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Polycystic ovary syndrome and postpartum depression symptoms: a population-based cohort study

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Abstract

BACKGROUND: Women with polycystic ovary syndrome are more likely to experience several pregnancy complications including hypertensive disorders, gestational diabetes mellitus, and preterm births than women without polycystic ovary syndrome. However, at present, there is limited research on whether polycystic ovary syndrome is associated with both anxiety and depression during pregnancy and whether this augments a woman's risk of postpartum depression, particularly among high-risk populations who have limited access to care.

OBJECTIVE: Our primary objective was to assess the association between prepregnancy polycystic ovary syndrome and postpartum depression, considering important baseline confounding factors. Our secondary objective was to evaluate the mediating role of prenatal depression and anxiety on the association between polycystic ovary syndrome and postpartum depression.

STUDY DESIGN: This study involved a population-based sample of 3906 postpartum (2–6 months) women who completed the Utah Pregnancy Risk Assessment Monitoring System Phase 8 questionnaire (2016–2018). Weighted adjusted prevalence ratios were used to assess the association between polycystic ovary syndrome and postpartum depression, considering potential confounding factors and assessing mediating effects of depression and anxiety experienced during pregnancy.

RESULTS: Following the exclusion criteria, 8.2% of women reported clinical polycystic ovary syndrome and 19.1%, 6.2%, and 4.4% reported irregular periods and acne, irregular periods and hirsutism, and all 3 symptoms, respectively. Moreover, 17.7% and 23.5% reported experiencing prenatal depression and anxiety and 9.5% and 10.2% reported experiencing postpartum depressed

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mood and anhedonia, respectively. Clinical polycystic ovary syndrome was associated with a 1.76 higher adjusted prevalence ratio (95% confidence interval, 1.03–3.00) for postpartum depressed mood or anhedonia after taking into consideration age, prepregnancy body mass index, race/ethnicity, education, and marital status. A similar higher prevalence was seen for irregular periods and acne (adjusted prevalence ratio, 1.65; 95% confidence interval, 1.13–2.41), irregular periods and hirsutism (adjusted prevalence ratio, 1.40; 95% confidence interval, 0.82–2.40), and all 3 symptoms (adjusted prevalence ratio, 1.75; 95% confidence interval, 0.96–3.19) and postpartum depressed mood or anhedonia. Prenatal depression and anxiety mediated 20% and 32% of the effect of clinical polycystic ovary syndrome on postpartum depressed mood and anhedonia, respectively.

CONCLUSION: Clinical polycystic ovary syndrome is associated with postpartum depressed mood and symptoms among this population-based sample inclusive of high-risk mothers. Prenatal depression and anxiety mediate this association, emphasizing the importance of prenatal psychological screening among women with polycystic ovary syndrome. An additional important clinical and public health implication of this study lies in the finding that nearly 20% of women in this population-based sample who reported at least 2 polycystic ovary syndrome symptoms (including at-risk women who may not have access to care) had not received a clinical diagnosis for polycystic ovary syndrome.

Keywords

anxiety; depression; polycystic ovary syndrome; postpartum depression; PRAMS; pregnancy

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine metabolic disorder in women of reproductive age worldwide.[1] PCOS is characterized by anovulation, hyperandrogenism, and polycystic ovarian morphology,[2] with a prevalence ranging between 4% and 12% (approximately 4 million women) in the United States.[1] The yearly economic impact on the United States healthcare system to identify and manage PCOS among women totals more than $4 billion.[1]

Women with PCOS are more likely to experience several pregnancy complications including hypertensive disorders, gestational diabetes, and preterm births and are substantially more likely to experience infertility and seek related treatment than those without the syndrome.[3–5] In addition, existing research has demonstrated that nonpregnant women with PCOS have increased susceptibility to depression (28%–64%) and anxiety (34%–57%), namely, infertile women.[6] Although the risk of depression and anxiety in pregnant women with PCOS is expected to be higher, previous research has reported higher prenatal and postpartum depression (PPD),[7] but not postnatal depression,[8] or postnatal depression or anxiety[9] in women with PCOS compared with those without the syndrome. Whether PCOS is associated with both anxiety and depression during pregnancy and whether this augments a woman's risk of PPD, particularly among high-risk populations who have limited access to care, remain to be studied. To address this knowledge gap, our primary objective was to assess the association between a prepregnancy diagnosis and symptoms of PCOS and prevalence of depression and anxiety during pregnancy and in the postpartum period among

a population-based sample. Our secondary objective was to assess whether prenatal depression, anxiety, and pregnancy complications mediate the association between PCOS and PPD.

Materials and Methods

Study participants and questionnaire

The study population included women who completed the Utah Pregnancy Risk Assessment Monitoring System (UT-PRAMS) Phase 8 questionnaire between 2016 and 2018. In collaboration with state health departments, PRAMS is conducted by the Centers for Disease Control and Prevention's Division of Reproductive Health. One key aspect of PRAMS is the stratified systematic sampling, which oversamples on features related to high-risk women (eg, mothers of low-birth-weight infants, those living in high-risk geographic areas, and racial/ethnic minority groups). A detailed description of the PRAMS surveillance system methodology and protocols is found elsewhere.[10]

UT-PRAMS Phase 8 (2016–2018) drew stratified (by maternal education and infant birthweight) samples of approximately 200 new mothers (2–6 months after delivery) every month. New mothers are contacted via mailed questionnaire (available in English and Spanish) multiple times and telephone follow-up. An informed consent document was included within each survey packet explaining the participants' rights. Consent is implied if the survey is completed. Similarly, the informed consent document is read verbally on phone interviews, and the participant verbally agrees to proceed with the survey. No written consent was required. The data are analyzed and presented in aggregate, with no individual case data published. The expected national PRAMS response rate is 60%. UT-PRAMS response rates were 65%, 66%, and 62% for 2016, 2017, and 2018, respectively.

Mothers' responses were linked to extracted birth certificate data items, including pregnancy complications for index birth. The PRAMS weighting process produces an analysis weight considering the stratified sampling along with nonresponse and noncoverage components. The analysis weight of the PRAMS data can be interpreted as the number of women like herself in the population that each respondent represents.[10] This study and the use of PRAMS data (deidentified) have been acknowledged by the University of Utah as a nonhuman subject research (University of Utah Institutional Review Board # 00130386).

Exposure

The presence of PCOS before pregnancy was assessed based on clinical PCOS and common symptoms. The PCOS diagnosis question asked, "Have you ever been told that you have Polycystic Ovarian Syndrome or PCOS by a doctor, nurse, or other healthcare worker?"—requiring a response of "yes or no" or "do not know." A PCOS symptomology question asked, "Have you ever experienced any of the following health problems?"—with the following choices: (1) "Irregular periods (menstruation)"; (2) "Skin condition that causes pimples (acne)"; (3) "Increased hair growth on the face, chest, or other parts of the body (hirsutism)"; and (4) "Being overweight or obese." PCOS symptomology was defined in

possible alternate ways as having (1) irregular periods and acne, (2) irregular periods and hirsutism, or (3) irregular periods, acne, and hirsutism.[11]

Outcomes

To assess the presence of prenatal or pregnancy depression and anxiety, women were asked, "During your most recent pregnancy, did you have any of the following health conditions?" —where depression and anxiety were listed as possible choices, with responses "yes or no." PPD was defined having answered "always" or "often" to either of the following 2 questions that captured PPD or a postpartum depressed mood (1) and anhedonia (2): (1) "Since your new baby was born, how often have you felt down, depressed, or hopeless?" and (2) "Since your new baby was born, how often have you had little interest or little pleasure in doing things you usually enjoyed?" Combined effect variables were created to include those who had (1) both pregnancy depression and pregnancy anxiety and (2) either pregnancy depression or pregnancy anxiety. Similarly, PPD effect variables were created for those who had (3) both postpartum depressed mood and anhedonia and (4) either postpartum depressed mood or anhedonia.

Covariates

Covariates included maternal age, body mass index (BMI), race/ethnicity, education, and marital status. Prepregnancy BMI was calculated from self-reported height and weight from the birth certificate data. Maternal age and BMI were assessed both continuously and categorically. Although birth certificate data captures more detailed race/ethnicity information, UT-PRAMS is restricted to providing information on White or nonwhite and Hispanic or non-Hispanic regarding race/ethnicity owing to privacy issues. Marital status was defined as "married or other." Finally, a previous preterm birth (<37 weeks) and infertility treatment for index pregnancy were reported as "yes or no."

Variables available from the PRAMS questionnaire included smoking (yes or no, last 2 years) and alcohol (yes or no, last 2 years). Maternal education was recategorized from 8 to 5 categories (0–8, 9–11, 12, 13–15, and ≥16 years). Those with less than 9th-grade education or high school without a diploma, college and associate degrees, and master's and professional degrees were combined for the analysis. Delivery modality was grouped into 2 categories: (1) cesarean delivery and (2) vaginal delivery (spontaneous vaginal, unsuccessful or successful forceps vaginal, or successful or unsuccessful vacuum vaginal). Preterm birth for index pregnancy was defined as less than 37 week of the gestational period. Small for gestational age (SGA) was defined as weight below the 10th percentile for gestational age.[12] Finally, gestational diabetes mellitus (GDM), hypertensive diseases of pregnancy (HDP), and 3-month previous pregnancy depression questions (yes or no) were available from the PRAMS questionnaire.

Statistical analysis

Sociodemographic and health history characteristics among women with and without PCOS were compared using the chi-square test for categorical and *t* test for continuous variables, considering the complex sampling design.[10] To test the association between PCOS and postpartum depressive symptoms, unadjusted and adjusted robust Poisson distribution

models were used to estimate prevalence ratio (PR) and 95% confidence intervals (CIs). This was done using the Stata SVY: GLM (Stata-Corp LP, College Station, TX) function to account for weighted survey data.

The selection of potential covariates was informed by previous literature[8,13,14] and assessed for confounding and mediation using directed acyclic graphs.[15] The final multivariate regression models were adjusted for age, race/ethnicity, maternal education, marital status, and prepregnancy BMI. Based on a priori hypothesis that depression and anxiety, along with pregnancy complications, may mediate the relationship between PCOS and postpartum depressive symptoms, a counterfactual approach to mediation analysis was applied to estimate the PR for the natural direct effect (NDE) and the natural indirect effect (NIE) of clinical PCOS and symptoms on postpartum depressive symptoms mediated through clinical and psychological factors (Figure 1).[16] This was done by using the Stata PARAMED (Stata-Corp LP) function for mediating variables for clinical PCOS and PCOS defined as 2 or more symptoms. We also estimated proportion mediated to reflect the extent of mediation,[17] where 100% indicates all of the total effect being mediated (no direct effect) and 0% indicates there is no mediation (all direct effect).

Given that preconception depression (up to 3 months before conception) and infertility treatment for index pregnancy may act as confounders (common causes of PCOS and postpartum depressive symptoms) or mediators (on the pathway between PCOS and postpartum depressive symptoms), they were assessed both ways. Multiple sensitivity analyses were conducted for those women with concordant answers for having had PCOS before pregnancy (3 months before) and having ever been diagnosed as having PCOS by a healthcare worker (n=3686).

Exclusion criteria

Among the total sample of 4101 women who completed the survey, 145 women whose infant was not living at the time they completed the survey and 152 women who had no information regarding the presence of PCOS were excluded. The 3906 women included in the analysis reflect an estimated population of 142,963 women as per the PRAMS sampling strategy. Analyses were performed in SAS 9.4 (SAS Institute, Cary, NC)[18] and STATA 15.0 (Stata-Corp LP).[19]

Results

In weighted analyses, of the 3906 women, 8.2% of women were diagnosed as having PCOS (Table 1). Those with clinical PCOS were older (μ=30.4 years vs 28.6 years; $P<.001$), had higher BMI (28.7 vs 25.8; $P<.001$), and were more likely to report prenatal depression (21.2% vs 17.4%; $P=.18$), prenatal anxiety (30.8% vs 22.9%), and postpartum depressed mood (12.0% vs 9.2%) or anhedonia (13.6% vs 9.9%) than those without the syndrome. Similarly, women with clinical PCOS were more likely to report irregular periods and acne, irregular periods and hirsutism, and irregular periods, acne, and hirsutism (48% vs 19%, 43% vs 6%, and 30% vs 4%) (Figure 2).

A higher adjusted prevalence of prenatal anxiety (adjusted PR [aPR], 1.07; 95% CI, 1.01–1.13), prenatal depression or anxiety (aPR, 1.32; 95% CI, 1.06–1.63), postpartum anhedonia (aPR, 1.54; 95% CI, 1.04–2.27), and postpartum depressed mood and anhedonia (aPR, 1.76; 95% CI, 1.03–3.00) was observed among those with clinical PCOS than those without the syndrome (Table 2). Consistent with primary analysis, most prevalence estimates were similar in magnitude but differed in significance in sensitivity analyses (Supplemental Tables 1 and 2).

Mediation analysis

Prenatal depression and anxiety mediated the association between clinical PCOS and postpartum depressed mood by 20% (Table 3) (NDE, 1.66; 95% CI, 1.10–2.50; NIE, 1.10; 95% CI, 1.05–1.13) after controlling for confounders. Similarly, prenatal depression and anxiety mediated the association of 2 or more PCOS symptoms and postpartum depressed mood by 32% (NDE, 1.30; 95% CI, 0.96–1.76; NIE, 1.11; 95% CI, 1.05–1.13) after controlling for confounders. There was little evidence for a mediating effect of GDM, delivery modality, HDP, preterm births for index pregnancy, and SGA in the relationship between PCOS and postpartum depressed mood and anhedonia (Table 3).

In sensitivity analyses, prepregnancy depression, but not infertility, had a substantial mediating effect on the association between PCOS diagnosis (proportion mediated, 16%) and symptomology (proportion mediated, 28%) and postpartum depressed mood and anhedonia (Supplemental Table 3). PR estimates between PCOS and psychological factors remained robust when considering preconception depression (3 months before) and infertility treatment as confounders (Supplemental Table 4).

Discussion

Our primary findings among a statewide sample of postpartum women, targeted at high-risk mothers, indicate that women with a clinical PCOS have a 32% higher prevalence of prenatal depression or anxiety and 76% higher prevalence of postpartum depressed mood or anhedonia; similar findings were observed assessing PCOS via symptomology. In addition, we found that prenatal depression and anxiety mediate 20% to 32% of the effect of PCOS on postpartum depressed mood and anhedonia, emphasizing the importance of preconception and prenatal psychological screening among at-risk women with clinical PCOS diagnosis or symptoms.

Our results are consistent with a previous study that reported a positive association between PCOS and prenatal depression or anxiety (odds ratio, 1.80).[9] Previous studies have been more mixed when assessing the effect of PCOS on prenatal depression and PPD alone without factoring in anxiety or anhedonia.[7,8] Indeed, our findings indicating a stronger relationship between PCOS and prenatal anxiety and postpartum anhedonia emphasize the importance of including these conditions when evaluating PCOS-related psychological distress.

We found notable consistency in the direction and magnitude of effects across various measures of PCOS, from physician diagnosis to PCOS symptoms, including irregular

periods, acne, or hirsutism. Similarly, although we did not have a direct medical diagnosis of PPD owing to the population-based data of our study design, our findings were consistent across different symptoms associated with PPD, namely, depressed mood or anhedonia. Clinical studies have shown that women with PCOS have increased susceptibility to depression and anxiety and postpartum depressed mood potentially owing to hormonal imbalance and distressed metabolic profiles such as elevated androgens,[20] hypersensitivity of the hypothalamic-pituitary-adrenal axis, and greater plasma adrenocorticotropic hormone and serum cortisol levels.[21] These conditions make women with PCOS less resilient compared with women without PCOS to similar stressful events caused by pregnancy, infertility treatment, and pregnancy-related complications.

This study considers a mediating effect of clinical and psychological factors on the relationship between PCOS and postpartum mental health. We found that although prenatal depression and anxiety explain up to a third of postpartum depressed mood and anhedonia, after taking into account important baseline confounding factors, infertility or pregnancy complications play little to no mediating role in the relationship between PCOS and postpartum mental health. This is in line with previous PRAMS research indicating a null relationship between infertility treatment and PPD symptoms.[22]

Strengths and limitations

Our study had a number of strengths, including being the first population-based study to the best of our knowledge to assess the relationship between clinical and symptomology-based PCOS and symptoms of anxiety or depression before, during, and after pregnancy. Although postpartum self-report of symptoms that occurred before pregnancy is vulnerable to recall bias, PRAMS purposively includes PCOS symptomology in addition to reporting of a PCOS diagnosis by a clinician to fully capture PCOS prevalence in a population of at-risk women who may have limited access to healthcare. Furthermore, we are unique in not only controlling for important sociodemographic and lifestyle confounding factors but also considering the mediating impact of psychological and reproductive health factors that occur between PCOS, which most often begins in adolescence around the start of menstruation, and PPD.

Nevertheless, this study had some limitations. The cross-sectional study design limits the ability to infer causality of the relationships. Although the PRAMS is susceptible to recall bias given that women retrospectively recall information that happened before, during, and after pregnancy, this is temporality built into the questionnaire, with recall taking place within a 1-year time frame. Because most data are self-reported 2 to 6 months after delivery, it is susceptible to recall bias. However, compared with commonly used screening tools for depression in clinical practice or research, the accuracy of the PRAMS has been shown comparable with the Patient Health Questionnaire-9, a 9-item validated self-reported screening instrument used in clinical practice in detecting PPD.[23] Although PRAMS is less comparable with the Edinburgh Postnatal Depression Scale, a common self-reported screening tool used in research, 1 anxiety item is common in both.

In addition, although UT-PRAMS follows strict sampling processes targeting at-risk mothers and had a higher than expected overall response rate in 2016 to 2018, the respondents were

predominantly White (91%) and non-Hispanic (84%), limiting generaliz-ability.[10] Furthermore, the PRAMS survey did not include a postpartum anxiety symptom assessment, which would be valuable to compare the change in depression and anxiety during and after pregnancy. Finally, although PCOS has been defined using different criteria available, the Rotterdam PCOS consensus workshop group concluded that a single diagnosis criterion is insufficient for clinical PCOS diagnosis.[24] In addition to clinical criteria in determining a PCOS diagnosis, of the following symptoms, our PCOS symptomology definition meets at least 2 needed criteria for a woman to be diagnosed as having PCOS: (1) irregular periods; (2) higher than normal blood levels of androgens; (3) signs of abnormally high levels of androgens, including excess facial and body hair (hirsutism), acne, or thinning of scalp hair; and (4) multiple cysts on 1 or both ovaries.[11] Although PCOS symptomology is not used in isolation in determining a clinical diagnosis of PCOS, our criteria likely meet both the Rotterdam and Androgen Excess and PCOS Society criteria.[1,24]

Self-reported PCOS diagnosis and depression status can result in the overestimation of the relationship between PCOS and postpartum depressed mood. However, our crude estimates were not radically different from that of another study that assessed PPD in a community setting of women.[8,9] Like-wise, we are unable to assess puerperal blues, which is a common but self-limited condition that lasts up to 2 weeks after childbirth, which also could lead to the overestimation of the results. However, women completed the UT-PRAMS survey in 2016 to 2018 on an average of 3.9 months (standard error, 0.02) after delivery and were categorized as having postpartum depressive mood and anhedonia, respectively, if they reported feeling “often” or “always” to being “down, depressed, or hopeless” or had “little interest or little pleasure in doing things [they] usually enjoyed” since their new baby was born. Therefore, the PRAMS assessment more accurately estimates postpartum depressed mood rather than puerperal blues.

Implications

These findings show that PCOS is associated with postpartum depressive mood or anhedonia among a population-based sample, targeted specifically at high-risk mothers. In addition, our findings indicate that preconception and prenatal depression and anxiety, but not pregnancy complications including GDM and HDP, mediate the association between PCOS and postpartum depressed mood. This emphasizes the value of prenatal psychological screening among women with clinical PCOS because symptoms associated with the syndrome are known to contribute to poor mental health and in turn are likely to elevate the risk of depression and anxiety. An additional important clinical and public health implication of this study lies in the finding that nearly 20% of women in this population-based sample who reported at least 2 PCOS symptoms (including at-risk women who may not have access to care) had not received a clinical diagnosis for PCOS.

Conclusion

Future studies with detailed medical records data will be needed to confirm PCOS diagnosis and therefore confirm our findings. Nevertheless, our findings highlight the importance of assessing for PCOS symptoms in addition to clinical diagnosis in nationally representative population-based surveys such as PRAMS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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AJOG at a Glance

Why was this study conducted?

Women with polycystic ovary syndrome (PCOS) have increased susceptibility to depression (28%–64%) and anxiety (34%–57%) outside of pregnancy, yet there is limited population-based research on whether PCOS is associated with both anxiety and depression during pregnancy and how this may augment a woman's risk of postpartum depression.

Key findings

Clinical PCOS was associated with a higher prevalence of postpartum depressed mood and anhedonia after adjusting for potential confounders. Prenatal depression and anxiety partially mediated the association between clinical PCOS and postpartum depressed mood and anhedonia.

What does this add to what is known?

Clinical PCOS and symptomology are associated with postpartum depressed mood among a population-based sample inclusive of high-risk mothers. Prenatal depression and anxiety mediate the association between PCOS and postpartum depressed mood, emphasizing the importance of prenatal psychological screening among women with PCOS.

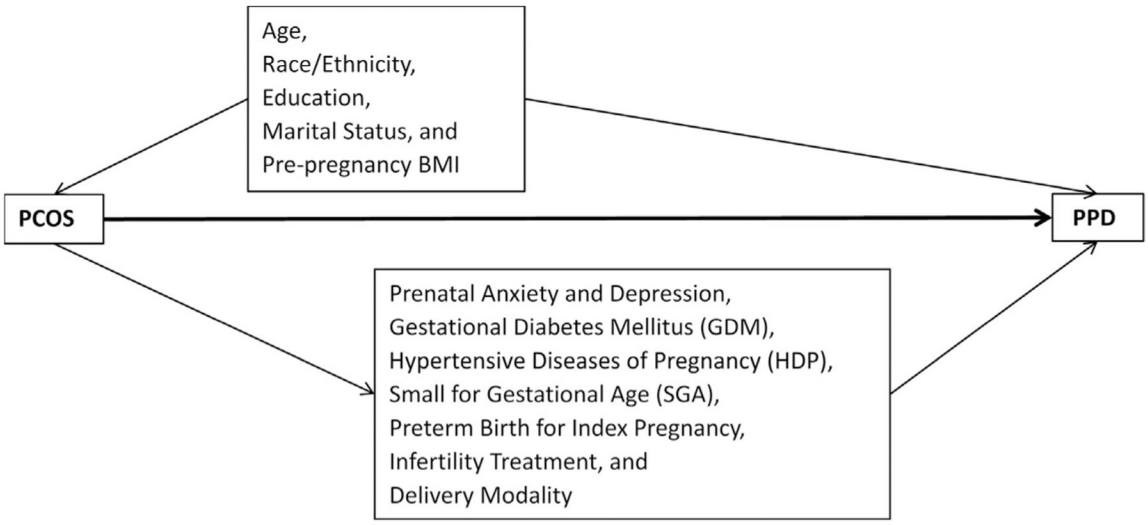

FIGURE 1. A directed acyclic graph demonstrating relationship between PCOS and PPD

Prenatal depression and infertility treatment for index pregnancy assessed as both potential confounders and mediators of the relationship between PCOS and postpartum depressed mood.

BMI, body mass index; *GDM*, gestational diabetes mellitus; *HDP*, hypertensive diseases of pregnancy*; PCOS*, polycystic ovary syndrome; *PPD*, postpartum depression.

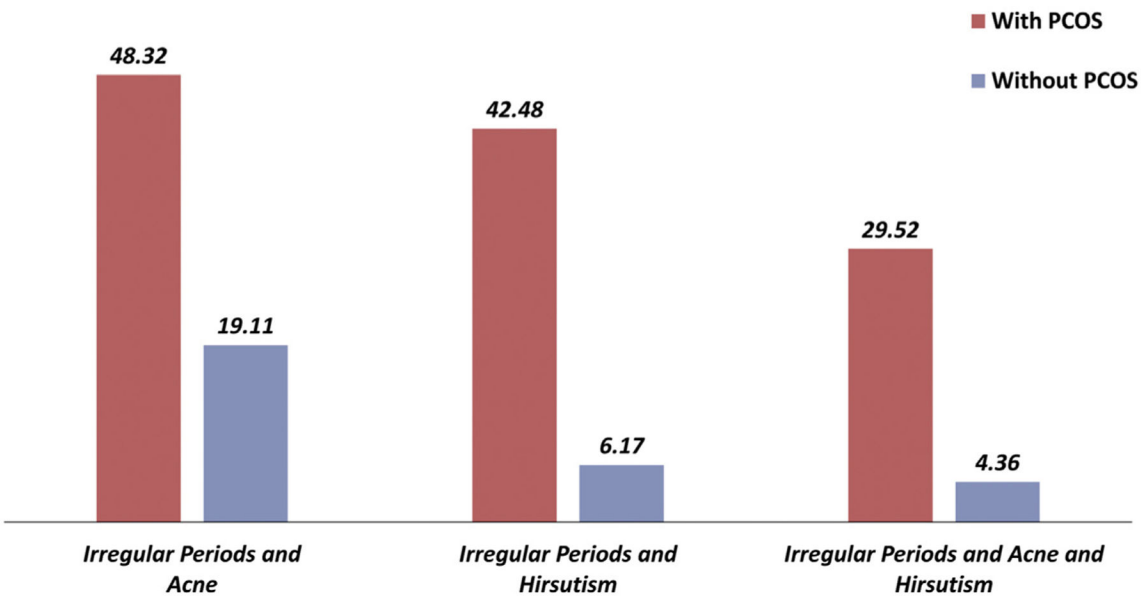

FIGURE 2. Proportion (%) of women with and without medical diagnosis of PCOS reporting 2 or more symptoms of PCOS

PCOS symptomology defined as irregular periods (menstruation) and skin conditions that cause pimples (acne) and increased hair growth on the face, chest, or other parts of the body. *PCOS*, polycystic ovary syndrome.

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TABLE 1

Characteristics of 3906[a] women by prepregnancy polycystic ovary syndrome diagnosis (2016–2018)

		Polycystic ovary syndrome		
Characteristics, %, *μ*±SD	**Total**	**Yes (8.19%)**	**No (91.81%)**	***P* value[b]**
Age, y	28.73±0.10	30.43±0.38	28.57±0.11	<.001
<18	0.72	0.14	0.78	
18–24	23.54	14.64	24.34	
25–29	33.14	30.24	33.40	
30+	42.60	54.98	41.48	
BMI, kg/m^2[c]	26.04±0.12	28.65±0.54	25.80±0.12	<.001
<18	6.11	4.40	6.26	
18–24	53.53	42.67	54.49	
25–29	18.19	15.44	18.44	
30+	22.17	37.49	20.81	
Ethnicity				
Non-Hispanic	84.50	85.77	84.38	.62
Hispanic	15.50	14.23	15.62	
Race				
Mother White	91.15	94.61	90.84	.04
Mother nonwhite	8.85	5.39	9.16	
Education[c]				
Up to 12th grade	8.08	4.32	8.41	<.001
High school	19.73	13.34	20.31	
Some college	34.45	32.87	34.59	
Bachelor’s degree	30.54	39.91	29.70	
Higher education	7.20	9.56	6.99	
Married	82.58	91.18	81.81	<.001
Smoker[c,d]	2.83	2.99	2.82	.88

		Polycystic ovary syndrome		
Characteristics, %, μ±SD	**Total**	**Yes (8.19%)**	**No (91.81%)**	***P* value[b]**
Drinker[d]	33.51	31.92	33.66	.62
Hypertensive diseases of pregnancy[c]	10.51	14.64	10.15	.04
Gestational diabetes mellitus for index pregnancy[c]	7.49	12.20	7.07	.01
Preterm births (<37 wk) for index pregnancy	8.12	11.81	7.79	.01
Previous preterm births (<37 wk)	5.46	8.61	5.18	.04
Small for gestational age[c]	2.04	2.89	1.96	.02
Infertility treatment	6.74	32.43	4.44	<.001
Delivery modality				
Vaginal	78.64	72.48	79.19	
Cesarean	21.36	27.52	20.81	.03
Previous depression (3 mo before pregnancy)	17.18	18.23	17.09	.67
Prenatal psychological symptoms				
Prenatal depression[c]	17.73	21.24	17.42	.18
Prenatal anxiety[c]	23.52	30.81	22.88	.02
Prenatal depression and anxiety	13.64	15.76	13.45	.37
Prenatal depression or anxiety	27.51	35.78	26.80	.01
Postpartum psychological symptoms				
Postpartum depressed mood[c]	9.46	11.97	9.24	.20
Postpartum anhedonia[c]	10.16	13.55	9.86	.10
Postpartum depressed mood and anhedonia	4.87	7.92	4.60	.04
Postpartum depressed mood or anhedonia	14.80	17.72	14.54	.24

BMI, body mass index; *SD*, standard deviation.

[a]Reflecting an estimated population size of 142,963 women;

[b]Two-sided chi-square test;

[c]Frequencies do not add up to 100% because of missing values;

[d] Smoker and drinker measured at the last 2 years before pregnancy.

TABLE 2

Adjusted prevalence ratios and 95% CIs on the relationship among PCOS, related symptoms, and psychological symptoms (2016–2018) (n = 3906[a])

Psychological characteristics	PCOS diagnosis	Irregular periods and acne	Irregular periods and hirsutism	Irregular periods, acne, and hirsutism
Prenatal psychological factors[b]				
Prenatal depression				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.03 (0.98–1.09)	1.05 (1.02–1.08)	1.03 (0.98–1.08)	1.03 (0.98–1.10)
Prenatal anxiety				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.07 (1.01–1.13)	1.07 (1.03–1.10)	1.05 (0.99–1.10)	1.05 (0.99–1.11)
Prenatal depression and anxiety				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.25 (0.88–1.77)	1.33 (1.07–1.65)	1.11 (0.80–1.54)	1.12 (0.76–1.65)
Prenatal depression or anxiety				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.32 (1.06–1.63)	1.36 (1.18–1.56)	1.27 (1.04–1.54)	1.30 (1.03–1.63)
Postpartum psychological factors[b]				
Postpartum depressed mood				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.34 (0.90–1.99)	1.43 (1.09–1.88)	1.03 (0.67–1.57)	1.08 (0.65–1.78)
Postpartum anhedonia				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.54 (1.04–2.27)	1.19 (0.90–1.56)	1.15 (0.77–1.71)	1.51 (0.98–2.33)
Postpartum depressed mood and anhedonia				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.33 (0.96–1.84)	1.20 (0.96–1.49)	0.99 (0.70–1.39)	1.14 (0.77–1.68)
Postpartum depressed mood or anhedonia				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.76 (1.03–3.00)	1.65 (1.13–2.41)	1.40 (0.82–2.40)	1.75 (0.96–3.19)

BMI, body mass index; *CI*, confidence interval; *PCOS*, polycystic ovary syndrome; *Ref.*, reference.

[a] Reflecting an estimated population size of 142,963 women;

[b] Models adjusted for age, prepregnancy BMI, ethnicity, race, education, and marital status.

TABLE 3

Adjusted direct, indirect, and total effect on the effects of PCOS (diagnosis by healthcare provider and symptomology) on postpartum depressed mood and anhedonia mediated through clinical and psychological factors (n = 3906[a])

Mediating factors	NDE, aPR (95% CI)	NIE, aPR (95% CI)	TE, aPR (95% CI)	Proportion mediated[b]
PCOS diagnosis[c]				
Prenatal depression and anxiety	1.66 (1.10–2.50)	1.10 (1.05–1.13)	1.81 (1.19–2.73)	20
Delivery modality[d]	1.73 (1.15–2.62)	1.00 (0.83–1.22)	1.74 (1.11–2.74)	0
GDM	1.77 (1.17–2.68)	0.99 (0.97–1.02)	1.76 (1.17–2.66)	2
HDP	1.74 (1.15–2.63)	1.01 (0.97–1.05)	1.76 (1.67–2.66)	2
Preterm births (<37 wk) for index pregnancy	1.68 (1.11–2.54)	1.03 (0.97–1.10)	1.74 (1.15–2.63)	7
Small for gestational age	1.72 (1.14–2.60)	1.01 (0.98–1.05)	1.74 (1.15–2.63)	2
PCOS symptomology (2+ symptoms)[c,e]				
Prenatal depression and anxiety	1.30 (0.96–1.76)	1.11 (1.07–1.15)	1.44 (1.07–1.95)	32
Delivery modality	1.44 (1.06–1.94)	1.00 (0.88–1.14)	1.44 (1.04–2.00)	0
GDM	1.43 (1.05–1.93)	1.00 (0.98–1.02)	1.43 (1.05–1.93)	0
HDP	1.44 (1.07–1.94)	1.01 (0.98–1.04)	1.45 (1.07–1.96)	3
Preterm births (<37 wk) for index pregnancy	1.44 (1.06–1.94)	1.01 (0.97–1.05)	1.45 (1.07–1.96)	3
Small for gestational age	1.44 (1.07–1.94)	1.00 (0.98–1.03)	1.44 (1.07–1.95)	0

aPR, adjusted prevalence ratio; *BMI*, body mass index; *CI*, confidence interval; *GDM*, gestational diabetes mellitus; *HDP*, hypertensive diseases of pregnancy; *NDE*, natural direct effect; *NIE*, natural indirect effect; *OR*, odds ratio; *PCOS*, polycystic ovary syndrome; *TE*, total effect.

[a]Reflecting an estimated population size of 142,963 women;

[b]Proportion mediated=(NDE/[NIE-1])/(NDE×NIE-1);

[c]Models adjusted for age, prepregnancy BMI, ethnicity, race, education, and marital status;

[d]Cesarean delivery is used as a reference;

[e]Defined as having a and b, a and c, or a, b, and c; 4 common PCOS symptoms include (1) skin conditions that cause pimples (acne); (2) irregular periods (menstruation); (3) increased hair growth on the face, chest, or other parts of the body; and (4) being overweight or obese.

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