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Cutaneous Manifestations of COVID-19 Vaccination and COVID-19 Infection: a Questionnaire-based, Multi-center Study in Korea

Ik Jun Moon[1*], Woo Jin Lee[1*], Hyun Chang Ko[2], Hyojin Kim[3], Chan Ho Na[4], Joonsoo Park[5], Jin Park[6], Hyun-Min Seo[7], Min Kyung Shin[8], Young Bok Lee[9], Yong Hyun Jang[10], Hye Jung Jung[11] and Yangwon Lee[12†]

[1]Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[2]Department of Dermatology, School of Medicine, Pusan National University, Busan, Korea
[3]Department of Dermatology, Inje University Busan Paik Hospital, Busan, Korea
[4]Department of Dermatology, Chosun University Hospital, Gwangju, Korea
[5]Department of Dermatology, Daegu Catholic University Hospital, Daegu, Korea
[6]Department of Dermatology, Jeonbuk National Univeristy Hospital, Jeonju, Korea
[7]Department of Dermatology, College of Medicine, Hanyang University, Seoul, Korea
[8]Department of Dermatology, College of Medicine, Kyung Hee University, Seoul, Korea
[9]Department of Dermatology, College of Medicine, The Catholic University of Korea, Seoul, Korea
[10]Department of Dermatology, School of Medicine, Kyungpook National University, Daegu, Korea
[11]Department of Dermatology, National Medical Center, Seoul, Korea
[12]Department of Dermatology, Konkuk University Medical Center, Seoul, Korea

Background: Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause various cutaneous complications, including dermatologic adverse reactions to SARS-CoV-2 vaccines reported by several studies.

Objective: To describe the clinical characteristics of cutaneous complications of SARS-CoV-2 infection and adverse reactions to SARS-CoV-2 vaccines, and to determine the risk factors for cutaneous manifestations.

Methods: A questionnaire-based survey in 12 hospitals in Korea.

Results: After receiving SARS-CoV-2 vaccinations, 20.23% and 5.94% of the respondents reported new-onset cutaneous lesions or aggravation of preexisting cutaneous conditions, respectively. Respondents who developed new cutaneous lesions after COVID-19 were significantly older than those who did not ($p = 0.001$). Systemic symptoms of SARS-CoV-2 vaccination (fever, chill, cough, sore throat, and myalgia) were associated with higher risk for new-onset cutaneous lesions ($p < 0.05$). Myalgia was the only systemic symptom of SARS-CoV-2 vaccination that was associated with higher risk for the aggravation of preexisting cutaneous conditions ($p = 0.011$). Following

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*These authors contributed equally as first authors.
†Corresponding: Yangwon Lee, Department of Dermatology, Konkuk University Medical Center, 120-1 Neungdong-ro, Gwangjin-gu, Seoul, 05030, Korea.
Phone: +82-2-2030-5172, Fax: +82-2-2030-5179, e-mail: 20050078@kuh.ac.kr

coronavirus 2019 (COVID-19) diagnosis, 13.3% and 9.7% of the respondents reported new skin lesions and aggravation of preexisting cutaneous conditions, respectively. Respondents with new cutaneous lesions were significantly older than those without new cutaneous lesions (p = 0.046). Systemic COVID-19 symptoms were significantly more common in respondents who developed new cutaneous lesions than in those who did not (p < 0.001). The proportion of respondents with underlying autoimmune diseases was significantly higher in those with cutaneous COVID-19 complications than in those without such complications (p = 0.038).

Conclusion: This study offers insights into the characteristics of cutaneous manifestations of SARS-CoV-2 vaccination and infection in Korea.

Key Words: Coronavirus disease 2019, Severe acute respiratory syndrome coronavirus 2, Skin disease, Skin eruption, Survey, Vaccination

INTRODUCTION

As of October 2023, nearly 45,000,000 Koreans received at least one vaccine dose against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and nearly 34,000,000 Koreans were diagnosed at least once with coronavirus disease 2019 (COVID-19)[1]. Although the global community rallied together to develop vaccines against SARS-CoV-2 following the emergence of the unprecedented COVID-19 pandemic, more than five million individuals across the globe died from the disease[2]. Furthermore, the urgent need for vaccines did not allow for a sufficient period of vaccine development, raising concerns regarding the efficacy and safety of the many newly developed vaccines and leading to vaccine refusal by some individuals. Nevertheless, concerted efforts by experts and government officials have led to the complete vaccination of a majority of the population, resulting in a subsiding trend in the COVID-19 pandemic.

Since the beginning of the global battle against the COVID-19 pandemic, numerous studies and case reports have documented the development of cutaneous reactions following SARS-CoV-2 vaccination or infection. Initial observations of cutaneous manifestations in vaccinated or infected patients have piqued the interest of researchers and clinicians alike. Previous studies have reported diverse dermatologic findings related to SARS-CoV-2 vaccination, including injection-site reactions, urticarial eruptions, papulosquamous eruptions, alopecia areata, and herpes zoster, among others[3-7]. The estimated incidence of cutaneous reactions following SARS-CoV-2 vaccination is 30%, albeit with a large variation among the studies[6]. Similarly, cutaneous manifestations of COVID-19 have been extensively documented, such as one study by Recalcati et al.[8], which identified various cutaneous lesions, including erythematous rash, vesicular eruptions, urticaria, and chilblain-like lesions, in afflicted individuals[9].

The majority of the large number of clinical studies elucidating the epidemiology of cutaneous manifestations of COVID-19 and those stemming from SARS-CoV-2 vaccination have been conducted in Western populations, and scholarly contributions originating from the Eastern Asian region are lacking from the current literature. The geographical imbalance in research output indicates a gap in our current understanding of the cutaneous reactions to SARS-CoV-2 infection and vaccination and highlights the need for the incorporation of the Eastern Asian perspective. Therefore, we conducted a questionnaire-based survey on the epidemiology and clinical characteristics of the cutaneous manifestations of SARS-CoV-2 infection and vaccination.

MATERIALS AND METHODS

1. Study design

This multicenter, questionnaire-based survey was performed in 12 university hospitals across the Republic of Korea as follows: Asan Medical Center, Uijeongbu St. Mary's Hospital, Kyung Hee University Hospital, Daegu Catholic University Hospital, Jeonbuk National University Hospital, Konkuk University Hospital, Kyungpook National University Hospital, Inje University Busan Paik Hospital, National Medical Center, Chosun University Hospital, Pusan National University Yangsan Hospital, and Hanyang University Guri Hospital. Approval was obtained from the Institutional Review Boards of all participating hospitals before the survey.

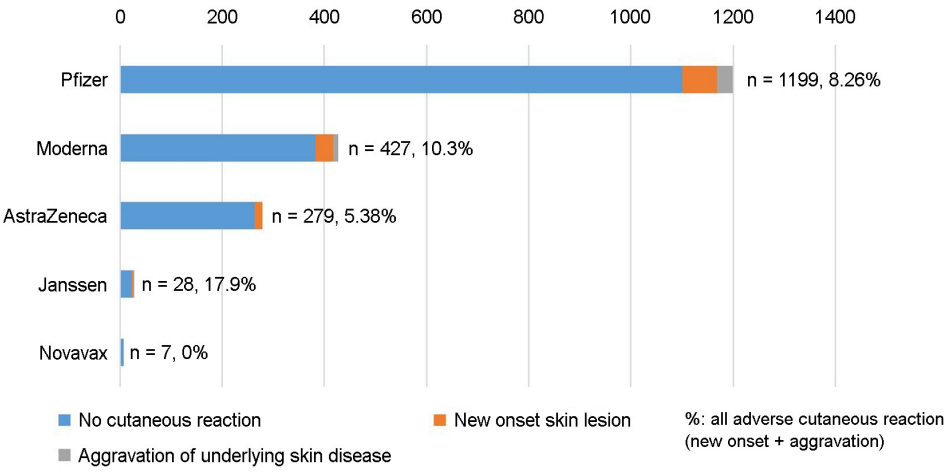

Fig. 1. Proportions of respondents who developed cutaneous reactions to specific SARS-CoV-2 vaccines

2. Questionnaire-based survey

The study questionnaire included 35 and 42 questions related to cutaneous manifestations observed after SARS-CoV-2 infection and vaccination, respectively. The questionnaire was administered to patients who visited the dermatology outpatient clinic of the participating hospitals. Informed consent was obtained from all survey participants. The survey was conducted between October 2022 and May 2023, and all responses were collected by July 31, 2023. Both the original Korean version and the English version of the questionnaire can be found in Supplementary Materials. After the collection of all responses, causality assessment was performed by a dermatologist, and the World Health Organization-Uppsala Monitoring Centre criteria were used for causality assessment based on the cutaneous lesions present at the time of the survey and the clinical information provided by respondents[10].

3. Statistical Analysis

Data were presented as numbers and percentages of responders. Unanswered questionnaire items were excluded from the analysis. The χ^2 or Fisher's exact test was used to compare categorical variables, and Student's *t* test was used to compare continuous variables. All statistical analyses were performed using IBM SPSS statistics version 22 (IBM, Armonk, NY, USA). A p value of <0.05 was considered statistically significant.

RESULTS

1. Cutaneous reactions to SARS-CoV-2 vaccination

A total of 707 participants who received SARS-CoV-2 vaccinations completed the questionnaire. Five different SARS-CoV-2 vaccines (AstraZeneca, Janssen, Moderna, Novavax, and Pfizer-BioNTech) were used in Korea during the CVID-19 pandemic. Fig. 1 summarizes the proportions of respondents who developed cutaneous reactions to specific SARS-CoV-2 vaccines.

1) Demographic characteristics of participant and risk for cutaneous manifestations after SARS-CoV-2 vaccination

The demographic characteristics of participants categorized by the vaccine type are presented in Table 1. The mean respondent age was 44.26 years, with a male/female ratio of 1:1.1. Following SARS-CoV-2 vaccination, 20.23% and 5.94% of the respondents reported the onset of new cutaneous lesions or aggravation of preexisting cutaneous conditions, respectively. Most of the respondents were patients visiting dermatology outpatient clinics, as reflected in their diverse dermatologic conditions. The most common dermatologic condition was atopic dermatitis, followed by psoriasis and hair loss, which included all types of hair loss diseases. The risk for the onset of new cutaneous lesions following SARS-CoV-2 vaccination varied from 10.71% (Janssen) to 0% (Novavax), albeit without statistically significant difference among the vaccines. Conversely, the risk for the aggravation of preexisting cutaneous conditions after SARS-CoV-2 vaccin-

Table 1. Demographics, general clinical information of participants and COVID-19 vaccine-associated skin manifestation

Characteristics	Pfizer (1st) (n=381)	Pfizer (2nd) (n=414)	Pfizer (3rd) (n=322)	Pfizer (4th) (n=82)	AZ (1st) (n=160)	AZ (2nd) (n=103)	AZ (3rd) (n=16)	Moderna (1st) (n=142)	Moderna (2nd) (n=157)	Moderna (3rd) (n=128)	Janssen (1st) (n=23)	Janssen (2nd) (n=5)	Novavax (1st) (n=1)	Novavax (2nd) (n=2)	Novavax (3rd) (n=4)	Total (n=707)
Sex																
Male	164 (43.04)	175 (42.27)	135 (41.93)	34 (41.46)	78 (48.75)	52 (50.49)	9 (56.25)	76 (53.52)	89 (56.69)	69 (53.91)	17 (73.91)	4 (80)	1 (100)	1 (50)	1 (25)	336 (47.52)
Female	217 (56.96)	229 (55.31)	187 (58.07)	48 (58.54)	82 (51.25)	51 (49.51)	7 (43.75)	66 (46.48)	68 (43.31)	59 (46.09)	6 (26.09)	1 (20)	0 (0)	1 (50)	3 (75)	371 (52.48)
Age	41.11 ±17.61	41.98 ±17.61	46.27 ±17.63	59.25 ±17.58	53.67 ±17.60	53.84 ±17.62	62.25 ±17.34	41.18 ±17.59	42.97 ±17.82	46.65 ±17.61	43.52 ±17.52	46.2 ±18.11	33	26 ±18.52	28.75 ±18.52	44.26 ±17.61
Past medical history																
Hypertension	42 (11.02)	50 (12.08)	40 (12.42)	22 (26.83)	25 (15.63)	12 (11.65)	4 (25)	24 (16.9)	28 (17.83)	26 (20.31)	4 (17.39)	1 (20)	0 (0)	0 (0)	0 (0)	111 (15.7)
Diabetes mellitus	21 (5.51)	25 (6.04)	24 (7.45)	12 (14.63)	18 (11.25)	8 (7.77)	2 (12.5)	8 (5.63)	12 (7.64)	11 (8.59)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	55 (7.78)
Respiratory disease	3 (0.79)	4 (0.97)	7 (2.17)	2 (2.44)	7 (4.38)	7 (6.8)	0 (0)	8 (5.63)	7 (4.46)	7 (5.47)	1 (4.35)	0 (0)	0 (0)	1 (50)	1 (25)	20 (2.83)
Autoimmune disease	5 (1.31)	5 (1.21)	5 (1.55)	3 (3.66)	3 (1.88)	2 (1.94)	0 (0)	4 (2.82)	4 (2.55)	3 (2.34)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	14 (1.98)
Malignancy	5 (1.31)	7 (1.69)	5 (1.55)	0 (0)	6 (3.75)	3 (2.91)	1 (6.25)	3 (2.11)	3 (1.91)	2 (1.56)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	16 (2.26)
Other	34 (8.92)	58 (14.01)	53 (16.46)	21 (25.61)	33 (20.63)	21 (20.39)	2 (12.5)	14 (9.86)	13 (8.28)	11 (8.59)	1 (4.35)	1 (20)	0 (0)	0 (0)	0 (0)	71 (10.04)
Past dermatologic history																
Atopic dermatitis	24 (6.3)	38 (9.18)	18 (5.59)	5 (6.1)	6 (3.75)	2 (1.94)	0 (0)	10 (7.04)	10 (6.37)	8 (6.25)	1 (4.35)	1 (20)	0 (0)	0 (0)	0 (0)	60 (8.49)
Psoriasis	34 (8.92)	36 (8.7)	29 (9.01)	6 (7.32)	9 (5.63)	6 (5.83)	4 (25)	8 (5.63)	10 (6.37)	7 (5.47)	4 (17.39)	1 (20)	0 (0)	0 (0)	0 (0)	57 (8.06)
Contact dermatitis	10 (2.62)	5 (1.21)	6 (1.86)	1 (1.22)	5 (3.13)	3 (2.91)	3 (18.75)	1 (0.7)	2 (1.27)	2 (1.56)	1 (4.35)	0 (0)	0 (0)	0 (0)	0 (0)	16 (2.26)
Urticaria	10 (2.62)	7 (1.69)	6 (1.86)	1 (1.22)	3 (1.88)	1 (0.97)	1 (6.25)	1 (0.7)	4 (2.55)	1 (0.78)	2 (8.7)	0 (0)	0 (0)	0 (0)	0 (0)	17 (2.4)

Table 1. Demographics, general clinical information of participants and COVID-19 vaccine-associated skin manifestation (Continued)

Characteristics	Pfizer (1st) (n=381)	Pfizer (2nd) (n=414)	Pfizer (3rd) (n=322)	Pfizer (4th) (n=82)	AZ (1st) (n=160)	AZ (2nd) (n=103)	AZ (3rd) (n=16)	Moderna (1st) (n=142)	Moderna (2nd) (n=157)	Moderna (3rd) (n=128)	Janssen (1st) (n=23)	Janssen (2nd) (n=5)	Novavax (1st) (n=1)	Novavax (2nd) (n=2)	Novavax (3rd) (n=4)	Total (n=707)
Alopecia	14 (3.67)	16 (3.86)	8 (2.48)	1 (1.22)	6 (3.75)	4 (3.88)	3 (18.75)	4 (2.82)	4 (2.55)	5 (3.91)	1 (4.35)	0 (0)	0 (0)	0 (0)	0 (0)	29 (4.1)
Acne	7 (1.84)	7 (1.69)	5 (1.55)	0 (0)	1 (0.63)	1 (0.97)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	8 (1.13)
Rosacea	7 (1.84)	8 (1.93)	8 (2.48)	3 (3.66)	2 (1.25)	1 (0.97)	0 (0)	1 (0.7)	1 (0.64)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (1.41)
Other	40 (10.5)	41 (9.9)	32 (9.94)	13 (15.85)	14 (8.75)	11 (10.68)	1 (6.25)	9 (6.34)	9 (5.73)	7 (5.47)	3 (13.04)	0 (0)	0 (0)	0 (0)	0 (0)	51 (7.21)
Systemic symptom after vaccination																
Fever	22 (5.77)	25 (6.04)	24 (7.45)	6 (7.32)	15 (9.38)	8 (7.77)	0 (0)	13 (9.15)	12 (7.64)	11 (8.59)	2 (8.7)	1 (20)	0 (0)	0 (0)	0 (0)	54 (7.64)
Chill	9 (2.36)	12 (2.9)	11 (3.42)	3 (3.66)	10 (6.25)	5 (4.85)	0 (0)	8 (5.63)	8 (5.1)	5 (3.91)	1 (4.35)	0 (0)	0 (0)	0 (0)	0 (0)	30 (4.24)
Cough	5 (1.31)	7 (1.69)	8 (2.48)	2 (2.44)	3 (1.88)	3 (2.91)	0 (0)	6 (4.23)	3 (1.91)	3 (2.34)	1 (4.35)	1 (20)	0 (0)	0 (0)	0 (0)	15 (2.12)
Sore throat	13 (3.41)	15 (3.62)	11 (3.42)	3 (3.66)	4 (2.5)	1 (0.97)	0 (0)	6 (4.23)	4 (2.55)	4 (3.13)	1 (4.35)	1 (20)	0 (0)	0 (0)	0 (0)	24 (3.39)
Myalgia	25 (6.56)	29 (7)	23 (7.14)	5 (6.1)	24 (15)	12 (11.65)	2 (12.5)	20 (14.08)	20 (12.74)	18 (14.06)	2 (8.7)	1 (20)	0 (0)	0 (0)	1 (25)	73 (10.33)
Other	7 (1.84)	6 (1.45)	9 (2.8)	2 (2.44)	5 (3.13)	4 (3.88)	0 (0)	2 (1.41)	1 (0.64)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	16 (2.26)
Skin condition after vaccination																
New onset skin lesion	20 (5.25)	16 (3.86)	24 (7.45)	8 (9.76)	9 (5.63)	4 (3.88)	2 (12.5)	4 (2.82)	14 (8.92)	17 (13.28)	2 (8.7)	1 (20)	0 (0)	0 (0)	0 (0)	143 (20.23)
Aggravation of pre-existing condition	13 (3.41)	11 (2.66)	6 (1.86)	1 (1.22)	0 (0)	0 (0)	0 (0)	4 (2.82)	1 (0.64)	4 (3.13)	1 (4.35)	1 (20)	0 (0)	0 (0)	0 (0)	42 (5.94)

AZ, AstraZeneca; Values are presented as absolute numbers only, mean ± standard deviation, or percentages (%)

Table 2. Characteristics of participants who reported cutaneous reactions after COVID-19 vaccination

Characteristics	Pfizer (n=68)	AZ (n=15)	Moderna (n=39)	Janssen (n=3)	Total (n=118)
Sex					
Male	28 (45.9)	6 (40)	22 (56.41)	2 (66.67)	58 (49.15)
Female	33 (54.1)	9 (60)	17 (43.59)	1 (33.33)	60 (50.85)
Age (years)	48.06±16.94	47.96±15.93	44.27±16.96	45.33±17.03	46.77±17.58
Onset (days)	47.05±73.76	13.00±19.73	40.90±54.93	3.5±1.09	39.81±51.50
Cutaneous reaction					
Urticaria and morbilliform eruption	38 (62.3)	10 (66.67)	25 (64.1)	0 (0)	73 (61.86)
Eczema	30 (49.18)	5 (33.33)	18 (46.15)	2 (66.67)	55 (46.61)
Vesicular eruption	6 (9.84)	3 (20)	3 (7.69)	0 (0)	12 (10.17)
Psoriasiform lesions	9 (14.75)	0 (0)	3 (7.69)	1 (33.33)	13 (11.02)
Acne and folliculitis	6 (9.84)	2 (13.33)	3 (7.69)	0 (0)	11 (9.32)
Hair loss	15 (24.59)	4 (26.67)	6 (15.38)	2 (66.67)	27 (22.88)
Hypopigmentation	3 (4.92)	1 (6.67)	0 (0)	0 (0)	4 (3.39)
Hyperpigmentation	4 (6.56)	1 (6.67)	6 (15.38)	0 (0)	11 (9.32)
Mass	2 (3.28)	0 (0)	2 (5.13)	0 (0)	4 (3.39)
Ulcer and necrosis	1 (1.64)	0 (0)	1 (2.56)	0 (0)	2 (1.69)
Herpes zoster	1 (1.64)	0 (0)	4 (10.26)	1 (33.33)	6 (5.08)
Local injection site reaction	8 (13.11)	5 (33.33)	6 (15.38)	0 (0)	19 (16.1)
Systemic symptoms					
Pruritus	52 (85.25)	7 (46.67)	37 (94.87)	3 (100)	99 (83.90)
Pain	10 (16.39)	2 (13.33)	10 (25.64)	1 (33.33)	23 (19.49)
Heating sensation	29 (47.54)	7 (46.67)	17 (43.59)	0 (0)	53 (44.92)
Sensory change	5 (8.2)	1 (6.67)	5 (12.82)	0 (0)	11 (9.32)
Timing of skin reaction					
After 1st vaccination	20 (32.79)	9 (60)	4 (10.26)	2 (66.67)	35 (29.66)
After 2nd vaccination	16 (26.23)	4 (26.67)	14 (35.9)	1 (33.33)	35 (29.66)
After 3rd vaccination	24 (39.34)	2 (13.33)	17 (43.59)	0 (0)	43 (36.44)
Others (4th and 5th)	8 (13.11)	0 (0)	4 (10.26)	0 (0)	12 (10.17)

AZ, AstraZeneca; Values are presented as absolute numbers only, mean ± standard deviation, or percentages (%)

ation was the lowest for the AstraZeneca vaccine (0%), which was significantly lower than that for the other vaccines (p = 0.018).

2) Clinical characteristics of the respondents with new-onset cutaneous lesions after SARS-CoV-2 vaccination

The new-onset cutaneous lesions reported after SARS-

Table 3. Data on the clinical course and risk factors of the common skin reactions after COVID-19 vaccination

Characteristics	Urticaria & morbilliform rash (n=125)	%	Eczema (n=55)	%	Hair loss (n=23)	%	*p*-value
Sex							0.326
Male	65	52.00	33	60.00	11	47.83	
Female	60	48.00	22	40.00	12	52.17	
Age	50.62±18.35		50.57±17.60		49.39±17.62		0.587
Time from vaccination to skin rash (days)	44.63±51.09		37.11±51.25		24.36±20.18		0.389
Systemic symptoms after vaccination							
Fever	35	28.00	18	32.73	7	30.43	0.722
Chill	16	12.80	8	14.55	3	13.04	0.956
Cough	10	8.00	6	10.91	2	8.70	0.653
Sore throat	20	16.00	11	20.00	5	21.74	0.941
Myalgia	47	37.60	27	49.09	12	52.17	0.484
Oral medication(s) to treat vaccine-related systemic symptoms							
Antipyretics	13	30.23	13	27.08	4	26.67	
Systemic corticosteroid	11	25.58	10	20.83	6	40.00	
Systemic antiviral agent	1	2.33	0	0.00	0	0.00	
Systemic antibiotics	4	9.30	5	10.42	1	6.67	
Systemic antihistamines	14	32.56	20	41.67	4	26.67	
Systemic anti-malarial agent	0	0.00	0	0.00	0	0.00	
Dermatologic symptoms							
Pruritus	94	75.20	53	96.36	11	47.83	
Pain	20	16.00	15	27.27	3	13.04	
Heating sensation	48	38.40	27	49.09	6	26.09	
Sensory change	9	7.20	7	12.73	1	4.35	
Treatment for cutaneous reaction							
Yes	27	21.60	29	52.73	15	65.22	
No	98	78.40	26	47.27	8	34.78	
Mode of treatment							
Observation at home (with or without OTC medication)	12	30.77	14	25.45	3	13.04	
Outpatient visit	26	66.67	26	47.27	20	86.96	

Table 3. Data on the clinical course and risk factors of the common skin reactions after COVID-19 vaccination (Continued)

Characteristics	Urticaria & morbilliform rash (n=125)	%	Eczema (n=55)	%	Hair loss (n=23)	%	*p*-value
Admission	1	2.56	1	1.82	0	0.00	
ICU care	0	0.00	0	0.00	0	0.00	
Final clinical outcome							
Persistent	57	50.44	24	43.64	11	47.83	0.898
Aggravation	14	12.39	13	23.64	2	8.70	0.04*
Partial remission	26	23.01	13	23.64	5	21.74	0.94
Complete remission	16	14.16	2	3.64	1	4.35	0.033*
Refused next vaccination	52	41.60	27	49.09	11	47.83	0.907
Presence of corresponding skin lesion at time of survey	29	23.20	49	89.09	21	91.30	
Causality assessment by dermatologist							
Certain	2	1.72	2	3.64	0	0.00	
Probable	13	11.21	4	7.27	3	13.04	
Possible	56	48.28	24	43.64	12	52.17	
Less likely	13	11.21	4	7.27	1	4.35	
Limited evaluation	13	11.21	4	7.27	2	8.70	
Unable to assess	19	16.38	14	25.45	4	17.39	

Values are presented as absolute numbers only, mean ± standard deviation, or percentages (%); $*p < 0.05$

CoV-2 vaccination were classified according to the vaccine product administered prior their development (Table 2). The types of the new-onset cutaneous lesions were not significantly different among the vaccine products. The most common cutaneous lesion was urticaria/morbilliform eruption, which accounted for 61.86% of all new-onset cutaneous lesions, followed by eczema (46.61%), hair loss (22.88%), local injection-site reaction (16.10%), and psoriasiform eruption (11.02%). Pruritus was the most common subjective symptom of the cutaneous lesions, reported by 92.37% of the respondents, followed by heating sensation (44.92%). Pain and sensory changes were reported by 19.49% and 9.32% of the respondents, respectively. Approximately 30% of all cutaneous lesions developed after the first vaccination. The same percentage of cutaneous lesions developed after the second vaccination, whereas 36.44% of the cutaneous lesions developed following the third vaccination. While 60% of the respondents who received the AstraZeneca vaccine developed new cutaneous lesions after the first vaccination, new cutaneous reactions were noted more frequently after the second or third vaccination in respondents who received the Pfizer or Moderna vaccine. Only 10.17% of all new-onset cutaneous lesions developed either the fourth or the fifth vaccination. The distribution of new-onset cutaneous lesion types is shown in the Supplementary Table 1. Overall, more than half of the new-onset cutaneous lesions were located on arms, legs, and back.

3) Demographic characteristics and the clinical course of respondents with common new-onset cutaneous lesions after SARS-CoV-2 vaccination

The questionnaire included queries on the clinical course of cutaneous lesions. However, sufficient data for analysis were available only for the three most common conditions

after the exclusion of the questions that were left blank by the respondents. Data on the clinical course and risk factors for the three most common cutaneous lesions (urticaria/morbilliform rash, eczema, and hair loss) are summarized in Table 3. Briefly, the male/female ratio, age, and the time of onset did not significantly differ among the three most common cutaneous reactions. Respondents reported various systemic symptoms associated with vaccination, among which myalgia was the most common. Albeit exhibiting variation, the frequency of systemic symptoms did not significantly differ among the respondents with different cutaneous reactions. Fewer than 30% of the respondents who had urticaria/morbilliform rash after vaccination received treatment. Conversely, 52.73% and 65.22% of the respondents who developed eczema and hair loss after vaccination, respectively, received treatment. The majority of the respondents either

Table 4. Demographics and clinical characteristics of participants with aggravation of underlying skin disease after COVID-19 vaccination according to type of vaccine

Characteristics	Pfizer (n=31)	%	AZ (n=0)	%	Moderna (n=9)	%	Janssen (n=2)	%	Total (n=42)	%
Sex										
Male	12	38.71	0	0.00	2	22.22	2	100.00	16	38.10
Female	19	61.29	0	0.00	7	77.78	0	0.00	26	61.90
Age (years)	42.56 ±17.55		N/A		51.56 ±17.69		37 ±18.15		45.02 ±17.70	
Underlying skin disease										
Atopic dermatitis	7	22.58	0	0.00	0	0.00	2	100.00	9	21.43
Psoriasis	5	16.13	0	0.00	1	11.11	0	0.00	6	14.29
Acne and folliculitis	1	3.23	0	0.00	0	0.00	0	0.00	1	2.38
Contact dermatitis	1	3.23	0	0.00	0	0.00	0	0.00	1	2.38
Urticaria	1	3.23	0	0.00	2	22.22	0	0.00	3	7.14
Hair loss	3	9.68	0	0.00	1	11.11	0	0.00	4	9.52
Vitiligo	1	3.23	0	0.00	0	0.00	0	0.00	1	2.38
Other / No response	13	41.94	0	0.00	5	55.56	0	0.00	18	42.86
Systemic symptoms after vaccination										
Fever	2	6.45	0	0.00	1	11.11	0	0.00	3	7.14
Chill	1	3.23	0	0.00	1	11.11	0	0.00	2	4.76
Cough	1	3.23	0	0.00	0	0.00	0	0.00	1	2.38
Sore throat	2	6.45	0	0.00	0	0.00	0	0.00	2	4.76
Myalgia	1	3.23	0	0.00	1	11.11	1	50.00	3	7.14
Timing of skin reaction										
After 1st vaccination	13	41.94	0	0.00	4	44.44	1	50.00	18	42.86
After 2nd vaccination	11	35.48	0	0.00	1	11.11	1	50.00	13	30.95
After 3rd vaccination	6	19.35	0	0.00	4	44.44	0	0.00	10	23.81
Others (4th and 5th)	1	3.23	0	0.00	0	0.00	0	0.00	1	2.38

AZ, AstraZeneca; Values are presented as absolute numbers only, mean ± standard deviation, or percentages (%)

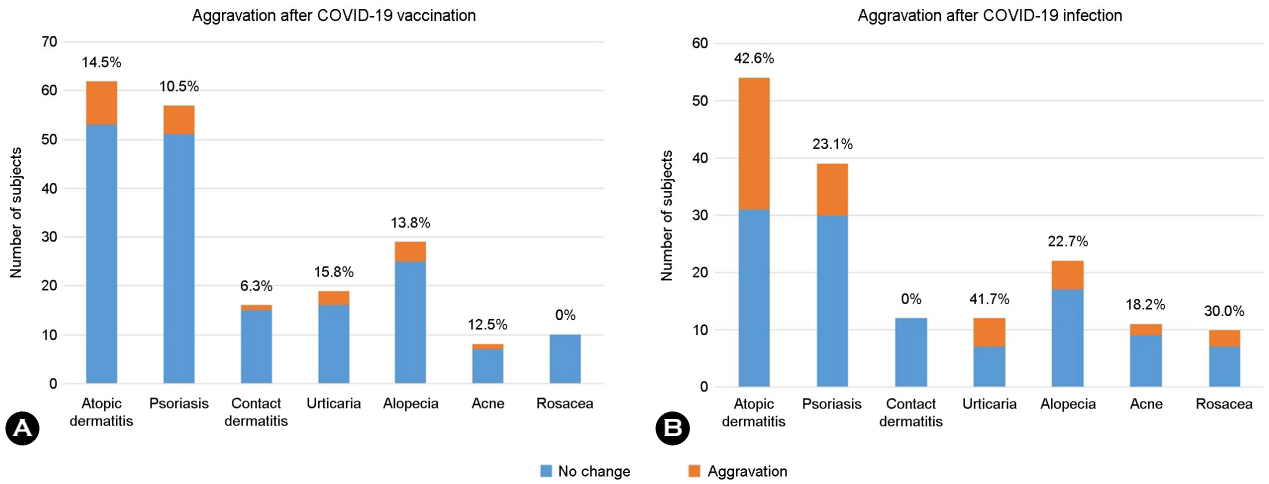

Fig. 2. Proportions of respondents who reported aggravation of specific preexisting cutaneous lesions after (A) SARS-CoV-2 vaccination and (B) SARS-CoV-2 infection

visited outpatient clinics for treatment or waited for spontaneous improvement. Only two respondents were admitted. The final outcome varied among the cutaneous lesion types. The proportion of respondents who reported worsening of the cutaneous lesions over time was significantly higher for eczema than for urticaria/morbilliform rash or hair loss (23.64% vs. X% and y%, respectively; $p = 0.040$). In contrast, 14.16% of the respondents with urticaria/morbilliform rash reported the complete clearance of cutaneous lesions at some point, which was significantly higher than that reported for eczema and hair loss (X% and Y%, respectively; $p = 0.033$).

4) Causality assessment of new-onset cutaneous lesions after SARS-CoV-2 vaccination

Based on the cutaneous lesion type and the clinical information including the time of onset, causality assessment was performed for each case by dermatologists. Only 9.3% (18 out of 194) of all cases were determined as unlikely to be caused by SARS-CoV-2 vaccination. Causality assessment could not be performed in 28.9% (56 out of 194) of the cases. The majority of the remaining cases were assessed as possibly caused by SARS-CoV-2 vaccination.

5) Demographic characteristics of respondents who reported aggravation of preexisting cutaneous conditions after SARS-CoV-2 vaccination

Aggravation of the preexisting cutaneous conditions was reported by 42 (5.94%) respondents, whose demographic characteristics are summarized in Table 4. Briefly, the male /female ratio was 1:1.63. None of the respondents who received the AstraZeneca vaccine reported aggravation of preexisting cutaneous conditions. There was no significant difference in the proportion of specific preexisting cutaneous diseases that exhibited aggravation among the different vaccines. Atopic dermatitis (21.43%) was the most commonly reported preexisting cutaneous condition that aggravated following vaccination. Although systemic symptoms was reported by respondents who experienced aggravation of preexisting cutaneous conditions after vaccination, the rates were low, below 8% for all. Across all vaccine products, 42.86% of the respondents experienced aggravation of cutaneous lesions after the first vaccination, with a consistently decline in the frequency of aggravation with each booster shot. Fig. 2A illustrates the proportions of respondents who reported aggravation of specific preexisting cutaneous conditions. The three most common preexisting cutaneous conditions were atopic dermatitis, psoriasis, and alopecia, which were reported to be aggravated after SARS-CoV-2 vaccination by comparable proportions of respondents. Interestingly, no respondent with rosacea reported aggravation.

6) Risk factors for the new onset and aggravation of preexisting cutaneous lesions after SARS-CoV-2 vaccination

We assessed the potential risk factors for the development of new cutaneous lesions and the aggravation of preexisting

Table 5. Analysis of risk factors associated with cutaneous reactions after COVID-19 vaccination

	No cutaneous reaction	%	New-onset skin lesion	%	*p*-value	Aggravation of skin disease	%	*p*-value
Sex								
M	296	47.06	58	49.15	0.639	16	38.10	0.425
F	333	52.94	60	50.85		26	61.90	
Age	43.29 ±17.63		48.51 ±16.97		0.001	45.02 ±16.17		0.269
Underlying disease								
Malignancy								
Yes	13	2.18	3	2.61	1	2	4.76	0.21
No	583	97.82	112	97.39		40	95.24	
HTN				0.00				
Yes	77	12.92	23	20.00	0.077	8	19.05	0.343
No	519	87.08	92	80.00		34	80.95	
DM				0.00				
Yes	43	7.21	8	6.96	1	2	4.76	0.759
No	553	92.79	107	93.04		40	95.24	
Respiratory disease				0.00				
Yes	13	2.18	5	4.35	0.362	2	4.76	0.26
No	583	97.82	110	95.65		40	95.24	
Autoimmune disease				0.00				
Yes	9	1.51	3	2.61	0.709	2	4.76	0.16
No	587	98.49	112	97.39		40	95.24	
Systemic symptom after vaccination								
Fever								
Yes	3	4.23	50	36.50	< 0.001	1	33.33	0.156
No	68	95.77	87	63.50		2	66.67	
Chill								
Yes	3	4.23	26	18.84	0.005	1	33.33	0.156
No	68	95.77	112	81.16		2	66.67	
Cough								
Yes	1	1.41	13	9.42	0.038	1	33.33	0.08
No	70	98.59	125	90.58		2	66.67	
Sore throat								
Yes	1	1.41	23	16.67	0.002	0	0.00	1
No	70	98.59	115	83.33		3	100.00	

Table 5. Analysis of risk factors associated with cutaneous reactions after COVID-19 vaccination (Continued)

	No cutaneous reaction	%	New-onset skin lesion	%	*p*-value	Aggravation of skin disease	%	*p*-value
Myalgia								
Yes	3	4.23	68	49.28	< 0.001	2	66.67	0.011
No	68	95.77	70	50.72		1	33.33	

Values are presented as absolute numbers only, mean ± standard deviation, or percentages (%)

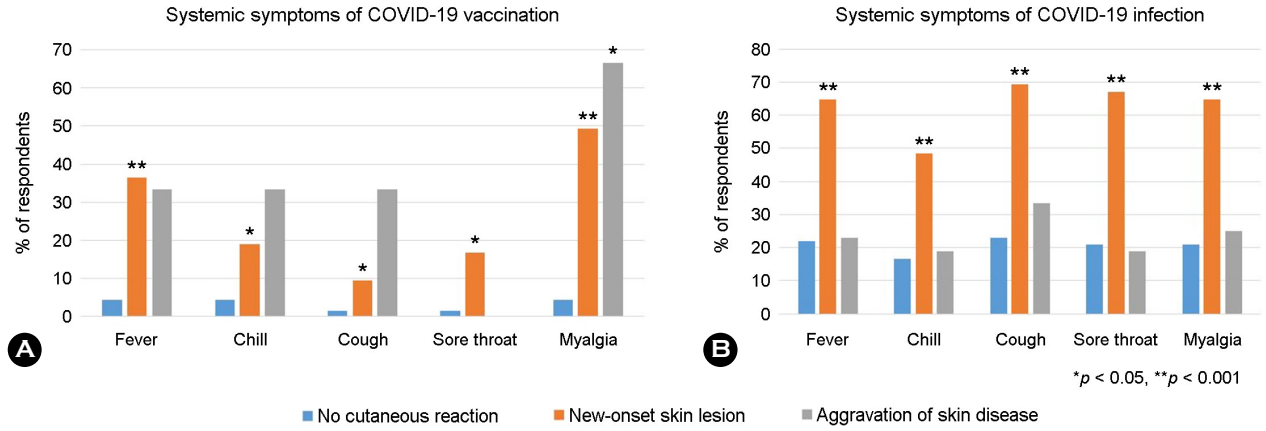

Fig. 3. Presence of systemic symptoms and risk for cutaneous reactions after (A) SARS-CoV-2 vaccination and (B) SARS-CoV-2 infection $*p < 0.05$ $**p < 0.001$

cutaneous lesions after SARS-CoV-2 vaccination (Table 5). The respondents who developed new cutaneous lesions after SARS-CoV-2 vaccination were significantly older than those who did not experience any cutaneous reactions (43.29 ± 17.63 vs. 48.51 ± 16.97 years, $p = 0.001$). The presence of underlying disease, including malignancy, hypertension, diabetes mellitus, respiratory disease, and autoimmune disease, was not associated with a higher risk for the onset or aggravation of cutaneous lesions after SARS-CoV-2 vaccination. Myalgia was the only systemic symptom following SARS-CoV-2 vaccination that was significantly associated with a higher risk for the aggravation of preexisting cutaneous conditions (odds ratio [OR] 45.33, 95% confidence interval [CI] 3.16~650.97, $p = 0.011$). However, the presence of systemic symptoms associated with SARS-CoV-2 vaccination was strongly associated with a higher risk for the new onset of cutaneous lesions; the observed increased risk was present for all five reported symptoms (fever: OR 13.03, 95% CI 4.74~48.92, $p < 0.001$; chill: OR 5.31, 95% CI 1.93~20.45, $p = 0.005$; cough: OR 7.34, 95% CI 1.50~11.53, $p = 0.038$; sore throat: OR 13.39, 95% CI 1.77~101.55, $p = 0.002$; and myalgia: OR 22.34, 95% CI 8.77~83.75, $p < 0.001$) (Fig. 3A).

2. Cutaneous complications of SARS-CoV-2 infection

1) Demographic and clinical characteristics of respondents who experienced cutaneous complications after SARS-CoV-2 infection

A total of 682 participants who were infected with SARS-CoV-2 completed the questionnaire. Table 6 shows the demographic and clinical characteristics of all respondents. Among these 682 respondents, 91 (13.3%) and 66 (9.7%) reported the development of new cutaneous lesions and the aggravation of preexisting cutaneous conditions, respectively, after COVID-19 diagnosis. Urticaria/morbilliform rash was the most common new-onset cutaneous lesion (72.53%), followed by hair loss (23.08%), vesicular eruption (15.38%), acne and folliculitis (13.19%), and eczema (9.89%). Only one respondent reported chilblain-like eruptions in acral regions. Among all respondents who reported aggravation

Table 6. Demographics and characteristics of participants who completed the questionnaire on the cutaneous manifestation of COVID-19 infection

Characteristics	No skin reaction (n=525)	%	New-onset skin lesion (n=91)	%	*p*-value	Aggravation of skin disease (n=66)	%	*p*-value	Total (n=682)	%
Sex										
Male	229	43.62	32	35.16	0.131	25	37.88	0.412	286	41.94
Female	296	56.38	59	64.84		41	62.12		396	58.06
Age (years)	39.57 ±15.95		43.43 ±15.90		0.046*	39.54 ±15.97		0.907	40.14 ±15.96	
Past medical history										
Hypertension	39	7.43	13	14.29	0.212	3	4.55	0.095	55	8.06
Diabetes mellitus	20	3.81	6	6.59	0.814	1	1.52	0.408	27	3.96
Respiratory disease	9	1.71	5	5.49	0.071	2	3.03	0.996	16	2.35
Autoimmune disease	6	1.14	4	4.40	0.014*	2	3.03	0.155	12	1.76
Malignancy	8	1.52	2	2.20	0.923	3	4.55	0.915	13	1.91
Other	29	5.52	20	21.98		2	3.03		51	7.48
New onset skin lesions							0.00			
Urticaria and morbilliform eruption	N/A	N/A	66	72.53		7	10.61		N/A	N/A
Vesicular eruption	N/A	N/A	14	15.38		N/A	N/A		N/A	N/A
Eczema	N/A	N/A	9	9.89		N/A	N/A		N/A	N/A
Chilblain-like change of the acral parts	N/A	N/A	1	1.10		N/A	N/A		N/A	N/A
Vasculitis	N/A	N/A	2	2.20		N/A	N/A		N/A	N/A
Acne and folliculitis	N/A	N/A	12	13.19		N/A	N/A		N/A	N/A
Hair loss	N/A	N/A	21	23.08		N/A	N/A		N/A	N/A
Hypopigmentation	N/A	N/A	1	1.10		N/A	N/A		N/A	N/A
Hyperpigmentaion	N/A	N/A	7	7.69		N/A	N/A		N/A	N/A
Ulcer and necrosis	N/A	N/A	1	1.10		N/A	N/A		N/A	N/A
Symptoms without skin lesion	N/A	N/A	4	4.40		N/A	N/A		N/A	N/A
Aggravated underlying skin disease										
Atopic dermatitis	N/A	N/A	N/A	N/A		23	34.85		N/A	N/A
Psoriasis	N/A	N/A	N/A	N/A		9	13.64		N/A	N/A
Hair loss	N/A	N/A	N/A	N/A		5	7.58		N/A	N/A
Acne and folliculitis	N/A	N/A	N/A	N/A		2	3.03		N/A	N/A
Rosacea	N/A	N/A	N/A	N/A		3	4.55		N/A	N/A
Urticaria	N/A	N/A	N/A	N/A		5	7.58		N/A	N/A
Others	N/A	N/A	N/A	N/A		10	15.15		N/A	N/A

Table 6. Demographics and characteristics of participants who completed the questionnaire on the cutaneous manifestation of COVID-19 infection (Continued)

Characteristics	No skin reaction (n=525)	%	New-onset skin lesion (n=91)	%	*p*-value	Aggravation of skin disease (n=66)	%	*p*-value	Total (n=682)	%
Symptoms of skin lesion										
Pruritus	N/A	N/A	69	75.82		57	86.36		N/A	N/A
Pain	N/A	N/A	15	16.48		11	16.67		N/A	N/A
Heating sensation	N/A	N/A	27	29.67		35	53.03		N/A	N/A
Sensory change	N/A	N/A	1	1.10		4	6.06		N/A	N/A
Systemic symptoms related to COVID-19										
Fever	21	21.88	59	64.84	< 0.001*	11	22.92	0.887	91	38.72
Chil	16	16.67	44	48.35	< 0.001*	9	18.75	0.756	69	29.36
Cough	22	22.92	63	69.23	< 0.001*	16	33.33	0.414	101	42.98
Sore throat	20	20.83	61	67.03	< 0.001*	9	18.75	0.365	90	38.30
Myalgia	20	20.83	59	64.84	< 0.001*	12	25.00	1	91	38.72
Mode of COVID-19 testing										
PCR	347	69.26	50	54.95		37	56.06		434	63.64
Rapid antigen test	120	23.95	33	36.26		17	25.76		170	24.93
Self-test	34	6.79	6	6.59		6	9.09		46	6.74

Values are presented as absolute numbers only, mean ± standard deviation, or percentages (%), $*p < 0.05$

of preexisting cutaneous lesions after SARS-CoV-2 infection, atopic dermatitis was the most common condition (34.85%), followed by psoriasis (13.64%), hair loss (7.58%), and urticaria (7.58%). Fig. 2B shows the number of respondents with specific cutaneous lesions and the proportion of those who reported aggravation after SARS-CoV-2 infection. Pruritus was the most common symptom of cutaneous complications. Respondents who developed new cutaneous lesions following COVID-19 were significantly older than those without new cutaneous lesions ($p = 0.046$). Systemic COVID-19 symptoms were more common in respondents who developed new cutaneous lesions than in those without new cutaneous lesions (fever: OR 7.49, 95% CI 3.93~14.29, $p < 0.001$; chill: OR 4.23, 95% CI 2.16~8.27, $p < 0.001$; cough: OR 6.42, 95% CI 3.40~12.12, $p < 0.001$; sore throat: OR 6.62, 95% CI 3.48~12.62, $p < 0.001$; and myalgia: OR 6.06, 95% CI 3.19~11.51, $p < 0.001$) (Fig. 3B). Moreover, the proportion of respondents with underlying autoimmune diseases was significantly higher in those who developed COVID-19-associated new-onset new cutaneous lesions than in those without new cutaneous lesions (OR 3.88; 95% CI, 1.22~12.31; $p = 0.038$). Other underlying diseases, including hypertension, diabetes mellitus, respiratory diseases, and malignancy, were not associated with an increased risk for the development of new cutaneous lesions. Neither underlying diseases nor systemic COVID-19 symptoms were associated with a higher risk for the aggravation of preexisting cutaneous lesions. Information on the final outcome of the new-onset cutaneous lesions following COVID-19 infection was available in 13 respondents. The cutaneous lesions persisted in 5 (38.5%) respondents, aggravated over time in 3 (23.1%) respondents, and exhibited partial and complete resolution in 3 (23.1%) and 2 (15.4%) respondents, respectively.

2) Clinical characteristics of respondents who experienced cutaneous complications of SARS-CoV-2 infection

Table 7 shows the clinical characteristics of respondents who developed the three most commonly reported new-onset cutaneous lesions and the risk factor analysis. Similar to that observed with the risk assessment for cutaneous

Table 7. Demographic characteristics and risk factor analysis of the common new-onset skin lesions following COVID-19 infection

Characteristics	No skin reaction (n=525)	%	Urticaria & morbilliform rash (n=66)	%	*p*-value	Vesicular eruption (n=14)	%	*p*-value	Hair loss (n=21)	%	*p*-value
Sex											
Male	229	43.62	23	18.40		8	57.14		7	33.33	
Female	296	56.38	43	34.40		6	42.86		14	66.67	
Age	39.57 ±15.95		45.76 ±15.96		0.004*	45.57 ±15.91		0.155	49.39 ±17.62		0.398
Systemic symptoms of COVID-19											
Fever	21	21.88	41	32.80	< 0.001*	9	64.29	0.002*	13	61.90	< 0.001*
Chill	16	16.67	27	21.60	0.001*	6	42.86	0.033*	11	52.38	< 0.001*
Cough	22	22.92	39	31.20	< 0.001*	10	71.43	0.001*	10	47.62	0.012*
Sore throat	20	20.83	39	31.20	< 0.001*	11	78.57	< 0.001*	13	61.90	< 0.001*
Myalgia	20	20.83	42	33.60	< 0.001*	9	64.29	0.002*	11	52.38	0.002*
Dermatologic symptoms											
Pruritus	N/A	N/A	57	45.60		12	85.71		13	61.90	
Pain	N/A	N/A	23	18.40		2	14.29		0	0.00	
Heating sensation	N/A	N/A	26	20.80		6	42.86		4	19.05	
Sensory change	N/A	N/A	1	0.80		0	0.00		0	0.00	
Presence of corresponding skin lesion at time of survey											
Yes	N/A	N/A	44	81.48		10	90.91		16	76.19	
No	N/A	N/A	10	18.52		1	9.09		5	23.81	
Causality assessment by dermatologist											
Certain	N/A	N/A	1	1.85		0	0.00		1	4.76	
Probable	N/A	N/A	2	3.70		0	0.00		3	14.29	
Possible	N/A	N/A	24	44.44		6	54.55		9	42.86	
Unable to assess	N/A	N/A	27	50.00		5	45.45		8	38.10	

Values are presented as absolute numbers only, mean ± standard deviation, or percentages (%), *p*-value: compared to the group without skin reaction, $*p < 0.05$

reactions to SARS-CoV-2 vaccination, all three common cutaneous reactions (urticaria/morbilliform rash, vesicular eruption, and hair loss) were associated with the presence of systemic COVID-19 symptoms. Moreover, the mean age of the respondents who developed urticaria/morbilliform rash was significantly higher than that of those who did not experience any cutaneous complications (39.57 ± 15.95 vs. 45.76 ± 15.96 years, $p = 0.004$). The anatomical distribution of the new-onset cutaneous lesions is presented in Supplementary Table 2.

DISCUSSION

In the present questionnaire-based survey study, which aimed to investigate the epidemiology and clinical characteristics of cutaneous reactions following SARS-CoV-2 infection and vaccination in the Republic of Korea, we found that 20.23% of the respondents reported cutaneous reactions after SARS-CoV-2 vaccination. Urticaria/morbilliform rash was the most common manifestation and often accompanied by pruritus. In general, new-onset cutaneous reactions occurred

at a similar rate (approximately 30%) for the first three vaccine administrations. Interestingly, the risk for cutaneous reactions was significantly higher for the first dose of the AstraZeneca vaccine than for the other four vaccines. A similar trend was observed in previous studies investigating all adverse reactions, not confined to the cutaneous reactions[11,12]. This discrepancy might be due to the difference in immunogenicity among the vaccine categories (viral vector vs. mRNA). Notably, only 10.17% of the cutaneous lesions developed after the fourth or fifth vaccination, indicating a decreasing risk with subsequent booster shots. The development of new-onset cutaneous lesions after SARS-CoV-2 vaccination was significantly associated with older age and the presence of vaccination-related systemic symptoms. In contrast, cutaneous complications following SARS-CoV-2 infection were observed in 13.3% of the respondents and urticaria/morbilliform rash was the most common presentation. The presence of systemic symptoms, such as fever, chill, cough, sore throat, and myalgia, was significantly associated with the development of new cutaneous lesions after infection. Furthermore, respondents who developed cutaneous complications after SARS-CoV-2 infection were significantly older than those without cutaneous complications.

The prevalence of cutaneous adverse effects following SARS-CoV-2 vaccination varies depending on the specific vaccine and population as well as the study design. The vast majority of previous studies reported the relative incidence of cutaneous side effects for different vaccine brands. However, Lacey et al. reported that cutaneous reactions subsequent to the administration of mRNA SARS-CoV-2 vaccines (Pfizer-BioNTech and Moderna) occurred in 1.9% of the vaccine recipients, which is considerably higher than that observed in the present study (6.33%)[13]. In the present study, we aimed to minimize the impact of selection bias by randomly distributing the questionnaire to patients in the participating clinics. Consequently, the rates of cutaneous complications resulting from SARS-CoV-2 vaccination observed in the present study should be considered a reliable estimate of the overall incidence of such cutaneous reactions. However, the discrepancy between the incidence of cutaneous reactions observed in the present study and that reported in previous studies may also stem from the different recording methods. In previous studies, physicians documented the cutaneous reactions, whereas the present study relied on respondents and involved more subjective assessment. Therefore, respondents might have attributed most of the cutaneous conditions to the SARS-CoV-2 vaccination, even in cases where the vaccines might not have been the cause. The accurate determination of the prevalence of SARS-CoV-2 vaccine-related cutaneous side effects requires larger-scale, cohort studies with the objective evaluation of cutaneous reactions by medical professionals, ideally dermatologists.

The association between age and the development of adverse reactions to SARS-CoV-2 vaccination has been demonstrated in previous studies[14-16], which reported an increased risk for adverse reactions in younger individuals. However, these studies included only injection-site reactions as adverse cutaneous reactions. Our analyses indicating a higher risk for adverse cutaneous reactions following both SARS-CoV-2 vaccination and injection in older respondents suggest differences in the underlying pathologic mechanism between systemic reactions, such as fever, fatigue, myalgia, nausea, and vomiting, and cutaneous reactions. Systemic reactions are caused by systemic innate immune response[17], whereas cutaneous vaccine reactions are classically considered a result of allergic response involving type I or type IV hypersensitivity reaction. Following the recent emergence of mRNA-based vaccines and the heightened public interest in vaccine-related adverse events, other potential mechanisms, including viral reactivation, molecular mimicry, antibody production, and immune complex deposition, have been proposed for cutaneous reactions[18-20]. Thus, the differential effect of age on vaccine-induced adverse reactions are likely due to mechanistic differences in reaction types.

The reported incidence of cutaneous manifestations of COVID-19 range from 0.19% to 20.45%[8,21,22]. In the present study, 13.3% of the respondents diagnosed with COVID-19 experienced cutaneous manifestations, which is likely a good estimate of the actual proportion of patients with COVID-19-related skin manifestations given that the data were based on over 600 respondents. Moreover, the questionnaire covered a broad spectrum of cutaneous conditions ranging from mild to severe forms and offered a more accurate estimate compared to prior clinical studies, which might have potentially overlooked mild skin reactions that might not be readily discernible to the evaluator. However, similar to the incidence of SARS-CoV-2 vaccination-related cutaneous reactions, the present study design might have overestimated the incidence of cutaneous manifestation of SARS-CoV-2 infection by including cutaneous conditions irrelevant to SARS-CoV-2 infection. Previous studies, mainly from North America and Europe, have indicated chilblain-like lesions as a main cutaneous reaction category in COVID-19, with an incidence ranging from 19% to 75%[8,23-25]. However, no respondent in the present study reported chilblain-like lesions. In fact, the reported incidence of such cutaneous lesions is lower than 1% in studies from Asian populations[22,26]. Therefore, our findings highlight the difference in the type of

cutaneous reactions to COVID-19 between different ethnic groups.

To our knowledge, this is the first study reporting that the likelihood of developing cutaneous reactions was significantly higher in respondents who experienced systemic symptoms, such as fever, chill, myalgia, sore throat, and myalgia, after SARS-CoV-2 vaccination or infection. Although the temporal relationship between the onset of systemic symptoms and cutaneous reactions could not be evaluated, our findings highlight the importance of vigilant monitoring for cutaneous reactions in patients who develop systemic symptoms after SARS-CoV-2 vaccination or infection. Furthermore, the association between systemic symptoms and cutaneous reactions suggest that the activation of innate immune response (systemic symptoms) might trigger subsequent hypersensitivity reaction, molecular mimicry, or autoimmune reaction, resulting in cutaneous manifestations. Our findings suggest the presence of a complex interplay of the factors contributing to cutaneous reactions after infection, including immune response and systemic disease manifestations. However, detailed cellular and molecular analyses are warranted to confirm this immunologic connection.

The limitations of our study should be acknowledged. First, the study included individuals seeking care at university hospitals and, therefore, may not be a full representation of the general population of the Republic of Korea. Furthermore, the classification of cutaneous lesions might not be accurate as their classification was solely based on the participants' response. To aid the participants, color images of typical cutaneous lesions were offered for each category. Although the lesion categories were relatively straightforward, mostly consisting of common cutaneous lesions, accurate assessment of the lesions might have been challenging for the participants, especially in cases where the lesions might have completely cleared at the time of the survey. Similarly, the medical history of the participants might not be fully accurate because the medical records of individual participants were not reviewed. The relatively small number of respondents who received certain vaccine products is another main study limitation. Finally, the risk of recall bias was present due to the study design.

In conclusion, this study offers valuable data on the prevalence, clinical characteristics, and risk factors for various cutaneous reactions observed in association with SARS-CoV-2 vaccination and infection, thereby contributing to our comprehensive understanding of the dermatologic impact of SARS-CoV-2.

CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Ik Jun Moon: 0000-0002-1123-4166
Woo Jin Lee: 0000-0002-0549-464X
Hyun Chang Ko: 0000-0002-3459-5474
Hyojin Kim: 0000-0003-0987-4938
Chan Ho Na: 0000-0001-5259-5382
Joonsoo Park: 0000-0003-1354-2311
Jin Park: 0000-0002-8830-5479
Hyun-Min Seo: 0000-0002-6897-494X
Min Kyung Shin: 0000-0001-9834-7931
Young Bok Lee: 0000-0002-8642-2479
Yong Hyun Jang: 0000-0003-1706-007X
Hye Jung Jung: 0000-0003-0995-5711
Yangwon Lee: 0000-0003-1268-1248

ETHICAL APPROVAL STATEMENT

The study was approved by the Institutional Review Board of (IRB No. 2022-1368). This study was conducted in accordance with the principles of the Declaration of Helsinki.

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Supplementary Table 1. Anatomical distribution of new-onset skin lesions developing after COVID-19 vaccination

	Urticaria / morbilliform rash (n=73)	Eczema (n=55)	Vesicular eruption (n=12)	Psoriasiform dermatitis (n=13)	Acne and folliculitis (n=11)	Hypo-pigmentation (n=4)	Hyper-pigmentation (n=11)	Mass (n=4)	Ulcer and necrosis (n=2)	Herpes zoster (n=6)	Overall (n=191)
Distribution											
Head and neck	27 (36.99)	27 (49.09)	8 (66.67)	5 (38.46)	9 (81.82)	4 (100)	3 (27.27)	3 (75)	0 (0)	1 (16.67)	87 (45.55)
Chest	27 (36.99)	22 (40)	9 (75)	2 (15.38)	4 (36.36)	1 (25)	4 (36.36)	0 (0)	0 (0)	1 (16.67)	70 (36.65)
Abdomen	32 (43.84)	26 (47.27)	7 (58.33)	4 (30.77)	2 (18.18)	1 (25)	6 (54.55)	0 (0)	0 (0)	1 (16.67)	79 (41.36)
Back	37 (50.68)	34 (61.82)	6 (50)	7 (53.85)	2 (18.18)	2 (50)	8 (72.73)	1 (25)	1 (50)	4 (66.67)	102 (53.4)
Perineum	16 (21.92)	15 (27.27)	4 (33.33)	2 (15.38)	1 (9.09)	0 (0)	3 (27.27)	0 (0)	0 (0)	2 (33.33)	43 (22.51)
Buttock	25 (34.25)	21 (38.18)	9 (75)	2 (15.38)	1 (9.09)	1 (25)	2 (18.18)	2 (50)	1 (50)	3 (50)	67 (35.08)
Arms	42 (57.53)	34 (61.82)	10 (83.33)	3 (23.08)	5 (45.45)	2 (50)	8 (72.73)	1 (25)	1 (50)	4 (66.67)	110 (57.59)
Legs	40 (54.79)	36 (65.45)	9 (75)	6 (46.15)	3 (27.27)	2 (50)	7 (63.64)	1 (25)	2 (100)	3 (50)	109 (57.07)
Hands	15 (20.55)	19 (34.55)	5 (41.67)	1 (7.69)	0 (0)	1 (25)	0 (0)	1 (25)	0 (0)	1 (16.67)	43 (22.51)
Feet	14 (19.18)	15 (27.27)	5 (41.67)	1 (7.69)	0 (0)	1 (25)	0 (0)	1 (25)	0 (0)	1 (16.67)	38 (19.9)
Generalized	7 (9.59)	3 (5.45)	2 (16.67)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	12 (6.28)
Symmetrical distribution											
Yes	26 (44.07)	26 (55.32)	4 (30.77)	4 (57.14)	4 (36.36)	0 (0)	5 (45.45)	1 (25)	0 (0)	2 (33.33)	72 (37.7)
No	33 (55.93)	21 (44.68)	9 (69.23)	3 (42.86)	7 (63.64)	4 (100)	6 (54.55)	3 (75)	2 (100)	4 (66.67)	92 (48.17)
Skin lesion on the injection site	9 (12.33)	4 (7.27)	3 (25)	0 (0)	1 (9.09)	0 (0)	2 (18.18)	1 (25)	1 (50)	2 (33.33)	23 (12.04)
Type of vaccine											
Pfizer	38 (52.05)	30 (54.55)	6 (50)	9 (69.23)	6 (54.55)	3 (75)	4 (36.36)	2 (50)	1 (50)	1 (16.67)	100 (52.36)
AZ	10 (13.7)	5 (9.09)	3 (25)	0 (0)	2 (18.18)	1 (25)	1 (9.09)	0 (0)	0 (0)	0 (0)	22 (11.52)
Moderna	25 (34.25)	18 (32.73)	3 (25)	3 (23.08)	3 (27.27)	0 (0)	6 (54.55)	2 (50)	1 (60)	4 (66.67)	65 (34.03)
Janssen	0 (0)	2 (3.64)	0 (0)	1 (7.69)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.67)	4 (2.09)
Total	73 (100)	55 (100)	12 (100)	13 (100)	11 (100)	4 (100)	11 (100)	4 (100)	2 (100)	6 (100)	191 (100)

Supplementary Table 2. Anatomical distribution of new-onset skin lesions developing after COVID-19 infection

	Urticaria / morbilliform rash (n=66)	Vesicular eruption (n=14)	Eczema (n=9)	Chilblain-like change of the acral parts (n=1)	Vasculitis (n=2)	Acne and folliculitis (n=12)	Hair loss (n=21)	Hypo-pigmentation (n=1)	Hyper-pigmentation (n=7)	Ulcer and necrosis (n=1)	Overall (n=134)
Distribution											
Head and neck	34 (51.52)	6 (42.86)	3 (33.33)	0 (0)	1 (50)	12 (100)	20 (95.24)	1 (100)	1 (14.29)	No data	78 (58.21)
Chest	24 (36.37)	8 (57.14)	0 (0)	0 (0)	0 (0)	5 (41.67)	0 (0)	0 (0)	3 (42.86)	No data	40 (29.85)
Abdomen	29 (43.94)	6 (42.85)	2 (22.22)	0 (0)	0 (0)	2 (16.67)	0 (0)	0 (0)	4 (57.14)	No data	43 (32.09)
Back	25 (37.88)	8 (57.14)	3 (33.33)	0 (0)	0 (0)	4 (33.33)	0 (0)	0 (0)	4 (57.14)	No data	44 (32.84)
Perineum	16 (24.24)	3 (21.43)	0 (0)	0 (0)	0 (0)	2 (16.67)	1 (4.76)	0 (0)	1 (14.29)	No data	23 (17.16)
Buttock	21 (31.82)	5 (35.71)	1 (11.11)	0 (0)	0 (0)	2 (16.67)	0 (0)	0 (0)	3 (42.86)	No data	32 (23.88)
Arms	44 (66.67)	13 (92.86)	0 (0)	0 (0)	0 (0)	5 (41.67)	0 (0)	0 (0)	6 (85.71)	No data	68 (50.75)
Legs	41 (62.12)	10 (71.43)	2 (22.22)	0 (0)	1 (50)	3 (25)	0 (0)	0 (0)	7 (100)	No data	64 (47.76)
Hands	15 (22.73)	3 (21.43)	2 (22.22)	1 (100)	1 (50)	2 (16.67)	0 (0)	0 (0)	0 (0)	No data	24 (17.91)
Feet	19 (28.79)	6 (42.86)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (42.86)	No data	28 (20.90)
Symmetrical distribution											
Yes	26 (44.83)	5 (35.71)	4 (44.4)	1 (100)	1(50)	5 (45.45)	2 (11.76)	0 (0)	2 (28.57)	No data	46 (38.33)
No	32 (55.17)	9 (64.29)	5 (55.56)	0 (0)	1 (50)	6 (54.55)	15 (88.24)	1 (100)	5 (71.43)	No data	74 (61.67)
Total	73 (100)	14 (100)	9 (100)	1 (100)	2 (100)	12 (100)	21 (100)	1 (100)	7 (100)	1 (100)	134 (100)

Values are presented as absolute numbers (%)