters were normal. [25]

Regarding the D-dimer in this study the results found a significant increase in the D- dimer level (p value ≤ 0.05) when comparing between the mean of D- dimer pre and post vaccination. the outcome of this study was concur with results that obtained by Muir KL et al which reported; a marked elevation in the d-dimer level after vaccination [26] and agreed with Kanack AJ et al study which found that D-dimer was markedly elevated in all patients, but differed in the onset of symptoms, which was 11 days (range 6–14 days) [27], also See I et al revealed; marked increase in the D-dimer level in post vaccination samples [15].

However Helene Brenna Haakonsen et al said; the D-dimer level was not elevated after receiving the Covid 19 vaccine. [28]

Finally Sharun K, Dhama K, Patel SK, et al conclude his results with; vaccine-induced thrombotic thrombocytopenia (VITT) and has been reported in approximately 3.2 cases per million after administration of Ad26.COV2.S (Janssen; Johnson & Johnson) vaccine. VITT is pathogenically linked to autoimmune heparin induced thrombocytopenia with the demonstration of antiplatelet factor 4 antibodies. VITT is associated with propensity for cerebral and splanchnic vein thrombosis, consumptive coagulopathy, and poor outcomes. [29]

Initial reports from Norway and Germany suggested female sex was a risk factor; 13 of the 16 patients in these reports were female. A female predominance seemed logical; heparin-induced thrombocytopenia, a related condition, tends to affect females, and immune disorders in general are more common in females, report on VITT cases associated with the Jonson and Jonson vaccine, rates were similar between males and females in all age, except in ages 30 to 49 years, where females were more likely to be affected. However the studied revealed that an association between the risk of VITT and younger age [30].

5. Conclusion

The conclusion of this study was significant decrease in the activated partial thromboplastin time (APTT), Prothrombin time (PT), and significant increase in fibrinogen and D-dimer level in the Sudanese individuals after the first dose of Johnson and Johnson Vaccine.

In Sudan Further studies with large sample size that cover all types of Covid -19 vaccines are required and the department of vaccination in the ministry of Health will further develop and refine resources for informed consent

that clearly convey the benefits and risks of Covid -19 vaccine.

References

- [1] Yamada S, Asakura H. Coagulopathy and Fibrinolytic Pathophysiology in COVID-19 and SARS-CoV-2 Vaccination. *International Journal of Molecular Sciences* 2022; 23 (6): 3338.
- [2] Sarkar M, Madabhavi IV, Quy PN, Govindagoudar MB. COVID-19 vaccine-induced immune thrombotic thrombocytopenia: A review. *Annals of Thoracic Medicine*. 2022; 17 (1): 1.
- [3] Long B, Bridwell R, Gottlieb M. Thrombosis with thrombocytopenia syndrome associated with COVID-19 vaccines. *The American journal of emergency medicine*. 2021; 49: 58-61.
- [4] Nagy A, Alhatlani B. An overview of current COVID-19 vaccine platforms. *Computational and structural biotechnology journal*. 2021; 19: 2508-17.
- [5] Klok FA, Pai M, Huisman MV, Makris M. Vaccine-induced immune thrombotic thrombocytopenia. *The Lancet Haematology*. 2021; 11.
- [6] Livingston EH, Malani PN, Creech CB. The Johnson & Johnson Vaccine for COVID-19. *Jama*. 2021; 325 (15): 1575-.
- [7] Pavord S, Scully M, Hunt BJ, Lester W, Bagot C, Craven B, Rampotas A, Ambler G, Makris M. Clinical features of vaccine-induced immune thrombocytopenia and thrombosis. *New England Journal of Medicine*. 2021; 385 (18): 1680-9.
- [8] Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. *Lancet*. 2020; 396 (10249): 467-478.
- [9] arawneh O, Tarawneh H. Immune thrombocytopenia in a 22-year-old post Covid-19 vaccine. *Am J Hematol*. 2021; 96 (5): E133-E134.12.
- [10] Lee EJ, Cines DB, Gernsheimer T, et al. Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination. *Am J Hematol*. 2021; 96 (5): 534-537.
- [11] Sharifian-Dorche M, Bahmanyar M, Sharifian-Dorche A, Mohammadi P, Nomovi M, Mowla A. Vaccine-induced immune thrombotic thrombocytopenia and cerebral venous sinus thrombosis post COVID-19 vaccination; a systematic review. *Journal of the neurological sciences*. 2021; 428: 117607.
- [12] Zazzeron L, Rosovsky RP, Bittner EA, Chang MG. Comparison of Published Guidelines for the Diagnosis and the Management of Vaccine-Induced Immune Thrombotic Thrombocytopenia. *Crit Care Explor*. 2021; 3 (9): e0519. doi: 10.1097/CCE.0000000000000519. PMID: 34514421; PMCID: PMC8425820.
- [13] Dotan A, Shoenfeld Y. Perspectives on vaccine induced thrombotic thrombocytopenia. *J Autoimmun*. 2021; 121: 102663. doi: 10.1016/j.jaut.2021.102663. Epub 2021 May 18. PMID: 34020254; PMCID: PMC8129886.

- [14] Chen VM, Curnow JL, Tran HA, Choi PY. Australian and New Zealand approach to diagnosis and management of vaccine-induced immune thrombosis and thrombocytopenia. *Med J Aust.* 2021 Sep 20; 215 (6): 245-249. e1. doi: 10.5694/mja2.51229. Epub 2021 Sep 6. Erratum in: *Med J Aust.* 2021 Nov 15; 215 (10): 453. PMID: 34490632; PMCID: PMC8661608.
- [15] See I, Su JR, Lale A, Woo EJ, Guh AY, Shimabukuro TT, Streiff MB, Rao AK, Wheeler AP, Beavers SF, Durbin AP. US case reports of cerebral venous sinus thrombosis with thrombocytopenia after Ad26. COV2. S vaccination, March 2 to April 21, 2021. *Jama.* 2021 Jun 22; 325 (24): 2448-56.
- [16] Gresele P, Momi S, Marcucci R, Ramundo F, De Stefano V, Tripodi A. Interactions of adenoviruses with platelets and coagulation and the vaccine-induced immune thrombotic thrombocytopenia syndrome. *Haematologica.* 2021; 106 (12): 3034-3045. doi: 10.3324/haematol.2021.279289. PMID: 34407607; PMCID: PMC8634187.
- [17] Sue Pavord, F. R. C. Path., Marie Scully, Beverley J. Hunt, William Lester, Catherine Bagot, Brian Craven, M. B., B. Ch., Alex Rampotas, Gareth Ambler, Ph.D., and Mike Makris. Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis. *nengl j med* 2021; 385 (18): 1680-1689.
- [18] Waggiallah, Hisham Ali. "Thrombosis formation after COVID-19 vaccination Immunological Aspects: Review article." *Saudi journal of biological sciences* vol. 29, 2 (2022): 1073-1078. doi: 10.1016/j.sjbs.2021.09.065
- [19] Sandhu, Bhuta, Carson, Konala, Biro, Manu, et al. [Internet]. *American Journal of Therapeutics.* [cited 2022Jun18]. Available from: <http://www.americantherapeutics.com/>
- [20] Warkentin TE, Cuker A. COVID-19: Vaccine-induced immune thrombotic thrombocytopenia (VITT). Update May. 2021; 7.
- [21] Schultz NH, Sørvoll IH, Michelsen AE, et al. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. *N Engl J Med* 2021; 384: 2124.
- [22] Amged Hussein Abdelrhman, Ahmed Hosham, Duaa Sala, Marwan Adel, Nadeen wahbi, Sara Abdelrahim, Waad Abdullah, et al. The Effect of Covid-19 Astrazeneca Vaccines on Some Coagulation Profile (Pt, Aptt) Among Sudanese Two Dose Vaccinated. *Journal of Medicine and Healthcare* 2022; 494 1-3.
- [23] Abou-Ismaïl MY, Moser KA, Smock KJ, Lim MY. Vaccine-induced thrombotic thrombocytopenia following Ad26.COVS vaccine in a man presenting as acute venous thromboembolism. *Am J Hematol.* 2021 Sep 1; 96 (9): E346-E349. doi: 10.1002/ajh.26265. Epub 2021 Jun 17. PMID: 34096082; PMCID: PMC8212083.
- [24] Aimò C, Mariotti EB, Corrà A, et al. Stevens-Johnson syndrome induced by Vaxvetria (AZD1222) COVID-19 vaccine. *Journal of the European Academy of Dermatology and Venereology: JEADV.* 2022; 36 (6): e417-e419. DOI: 10.1111/jdv.17988. PMID: 35133674; PMCID: PMC9114927.
- [25] Gattringer T, Gressenberger P, Gary T, et al Successful management of vaccine-induced immune thrombotic thrombocytopenia-related cerebral sinus venous thrombosis after ChAdOx1 nCov-19 vaccination Stroke and Vascular Neurology 2022; 7: doi: 10.1136/svn-2021-001142
- [26] Muir KL, Kallam A, Koepsell SA, Gundabolu K. Thrombotic thrombocytopenia after Ad26. COV2. S vaccination. *New England Journal of Medicine.* 2021 May 20; 384 (20): 1964-5.
- [27] Kanack AJ, Singh B, George G, Gundabolu K, Koepsell SA, Abou-Ismaïl MY, Moser KA, Smock KJ, Green D, Major A, Chan CW. Persistence of Ad26. COV2. S-associated vaccine-induced immune thrombotic thrombocytopenia (VITT) and specific detection of VITT antibodies. *American journal of hematology.* 2022 May; 97 (5): 519-26.
- [28] Haakonsen HB, Nystedt A. Deep vein thrombosis more than two weeks after vaccination against COVID-19. *Tidsskr Nor Laegeforen.* 2021 Apr 28; 141. English, Norwegian. doi: 10.4045/tidsskr.21.0274. PMID: 33928773.
- [29] Ben Saida I, Maatouk I, Toumi R, Bouslama E, Ben Ismaïl H, Ben Salem C, Boussarsar M. Acquired Thrombotic Thrombocytopenic Purpura Following Inactivated COVID-19 Vaccines: Two Case Reports and a Short Literature Review. *Vaccines (Basel).* 2022 Jun 24; 10 (7): 1012. doi: 10.3390/vaccines10071012. PMID: 35891176; PMCID: PMC9319973.
- [30] Pai M. Epidemiology of VITT. *Semin Hematol.* 2022; 59 (2): 72-75. doi: 10.1053/j.seminhematol.2022.02.002. Epub 2022 Feb 8. PMID: 35512903; PMCID: PMC8820951.