Correlation between a few hematological variables and D-Dimer in non-vaccinated individuals and individuals who received Pfizer vaccine

Ismael Hasan Mohammed [1*]

Abstract

Background and objective: When a blood clot forms in an artery or a vein, it is called thrombosis. Thus, D-dimer can be thought of as a biomarker of activation of coagulation and fibrinolysis, and it is frequently used to rule out venous thromboembolism (VTE). This study was conducted to find out the relationship between RBC, WBC, Hb, platelets with the thrombotic variable, which is represented by D-dimer and impact of Pfizer vaccine on these variables.

Methods: Forty male and female patients aged 40 – 65 years with complete data records were included in this analysis for evaluation the correlations among RBC, Hb, WBC, platelets, and d-dimer. Ten students (male and females) aged 19-22 years and 10 old subjects aged 44-73 years were used for estimation the effect of the Pfizer vaccination on previous parameters.

Results: The results of this study showed that there is no correlation between all these measures and the D-dimer. Only there was a positive correlation between RBC and Hb, and between WBC and Hb. In addition, there was an increase in WBC, platelets and D-Dimer after one week of receiving the Pfizer vaccine in young and old groups.

Conclusion: There is no correlation between a rise or a decrease in the counts or levels of hematological measures (RBC, WBC, Hb, platelets) with the occurrence of thrombosis. The study also revealed that the Pfizer vaccine had an elevated effect on the WBC, platelets, and d-dimer measurements after one week.

Keywords: D-Dimer; Pfizer; RBC; WBC; WBC; Platelets.

Introduction

The development of a blood clot (partial or whole blockage), whether in venous or arterial blood vessels, limits the blood's normal flow and has clinical consequences. Blood cells (including platelets), plasma proteins, coagulation factors, inflammatory factors and cytokines, and the endothelial lining of arteries and veins all work together to maintain a complex homeostasis that allows blood to flow freely in vessels.

A thrombosis may be more likely to develop than a coagulopathy (increased risk of bleeding) when this physiological process is out of balance. Patients may experience an increased risk of both thrombosis and bleeding under specific clinical conditions such as disseminated intravascular coagulopathy (DIC), or coagulopathy in patients with underlying malignancy.[1]

Due to its frequency, erythrocytosis frequently results in a referral for a hematological evaluation; however, it is a poorly understood entity in clinical practice. Since secondary causes of erythrocytosis typically take longer to diagnose and frequently end up being inconclusive, the assessment primarily focuses on ruling out the primary causes of erythrocytosis. Undiagnosed conditions can have an impact on a patient's quality of life, and some studies indicate that some secondary etiologies may make thrombosis

[1] **Department of Medical Microbiology, Faculty of Science and Health, Koya University, Erbil, Iraq.**
Correspondence: ismael.hasan@koyauniversity.org

more likely.[2]

Leukocytes have been discovered to have a part in coagulation by releasing chemicals that boost systemic thrombogenicity and are known as leukocyte-released procoagulant mediators. Leukocytes are actively drawn to the site of thrombus development through interactions with platelets and endothelial cell adhesion molecules.[3]

Small, anucleate cells called platelets are produced in the bone marrow from megakaryocytes. At sites of vascular injury, platelets in circulation can quickly adhere and aggregate, forming the platelet plug (initial hemostasis wave). Additionally, negatively charged, phosphatidylserine-rich membrane surfaces from activated platelets can help cells produce more thrombin, which promotes blood coagulation (the second phase of hemostasis). Therefore, platelets are crucial to hemostasis. However, this advantage of hemostasis occasionally carries the risk of blood clotting and blood vessel blockage, which is the most common mechanism in the development of heart attacks and strokes after the break of an atherosclerotic mass.[4]

A fibrin breakdown product called D-dimer, which has several cross-linked D and/or E domains from the original fibrinogen molecule, may only potentially form when the fibrinolysis and hemostasis pathways are simultaneously active.[5]

The D-dimer test has gained popularity as a way to rule out venous thromboembolism. The appropriate use of D-dimer testing has significantly reduced the number of radiological examinations in this clinical context. The diagnosis of systemic coagulation illnesses, notably disseminated intravascular coagulation, also clinical management of coronavirus disease 2019 (COVID-19) requires D-dimer testing in addition to other coagulation assays.[5,6]

Corona viruses have posed a significant threat to the health of the general public worldwide. The evidence for abnormalities in common laboratory tests, particularly hematological tests and DD, which frequently accompany corona virus infection, has improved recently. They simultaneously have the potential to point out, in a time- and money-efficient manner, that may help with the diagnosis of SARS-CoV-2 infection, as well as help with the prognosis of the illness and the improvement of its clinical monitoring.[7]

The objective of this study is to investigate the correlation between hematological factors such RBC, WBC, Hb, and platelets, which are related to blood viscosity, and D-dimer, one of the thrombosis indicators. Also, to know the effect of the Pfizer vaccine after a week on these blood variables and D-Dimer.

Methods

This study was conducted in November 2021 - April 2022 as convenience sample study to evaluate the correlation among hematological variables that include RBC, Hb, WBC, platelets and D-dimer in male and female patients aged 40 – 65 years.

The data was gathered from patients who underwent examinations at the Shahid Doctor Khalid Hospital at Koya city and Rizgari Teaching Hospital at Erbil city during November in 2021 and April 2022 at Kurdistan-Iraq. Forty male and female patients aged 40 – 65 years, those who visited the hospital were given the results of RBC, Hb, WBC, platelets, and d-dimer for evaluation the correlations among them.

Convenience sample study is used to know the effect of Pfizer vaccine after one week on hematological parameters (RBC, WBC, Hb, platelets) and D-Dimer. Ten normal students (male and females) aged 19-22 years from Koya University in the Kurdistan region of Iraq, as well as ten normal old participants aged 44-73 years, were utilized to estimate the vaccination's effects of the Pfizer on previous parameters. The parameters were measured before the vaccination and one week after vaccination. The data was taken from

a venous blood sample that was collected into EDTA tubes for the purpose of establishing an automated method for determining complete blood counts (CBCs). Blood counts were conducted using a fully automated hematology analyzer CBC Machine 3PART, For Laboratory, Model Name/Number: PE6800.

Statistical analysis of data

Data analysis was carried out using IBM SPSS ver. 22 (SPSS Inc., Chicago, IL, USA). Correlation between each two parameters was performed by correlation coefficient (Bivariate correlations-Pearson) and the graphs were performed by chart builder –Scatter/Dot. Paired t test was used to evaluate the effect of Pfizer vaccine, comparing readings before and after the vaccination. A P value of ≤0.05 was considered as statistically significant.

Ethical consideration

The study was conducted in accordance with the ethical principles established in the Declaration of Helsinki. The study protocol and the subjects' information and permission form were evaluated and approved by a local ethics committee. The ethics committee approved this study at Koya University, Faculty of Science and Health.

Results

The results revealed that there is no significant positive or negative correlation between any of the blood variables included in this study, with the exception of a significant positive correlation between RBC and Hb at the 0.01 level (r = 0.484, P-value = 0.009) (Figure 1) and a significant positive correlation between WBC and Hb at the 0.05 level (r = 0.414, P-value = 0.28) (Figure 2).

Receiving Pfizer vaccine showed no change in the parameters of RBC and Hbone week after receiving the vaccination in both the young and old groups. While there was an increase in each of the WBC, platelets, and D-dimer one week after receiving the Pfizer vaccination in both the young and old groups (Table 1 and Table 2).
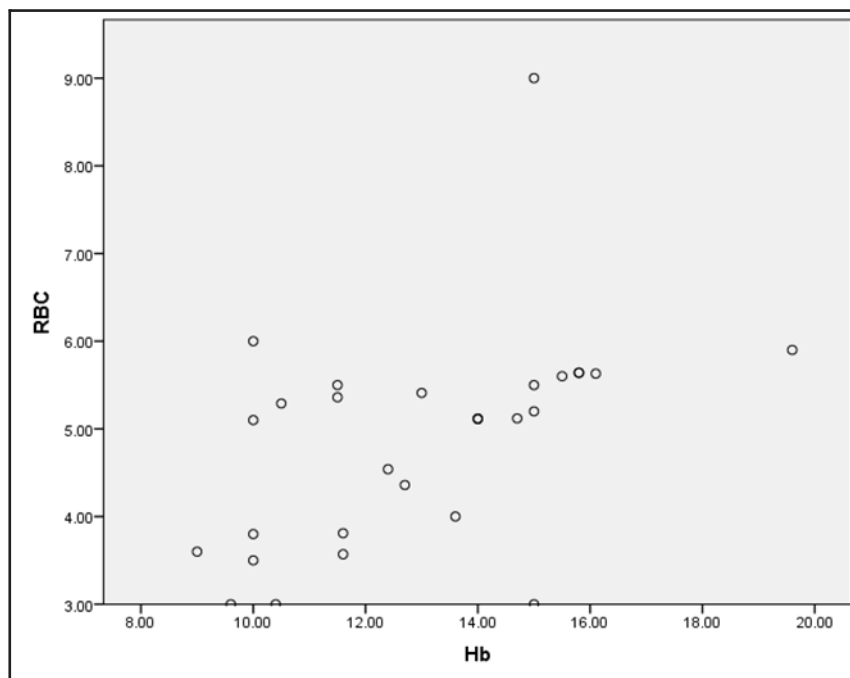

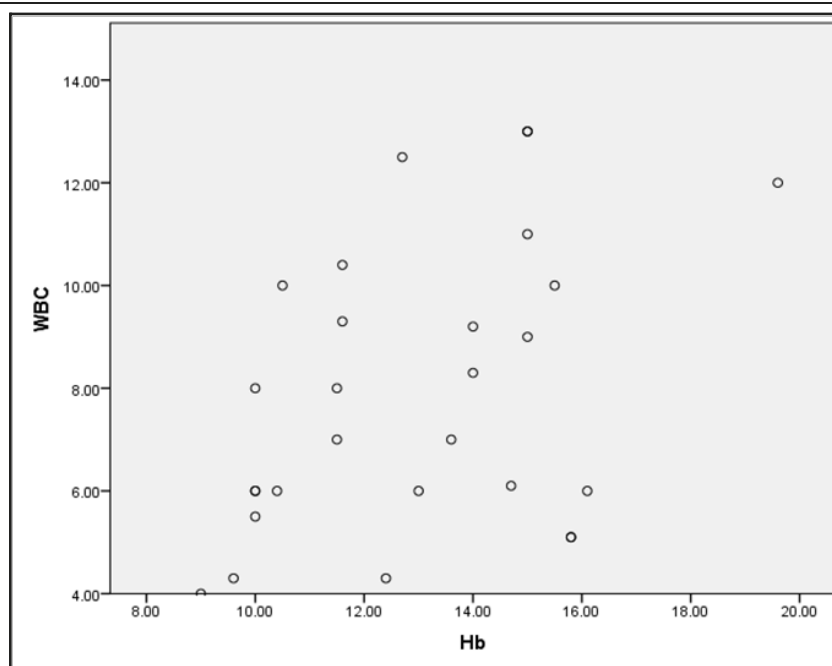**Figure 1** Correlation between RBC and Hb concentrations

Figure 2 Correlation between WBC and Hb concentrations

Table 1 Effect of Pfizer vaccine on a number of hematological parameters and d-dimer in 10 young students

Parameters	Before vaccination	After one week from the vaccination	*P*-value
RBC (106/mm3)	4.5510 ± 0.6259	4.5280 ±0.6248	0.603
WBC (103/mm3)	6.7900 ±1.9122	7.4120 ±1.9198*	0.0003
Hb (g/dL)	13.3100 ±1.2351	13.4390 ±1.2002	0.304
Platelets (103/mm3)	252.80 ±44.87	259.10 ±43.46*	0.001
D-Dimer (µg/ml)	0.2188 ±0.1029	0.3000 ±0.1178*	0.001

All the values are expressed as mean ± SD (n= 10 for each group). * Significantly different from the before vaccination at *P* <0.05 by T-test

Table 2: Effect of Pfizer vaccine on a number of hematological parameters and d-dimer in 10 old subjects

Parameters	Before vaccination	After one week from the vaccination	*P*-value
RBC (106/mm3)	4.6690 ± 0.5810	4.7440 ±0.5708	0.233
WBC (103/mm3)	7.4700 ±1.8536	7.7830 ±1.7257*	0.014
Hb (g/dL)	12.8800 ±1.1555	12.9080 ±1.1297	0.762
Platelets (103/mm3)	287.40 ±79.19	290.40 ±78.64*	0.026
D-Dimer (µg/ml)	1.1320 ±0.6793	1.8350 ±0.9298*	0.004

All the values are expressed as mean ± SD (n= 10 for each group). * Significantly different from the before vaccination at *P* <0.05 by T-test

Discussion

We retrospectively analyzed the data of forty patients to assess the correlation between D-Dimer and RBC, Hb, WBC and platelets. The present study is the first study in Kurdistan-Iraq.

Numerous studies demonstrate that a rise in the number of red blood cells causes the blood's viscosity to rise. This, in turn, may have an impact on capillaries and raise the risk of thrombosis in the arteries and veins.[8] Furthermore, patients with untreated polycythemia vera have a high incidence of fatal cerebrovascular strokes.[9] Recent study showed that RBC did not have an any correlation with D-Dimer, platelets and white blood cells, only showed that it had a significant positive correlation with hemoglobin, which is expected because Hb is considered a major macromolecular fraction of red blood cells (RBCs).[10]

Certain investigations corroborated the conclusions of this research. Observational studies have shown that thrombosis is not associated with most forms of polycythemia vera.[11] However, other researchers found that the phlebotomy for patients with polycythemia vera PV and secondary erythrocytosisdoes not reduce the incidence of thrombosis, and this indicates that there is no relationship between hematocrit, viscosity, and thrombosis.[12,13] Also, other researchers via observational studies have shown that thrombosis does not accompany most forms of erythrocytosis.[11]

While other researches shown that occurrence of venous thromboembolism in men and women are more likely to occur when their hematocrit is high. It is well known that a high hematocrit is linked to an increase in hemoglobin and red blood cell count because they are directly related.[14]

Regarding white blood cells, the current study only showed that has a positive relationship with hemoglobin. While some research suggest that the vascular risk is significantly linked to an increase in white blood cells, or leukocytosis. Leukocytes can adhere to the endothelium monolayer when there is inflammation because adhesion molecules, which are cell surface proteins, are present. Pro-inflammatory cytokines in the arterial plaque encourage leukocyte migration into the intima.[15]

The pathogenesis of atherosclerosis is significantly influenced by oxidative mechanisms. White blood cell numbers have been theorized to play a role in the oxidative breakdown of LDL, which encourages atherosclerosis and arterial thrombi.[16]

Even the platelets in the current study did not appear to have a relationship with D-Dimer, which usually expresses the presence of the thrombosis state and with the rest of the factors. By gathering and coagulating, platelets produce thrombosis. The rupture site of the atherosclerotic plaque is the optimum location for thrombotic events to happen, and this may result in a heart attack or stroke, the two leading causes of death. Many studies have demonstrated that platelets play an important part in the initiation of atherosclerosis as well as the function they play in thrombosis, which is an outcome of atherosclerosis.[17] In a study on Covid-19 patients, it was observed that an increase in the number of blood platelets over the first week of hospitalization of Covid-19 patients was associated with an improvement in survival rates and a reduction in the risk occurrence of the thrombosis. Additionally, it was observed that when the blood platelet count increased, the levels of D-dimer reduced.[18]

Only there was a positive correlation between RBC and Hb, and between WBC and Hb, and this is normal, because usually blood cells increase together and decrease together, and since Hb is part of red blood cells, therefore their increase means an increase in red blood cells and vice versa. But, the positive correlation between WBC and Hb, we did not find a scientific explanation for it.

The Pfizer vaccine did not show any effect

on RBC and Hb after a week of taking the vaccine in both groups (young and old). But it showed a significant increase ($P <0.05$) in WBC in both groups. While majority of research found a decrease in white blood cells after the second and third doses of the covid vaccination. Leukopenia following vaccination is not fully understood, however a drop in lymphocyte count was seen, which may account for the low level of white blood cells. It's probable that the suppression of the bone marrow, which reduces white blood cell formation, is what's causing the decline in white blood cell count later after vaccination, or after the second and third dose.[19] However, a research was shown that people who test positive for COVID-19 but have no symptoms typically have a high WBC count, particularly lymphocytes.[20] This may corroborates the increase in white blood cells seen in the current study.

This study found that both the young group and the old group's platelet counts rose ($P <0.05$) one week after receiving the Pfizer vaccination. Even while numerous reports mentioning a drop in blood platelet counts two weeks after receiving the Pfizer vaccination, some individuals experienced bleeding episodes as a result of a paucity of platelets.[21]

According to the findings of current study, both groups experienced an increase in D-dimer one week after receiving the Pfizer vaccination. It was noted that after receiving the covid vaccine, particularly AstraZeneca, a thrombosis developed along with an increase in D-dimer, a deficiency in platelets, and a decrease in fibrinogen levels. The cause is thought to be the development of antibodies following vaccination that impede the formation of the heparin-PF4 complex, which is required to prevent the development of thromboembolism. Furthermore, the release of PF4 from the platelets, which is what causes a hypercoagulability, will be unhindered in the absence of the formation of this complex.[22]

In particular, AstraZeneca has found that people who had thromboembolism after receiving the covid vaccine had antibodies that prevented the formation of the heparin -PF4 complex.[23]

Conclusion

This study suggested that there may be no correlation between blood variables (RBC, WBC, Hb, platelets) that related to blood viscosity and the D- dimer variable, which is one of the most significant thrombotic indicators. It also showed, a week after receiving the Pfizer vaccination, various blood parameters, such as WBC, platelets, and D-dimer, increase.

Competing interests

The author declares that he has no competing interests.

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