Cutaneous Reactions Among Thai COVID Patients: A Preliminary Questionnaire-based Study

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Abstract

COVID-19 outbreak was an emerging disease since 2019. Despite respiratory symptoms, cutaneous manifestations related with COVID-19 was increasingly reported worldwide. The prevalence and morphology of skin eruptions in Asia, particularly in Thailand were lacking. Limited data have been reported. This retrospective, observational study was conducted to assess the prevalence and patterns of COVID-associated cutaneous eruptions, hair loss, and exacerbation of preexisting skin diseases among Thai patients. The online survey was developed using Google Form and distributed via social media platforms between November and December 2022. One hundred post-infected participants completed the survey. Our study discovered that within one month after infection, 6% of Thai patients developed cutaneous lesions. Regarding COVID-19 related cutaneous presentations, maculopapular and urticaria were the most common lesions. There was only one case of papulovesicles and petechiae rash. Vesicular, livedo and pseudo-chilblain were not found in any participants. According to the study, COVID-19 associated cutaneous eruptions revealed a lower prevalence than reports from other continents. Maculopapular and urticaria were common clinical patterns among Thais. In contrast, pseudo-chilblain, a condition commonly seen in Europeans, was not observed in our study.

Keywords: *SAR-CoV-2, COVID-19, Rash, Thai*

1. Introduction

Known as COVID-19, the novel Coronavirus disease was caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SAR-CoV-2). The very first outbreak was reported in Wuhan, China, in December 2019. By March 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic (Ochani et al., 2021).

COVID-19 is a highly contagious disease and the incubation period had been reported around 1-14 days. It was transmitted from human to human by airborne transmission. During COVID-19 infection, a wide range of clinical manifestations existed, ranging from asymptomatic presentation to critical illness with respiratory failure or multiorgan dysfunction. Common clinical presentations were non-specific upper respiratory tract symptoms. As a result of infection, a patient may experience fever, fatigue, cough, rhinorrhea, shortness of breath, and myalgia. Acute illness may cause ageusia or anosmia in some individuals (Ochani et al., 2021; Tsai et al., 2021).

Aside from respiratory symptoms, patients with COVID-19 may also experience a number of extrapulmonary symptoms, including cardiac dysfunction, acute coronary syndrome, thromboembolism, acute kidney injury, impaired hepatic function, neurological deficits, and dermatological complications (Tsai et al., 2021).

From literature review, A total of 4-20.4% of infected patients presented with skin manifestations in relation to COVID-19.(Huynh, Sanchez-Flores, Yau, & Huang, 2022) According to the morphology of rashes, six clinical patterns can be distinguished, including urticarial rash, maculopapular or morbiliform rash, papulovesicular rash, pseudochilblain rash, livedo rash, and purpuric vasculitis rash.(Arefinia, Ghoreshi, Alipour, Iranmanesh, Mehrolhasani, Shamsi-Meymandi, & Sarvari, 2022; Genovese, Moltrasio, Berti, & Marzano, 2021; Li, Wen, Mu, Du, & Han, 2022) Other rare COVID-19-related skin conditions that have been

seen are including ertyhema multiforme-like eruption, pityriasis rosea-liked rash, kawasaki-liked and multisystem inflammatory syndrome in children (Wang & Worswick, 2021).

As compared to European studies, Asian studies have reported lower prevalence and different clinical patterns of cutaneous manifestations.(Li et al., 2022; Tamai, Maekawa, Goto, Ge, Nishida, Iwahashi, & Yokomi, 2020). Therefore, the purpose of this study is to evaluate the prevalence of skin abnormalities associated with COVID-19 illness among Thai patients.

2. Objectives

1) To assess the prevalence of cutaneous manifestations among COVID patients in Thailand
2) To assess the clinical features of cutaneous manifestations in among COVID patients in Thailand

3. Materials and Methods

This is a retrospective, cross-sectional, observational study conducted in Thailand as an online survey between November 2022 - December 2023. An open ended, self-reported questionnaire was used in this study to examine cutaneous manifestations during COVID infection among Thai individuals.

The study was carried out at Benchakitti Park Hospital and Sukhumvit Hospital, Bangkok, Thailand. To reach potential participants, the poster was promoted in both outpatient Department (OPD) and Inpatient Department (IPD). In addition, to recruit participants online, the poster and link/QR code were shared through the Line OA of Home Isolation Projects and various social media platforms.

The standardized survey was developed as an online survey tool using Google Forms and reviewed by board certified dermatologists. The survey consists of three main sections, including demographic data, COVID-19 data, and cutaneous data. Links or Quick Response codes (QR codes) to the questionnaire were distributed to Thai post-COVID patients via social media and online platforms. The inclusion criteria were as follows: 1) Thai post-infected patients with positive antigen test kit (ATK) or Real-time polymerase chain reaction (RT-PCR) results 2). Adults over the age of 18 3) Be able to read and understand the Thai language. The patient would select one clinical pattern that was most similar to his/her lesion if cutaneous eruptions appeared within the first month after diagnosis. Moreover, participants with any changes to their hair or skin can upload photographs to the platform.

Categorical data were expressed in frequency and percentage, whereas median and interquartile range were used for continuous data. All statistics in this study were computed by IBM SPSS statistics version 29.0.0.0

4. Results and Discussion

4.1 Results

A total of 100 post-COVID-19 patients participated in this study. According to Table 1, all patients had the following demographic characteristics. In terms of age, the median participant was 32 years old (IQR 32-46 years old). A majority of cases were female, accounting for 61% of all cases.

According to the National Institutes of Health guideline, COVID-19 severity was classified into five subgroups: asymptomatic, mild, moderate, severe, and critical (NIH, 2023). Asymptomatic patients were those who had tested positive for SAR-CoV-2 but did not exhibit any clinical symptoms. Mild symptoms were present in patients who had developed symptoms but not lower respiratory symptoms. Moderate severity was characterized by the development of abnormal lower respiratory symptoms, an abnormal chest X-ray, and a SpO2 level of at least 94%. Severe cases were identified as patients with a SpO2 level below 94% or pulmonary infiltration greater than or equal to 50%. Finally, critical patients were those who experienced respiratory failure during the infection. Regarding our findings, the majority of participants had mild symptoms (60%), while 22% had moderate symptoms. Asymptomatic and severe groups each represented 7% of the participants. There were no critically ill patients reported in our study.

According to Thai COVID-19 vaccination status, any patients who got at least two doses of eligible vaccines were referred to complete vaccination. The approved COVID-19 vaccines required either two doses

of Coronavac or AstraZeneca, Comirnaty or mRNA-1273. To address the urgent need to contain the spread of the virus, the administration allowed the combination of different vaccines, such as starting with Coronavac followed by AstraZeneca or Comirnaty. Ones who did not complete 2 doses of primary series of vaccines were labelled with incomplete vaccination (Ministry of public health of Thailand, 2021). In our report, 99% of the participants were fully vaccinated with any kind of COVID-19 vaccine. Meanwhile, no patient had received only one dose of COVID-19 vaccination. Only one person refused to receive the vaccine.

Table 2 Clinical characteristics of COVID-19 patients

Clinical characteristics	**Total (%)**
Age	32 (IQR 30-46)
Gender	
Male	39 (39)
Female	61 (61)
Disease severity	
Asymptomatic	7 (7)
Mild	60 (60)
Moderate	22 (22)
Severe	7 (7)
Critical	0
Vaccination	
None	1 (1)
Partial vaccination	0 (0)
Complete vaccination	99 (99)

4.1.1 Cutaneous manifestations

As a result of the study, 6 participants (6% of the 100 participants) experienced abnormal cutaneous eruptions during COVID-19 illness, which were classified into 2 categories. These are depicted in Table 2 as Group 1: relevant manifestations, and Group 2: other. The relevant findings represented abnormal cutaneous eruptions that had been indicated as COVID skin sign. While, other manifestations accounted for any eruptions that not directly caused by COVID. According to our study, maculopapular lesions were the most prevalent in Thai individuals, accounting for 2 cases. Another most common symptom was urticaria, which was also reported by 2 patients. There was only one case reported with petechiae eruptions. Among post-COVID-19 participants, there was neither vesicles, livedo, and pseudo-chilblain observed.

As a final observation, one case developed a maculopapular eruption. A diagnosis of Favipiravir allergy has been made in this patient, which resolved spontaneously with symptomatic treatment.

Table 2 Morphologies of cutaneous manifestations

Cutaneous manifestations	Total (%)
Total	6 (6)
Relevant manifestations	
Maculopapules	2 (33.33)
Urticaria	2 (33.33)
Vesicles	0 (0)
Petechaie/purpura	1 (16.67)
Livedo	0 (0)
Pseudo-chilblain	0 (0)
Others	
Drug eruption	1 (16.67)

4.2 Discussion

Initial outbreaks of COVID-19 occurred in Wuhan, China and rapidly spread to other parts of the world. Thailand was the very first country to record a confirmed case outside republic of China in mid-January 2020 (Srisawat, Iamsirithaworn, Tantawichien, & Thisyakorn, 2021).

As the number of patients with COVID-19 increased, associated skin manifestations were identified. Based on data collected from European countries, cutaneous eruptions may occur in up to 20% of all cases of infection (Recalcati, 2020). In Asia, some researchers have found that the incidence was much lower. It was reported in a study from China that only 0.18 percent of patients post-COVID-19 had concurrent rash during their infection (Guan et al., 2020). There has been speculation that differences in race and genetics may contribute to Asian participants' decreased incidence of COVID-19-related cutaneous eruptions (Punyaratabandhu & Chirachanakul, 2021). Our study revealed cutaneous complications in approximately 6% of the subjects. Another observational study conducted in Thailand reported a prevalence of 2.45%, 8%, respectively (Punyaratabandhu & Chirachanakul, 2021; Rerknimitr et al., 2020).

Similarly to previous observational studies in Thailand, maculopapular and urticaria were the most common cutaneous features (Punyaratabandhu & Chirachanakul, 2021; Rerknimitr et al., 2020). Even though, the data from Freeman et al. (2020) revealed almost one fifth of confirmed cases in Europe developed clinical of chilblain liked. In our study, we found that there were no instances of pseudo-chilblain seen among Thai individuals. Some researcher hypothesized that difference in climate, or a less virulent strain of the virus, may contribute this phenomenon of lower prevalence of chilblain in Asian (Rerknimitr et al., 2020). Apart from pseudo-chilblain, there was also no report of any vesicular lesions, pityriasis rosea-liked, erythema multiforme-liked in any of our participants. In our point of view, due to our small sample size and the low rate of these eruptions, the lesions were not visible in our report.

Several theories have been proposed to explain the mechanism of common COVID-19-related cutaneous eruptions. It has been hypothesized that maculopapular rashes are caused by secondary immune responses to the SAR-CoV-2 virus, which may correspond with the viremia phase (Tan, Tam, & Oh, 2021). As regards urticaria, pathogenesis had been associated with direct mast cell degranulation, bradykinin release, and complement activation (Do, Stewart, & Harp, 2021). A research found that petechiae or purpuric eruptions may result from endothelial damage caused by viruses or dysregulated immune responses. In some cases of purpuric rash, thrombocytopenia or disseminated intravascular coagulation may be present (Do et al., 2021; Genovese et al., 2021). As a result of a literature review, it was unclear how pseudochilblain develops. According to Garcia-Lara, Linares-González, Ródenas-Herranz, & Ruiz-Villaverde (2020) peripheral edema and erythema of toes were caused by vasospasm, immune dysregulation, vessel thrombosis, vasculitis, and neoangiogenesis mechanisms. Similarly to chilblain-like lesions, livedo eruptions can be followed by thrombosis within the infected endothelium with the SAR-CoV-2 virus that resulted in reticulated erythematous rings (Conforti et al., 2020).

Of the 46 patients who received Favipiravir therapy, only one patient experienced a maculopapular rash eruption, which represented 2.2% of the total sample. Research had indicated that the incidence of cutaneous adverse reactions to Favipiravir was generally low, with most reports documenting mild reactions, such as maculopapular rashes and urticaria. There had been some instances where major adverse eruptions have been observed. According to a review of the literature, there had been one report of Steven-Johnson syndrome and one report of angioedema (Ergur Ozturk, Ozturk, & Ates, 2022; Punyaratabandhu & Vanitchpongphan, 2022; Sriwijitalai & Wiwanitkit, 2022). Given the rising incidence of cutaneous eruptions, it is of utmost importance for physicians to investigate potential drug causes in these individuals. Despite the lower incidence of drug allergy compared to COVID rash, the reactions can be life-threatening. Therefore, if a drug eruption was suspected, the responsible medication must be immediately discontinued to treat the patient's potentially fatal condition.

This study was a preliminary questionnaire-based survey to determine the prevalence and characteristics of COVID-related skin eruptions among individuals in Thailand. Our results were consistent with those of previous studies. However, additional data collection is needed to establish more precise incidence rates and identify specific features of the eruptions. In our future work, we plan to explore potential

associations between demographic factors and the prevalence of cutaneous lesions. These findings will help to expand our understanding of COVID-related skin manifestations and inform clinical practice.

There were some limitations in our study. Firstly, our sample size was small. We planned to collect more data in further study to gain more information about COVID-19 rash in Thai population. Secondly, this was a retrospective observational study. The survey needed participants to recall their abnormal cutaneous events during a month of infection which may be unreliable due to recall bias. One last limitation was self-reported questionnaire. Since physicians could not assess the skin lesions carefully, the report may be unreliable

5. Conclusion

According to the study, COVID-19 associated cutaneous eruptions revealed a lower prevalence than reports from other continents. Maculopapular and urticaria were common clinical patterns among Thais. In contrast, pseudo-chilblain, a condition commonly seen in Europeans, was not observed in our study.

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