ORIGINAL REPORT

Exploring the Risk Factors of Rosacea Exacerbation Associated with COVID-19 Infection or Vaccination: A Cross-sectional Study

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COVID-19 can affect the skin, with rosacea flare-ups reported after infection or vaccination. This study compared rosacea patients with and without post-COVID-19 exacerbation to identify contributing factors. A customized electronic questionnaire was administered to rosacea patients, gathering COVID-19 infection/vaccination status, demographics, and rosacea features. Participants were classified by post-COVID-19 rosacea exacerbation vs none. Multivariable logistic regression identified risk factors. Finally, a total of 104 patients were analysed; 15.4% experienced rosacea exacerbation after COVID-19 vaccination and 28.8% after infection. Comorbidities such as metabolic diseases or allergic diseases were associated with a higher risk of rosacea exacerbation after vaccination or infection (OR = 11.083, 95% CI: 1.136–108.135). Burning and stinging symptoms predicted higher exacerbation risk after vaccination (OR = 8.978, 95% CI 1.968–40.969). Papulopustular rosacea was associated with lower risk (OR = 0.276, 95% CI: 0.066–1.160). Higher body mass index (BMI) was associated with lower exacerbation risk after vaccination (OR = 0.646, 95% CI 0.450–0.928) and infection (OR = 0.731, 95% CI: 0.572–0.933). Frequent rosacea episodes increased exacerbation risk after infection (OR = 8.288, 95% CI: 2.044–33.608). In conclusion, lower BMI was associated with higher risk of rosacea exacerbation after COVID-19 vaccination or infection. Patients with burning and stinging symptoms or a non-papulopustular subtype were more likely to experience exacerbation after vaccination.

Key words: COVID-19; COVID-19 vaccination; rosacea; neurogenic inflammation.

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SIGNIFICANCE

COVID-19 can cause worse skin conditions including rosacea. The relationship between COVID-19 and rosacea has not been reported. Patients with rosacea have a risk of exacerbation following COVID-19 infection or vaccination, especially those with metabolic diseases or allergic diseases, burning or stinging sensations, low body mass index (BMI), and the non-papulopustular subtype. Tailored management strategies for rosacea patients are recommended in the context of COVID-19 epidemic.

Rosacea is a chronic skin condition that affects a substantial number of individuals globally, characterized by erythema, inflammatory papules/pustules, phymatous changes, and/or ocular manifestations (1). In addition to the cutaneous damage it causes, rosacea often presents with subjective symptoms such as burning and stinging, significantly impacting patients' quality of life (2). Recent studies indicate that the pathogenesis of rosacea is involved not only with innate and adaptive immune responses but also intricate neurovascular regulation mechanisms (3). Neurovascular dysregulation and alterations in immune responses are recognized as key pathophysiological factors contributing to the clinical manifestations.

Since January 2020, the coronavirus disease 19 (COVID-19) pandemic has been a global emergency, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Apart from affecting the respiratory system, COVID-19 also impacts multiple organ systems, including the skin (4). Excluding anaphylactic reaction caused by the virus, some pre-existing skin diseases are found to be exacerbated following SARS-CoV-2 infection (5, 6), such as rosacea (7, 8). Additionally, COVID-19 vaccine has also been considered a potential trigger of autoimmune reactions. Several cases have reported rosacea-like eruptions after COVID-19 vaccination (9–11). The association between the COVID-19 infection or vaccination and the onset of rosacea suggests their possible involvement in rosacea exacerbation. However, further evidence is needed to establish this relationship conclusively.

As the world is still in the COVID-19 pandemic, it is essential to investigate its impact on patients with rosacea. COVID-19 vaccination confers a certain level of protection against COVID-19, but it also partly mimics the infection of a low-virulence virus (12). This cross-sectional study focused on rosacea patients, analysing the differences in demographic and clinical features between those with and without rosacea exacerbation following

COVID-19 vaccination or infection (13–16). The factors were selected based on prior literature and clinical observations associated with rosacea. The study aimed to explore potential factors influencing the exacerbation of rosacea after COVID-19 infection or vaccination.

MATERIALS AND METHODS

Participants and selection criteria

A cross-sectional survey was conducted among rosacea patients attending outpatient clinics at Shanghai Skin Disease Hospital between August 2023 and February 2024 to assess their COVID-19 infection and vaccination status. The establishment of a clinical diagnosis of rosacea in patients was made through face-to-face interviews and examinations by a trained dermatologist. The collection of COVID-19 data was carried out by collecting questionnaires. Patients were asked to complete an online questionnaire after they agreed to participate in this study. To ensure data quality, at least 1 trained physician was present to provide guidance to patients during questionnaire completion. Eventually, 113 questionnaires were received. This study was approved by the Ethics Committee of the Skin Disease Hospital of Tongji University (2024-31). All patients provided electronic informed consent before the questionnaire interview.

Patients with a clinical diagnosis of rosacea before COVID-19 infection or COVID-19 vaccination were included in this study, regardless of age, gender, and manufacturers of vaccine. Each patient was asked to show evidence related to COVID-19 infection (such as diagnosis in the medical record, antigen or PCR test results) and online record of COVID-19 vaccination. Exclusion criteria included (a) those who refused to provide the informed consent, (b) unable to understand the content of the questionnaire, and (c) with communication barriers.

Questionnaire design

A customized electronic structured questionnaire evaluated by a dermatologist was used. The main contents of the questionnaire were summarized into 5 parts as follows: (*i*) demographic characteristics: age, gender, marriage, body mass index (BMI); (*ii*) rosacea clinical features: disease symptom (based on duration of disease, subtype of rosacea, mean frequency and duration of episodes, phenotypes, comorbidities such as other inflammatory skin diseases, metabolic diseases, mental disease, allergic diseases etc.); (*iii*) exacerbation status following vaccination, vaccination related adverse reactions, aggravation or new symptoms after vaccination (if exacerbation); (*iv*) exacerbation status following infection, aggravation, or new symptoms after COVID-19 infection (if exacerbation); (*v*) relation between exacerbation and mask-wearing: mask-wearing frequency (divided into ≥ 4 h and < 4 h per day), patient self-assessment of association between mask-wearing and rosacea exacerbation (if exacerbation). Rosacea exacerbation was described as the appearance of new symptoms or exacerbation of existing symptoms in 2 weeks.

Screening and grouping

Patients who received at least 1 dose of COVID-19 vaccine and infection with COVID-19 were included in the analysis. Questionnaires with abnormal data were defined as invalid questionnaires and were deleted. After screening, 104 questionnaires were enrolled in the final analysis. Four grouping situations were analysed: (*i*) exacerbation after vaccination vs non-exacerbation after vaccination; (*ii*) exacerbation after infection vs non-exacerbation after infection; (*iii*) exacerbation after vaccination and infection vs non-exacerbation after vaccination and infection; (*iv*) exacerbation after vaccination or infection vs non-exacerbation after vaccination or infection.

Statistical analysis

The statistical analysis in this study was conducted using IBM® SPSS® Statistics 26 (IBM Corp, Armonk, NY, USA). Quantitative variables with normal distribution were described as means ± standard deviation (SD) and were compared using a *t*-test. Quantitative variables with non-normal distributions were summarized as median and interquartile range (IQR), and a non-parametric rank-sum test was done to test the statistical difference between groups. Qualitative variables were expressed as frequencies with proportions (%) and were compared using the χ^2 test or Fisher's exact test. A multivariable logistic regression model was used to detect the independent factors for disease exacerbation among patients with rosacea after vaccination or COVID-19 infection by calculating the odds ratio (OR) and 95% confidence interval (95% CI). Variables with *p*-values less than 0.2 in univariate analysis were included in the multivariable logistic regression model with the adjustment of age, gender, and BMI. In this study, a *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Patient general information

After screening, 104 questionnaires were included in the data analysis (**Fig. 1**). General information on the 104 patients is given in **Table I**. Some 16 (15.4%) patients reported post-vaccination exacerbation and 30 (28.8%) patients reported post-infection exacerbation. Patients who experienced rosacea exacerbation after vaccination were more likely to exacerbate again following COVID-19 infection ($p < 0.001$).

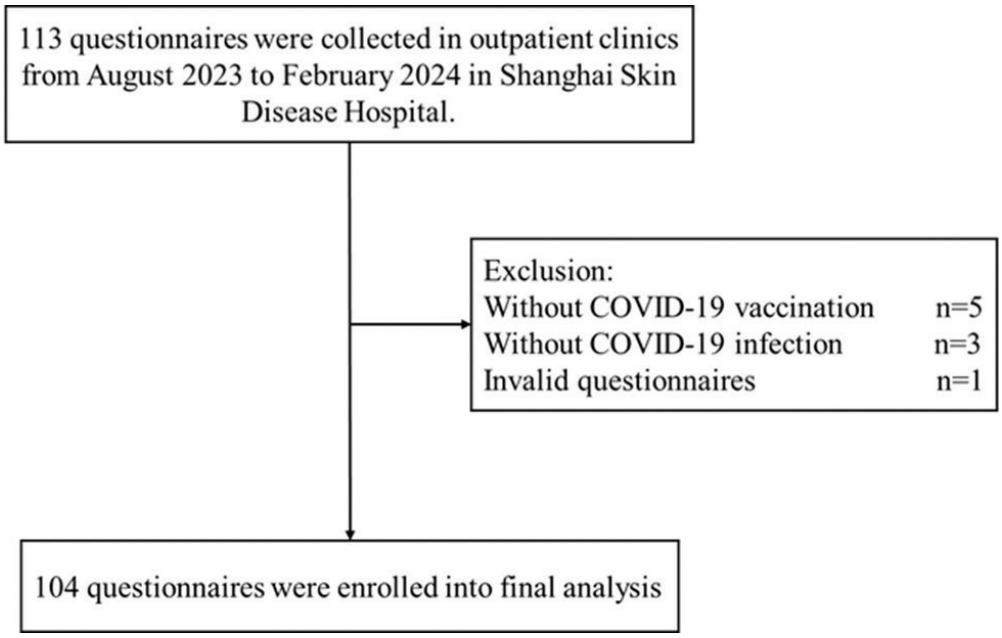

Fig. 1. Flowchart.

Factors associated with rosacea exacerbation after COVID-19 vaccination

Table II presents the univariable and multivariable analyses of potential factors associated with rosacea exacerbation after vaccination. In the univariable analysis, no significant association was observed between age, gender, or marital status and post-vaccination rosacea exacerbation ($p > 0.05$). Patients whose condition was complicated by metabolic diseases or allergic diseases reported more exacerbation of rosacea (12.5% vs 3.4%, 12.5% vs 0), with a significant difference observed in those with allergic diseases ($p = 0.022$). BMI was lower in the exacerbation group compared with the non-exacerbation group (20.16 ± 2.53 vs 21.12 ± 2.85, $p = 0.205$), with a statistically significant association in the multivariable model (OR = 0.646, 95% CI: 0.450–0.928, $p = 0.018$). Regarding disease characteristics, the median disease duration did not differ significantly between groups (18 months [IQR: 7–45] vs 24 months [IQR: 12–48], $p = 0.342$). Patients with papulopustular rosacea (PPR) had a lower risk of exacerbation, however, with no statistically significant association in the multivariable model (OR = 0.276, 95% CI: 0.066–1.160, $p = 0.079$). The frequency and duration of rosacea episodes were similar between groups ($p > 0.05$). Among clinical phenotypes, persistent flushing (56.3% vs 62.5%), transient flushing (68.8% vs 53.4%), papules (43.8% vs 53.4%), pustules (18.8% vs 30.7%), telangiectasia (31.3% vs 39.8%), and dry appearance (25.0% vs 22.7%) did not show significant associations with exacerbation ($p > 0.05$). However, patients experiencing burning or stinging sensations had a significantly increased risk of exacerbation (OR = 8.978, 95% CI: 1.968–40.969, $p = 0.005$). Oedema, phymatous changes, and ocular manifestations were infrequent and not significantly associated with exacerbation. The frequency of wearing masks seems to show no difference between progress patients and non-progress patients ($p > 0.05$). Lastly, vaccination-related adverse reactions were reported more frequently in the exacerbation group (37.5% vs 15.9%), with statistical significance in the multivariable analysis (OR = 5.101, 95% CI: 1.173–22.183, $p = 0.030$).

Factors associated with rosacea exacerbation after COVID-19 infection

Table III summarizes the univariable and multivariable analyses of factors associated with post-infection rosacea exacerbation. In the univariable analysis, age, gender, marital status, and the presence of comorbidities did not show significant associations with rosacea exacerbation ($p > 0.05$). Patients with different comorbidities did not show association with rosacea progression ($p > 0.05$). However, a lower BMI was observed in the exacerbation group (20.09 ± 0.32) compared with the non-exacerbation group (21.34 ± 0.35), and this association remained significant in the multivariable model (OR = 0.731, 95% CI: 0.572–0.933, $p = 0.012$). Disease duration did not significantly differ between groups (22 months [IQR: 7.5–39] vs 24 months [IQR: 12–48], $p = 0.301$). Regarding rosacea subtypes, erythematotelangiectatic rosacea was present in all exacerbation patients (100%) but was not significantly associated with exacerbation ($p = 0.253$). Other subtypes, including papulopustular, phymatous, and ocular rosacea, also did not show significant differences between groups ($p > 0.05$). The frequency of rosacea episodes was significantly asso-

Table I. General information on the 104 patients

Item	Total patients ($n=104$)
Age, years, *n* (%)	
<25	25 (24.0)
≥25	79 (76.0)
Gender, *n* (%)	
Male	7 (6.7)
Female	97 (93.3)
Marriage, *n* (%)	
Married	37 (35.6)
Unmarried/divorce	67 (64.4)
Comorbidity, *n* (%)	
Other inflammatory skin diseases (acne, psoriasis, etc.)	36 (34.6)
Metabolic diseases (type 2 diabetes mellitus, thyroid dysfunction, etc.)	5 (4.8)
Mental disease (depressive disorder, anxiety disorder, etc.)	3 (2.9)
Allergic diseases (rhinitis, asthma, etc.)	2 (1.9)
BMI, kg/m^2, mean±SD	20.93±2.79
Disease duration, months, median (IQR)	24 (12-48)
Subtype of rosacea, *n* (%)	
Erythematotelangiectatic	98 (94.2)
Papulopustular	65 (62.5)
Phymatous	2 (1.9)
Ocular	6 (5.8)
Mean frequency of episodes, *n* (%)	
≤3 times a week	80 (76.9)
>3 times a week	24 (23.1)
Mean duration of episodes, *n* (%)	
≤2 h	70 (67.3)
>2 h	34 (32.7)
Phenotypes, *n* (%)	
Persistent flushing	64 (61.5)
Transient flushing	58 (55.8)
Papules	54 (51.9)
Pustules	30 (28.8)
Telangiectasia	40 (38.5)
Burning or stinging	24 (23.1)
Oedema	10 (9.6)
Dry appearance	24 (23.1)
Phymatous changes	2 (1.9)
Ocular manifestations	6 (5.8)
Daily duration of mask use (hours)	
<4	10 (9.6)
≥4	94 (90.4)
Vaccination related adverse reaction, *n* (%)	20 (19.2)
Post-vaccination exacerbation, *n* (%)	16 (15.4)
Post-infection exacerbation, *n* (%)	30 (28.8)

BMI: body mass index; IQR: interquartile range; SD: standard deviation.

ciated with exacerbation, with more frequent episodes (>3 times per week) being a risk factor in the multivariable analysis (OR=8.288, 95% CI: 2.044–33.608, $p=0.003$). Conversely, shorter episode durations (≤2 h) were associated with a lower risk of exacerbation (OR=0.189, 95% CI: 0.048–0.738, $p=0.017$). Analysis of rosacea phenotypes showed no significant differences in the presence of persistent flushing (63.3% vs 60.8%), transient flushing (63.3% vs 52.7%), papules (50.0% vs 52.7%), pustules (23.3% vs 31.1%), telangiectasia (30.0% vs 41.9%), burning or stinging sensations (23.3% vs 23.0%), oedema (6.7% vs 10.8%), and phymatous changes (3.4% vs 1.4%) ($p>0.05$). However, patients with a dry skin appearance were less likely to experience disease exacerbation in the multivariable model (OR=0.255, 95% CI: 0.068–0.954, $p=0.042$). No difference was found in the frequency of mask-wearing between the 2 groups ($p>0.05$).

Factors associated with rosacea exacerbation after COVID-19 vaccination and/or infection

The combinatory analysis of the post-vaccination and post-infection exacerbation groups showed consistent results (Tables SI and SII). Patients whose condition was complicated by metabolic diseases (OR=11.083, 95% CI: 1.136–108.135) or allergic diseases ($p=0.012$) reported more exacerbation of rosacea. When considering exacerbation after vaccination and infection vs non-exacerbation after vaccination and infection, BMI was significantly lower in the exacerbation group (19.37±1.76 vs 21.19±2.87, $p=0.035$), and this remained significant in the multivariable analysis (OR=0.630, 95% CI: 0.427–0.931, $p=0.020$). Regarding rosacea subtypes, the papulopustular form was less frequent in exacerbation patients (33.3% vs 66.3%), showing a significant association with lower exacerbation risk (OR=0.169, 95% CI: 0.040–0.712, $p=0.015$). The frequency and duration of episodes, as well as specific phenotypic features such as flushing, papules, pustules, telangiectasia, and burning sensations, did not show significant associations with exacerbation ($p>0.05$). When considering exacerbation after vaccination or infection vs non-exacerbation after vaccination or infection, similar to previous findings, BMI was lower in the exacerbation group (20.37±2.06 vs 21.27±3.09, $p=0.127$) and was a significant predictor in the multivariable model (OR=0.705, 95% CI: 0.549–0.905, $p=0.006$). Patients with more frequent episodes (>3 times per week) had a higher likelihood of exacerbation in the univariable analysis (35.3% vs 17.1%, $p=0.039$) with statistical significance in the multivariable model ($p=0.034$). No difference was found in the frequency of mask-wearing between the 2 groups ($p>0.05$).

Disease characteristics of rosacea exacerbation

Persistent erythema and transient flushing were the most commonly reported exacerbated or newly emerged symptoms in patients experiencing rosacea exacerbation following COVID-19 vaccination or infection (Fig. S1). Notably, patients with post-infection rosacea exacerbation exhibited a higher prevalence of newly developed papules and pustules compared with those with post-vaccination exacerbation (Fig. S1). Furthermore, the majority of patients (88.2%) reported that their symptom exacerbation could not be solely attributed to the increased frequency of mask-wearing during the COVID-19 pandemic. Importantly, neither the mean frequency nor the mean duration of rosacea episodes changed significantly following symptom exacerbation ($p>0.05$).

DISCUSSION

COVID-19 has significantly impacted human health, including dermatological conditions like rosacea. Our

Table II. Univariable and multivariable analysis of factors in post-vaccination exacerbation patients

	Univariable			Multivariable	
Variables	Progress patients ($n=16$)	Non-progress patients ($n=88$)	p-value	OR (95% CI)	p-value
Age, years, *n* (%)			1.000	1.179 (0.287–4.840)	0.819
<25	4 (25.00)	21 (23.1)			
≥25	12 (75.00)	67 (76.1)			
Gender, *n* (%)			1.000	0.645 (0.057–7.355)	0.724
Male	1 (6.3)	6 (6.8)			
Female	15 (93.8)	82 (93.2)			
Marriage, *n* (%)			0.458		
Married	7 (43.8)	30 (34.1)			
Unmarried/divorce	9 (56.3)	58 (65.9)			
Comorbidity, *n* (%)					
Other inflammatory skin diseases (acne, psoriasis, etc.)	6 (37.5)	30 (34.1)	0.792		
Metabolic diseases (type 2 diabetes mellitus, thyroid dysfunction, etc.)	2 (12.5)	3 (3.4)	0.168	6.991 (0.492–99.249)	0.151
Mental disease (depressive disorder, anxiety disorder, etc.)	0 (0)	3 (3.4)	1.000		
Allergic diseases (rhinitis, asthma, etc.)	2 (12.5)	0 (0)	**0.022**		
BMI, kg/m^2, mean±SD	20.16±2.53	21.12±2.85	0.205	0.646 (0.450–0.928)	**0.018**
Disease duration, months, median (IQR)	18 (7–45)	24 (12–48)	0.342		
Subtype of rosacea, *n* (%)					
Erythematotelangiectatic	16 (100)	82 (93.2)	0.587		
Papulopustular	7 (43.8)	58 (65.9)	0.092	0.276 (0.066–1.160)	0.079
Phymatous	1 (6.3)	1 (1.1)	0.285		
Ocular	0 (0)	6 (6.8)	0.587		
Mean frequency of episodes, *n* (%)					
≤3 times a week	12 (75.0)	68 (77.3)	1.000		
>3 times a week	4 (25.0)	20 (22.7)			
Mean duration of episodes, *n* (%)					
≤2 h	11 (68.8)	59 (67.0)	0.894		
>2 h	5 (31.3)	29 (33.0)			
Phenotypes, *n* (%)					
Persistent flushing	9 (56.3)	55 (62.5)	0.636		
Transient flushing	11 (68.8)	47 (53.4)	0.256		
Papules	7 (43.8)	47 (53.4)	0.477		
Pustules	3 (18.8)	27 (30.7)	0.503		
Telangiectasia	5 (31.3)	35 (39.8)	0.519		
Burning or stinging	7 (43.8)	17 (19.3)	0.070	8.978 (1.968–40.969)	**0.005**
Oedema	0 (0)	10 (11.4)	0.338		
Dry appearance	4 (25.0)	20 (22.7)	1.000		
Phymatous changes	1 (6.3)	1 (1.1)	0.285		
Ocular manifestations	0 (0)	6 (6.8)	0.587		
Daily duration of mask use (hours)					
<4	4 (25.0)	20 (22.7)	1.000		
≥4	12 (75.0)	68 (77.3)			
Vaccination-related adverse reaction	6 (37.5)	14 (15.9)	0.095	5.101 (1.173–22.183)	**0.030**

BMI: body mass index; IQR: interquartile range; SD: standard deviation. Bolded fonts indicate a statistically significance (p-value less than 0.05).

study identified an association between COVID-19 infection and vaccination and rosacea exacerbation: 28.8% of rosacea patients reported symptoms exacerbation following COVID-19 infection and 15.4% after vaccination. This aligns with case reports and prior studies reporting post-COVID-19 infection or vaccination skin reactions and disease aggravation (17–19). Notably, patients who experienced a rosacea flare after vaccination were more likely to flare again following COVID-19 infection ($p<0.001$). These findings suggest that viral-induced immune dysregulation and systemic alterations may contribute to rosacea pathogenesis, warranting further investigation.

Patients reporting baseline burning or stinging sensations were more likely to experience rosacea exacerbations after COVID-19 vaccination, which may reflect underlying neuroimmune dysfunction, vascular hyperreactivity, and heightened cytokine responses (20, 21). COVID-19 vaccines often contain toll-like receptor (TLR) agonists that activate NF-κB and elevate proinflammatory cytokines IL-1β, IL-6, and TNF-α (22, 23), which stimulate TRPV1 nociceptors and induce release of neuropeptides (CGRP, VIP), intensifying burning and stinging sensations (24). In rosacea, CGRP is upregulated, promoting neurogenic inflammation by activating γδ T cells, which secrete IFN-γ and IL-17. IL-17 drives keratinocyte activation, neutrophil recruitment, and angiogenesis, contributing to erythema and papulopustular lesions, while IFN-γ enhances macrophage activation, exacerbating inflammation (23, 25). Increased CGRP release post-vaccination, a mechanism also implicated in vaccine-induced migraines, may further aggravate neurovascular inflammation (25, 26). Given the abundance of γδ T cells and CGRP receptors (RAMP1) in rosacea lesions, excess CGRP can amplify neuroimmune dysregulation and worsen rosacea symptoms. However, we did not observe a significant increase in burning/stinging in infection-related exacerbations, possibly because a

Table III. Univariable and multivariable analysis of factors in post-infection exacerbation patients

	Univariable			Multivariable	
Variables	Progress patients ($n = 30$)	Non-progress patients ($n = 74$)	p-value	OR (95% CI)	p-value
Age (years), *n* (%)					
< 25	5 (16.7)	20 (27.9)	0.263	3.097 (0.892–10.754)	0.075
≥ 25	25 (83.3)	54 (73.0)			
Gender, *n* (%)			0.654	1.024 (0.081–12.899)	0.985
Male	1 (3.3)	6 (8.1)			
Female	29 (96.7)	68 (91.9)			
Marriage, *n* (%)					
Married	19 (63.3)	48 (64.9)	0.882		
Unmarried/divorced	11 (36.7)	26 (35.1)			
Comorbidity, *n* (%)					
Other inflammatory skin diseases (acne, psoriasis, etc.)	8 (26.7)	28 (37.8)	0.278		
Metabolic diseases (type 2 diabetes mellitus, thyroid dysfunction, etc.)	3 (10.0)	2 (2.7)	0.285		
Mental disease (depressive disorder, anxiety disorder, etc.)	0 (0)	3 (4.1)	0.555		
Allergic diseases (rhinitis, asthma, etc.)	2 (6.7)	0 (0)	0.081		
BMI (kg/m^2), mean ± SD	20.09 ± 1.73	21.34 ± 3.09	**0.005**	0.731 (0.572–0.933)	**0.012**
Disease duration (months), median (IQR)	22 (7.5–39)	24 (12–48)	0.301		
Subtype of rosacea, *n* (%)					
Erythematotelangiectatic	30 (100)	68 (91.9)	0.253		
Papulopustular	17 (56.7)	48 (64.9)	0.434		
Phymatous	1 (3.3)	1 (1.4)	0.496		
Ocular rosacea	3 (10.0)	3 (4.1)	0.475		
Mean frequency of episodes, *n* (%)			**0.036**	8.288 (2.044–33.608)	**0.003**
≤ 3 times a week	19 (63.3)	61 (82.4)			
> 3 times a week	11 (36.7)	13 (17.6)			
Mean duration of episodes, *n* (%)					
≤ 2 h	23 (76.7)	47 (63.5)	0.195	0.189 (0.048–0.738)	**0.017**
> 2 h	7 (23.3)	27 (36.5)			
Phenotypes, *n* (%)					
Persistent erythema	19 (63.3)	45 (60.8)	0.811		
Transient flushing	19 (63.3)	39 (52.7)	0.323		
Papules	15 (50.0)	39 (52.7)	0.803		
Pustules	7 (23.3)	23 (31.1)	0.429		
Telangiectasia	9 (30.0)	31 (41.9)	0.259		
Burning or stinging	7 (23.3)	17 (23.0)	0.968		
Oedema	2 (6.7)	8 (10.8)	0.778		
Dry appearance	4 (13.3)	20 (27.0)	0.133	0.255 (0.068–0.954)	**0.042**
Phymatous changes	1 (3.4)	1 (1.4)	0.496		
Ocular manifestations	3 (10.0)	3 (4.1)	0.475		
Daily duration of mask use (hours)					
< 4	7 (23.3)	19 (25.7)	0.803		
≥ 4	23 (76.7)	55 (74.3)			

BMI: body mass index; IQR: interquartile range; SD: standard deviation.

higher proportion of those cases were PPR (56.7% vs 43.8%), which might mask these sensations. Further studies are needed to clarify this discrepancy.

Skin dryness – indicative of reduced sebum production – may modulate rosacea exacerbation risk through microbiome and immune effects. Demodex mites rely on sebum and trigger inflammation via TLR2; hence, lower sebum might reduce Demodex density and attenuate this inflammatory stimulus, potentially mitigating rosacea flares after COVID-19 infection or vaccination (27). Beyond microbial factors, COVID-19 can disrupt lipid metabolism by increasing bile acid levels and decreasing triglycerides. In patients with higher sebum output, excess bile acids could activate the GPBAR1 (TGR5) receptor and exacerbate inflammation (28, 29). Additionally, sebaceous lipids (e.g., squalene and wax esters) serve as CD1a ligands, stimulating CD1a-autoreactive T cells, and fuel skin inflammation (30). In dry skin, reduced CD1a antigen presentation may limit T cell activation, dampening the inflammatory cascade that could otherwise worsen rosacea post-infection or vaccination. These findings highlight lipid dysregulation as a key factor in post-infection rosacea exacerbation, particularly in individuals with increased sebaceous gland activity.

Rosacea subtype also influenced exacerbation risk. Patients with PPR had a lower risk of disease exacerbation following COVID-19 vaccination or infection, possibly due to its distinct pathophysiology: PPR lesions show persistent IL-1β elevation and MAPK/TNF pathway activation (31, 32). As COVID-19 vaccination and infection also upregulate these inflammatory markers (33), PPR patients might be less reactive to additional systemic immune stimulation (i.e., a form of tolerance).

There was no significant difference in rosacea progression with the duration of mask-wearing per day, consistent with findings from some previous studies (8, 34). However, other studies suggested prolonged exposure time may be a significant risk factor for rosacea aggravation (35, 36). Our findings indicate a potential

independent association between COVID-19 vaccination or infection and rosacea progression.

In this study, a lower BMI was significantly associated with an increased risk of rosacea exacerbation following COVID-19 infection or vaccination. Additionally, patients with rosacea progression exhibited a significantly greater prevalence of comorbidities such as diabetes mellitus and asthma. These findings suggest that both body composition and systemic health factors may play a role in the worsening of rosacea. Mechanistically, obesity is associated with reduced vaccine-induced immunity (37). In contrast, individuals with a very low body mass index may exhibit an exaggerated inflammatory response to infections or vaccinations, potentially triggering rosacea flares (38). Moreover, BMI is closely associated with metabolic and cardiovascular diseases, which may contribute to the development of rosacea through shared underlying mechanisms such as chronic low-grade inflammation, insulin resistance, and vascular dysfunction. Although our multivariable model was adjusted for metabolic comorbidities, BMI remained an independent predictor. Additionally, the limited number of patients with comorbidities in our cohort undermines the robustness of these findings and precludes a comprehensive evaluation of the independent and interactive effects of specific systemic conditions. Despite these limitations, our results suggest that a low BMI may independently contribute to the risk of rosacea exacerbation under immune activation. Further verification in larger and more diverse populations is necessary to confirm these findings.

Limitations

This study is limited by its single-centre design and small sample size, which constrain generalizability. By 2023, 95.2% of adults had either been vaccinated or infected with SARS-CoV-2, making it virtually impossible to find rosacea patients unexposed to COVID-19 or vaccination during 2021–2023. This pervasive exposure complicates attribution of rosacea flares specifically to COVID-19 triggers, though it mirrors real-world post-pandemic conditions. We used an unvalidated questionnaire and relied on self-reported symptom exacerbations, introducing potential recall and reporting biases. To minimize patient burden, we did not collect information on other possible triggers (e.g., stress or diet), which is another limitation. Future multi-centre studies with larger cohorts, validated tools, and objective measures of rosacea activity are needed to confirm these findings and elucidate underlying mechanisms.

Conclusion

Our findings underscore rosacea's complex systemic nature. Immune disturbances from COVID-19 infection or vaccination can exacerbate rosacea, suggesting that other infections or immunologic stimuli might similarly provoke flares. Notably, vaccination appears to pose a lower risk of exacerbation than infection. Vaccination and other preventive measures remain important, but clinicians should stay vigilant for rosacea flares and manage at-risk patients proactively after COVID-19 vaccination or infection.

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