Androgenetic alopecia present in the majority of patients hospitalized with COVID-19: The "Gabrin sign"

To the Editor: Dr Frank Gabrin was the first American physician to die of severe acute respiratory syndrome coronavirus (SARS-CoV)-2 infection. Dr Gabrin suffered from androgenetic alopecia and was a long-term survivor of bilateral testicular cancer.[1] The association between SARS-CoV-2 infectiveness and the androgen pathway has been previously described.[2] Androgen-mediated SARS-CoV-2 vulnerability may help explain the disproportioned mortality rate among men.[3] We present further epidemiologic evidence that androgen sensitivity might be associated with severe symptoms leading to hospitalization due to COVID-19.

Previously, we reported a possible association between male patients hospitalized with COVID-19 and androgenetic alopecia (AGA); however, the study was limited by its population size of 41 men.[4] In this communication, we present additional data from patients with confirmed COVID-19 admitted

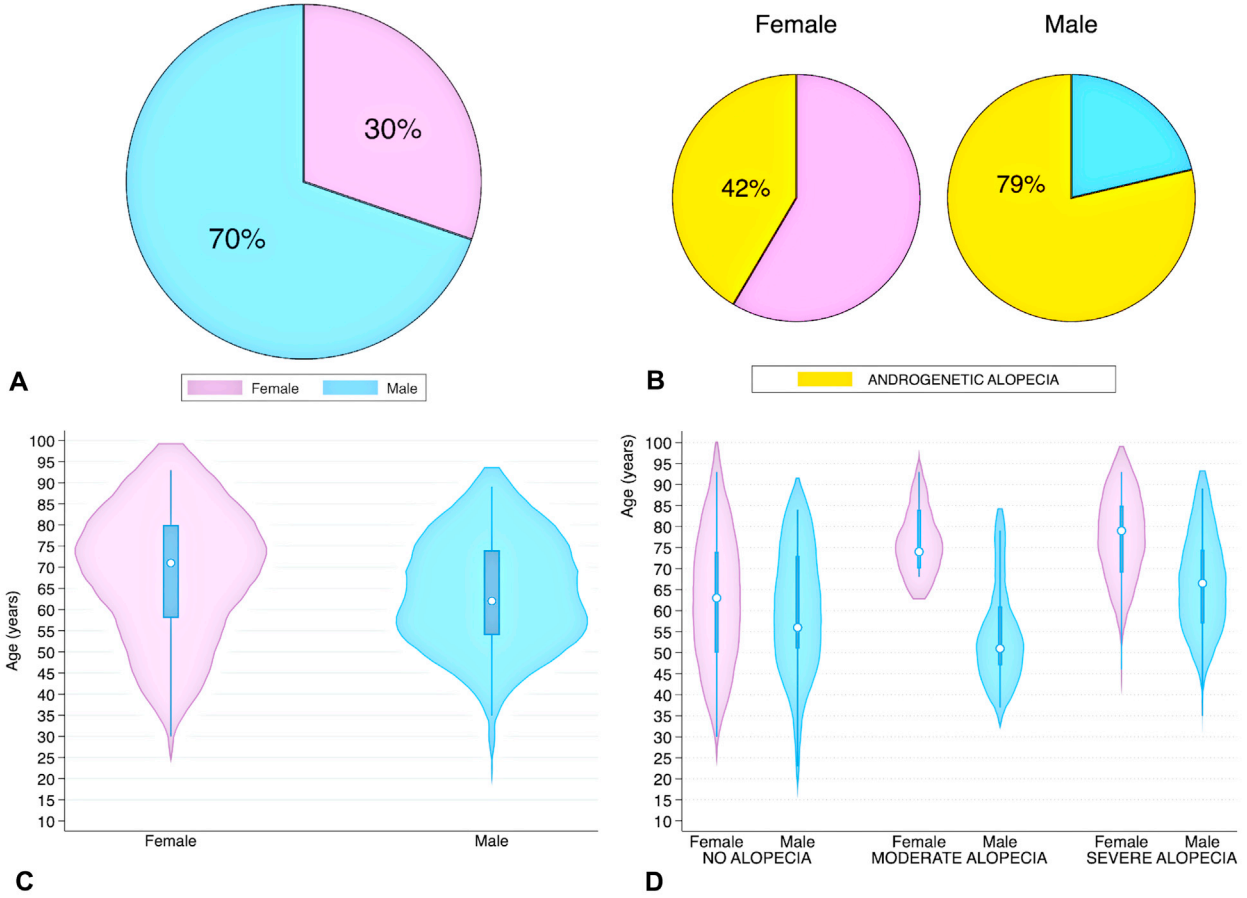

Fig 1. Epidemiologic characteristics of 175 individuals hospitalized due to severe symptoms of COVID-19 from March 23, 2020, to April 12, 2020. **A**, The study population had male-to-female ratio of 2.3:1. **B**, Androgenetic alopecia (AGA) was present in 42% of the women and in 79% of the men. **C**, Notably, the violin plots demonstrate there was an older age distribution in the women compared with the men. AGA severity was categorized by specific sex scales: Hamilton–Norwood scale (HNS) for men and Ludwig scale (LS) for women into groups: "no alopecia" for HNS = 1 or LS = 0; "moderate AGA" for HNS = 2 or LS = 1; or "severe AGA" for HNS >2 or LS >1. **D**, Although age was widely proportional among patients with no alopecia, moderate AGA, and severe AGA, there was a slight tendency for younger age in men with moderate AGA and in women with no alopecia compared with the respective severe AGA groups. The *white circle* represents the median, the *bar* in the center represents the interquartile range, and the *thin lines* represent the 95% confidence interval. The wider sections of the violin plot represent a higher probability that members of the population will take on the given value and the thinner sections represent a lower probability.

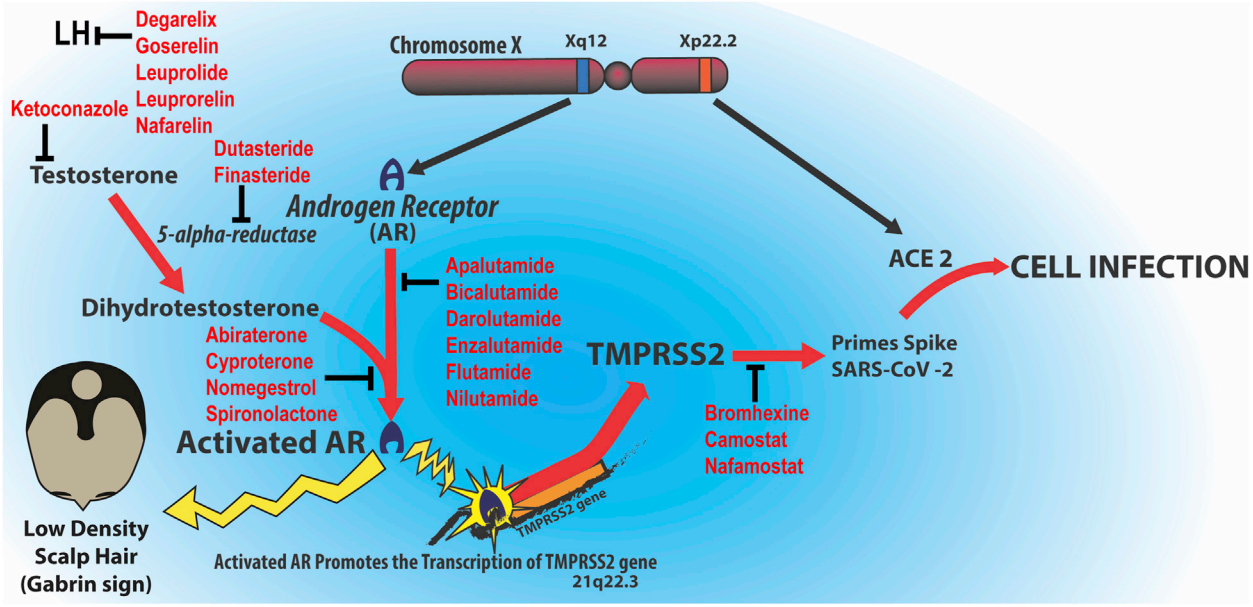

Fig 2. Possible targets of the androgen pathway for severe acute respiratory syndrome coronavirus 2 (*SARS-CoV-2*) prophylaxis and adjuvant therapy. Antiandrogen therapies include gonadotropin-releasing hormone (*GnRH*) analogs (degarelix, goserelin, leuprolide, leuprorelin, nafarelin), which stop luteinizing hormone (*LH*) secretion and induce chemical castration. Testosterone is regarded as the main androgen hormone, and its production is inhibited by ketoconazole, an inhibitor of steroidogenesis. Dutasteride and finasteride, 5-α-reductase inhibitors, target synthesis of dihydrotestosterone, the most potent intrinsic androgen hormone. Androgen receptor inhibitors may be steroidal (abiraterone, cyproterone, nomegestrol, or spironolactone), or nonsteroidal (apalutamide, bicalutamide, darolutamide, enzalutamide, flutamide, or nilutamide). Transmembrane protease, serine 2 (*TMPRSS2*) blockers include bromhexine, camostat, and nafamostat. *ACE*, Angiotensin converting enzyme.

due to severity criteria (mainly low peripheral oxygen saturation) to 3 tertiary hospitals in Madrid, Spain. The patients were randomly examined by dermatologists who were assisting with the overwhelming number of admitted patients. The study took place from March 23, 2020, to April 12, 2020.

Upon admission, the dermatologists recorded the age, sex, and alopecia diagnosis. Alopecia severity was evaluated using the Hamilton–Norwood scale (HNS) for men and the Ludwig scale (LS) for women. The scores were categorized into groups: "no alopecia" for HNS = 1 or LS = 0; "moderate AGA" for HNS = 2 or LS = 1; and "severe AGA" for HNS >2 or LS >1.

A total of 175 individuals with confirmed COVID-19 were evaluated. Among the patients, 122 were men and 53 were women. Overall, 67% of the patients (95% confidence interval, 60%-74%) presented with clinically relevant AGA. The frequency of AGA in men was 79% (95% confidence interval, 70%-85%) The frequency of AGA in women was 42% (95% confidence interval, 29%-55%). The median age of female patients was 71 years (interquartile range, 22 years). The median age of male patients was 62.5 years (interquartile range, 20 years) (Fig 1, *A-C*). Raw data available in Supplement 1 (available via Mendeley at https://data.mendeley.com/datasets/tphxzjkrh8/1). In both sexes, age presented great variation for those with "no alopecia," whereas those with severe AGA presented an older age distribution and median (Fig 1, *D*).

The prevalence of age-matched men in a similar white population was estimated to be 31% to 53%,[4] whereas in women, the highest AGA prevalence reported (with dermatologist evaluation) was 38% in patients aged >69 years.[5] Age group comparison with other references available in Supplement 2 (available via Mendeley at https://data.mendeley.com/datasets/jk63cthxbr/2). In our data, 57% of females >69 years old were diagnosed with AGA. These results indicate that a substantial proportion of individuals hospitalized for severe COVID-19 in your centers have AGA.

The hypothesis of androgen-mediated COVID-19 severity requires validation in larger studies. Antiandrogen treatments that could be theoretically studied in the treatment and prophylaxis of severe

COVID-19 are indicated in Fig 2. Therapeutic randomized controlled clinical trials with bicalutamide (NCT04374279), degarelix (NCT04397718), and spironolactone (NCT04345887) are currently underway.

The sample size and lack of a control group and outcomes are limitations of this study. Because dermatologists actively graded AGA, observer bias was possible. The precise AGA rate in an age-matched, not-admitted population with COVID-19 is still unknown to draw further conclusions. Future studies could evaluate whether lung involvement correlates with the severity of AGA or whether the proportion of AGA is higher in intensive care/fatal COVID-19. AGA severity reflects androgen activity over age, which are 2 vulnerability characteristics for COVID-19. AGA is a primary individual characteristic, different from telogen effluvium, which occurs after months of the stress of illness.

Finally, because Dr Gabrin was the first physician to die from COVID-19 in the United States, we propose the use of the eponym the "Gabrin sign" to visually identify patients at higher risk for severe symptoms after COVID-19 infection.

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Retrospective analysis of smell and taste disturbances associated with dermatologic medications reported to the United States Food and Drug Administration and relevance to COVID-19 infections

To the Editor: Smell and taste disturbances are more recently reported symptoms of the novel coronavirus disease 2019 (COVID-19).[1] Many commonly used dermatologic medications can also cause smell/taste changes. With COVID-19 testing shortages in the United States, these medication adverse events warrant careful consideration. In this study, we analyzed the United States Food and Drug Administration Adverse Event Reporting Database (FAERS) for the most common dermatologic medications associated with smell/taste disturbances and their relevance to COVID-19 infections.

The FAERS database was searched for the most common medications causing smell/taste disturbances and then filtered for dermatologic drugs. The data were substantiated using 2 other databases and recorded. The National Institute of Health Clinical Studies Database was queried for clinical trial data, and PubMed was examined for case reports/series on