Risk of severe acute respiratory syndrome coronavirus 2 infection among women with polycystic ovary syndrome

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Objective: To determine whether women with polycystic ovary syndrome (PCOS) had a higher incidence of testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) than those without PCOS and evaluate whether PCOS diagnosis independently increased the risk of moderate or severe disease in those with positive SARS-CoV-2 test results.
Design: Retrospective cohort study using the National COVID Cohort Collaborative (N3C).
Setting: National COVID Cohort Collaborative.
Patient(s): Adult nonpregnant women (age, 18–65 years) enrolled in the N3C with confirmed SARS-CoV-2 testing for any indication. Sensitivity analyses were conducted in women aged 18–49 years and who were obese (body mass index, ≥ 30 kg/m^2).
Intervention(s): The exposure was PCOS as identified by the N3C clinical diagnosis codes and concept sets, which are a compilation of terms, laboratory values, and International Classification of Diseases codes for the diagnosis of PCOS. To further capture patients with the symptoms of PCOS, we also included those who had concept sets for both hirsutism and irregular menses.
Main Outcome Measure(s): Odds of testing positive for SARS-CoV-2 and odds of moderate or severe coronavirus disease 2019 (COVID-19) in the PCOS cohort compared with those in the non-PCOS cohort.
Result(s): Of the 2,089,913 women included in our study, 39,459 had PCOS. In the overall cohort, the adjusted odds ratio (aOR) of SARS-CoV-2 positivity was 0.98 (95% confidence interval [CI], 0.97–0.98) in women with PCOS compared to women without PCOS. The aORs of disease severity were as follows: mild disease, 1.02 (95% CI, 1.01–1.03); moderate disease, 0.99 (95% CI, 0.98–1.00); and severe disease, 0.99 (95% CI, 0.99–1.00). There was no difference in COVID-19–related mortality (aOR, 1.00; 95% CI, 0.99–1.00). These findings were similar in the reproductive-age and obese reproductive-age cohorts.
Conclusion(s): Women with PCOS had a similar likelihood of testing positive for SARS-CoV-2. Among those who tested positive, they were no more likely to have moderate or severe COVID-19 than the non-PCOS cohort. Polycystic ovary syndrome is a chronic condition associated with several comorbidities, including cardiovascular disease and mental health issues. Although these comorbidities are also associated with COVID-19 morbidity, our findings suggest that the comorbidities themselves, rather than PCOS, drive the risk of disease severity. (Fertil Steril® 2023;119:847–57. ©2023 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: PCOS, polycystic ovaries, SARS-CoV-2, COVID-19, coronavirus

Coronavirus disease 2019 (COVID-19) has affected >305 million people worldwide within 2 years and resulted in >5.4 million deaths as of December 2021 (1). Given the profound impact COVID-19 has had on the loss of life, health impairment, and financial costs (2), the health care community has sought ways to identify individuals at higher risk of contracting the virus associated with COVID-19—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—and/or those who have a greater severity of disease. The Centers for Disease Control and Prevention (CDC) has recognized several medical conditions associated with a higher risk of severe COVID-19, which is defined as a greater likelihood of hospitalization, intensive care admission, ventilator support, or death. These conditions include diabetes, heart disease,

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mental health conditions (e.g., depression), and obesity (3), all of which are also highly prevalent in the population with polycystic ovary syndrome (PCOS).

Polycystic ovary syndrome is the most common endocrine disorder in reproductive-age women, with a prevalence of 8%–13% globally depending on region and ethnicity (4). In the United States, it is estimated that 5 million women are affected by PCOS (5). Up to 80% of women with PCOS in the United States are also obese (6), and those with PCOS have been shown in meta-analyses to be at higher risk of metabolic conditions (7), such as diabetes, as well as mental health conditions, including depression (8). Although data surrounding cardiovascular disease are limited especially with regard to longitudinal studies, there are longitudinal data on cardiometabolic disease risk factors persisting beyond the reproductive years (7, 9, 10). Because these conditions are recognized risk factors affecting the severity of COVID-19, to appropriately counsel women with PCOS, it is important to determine whether PCOS status is independently associated with a greater risk of severe COVID-19.

In the literature, only one study in humans has been conducted to date to evaluate this association. In a population-based cohort study in the United Kingdom, Subramanian et al. (11) reported that women with PCOS had a 28% higher risk of suspected/confirmed COVID-19. Importantly, however, testing was not required to diagnose COVID-19 given the low utilization of outpatient testing at the time of the study. Therefore, confirmed COVID-19 codes were only present in 0.1% (n = 14) of women with PCOS.

When exploring the pathophysiology of why women with PCOS may be at greater risk of COVID-19, various mechanisms have been proposed. Elevated androgen levels, the hallmark of PCOS (12, 13), may partially explain why men are at greater risk of COVID-19 than women, with testosterone suppressing the immune response and modulating proteins that facilitate entry of the SARS-CoV-2 virus into host tissue (14). Rodent studies show that dihydrotestosterone upregulated priming proteins for SARS-CoV-2 entry, particularly in organs expressing androgen receptors, such as the lungs and kidneys. Hyperandrogenism also potentiates hyperinsulinemia, causing adipocyte dysfunction and a chronic inflammatory state in PCOS (14). As mentioned previously, women with PCOS are more likely to be obese. Obesity has been associated with a 1.45-fold greater risk of COVID-19 mortality (95% confidence interval [CI], 1.30–1.61) (15) possibly through low-grade inflammatory pathways (16) and with other high-risk conditions, such as diabetes and hypertension. Other proposed mechanisms include compensatory hyperglycemia and vitamin D deficiency (17).

Given the multitude of mechanisms by which PCOS may be associated with COVID-19, our objectives were to determine the incidence of positive SARS-CoV-2 test results in adult women with PCOS in the United States and COVID-19 severity in this population. Our primary outcomes were the odds of a positive SARS-CoV-2 test result in those with PCOS compared with that in those without PCOS and odds of disease severity (defined as mild, moderate, severe, and death) in those with PCOS compared with that of those without.

MATERIALS AND METHODS

This was a retrospective cohort study conducted using the National COVID Cohort Collaborative (N3C). With this study design, the exposure and outcome were PCOS status and the incidence of COVID-19, respectively. Incidence was used rather than prevalence given the timeframe of the database (starting January 2020) before which COVID-19 was unlikely to be present in the general population. In addition, during this time, COVID-19 was primarily manifesting as an acute infection. The N3C is a centralized electronic health record–derived data resource. As outlined in a previous manuscript using the N3C, it is a partnership that includes the Clinical and Translational Science Awards Program hubs, National Center for Advancing Translational Science, Center for Data to Health, and community (18). The N3C Data Enclave is approved under the authority of the National Institutes of Health (NIH) Institutional Review Board. Each N3C site maintains an institutional review board–approved data transfer agreement (18). The N3C harmonizes data that are transmitted from electronic health records throughout the United States using rigorous data quality review that relies on both automated and manual approaches (19). Within the N3C are various data sets, including a deidentified data set (level 2) that is continuously updated with new patients. The N3C identifies laboratory-confirmed and suspected cases of SARS-CoV-2 infection and demographically matches them on age group, sex, etc who have tested negative or equivocal for SARS-CoV-2 in a 1:2 ratio. Details about the N3C cohort features and data classification are published elsewhere (20). As of December 2021, the N3C consisted of >10.0 million patients, >3.4 million of whom are SARS-CoV-2 positive.

Data were pulled, and queries run October 15–21, 2021, which included data from January 2020 onward. The first step was identifying the exposure: PCOS. Women with PCOS were defined as the exposed cohort, and those without PCOS were defined as the nonexposed cohort. To identify those with PCOS, the N3C Concept Sets were used. Concept Sets in the N3C are a compilation of terms, laboratory values, and International Classification of Diseases, 9th and 10th Revisions, codes associated with a particular diagnosis (Supplemental Table 1, available online). Patients with PCOS had concept sets indicating PCOS, and to further capture patients with the symptoms of PCOS, we included those with concept sets for both hirsutism and irregular menses. Those without these codes were defined as the non-PCOS cohort.

We included all adult females (aged 18–65 years) who had laboratory testing for SARS-CoV-2 in the N3C data set. Therefore, cases suspected of COVID-19 that lacked confirmatory laboratory testing for SARS-CoV-2 were excluded. The decision to include women beyond reproductive age in the overall cohort is because of PCOS being a lifelong condition with evidence indicating the presence of cardiometabolic risk beyond the reproductive years in women with PCOS (21, 22). The upper limit of 65 years was set because of previous evidence identifying the age of >65 years as a significant risk factor for severe COVID-19, with >81% of COVID-19 deaths occurring in people aged >65 years (3). Moreover, because the first

diagnostic criteria for PCOS were published in 1990, it is difficult to ascertain how the diagnosis of PCOS was established in this elderly population (23). In addition, because pregnancy is an independent risk factor for severe SARS-CoV-2 infection (24), pregnant women were excluded.

Data collected through the N3C included patient age (in years), race, ethnicity, body mass index (BMI) (in kg/m^2), smoking status, substance use, SARS-CoV-2 laboratory status, COVID-19 severity, and the presence of confounders, including diabetes, heart disease, stroke, cerebrovascular accident, cancer, chronic kidney disease, chronic lung disease, dementia, human immunodeficiency virus infection, liver disease, antiandrogen use, hormonal contraceptive use, and depression. The SARS-CoV-2 laboratory status was categorized as positive or negative. All patients with COVID-19 included in this study were SARS-CoV-2 positive. The severity of COVID-19 was derived from patient severity data in the form of clinical, laboratory, and imaging findings at the time of labeling within the N3C (i.e., mild, mild emergency department, moderate, severe, or death). The N3C follows the World Health Organization's COVID Severity Scale. This scale distinguishes mild, moderate, and severe on the basis of the clinical signs of pneumonia and other factors, including respiratory rate and oxygen saturation on room air (25). For example, mild is defined as the absence of viral pneumonia or hypoxia, and moderate is defined as the presence of clinical signs of pneumonia (fever, cough, dyspnea, and fast breathing) but absence of signs of severe pneumonia, including an oxygen saturation level of $\geq$90% on room air. For the purpose of this study, mild emergency department (defined in the N3C as mild cases of patients who presented in the emergency department) and mild disease were combined. Those patients having diagnosis codes for any of the confounders included in this study were classified as having the condition in a binary fashion.

Categorical outcomes were analyzed using the χ^2 analysis, whereas continuous outcomes were analyzed using Student's t test. Multivariate logistic regression modeling was performed to evaluate whether women with PCOS had a higher incidence of positive SARS-CoV-2 laboratory status than those without PCOS. We investigated further those with COVID-19 using logistic regression to determine whether COVID-19 severity differed between the 2 cohorts. We controlled for patient comorbidities on the basis of either PCOS comorbidities or CDC comorbidities for COVID-19. These were determined on the basis of significant associations in univariate regression models and a priori and included age, BMI, diabetes, cardiovascular disease, obstructive sleep apnea, cancer, chronic kidney disease, chronic lung disease, liver disease, substance abuse, depression, and demographic variables, such as race, ethnicity, and smoking. To capture a portion of the population with either biochemical or clinical hyperandrogenemia, a variable was created for those determined through the data set to be on any of the following antiandrogen medications commonly prescribed for hirsutism: spironolactone; flutamide; and finasteride. Given that combined hormonal contraceptives are often prescribed as first-line therapy for hirsutism management and have an antiandrogenic effect, the use of combined hormonal contraceptives during the study period was also captured (Supplemental Table 2). When modeling race, our comparison variable was white race, and we grouped all non-White and non-Black patients into an other race variable. We combined these groups because of the low frequencies of non-White and non-Black patients. For ethnicity, we compared those identifying as "Hispanic" with those either who were listed as "non-Hispanic" or whose variable was missing.

We also performed sensitivity analyses to evaluate for differences related to aging. Therefore, we restricted to reproductive-age women (aged 18–49 years) in our sensitivity analysis, given that PCOS is primarily a disease of reproductive-age women. For a second sensitivity analysis, we also included an additional restriction to investigate only those who were of reproductive age and obese (BMI, $\geq$30 kg/m^2) given the higher prevalence of obesity in the population with PCOS. We modeled the relationship between PCOS and COVID-19 using logistic regression to adjust for the comorbidities previously mentioned, within the models.

All analyses were conducted within the N3C platform using level 2 data, in the Palantir framework. The N3C data transfer to the National Center for Advancing Translational Science is performed under a Johns Hopkins University Reliance Protocol No. IRB00249128 or individual site agreements with the NIH. The N3C Data Enclave is managed under the authority of the NIH; information can be found at https://ncats.nih.gov/n3c/resources. The code was written using the R programming language and uploaded there. Code will be available on GitHub after publication (https://github.com/bolandlab). This research was deemed exempt status by the institutional review boards from the University of Pennsylvania and University of Rochester because of its use of deidentified data.

RESULTS

Demographic Characteristics

We identified 7.6 million unique patients in the N3C data set as of October 2021, 4.1 million of whom were female. After accounting for the exclusion criteria, 2,089,913 women were included in the study, and 39,459 (1.9%) had PCOS (Supplemental Fig. 1). Women with PCOS were younger (mean age, 34.3 vs. 43.2 years), had a higher BMI (mean BMI, 36.7 vs. 30.0 kg/m^2), and had a higher prevalence of several conditions, including diabetes (28.3% vs. 14.7%) and depression (34.0% vs. 11.1%), than those without PCOS (Table 1). There were 1,290,243 reproductive-age (age, 18–49 years) women in the N3C. Of these, 36,472 (2.8%) had PCOS. Similar demographic characteristics were noted in the reproductive-age cohort compared with the overall cohort (Table 2).

Overall Cohort

In the overall cohort, the incidence of SARS-CoV-2-positive women with PCOS was 23.8%, compared with 28.3% in those without PCOS ($P<.001$). In unadjusted analyses, among those positive for SARS-CoV-2, 11.5% of women with PCOS had

TABLE 1

Demographic characteristics of the overall cohort.

Characteristic	PCOS (n = 39,459)	Non-PCOS (n = 2,050,454)	*P* value
Age, y (mean ± SD)	34.4 ± 9.7	43.2 ± 13.7	<.001
BMI (mean ± SD)	36.7 ± 10.1	30.0 ± 8.4	<.001
Race, n (%)			<.001
White	26,755 (67.8)	1,302,228 (63.5)	
Black	5,527 (14)	324,657 (15.8)	
Asian	1,067 (2.7)	56,008 (2.7)	
Hawaiian/Pacific Islander	81 (0.2)	3,340 (0.2)	
Other	393 (1)	16,989 (0.8)	
Missing	5,636 (14.3)	347,232 (16.9)	
Ethnicity, n (%)			<.001
Hispanic/Latino	5,305 (13.4)	244,725 (11.9)	
Not Hispanic/Latino	30,596 (77.5)	1,570,543 (76.6)	
Missing	3,558 (9)	235,186 (11.5)	
Smoking status, n (%)			<.001
Current/former	8,867 (22.5)	434,144 (21.2)	
Nonsmoker	30,592 (77.5)	1,616,310 (78.8)	
Antiandrogen medication use, n (%)	6,013 (15.2)	67,257 (3.3)	<.001
Hormonal contraceptive use, n (%)	9,659 (24.5)	158,013 (7.7)	<.001
Substance abuse	1,030 (2.6)	66,853 (3.3)	<.001
Depression	13,418 (34.0)	228,019 (11.1)	<.001
Diabetes	11,177 (28.3)	301,289 (14.7)	<.001
Cardiovascular disease	1,605 (4.1)	106,567 (5.2)	<.001
Obstructive sleep apnea, n (%)	6,509 (16.5)	143,565 (7.0)	<.001
Cerebrovascular accident	145 (0.4)	12,955 (0.6)	<.001
Chronic kidney disease	1,157 (2.9)	71,809 (3.5)	<.001
Chronic lung disease	651 (1.6)	72,022 (3.5)	<.001
Liver disease	1,272 (3.2)	41,606 (2)	<.001
Cancer	2,417 (6.1)	155,832 (7.6)	<.001
HIV/immunocompromised	100 (0.3)	8,223 (0.4)	<.001
Dementia	96 (0.2)	8,958 (0.4)	<.001

Note: HIV = human immunodeficiency virus; PCOS = polycystic ovary syndrome; SD = standard deviation.

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moderate COVID-19 compared with 10.5% of those without PCOS (P=.003). Death with COVID-19 occurred in 0.4% of those with PCOS compared with 0.7% of those without PCOS (P<.001). In analyses adjusted for age, BMI, race, smoking, antiandrogen use, hormonal contraceptive use, substance abuse, depression, cancer, cardiovascular disease, obstructive sleep apnea, chronic lung disease, chronic kidney disease, liver disease, and diabetes, the adjusted odds ratio (aOR) of SARS-CoV-2 positivity was 0.98 (95% CI, 0.97–0.98) in women with PCOS compared with those without PCOS. The aOR of mild disease was 1.02 (95% CI, 1.01–1.03). Subjects with PCOS were as likely to have moderate disease (aOR, 0.99; 95% CI, 0.98–1.00), severe disease (aOR, 0.99; 95% CI, 0.99–1.00), and death with COVID-19 (aOR, 1.00; 95% CI, 0.99–1.00) compared with those without PCOS (Table 3).

Sensitivity Analyses

In the reproductive-age cohort, the incidence of a positive SARS-CoV-2 test result in women with PCOS was 24%, compared with 30.3% in those without PCOS (P<.001). Among those who were positive, in unadjusted analyses, 88.5% of those with PCOS had mild COVID-19 compared with 91.7% of those without PCOS (P<.001). Moreover, 10.9% of patients with PCOS had moderate COVID-19 compared with 7.8% of those without PCOS (P<.001). In analyses adjusted for age, BMI, race, smoking, antiandrogen use, hormonal contraceptive use, substance abuse, depression, cancer, cardiovascular disease, obstructive sleep apnea, chronic lung disease, chronic kidney disease, liver disease, and diabetes, findings were similar to those observed in the overall cohort: SARS-CoV-2 positivity, aOR, 0.98 (95% CI, 0.98–0.99); mild disease, aOR, 1.02 (95% CI, 1.01–1.03); moderate disease, aOR, 0.99 (95% CI, 0.98–1.00); severe disease, aOR, 0.99 (95% CI, 0.99–1.00); and death with COVID-19, aOR, 1.00 (95% CI, 1.00–1.00) (Table 4). On further restriction to obese (BMI, ≥30 kg/m^2) reproductive-age women (n = 54,992), findings were similar to those observed in the overall reproductive-age cohort: SARS-CoV-2 positivity, aOR, 0.98 (95% CI, 0.98–0.99); mild disease, aOR, 1.02 (95% CI, 1.01–1.03); and moderate disease, aOR, 0.99 (95% CI, 0.98–1.00) (Supplemental Table 3). Severe disease and death could not be calculated because of low counts and the N3C policy.

DISCUSSION

To our knowledge, our study is the first to explore the impact of PCOS status on the incidence of a positive SARS-CoV-2 test result and COVID-19 severity in the United States. In our population cohort study, we found that women with PCOS had a statistically lower incidence of a positive SARS-CoV-2 test result than those without PCOS. In those who tested positive

TABLE 2

Demographic characteristics of the reproductive-age (18–49 years) cohorts.

Characteristic	PCOS (n = 36,472)	Non-PCOS (n = 1,253,771)	*P* value
Age, y (mean ± SD)	32.8 ± 8.1	34.2 ± 9.4	<.001
BMI (mean ± SD)	36.6 ± 10.1	29.5 ± 8.5	<.001
Race, n (%)			<.001
White	24,396 (66.9)	778,212 (62.1)	
Black	5,215 (14.3)	193,981 (15.5)	
Asian	1,018 (2.8)	37,304 (3)	
Hawaiian/Pacific Islander	78 (0.2)	2,374 (0.2)	
Other	367 (1)	11,934 (1)	
Missing	5,398 (14.8)	229,966 (18.3)	
Ethnicity, n (%)			<.001
Hispanic/Latino	5,143 (14.1)	167,360 (13.3)	
Not Hispanic/Latino	28,048 (76.9)	936,084 (74.7)	
Missing	3,281 (9)	150,327 (12)	
Smoking status, n (%)			<.001
Current/former	8,182 (22.4)	245,378 (19.6)	
Nonsmoker	28,290 (77.6)	1,008,393 (80.4)	
Antiandrogen medication use, n (%)	5,476 (15.0)	35,755 (2.9)	<.001
Hormonal contraceptive use, n (%)	9,541 (26.2)	148,234 (11.8)	<.001
Substance abuse	952 (2.6)	38,599 (3.1)	<.001
Depression	13,418 (36.8)	228,019 (18.2)	<.001
Diabetes	9,558 (26.2)	102,416 (8.2)	<.001
Cardiovascular disease	1,108 (3)	24,883 (2)	<.001
Obstructive sleep apnea, n (%)	5,533 (15.2)	52,609 (4.2)	<.001
Cerebrovascular accident	98 (0.3)	3651 (0.3)	.431
Chronic kidney disease	806 (2.2)	20,473 (1.6)	<.001
Chronic lung disease	456 (1.3)	12,756 (1)	<.001
Liver disease	1,095 (3)	17,227 (1.4)	<.001
Cancer	1,892 (5.2)	51,685 (4.1)	<.001
HIV/immunocompromised	90 (0.2)	3,950 (0.3)	.021
Dementia	64 (0.2)	1,760 (0.1)	.079

Note: HIV = human immunodeficiency virus; PCOS = polycystic ovary syndrome; SD = standard deviation.

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for SARS-CoV-2, they were more likely to have mild disease but were as likely to have severe disease or death with COVID-19 compared with women without PCOS, after adjusting for several known risk factors. These findings were similar when restricting the cohort to a younger reproductive-age population. However, it is important to note that all aORs closely approximated, if not encompassed, 1, making them clinically not significant differences.

Our findings are in contrast to those of the only other population-based study exploring the association between PCOS and COVID-19 (11). There are several possible reasons for this. The prior study included a cohort identified from The Health Improvement Network database, which consists of 365 active general practices in the United Kingdom. The composition of this cohort may be inherently different from the N3C, which also consists of inpatient and emergency

TABLE 3

Odds of COVID-19 in women with PCOS compared with that of those without PCOS in the overall cohort.

	N (%)		
Characteristic	PCOS	Without PCOS	aOR[b] (95% CI)
Positive SARS-CoV-2 test	9,374 (23.8)	580,933 (28.3)	0.98 (0.97–0.98)
Mild COVID-19[a]	8,227 (87.8)	513,238 (88.3)	1.02 (1.01–1.03)
Moderate COVID-19	1,075 (11.5)	61,013 (10.5)	0.99 (0.98–1.00)
Severe COVID-19	39 (0.4)	2,725 (0.5)	0.99 (0.99–1.00)
Death from COVID-19	33 (0.3)	3,957 (0.7)	1.00 (0.99–1.00)

Note: aOR = adjusted odds ratio; CI = confidence interval; COVID-19 = coronavirus disease 2019; PCOS = polycystic ovary syndrome; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

[a] We combined mild COVID-19 with mild emergency department in the National COVID Cohort Collaborative for a combined mild COVID-19 group.

[b] Adjusted odds ratio. Variables controlled for were age, body mass index, diabetes, cardiovascular disease, obstructive sleep apnea, cancer, chronic kidney disease, chronic lung disease, liver disease, substance abuse, antiandrogen use, hormonal contraceptive use, depression, and demographic variables, such as race, ethnicity, and smoking.

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TABLE 4

Odds of COVID-19 in women with PCOS compared with that of those without PCOS in the reproductive-age cohort.

	N (%)		
Characteristic	**PCOS**	**Without PCOS**	**aOR[b] (95% CI)**
Positive SARS-CoV-2 test	8,754 (24.0)	380,144 (30.3)	0.98 (0.98–0.99)
Mild COVID-19[a]	7,745 (88.5)	348,673 (91.7)	1.02 (1.01–1.03)
Moderate COVID-19	956 (10.9)	29,559 (7.8)	0.99 (0.98–1.00)
Severe COVID-19	33 (0.4)	1,022 (0.3)	0.99 (0.99–1.00)
Death from COVID-19	20 (0.2)	890 (0.2)	1.00 (1.00–1.00)

Note: aOR = adjusted odds ratio; CI = confidence interval; COVID-19 = coronavirus disease 2019; PCOS = polycystic ovary syndrome; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

[a] We combined mild COVID-19 with mild emergency department in the National COVID Cohort Collaborative for a combined mild COVID-19 group.

[b] Adjusted odds ratio. Variables controlled for were age, body mass index, diabetes, cardiovascular disease, obstructive sleep apnea, cancer, chronic kidney disease, chronic lung disease, liver disease, antiandrogen use, hormonal contraceptive use, substance abuse, depression, and demographic variables, such as race, ethnicity, and smoking.

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room data. As mentioned earlier, perhaps the biggest difference is that our study included only laboratory-confirmed SARS-CoV-2–positive cases and excluded cases suspected of COVID-19. The number of confirmed SARS-CoV-2–positive individuals with PCOS was also higher in our study (n = 9,391, compared with n = 14 in the UK cohort) (11). Although they adjusted for several factors, such as BMI, androgen excess, impaired glucose regulation, and cardiovascular disease, we were able to control for additional confounders, including socioeconomic variables, such as race and substance use, chronic kidney and lung disease, and cancer. Finally, it is possible that the demographic characteristics and socioeconomic differences in the 2 populations may explain the differences in our findings.

Given the known risk factors associated with PCOS, it is surprising that PCOS by itself was not associated with a higher odds of testing positive for SARS-CoV-2 or having a more severe COVID-19 course. When evaluating the features driving an increased risk of COVID-19, we found that several chronic conditions were significantly associated with moderate disease. For example, in the overall cohort, those with cardiovascular and chronic kidney diseases had 1.11 (95% CI, 1.10–1.12) and 1.16 (95% CI, 1.15–1.17) higher odds of moderate disease, respectively. Black race and substance abuse also had increased odds of moderate disease of 1.09 (95% CI, 1.09–1.10) and 1.12 (95% CI, 1.11–1.13), respectively. These factors have all been shown in other studies to drive COVID-19 risk (3, 26–28). Therefore, it is possible that although PCOS may predispose to certain long-term morbidities, overall, it is not a significant driver of severe COVID-19 risk by itself.

Although our findings are reassuring to the millions of women diagnosed with PCOS, a large proportion with associated comorbidities are, in fact, at increased risk of severe COVID-19. Moving forward, we need to continue monitoring outcomes with different types of SARS-CoV-2 variants and long COVID-19 syndrome in PCOS. Future studies should also explore whether the incidence of pregnancy complications with COVID-19 differs between those with PCOS and those without.

Our study has several strengths. Our sample size was large and distributed over a wide geographic area, with a racially diverse group of approximately 39,000 women with PCOS and >9,000 of whom tested positive for SARS-CoV-2. To decrease the heterogeneity of the group and increase the validity of our findings, we restricted our cohort to those with confirmed SARS-CoV-2 testing, excluding those with suspected COVID-19 but no testing, given the known overlap in symptomatology with other viral conditions. We also controlled for multiple known confounders, including major risk factors identified by the CDC, such as chronic kidney disease, depression, and diabetes (3, 15, 29). We were able to restrict our analysis for both age and BMI, thereby adding to the robustness of our findings and to better counsel our patients.

However, our study has some limitations. Because of the nature of the data set used, the prevalence of PCOS was lower than expected in the United States. It is, therefore, possible that those with PCOS were misclassified as not having PCOS. In such a situation, we would anticipate nondifferential misclassification, potentially resulting in more conservative estimates. The lower prevalence could also affect the generalizability of the findings. Body mass index data were also not available in approximately 48% of patients, therefore limiting the number of patients available for this sensitivity analysis. However, BMI data were assumed to be missing at random, and a complete case analysis was performed, given the limitations of conducting multiple imputation with large percentages of missing data (30). The data set did not have detailed information for us to differentiate phenotypes of PCOS and evaluate whether certain phenotypes, such as hyperandrogenic, carry different risk profiles for COVID-19 severity. We were able to control for antiandrogen medication and hormonal contraceptive use, which was used in a significantly larger proportion of women with PCOS. However, compliance with the medications cannot be assessed as well as the temporal use of these medications in relation to the COVID-19 diagnosis. In addition, although the N3C is a national data set, organizations have to elect to enroll; data are, thus, limited to contributing organizations. We also did

not assess the causality of our findings. Therefore, we caution against causal interpretations of our results without follow-up studies.

CONCLUSION

In conclusion, our study found that those with PCOS did not have a higher odds of testing positive for SARS-CoV-2. Furthermore, when they developed COVID-19, they were no more likely to have moderate or severe COVID-19. These findings differ from those of a prior study using UK data. Reasons for this could include a smaller PCOS sample size in the prior study resulting in lower power or potentially social and demographic differences between the United Kingdom and the United States.

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REFERENCES

1. Worldometer. Coronavirus cases. Available at: https://www.worldometers.info/coronavirus/coronavirus-cases/. Accessed January 14, 2022.
2. Cutler DM, Summers LH. The COVID-19 pandemic and the $16 trillion virus. J Am Med Assoc 2020;324:1495–6.
3. National Center for Immunization and Respiratory Diseases (NCIRD) Division of Viral Diseases. People with certain medical conditions. Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Accessed January 14, 2022.
4. Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril 2018;110:364–79.
5. Centers for Disease Control and Prevention. Polycystic ovary syndrome and diabetes. Available at: https://www.cdc.gov/diabetes/basics/pcos.html#:~:text=PCOS%20is%20one%20of%20the,beyond%20the%20child%2Dbearing%20years. Accessed February 2, 2022.
6. Dumesic DA, Oberfield SE, Stener-Victorin E, Marshall JC, Laven JS, Legro RS. Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome. Endocr Rev 2015;36:487–525.
7. Wekker V, van Dammen L, Koning A, Heida KY, Painter RC, Limpens J, et al. Long-term cardiometabolic disease risk in women with PCOS: a systematic review and meta-analysis. Hum Reprod Update 2020;26:942–60.
8. Cooney LG, Lee I, Sammel MD, Dokras A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod 2017;32:1075–91.
9. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update 2018;24:455–67.
10. Lim SS, Kakoly NS, Tan JWJ, Fitzgerald G, Bahri Khomami M, Joham AE, et al. Metabolic syndrome in polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. Obes Rev 2019;20:339–52.
11. Subramanian A, Anand A, Adderley NJ, Okoth K, Toulis KA, Gokhale K, et al. Increased COVID-19 infections in women with polycystic ovary syndrome: a population-based study. Eur J Endocrinol 2021;184:637–45.
12. Lizneva D, Kirubakaran R, Mykhalchenko K, Suturina L, Chernukha G, Diamond MP, et al. Phenotypes and body mass in women with polycystic ovary syndrome identified in referral versus unselected populations: systematic review and meta-analysis. Fertil Steril 2016;106:1510–20.e2.
13. Pasquali R, Zanotti L, Fanelli F, Mezzullo M, Fazzini A, Morselli Labate AM, et al. Defining hyperandrogenism in women with polycystic ovary syndrome: a challenging perspective. J Clin Endocrinol Metab 2016;101:2013–22.
14. Dilbaz B. Are women with polycystic ovary syndrome more vulnerable to COVID-19 infection? Turk J Obstet Gynecol2021;18:221-223.
15. Mahamat-Saleh Y, Fiolet T, Rebeaud ME, Mulot M, Guihur A, El Fatouhi D, et al. Diabetes, hypertension, body mass index, smoking and COVID-19-related mortality: a systematic review and meta-analysis of observational studies. BMJ Open 2021;11:e052777.
16. Ilias I, Goulas S, Zabuliene L. Polycystic ovary syndrome: pathways and mechanisms for possible increased susceptibility to COVID-19. World J Clin Cases 2021;9:2711-2720.
17. Morgante G, Troìa L, De Leo V. Coronavirus disease 2019 (SARS-CoV-2) and polycystic ovarian disease: is there a higher risk for these women? J Steroid Biochem Mol Biol 2021;205:105770.
18. Haendel MA, Chute CG, Bennett TD, Eichmann DA, Guinney J, Kibbe WA, et al. The National COVID Cohort Collaborative (N3C): rationale, design, infrastructure, and deployment. J Am Med Inform Assoc 2021;28:427–43.
19. Pfaff ER, Girvin AT, Gabriel DL, Kostka K, Morris M, Palchuk M, et al. Synergies between centralized and federated approaches to data quality: a report from the National COVID Cohort Collaborative. J Am Med Inform Assoc 2022;29:609–18.
20. Bennett TD, Moffitt RA, Hajagos JG, Amor B, Anand A, Bissell MM, et al. Clinical characterization and prediction of clinical severity of SARS-CoV-2 infection among US adults using data from the US National COVID Cohort Collaborative. JAMA Netw Open 2021;4:e2116901.
21. Cooney LG, Dokras A. Beyond fertility: polycystic ovary syndrome and long-term health. Fertil Steril 2018;110:794–809.
22. Behboudi-Gandevani S, Ramezani Tehrani F, Hosseinpanah F, Khalili D, Cheraghi L, Kazemijaliseh H, et al. Cardiometabolic risks in polycystic ovary syndrome: long-term population-based follow-up study. Fertil Steril 2018;110:1377–86.
23. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 194: polycystic ovary syndrome. Obstet Gynecol 2018;131:e157–71.
24. Metz TD, Clifton RG, Hughes BL, Sandoval GJ, Grobman WA, Saade GR, et al. Association of SARS-CoV-2 infection with serious maternal morbidity and mortality from obstetric complications. J Am Med Assoc 2022;327:748–59.
25. World Health Organization. Living guidance for clinical management of COVID-19. Geneva: World Health Organization; 2021.
26. Baillargeon J, Polychronopoulou E, Kuo YF, Raji MA. The impact of substance use disorder on COVID-19 outcomes. Psychiatr Serv 2021;72:578–81.
27. National Center for Immunization and Respiratory Diseases (NCIRD) Division of Viral Diseases. Risk for COVID-19 infection, hospitalization, and death by race/ethnicity, Available at: https://www.cdc.gov/coronavirus/2019-ncov/

covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html. Accessed January 14, 2022.
28. Singh AK, Gillies CL, Singh R, Singh A, Chudasama Y, Coles B, et al. Prevalence of co-morbidities and their association with mortality in patients with COVID-19: a systematic review and meta-analysis. Diabetes Obes Metab 2020;22:1915–24.
29. ERA-EDTA Council, ERACODA Working Group. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. Nephrol Dial Transplant 2021;36:87–94.
30. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ 2009;338:b2393.

Riesgo del síndrome respiratorio agudo grave por infección con coronavirus 2 en mujeres con síndrome de ovario poliquístico.

Objetivo: Determinar si las mujeres con síndrome de ovario poliquístico (SOP) tuvieron una mayor incidencia del síndrome respiratorio agudo severo por el coronavirus 2 (SARS-CoV-2) que aquellas sin SOP y evaluar si el diagnóstico de SOP de forma independiente aumentó el riesgo de enfermedad moderada o grave en aquellas con resultados positivos de la prueba de SARS-CoV-2.

Diseño: Estudio de cohorte retrospectivo utilizando el National COVID Cohort Collaborative (N3C).

Lugar: Cohorte Nacional colaborativo de COVID.

Paciente(s): Mujeres adultas no embarazadas (edad, 18–65 años) inscritas en el N3C con pruebas confirmadas de SARS-CoV-2 para cualquier indicación. Se realizaron análisis de sensibilidad en mujeres de 18 a 49 años que eran obesas (índice de masa corporal, $\geq$30 kg/m^2).

Intervención(es): La exposición fue SOP identificada por los códigos de diagnóstico clínico N3C y conjuntos de conceptos, que son una compilación de términos, valores de laboratorio y códigos de la Clasificación Internacional de Enfermedades para el diagnóstico de SOP. Para captar aún más pacientes con los síntomas del SOP, también incluimos a aquellas que tenían conjuntos de conceptos tanto para el hirsutismo como para la menstruación irregular.

Principal(es) medida(s) de resultado: Probabilidad de dar positivo para SARS-CoV-2 y probabilidad de enfermedad por coronavirus 2019 moderada o grave (COVID-19) en la cohorte de SOP en comparación con las de la cohorte sin SOP.

Resultado(s): De las 2,089,913 mujeres incluidas en nuestro estudio, 39,459 tenían SOP. En la cohorte general, el odds ratio (aOR) ajustado de positividad al SARS-CoV-2 fue de 0.98 (intervalo de confianza [IC] 95 %, 0.97–0.98) en las mujeres con SOP en comparación con la de las mujeres sin SOP. Los aOR de gravedad de la enfermedad fueron los siguientes: enfermedad leve, 1.02 (IC 95 %, 1.01–1.03); enfermedad moderada, 0.99 (IC 95 %, 0.98–1.00); y enfermedad grave, 0.99 (IC 95 %, 0.99–1.00). No hubo diferencias en la mortalidad relacionada con COVID-19 (aOR, 1.00; IC 95 %, 0.99–1.00). Estos hallazgos fueron similares en las cohortes de edad reproductiva y edad reproductiva obesa.

Conclusión(es): Las mujeres con SOP tenían una probabilidad similar de dar positivo para el SARS-CoV-2. Entre las que dieron positivo, no tenían más probabilidad de tener COVID-19 moderado o grave que la cohorte sin SOP. El síndrome de ovario poliquístico es una afección crónica asociada con varias comorbilidades, incluyendo enfermedad cardiovascular y problemas de salud mental. Aunque estas comorbilidades también están asociadas con la morbilidad por COVID-19, nuestros hallazgos sugieren que las comorbilidades en sí mismas, en lugar del SOP, impulsan el riesgo de gravedad de la enfermedad.