Assessment of Coagulation Profile in Adults Vaccinated Against SARS-CoV-2 (COVID-19) in Qena Governorate

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Abstract

Background: Egypt is just one of many countries around the world that have approved or granted emergency use authorization (EUA) for six different vaccines to prevent COVID-19: Moderna (mRNA-1273), Oxford/AstraZeneca (ChAdOx1 nCoV-19), Janssen (Ad26.COV2. S), Pfizer BioNTech (BNT162b2), Sinopharm COVID-19 vaccine and Sinovac-CoronaVac COVID-19 vaccine.

Objectives: to evaluate the platelet count and blood coagulation profile in COVID-19 vaccine recipients.

Patients and methods: this cross-sectional study was at Qena University Hospital and Clinical Pathology Departments involving 400 adult individuals with male to female ratio 1:1 vaccinated against COVID-19 over 6 months from 1/12/2021 to 1/6/2022: 135(33.8%) received Sinopharm vaccine, 123(30.8%) received Sinovac vaccine, 68(17%) received Pfizer vaccine, 51(12.8%) received AstraZeneca vaccine, 12(3%) received Moderna vaccine, and 11(2.8%) received Janssen vaccine.

Results: the mean age of 39.75 ± 13.56 years with a range 18-95 years, the mean platelets count was 229-487 $x10^3/mm^3$ with a range 280.56 ± 96.62 $x10^3/mm^3$, the mean value of PT was 13.02 ± 0.7 sec and ranged between 12-16.8 sec, the mean value of PTT was 30.09 ± 3.45 sec and ranged between 24-50 sec, the mean value of D-dimer was 0.35 ± 0.13 mg/l and ranged between 0.19-0.57 mg/l. There were insignificant differences in all types of vaccinations concerning the platelet count, D-dimer, PT, PTT, and INR.

Conclusion: Vaccination versus SARS-CoV-2 remains crucial for controlling the COVID-19 pandemic. There is no significant difference in all types of vaccinations concerning D-dimer, PT, PTT, and INR or concerning platelet count.

Keywords: Egypt; AstraZeneca vaccine; Janssen vaccine; Moderna vaccine; Pfizer vaccine.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak of 2019 (abbreviated as COVID-19) is a recognized global pandemic. In late 2019, an infectious sickness began in Wuhan, China & has since spread around the world, infecting over 245 million individuals as well as killing approximately 4.98 million (**Fujita et al., 2021**).

Until reliable vaccinations can be produced and a worldwide immunization campaign is completely launched, it is widely believed that, notwithstanding the necessity of infection control measures to minimize or reduce SARS-CoV-2 transmission, the globe will not return to its pre-pandemic normalcy (**WHO, 2020**).

Many countries around the world, including Egypt, have approved or granted emergency use authorization (EUA) for 6 vaccines to prevent COVID-19: Pfizer BioNTech (BNT162b2), Janssen (Ad26.COV2. S), Moderna (mRNA-1273), Oxford/AstraZeneca (ChAdOx1 nCoV-19), Sinopharm COVID-19 vaccine as well as Sinovac-CoronaVac COVID-19 vaccine (**Greinacher et al., 2021**).

Side effects have been reported after receiving COVID-19 vaccines, some of which are short-term and resolve after a few days without any medical intervention as in Moderna (mRNA-1273), Pfizer BioNTech (BNT162b2) and Sinopharm COVID-19 vaccine . However, some more severe side effects have also been reported. Common side effects after receiving the first dosage of COVID-19 vaccines include injection site tenderness, injection site pain, fatigue, headache, malaise, myalgia, pyrexia and feverishness, and fever >38 °C. Oxford/AstraZeneca (ChAdOx1 nCoV-19) showed some severe side effects include dizziness, muscle spasm, and paresthesia. Sporadic symptoms such as tremors, diplopia, tinnitus, dysphonia, epilepsy, allergic reactions including anaphylaxis, and reactivation of herpes zoster appear after vaccination (**Atyabi et al., 2022).**

Following receiving the Oxford/AstraZeneca (ChAdOx1 nCoV-19) vaccine, numerous individuals late in February 2021 experienced a novel clinical syndrome that consisted of thrombosis at unexpected places accompanied by thrombocytopenia. Similar clinical sequelae were documented in April 2021 among those who had received the Janssen (Ad26.COV2. S) vaccine; nonetheless, the occurrence of significant adverse events has remained extremely rare, even after more than 400 million people were vaccinated throughout the world (**Greinacher et al., 2021; Muir et al., 2021)**

Follow-up and assessment of coagulation profile in vaccinated individuals can help in the acceptance of different vaccines and make sure of their safety.

Patients and methods

It was a cross-sectional trial that looked at 400 adult subjects vaccinated against SARS-COV-2 (COVID-19) from 5th to 29th days in Qena Governorate at Qena University Hospital in the Clinical and Chemical Pathology Department over, over 6 months from 1/12/2021 to 1/6/2022.

Inclusion criteria: adult individuals vaccinated against SARS-COV-2 (COVID-19) who received the vaccine from 5th to 29th days.

Exclusion criteria: Patients on anticoagulants, Patients with severe liver disorders, Patients with vitamin K deficiency, cases with inherited clotting factor deficiencies such as von Willebrand disease, Haemophilia, and factors XII and XI deficiency, cases with active malignancy and Patients with a history of thrombosis, disseminated intravascular coagulation (DIC), pulmonary embolism or deep venous thrombosis (DVT).

Ethical approval: The study was conducted after the approval by the institutional ethics committee at Qena Faculty of Medicine, The ethical approval code was SVU-MED-CCP031-12111273.

Methods

All of the subjects underwent:

A. History taking:

-Including personal history (name, age, and sex), associated medical conditions, family history, and history of coagulation disorders.

-Type, number of doses, and timing of vaccines: Pfizer BioNTech (BNT162b2) is administered in 2 intramuscular (IM) doses (0.3 mL each) 3 weeks apart **(Dooling et al., 2021)**. Janssen (Ad26.COV2. S) is given in a single 0.5 mL IM injection **(Mascellino et al., 2021)**. Moderna (mRNA-1273) is administered in 2 IM doses (0.5 mL each) 28 days apart **(Jackson et al., 2020)**. Oxford/Astrazeneca (ChAdOx1 nCoV-19) is administered in 2 IM doses (0.5 mL each) 28 days apart **(Vilches et al., 2021)**. Sinopharm COVID-19 is administered in 2 IM doses (0.5 mL each) fourteen or twenty-one days apart **(Xia et al., 2022)**. Sinovac-CoronaVac COVID-19 vaccine is administered in 2 IM doses (0.5 mL each), fourteen or twenty-eight days apart **(WHO, 2021)**.

B. Blood sampling for Laboratory investigations:

Under aseptic conditions, 5 ml venous blood was divided into EDTA and sodium citrate tubes with a 9:1 blood volume to anticoagulant ratio, utilizing the standard operating procedure (SOP), platelet-poor plasma (PRP) was obtained by spinning the citrate tube at 3000 x g for 15 minutes while kept at room temperature.

CBC: using Cell Dyne-Ruby automated cell counter (Abbott Diagnostics -Santa Clara-Ca-USA) and the peripheral blood smear was done using Leishman's stain.

Prothrombin time (PT) and partial thromboplastin time (PTT) are measured using automated blood coagulation analyzers, CS-1600-Sysmex Corporation.-Kobe, Japan. Normal PT is from 10.5 to 13.3 seconds. Normal PC is from 80.3% to 102.3%. Normal INR is from 0.92 to 1.16. Normal PTT is from 28.9 to 36.7 seconds.

D-Dimer: using particle-enhanced D-Dimer assay with turbidimetric immunoassay on automated blood coagulation analyzer CS-1600-Sysmex Corporation.-Kobe, Japan. A normal D-dimer is considered less than 0.5 µ/mL

Statistical analysis

The SPSS 25.0, was used to process and analyze the data. IBM Corp., Armonk, New York. The Kolmogorov-Smirnov test was performed to ensure a normally distributed sample. Qualitative data were described using numbers and percentages. The minimum and maximum values, as well as the mean ±SD, were utilized to characterize the quantitative data. The one-way ANOVA test was used for testing the significance between non-parametric quantitative variables in more than two groups. The five percent significance threshold was utilized to evaluate the findings.

Results

This cross-sectional study was conducted at Qena University Hospital in the Clinical and Chemical Pathology Department on 400 adult subjects given the SARS-COV-2 (COVID-19) vaccine from the 5th to 29th days in Qena Governorate. The ages of the participants extended from eighteen to ninety-five with an average age of 39.75±13.56 years. Two hundred (50%) of the cases were male and two hundred (50%) were female. 7(1.75%) had diabetes mellitus, 33(8.30%) had hypertension, 5(1.30%) had both and 355(88.80%) had no diabetes nor hypertension. The mean platelets count was 229-487 x10^3/mm^3 with a range between 280.56±96.62 x10^3/mm^3, the mean value of PT was 13.02±0.7 sec and ranged between 12-16.8 sec, the mean value

of PTT was 30.09±3.45 sec and ranged between 24-50 sec, the mean value of D-

dimer was 0.35±0.13 mg/l and ranged between 0.19-0.57 mg/l **(Table. 1)**.

Table 1. Demographic data, co-morbidity and laboratory values

Demographic data	Number (No=400)	
Age (years)		
Range	18-95	
Mean ± S.D.	39.75 ± 13.56	
Age distribution	*No*	*%*
18-30 years	138	34.5%
31-50 years	173	43.25%
51-70 years	83	20.75%
71-95 years	6	1.5%
Gender	*No*	*%*
Male	200	50%
Female	200	50%
Co-morbidity	*NO*	*%*
Diabetes	7	1.75%
Hypertension	33	8.3%
Diabetes and hypertension	5	1.3%
History of previous coagulopathy	0	0%
No	355	88.8%
Laboratory finding	**Mean**	**Range**
Platelts count x10^3/mm^3	229-487	280.56±96.62
PT sec	13.02±0.7	12-16.8
PTT sec	30.09±3.45	24-50
D-dimer mg/l	0.35±0.13	0.19-0.57

11(2.8%) of the subject received Janssen vaccine, 12(3%) received Moderna vaccine, 68(17%) received Pfizer vaccine, 135(33.8%) received Sinopharm vaccine, 51(12.8%) received AstraZeneca vaccine and 123(30.8%) received Sinovac vaccine, **(Table. 2).**

Table 2. The type of vaccination received

Vaccination received	Number	Percent
AstraZeneca	51	12.75%
Janssen	11	2.75%
Moderna	12	3%
Pfizer	68	17%
Sinopharm	135	33.75%
Sinovac	123	30.75%
Total	400	100%

There were 44(22.0%) males and 7(3.5%) females received the AstraZeneca vaccine, 7(3.5%) males and 4(2.0%) females received Janssen vaccine, 3(1.5%) males and 9(4.5%) females received Moderna vaccine, 10(5.0%) males and 58(29.0%) females received Pfizer vaccine, 72(36.0%) males and 63(31.5%) females received Sinopharm vaccine, and 64(32.0%) males and 59(29.5%) females received Sinovac vaccine (**Fig.1 and Table.3).**
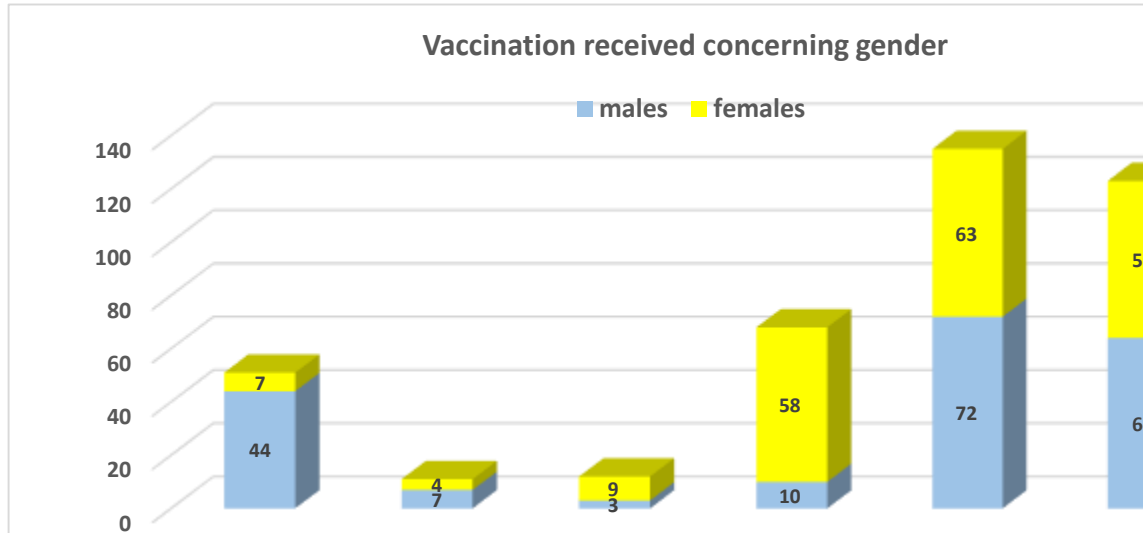

Fig.1. Vaccination received concerning gender

Table 3. The type of vaccination received concerning gender

Vaccination received	Male		Female	
	No	%	No	%
AstraZeneca	44	22%	7	3.5%
Janssen	7	3.5%	4	2%
Moderna	3	1.5%	9	4.5%
Pfizer	10	5%	58	29%
Sinopharm	72	36%	63	31.5%
Sinovac	64	32%	59	29.5%
Total	200	50%	200	50%

A 32(63%) of subject received the 1st dose of AstraZeneca vaccine and 19(37%) received the 2nd dose, 11(100%) received the 1st dose of Janssen vaccine, 12(100%) received the 1st dose of Moderna vaccine, 35(51%) of received the 1st dose of Pfizer vaccine, and 33(49%) received the 2nd dose, 73(54%) of received the 1st dose of Sinopharm vaccine and 62(46%) was the 2nd dose and 59(48%) of received the 1st dose of Sinovac vaccine and 64(52%) received the 2nd dose, **(Table. 4)**.

Table 4. The type of vaccination concerning the number of doses received

Vaccination received	Total No	1st dose		2nd dose	
		No	%	No	%
AstraZeneca	51	32	63%	19	37%
Janssen	11	11	100%	0	0%
Moderna	12	12	100%	0	0%
Pfizer	68	35	51%	33	49%
Sinovac	123	59	48%	64	52%
Sinopharm	135	73	54%	62	46%

There was an insignificant difference in all types of vaccinations concerning the mean D-dimer value. **(Table. 5)**, PT, **(Table. 6)** INR value, **(Table. 7),** PTT, **(Table. 8),** and platelet count **(Table. 9)**.

Table 5. D-dimer level concerning the type of vaccinations received

Vaccinations received	D-dimer mg/l		
	Range	Mean ±SD	P value
AstraZeneca (no=51)	0.19-1	0.36±0.15	
Janssen (no=11)	0.19-0.55	0.38±0.14	
Moderna (no=12)	0.19-0.5	0.34±0.09	
Pfizer (no=68)	0.19-0.57	0.33±0.11	0.7
Sinopharm (no=135)	0.19-1	0.34±0.13	
Sinovac (no=123)	0.19-1	0.36±0.13	

One way ANOVA

Table 6. PT time concerning the type of vaccinations received

Vaccinations received	PT sec		
	Range	Mean ±SD	P value
AstraZeneca (no=51)	12.1-14.8	13.02±0.47	
Janssen (no=11)	12.1-13.2	12.8±0.39	
Moderna (no=12)	12-13.4	12.73±0.49	
Pfizer (no=68)	12-15.6	12.93±0.52	0.319
Sinopharm (no=135)	12-16.8	13.09±0.82	
Sinovac (no=123)	12-16.7	13.04±0.74	

One way ANOVA

Table 7. INR concerning the type of vaccinations received

Vaccinations received	INR		
	Range	Mean ±SD	P value
AstraZeneca (no=51)	1-1.3	1.04±0.08	0.159

Janssen (no=11)	1-1.2	1.03±0.06	
Moderna (no=12)	1-1.3	1.03±0.09	
Pfizer (no=68)	1-1.4	1.04±0.07	
Sinopharm (no=135)	1-1.7	1.07±0.13	
Sinovac (no=123)	1-1.8	1.07±0.13	

One way ANOVA

Table 8. PTT time concerning the type of vaccinations received

Vaccinations received	PTT sec		
	Range	**Mean ±SD**	**P value**
AstraZeneca (no=51)	25.5-39	29.98±3.02	
Janssen (no=11)	26.7-33.8	30.07±2.40	
Moderna (no=12)	25.9-35.7	30.04±3.34	0.298
Pfizer (no=68)	24.3-39	29.26±3.16	
Sinopharm (no=135)	24-38	30.15±3.50	
Sinovac (no=123)	24.4-50	30.54±3.76	

One way ANOVA

Table 9. Platelet count concerning the type of vaccinations received

Vaccinations received	Platelet count x 10^3/mm3		
	Range	**Mean ±SD**	**P value**
AstraZeneca (no=51)	122-650	283.1±95.2	
Janssen (no=11)	167-377	256.73±60.25	
Moderna (no=12)	130-370	253.17±84.51	0.229
Pfizer (no=68)	93-484	265.12±84.86	
Sinopharm (no=135)	100-656	284.94±101.8	
Sinovac (no=123)	29-787	288.04±100.98	

One way ANOVA

Discussion

Vaccination is one of the most practical ways to stop the epidemic and protect against its effects. Although herd immunity within the population, often achieved through infection or vaccination, needs to be established to halt the COVID-19 pandemic. Vaccine development initiatives targeting SARS-CoV-2 have been initiated by some academic as well as commercial institutes and firms. Although public opinion and acceptance of vaccines play crucial roles (**Jackson et al., 2020**).

In our study, the ages of the participants varied from 18 to 95 years, with a mean age of 39.75 ±13.56 years. Two hundred men and two hundred women were investigated after vaccination, however in the study of **Baden et al., 2021,** the average age of the participants was 51.4, 24.8% were 65 or older, and 16.7% were younger than 65.47.3% of the participants were female. The study by **Adejumo et al., 2021** included

1,470 people. Around 38.2 percent of the cases were between 31 and 40 years old, with an average age of 40±6 years.

In this study, vaccinations received showed that 51 (12.8%) of subjects received AstraZeneca vaccine, 11 (2.8%) received Janssen vaccine, 12 (3%) received Moderna vaccine, 68 (17%) received Pfizer vaccine, 135 (33.8%) received Sinopharm vaccine, and 123 (30.8%) received Sinovac vaccine. 44(22.0%) males and 7(3.5%) females received AstraZeneca vaccine, 7(3.5%) males and 4(2.0%) females received Janssen vaccine, 3(1.5%) males and 9(4.5%) females received Moderna vaccine, 10(5.0%) males and 58(29.0%) females received Pfizer vaccine, 72(36.0%) males and 63(31.5%) females received Sinopharm vaccine and 64(32.0%) males and 59(29.5%) females received Sinovac vaccine. The range of the vaccination time was 5th -29th days and its mean was 14.54±4.97.

In the study of **Chung et al., 2021,** by the index date, 77% of (PfizerBioNTech) and 76% of–Moderna (mRNA-1273) had taken one dosage. Vaccinated persons were older, less likely to be male, and more likely to have had several SARS-CoV-2 tests three months before the immunization program, comorbidities, and an influenza vaccine. Users of the (PfizerBioNTech) vaccination were younger and more likely to be female in comparison to Moderna (mRNA-1273) vaccine users.

In this study, the mean platelets count was 229-487 $x10^3$/mm^3 with a range of 280.56±96.62 $x10^3$/mm^3, PT ranged between 12-16.8 sec with a mean value of 13.02±0.7 sec, PTT ranged between 24-50 sec with a mean value of 30.09±3.45 sec. D-dimer ranged between 0.19-4 mg/l with a mean value of 0.35±013 mg/l. Our findings indicated that in all types of vaccinations, there were no differences concerning D-dimer, PT, INR, PTT, and platelet count.

Our outcomes were in line with the finding by **Uaprasert et al., 2021,** in their meta-analysis, they reported 8 randomized controlled trials (RCTs) involving 195,196 people who used 4 different vaccination platforms including 2 mRNA vaccines (BNT162b2 and mRNA-1273), 3 adenoviral vector vaccines (Ad26.COV.2S, ChAdOx1 and rAD26/rAD5), 1 inactivated vaccine (2 studies of CoronaVac) and 1 protein subunit vaccine (NVX-CoV23). Risks of thromboembolism (risk ratio [RR], 1.14; 95% CI [confidence interval], 0.61-2.14; I2 = 35%), hemorrhage (RR, 0.97; 95% CI, 0.35-2.68; I2 = 0), and mortality from thromboembolism/hemorrhage were all similar after receiving a SARS-CoV-2 vaccination. Risk changes with vaccinations were extremely minor and not substantially different contrasted with the baseline estimated risk of these events in those given placebos. These results were true across all four vaccine delivery systems in the subgroup study.

However, in the study by **Hippisley-Cox et al., 2021,** There was a greater likelihood of thrombocytopenia 8-14 days and 22-28 days after administering the Oxford-AstraZeneca vaccine, correspondingly (incidence rate ratio 1.33, 95% CI 1.19 to 1.47 and 1.26, 1.13 to 1.44). This was because there was a higher chance of thrombocytopenia. In addition, a positive SARS-CoV-2 test was connected with a higher risk (1-7 days: 14.04, 12.08 to 16.31; 8-14 days: 5.27, 4.34 to 6.40; 15-21 days: 1.91, 1.44 to 2.54; 22-28 days: 1.50, 1.10 to 2.05). A greater chance of venous thromboembolism was detected at eight to fourteen days following a positive SARS-CoV-2 test (1-7 days: 13.78, 12.66 to 14.99; 8-14 days: 13.86, 12.76 to 15.05; 15-21 days: 7.88, 7.18 to 8.64; 22-28 days: 3.38, 3.00 to 3.81) or after administering the Oxford-AstraZeneca vaccine.

According to the study by **Ceschia et al., 2021**, 2 weeks after receiving of Oxford-AstraZeneca vaccine the patient had thrombocytopenia (nadir value $20 \times 1000/mm^3$ with normal value $130–400 \times 1000/mm^3$) and elevated D-dimer concentrations (32,559 μg/ifEU with normal value < 500 μg/ifEU), considering the high clinical probability of pulmonary embolism (PE).

While in the study of **Ostrowski et al., 2021**, the study included 80 participants recently vaccinated (median of 11 days (range 8-16) post-vaccination) with either AZ (n=55, Oxford/AstraZenica [AZD1222/ChAdOx1]) or mRNA (n=25 in total: n=16 Pfizer/BioNTech [BNT162b2] and n=9 Moderna [mRNA-1273]) vaccines. Pre-vaccination samples were available from all participants, as they were participants in the ENFORCE study. and 25 non-vaccinated age- and gender matched healthy controls. The main findings where that both vaccines enhanced inflammation and platelet activation, though Oxford/ AstraZeneca vaccination induced a more pronounced increase in several inflammatory and platelet activation markers compared to mRNA vaccination and that post-vaccination thrombin generation was higher following AZ vaccination compared to mRNA vaccination. No difference in neither the PF4 antibody level nor the proportion of individuals with positive PF4 antibodies were observed between the vaccine groups.

Greinacher and colleagues reported on 11 patients who presented 5 to 16 days after AZ vaccination with multiple thromboses and thrombocytopenia. Nine of the patients had cerebral venous sinus thrombosis (CVST), 3 had splanchnic vein thrombosis, three had pulmonary embolism, and other types of thrombosis were detected in 4 patients. In one patient who died from cerebral bleeding, CVST could not be excluded. Using an ELISA assay, the authors showed that the patients had circulating antibodies against PF4-heparin and also that there was platelet activation which could be inhibited by immune globulin providing support for a proposed treatment for autoimmune heparin-induced thrombocytopenia, and it also inhibited platelet activation (**Greinacher et al., 2021).**

Our findings were in agreement with the findings reported in the trial of **Scully et al., 2021,** Consistent with the sporadic character of this condition, Vaccination against SARS-CoV-2 does not appear to raise the risk of thrombocytopenia or venous thromboembolism beyond what is seen in the general population.

The current study has got some limitations. The study only involved one location. There was also the absence of a healthy, unvaccinated control group. Finally, we did not do a functional, platelet-activation experiment to clarify the platelet-activating potential of anti-PF4 antibodies in participants who tested positive or strongly positive with the ELISA immunologic testing.

Conclusion

Preventing the COVID-19 pandemic will depend heavily on the success of the SARS-CoV-2 vaccination program. There is no variation in all types of vaccinations concerning D-dimer, PT, INR, PTT, and platelet count. The different types of SARS-CoV-2 vaccines given don't increase thrombocytopenia or venous thromboembolism risk.

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