Cutaneous adverse effects of COVID- 19 vaccines: A cross-sectional study among AstraZeneca and Sinovac vaccine recipients at UERMMMCI*

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Abstract

Introduction COVID-19 has emerged as a global problem with vaccines being established as one of the best tools in its control. Of particular interest in dermatology are risks and manifestations of cutaneous reactions from such countermeasures, with strides made in documenting and associating skin reactions with vaccines against COVID-19. This study aimed to determine the incidence of cutaneous adverse reactions in recipients of recombinant ChAdOx1-S and inactivated SARS-COV-2 vaccines among healthcare personnel and employees of UERMMMCI.

Methods A cross-sectional study was done were respondents, chosen through randomized stratified cluster sampling, were given a questionnaire to elicit cutaneous adverse effects associated with COVID-19 vaccines.

Results There were198 respondents, of which 29.3% were male and 70.7% were female, with a mean age of 26.07 years. Of these respondents, 72 (36.36%) received recombinant ChAdOx1-S and 126 (63.64%) received inactivated SARS-COV-2 vaccine. For the first dose, cutaneous reactions developed in 6 (8.33%) recipients of recombinant ChAdOx1-S, and 2 (1.59%) recipients of inactivated SARS-COV-2. For the second dose, no reactions followed vaccination with recombinant ChAdOx1-S while 4 (3.17%) reactions developed after inactivated SARS-COV-2 vaccination. Lesions were mostly confined to the injection site presenting with erythema for both vaccine types. One urticarial, widespread reaction was associated with a second dose of inactivated SARS-COV-2 vaccine.

Conclusions Adverse reactions to COVID-19 vaccinations have been documented which may be attributed to respective excipients rather than vaccine antigens. Due to the rare occurrence of severe anaphylactic reactions, vaccine use is recommended as they confer protection even to those with prior infections. Documented reactions in this study were observed to be mild and self- limiting similar to larger studies.

Key words: vaccine, drug reaction, COVID-19, pandemic

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The coronavirus disease 2019 (COVID-19) with the causative agent of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a global problem. The impact of the aforementioned disease was significant enough for the World Health Organization (WHO) to declare it as a global pandemic

as of March 11, 2020.[1] Upon acquiring the infection, cases may drastically range from asymptomatic presentations to those that become critically ill with severe respiratory distress, lung infection, and even death. As such, protective behaviors become key to improving the circumstances.[2] The use of vaccines has been established as one of the best tools in public health in infectious disease cases where no absolutely effective treatments have been found. The same rings especially true in cases of global pandemics.[1]

Of particular interest in the field of dermatology are the risk and manifestation of cutaneous reactions from such countermeasures. Strides have been made in documenting and associating certain skin reactions with vaccines against Covid-19 infections. Specifically, the mRNA-1273 vaccine against SARS-CoV-2 being developed by Moderna has been observed to cause both immediate (84.2%) and delayed (0.8%) cutaneous reactions in a study of 30,402 participants.[3] A case series from phase III efficacy trials has also shown that the extent of these manifestations can range from localized erythema and swelling, termed as "Covid arm", to larger and more generalized erythrodermic and urticarial reactions after being administered with the same vaccine.[4] Specifically, as well, no studies have yet been done on cutaneous reactions to the abovementioned vaccine brands Sinovac, Moderna, and AstraZeneca.

In particular interest to dermatologists is the onset of cutaneous manifestations of these reactogenic occurrences. Presently, there is a lack of studies exploring the various dermatologic sequelae in patients receiving these vaccines in the Philippine setting. Results of this study can help promote better understanding on how to better manage the expectations for both those administering and receiving this crucial vaccine during this time of a pandemic. Hence, this study aimed to determine the incidence and prevalence of cutaneous adverse reactions in recipients of AstraZeneca and Sinovac vaccines among healthcare personnel and employees of UERMMMCI.

Methods

Study design and subject selection

This cross- sectional study determined the prevalence of cutaneous manifestations in recipients of AstraZeneca and Sinovac vaccination among healthcare workers and employees in the UERM community. The research protocol was approved by the UERMMMCI Ethics Review Committee.

A minimum of 192 patients were needed to determine the proportion patients who had adverse cutaneous reactions to COVID-19 vaccines, based on the assumption that 52% of all who receive COVID vaccinations present with adverse cutaneous reactions, as per the study of McMahon et al. (2021).[5] This was computed with a precision of + 0.10 and at 5% alpha level of significance.

Descriptive statistics were used to summarize the general and clinical characteristics of the study participants. Missing data were neither replaced nor estimated. STATA 15.0 was used for data analysis.

Results

A total of 206 respondents agreed to participate in this study. Eight (8) of them have received a different brand of COVID-19 vaccine and were excluded from this study. Of the remaining 198 participants, majority were aged between 20-29 years old (93.9%). Mean age was 26 years. There were 56 (28.2%) males, and 142 (71.7%) females. Seventy (35.4%) of the respondents received the AstraZeneca brand while 128 (64.6%) received the Sinovac brand of vaccination for both 1st and 2nd doses of vaccination (Table 1). Brands were not mixed as per protocol for consequent doses. Out of 198 respondents, the first dose of vaccination yielded a total of 8 cutaneous reactions.

Table 1. Demographic data of respondents.

	n	Frequency (%)
Age (in years)		
20-29	186	93.9%
30-39	11	5.6%
40-49	1	0.5%
Sex		
Male	56	28.2%
Female	142	71.7%
Brand of Vaccine Received		
AstraZeneca	70	35.4%
Sinovac	128	64.6%

From this total, 6 (75%) were documented with AstraZeneca while 2 (25%) were seen with Sinovac. Comparing recipients with non-reactions, 6 (8.57%) and 2 (1.56%) were noted to develop cutaneous manifestations with AstraZeneca and Sinovac, respectively. For the first dose (Table 2), reactions were characterized according to extent, size, onset, and time of resolution. All reactions were seen to be localized to the injection site at this time with variation in size of 1-2 cm (50%) and >5cm (50%). Onset of symptoms to all was seen within 2-24 hours of vaccine administration while resolution ranged from less than 24 hours (25%), 2-24 hours (50%), and within 1 week (25%).

Table 2. Cutaneous manifestations after first COVID-19 vaccination..

	Astra Zeneca (n=6)	Sinovac (n=2)
Type of cutaneous reaction		
Localized to site of injection	6 (75%)	2 (25%)
Size		
1-2 cm	4 (50%)	2 (25%)
>5cm	2 (25%)	0
Onset		
Within 2-24 hours	6 (75%)	2 (25%)
Resolution		
<24 hours	2 (25%)	0
2-24 hours	2 (25%)	2 (25%)
Within 1 week	2 (25%)	0

The cutaneous manifestations were also characterized by a range of accompanying symptoms including redness, warmth, swelling, tenderness, and itching which were not mutually exclusive amongst each other. Prolonged redness after vaccine administration was noted to be the most common associated finding. No constitutional symptoms were recorded during the first dose of vaccination (Table 3).

The second dose of vaccination yielded a total of only 4 cutaneous reactions and were only seen with the Sinovac brand. Comparing recipients with non-reactions, 4 (3.16%) were noted to develop cutaneous manifestations with the aforementioned brand. For the second dose, reactions were characterized with the same parameters. Reactions were noted to mostly be

Table 3. Associated symptoms after first COVID-19 vaccination.

	Astra Zeneca (n=6)	Sinovac (n=2)
Type of associated symptoms		
Redness	6	1
Warmth	4	0
Swelling	4	0
Tenderness	4	0
Itchiness	0	2

localized to injection site (75%), however, one (25%) patient experienced urticarial lesions extending to distant sites of the body. Onset of symptoms were mostly seen within 2-24 hours (75%) of vaccine administration with the exception of the urticarial eruption occurring within 14- 30 days (25%) of vaccination. Resolution ranged from 2-24 hours (75%) and within 1 week (25%) since symptom onset (Table 4).

Table 4 Cutaneous manifestations after second COVID-19 vaccination.

	Astra Zeneca (n=0)	Sinovac (n=4)
Type of cutaneous reaction		
Localized to site of injection	0	3 (75%)
Urticarial	0	1 (25%)
Size		
1-2 cm	0	4 (100%)
Onset 0		
Within 2-24 hours	0	3 (75%)
	Astra Zeneca (n=0)	Sinovac (n=4)
Within 14-30 days	0	1 (25%)
Resolution		
2-24 hours	0	3 (75%)
Within 1 week	0	1 (25%)

The accompanying symptoms for the second dose was limited to redness, warmth, and itching only which were still not mutually exclusive among each other. Prolonged redness and itchiness were equally the most common associated finding. No constitutional symptoms were recorded during the second dose of vaccination (Table 5).

Table 5. Associated symptoms after seconds COVID-19 vaccination.

	Astra Zeneca (n=0)	Sinovac (n=4)
Type of associated symptoms		
Redness		4
Warmth		2
Itchiness		4

Over the course of 2 doses, a total of 140 injections for AstraZeneca and 256 for Sinovac were given. Cumulatively, administration of consequent doses for both brands of COVID-19 vaccines were tallied showing a recorded frequency of cutaneous manifestations of 4.29% for AstraZeneca and 2.34% for Sinovac (Table 6).

Table 6. Cumulative incidence for both doses of COVID-19 vaccination.

	Astra Zeneca (n=140)	Sinovac (n=256)
Presence of cutaneous reaction		
With cutaneous reaction	6 (4.29%)	6 (2.34%)
Without cutaneous reaction	134 (95.71%)	250 (97.66%)

Discussion

The study aimed to determine the prevalence of cutaneous manifestations in recipients of AstraZeneca and Sinovac vaccination among healthcare workers and employees in a tertiary hospital with ready access to the abovementioned vaccines. As of May 2021, more than 1.5 billion vaccine doses have been administered worldwide and especially in the background of an ongoing epidemic, any information that could be gleaned to better understand the safety profile of these drugs are of utmost importance.[6]

Nine out of the 12 (75%) of the study participants with cutaneous manifestations were females. From this data, 4 were recipients of AstraZeneca and 5 were recipients of Sinovac vaccines. This demographic was comparable with a study by McMahon et.al with 414 unique patients with cutaneous reactions showing 90% of them were also females.[5] In the same study, 63% of patients with cutaneous adverse effects developed their symptoms after the second dose. This was followed by the first dose and both doses in terms of frequency of eruption. Interestingly, the participants of this current study showed a split result in terms of the brand of vaccine. AstraZeneca showed a higher percentage (8.57%, n=70) of cutaneous adverse effects among recipients during the first dose while Sinovac exhibited the same observation (3.16%, n=128) during the second dose. An additional finding showed that 2 participants experienced cutaneous adverse effects during both doses of Sinovac.

The cutaneous manifestations post-COVID-19 vaccination have been noted to mostly be self-limiting and transient with the appearance of non-specific rashes such as macules, papules, and urticarial lesions. However, as seen in another study, these reactions could sometimes lead to more extensive diseases such as functional angiopathies and auto-immune mediated reactions, and reactivation of viral infections.[6] Other examples include pityriasis rosea-like rash[7], herpes zoster[8], and Stevens-Johnson syndrome.[9] The findings of this current study seemed to appear in line with these larger studies showing majority of symptomatic participants experienced nonspecific and self-limiting skin problems. The most extensive of them only included one episode of generalized urticarial rash without progression of more severe signs and symptoms. Constitutional symptoms such as fever, malaise, nausea, and difficulty of breathing were all absent in all participants, regardless of the appearance of cutaneous manifestations.

As per the findings of this study, most cutaneous vaccine reactions were noted to be immediate in onset. Type 1 or immunoglobulin E-mediated allergic reactions are not often caused by viral particles constituting these vaccines. Instead, they may be the due to the excipients added to these drugs that may have inadvertently caused these hypersensitivity reactions. Examples would include polysorbate 80 found in AstraZeneca and aluminum adjuvants found in Sinovac which are ideally inert but have been suspected to cause allergic reactions to their recipients.[10]

Lastly, in balancing the need for the protection conferred by these vaccines against the potential risk of cutaneous adverse effects, the current recommendation would still be to receive administration even if with prior mild to moderate reactions.[11] Correlating with the findings of the study, the observed frequency of developing evanescent symptoms for both AstraZeneca

(4.29%) and 2.34% for Sinovac (2.34%) were quite low enough to support this stance, especially during a pandemic.

Conclusion

Adverse reactions to COVID-19 vaccinations have been documented which may be attributed to respective excipients rather than vaccine antigens due to their onset and resolution. Documented reactions in this study were observed to be mild and self-limiting similar to larger studies. Due to the rare occurrence of severe reactions, vaccine use is recommended as they confer protection even to those with prior infections or with previous mild to moderate adverse effects upon vaccine administration particularly for healthcare workers in the setting of a pandemic.

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