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Effect of different COVID-19 vaccines on some biomarkers in diabetics

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***Abstract*— After the emergency approval of different COVID-19 vaccines the administration of millions of doses, many concerns arise for adverse effects, especially in vulnerable groups such as diabetics. In this study, we investigate what effects different COVID vaccines could have on several biomarkers in diabetic patients and whether that raises a concern for this group or not. Materials and methods: this study includes two groups of diabetics each group consists of 20 participants ; One of the groups under study, where they received the COVID-19 vaccine either AstraZeneca or Pifizr-BioNTech vaccine and the other groups were controlled or the Pfizer-BioNTech vaccine, the other group-the control group-did not take any vaccine. Blood samples were taken from both groups about a week after the first dose and statistical studies were conducted on the results. Results: Noticed an increase in all biomarkers. Increase in RBS could simply be due to immune response, same thing could be said for the CRP increase. Ferritin increase was not important; it was only apparent in three patients and that could be due to active infection. The increase in D-dimer levels was apparent in all patients and that raises the biggest concern. Conclusion: the biggest issue was seen in the rising of D-dimer levels because it raises concern about clotting disorders and heart disease which is already a concern for diabetic patients. Further investigation should be done and careful monitoring for clotting risks is necessary after the vaccine.**

***Keywords*— SARS-CoV-2,AstraZeneca, Pfizer-BioNTech, RBS, CRP, Ferritin, D-dimer.**

I. INTRODUCTION

Corona virus pandemic is an ongoing global pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (Ali et al., 2022). Efforts are focused on the role of extensive vaccination for preventing, the transmission of the disease and controlling it.

Due to the urgency of the matter, vaccines development and production have accelerated at an unprecedented speed. Currently, there are 194 candidate vaccines in preclinical development and 137 in clinical stages of development (WHO, 2020). Recent data indicate that there are 22 COVID-19 vaccines approved and are currently in use in different parts of the world (Machingaidze and Wiysonge, 2021).

Vaccination is necessary for vulnerable groups and one such group that tends to have a poor prognosis when it comes to SARS-CoV-2 infection is diabetics (Muhar et al., 2022), which makes getting the vaccine particularly important for them (Baiden et al., 2015).

However, vaccination could have some negative side effects on the people who take it (Kudlay and Svistunov, 2022). This leaves us questioning whether those side effects can be worse for diabetic patients, and whether any disruption to the proper function of their bodies can occur due to the vaccine (Yap et al., 2021). This is why monitoring this group for any adverse effects is necessary.

II. MATERIALS AND METHODS

A. Studied groups and Data collection

In this study focused primarily on biomarkers that have close association to either Diabetes mellitus (DM) or the general inflammatory state of the body. Data were obtained from a randomly controlled clinical trial. Twenty diabetic patients who took the COVID 19 vaccine were randomly selected (10 males, 10 females, age range: 18-82 years). Another group of twenty diabetic patients who didn't take the COVID 19 vaccine were also randomly selected as a control group (13 males, 7 females, age range: 16-82 years) (Krause et al., 2022).

Samples were obtained one to two weeks after taking the vaccine for the first group and around the same period of time for the control group. The four studied biomarkers were Random Blood Sugar (RBS), C-reactive protein (CRP), Ferritin and D-dimer blood levels (Falissard et al., 2012).

B. Random Blood Sugar (RBS):

RBS measures the glucose level in the blood of non-fasting level. Usually, blood sugar levels that are 200 mg/dL or higher indicates that the patient has diabetes (Morley and Kushner 1982).

C. Reactive Protein (CRP):

C-reactive protein is a plasma It rises in response to inflammation in the acute phase . CRP measurement unit is milligrams per liter (mg/L). Standard results for a CRP test are interpreted the following way: Less than 10 mg/L is

considered normal. Equal to or greater than 10 mg/L is considered elevated (Morley and Kushner 1982).

D. Ferritin:

Serum ferritin levels are usually measured when studying case that are related to iron-deficiency anemia. However, serum ferritin is also a well-known inflammatory marker. Ferritin levels usually increase as result of acute or chronic inflammation, chronic consumption of alcohol, liver diseases, renal failure, malignancies, or metabolic syndrome rather than iron overload. Normal serum ferritin levels differ from a laboratory to another but generally concentrations that are >300 µg/L in men and postmenopausal women and >200 µg/L in premenopausal women are considered elevated levels (Adams 2008).

E. D-dimer:

D-dimer is a biomarker that's in the blood and marks the formation and degradation of fibrin. It can be measured using whole blood samples or just plasma. Individuals that are healthy have low levels of D-dimer circulating in the blood, because elevated levels are usually found in conditions related to thrombosis. Normal concentration of D-dimer is < 250 ng/mL, or < 0.4 mcg/mL (Jeffrey et al., 2017).

F. Vaccination:

The vaccinated group consisted of: 1- patients who took the AstraZeneca vaccine (9 patients) and 2- patients who took the Pfizer-BioNTech vaccine (11 patients). AstraZeneca vaccine (ChAdOx1 nCoV-19 vaccine) was developed by the University of Oxford jointly with AstraZeneca pharmaceutical and biotechnology company. The action of the vaccine is carried out by introducing the genetic code of the SARS-CoV-2 spike protein to the body. Once this code is inside the cell, it produces the spike protein which in turn causes an immune response by the body, this is generally similar to other mRNA vaccines. After the immune response the body will be able to recognize the spike protein of the coronavirus in case of later infection which will make the immune system have a quick response and destroy the before it causes infection (Merrick et al. 2017).
Pfizer-BioNTech vaccine (BNT162b2 vaccine) was developed by Pfizer and BioNTech, it uses mRNA technology and contains the genetic code of the spike protein (Han et al., 2021). After the mRNA is inside the cell, it follows a similar pathway in producing the spike protein which in turn will cause an immune response that will protect the body in case of future infection (Petruccelli et al., 2019)

G. Blood Samples collection:

Blood was collected from patients who took the vaccine one to two weeks after the first dose of the vaccine. The control group blood samples were taken at about the blood samples of the control group were taken in the same period (Angelakis et al., 2020).

III. RESULTS AND DISCUSSION

This study findings see based on the two tables listed at the end of the study a big increase in the Mean of all the biomarkers in the vaccinated group compared to the non-vaccinated group. Now we'll discuss each biomarker in detail.

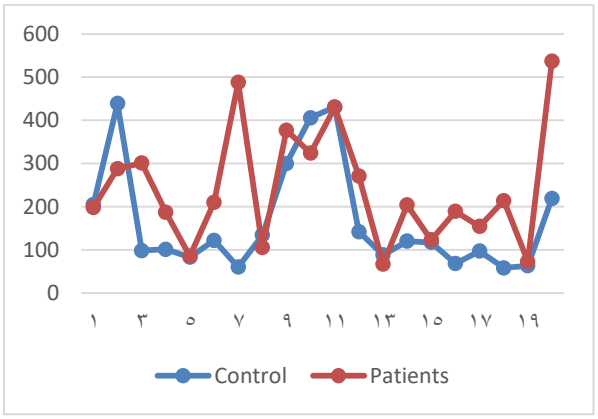

Figure 1 The random blood sugar (RBS) results in this study

Generally, it was noticed that there is an increase in the Mean of Random Blood Sugar (RBS) in the vaccinated group. also notice a big variance of this biomarker between patients, which makes the link between vaccination and the increase of RBS levels unclear.

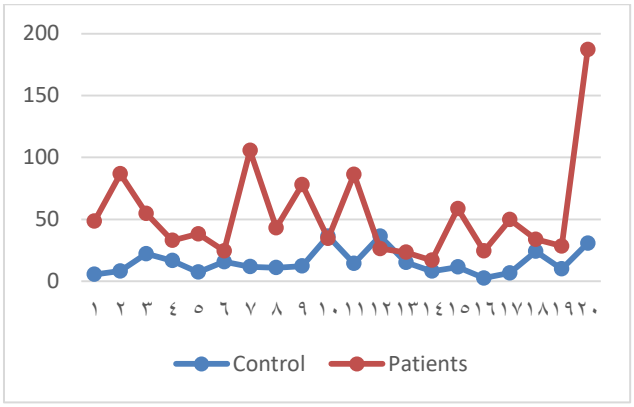

Figure 2 The C-reactive protein (CRP) levels in this study

A remarked increase was seen in the Mean of the inflammatory protein CRP in the vaccinated group; three times the Mean in the control group. The data shows us a general tendency toward big increases in this protein in the vaccinated group.

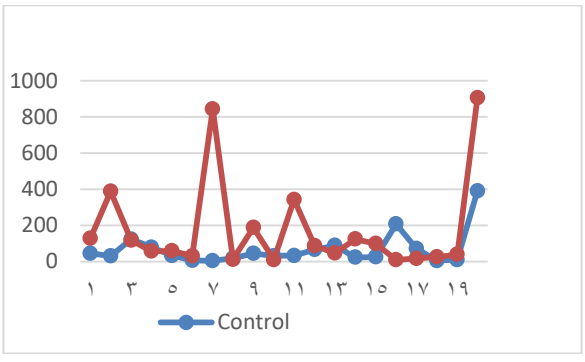

Figure 3 The serum ferritin levels in this study

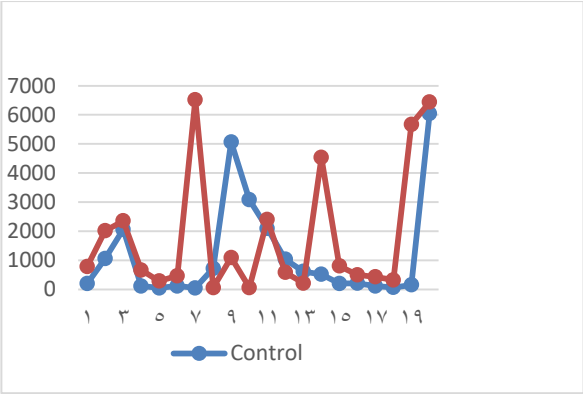

Figure 4 D-dimer levels in this study

TABLE 1. THE DISTRIBUTION OF VACCINATED GROUP ACCORDING TO SOME BIOMARKERS

No.	Age	Gender	RBS	CRP	Ferritin	D-dimer
1	54	male	198	48.5	128.43	785.6
2	72	male	288	86.7	387.65	2013
3	66	male	301	54.8	118.08	2358
4	51	male	187	32.9	56.876	667.5
5	22	male	85	38.2	58.865	287.3
6	42	male	210	24.6	31.457	467.2
7	82	female	488	105.6	843.76	6521
8	21	female	105	43.1	11.325	63.98
9	64	female	377	78.1	187.976	1097
10	18	female	324	34.5	9.764	60.81
11	57	male	430	86.3	342.907	2398
12	60	male	271	26.3	87.965	583.8
13	22	male	67	23.4	45.871	215.7
14	60	male	204	16.9	123.787	4532
15	39	male	123	58.7	99.125	806.4
16	51	female	189	24.4	8.974	500.3
17	49	female	154	49.7	16.987	432.8
18	55	female	214	33.9	24.873	327.4
19	33	female	73	28.4	38.982	5673
20	80	female	537	187.2	905.129	6439
General Mean	49.9		241.25	54.11	176.43915	1811.4895
Mean (females)	50.33333		273.4444	64.988889	227.53	2346.1433
Mean (males)	49.54545		214.9091	45.209091	134.6375455	1374.0455

Noticed that a 150% increase in the Mean of the levels of ferritin in the vaccinated group. This finding on its own is not enough because we notice that three patients of the vaccinated sample have exceptionally high levels of ferritin which in turn resulted in the increase of the Mean. Generally, for the rest of the group, levels of Ferritin stayed in the normal range or slightly higher.

Both groups show an increase in the Mean of D-dimer levels, however, the Mean in the vaccinated group is 60% higher than the control group. This shows us that there is a link between vaccination and the increase in the levels of D-dimer protein.

In the tables 1 and 2, the distribution in both cases and controls for the biomarkers in correlation to gender, it was noted that in control group, The mean RBS, CRP, and ferritin were markedly elevated in males than females while the D-dimer was slightly different (doubled once) in males over females. While in case group there were slightly increase in RBS and CRP levels in males than females while both ferritin and D-dimer were markedly elevated in males too.

IV. DISCUSSION

In this study can see from the results have that the vaccine did increase Random Blood Sugar, which is normal because immune response normally raises blood sugar. Also, there was variance between RBS levels in the vaccinated group which needs further investigation to find other links or explanations (Falissard *et al.*, 2012).

The vaccination also increased the levels of biomarkers associated with inflammation. But since the COVID-19 vaccination Function is generating an immune response, which means an increased inflammation, the dose will obviously elevate CRP levels temporarily (Potempa *et al.*, 2020), but generally, this is not a cause for concern since the temporary increase in CRP after a vaccine is not the same as long-term elevation associated with the risk of other diseases. It is also not the same as dangerously high levels of CRP seen as a result of infection with the coronavirus itself. Can also note that the temporary increase in CRP levels has also been seen after taking other vaccines, such as the influenza vaccine and the pneumococcal pneumonia vaccine (Miller *et al.*, 2013).

Moving to Ferritin levels, don't see clear association between vaccination and increased levels. Some patients did have a big increase in Ferritin levels which affected the average results but it could because to other conditions such as an active infection in those patients (Lichstein *et al.*, 2019).

Lastly, that we saw an apparent increase in D-dimer levels after the vaccination. This is especially concerning for diabetics since they're already at a greater risk for clotting and heart disease. There is also a risk for the rare incidence of Vaccine-induced immune thrombotic thrombocytopenia (VITT) associated with the AstraZeneca vaccine. Further investigation should be focused on this issue. Also monitoring diabetic patients during the month after vaccination is necessary to prevent any risk for clotting.

V. CONCLUSION

The biggest issue was seen in the rising of D-dimer levels because it raises concern about clotting disorders and heart disease which is already a concern for diabetic patients. Further investigation should be done and careful monitoring for clotting risks is necessary after the vaccine.

TABLE 2. THE DISTRIBUTION OF CONTROL GROUP ACCORDING TO SOME BIOMARKERS

No.	Age	Gender	RBS	CRP	Ferritin	D-dimer
1	38	male	205	5.5	45.7	200
2	82	male	439	8.3	29.9	1056
3	36	male	98	22.2	123.5	2065
4	29	male	101	16.7	78.9	120
5	23	male	83	7.4	32.7	48.98
6	48	female	122	15.7	5.9	116.7
7	28	female	60	11.8	3.8	50.53
8	46	female	134	10.9	18.6	719.9
9	77	male	300	12.3	44.8	5067
10	70	female	406	36.4	30.8	3084
11	65	male	431	14.3	32.8	2097
12	54	female	142	36.4	65.2	1034
13	32	male	88	15.2	88.98	619
14	42	male	120	8.1	22.8	521
15	43	male	117	11.5	25.2	208
16	19	male	68	2.5	207.5	213
17	23	male	97	6.7	71.8	118
18	16	female	58	24.1	4.87	65.83
19	32	female	63	9.9	10.21	154.9
20	65	male	219	30.7	390.6	6040
General Mean	43.4		167.55	15.33	66.728	1179.942
Mean (males)	44.15385		182	12.41538	91.93692	1413.306154
Mean (females)	42		140.7143	20.74286	19.91143	746.5514286

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