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Original Article

Measurement of D-dimer Level Among COVID-19 Vaccinated Individuals at Khartoum State, Sudan

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Abstract

Introduction: The COVID-19 pandemic affects millions of people worldwide with a high number of morbidities and mortality. The virus was first identified and reported from Wuhan, China, in December 2019. Several COVID-19 vaccines were developed and disseminated worldwide. Several hemostatic changes were found in individuals who took the COVID-19 vaccine. The aim of this study was to measure the D-dimer level among individuals who have taken the COVID-19 vaccine and to compare them to unvaccinated individuals (control) in Khartoum State in 2023.

Methods: This study was a case-control descriptive study conducted at Al-Riada Modern Medical Laboratory in Khartoum State during the period from January 2023 to April 2023 on 100 samples to measure D-dimer level. For each participant, 2.8 ml of blood was collected in a trisodium citrate anticoagulant container with a volume ratio of 1:9, and platelet-poor plasma was prepared by sample centrifugation at 3500 for 15 minutes. The D-dimer was assessed by the sandwich immunodetection method (Finecare™).

Results: The gender distribution was (20, 30) in the case group and (26, 24) in the control group for males and females, respectively. The mean age of the case group was 38 years, while the mean age of the control group was 40 years. The frequency of COVID-19 vaccine types was 26, 9, 8, 7, AstraZeneca, Johnson, Pfizer, and Sinopharm, respectively. The mean post-vaccination exposure duration in the case group was 23. The study showed the D-dimer mean was significantly increased in the case group compared to the control group (0.97 mg/LL and 0.214 mg/LL respectively) (*P* value: 0.000).

Conclusion: D-dimer was significantly increased among individuals vaccinated with the COVID-19 vaccine compared to unvaccinated individuals in the control group. None of the gender, age, or vaccine type showed a significant correlation with D-dimer level.

Keywords: D-dimer, COVID-19, Measurement, Vaccinated, Khartoum state, Sudan

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Introduction

The COVID-19 pandemic affects millions of people worldwide with high morbidity and mortality (1-3). The virus was first identified and reported in Wuhan, China, in December 2019 (2-6). SARS-CoV-2 is a coronavirus designated as COVID-19 by the World Health Organization (WHO) (1,2,7). Bats and birds serve as the typical coronavirus hosts (1,8). In December 2019, an outbreak of a new type of coronavirus was noted (1,9). The viral reservoir may be bats, given the high homology of SARS-CoV-2 to other SARS-like viruses found in bats (9-11). SARS-CoV-2 is like SARS and Middle East respiratory syndrome viruses in the Coronaviridae family (1,12). These peplomers are known as spike proteins and are thought to be responsible for the tropism they display as they engage only with specific receptors on the cell surfaces of target organisms (1,13). SARS-CoV-2 appears to preferentially target respiratory epithelium, where it enters host cells through the angiotensin-converting enzyme 2 (ACE2) receptor, similar to severe acute respiratory syndrome coronavirus (SARS-CoV) (13-15). Hundreds of viruses belong to the coronavirus family (2,16). Among them are the SARS-CoV reported in November 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) reported in September 2012, which emerged in the human population from animal reservoirs and caused severe respiratory illness with high mortality rates (2,17,18). Initial reporting of findings from China has helped inform and guide the world (19). Guidance from subspecialists is critically important to help clinicians engaged in COVID-19 patient care, especially as multiple specialties are needed for patient management in intensive care units (ICUs) and non-ICU settings (20). Several vaccines have been developed and are currently being used to reduce disease incidence and mortality in many countries (21,22). Lately,

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rare but life-threatening events such as thrombosis with thrombocytopenia syndrome (TTS) (also called VITT—vaccine-induced thrombocytopenia and thrombosis) have been reported with some COVID-19 vaccines (21,23). Recent reviews of TTS following COVID-19 vaccinations have not included clinical management guidelines (21,24). The COVID-19 virus has caused increased morbidity and mortality worldwide (25). The number of deaths due to infection with the coronavirus has exceeded six million around the world since the first cases were discovered in China in December 2019 (26). As of April 18, 2020, WHO reported more than 2.1 million confirmed cases of COVID-19, including 142 229 deaths in 213 countries (2). The United States of America, Spain, Italy, Germany, France, the United Kingdom, China, Iran, Turkey, Belgium, the Russian Federation, Canada, and Brazil are the most impacted nations with over 30,000 confirmed cases of SARS-CoV-2 (2,27). However, Africa is expected to be the most vulnerable continent where COVID-19 spreading will have a major impact (28). As of April 18, 2020, Africa reported 19,895 confirmed cases, including 1017 deaths. The routine clinical diagnosis of COVID-19 is primarily based on epidemiological history and clinical manifestations and confirmed by a variety of laboratory detection methods, including computed tomography scans and serological techniques. The current standard for SARS-CoV-2 diagnosis is reverse transcription polymerase chain reaction (RT-PCR) (29-33). The amplification of a specific target gene is the aim of PCR. Primer-specific small amounts of template DNA and the target gene are heated and cooled in cycles, allowing the primers to attach to the gene and amplify it into millions of copies (34). Nucleic acid amplification tests (e.g., PCR) and immunoassays (e.g., enzyme-linked immunosorbent assay) are among the most utilized tools in today's COVID-19 diagnostic testing landscape (35). Approximately 20% of patients infected with SARS-CoV-2 (COVID-19) develop potentially life-threatening pathologies involving hyperinflammation, septic shock complications, and coagulation dysfunction (36). Routine laboratory data in the early stage of the COVID-19 epidemic are similar to those of a common viral infection: lymphopenia, prolonged prothrombin time, elevated D-dimer, liver enzymes (alanine aminotransferase), total bilirubin, and lactate dehydrogenase, with worsening data in ICU cases. The COVID-19 pandemic has sent shock waves through the global economy, causing the largest global economic crisis in more than a century, this crisis has led to a sharp increase in inequality within and between countries (37). Initial evidence indicates that recovery from this crisis will be as uneven as its initial economic effects, as emerging economies and economically disadvantaged groups need much longer to compensate for the losses resulting from the pandemic in terms of loss of income and livelihoods (38,39). COVID-19 vaccines help our bodies develop immunity to the virus that causes COVID-19 without us having to get the illness (40-42). Different types of vaccines work in different ways to offer protection (43). But with all types of vaccines, the body is left with a supply of "memory" T-lymphocytes as well as B-lymphocytes that will remember how to fight that virus in the future (44). None of the COVID-19 vaccines can give you COVID-19 (45). Bringing new vaccines to the public involves various steps, all of which must be followed before they are made available for use (46).

Materials and Methods

Study Design

This case-control descriptive study was carried out at the Al-Riada Modern Medical Laboratory in Khartoum State from January to April 2023. The samples were collected from Alingas Family Centre and Al-Ailfoun, east of the Nile. Individuals vaccinated with the COVID-19 vaccine were enrolled in this study as a case group. While individuals unvaccinated with the COVID-19 vaccine were enrolled as the control group.

Inclusion Criteria

Individuals vaccinated with the COVID-19 vaccine depend on the design of the vaccine type. Healthy participants who had not taken any type of corona vaccine before were selected as a control.

Exclusion Criteria

Participants who have a history of bleeding, thrombosis, anticoagulant drugs, or have been infected with the coronavirus before.

Data Collection

The data for this study was collected from both populations using a structured questionnaire.

Sample Collection

For each participant, 2.8 mL of blood sample was collected in a trisodium citrate anticoagulant container with a volume ratio of 1:9, and platelet-poor plasma was prepared by sample centrifugation at 3500 for 15 minutes.

Data Analysis

Data was entered and organized into a Microsoft Office Excel 2010 datasheet, and then for the analysis, SPSS version 23 statistical software (SPSS Inc., IL, USA) was used. The data was expressed as means and standard deviations. The statistical analysis was performed by the analysis of variance. A P value < 0.05 was considered statistically significant.

Results

This was a case-control descriptive study conducted at Al-Riada Modern Medical Laboratory on 100 samples; 50 of

them were case groups and 50 were control. The gender distribution was (20, 30) in the case group and (26, 24) in the control group, for males and females, respectively. The mean age of the case group was 38 years, while the mean age of the control group was 40 years. The case group was categorized according to the types of COVID-19 vaccines: AstraZeneca 26 (52%), Johnson 9 (18%), Pfizer 8 (16%), and Sinopharm 7 (14%). The mean post-vaccination exposure duration in the case group was 23. The study showed a significant increase in the D-dimer mean among the case group compared to the control (0.979 mg/LL and 0.214 mg/LL respectively), with a *P* value of 0.000 (Tables 1-8).

Discussion

COVID-19 has been classified as a pandemic disease that affects millions of people worldwide with high morbidity and mortality. The virus was first identified and reported from Wuhan, China, in December 2019. SARS-CoV-2 is a coronavirus with a human infection designated as COVID-19 by the WHO. COVID-19 vaccines have recently become a worldwide vaccination policy. Vaccination with COVID-19 vaccines helps our bodies develop immunity against COVID-19. But very recently, unusual thrombotic events in combination with severe thrombocytopenia have been reported. VITT (vaccine-induced immune thrombotic thrombocytopenia) has been associated with a high risk of fatal outcomes with both ischaemic and hemorrhagic complications. The study was conducted at Al-Riada Modern Medical Laboratory in Khartoum State. In the period from January to April 2023, 100 samples were collected to assess the D-dimer among the COVID-19-vaccinated population. The study showed a significantly increased D-dimer level among the COVID-19 vaccinated population compared to the control; this finding was matched with Hassan and colleagues, who reported increased D-dimer levels. The D-dimer in the COVID-19 vaccinated population was 387.11, whereas the control was 244.81 among the Sudanese population in Shendi town (47). The finding was in line with Schultz et al, who described five healthcare workers aged 32–54 who presented with severe venous thromboembolism at unusual sites. All five patients had elevated D-dimer levels (48). The finding was in agreement with Greinacher et al, who found that 11 patients, aged 22–49 years, developed cerebral venous thrombosis, three developed splanchnic-vein thrombosis, three developed pulmonary embolism, and four developed other types

Table 1. D-dimer Levels Among Case and Control Groups

Study population		*P* value
Case	Control	0.000
0.979	0.214	

Table 2. Distribution of Age, and Duration Among Both Groups

Variable	Case Age	Case Post-vaccination Exposure Duration	Case D-dimer	Control Age	Control D-dimer
Mean	38.04	23.14	0.97920	40.64	0.21462
Standard Error of Mean	1.793	1.548	0.293283	1.719	0.018937
Median	40.00	17.00	0.30000	45.00	0.16000
Mode	55	16	0.140	55	0.100
Standard Deviation	12.681	10.949	2.073826	12.153	0.133906
Variance	160.815	119.878	4.301	147.704	0.018
Range	37	36	9.900	37	0.479
Minimum	18	12	0.100	18	0.001
Maximum	55	48	10.000	55	0.480

Table 3. Gender Distribution Among Case Group

Gender	≤0.5 (Normal)		>0.5 (High)	
Male	13	26%	7	14%
Female	20	40%	10	20%

P value: 0.903.

Table 4. Distribution of Age Among Case Group

Age	≤0.5 (Normal)		>0.5 (High)	
18-35	14	28%	6	12%
36-55	19	38%	11	22%

P value: 0.626

Table 5. Distribution of Vaccine Types Among Case Group

Vaccine Types	≤0.5 (Normal)		>0.5 (High)	
AstraZeneca	19	38%	7	14%
Johnson	7	14%	2	4%
Sinopharm	3	6%	4	8%
Pfizer	4	8%	4	8%

P value: 0.293

Table 6. Distribution of Post-vaccination Exposure Duration Among Case Group

Post-vaccination	≤0.5 (Normal)		>0.5 (High)	
12-31	14	28%	6	12%
32-48	19	38%	11	22%

P value: 0.296

Table 7. Distribution of Gender Among the Control Group

Gender	≤0.5 (Normal)	
Male	26	52%
Female	24	48%

Table 8. Distribution of Age Among the Control Group

Age	≤0.5 (Normal)	
18-35	16	32%
36-55	34	68%

of thrombi. Seven patients tested for D-dimers, all had elevated levels ranging from 1.8 to 142 mg/L (reference value: 0.5 mg/L) (49). The finding was matched with Scully et al, who concluded that 22 patients with no history of prothrombotic conditions all received the first dose of the ChAdOx1 nCoV-19 vaccine. All the patients had elevated D-dimer levels at presentation (50). The finding was in line with Iba et al, who reported that vaccine-induced immune thrombotic thrombocytopenia manifests most often as unusual thrombosis and D-dimer elevation (51). The finding was in agreement with Hocking et al, who concluded that a 44-year-old male healthcare worker presented with fevers, fatigue, and abdominal discomfort after receiving his first dose of the COVID-19 vaccine (ChAdOx1-S [recombinant]), (AstraZeneca) (52). He had no prior thrombosis or exposure to heparin (53-57). There is a markedly elevated D-dimer of 114 mg/L (upper limit of normal, 0.5 mg/L) (28). Also, the finding was matched with Preethi Suresh et al. 2021, who found that a 27-year-old fit and well man, after having the first dose of the ChADOx1 nCOV-19 vaccine (Vaxzevria, previously AstraZeneca COVID-19 vaccine; AstraZeneca), blood showed raised D-dimer (58-61). This is likely because of the activation of coagulation proteins in response to the COVID-19 vaccination process. The study found no significant correlation between D-dimer levels and gender, age, or types of COVID-19 vaccines. This contrasts with the findings of Al-Dolaimy and Al-Samarrai (4), who reported that D-dimer levels did not differ significantly between pre-vaccination and post-vaccination.

Conclusion

D-dimer was significantly increased among those individuals vaccinated with the COVID-19 vaccine when compared to unvaccinated individuals in the control group. None of the gender, age, or vaccine type showed a significant correlation with D-dimer level.

Recommendation

1. Enroll the D-dimer test as a part of routine screening investigations in COVID-19-vaccinated individuals to screen their coagulation status.
2. Applying molecular techniques to detect genetic polymorphisms among the COVID-19-vaccinated population.
3. Further study of the D-dimer test on a larger population is recommended to obtain more reliable data on the COVID-19-vaccinated population.
4. More hemostatic investigations are suggested for vaccinated, healthy individuals. With COVID-19 vaccines, it is important to determine the risk factors and thrombotic markers to predict thrombotic risk among vaccinated healthy individuals.

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Competing Interests

The authors declare no potential conflicts of interest relevant to this article.

Ethical Approval

Ethical committee approval was obtained from the faculty of graduate studies and scientific research at the National University of Sudan, Faculty of Medical Laboratory Science. A structured formal consent that included information was provided with written informed consent from the population that was enrolled in this study.

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