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Title: COVID-19 related masks increase severity of both acne (Maskne) and rosacea (Mask rosacea): Multi-center, real-life, telemedical, observational prospective study

Running head: Maskne and Mask rosacea

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ABSTRACT

Background

Masks are essential for COVID-19 prevention, but recently they were suggested to modify cutaneous facial microenvironment and trigger facial dermatoses.

Objective

To evaluate mask- related rosacea and acne (maskne) in untreated patients during lockdown

Methods

In this multi-center, real-life, observational prospective study, we enrolled stable, untreated acne and rosacea patients that wore masks during lockdown at least 6h/day. They underwent two teledermatological consultations, at the baseline and after 6 weeks. Clinical, pharmacological and psychological data were recorded.

Results

A total 66 patients, 30 (median age: 34.0 [30.25-29.75] yoa) with acne and 36 patients (median age: 48 [43-54] years) with rosacea, were enrolled in this study. After 6 weeks of mask and quarantine, patients with acne displayed an increased Global Acne Grading Scale (GAGS) score in mask-related areas ($P<0.0001$). Likewise, after 6 weeks of mask and quarantine, patients with rosacea displayed a worsen in both physician ($P<0.0001$) and patient ($P<0.0001$) reported outcomes. Remarkably, patients reported also a statistically significant decrease in their quality of life ($P<0.0001$).

Conclusions

masks appear to trigger both acne and rosacea flares. Additional studies are needed to generate evidence and inform clinical decision-making.

Keywords: COVID-19, pandemics, mask rosacea, maskne, rosacea due to masks, acne due to masks.

INTRODUCTION

During COVID-19 pandemics, the introduction of personal protective equipments (PPE), such as masks and gloves, drastically changed facial and hand dermatoses dermatoepidemiology [1, 2]. Focusing on facial dermatoses, Hua and colleagues evaluated the short-term cutaneous impact of wearing surgical masks (SM) and PPE on the skin finding a relevant modification in the level of

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hydration, trans-epidermal water loss, pH, erythema and sebum production [3]. Masks are usually coupled with dressing and moisturizers to prevent both dehydration and pressure ulcers [4], but topical agents may be comedogenic and detrimental for pre-existing facial inflammatory dermatoses, especially for acne [5]. In fact, maskne or mask-related acne is a well-recognized comorbidity due to PPE during COVID-19 pandemic both in healthcare workers [6] and less in the general population [7]. At the same time, rosacea may be also triggered by the cutaneous modification due to masks, but no conclusive data available [2].

During the first Italian lockdown several patients refused to attend dermatological visits [8,9] and discontinued lifesavings therapies [10], offering an opportunity for the evaluation of mask-triggered facial dermatoses with teledermatology.

MATERIALS AND METHODS

This is a prospective observational study focusing on patients with acne vulgaris and rosacea that involved three primary dermatology referral centers with a telemedicine service in Italy (IRCCS Istituto Ortopedico Galeazzi, IRCCS Istituto San Gallicano and Ospedale Maggiore della Carità) during the first Italian lockdown (March 11th- May 4th 2020).

Inclusion criteria

We included adult (>18 years old) patients with a diagnosis of acne vulgaris or rosacea that before lockdown underwent topical therapies and during lockdown they were not able to attend dermatological in-person visits, leading to discontinuation of their topical medications. They were stable (<20% variation in severity scores in the previous two consecutive visits ~ 2 months without a therapy) and accepted to have teledermatological visits every four weeks only for a clinical evaluation. We decided to include only stable patients not undergoing a treatment (topical or systemic ones) to avoid confounders due to therapy, such as drug, posology, administration method and therapy duration. They had to wear masks for at least 6 hours per day, an approved SM or FFP2

for Italian laws (<http://www.governo.it/it/articolo/coronavirus-conte-firma-il-dpcm-11-marzo-2020/14299>)[11].

Exclusion criteria

We excluded acne and rosacea adult patients that a) smoke cigar, cigarettes and e-cigarettes, b) did not discontinue topical and/or systemic therapies, c) have facial dermatoses other than acne and rosacea, d) undergoing special diets (i.e. vegans, vegetarians [12], Ramadan fasting [13-15] and keto diet [16]) capable to influence inflammation, e) infected by SARS-CoV-2, f) with a diagnosis or even a positive medical history for alcoholism, f) with comorbidities capable to trigger acne or rosacea flares, g) wear community masks or approved masks for less than 6 hours, g) history of patch test positivity for formaldehyde [17].

Teledermatological evaluation

Patients fulfilling the inclusion criteria were enrolled and underwent a teledermatological evaluation at the baseline (T0) and after 6 weeks of quarantine (T1) with a 15 minutes videocall on FaceTime or WhatsApp or Skype or Zoom. To increase comparability and ensure consistency we choose for each patient the same videocall program at T0.

To stage acne vulgaris patients we used Global Acne Grading Scale (GAGS) [18] and Dermatology Life Quality Index (DLQI) [19]. In particular, we reported both total GAGS score and GAGS for the single location (forehead, left and right cheeks, nose, chin, chest and upper back) to topographically evaluate mask-covered vs non mask-covered sites.

To stage rosacea we used Clinician's Erythema Assessment (CEA) [20], Global Flushing Severity Score (GFSS) [21], Investigator Global Assessment (IGA) [21], Patient Self-Assessment (PSA) [21] and DLQI [19]. Each patient signed an electronic informed consent form.

Statistical analysis

Normal distribution for each variable was investigated by performing the Kolmogorov-Smirnov test. Based on the distribution, parametric (Student's T-test) and non-parametric (Mann-Whitney test or Wilcoxon test) tests for paired or independent samples were applied to analyze the scores' variation between the baseline (T0) and after 6 weeks of quarantine (T1) in the investigated population. Patients affected by rosacea were further subcategorized based on the type of disease (predominant phenotype or papulopustular (PP) or erythematotelangiectatic phenotype (EE)) and the statistical analysis repeated. Multivariate regression analysis was conducted by using an "Enter" approach to analyze the influence of selected variables on the scores' variation after 6 weeks of quarantine. Data were reported as mean \pm standard deviation as well as percentage and all the analyses were conducted by using the MedCalc Statistical Software version v19.0.3 (MedCalc Software bvba, Ostend, Belgium), with a P value considered significant when less than 0.05.

RESULTS

Maskne or Acne due to Masks

A total of 30 patients (median: 34.0 [30.25-29.75] yoa) with acne were enrolled in this study, specifically 12 (40%) males and 18 (60%) females. Of those, 6 (33.3%) were affected by polycystic ovary syndrome. Patients reported to wear a mask for an median time of 8 [7-8.75] hours/day.

Acne severity was evaluated by GAGS scores for the six areas (forehead, each cheek, nose, chin and chest/upper back) and by DLQI, at the baseline (T0) and after 6 weeks of quarantine (T1). Results are reported in the Table 1. DLQI and all the GAGS scores mask-related significantly worsen ($P < 0.0001$) after 6 weeks of quarantine, with the exception of GAGS score for forehead and chest/upper back, which did not show any variation. Age, gender and number of hours/day wearing a mask did not significantly influence the global GAGS scores at T0 ($P = 0.84$) and T1 ($P = 0.95$), explaining only 3.0% and 1.3% of scores variability in our population, respectively (Supplementary Table 1).

Mask rosacea or Rosacea due to Masks

A group of 36 patients (median age: 48 [43-54] yoa) were included in this study, with a higher prevalence of women (n=22, 61.1%) than men (n=14, 38.9%). Patients were mainly affected by papulopustular (n=23, 63.9%), followed by erythematotelangiectatic (n=13, 36.1%), and they reported to wear a mask on average for 8 [7-9] h/day. As reported in Table 2, all the scores (CEA, DLQI, GFSS, IGA, PSA) showed a significant increase at T1. The same results were obtained when patients were further subcategorized into 2 rosacea phenotypes, PP and EE. PP patients showed a higher median age (49 [45-54] years) than EE patients (44 [37-51] years) (P=0.039) while no difference was observed in the average time wearing a mask/day (8 [7.5-9] vs 8 [7-9] hours/day, respectively; P=0.94).

Based on multivariate regression analyses, the variations observed in the scores for the global population analyzed occurred regardless the age, the hours wearing a mask/day and the gender (Supplementary Table 2).

DISCUSSION

In our real-world study, acne vulgaris and rosacea appeared to worsen in untreated patients wearing masks. Maskne is a recognized subtype of acne mechanica [5], and mask rosacea is a potential new entity triggered by mask-wearing during the pandemic.

Recently, Teo suggested that maskne should be diagnosed in case of a) *de novo* acne occurred 6 weeks after a regular mask wear or b) worsen of pre-existen acne in mask covered by areas after regular mask wearing, c) after exclusion of the main differential diagnoses (i.e. seborrheic dermatitis).

Remarkably, in this study authors used the same temporal criteria (6 weeks presence) to define also rosacea due to mask. In literature, a few case reports described worsening of rosacea after wearing masks [2].

Hua and colleagues evaluated cutaneous short term changes in patients wearing SM and N95, finding that masks induce microenvironment changes in the skin by dehydration, increased sebum and increased PH [3]. Furthermore, dehydration, transepidermal water loss and sebum dysregulation are pro-comedogenic factors, capable to promote *Cutibacterium acnes* multiplication, and hence innate immune response and leading to inflammatory lesions (papules and pustules) [24]. Likewise, also *Demodex folliculorum*, regarded as the a trigger in rosacea, takes advantage from sebum overproduction producing/amplifying inflammation (papules, pustules and erythema) [25].

Lab results further support the clinical findings, since in our study severity scores and DLQI worsened in both acne and rosacea patients after 6 weeks of masks, in agreement with previous reports described a detrimental influence on quality of life in patients affected by these dermatoses [22,23].

Unfortunately, beside the suggestion to not discontinuing isotretinoin (<https://www.aad.org/public/diseases/acne/derm-treat/isotretinoin/coronavirus-pandemic>) in severe acne and to preserve teledermatology consultations every 4 weeks, no other recommendations available to guide dermatologists that treat acne and rosacea patients during pandemics. Thus, real-world evidence can help inform clinical decision-making for dermatologists treating acne and rosacea patients.

This study was performed during lockdown where acne and rosacea visits were re-prioritized in Italian dermatologic referral centers [26], so the limitation of in-person visits excluded the possibility to test facial microbiome changes.

Since mask wearing worldwide was maintained due to COVID-19 pandemics, we expect an increase in the prevalence of maskne and mask rosacea and establishing recommendations/guidelines to support dermatologists and family doctors in the differential diagnosis and management is needed. Further studies on mask-related dermatoses are needed to better understand the pathophysiologic mechanism of face mask wearing in rosacea, in order to evaluate the best therapeutic approaches and counteract the pro-inflammatory effect of masks.

REFERENCES

1. Blicharz L, Czuwara J, Samochocki Z, et al. Hand eczema-A growing dermatological concern during the COVID-19 pandemic and possible treatments. *Dermatol Ther.* 2020;33(5):e13545.
2. Giacalone S, Minuti A, Spigariolo CB, et al. Facial dermatoses in the general population due to wearing of personal protective masks during the COVID-19 pandemic: first observations after lockdown. *Clin Exp Dermatol.* 2020:10.1111/ced.14376.
3. Hua W, Zuo Y, Wan R, et al. Short-term skin reactions following use of N95 respirators and medical masks. *Contact Dermatitis.* 2020;83(2):115-121.
4. Gasparino RC, Lima MHM, de Souza Oliveira-Kumakura AR, et al. Prophylactic dressings in the prevention of pressure ulcer related to the use of personal protective equipment by health professionals facing the COVID-19 pandemic: A randomized clinical trial. *Wound Repair Regen.* 2020. doi: 10.1111/wrr.12877.
5. Teo WL. Diagnostic and Management Considerations for 'Maskne' in the Era of COVID-19. *J Am Acad Dermatol.* 2020:S0190-9622(20)32664-5.
6. 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:e14346
7. Kutlu Ö, Metin A. Relative changes in the pattern of diseases presenting in dermatology outpatient clinic in the era of the COVID-19 pandemic. *Dermatol Ther.* 2020:e14096.
8. Gironi LC, Boggio P, Giorgione R, et al. The impact of COVID-19 pandemics on dermatologic surgery: real-life data from the Italian Red-Zone. *J Dermatolog Treat.* 2020:1-7.
9. Pacifico A, Ardigò M, Frascione P, et al. Phototherapeutic approach to dermatology patients during the 2019 coronavirus pandemic: real-life data from the Italian red zone. *Br J Dermatol.* 2020;183(2):375-376.
10. Bragazzi NL, Riccò M, Pacifico A, et al. COVID-19 knowledge prevents biologics discontinuation: Data from an Italian multicenter survey during RED-ZONE declaration. *Dermatol Ther.* 2020;33(4):e13508.
11. Tatapudi H, Das R, Das TK. Impact assessment of full and partial stay-at-home orders, face mask usage, and contact tracing: An agent-based simulation study of COVID-19 for an urban region. *Glob Epidemiol.* 2020 Nov;2:100036.
12. Lithell H, Bruce A, Gustafsson IB, Höglund NJ, Karlström B, Ljunghall K, Sjölin K, Venge P, Werner I, Vessby B. A fasting and vegetarian diet treatment trial on chronic inflammatory disorders. *Acta Derm Venereol.* 1983;63(5):397-403.
13. Damiani G, Mahroum N, Pigatto PDM, et al. The Safety and Impact of a Model of Intermittent, Time-Restricted Circadian Fasting ("Ramadan Fasting") on Hidradenitis Suppurativa: Insights from a Multicenter, Observational, Cross-Over, Pilot, Exploratory Study. *Nutrients.* 2019;11(8):1781.
14. Adawi M, Damiani G, Bragazzi NL, et al. The Impact of Intermittent Fasting (Ramadan Fasting) on Psoriatic Arthritis Disease Activity, Enthesitis, and Dactylitis: A Multicentre Study. *Nutrients.* 2019;11(3):601.
15. Damiani G, Watad A, Bridgwood C, et al. The Impact of Ramadan Fasting on the Reduction of PASI Score, in Moderate-To-Severe Psoriatic Patients: A Real-Life Multicenter Study. *Nutrients.* 2019 ;11(2):277.
16. Afifi L, Danesh MJ, Lee KM, et al. Dietary Behaviors in Psoriasis: Patient-Reported Outcomes from a U.S. National Survey. *Dermatol Ther (Heidelb).* 2017;7(2):227-242.

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17. Aerts O, Dendooven E, Foubert K, et al. Surgical mask dermatitis caused by formaldehyde (releasers) during the COVID-19 pandemic. *Contact Dermatitis*. 2020;83(2):172-173.
 18. Adityan B, Kumari R, Thappa DM. Scoring systems in acne vulgaris. *Indian J Dermatol Venereol Leprol* 2009;75:323-6
 19. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19(3):210-6.
 20. Tan J, Liu H, Leyden JJ, Leoni MJ. Reliability of Clinician Erythema Assessment grading scale. *J Am Acad Dermatol*. 2014;71(4):760-3.
 21. Gallo RL, Granstein RD, Kang S, et al. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol*. 2018;78(1):148-155.
 22. Husein-ElAhmed H, Steinhoff M. Efficacy of topical ivermectin and impact on quality of life in patients with papulopustular rosacea: A systematic review and meta-analysis. *Dermatol Ther*. 2020;33(1):e13203.
 23. Smith H, Layton AM, Thiboutot D, et al. Identifying the Impacts of Acne and the Use of Questionnaires to Detect These Impacts: A Systematic Literature Review. *Am J Clin Dermatol*. 2020. doi: 10.1007/s40257-020-00564-6
 24. Jusuf NK, Putra IB, Sari L. Differences of Microbiomes Found in Non-Inflammatory and Inflammatory Lesions of Acne Vulgaris. *Clin Cosmet Investig Dermatol*. 2020;13:773-780.
 25. Daou H, Paradiso M, Hennessy K, Seminario-Vidal L. Rosacea and the Microbiome: A Systematic Review. *Dermatol Ther (Heidelb)*. 2020. doi: 10.1007/s13555-020-00460-1.
 26. Cristaudo A, Pigliacelli F, Pacifico A, et al. Teledermatology and hygiene practices during the COVID-19 pandemic. *Contact Dermatitis*. 2020;83(6):536.

TABLES LEGEND

Table 1: GAGS scores and DLQI are reported at the baseline (T0) and after 6 weeks of quarantine (T1).

Table 2: The following scores were calculated to assess the rosacea severity at the baseline (T0) and 6 weeks of quarantine (T1).

SUPPLEMENTARIES

Supplement Table 1 (S1): Global GAGS scores at the baseline (T0) and after 6 weeks quarantine (T1).

Supplementary Table 2: Multivariate regression analysis (Enter approach) to investigate the variables associated with the worsening of rosacea scores after 1 month of quarantine.

Table 1: GAGS scores and DLQI are reported at the baseline (T0) and after 6 weeks of quarantine (T1).

Variables	T0 (median [IQR])	T1 (median [IQR])
GAGS forehead	<u>2 [2-4]</u>	<u>2 [2-4]</u>
GAGS left cheek	<u>2 [0-3.5]</u>	<u>4 [4-4]</u> ***
GAGS right cheek	<u>2 [0-3.5]</u>	<u>4 [4-4]</u> ***
GAGS nose	<u>1 [0-2]</u>	<u>2 [2-2]</u> ***
GAGS chin	<u>1 [0-1]</u>	<u>2 [1-2]</u> ***
GAGS chest and upper back	<u>3 [0-3]</u>	<u>3 [0-3]</u>
GAGS cheeks, nose and chin	<u>5 [4-6]</u>	<u>12 [11-13]</u> ***
Global GAGS	<u>9.5 [7-14]</u>	<u>17.5 [15-21]</u> ***
DLQI	<u>8 [6-9]</u>	<u>11 [10-13]</u> ***

*** P value<0.0001.

DLQI: Dermatology Life Quality Index, GAGS: Global Acne Grading Scale, IQR: Interquartile range

Table 2: The following scores were calculated to assess the rosacea severity at the baseline (T0) and 6 weeks of quarantine (T1).

Variables	All population (N=36), <u>median [IQR]</u>		Papulo-pustular patients (N=23), <u>median [IQR]</u>		Erythematotelangiectatic patients (N=13), <u>median [IQR]</u>	
	T0	T1	T0	T1	T0	T1
CEA	2 [0-3]	3 [0-4]***	1 [0-2]	2 [0-3]**	2 [2-3]	4 [3-4]**
DLQI	7 [5-8]	10 [9-11]***	7 [6-9]	11 [9-12]***	6 [4-6]	9 [8-9]***
GFSS	2.5 [0-4]	4.5 [0-6]***	2 [0-3]	3 [0-5.5]**	4 [3-5]	6 [5-7]***
IGA	2 [1-2.25]	3 [2-4]***	1 [0-2]	3 [0-3.5]**	2 [2-3]	4 [3-4]**
PSA	2 [0.75-3]	3 [2-4]***	1 [0-2.5]	2 [0-4]**	2 [2-3]	4 [3-4]**

*** P value<0.0001, ** P value<0.01. P values were calculated in comparison with the relative T0.

CEA: Clinician's Erythema Assessment, DLQI: Dermatology Life Quality Index, GFSS: Global Flushing Severity Score, IGA: Investigator Global Assessment, IQR: Interquartile range; PSA: Patient Self-Assessment