

## Cutaneous Reaction SARS-CoV-2 Vaccination: A Cross-Sectional Study

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### ABSTRACT

**Background:** Following the COVID-19 virus pandemic, the globe has begun immunization programmers using a variety of vaccines. **Objective:** Our study aimed to recognize dermatological responses emerging in response to the COVID-19 vaccines delivered in Egypt and to ascertain their clinical characteristics and potential contributing variables.

**Materials and method:** Individuals over the age of 18 who experienced dermatological reactions after receiving the COVID-19 vaccine were included in the study between December 2021 and December 2022. The evaluation used an electronic survey on Google forms that were created by the research team and had its validity and reliability evaluated by five dermatology-specific doctors. A routine survey that questioned questions about age, gender, place of residence, smoking, medical history, allergy, number of doses and when cutaneous reactions started after immunization. According to the severity of the symptoms following the vaccination, dermatological reactions were grouped.

**Result:** The study comprised a total of 1000 patients, of which 413 men (41.3%) and 587 women (58.7%). It was found that COVID arm (25.2%), pityriasis rosea (13.6%), vasculitis (11.4%), and lichen planus (9.2%) were the dermatological conditions and reactions that arose most commonly following immunization. After delivery of the vaccine, the rate of dermatological reactions was 63.8% (with 41.6% reported mild symptoms, 15.6% reported moderate symptoms, and 6.6% reported severe symptoms). The patients who received the immunizations experienced a statistically significantly increased number of responses ( $p = 0.001$ ).

**Conclusion:** The most common reactions in our sample were COVID arm, pityriasis rosea, and Vasculitis.

**Keywords:** COVID, Vaccination, Skin manifestations.

### INTRODUCTION

In December 2019, a huge number of inexplicable and fatal pneumonia cases emerged in Wuhan. The SARS-CoV-2 virus, which was identified from the lower respiratory tracts of infected patients, is the culprit that causes the sickness known as coronavirus disease. The COVID-19 pandemic led to a global effort to develop vaccines to protect against the disease. While these vaccines have been shown to be highly effective, they can also cause a range of side effects, including cutaneous manifestations. Cutaneous manifestations are skin reactions that can occur after receiving the COVID-19 vaccine. These reactions ranged from mild to severe and presented in various forms, including rashes, hives, and blisters. In some cases, these reactions were a sign of an allergic reaction to the vaccine, although they can also occur in individuals without a history of allergies. While, cutaneous manifestations after COVID-19 vaccination can be concerning, it's important to note that they are generally mild and resolve on their own within a few days. This topic has garnered significant interest among healthcare professionals, researchers, and the general public, as understanding the nature and prevalence of these cutaneous reactions is crucial to ensuring the safety and efficacy of COVID-19 vaccination programs<sup>(1)</sup>. The most common cutaneous manifestations after COVID-19 vaccination are erythema (redness), swelling, and pain at the injection site. These symptoms typically occur within a few

hours to a few days after vaccination and are usually mild to moderate in severity. Other common cutaneous manifestations include itching, warmth, and induration (hardening) at the injection site. In addition, to local reactions at the injection site, some individuals may experience rashes or hives on other parts of the body after COVID-19 vaccination. These reactions can occur anywhere from a few days to a few weeks after vaccination and may be accompanied by other symptoms such as fever, fatigue, and muscle aches<sup>(2)</sup>. The aim of this study was to identify the cutaneous reactions brought on by the COVID-19 vaccines given in Egypt, their initiation, clinical characteristics, and risk factors that can contribute to their occurrence.

### MATERIALS AND METHOD

**Setting:** A cross-sectional survey was conducted to determine the prevalence and contributing variables about skin reaction after COVID-19 vaccine among university students at Misr University for Science and Technology (MUST). The study was carried out in Egypt between December 2021 and December 2022, during the COVID-19 Pandemic.

**Participant's selection:** Data were gathered using an online self-administered survey form. Students at universities were given access to the poll through a variety of social media channels, including Facebook, WhatsApp, and Twitter. Participants between the ages of 18 and < 65 were included. 1000 responses made up

the computed sample size. 58.7% are females and 41.3% are men.

**Inclusion criteria:** Rural and urban. Both sexes. All nationalities. Age group: 18 to < 65 years. +ve medical history or not.

**Exclusion criteria:** Age < 18 or > 65 years. Subjects who have severe allergy to any types of foods or medicines. Individuals who didn't take the vaccine.

**Twenty multiple-choice questions were included in the survey, and they were organised into four main categories as follows:** (1) Demographic information, such as place of residence, age, gender, and profession. (2) Information about medical history, smoking or not and any allergy of food or medication. (3) Vaccination history about if infected with COVID-19 before vaccination, type of COVID-19 vaccines have been received such as (AstraZeneca/Oxford, Moderna, Sinovac, Sinopharm, Johnson & Johnson, and Pfizer-BioNTech), and Number of doses have been received. (4) Symptoms after vaccination among studied sample, any noticed symptoms following vaccination (mild, moderate, severe, pain & swelling at site of injection, any noticed bruises on the body, irritation and allergic skin reactions), time to symptoms appearance after injection with a COVID-19 vaccine, duration of symptoms with hours, days, months or years, symptoms picture such as (COVID arm, CLL, herpes zoster, vasculitis, pityriasis rosea).

**Ethical approval:** The Ethics Committee of Misr University for Science and Technology has authorized this work. After receiving all of the information, each student signed his consent. The Helsinki Declaration was followed throughout the course of the investigation.

**Statistical analysis**

The statistical programme for social sciences (SPSS), version 26.0, was used to accomplish these computations. Quantitative data were given as a number and a percentage, whereas qualitative data were expressed as a percentage and number. Quantitative data were evaluated for normality using the Kolmogorov-Smirnov test before being described using the mean and standard deviation for normally distributed data and the median and range for non-normally distributed data. With the proposed tests listed below, the appropriate statistical test was applied based on the kind of data: Spearman or Chi square for categorical variables and continuous variables were correlated using Pearson correlation. At the start of the survey, permission was gained once the study's goals were stated. Chi-square was utilised in the study, measures of central tendency were used to determine the continuous variables, and categorical variables were calculated using frequencies and percentages. P-values ≤ 0.05 were regarded as statistically significant.

**RESULTS**

Table (1) showed that there were 47.9% aged from 18-23 years, 12.5% from 24 to 29 years, 8.6% from 42 to 47 years, and 58.7% were females and 91.6% were urban residence. Also, 18.2% had positive medical history, 15.2% were smokers and 22.6% had allergy to food & drugs.

**Table (1):** Sociodemographic characteristics of the studied sample

		n=1000	%
<b>Age/years</b>	18-23	479	47.9
	24-29	125	12.5
	30-35	72	7.2
	36-41	84	8.4
	42-47	86	8.6
	48-53	75	7.5
	54-59	48	4.8
	60-65	21	2.1
	> 65	10	1.0
<b>Sex</b>	Male	413	41.3
	Female	587	58.7
<b>Residence</b>	Rural	84	8.4
	Urban	916	91.6
<b>Medical history</b>	-ve	818	81.8
	+ve	182	18.2
<b>Smoking</b>	No	848	84.8
	Yes	152	15.2
<b>Allergy to any types of foods or medicines</b>	No	597	59.7
	Yes	226	22.6
	Don't know	177	17.7

Table (2) demonstrated that 34.4% have been infected with COVID-19 before vaccination. Among studied cases; 27.6% were Pfizer-BioNTech, 26.7% were AstraZeneca/Oxford, 24.5% were Sinopharm, 19.9% were Sinovac, 8.1% were Johnson & Johnson and 3.2% received Moderna. As regards number of doses; 62.2% received 2 doses, 22.4% three doses and 15.4% one dose.

**Table (2):** Vaccination history among studied cases

		n=1000	%
<b>Infected with COVID-19 before vaccination</b>	No	486	48.6
	Yes	344	34.4
	Maybe	170	17.0
<b>Type of COVID-19 vaccines have been received</b>	AstraZeneca/Oxford	267	26.7
	Moderna	32	3.2
	Sinovac	199	19.9
	Sinopharm	245	24.5
	Johnson & Johnson	81	8.1
	Pfizer-BioNTech,	276	27.6
<b>Number of doses have been received</b>	One dose	154	15.4
	Two doses	622	62.2
	Three doses	224	22.4

Table (3) showed that 63.8% had symptoms (41.6% had mild symptoms, 15.6% had moderate symptoms and 6.6% had severe symptoms); 81.3% of them had pain & swelling at site of injection, 11.1% bruises and 15% irritation & skin allergy. Among cases with symptoms after vaccination; 47% appeared from 5 to 8 hours, 22.7% from 9 to 12 hours, 17.9% from 12 to 24 hours, 5% from 24 to 48 hours, 4.5% days after and

2.8% weeks after injection. Symptoms lasted for days among 59.7%, 37.3% lasted for hours and 2.5% for months. Symptoms' pictures were detected as follows; 25.2% COVID arm, 13.6% pityriasis rosea, 11.4% vasculitis, 9.2% lichen planus and 8.6% erythema multiform. Among studied sample; 11.1% try to treat the reaction.

**Table (3):** Symptoms after vaccination among studied sample

	n=1000	%
<b>Noticed any symptoms following vaccination</b>		
No	362	36.2
Mild symptoms	416	41.6
Moderate	156	15.6
Severe	66	6.6
	n=638	
Pain & swelling at site of injection	519	81.3
Noticed any bruises on your body	71	11.1
Irritation and allergic skin reactions, or itchy skin	96	15.0
<b>Time to symptoms appear after injection with a COVID-19 vaccine</b>		
5-8h	300	47.0
9-12h	145	22.7
12-24	114	17.9
24-48	32	5.0
Days after	29	4.5
Weeks after	18	2.8
<b>Duration of symptoms</b>		
Hours	238	37.3
Days	381	59.7
Months	16	2.5
Year or more	3	0.5
<b>Symptoms picture</b>		
COVID arm	161	25.2
CLL	7	1.1
Purpuric reaction	19	3.0
Herpes Zoster	12	1.9
Rowell syndrome	4	0.6
Erythema multiforms	55	8.6
Lichen planus	59	9.2
Vasculitis	73	11.4
Pityriasis rosea	87	13.6
<b>Try to treat reaction</b>		
No	567	88.9
Yes	71	11.1

Table (4) demonstrated a statistically significant relation between symptoms after vaccination and the following; allergy to any types of foods or medicines, type of COVID-19 vaccines have been received and number of doses of vaccine received. A higher frequency of severe symptoms is detected among studied sample with no allergy, those with positive history of infection with COVID-19 before vaccination, more also with AstraZeneca/Oxford and Pfizer-BioNTech. More severe reaction occurs with two doses of vaccine, three doses and one dose of vaccine, respectively.

**Table (4):** Relation between symptoms after vaccination and covid-19 vaccine characters

	Symptoms after vaccination				Test of significance
	No n=362(%)	Mild n=416(%)	Moderate n=156(%)	Severe n=17(%)	
<b>Allergy to any types of foods or medicines</b>					
No	244(79.5)	236(69.8)	88(68.2)	29(59.2)	$\chi^2=14.27$ p=0.003*
Yes	63(20.5)	102(30.2)	41(31.8)	20(40.8)	
<b>infected with COVID-19 before vaccination</b>					
No	212(58.6)	187(45)	63(40.4)	24(36.4)	$\chi^2=27.68$ p<0.001*
Yes	94(26.0)	153(36.8)	66(42.3)	31(47.0)	
May be	56(15.5)	76(18.3)	27(17.3)	11(16.7)	
<b>Type of COVID-19 vaccines have been received</b>					
AstraZeneca/Oxford					$\chi^2=64.73, p<0.001^*$ $\chi^{2MC}=14.21, p=0.003^*$ $\chi^2=47.45, p<0.001^*$ $\chi^2=30.66, p<0.001^*$ $\chi^2=1.79, p=0.617$ $\chi^2=37.27, p<0.001^*$
Moderna	47(13.0)	131(31.5)	56(35.9)	33(50.0)	
Sinovac	4(1.1)	18(4.3)	10(6.4)	0	
Sinopharm	105(29)	81(19.5)	12(7.7)	1(1.5)	
Johnson & Johnson	120(33.1)	91(21.9)	30(19.2)	4(6.1)	
Pfizer-BioNTech	24(6.6)	36(8.7)	15(9.6)	6(9.1)	
	81(22.4)	98(23.6)	67(42.9)	30(45.5)	
<b>Number of doses have been received</b>					
One dose	50(13.8)	73(17.5)	16(10.3)	15(22.7)	$\chi^2=16.65, p=0.01^*$
Two doses	246(68)	247(59.4)	95(60.9)	34(51.5)	
Three doses	66(18.2)	96(23.1)	45(28.8)	17(25.8)	

$\chi^2$ : Chi-Square test, \*statistically significant, MC: Monte Carlo test.

## DISCUSSION

It has been noticed that urticaria, pain, swelling, itching, bruises and skin changes can happen at injection site on studying cutaneous manifestations after Covid-19 vaccines. In this study, patients mostly developed pain and swelling at injection site (n: 519, 81.3%), irritation and allergic skin reactions (n: 96, 15%) and bruises (n: 71, 11.1%) to a lesser degree. The time for symptoms to appear was disparate between the patients. For most patients it took 5 to 8 hours for the symptoms to appear (n: 300, 47%) and for few patients (n: 18, 2.8%) the symptoms appeared weeks after vaccination.

The COVID arm as called by the centers for disease control and prevention (CDC) is a delayed skin reaction that appears in large number of patients few days after the first dose of the vaccine and in much fewer number of patients after the second dose of the vaccine. It appears as red itchy or painful indurated plaque. The incidence of covid arm is reported to be higher among those who received the mRNA vaccines (Pfizer-BioNTech and Moderna) compared to those who received the viral vector vaccine (Johnson & Johnson). This is likely due to differences in the way the two types of vaccines work. The mRNA vaccines work by using a small piece of genetic material from the virus to instruct cells in the body to produce a protein found on the surface of the virus. This protein then triggers an immune response, which helps the body recognize and fight the virus in the future. The

immune response to the mRNA vaccines may be stronger and more localized, which could explain why covid arm is more common with these vaccines<sup>(3-5)</sup>.

In contrast, the viral vector vaccine works by using a harmless virus to deliver genetic material from the COVID-19 virus into cells in the body. This genetic material then instructs cells to produce the same protein found on the surface of the virus, triggering an immune response. The immune response to the viral vector vaccine may be more widespread throughout the body, which could explain why covid arm is less common with this vaccine. Also, it was reported in a Spanish cross-sectional study that COVID arm was reported more in females than in males. One possible explanation for this gender difference is that females tend to have a more robust immune response to vaccines than males. This is believed to be due to hormonal differences between males and females, as well as genetic and environmental factors<sup>(5-7)</sup>. Additionally, some studies have suggested that females may be more likely to report vaccine side effects than males, which could contribute to the perception that Covid arm is more common among females. In our study between all the symptoms that were reported after receiving the vaccine, COVID arm was the most common symptom (n:161, 25,2%). It usually did not interfere with receiving the next dose of the vaccine and patients are encouraged to do so. Most time COVID arm did not require treatment and it resolves spontaneously. If

needed topical glucocorticoids or an oral antihistaminic may be prescribed<sup>(8-10)</sup>.

According to a Spanish cross sectional study varicella zoster virus (VZV) reactivation (herpes zoster) was mostly reported in patients after receiving BNT162b2 (Pfizer/BioNTech) vaccine and it was reported more in males than in females. One case report published in the Journal of the European Academy of Dermatology and Venereology in July 2021 described a case of herpes zoster (shingles) occurring in a male patient after receiving the Pfizer-BioNTech COVID-19 vaccine. However, this is just a single case report and does not provide evidence of gender differences in the incidence of VZV reactivation after COVID-19 vaccination. In our study it was reported that 12 (1.9%) of the patients noted VZV reactivation. A fewer number of patients reported herpes simplex virus (HSV) reactivation and that is mostly because HSV patients do not usually seek medical advice<sup>(11-13)</sup>.

A purpuric reaction was reported mostly after the BNT162b2 (Pfizer/BioNTech) and AZD1222 (AstraZeneca) vaccines, and about 19 patient (3%) had it. The exact cause of purpuric reactions after COVID-19 vaccination is not yet fully understood. However, it is believed to be an immune-mediated response to the vaccine components, specifically the spike protein of the SARS-CoV-2 virus. In some cases, the purpuric reactions have been associated with thrombocytopenia<sup>(14)</sup>.

A Pityriasis rosea like rash was the second most common skin reaction in our study it was reported in about 87 (13.6%) patients. In a Turkish study, 12 patients (4.5%) experienced it. It is mostly due to human herpes virus (HHV) 6 & 7 reactivation. It could also be attributed to SARS CoV 2 infection or due to other vaccines such as hepatitis B or influenza vaccines. Reports of pityriasis rosea occurring after COVID-19 vaccination, particularly after the second dose of the Pfizer-BioNTech vaccine. The exact cause of this reaction is not yet fully understood, but it is believed to be an immune-mediated response to the vaccine. One theory is that the vaccine may trigger an immune response that leads to the development of pityriasis rosea in individuals who are genetically predisposed to the condition. Another theory is that the rash may be a result of a viral infection or reactivation of a latent virus, such as human herpes virus 6 (HHV-6), which has been associated with pityriasis rosea<sup>(2, 15)</sup>.

Vasculitis was reported in 73 (11.4%) patients in our study while in another Turkish study 3.7% of the patients reported vasculitis one of them was urticarial vasculitis, while all the others were leukocytoclastic vasculitis. Leukocytoclastic vasculitis (LCV) is a type of skin inflammation that affects the small blood vessels, which can lead to the development of petechiae, purpura, and other skin lesions. Urticarial vasculitis (UV) is another type of

skin inflammation that affects the blood vessels and is characterized by the development of hives and other urticarial lesions. There have been reports of LCV occurring after COVID-19 vaccination, particularly after the Pfizer-BioNTech vaccine. The exact cause of LCV after COVID-19 vaccination is not yet fully understood, but it is believed to be an immune-mediated response to the vaccine. One theory is that the vaccine may trigger an immune response that leads to the development of LCV in individuals who are genetically predisposed to the condition. Another theory is that the rash may be a result of a viral infection or reactivation of a latent virus, such as herpes simplex virus or varicella-zoster virus. In contrast, UV has not been reported as frequently after COVID-19 vaccination. This may be due to differences in the immune response triggered by the vaccine, as well as differences in the genetic and environmental factors that contribute to the development of UV<sup>(2)</sup>.

There have been reports of individuals developing new allergies to food or medication after receiving the COVID-19 vaccine, but the exact cause of these reactions is not yet fully understood. It is possible that the immune response triggered by the vaccine may cause changes in the immune system that lead to the development of new allergies. For example, the vaccine may cause the immune system to become more reactive to certain allergens, or to produce antibodies that cross-react with allergens in food or medication. However, it is important to note that most individuals who receive the vaccine do not experience any allergic reactions<sup>(3)</sup>.

In our study, cutaneous side effects were observed in 27.6% of the study group who received Pfizer-BioNTech vaccine, 26.7 % in who received AstraZeneca/Oxford vaccine, followed by 24.5% in who received Sinopharm vaccine and 19.9% in who received Sinovac vaccine. The least cutaneous manifestations occurred with persons who had been administered Johnson & Johnson vaccine (8.1%) and Moderna vaccine (3.2%).

It was noted that most of the cutaneous reactions after COVID vaccines were mild requiring no treatment. Patients with mild or moderate symptoms should be encouraged to receive the second dose and, in some cases, prophylactic treatment such as antihistaminic or glucocorticoids may be given. In cases with moderate or severe reactions using a different type of the vaccine for the second dose may be of benefit for the patient. In a few severe cases with severe hypersensitivity reactions (such as anaphylaxis which is very rare), receiving of the second dose may be contraindicated.

## CONCLUSION

This study highlighted the various cutaneous manifestations that can occur after receiving COVID-19 vaccines. While, most patients experience mild

symptoms or no symptoms at all, some may experience moderate to severe reactions such as COVID arm, VZV reactivation, purpuric reaction, vasculitis, and pityriasis rosea like rash. These reactions may occur at varying times after vaccination and can be more common with certain types of vaccines. Physicians should be aware of these potential side effects and develop appropriate treatment strategies. Most cutaneous reactions do not require treatment, and patients should be encouraged to receive their second dose of the vaccine. In rare cases of severe hypersensitivity reactions, receiving of the second dose may be contraindicated. Further studies are needed to better understand the incidence and clinical features of these cutaneous reactions.

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**Financial disclosures:** None.

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