



Facial dermatoses and use of protective mask during Covid-19 pandemic: A clinical and psychological evaluation in patients affected by moderate–severe atopic dermatitis under treatment with dupilumab

Mazzoletti Vanessa¹ | Esposto Elia¹ | Veronese Federica²  |
Cammarata Edoardo³  | Airoidi Chiara⁴ | Graziola Francesca² | Savoia Paola¹

¹Department of Health Sciences, University of Eastern Piedmont, Novara, Italy

²SCDU Dermatologia, AOU Maggiore della Carità, Novara

³SSD Dermatologia e Allergologia, Ospedale Beauregard, Aosta, Italy

⁴Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy

Correspondence

Federica Veronese, SCDU Dermatologia, AOU Maggiore della Carità, C.so Mazzini 18, 28100 Novara, Italy.

Email: federica.veronese@med.uniupo.it

Abstract

During the SARS-COV-2 pandemic, using face masks became mandatory in many countries. Although evidence suggests that masks can exacerbate several inflammatory skin diseases, few studies focus on their real impact on eczema localized to the face in atopic dermatitis (AD) patients. The aim of this study is to evaluate facial eczema prevalence during pandemic and its psychological impact in AD patients pre-assessed for systemic treatment and/or in therapy with dupilumab. This study includes 71 patients affected by moderate–severe AD, treated with dupilumab at SCDU of Dermatology in Novara, Italy. We calculated the number of subjects with facial involvement in pre- and post-pandemic periods and the related localization trend. We evaluated, in the two groups, clinical and psychological indicators recorded at each visit and the score modifications during the observational period. No statistically significant differences were observed in facial eczema prevalence, between pre- and post-pandemic periods ($p = 0.7618$) and in facial eczema remission among the two groups ($p = 0.1903$). In post-pandemic period, psychological scores were significantly lower (DLQI and HADS respectively with $p < 0.0001$ and $p = 0.0025$) and the reduction in EASI score during observational period was significantly greater ($p = 0.0001$). Our analysis revealed a potential protective effect of masks on face eczema, suggesting that they could enhance dupilumab efficacy. Face masks, covering sensitive areas, can positively contribute to mental distress in patients with facial eczema, and being associated with a lower allergic diseases incidence may sustain dupilumab in reducing AD severity.

KEYWORDS

atopic dermatitis, Covid-19, dupilumab, face mask, facial dermatoses

Vanessaa Mazzoletti and Elia Esposto contributed equally to the present work.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2022 The Authors. *Dermatologic Therapy* published by Wiley Periodicals LLC.

1 | INTRODUCTION

The severe acute respiratory infection caused by SARS-COV-2 (Covid-19), emerged in China in December 2019, and subsequently spread around the world.¹

Because the main SARS-COV-2 transmission route is by respiratory droplets, even from asymptomatic and pre-symptomatic patients,² one of the control measures to minimize the risk of infection is the routine use of respiratory protective equipment (RPE), such as face masks; in particular, surgical masks blocking large particles and FFP2 face masks blocking almost 95% of 0.3-micron particles.^{1,3,4}

During the pandemic a growing number of countries (including USA and many European Union areas) introduced the mandatory use of the face mask in public areas. So, wearing masks quickly became a daily routine in most countries.^{1,2}

The impact on the skin of this personal protective equipment was considerable, and several dermatological manifestations associated with RPE increased in the pandemic context: specific face areas, in particular cheeks, back of the nose, and ears, have been affected by adverse skin reactions.²

Han et al³ evaluated changes in skin characteristics after the use of RPE (KN94 masks—equivalent to European FFP2 masks—and surgical masks) among health care workers. They observed that skin hydration, trans-epidermal water loss (TEWL), skin rash, skin temperature, sebum secretion, and pH, increase over time in RPE-covered areas. In addition, they observed that after a night without RPE use, an increase in hydration, TEWL, sebum secretion, and pH persists. These phenomena can be due to continuous exhalation and prolonged occlusion, resulting in local humidity and sweating increase and leading to local disruption of the skin barrier, which can contribute to the development of various dermatoses related to mask use. In fact, RPE-covered skin may become more susceptible to various allergens or chemical irritants contained in facial masks, with an increased risk of allergic contact dermatitis.^{1,3}

Although the incomplete or absent disclosure of chemicals used in RPE manufacture probably do not allow to identify many relevant allergens, among molecules responsible for RPE-related allergic contact dermatitis are described: rubber accelerators and antioxidants, such as N-isopropyl-N-phenyl paraphenylenediamine (in mask elastics), nickel, and cobalt metal ions (in metal wires to shape face masks), polyurethanes (in sponge strips), adhesive chemicals, such as methyl dibromo glutaronitrile, formaldehyde and other preservatives.^{4,5}

Irritant contact dermatitis (ICD), on the other hand, derives from cytotoxic damage due to direct contact with chemical substances or physical irritants and its severity depends on irritant and on chronic exposure. People with atopic history are more susceptible to irritants because they already have a skin barrier defect. During pandemics, hands are the most frequent site of work-related ICD, but many reports show involvement of cheek and nasal dorsum, mainly due to prolonged mask exposure.⁴

Furthermore, Hye and Jiade have been shown that increasing pH levels leads to a loss of both epidermal barrier homeostasis and non-specific skin antimicrobial defense, with consequent skin irritation and

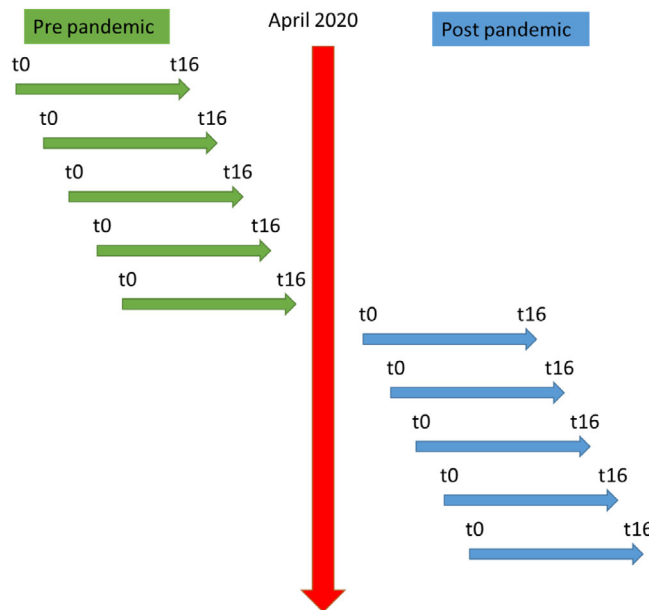


FIGURE 1 Graphic representation of the two study groups, before and after the mandatory use of mask in the population

infections increased risk.^{3,4} Precisely, the importance of skin integrity, in terms of both physical and homeostatic barrier and antimicrobial defense, has led us to hypothesize a positive correlation between face mask use in atopic dermatitis (AD) patients (intrinsically characterized by epidermal dysfunction) and the onset of facial eczema during Covid-19 pandemic.

In particular, the aim of our study is to evaluate the prevalence of facial eczema in AD patients pre-assessed for systemic treatment with dupilumab in the Covid-19 phase, and in those already on therapy. The current Covid-19 pandemic is raising many doubts about the management of chronic immunosuppressive and target dermatological therapies. Recently, the European Task Force on Atopic Dermatitis has not considered dupilumab as a drug able to increase the risk for viral infections and, thus, should be preferred over conventional systemic immuno-suppressive treatments (cyclosporine, corticosteroids) during current Covid-19 pandemic.⁶ As a secondary objective, we set the analysis of psychological scores, assuming to find worse scores among the subjects evaluated in the Covid-19 era.

2 | MATERIALS AND METHODS

In our retrospective analysis, we included all the patients aged ≥ 18 y/o, affected by moderate–severe AD and treated with dupilumab at the SCU of Dermatology in Novara, Italy, from 2018 until the end of 2021.

To assess the Covid-19 pandemic impact on the disease, two distinct time periods were considered: (i) pre-pandemic, in which pre-assessment dermatological evaluation, dupilumab initiation and the 16-weeks follow-up visit were performed before April 01, 2020 and (ii) post-pandemic, which includes patients enrolled after April

01, 2020. This date was chosen to define a cut-off time distinguishing the phases preceding and following the mandatory mask use (Figure 1) and were collected from the database of our AD patients.

2.1 | Statistical analysis

First, we calculated the absolute and relative number of subjects with facial involvement in pre-pandemic and post-pandemic periods. To analyze if, between the two groups, there were differences in terms of improvement, worsening, or clinical stability of facial eczema, at t16, the facial dermatitis localization trend (variation between t0 and t16) was compared within the two groups of patients, using the Chi-Square or Fisher Exact test, as appropriate.

In addition, clinical and psychological indicators (EASI, POEM, NRS sleep, NRS pruritus, DLQI, HADS) relating to the disease and recorded both at baseline and at follow-up visit were evaluated; we calculated, with a *t*-test, score differences at initial visit (t0), both in the pre-pandemic and in the post-pandemic period, to assess if the two patient groups presented with different clinical-psychological conditions.

Subsequently, we assessed score modifications from t0 to t16 between the two groups through ANCOVA models.

The significance value was set at two-tailed 0.05 and the analysis was performed using SAS 9.4 software.

3 | RESULTS

Overall, patients affected by moderate-severe AD treated with dupilumab at our Division from December 2018 to December 2021 were 71.

Of these, 36 patients underwent evaluation in the pre-pandemic period (before April 1, 2020) and 28 in the pandemic period (after April 1, 2020); 7 patients were excluded because their t0 and t16 were, respectively, in the pre-pandemic and post-pandemic period. So, we included in our study 64 subjects.

First of all, it was investigated for each group the number of patients with facial involvement at t0; despite the hypothesis that in the post-pandemic period this condition was more frequent due to the mask use, no statistically significant differences emerged between the two periods (p -value = 0.7618). In fact, in the pre-pandemic group, 29 out of 36 subjects (80.56%) had facial involvement at t0, compared to 21 out of 28 subjects (75%) in the pandemic group.

Furthermore, it was compared whether the percentages, for each combination of the second group, differ in terms of statistical significance compared to those of the first group. It emerged that, among patients with facial involvement at t0, remission was obtained in 32% in the post-pandemic period, compared with approximately 28% in the pre-pandemic period. However, this difference was not statistically significant (p -value 0.1903, Table 1).

Table 2 shows clinical indicators (EASI, POEM, NRS pruritus, and NRS sleep) and psychological indicators (DLQI and HADS) relative to AD, analyzed between the two groups at t0.

The scores concerning the clinical evaluations were almost homogeneous, without statistically significant differences between the two groups. On the contrary, the scores concerning the psychological assessments were significantly lower in the post-pandemic period (DLQI and HADS: respectively, p -value <0.0001 and p = 0.0025, see Table 2). Particularly, the DLQI and HADS scores were lower by about 10 and 7 points between post- and pre-pandemic, respectively. This result is not only statistically significant but it points out also a clinically relevant difference.

Finally, we evaluated differences in clinical and psychological behaviors (in terms of improvement or worsening), from t0 and t16, between the two study groups. The reduction in the EASI score (and therefore the clinical benefit as can be seen in Figure 2) between t0 and t16 was significantly greater in the pandemic period with about 4 points lower, while no significant variations were observed as regards the other parameters (Table 3).

4 | DISCUSSION

Several publications concerning inflammatory skin diseases worsened by RPE have been recently disclosed in literature.⁷⁻¹¹ Notably, face masks can cause adverse facial dermatoses and exacerbate underlying dermatology conditions, like acne, rosacea, and seborrheic dermatitis.⁷⁻⁹ However, very few studies focus on the impact of masks on face eczema in AD patients. It is universally known that AD pathophysiology is based on skin barrier dysfunction¹² and can therefore be speculated a possible correlation between prolonged face mask use, during pandemic, and the onset of facial eczema in AD patients. Based on these assumptions we compared patients affected by moderate/severe AD under treatment with dupilumab at our Clinic in the pre-pandemic and pandemic period.

Considering current studies,⁷⁻¹¹ we might have expected a higher prevalence of patients with facial eczema in the group taken in charge and treated in the post-pandemic period, because of mask use; however, our analysis did not reveal statistically significant differences between the two periods (p -value = 0.7618). This result is, however, only apparently in contrast with literature: previous studies, have reported that AD patients are more prone to adverse face skin reactions but these assessments have been limited to healthcare workers (HCWs) who wear masks daily and for several consecutive hours. A study conducted in Germany during the SARS-COV-2 pandemic, on facial mask dermatitis in the general population, demonstrated that there was no increase in symptoms in participants with atopic diathesis.² Our results can therefore be justified by the fact that the sample examined did not include HCWs, but only patients with non-continuous use of the mask.

Furthermore, we investigated whether facial masks can affect the dupilumab efficacy in inducing facial eczema remission. We observed that masks do not compromise the treatment efficacy: among patients with facial involvement at t0, almost half healed in the post-pandemic period, compared to about one third of the subjects in the pre-pandemic period, but this difference is not statistically significant. This

TABLE 1 Outline of the study design

	t0	t16	Pre-pandemic (n = 36)	Post-pandemic (n = 28)
Face	No	No	5 (13.89%)	7 (25.00%)
		Yes	2 (5.56%)	0
	Yes	No	10 (27.78%)	9 (32.14%)
		Yes	19 (52.78%)	12 (42.86%)

TABLE 2 Clinical and psychological AD indicators analyzed between the two groups at T0. Means and standard deviations are reported

	Pre-pandemic t0	Post-pandemic t0	p-Value
EASI	27.53 (4.71)	26.57 (7.38)	0.5531
POEM	21.81 (5.96)	20.41 (6.59)	0.3822
NRS pruritus	8.42 (1.61)	8.36 (1.68)	0.8861
NRS sleep	6.50 (2.86)	6.64 (2.51)	0.8353
DLQI	23.06 (5.03)	13.14 (7.53)	<0.0001
HADS	20.06 (10.43)	13.04 (7.19)	0.0025

TABLE 3 Differences in clinical and psychological behaviors (in terms of improvement or worsening), from t0 and t16, between the two study groups. Means and standard deviations are reported, and p-values derived from ANCOVA analysis

	Pre-pandemic Δ	Post-pandemic Δ	p-Value
EASI	-17.83 (4.88)	-21.46 (6.78)	0.0001
POEM	-13.69 (7.61)	-12.56 (7.36)	0.9172
NRS pruritus	-5.06 (2.93)	-5.11 (3.01)	0.8583
NRS sleep	-4.06 (3.03)	-4.89 (3.45)	0.2267
DLQI	-18.78 (6.76)	-9.25 (6.43)	0.3428
HADS	-11.19 (10.05)	-4.19 (6.08)	0.1738

**FIGURE 2** (1A, 1B) Young female with severe face eczema at t0 and at t16, respectively; (2A, 2B) another young woman with facial involvement pre-assessed for systemic therapy and at 16-weeks follow-up visit. Both patients were evaluated in the post-pandemic period

result could simply be justified to the small sample examined; however, we can also hypothesize that mask use may even have a protective role. Specific climatic conditions, in particular low humidity levels and low temperatures, can trigger atopic eczema frequency (AD flare-up). In the northern hemisphere, newborn exposure to cold and dry seasons—such as autumn and winter—can facilitate AD development.^{13,14} Therefore, moderate use of masks, increasing local heat and humidity, could enhance dupilumab effectiveness with face eczema resolution.

In this paper, we also compared clinical-psychological conditions at baseline between patients enrolled in the two different periods. While clinical scores (EASI, POEM, NRS pruritus, and NRS sleep) were homogeneous, psychological ones were different. In everyday practice it is easy to find clinical pictures which, although not excessively extensive, do however, involve visible areas (such as face) and therefore have a negative impact on patient quality of life. The RPE has been shown to have a mild to moderate influence on the quality of life in most HCWs, and DLQI scores are worse in those with skin symptoms related to device use¹⁵; so, we would have expected a worse mental health status in the pandemic period. On the contrary, significantly lower DLQI and HADS scores were recorded, compared to those in the pre-pandemic group (p -value <0.0001 and p -value = 0.0025). These data agree with those reported by Merhand et al: the French Eczema Association examined the impact of masks on daily life in AD patients and showed, surprisingly, that wearing RPE can improve quality of life, allowing them to hide their dermatoses.¹⁶ Therefore, despite a comparable AD severity, mental distress appears to be lower within the pandemic group: this may partially be explained by the fact that social distancing and the use of the face mask outside

the home reduce the discomfort resulting from the presence of lesions on visible areas, such as the face. This confirms the negative role of AD on the life-quality of affected patients and underlines the importance of including the psychological indicators in clinical practice.¹⁷ The combined use of these scores could offer a broader overview of the impact of AD on quality of life, integrating skin examination with health as perceived by the patient, representing a valuable support in the process of choosing therapy and response to treatment.¹⁸

Finally, after 16 weeks of dupilumab treatment, a better clinical improvement was observed in the pandemic group, with a statistically significant difference (Δ EASI post-pandemic = 21.46 vs. Δ EASI pre-pandemic = 17.83, p -value ANCOVA = 0.0001). Choi et al evaluated allergic asthma and rhinitis incidence in adolescents before and after the SARS-COV-2 pandemic in Korea. In 2020, because of wearing masks which reduces airborne particles exposure, the incidence of these allergic diseases decreased statistically significantly, while they did not observe differences in the incidence of atopic dermatitis.¹⁹ In our study population, mask use, together with physical isolation measures such as "smart working" and confinement to own home (lock-down), can potentially have contributed to minimizing allergic diseases related to atopic diathesis; thus, in patients treated with dupilumab, it may have resulted in a greater reduction in atopic dermatitis severity at t16.

In conclusion, our analysis did not reveal differences in facial eczema prevalence between AD patients evaluated before and after the COVID19 pandemic. The main difference compared to the studies published so far in the literature is represented by a sample of patients that excluded HCWs, therefore with non-continuous use of the mask. In our experience, face masks use has not a negative impact on face eczema and, due to the local heat and humidity increase and to the protective effect from cold and dry weather, could enhance dupilumab effectiveness.

The lower scores of DLQI and HADS in the post-pandemic patient group highlighted that, in patients affected by dermatoses localized in sensitive and visible areas, physical isolation and the possibility to cover them with masks, can positively contribute to patients' mental distress.

Finally, an important EASI improvement was recorded in post-pandemic subjects and then, mask use is probably associated with disease control and reduction of exposure to allergens and air pollutants, decreasing allergic asthma and rhinitis. A lower allergic diseases incidence in patients treated with dupilumab may have contributed to a more important reduction in atopic dermatitis severity.

However, our sample includes a limited number of patients and to confirm our data, further studies regarding mask impact on AD subjects will be needed.

AUTHOR CONTRIBUTIONS

Conceptualization: Federica Veronese. **Data curation:** Vanessa Mazzeletti, Elia Esposto. **Formal analysis:** Chiara Airoidi; **Investigation:** Federica Veronese, Francesca Graziola. **Methodology:** Paola Savoia, Federica Veronese. **Supervision:** Paola Savoia, Federica Veronese.

Validation: Paola Savoia. **Writing—original draft:** Vanessa Mazzeletti, Elia Esposto. **Writing—Review & Editing:** Paola Savoia, Federica Veronese, Edoardo Cammarata. All authors have read and agreed to the submitted version of the manuscript.

ACKNOWLEDGMENTS

The authors thank all patients who participated to this study; all of them have given written informed consent to publication of their case details. Open Access Funding provided by Università degli Studi del Piemonte Orientale Amedeo Avogadro within the CRUI-CARE Agreement.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions. The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Veronese Federica  <https://orcid.org/0000-0001-6438-5171>

Cammarata Edoardo  <https://orcid.org/0000-0002-7844-6956>

REFERENCES

- İnan Doğan E, Kaya F. Dermatological findings in patients admitting to dermatology clinic after using face masks during Covid-19 pandemic: a new health problem. *Dermatol Ther*. 2021;34(3):e14934. doi:10.1111/dth.14934
- Niesert AC, Opiel EM, Nellesen T, et al. "Face mask dermatitis" due to compulsory facial masks during the SARS-CoV-2 pandemic: data from 550 health care and non-health care workers in Germany. *Eur J Dermatol*. 2021;31(2):199-204. doi:10.1684/ejd.2021.4007
- Han HS, Shin SH, Park JW, Li K, Kim BJ, Yoo KH. Changes in skin characteristics after using respiratory protective equipment (medical masks and respirators) in the COVID-19 pandemic among healthcare workers. *Contact Dermatitis*. 2021. doi:10.1111/cod.13855
- Yu J, Chen JK, Mowad CM, et al. Occupational dermatitis to facial personal protective equipment in health care workers: a systematic review. *J Am Acad Dermatol*. 2021;84(2):486-494. doi:10.1016/j.jaad.2020.09.074
- Xie Z, Yang YX, Zhang H. Mask-induced contact dermatitis in handling COVID-19 outbreak. *Contact Dermatitis*. 2020;83(2):166-167. doi:10.1111/cod.13599
- Wollenberg A, Flohr C, Simon D, et al. European task force on atopic dermatitis statement on severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) infection and atopic dermatitis. *J Eur Acad Dermatol Venerol*. 2020;34(6):e241-e242.
- Damiani G, Gironi LC, Grada A, et al. COVID-19 related masks increase severity of both acne (maskne) and rosacea (mask rosacea): multi-center, real-life, telemedical, and observational prospective study. *Dermatol Ther*. 2021;34(2):e14848. doi:10.1111/dth.14848
- Damiani G, Gironi LC, Pacifico A, et al. COVID-19 dermatologic Italian task force, young dermatologists Italian network. Masks use and facial dermatitis during COVID-19 outbreak: is there a difference between CE and non-CE approved masks? Multi-center, real-life data from a large Italian cohort. *Ital J Dermatol Venerol*. 2021;156(2):220-225. doi:10.23736/S2784-8671.21.06895-4

9. Thatiparthi A, Liu J, Martin A, Wu JJ. Adverse effects of COVID-19 and face masks: a systematic review. *J Clin Aesthet Dermatol*. 2021; 14(9 suppl 1):S39-S45.
10. Kaul S, Kaur I, Jakhar D. Facial mask-related acne and acneiform eruption during the coronavirus disease 2019 pandemic: a case series. *J Clin Aesthet Dermatol*. 2021;14(10):32-34.
11. Skiveren JG, Ryborg MF, Nilausen B, Bermark S, Philipsen PA. Adverse skin reactions among health care workers using face personal protective equipment during the coronavirus disease 2019 pandemic: a cross-sectional survey of six hospitals in Denmark. *Contact Dermatitis*. 2021;86:266-275. doi:10.1111/cod.14022
12. Kim J, Kim BE, Leung DYM. Pathophysiology of atopic dermatitis: clinical implications. *Allergy Asthma Proc*. 2019;40(2):84-92. doi:10.2500/aap.2019.40.4202
13. Ibekwe PU, Ukonu BA. Impact of weather conditions on atopic dermatitis prevalence in Abuja. *Nigeria J Natl Med Assoc*. 2019;111(1):88-93. doi:10.1016/j.jnma.2018.06.005
14. Sendrasoa FA, Ranaivo IM, Razanakoto NH, et al. Epidemiology and associated factors of atopic dermatitis in Malagasy children. *Allergy Asthma Clin Immunol*. 2020;16:4. doi:10.1186/s13223-019-0398-2
15. Daye M, Cihan FG, Durduran Y. Evaluation of skin problems and dermatology life quality index in health care workers who use personal protection measures during COVID-19 pandemic. *Dermatol Ther*. 2020;33(6):e14346. doi:10.1111/dth.14346
16. Merhand S, Misery L, Delvigne V, Le Floch C, Taïeb C. Wearing a mask and skin disease: patients with atopic dermatitis speak it out. *J Eur Acad Dermatol Venereol*. 2021;35(3):e185-e187. doi:10.1111/jdv.16917
17. Stingeni L, Marietti R, Tramontana M, Bianchi L, Hansel K. Patient-reported outcomes in adult atopic dermatitis are useful in both clinical trials and real-life clinical practice. *J Eur Acad Dermatol Venereol*. 2022;36(3):326-327. doi:10.1111/jdv.17956
18. Russo F, Flori ML, Gola M, Milanese N. Severe adult atopic dermatitis: clinical challenges. *Dermatitis*. 2020;31(4):e48-e49.
19. Choi HG, Kong IG. Asthma, allergic rhinitis, and atopic dermatitis incidence in Korean adolescents before and after COVID-19. *J Clin Med*. 2021;10(15):3446. doi:10.3390/jcm10153446

How to cite this article: Vanessa M, Elia E, Federica V, et al. Facial dermatoses and use of protective mask during Covid-19 pandemic: A clinical and psychological evaluation in patients affected by moderate-severe atopic dermatitis under treatment with dupilumab. *Dermatologic Therapy*. 2022;35(7): e15573. doi:10.1111/dth.15573