

**Reply to letter to the editor: “A response to ‘Male balding is a major risk factor for severe COVID-19’”**



*To the Editor:* We appreciate the interest regarding “Male balding is a major risk factor for severe COVID-19”<sup>1</sup> by Thatiparthi et al.<sup>2</sup> These authors propose a potential causal relationship between COVID-19 and scalp balding. They suggest that balding could possibly allow the virus to transverse the cutaneous barrier through accelerated photo-aging, oxidative stress, loss of elasticity, and reduced moisturization. Although the possibility of COVID-19 percutaneous transmissibility is a novel perspective, further investigation is needed to determine if SARS-CoV-2 infects epidermal keratinocytes and whether SARS-CoV-2 skin inoculation leads to systemic disease.

Prevalent in health care workers, hand eczema represents an alternative skin disease for further inquiry into the relationship between COVID-19 and skin barrier disruption. Hand eczema erodes the epidermis thereby shortening the transmission route needed for SARS-CoV-2 binding to ACE2 receptors in the epidermal basal layer. Among tested United Kingdom Biobank participants, 1450 of 18,221 (8.0%) participants tested COVID-19 positive compared with 14 of 139 (10.1%) participants with physician-diagnosed hand eczema.

The common types of balding in men are male pattern balding and senescent balding. Although our study did not differentiate between these 2 types, it is possible that both balding types are associated with COVID-19, as both male sex and advanced age are strong COVID-19 risk factors. In an analysis covering 40% of all patients in England, COVID-19-related death was associated with male sex (hazard ratio [HR], [95% confidence interval], 1.59 [1.53-1.65]) and increasing age (60-69 years; HR, 2.40 [2.16-2.66]; 70-79 years, HR, 6.07 [5.51-6.69]; 80+ years, HR, 20.60 [18.70-22.68]).<sup>3</sup>

The association between COVID-19 and male sex may be related to the androgen-mediated

COVID-19 hypothesis,<sup>4</sup> in which testosterone upregulates transmembrane serine protease 2 (TMPRSS2) facilitating SARS-CoV-2 entry into host cells via ACE2. Poor outcomes of COVID-19 in the elderly are most likely related to the aging immune system’s inability to neutralize virus thereby triggering a pro-inflammatory state in COVID-positive patients. As balding also presents a manifestation of cellular senescence, we suggest that balding may also function as a highly visible biomarker for immunosenescence. Thus, the association between balding and severe COVID-19 may be considered one of the factors that clinicians can use to rapidly identify patients at higher risk.

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