Impact of COVID-19 on the Risk of Developing Dermatological Conditions

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Abstract
Introduction: The COVID-19 pandemic, caused by SARS-CoV-2, has impacted global health across various medical domains, including dermatology. Dermatological manifestations are increasingly recognized in COVID-19 patients. This study aimed to evaluate the risk of developing dermatological conditions in patients with COVID-19 compared to non-COVID patients.
Methods: This retrospective cohort study analyzed electronic health records (EHRs) from January 1, 2020, to January 1, 2022, including two cohorts: COVID-19 patients with confirmed diagnoses and non-COVID patients. The primary outcome was the development of new dermatological conditions within three months of the index date. Risk differences and risk ratios (RRs) were calculated to compare the cohorts. Confounding factors such as age, sex, race, and ethnicity were controlled during the statistical analysis. Statistical significance was set at $p < 0.05$.
Results: COVID-19 patients exhibited a significantly reduced risk for various dermatological conditions, including acne vulgaris (RR = 0.671), atopic dermatitis (RR = 0.649), and seborrheic dermatitis (RR = 0.606), among others. Certain rarer conditions, such as lichen planus (RR = 0.585) and basal cell carcinoma (RR = 0.517), also showed a decreased incidence. However, pallor was significantly more prevalent in COVID-19 patients (RR = 2.328), suggesting systemic vascular involvement.
Conclusion: The findings indicate a reduced risk for many dermatological conditions in COVID-19 patients, possibly due to immune modulation and vascular alterations by the virus. Pallor's increased prevalence in these patients underscores the broader systemic effects of COVID-19. These results contribute to our understanding of COVID-19's dermatological impacts, offering insights for better patient management and future research into the long-term effects on skin health.

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Keywords: COVID-19, Dermatological manifestations, Risk assessment

Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has posed unprecedented challenges to global health since its emergence in Wuhan, China, in December 2019 [1]. As of June 1, 2022, over 540 million confirmed cases and more than 6 million deaths have been reported worldwide, highlighting the virus's high transmissibility and substantial morbidity and mortality rates [2].

Clinically, COVID-19 exhibits a wide spectrum of manifestations, ranging from asymptomatic infections to severe respiratory illness characterized by acute respiratory distress syndrome (ARDS), multi-organ failure, and death [3]. Common symptoms include fever, dry cough, fatigue, sputum production, shortness of breath, loss of smell (anosmia), and loss of taste (ageusia) [4]. Beyond respiratory involvement, SARS-CoV-2 infection has been associated with various extrapulmonary effects, including cardiovascular, renal, neurological, gastrointestinal, and dermatological manifestations [5].

Dermatological manifestations in COVID-19 patients have garnered increasing attention, with estimated incidence rates between 4% and 20% among infected individuals [6]. These cutaneous findings are diverse and can include maculopapular eruptions, urticarial rashes, vesicular lesions, chilblain-like acral lesions (often referred to as "COVID toes"), and vascular phenomena such as livedo reticularis and necrosis [7]. The underlying mechanisms for these skin manifestations are not yet fully understood. Proposed theories suggest direct viral invasion of skin cells expressing angiotensin-converting enzyme 2 (ACE2) receptors, immune system hyperactivity leading to cytokine release, microthrombi formation, and vasculitis [5].

To systematically document and analyze these dermatological presentations, organizations like the American Academy of Dermatology (AAD) and the International League of Dermatological Societies (ILDS) have established online registries [8]. These registries aim to capture a broad spectrum of skin lesions associated with SARS-CoV-2 infection, aiding in the characterization and understanding of COVID-19-related dermatological conditions [8].

Currently, there is a lack of comprehensive studies comparing the risk of developing specific dermatological conditions in patients with COVID-19 versus those without the infection. Understanding this relationship is crucial for several reasons. Firstly, it can enhance clinical awareness, allowing healthcare providers to recognize skin manifestations as potential indicators of SARS-CoV-2 infection, especially in cases where respiratory symptoms are absent or minimal. Secondly, it can improve patient management by facilitating timely diagnosis and appropriate treatment of skin conditions associated with COVID-19. Lastly, it contributes to public health efforts by aiding in the early detection and isolation of infected individuals, thereby helping to control the spread of the virus. As such, in this study we evaluate the risk of developing various dermatological conditions in patients with COVID-19 and those without COVID-19.

Methods

This retrospective cohort study utilized data extracted from electronic health records (EHRs) of patients with healthcare encounters between January 1, 2020, and January 1, 2022. The study population consisted of patients aged 0 to 80 years who had at least one documented healthcare visit during the study period. Two cohorts were formed: the COVID-19 cohort, which included patients with a confirmed COVID-19 diagnosis, and the non-COVID cohort, composed of patients with no recorded history of COVID-19. The primary objective was to assess the development of new dermatological conditions within three months of the index date, defined as the date of COVID-19 diagnosis for the COVID-19 cohort and the date of the healthcare encounter for the non-COVID cohort. This was determined by conducting a retrospective review of the patients' medical records. Patients with pre-existing dermatological conditions before the index date, as well as those with incomplete medical records, were excluded from the study.

The primary outcome measure was the proportion of patients in each cohort who developed a new dermatological condition during the three-month follow-up period. To compare the risk of developing dermatological conditions between the two cohorts, risk differences were calculated. Additionally, risk ratios (RRs) were used to quantify the relative risk of developing a dermatological condition in the COVID-19 cohort compared to the non-COVID cohort. A risk ratio (relative risk) estimates the likelihood of a health event by dividing the incidence rate in the COVID-19 cohort by the incidence rate in the non-COVID cohort. To control for potential confounding factors, such as age, sex, race, and ethnicity, these variables were adjusted for during statistical analysis to ensure the robustness of the results.

All statistical analyses were performed using R version 4.0.2. Risk ratios (RRs) and risk differences were computed for each dermatological condition, with 95% confidence intervals (CIs) provided to assess the precision of the estimates. A p-value of less than 0.05 was considered statistically significant.

Results

Patients with COVID-19 exhibited a significantly reduced risk for a wide range of dermatological conditions when compared to non-COVID patients. These included acne vulgaris (RR = 0.671), atopic dermatitis (RR = 0.649), rosacea (RR = 0.65), and seborrheic dermatitis (RR = 0.606) (Figure 1). Other conditions with reduced risk included contact dermatitis (RR = 0.704), vitiligo (RR = 0.552), melasma (RR = 0.479), and tinea unguium (RR = 0.72) (Figure1). Additionally, there was a reduced risk for alopecia areata (RR = 0.682), lichen planus (RR = 0.585), basal cell carcinoma (RR = 0.517), and squamous cell carcinoma (RR = 0.647).

Further reduced risks were observed for perioral dermatitis (RR = 0.749), pityriasis rosea (RR = 0.536), actinic keratosis (RR = 0.448), pityriasis versicolor (RR = 0.563), and seborrheic keratosis (RR = 0.411) (Figure 1). Rarer conditions such as pyogenic granuloma (RR = 0.647), granuloma annulare (RR = 0.712), lichen sclerosus et atrophicus (RR = 0.607), and prurigo nodularis (RR = 0.667) also demonstrated reduced risk in COVID-19 patients (Figure 1). Moreover, xerosis cutis (RR = 0.837) and tinea pedis (RR = 0.748) were less frequent in COVID-19 patients compared to non-COVID patients.

In contrast, pallor was notably more common in patients with COVID-19, with a significant increase in risk (RR = 2.328), highlighting it as one of the few conditions with an elevated risk in this patient population.

Table 1: Comparison of dermatological condition risks between patients with COVID-19 and those without COVID-19. The table presents the risk percentages of various dermatological conditions in both cohorts, showing the risk difference between patients with and without COVID-19. The 95% confidence intervals (CIs), p-values, and risk ratios (RRs) are provided to indicate statistical significance and the relative risk comparison

S.no	Condition	Risk in Patients with COVID-19	Risk in Patients without COVID-19	Risk Difference	95 % CI	*p*	Risk Ratio	95 % CI
1	Acne vulgaris	0.097%	0.144%	-0.05%	(-0.057%,-0.037%)	0.0001	0.671	(0.617,0.73)
2	Atopic dermatitis	0.092%	0.142%	-0.050%	(-0.06%,-0.04%)	0.0001	0.649	(0.595,0.706)
3	Rosacea	0.041%	0.062%	-0.022%	(-0.028%,-0.015%)	0.0001	0.65	(0.572,0.739)
4	Seborrheic dermatitis	0.089%	0.146%	-0.058%	(-0.067%,-0.048%)	0.0001	0.606	(0.556,0.66)
5	Contact dermatitis	0.085%	0.121%	-0.036%	(-0.045%,-0.027%)	0.0001	0.704	(0.644,0.77)
6	Vitiligo	0.006%	0.010%	-0.005%	(-0.007%,-0.002%)	0.0002	0.552	(0.401,0.761)
7	Melasma	0.021%	0.043%	-0.022%	(-0.027%,-0.017%)	0.0001	0.479	(0.406,0.565)
8	Tinea unguium	0.109%	0.151%	-0.042%	(-0.052%,-0.032%)	0.0001	0.72	(0.666,0.779)
9	Alopecia areata	0.009%	0.012%	-0.004%	(-0.007%,-0.001%)	0.0059	0.682	(0.519,0.897)
10	Lichen planus	0.005%	0.009%	-0.004%	(-0.006%,-0.001%)	0.0014	0.585	(0.419,0.816)
11	Basal cell carcinoma	0.031%	0.060%	-0.029%	(-0.035%,-0.023%)	0.0001	0.517	(0.451,0.593)
12	Squamous cell carcinoma	0.018%	0.028%	-0.010%	(-0.014%,-0.006%)	0.0001	0.647	(0.537,0.78)
13	Perioral dermatitis	0.019%	0.025%	-0.006%	(-0.01%,-0.002%)	0.0021	0.749	(0.622,0.901)
14	Pityriasis rosea	0.006%	0.012%	-0.006%	(-0.008%,-0.003%)	0.0001	0.536	(0.398,0.721)
15	Actinic keratosis	0.052%	0.117%	-0.064%	(-0.072%,-0.056%)	0.0001	0.448	(0.405,0.496)
16	Pityriasis versicolor	0.017%	0.030%	-0.013%	(-0.017%,-0.009%)	0.0001	0.563	(0.468,0.678)
17	Seborrheic keratosis	0.113%	0.275%	-0.162%	(-0.174%,-0.15%)	0.0001	0.411	(0.383,0.44)
18	Pyogenic granuloma	0.004%	0.007%	-0.002%	(-0.004%,0%)	0.0233	0.647	(0.443,0.945)
19	Granuloma annulare	0.009%	0.012%	-0.003%	(-0.006%,-0.001%)	0.0204	0.712	(0.534,0.95)
20	Lichen sclerosus et atrophicus	0.009%	0.014%	-0.006%	(-0.009%,-0.002%)	0.0004	0.607	(0.459,0.803)
21	Prurigo nodularis	0.008%	0.012%	-0.004%	(-0.007%,-0.001%)	0.0073	0.667	(0.495,0.898)
22	Xerosis cutis	0.088%	0.105%	-0.017%	(-0.026%,-0.008%)	0.0002	0.837	(0.762,0.919)
23	Pallor	0.014%	0.006%	0.008%	(0.005%,0.011%)	0.0001	2.328	(1.697,3.193)
24	Tinea pedis	0.046%	0.061%	-0.015%	(-0.022%,-0.009%)	0.0001	0.748	(0.659,0.849)

Discussion

The findings from this analysis reveal a notable reduction in the risk of various dermatological conditions in patients with COVID-19 compared to those without the infection. This trend highlights the complex interplay between SARS-CoV-2 and the skin, potentially linked to the virus's unique effects on immune regulation, inflammation, and vascular function.

Reduced Risk of Inflammatory Dermatoses

The significantly lower risk of inflammatory skin conditions, such as acne vulgaris, atopic dermatitis, rosacea, and seborrheic dermatitis, in COVID-19 patients can be partly explained by SARS-CoV-2's broad tropism for cells expressing the angiotensin-converting enzyme 2 (ACE2) receptor. This receptor is found not only in respiratory tissues but also in other tissues, including the skin [5]. The virus's ability to bind to ACE2 receptors may disrupt normal immune responses in these tissues. Moreover, the cytokine storm induced by the virus likely alters immune signaling pathways, reducing inflammatory processes that normally drive these dermatoses [9]. This immune modulation could suppress or alter pathways that contribute to chronic inflammatory skin conditions like contact dermatitis and lichen planus, which also showed reduced incidence in COVID-19 patients.

Lower Incidence of Skin Cancers and Pre-Cancerous Lesions

Interestingly, the analysis shows a reduced risk of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and actinic keratosis (AK) in patients with COVID-19. These findings may reflect immune-modulatory effects of the virus, as recent research suggests that viral infections can alter the skin's tumor microenvironment and immune surveillance, thereby affecting cancer development [10]. Moreover, it is possible that SARS-CoV-2 infection modifies the activity of pathways involved in cell growth and repair, leading to a temporary reduction in the initiation or progression of these skin cancers. Additionally, during the pandemic, many patients avoided outdoor activities, leading to reduced UV exposure—a key risk factor for AK, BCC, and SCC.

Reduced Risk of Autoimmune and Other Skin Conditions

Autoimmune-driven skin conditions such as alopecia areata and lichen planus were also less common in COVID-19 patients, supporting the notion that the virus may suppress immune-mediated damage. Conditions like pityriasis rosea and granuloma annulare, which involve immune dysregulation, were similarly reduced in the COVID-19 cohort. These observations point to a potential interaction between SARS-CoV-2 and autoimmune mechanisms, suggesting that the virus may downregulate specific immune pathways involved in these conditions [11].

Increased Risk of Pallor

In contrast, pallor was notably more common in COVID-19 patients, which is consistent with reports of vascular involvement and anemia in COVID-19 [12]. The virus's impact on blood flow and its ability to cause endothelial dysfunction may lead to hypoxia and reduced tissue perfusion, which can manifest as pallor. Additionally, systemic inflammation and viral effects on hematopoiesis can result in anemia, further contributing to pallor in these patients.

Conclusion

This study demonstrates a significant reduction in the risk of several dermatological conditions, including inflammatory

skin diseases, autoimmune disorders, and certain skin cancers, in patients with COVID-19 compared to those without the infection. These findings highlight an important association between COVID-19 and altered dermatological health. In contrast, pallor was notably more common in COVID-19 patients, underscoring the virus's potential systemic effects. These insights provide a foundation for further investigation into the long-term impact of SARS-CoV-2 on skin health and emphasize the importance of recognizing dermatological manifestations in managing COVID-19 patients.

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