Title

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Androgens and women: COVID-19 outcomes in women with acne vulgaris, polycystic ovarian syndrome, and hirsutism

Dear Editor,

Disproportionately increased COVID-19 severity in men has resulted in investigation into androgen-regulated transcription of transmembrane protease-serine 2 (TMPRSS2), which mediates SARS-CoV-2 infectivity.[1] Several dermatologic disorders are associated with androgen excess, such as polycystic ovarian syndrome (PCOS), acne cystica, and hirsutism in women.[2] Considering the implication that androgens play a role in COVID-19 infection-related outcomes in men, we examined COVID-19 incidence and severity in women with these dermatologic conditions.

The HIPAA-limited University of California COVID Research Data Set (UC CORDS) provides access to health records for patients tested for COVID-19 across UC medical institutions.[3] As of October 8, 2020, it had COVID-19 test results, demographics, hospitalization, and mortality on 117,529 women, age 0–65. Data on diagnoses of acne vulgaris, PCOS, or hirsutism, and concomitant use of spironolactone, estradiol (proxy for oral contraceptive pills), or metformin for at least 30 days were collected. Chi-squared and Fisher's exact tests were used for statistical analysis.

The UC CORDS female population had a 4.0% (n = 4,693, age: 0–65, avg age: 35) COVID-19-positive test rate. Of these, 6,195 had acne vulgaris, with a 3.2% (n = 201, age: 0–65, avg age: 33) COVID-19 infection rate, 1,590 women had PCOS, of which 3.1% (n = 49, age: 18–50, avg age: 34) were COVID-19 positive, and 687 had hirsutism, with a 3.6% (n = 25, age: 19–65, avg age: 38) COVID-19-positive rate, none of which were different from women without these conditions ($P = 0.002$, $P = 0.062$, $P = 0.635$, respectively) (Table 1).

Table 1 Women in the UC CORDS with and without acne vulgaris, PCOS, or hirsutism who tested positive for COVID-19

	COVID-19-positive patients			COVID-19-positive hospitalizations			COVID-19-positive mortality[b]	
	Disorder of androgen excess (No., %)	Control (No., %)[a]	*P*-value	Disorder of androgen excess (No., %)	Control (No., %)[a]	*P*-value	Disorder of androgen excess (No., %)	Control (No., %)[a]
Acne vulgaris	201 (3.2%)	4,492 (4.0%)	0.002	9 (4.5%)	526 (11.7%)	0.002	0	22 (0.5%)
PCOS	49 (3.1%)	4,644 (4.0%)	0.062	3 (6.1%)	532 (11.5%)	0.363	0	22 (0.5%)
Hirsutism	25 (3.6%)	4,668 (4.0%)	0.635	2 (8.0%)	533 (11.4%)	1.0	0	22 (0.5%)

[a]UC CORDS COVID-19-positive patients without acne vulgaris, PCOS, or hirsutism.
[b]Death any time after positive COVID-19 test.

Table 2 COVID-19 infection rate and hospitalization rate for women with and without acne vulgaris, PCOS, or hirsutism on spironolactone, estradiol, or metformin in the UC CORDS as of October 8, 2020

	Acne vulgaris			PCOS			Hirsutism		
Medication	Patients on medication (No., %)	Control (No., %)[a]	*P*-value[b]	Patients on medication (No., %)	Control (No., %)[a]	*P*-value[b]	Patients on medication (No., %)	Control (No., %)[a]	*P*-value[b]
COVID-19-positive patients									
Spironolactone	17 (8.5%)	184 (3.3%)	0.622	1 (2.0%)	48 (3.3%)	0.081	2 (8.0%)	23 (3.9%)	0.559
Estradiol	33 (16.4%)	168 (3.4%)	0.292	10 (20.4%)	39 (3.1%)	0.933	5 (20.0%)	20 (3.5%)	0.789
Metformin	7 (3.5%)	194 (3.2%)	0.653	10 (20.4%)	39 (3.0%)	0.743	3 (12.0%)	22 (3.7%)	1.0
COVID-19-positive hospitalization									
Spironolactone	0	9 (4.9%)	N/A	0	3 (6.3%)	N/A	1 (50%)	1 (4.4%)	0.157
Estradiol	2 (6.1%)	7 (4.2%)	0.644	1 (10.0%)	2 (5.1%)	0.504	0	2 (10.0%)	N/A
Metformin	1 (14.3%)	8 (4.1%)	0.278	1 (10.0%)	2 (5.1%)	0.504	0	2 (9.1%)	N/A

[a]UC CORDS COVID-19-positive patients with acne vulgaris, PCOS, or hirsutism and not on the specified medication.
[b]Statistical analysis using Chi-squared for >5 or Fisher's exact for <5 patients; significant if <0.05.

Analysis of hospitalization rates among COVID-19-positive women (n = 4,693) in the UC CORDS indicated that 11.4% (n = 535, avg age: 41) were hospitalized within 2 weeks (1 week prior or subsequent) of testing. COVID-19-positive women with acne (n = 201) had a 4.5% (n = 9, average age: 38) hospitalization rate ($P = 0.002$). COVID-19-positive women with PCOS or hirsutism had 6.1% (n = 3, average age 32) and 8.0% (n = 2, average age 40) hospitalization, respectively, which was not significantly different from those without ($P = 0.363$, $P = 1.0$, respectively). Lastly, these women did not have significantly different mortality rates compared to those without these conditions (Table 1).

Further analysis of the populations on targeted therapies revealed no significant associations in both the COVID-19 infection rates or hospitalization rates of women with acne, PCOS, or hirsutism on spironolactone, estradiol, or metformin ($P > 0.05$) (Table 2).

Our results suggest that there is no evidence for an increased risk of COVID-19 infection, hospitalization, or mortality in women with acne vulgaris, PCOS, or hirsutism. Additionally, management with common medications was not associated with COVID-19 infection risk. In particular, spironolactone, which was speculated early in the pandemic to increase the risk of COVID-19 infection by increasing circulating angiotensin converting enzyme (ACE), did not appear to influence infection risk in our patients. The lower COVID-19 rates of infection and hospitalization among women with acne were possibly related to the younger average age (acne: 33 years vs. non-acne: 35 years). Still, these data are all suggestive, as serum hormone levels were not collected in these women, and thus there is no direct evidence of the impact of androgens. Limitations include the use of a database reflective of tertiary care facilities, low case frequency, and lack of clinical details due to the de-identified database.

While androgens likely play a role in COVID-19 outcomes, there are several other sex differences to account for, like varying immune response and the potential protective effect of estrogens/progesterone.[4] Results from ongoing trials with TMPRSS2 inhibitors and anti-androgen therapy may elucidate the impact of androgens in both sexes and have a potential role in future COVID-19 management.[5] Insight on the role of sex hormones on disease incidence and severity will contribute to better understanding of at-risk populations.

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