VIA MEDICA

ORIGINAL PAPER / OBSTETRICS

Ginekologia Polska
2024, vol. 95, no. 5, 365–372

ISSN 0017–0011, e-ISSN 2543–6767

DOI: 10.5603/gpl.92311

Preeclampsia in pregnant women with polycystic ovary syndrome: risk factor analysis based on a retrospective cohort study

Ruoan Jiang[1], Yingsha Yao[1], Ting Wang[1], Baohua Li[1], Peiyue Jiang[1], Fangfang Wang[1], Fan Qu[2]

[1]Department of Obstetrics and Gynecology, Women's Hospital Zhejiang University School of Medicine, Hangzhou, China
[2]Women's Hospital Zhejiang University School of Medicine, Hangzhou, China

ABSTRACT

Objectives: To compare the clinical characteristics of pregnant women with polycystic ovary syndrome (PCOS) and perinatal outcomes with or without preeclampsia (PE) and to factors that are potentially associated with the onset of PE.

Material and methods: This was a retrospective study of pregnant women diagnosed with PCOS from January 2017 to December 2021. Eligible patients were divided into two groups based on the presence or absence of preeclampsia: a PE group and a non-PE group. Demographics, clinical characteristics, maternal and perinatal outcomes, and potential factors linked to disease recurrence were analyzed.

Results: In total, 616 patients were enrolled and respectively classified into the PE group (n = 51) and the non-PE group (n = 565). The incidence of PE in pregnant women with PCOS was 8.28%; this was significantly higher than that in non-PCOS pregnant women (3.22%, $p < 0.001$). Logistic regression analysis of the predictive factors for PE in women with PCOS revealed that the combination of maternal hyperandrogenism, a pre-pregnancy BMI ≥ 24 kg/m^2, and a family history of cardiovascular disease (CVD) and assisted reproductive techniques (ART) exhibited the steepest receiver-operating characteristic (ROC) curve value at 0.797 [95% confidence interval (CI): 0.733–0.862].

Conclusions: Patients with PCOS have a higher incidence of PE. We identified a series of significant and independent factors associated with PE in PCOS: maternal hyperandrogenism, a pre-pregnancy BMI ≥ 24 kg/m^2, and a family history of CVD and ART.

Keywords: PCOS; obstetric outcomes; predictors; preeclampsia; hyperandrogenism

Ginekologia Polska 2024; 95, 5: 365–372

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a disorder that is characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries [1] and leads to several health complications, including menstrual dysfunction, infertility, hirsutism, acne, obesity, and metabolic syndrome [2]. The estimated prevalence of PCOS varies from 3–20% depending on the diagnostic criteria used [3].

Pregnant women with PCOS are at increased risk for pregnancy complications and neonatal complications. Previous meta-analyses on pregnancy and delivery complications report an increased risk for miscarriage, gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), preterm birth and caesarean section (CS) in women with PCOS [4]. After controlling for all potential confounding effects, Mills reported that women with PCOS have a 50% increased risk for the development of PIH and a 30% increased risk of developing preeclampsia (PE) than women without PCOS; these authors also concluded that PCOS is an independent risk factor for GDM and PIH [5]. A stronger association between PCOS and hypertensive disorders has also been reported [6]. PCOS in pregnancy was also shown to be associated with the increased risk of PIH and PE [7]. Collectively, these studies indicated that PCOS may be one of the risk factors of PIH or PE.

Corresponding author:
Fan Qu
Women's Hospital Zhejiang University School of Medicine, Hangzhou 310006, China
e-mail: syqufan@zju.edu.cn

Received: 20.10.2022 Accepted: 03.10.2023 Early publication date: 20.10.2023

Preeclampsia is one of the most feared and challenging complications of pregnancy and a significant focus of our research. In a previous study, we found that the incidence of PE in PCOS was 6.9–9.6%, much higher than the incidence of PE in the general population reported in previous studies (1.4–2.1%) [8, 9]. In addition to the risk factors for PE that have been described in previous guidelines (*e.g.*, previous pregnancy with preeclampsia, multifetal gestation, renal disease, autoimmune disease, type 1 or type 2 diabetes mellitus, and chronic hypertension), some studies have found that hyperandrogenemia [10] and obesity [11] might also be high-risk factors for PCOS complicated with PE.

In the present study, we performed a systematic analysis of the risk factors for PE in pregnant women with PCOS based on a retrospective cohort study. Our intention was to provide guidance for the prevention of PE in patients with PCOS.

MATERIAL AND METHODS

Patients

This retrospective study was conducted in the Women's Hospital, Zhejiang University School of Medicine, China. We analyzed the clinical characteristics, laboratory indices, and maternal-fetal and neonatal complications of patients who had a history of PCOS and delivered in our hospital between January 2017 and Dec 2021. The inclusion criteria were as follows: (1) PCOS was diagnosed in our hospital before pregnancy, and (2) delivery in our hospital with a complete dataset and postpartum follow-up. Patients were excluded if they had chronic hypertension. Patients who met the inclusion and exclusion criteria were enrolled in the study and separated into two groups based on the presence or absence of PE.

The diagnosis of PCOS was made according to the Rotterdam criteria (2003) and at least two of the following three criteria were met: clinical and/or biochemical signs of hyperandrogenism, oligo-ovulation and/or anovulation, and a polycystic ovary on ultrasonography, with the exclusion of any related diseases, such as adrenal congenital hyperplasia, Cushing syndrome, androgen-secreting tumors, or Hashimoto's thyroiditis [1]. Preeclampsia was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on two recordings four hours apart and proteinuria of at least 300 mg/24 hours or at least 1+ or more on dipstick testing in a random urine sample on at least two occasions [12]. Gestational diabetes was, according to a one-step approach, defined as any single threshold value that met or exceeded a fasting value of 92 mg/dL, a 1-hour value of 180 mg/dL, or a 2-hour value of 153 mg/dL) [13]. Intrahepatic cholestasis of pregnancy (ICP) was diagnosed according to the following criteria: bile acid > 10 μmol/L and pruritus, with or without elevated transaminase [14].

Clinical assessment

We collected a range of anthropometric measurements, including weight, height, along with the levels of follicle-stimulating hormone (FSH) (mIU/mL), luteinizing hormone (LH) (mIU/mL), prolactin (PRL) (ng/mL), estradiol (E2) (pg/mL), progesterone (ng/mL), total testosterone (TT) (ng/mL), dehydroepiandrosterone sulfate (DHEA-S) (μg/dL) and sex hormone-binding globulin(SHBG) (nmol/L) obtained on the morning of the third to fifth day of the menstrual cycle.

Maternal age (years) at birth was recorded and the women were categorized as advanced age if aged ≥ 35 years. Body mass index was also calculated [weight (kg)/ (height (m)^2]. Parity was classified as nulliparous or parous. The medical birth registers also contained information on whether the pregnancy was conceived by assisted reproductive technology (ART), ovarian stimulation, artificial insemination or not, and information was acquired relating to concurrent diseases such as pregestational diabetes mellitus, autoimmune disease, thyroid dysfunction and medication during pregnancy. Infants born small for gestational age were defined as having birth weights of less than 2 standard deviations below the mean for gestational age and sex of the infant. Preterm birth at delivery that was less than 37 weeks of gestation, was classified as moderate (32 + 0 to 36 + 6 weeks) and very preterm birth (< 32 weeks). Perinatal mortality was defined as intrauterine fetal death after 28 weeks of gestation or death of the infant from 0 to 27 days after birth.

Ethics statement

The current study was approved by the ethics committee of Women's Hospital, Zhejiang University School of Medicine (Ethics NO. IRB-20220220-R). This study is a retrospective study of medical records and archived samples with no harm to patients' interests and no harm to patients' privacy. We ensure that we have discussed whether all data were fully anonymized before you accessed them, and the ethics committee waived the requirement for informed consent. And our study did not include minors.

Statistical analysis

Descriptive data are presented as medians and interquartile ranges for continuous variables and as numbers and percentages for categorical variables. Binary logistic regression analysis was performed to determine the significant independent contribution of those variables yielding a p value < 0.05. Logistic regression analysis was subsequently used to investigate the significant factors as predictors. Receiver-operating characteristic (ROC) curves were constructed, and the area under the curve (AUC) was used to compare the predictive value. Then, we estimated the sensitivity, specificity, predictive values, and likelihood ratios.

A two-sided alpha level of < 0.05 was selected to represent statistical significance. The statistical software packages SPSS 26.0 (SPSS Inc., Chicago, IL, USA), GRAPHPAD (GraphPad Software, San Diego, CA, USA) and MEDCALC (MedCalc Software, Mariakerke, Belgium) were used for data analyses.

RESULTS

A total of 887 pregnant patients with PCOS were diagnosed in our gynecological clinic between January 2017 and December 2021. In total, 616 cases were included in this study once the inclusion and exclusion criteria had been applied. Of the 616 patients, 51 cases were diagnosed with PE. During the same period, 96532 deliveries took place in our hospital, and PE was diagnosed in 3148 patients between January 2017 and December 2021. The incidence of PE in PCOS pregnant women was 8.28%, significantly higher than that in non-PCOS pregnant women (3.22%, p < 0.001). The screening process of cases according to the inclusion and exclusion criteria is shown in Figure 1.

The demographic and laboratory characteristics of pregnant women diagnosed PCOS are described in Table 1. There were no significant differences between the two groups in terms of multipara, natural conception, ovarian stimulation, artificial insemination (AI), or medication during pregnancy. Similarly, there were no significant differences in the incidences of complications of pregnancy, including thyroid dysfunction, autoimmune disease. As shown in Table 1, the mean age of pregnant women in the PE group was significantly higher than that in the non-PE group (31.71 ± 3.64 vs 29.79 ± 3.58 years, p < 0.001). The rate of maternal hyperandrogenism in the PE group was 27.45% (14 cases); this was significantly higher than that in the non-PE group (5.66%; 32 cases; p < 0.001). The incidence of a family history of cardiovascular disease (CVD) in the PE group was 31.37% (16 cases); this was significantly higher than that in the non-PE group (7.79%; 44 cases; p < 0.001). Pre-pregnancy body mass index (BMI) in the PE group was significantly higher than that in the non-PE group (24.07 ± 3.72 vs 22.05 ± 3.45 kg/m^2, p < 0.001). We also found that the proportion of cases involving ART in the PE group was significantly higher than that in the non-PE group (43.14% vs 23.54%, p < 0.001). The rate of multifetal gestation in the PE group was significantly higher than that in the non-PE group (25.49% vs 12.92%, p = 0.040). The prevalence of pregestational diabetes mellitus (PGDM) in the PE group was 7.84% (4 cases); this was significantly higher than in the non-PE group (2.12%; 12 cases; p = 0.014). With regards to the outcome of complications of pregnancy, this study showed that the incidence of FGR in the PE group was significantly higher than that in the non-PE group (9.80% vs 1.42%, p < 0.001), and the rate of cesarean section in the PE group was significantly higher than that in the non-PE group (80.39% vs 43.36%, p < 0.001).

Furthermore, we compared perinatal outcomes between the two groups. Compared to the non-PE group, the number of gestational weeks for newborns in the PE group was significantly lower (257.57 ± 17.68 *vs.* 268.44 ± 18.26 days, p = 0.001) and the probability of premature delivery was significantly higher (43.14% vs 16.28%, p = 0.001). The incidence of SGA in the PE group was significantly higher than that in the non-PE group (7.81% vs 1.88%, p = 0.003). In addition, newborns in the PE group had a significantly lower birth weight than those in the non-PE group (2589.76 ± 721.04 vs 3012.50 ± 700.73 g, p < 0.001), as well

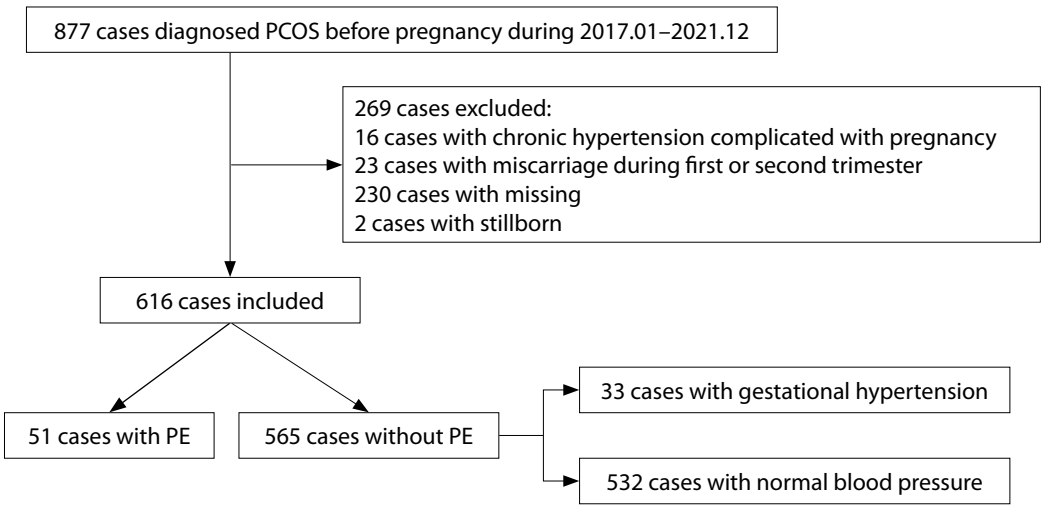

Figure 1. Case screening flowchart of this study; PCOS — polycystic ovary syndrome; PE — preeclampsia

Table 1. Demographic and clinical characteristics of pregnant women diagnosed polycystic ovary syndrome (PCOS) with preeclampsia (PE) and non-PE

	PE (n = 51)	non-PE (n = 565)	p value
Age (mean ± SD) [year]	31.71 ± 3.64	29.79 ± 3.58	0.000
Parity (n, %)			0.235
Nulliparous	46 (90.20)	474 (83.89)	
Multiparous (n, %)	5 (9.80)	91 (16.11)	
Hyperandrogenism (n, %)	14 (27.45)	32 (5.66)	0.000
Family history of CVD (n, %)	16 (31.37)	44 (7.79)	0.000
Pre-pregnancy BMI [kg/m^2]	24.07 ± 3.72	22.05 ± 3.45	0.000
Pregnancy method (n, %)			
Natural conception	21 (41.18)	315 (55.75)	0.346
Ovarian stimulation	29 (56.86)	250 (44.25)	0.083
AI	2 (5.88)	26 (4.60)	0.823
ART	22 (43.14)	133 (23.54)	0.000
Type of pregnancy (n, %)			0.040
Singleton	38 (74.51)	492 (87.08)	
Twin	13 (25.49)	72 (12.74)	
Triplet	0 (0.00)	1 (0.18)	
Medication during pregnancy (n, %)			
Aspirin	12 (23.53)	88 (15.57)	0.140
Metformin	3 (5.88)	18 (3.19)	0.309
Complications of pregnancy (n, %)			
PGDM	4 (7.84)	12 (2.12)	0.014
Thyroid dysfunction	7 (13.73)	45 (7.96)	0.156
Autoimmune disease	1 (1.96)	7 (1.24)	0.663
Delivery outcome			
GDM	6 (11.76)	74 (13.10)	0.786
ICP	3 (5.88)	15 (2.65)	0.190
PROM	5 (9.80)	115 (20.35)	0.068
FGR	5 (9.80)	8 (1.42)	0.000
Delivery way (n, %)			0.000
Vaginal delivery	10 (19.61)	320 (56.64)	
CS	41 (80.39)	245 (43.36)	

Data are presented as mean ± standard deviation (SD), median (interquartile range) and n (%); AI — artificial insemination; ART —assisted reproductive techniques; CS — caesarean section; CVD — cardiovascular disease; FGR — fetal growth restriction; GDM — gestational diabetes mellitus; ICP — intrahepatic cholestasis of pregnancy; PGDM — pregestational diabetes mellitus; PROM — premature rupture of membranes

as a higher risk of admission to the neonatal unit (23.43% vs 14.24%, p = 0.050) (Tab. 2).

Next, univariate, and multivariate regression models were used to determine the relationship between the clinical characteristics of pregnant women with PCOS and the occurrence of PE. Univariate logistic analysis revealed an association between disease occurrence and maternal hyperandrogenism, a family history of CVD, advanced age, a pre-pregnancy BMI ≥ 24 kg/m^2 and ART. Furthermore, multivariate logistic analysis revealed that maternal hyperandrogenism [odds ratio (OR) = 7.397, 95% confidence interval (CI): 3.302–16.570, p < 0.001], a family history of CVD (OR = 6.036, 95% CI: 2.857–12.754, p < 0.001), a pre-pregnancy BMI ≥ 24 kg/m^2 (OR = 2.813, 95% CI: 1.464–5.402, p = 0.002) and ART (OR = 2.838, 95% CI: 1.476–5.459, p = 0.002) were independent predictive factors of PE in pregnant women with PCOS (Tab. 3).

Finally, ROC curves were generated for maternal hyperandrogenism, a pre-pregnancy BMI ≥ 24 kg/m^2, a family history of CVD and ART, as well as a combination of these four factors. The AUC values were 0.609 (95% CI, 0.518–0.699) for maternal hyperandrogenism, 0.644 (95% CI, 0.559–0.730) for a pre-pregnancy BMI ≥ 24 kg/m^2, 0.628 (95% CI, 0.538–0.718) for a family history of CVD, 0.598 (95% CI, 0.512–0.684)

Table 2. Neonatal outcomes of pregnant women diagnosed polycystic ovary syndrome (PCOS) with preeclampsia (PE) and non-PE

	PE (n = 64)	non-PE (n = 639)	p value
Gestational age at delivery (mean ± SD) [day]	257.57 ± 17.68	268.44 ± 18.26	0.001
Preterm birth (n, %)	22 (43.14)	92 (16.28)	0.000
SGA (n, %)	5 (7.81)	12 (1.88)	0.003
Neonate birth weight (mean ± SD) [g]	2589.76 ± 721.04	3012.50 ± 700.73	0.000
Neonatal asphyxia (n, %)		24 (3.75)	0.766
Mild neonatal asphyxia	3 (4.69)	4 (0.63)	
Severe neonatal asphyxia	0 (0)		
Perinatal mortality (n, %)	0 (0)	3 (0.47)	0.583
Neonatal unit admission (n, %)	15 (23.43)	91 (14.24)	0.050
Intubation (n, %)	4 (6.25)	16 (2.50)	0.086

Data are presented as mean ± standard deviation (SD), median (interquartile range) and n (%); SGA — small for gestational age

Table 3. Univariate and multivariate logistic regression analysis for the prediction of preeclampsia (PE) in polycystic ovary syndrome (PCOS) pregnant women

n, %	Univariate		Multivariate	
	OR 95% CI	p value	OR 95% CI	p value
Hyperandrogenism	6.302 (3.096–12.831)	0.000	7.397 (3.302–16.570)	0.000
Family history of CVD	5.920 (3.065–11.438)	0.000	6.036 (2.857–12.754)	0.000
Advanced age	2.174 (1.033–4.572)	0.041	2.087 (0.897–4.856)	0.088
Pre-pregnancy BMI ≥ 24 kg/m^2	3.804 (2.117–6.836)	0.000	2.813 (1.464–5.402)	0.002
ART	2.464 (1.370–4.433)	0.003	2.838 (1.476–5.459)	0.002
PGDM	3.614 (1.133–11.522)	0.030	1.606 (0.420–6.141)	0.489
Multifetal gestation	2.306 (1.173–4.533)	0.015	1.743 (0.739–4.114)	0.205

ART — assisted reproductive techniques; BMI — body mass index; CI — confidence interval; CVD — cardiovascular disease; OR — odds ratio; PGDM — pregestational diabetes mellitus

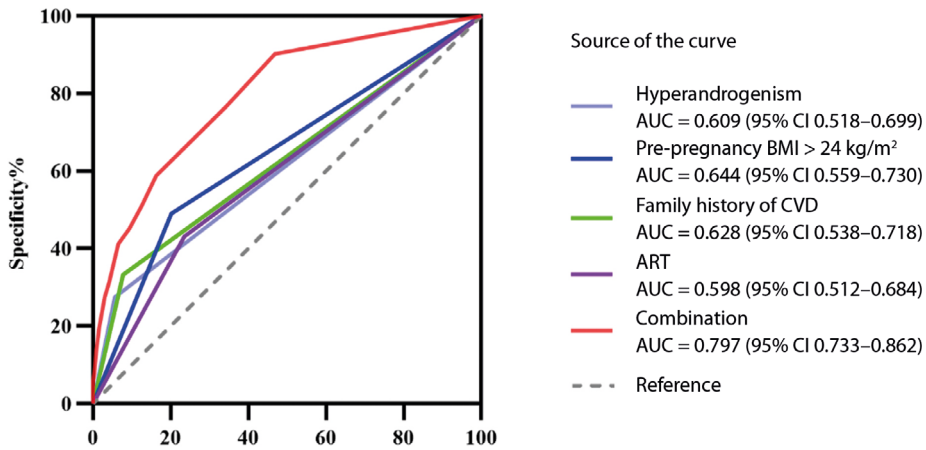

Figure 2. ROC curves of the predictive factors for preeclampsia (PE) in polycystic ovary syndrome (PCOS) pregnant women; AUC — area under curve; CI — confidence interval; BMI — body mass index; CVD — cardiovascular disease; ART — assisted reproductive techniques

for ART, and 0.797 (95% CI: 0.733–0.862) for the combination of all four factors, respectively, as shown in Figure 2. The sensitivity of maternal hyperandrogenism was 0.255, and specificity of was 0.943. The sensitivity for a pre-pregnancy BMI ≥ 24 kg/m^2 was 0.490 while the specificity was 0.798. The sensitivity and specificity for a family history of CVD were 0.333 and 0.922, respectively. The sensitivity of ART was 0.431 while the specificity was 0.765. Finally, the sensitivity and specificity of the combination prediction model were 0.902 and 0.531, respectively. These data suggested that the

combination of maternal hyperandrogenism, a pre-pregnancy BMI ≥ 24 kg/m^2, and a family history of CVD and ART, had a moderate predictive value for PE in pregnant women with PCOS.

DISCUSSION

At present, there are many prediction models for PE, such as the prediction model for preterm PE of the Fetal Medicine Foundation (FMF) [7, 15]. Most of these predictive models include maternal risk factors, such as a history of preeclampsia, multifetal gestation, type 1 or 2 diabetes, and renal disease[16–18]; however, PCOS was not included as a high or moderate risk factor. In this study, we found that the incidence of PE in PCOS was much higher than that in the general population. In addition to the maternal risk factors for PE, we also found that maternal hyperandrogenism, a family history of cardiovascular disease, a pre-pregnancy BMI ≥ 24 kg/m^2, and ART were all independent risk factors for PE in pregnant women with PCOS. This is an interesting phenomenon and may be one of the reasons for the increased risk of PE in pregnant women with PCOS.

Hyperandrogenism is one of the diagnostic features of PCOS and is defined based on clinical and/or biochemical criteria [19]. The clinical features of female hyperandrogenism include hirsutism, acne, and alopecia. Biochemical features (termed hyperandrogenemia) include elevated serum levels of androgens [increased total testosterone, androstenedione, dehydroepiandrosterone (DHEAS), and free androgen index, which is influenced by the suppression of SHBG levels [19]]. It is hypothesized that hyperandrogenism in women with PCOS may be associated with hypertension [20]. We found that pre-pregnancy maternal hyperandrogenism was associated with subsequent preeclampsia (OR = 7.397, 95% CI: 3.302–16.570), as reported previously [11]. In a cross-sectional study of 151 young women with PCOS, Chen et al. found that the serum bioavailable and total testosterone levels were significantly and positively correlated with both systolic pressure and diastolic pressure in young women with PCOS in a manner that was independent of insulin resistance, obesity, and dyslipidemia [21].

The mechanisms by which androgens initiate hypertension have not been clearly elucidated. A previous study reported that androgen may directly upregulate the proximal tubule renin-angiotensin system and increase the volume resorptive rate, thereby increasing extracellular volume and blood pressure [22]. Furthermore, androgens may contribute to abnormal placental morphology and may be related to adverse pregnancy outcomes [23]. Palomba et al. compared the placentas of pregnant women with PCOS with those of healthy controls and observed a number of microscopic alterations including utero-placental vascular lesions, chronic villitis, intervillositis, and abnormal villus maturity, along with an absence of physiological change in the spiral vessels [24]. These authors also found that microscopic placental lesions were significantly influenced by the basal free androgen index (FAI) [testosterone (nmol/L)/SHBG × 100], thus suggesting a potential for hyperandrogenism in the underlying pathogenesis [24]. A recent study of a select group of women from Hvidovre University Hospital showed that women with PCOS and hyperandrogenemia had a more than two-fold increased risk of pre-eclampsia when compared with the background population, whereas normoandrogenic women with PCOS were not at an increased risk, thus indicating hyperandrogenemia rather than PCOS as a marker of PE [25].

In our study, the women were categorized as underweight (BMI < 18.5 kg/m^2), normal weight (18.5 kg/m^2 ≤ BMI < 24 kg/m^2), overweight (24 kg/m^2 ≤ BMI < 28 kg/m^2), or obese (BMI ≥ 28 kg/m^2) [26]. Obesity and features of metabolic syndrome are associated with hypertensive disorders during pregnancy [25, 27]. There is a common misconception that all women with PCOS are obese. However, the mean BMI before pregnancy in women with PCOS in our study was 22.22 kg/m^2 and were within the normal weight range; this concurs with previous reports [28, 29]. The mean BMI before pregnancy in PE group was 24.07 kg/m^2; this was significantly higher than that in the non-PE group. Previous studies of PCOS and hypertensive disorders in pregnancy have addressed possible associations with BMI, although conclusions have been inconsistent. Lønnebotn found a significant association between PCOS and hypertensive disorders in pregnancy among those who were underweight (BMI < 18.5 kg/m^2) and obese (BMI ≥ 30 kg/m^2) but not among those of normal weight or slightly overweight when stratifying by BMI [29]. Nevertheless, Khomami concluded that PE was not associated with PCOS by comparing BMI- matched studies in a meta-analysis [30]. In this study, we found that for Chinese pregnant women with PCOS, the pre-pregnancy BMI ≥ 24 kg/m^2 of those with PE was significantly higher than that in women without PE. This finding suggests that a BMI ≥ 24 kg/m^2 may be an independent risk factor for PE in pregnant women with PCOS. Under this condition, both obese PCOS patients and those who are overweight should be admitted into pre-pregnancy weight control management to prevent obstetric complications. It is well documented that modest weight loss improves an array of abnormal factors in pre-pregnancy PCOS women, including reducing the incidence of PE during pregnancy. Obstetricians should consider the well-established benefits of exercise training and its recommendation as a cornerstone of PCOS pregnancy management.

A view prevails among some experts that pregnancies following ART are associated with a higher risk of hypertensive disorders of pregnancy [31–33]. Regardless of ovulation induction, mild mono/bi-follicular stimulation and ART, or multiple follicular stimulation and ART, PCOS women have been shown to have an increased risk of PIH [34]. However, some researchers have the opposite opinion. Liu also found that the incidence of PIH or PE was not significantly different when compared between groups with and without ART, thus suggesting that ART is a relatively safe and effective method with which to address infertility problems in women with PCOS [35]. We found that ART increased the incidence of PE in PCOS women, although ovarian stimulation did not increase this risk; this may be related to the medication given after ART or the modes of ovulation induction. We also found that a family history of CVD is also a risk factor for PE, thus suggesting that we should also consider family susceptibility, the influence of diet, and genetic factors.

Our study also has some limitations that need to be considered. Because this was a single-center, retrospective cohort study, we were unable to acquire a complete set of relevant information for analysis. For instance, data relating to the clinical features of female hyperandrogenic issues (such as hirsutism, acne and alopecia) were incomplete; therefore, biochemical features were used as a diagnostic basis in this study. Furthermore, we are planning to conduct a prospective study to study the risk of PE in patients with different phenotypes of hyperandrogenic PCOS, and to verify the prediction of PE in PCOS patients. In addition, the selection of ovarian stimulation should be further investigated.

CONCLUSIONS

Patients with PCOS have a higher rate of PE, in which maternal hyperandrogenism, a pre-pregnancy BMI ≥ 24 kg/m^2, a family history of CVD and ART are significant independent factors.

Article information and declarations

Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics statement

Compliance with ethical standards. Informed consent Informed consent was obtained from all individual participants included in the study. This study is a retrospective study of medical records and archived samples with no harm to patients' interests and no harm to patients' privacy. We ensure that we have discussed whether all data were fully anonymized before you accessed them, and the ethics committee waived the requirement for informed consent. And our study did not include minors. It has been approved by the Ethics Committee of Women's Hospital Zhejiang University School of Medicine, ethics Number IRB-20220220-R.

Author contributions

Conception and design: Ruoan Jiang, Yingsha Yao, Fan Qu.
Acquisition and data: Ruoan Jiang, Yingsha Yao, Ting Wang, Fangfang Wang.
Analysis and interpretation of data: Ruoan Jiang, Yingsha Yao, Ting Wang.
Drafting of the manuscript: Ruoan Jiang, Yingsha Yao, Peiyue Jiang.
Critical revision of the manuscript for important intellectual content: Fan Qu.
Statistical analysis: Ruoan Jiang, Yingsha Yao, Baohua Li.
Supervision: Fan Qu.

Funding

This study was funded by the Clinical Research Foundation of Women's Hospital, School of Medicine, Zhejiang University (ID# 20210263, principal researcher MD Li). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of interests

The authors declare that they have no conflict of interest.

REFERENCES

1. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004; 81(1): 19–25, doi: 10.1016/j.fertnstert.2003.10.004, indexed in Pubmed: 14711538.
2. Meier RK. Polycystic Ovary Syndrome. Nurs Clin North Am. 2018; 53(3): 407–420, doi: 10.1016/j.cnur.2018.04.008, indexed in Pubmed: 30100006.
3. Carmina E, Azziz R. Diagnosis, phenotype, and prevalence of polycystic ovary syndrome. Fertil Steril. 2006; 86 Suppl 1: S7–S8, doi: 10.1016/j.fertnstert.2006.03.012, indexed in Pubmed: 16798288.
4. Palomba S, de Wilde MA, Falbo A, et al. Pregnancy complications in women with polycystic ovary syndrome. Hum Reprod Update. 2015; 21(5): 575–592, doi: 10.1093/humupd/dmv029, indexed in Pubmed: 26117684.
5. Mills G, Badeghiesh A, Suarthana E, et al. Polycystic ovary syndrome as an independent risk factor for gestational diabetes and hypertensive disorders of pregnancy: a population-based study on 9.1 million pregnancies. Hum Reprod. 2020; 35(7): 1666–1674, doi: 10.1093/humrep/deaa099, indexed in Pubmed: 32535629.
6. Kjerulff LE, Sanchez-Ramos L, Duffy D. Pregnancy outcomes in women with polycystic ovary syndrome: a metaanalysis. Am J Obstet Gynecol. 2011; 204(6): 558.e1–558.e6, doi: 10.1016/j.ajog.2011.03.021, indexed in Pubmed: 21752757.
7. Francisco C, Wright D, Benkő Z, et al. Competing-risks model in screening for pre-eclampsia in twin pregnancy by maternal characteristics and medical history. Ultrasound Obstet Gynecol. 2017; 50(4): 501–506, doi: 10.1002/uog.17529, indexed in Pubmed: 28508528.
8. Foroozanfard F, Asemi Z, Bazarganipour F, et al. Comparing pregnancy, childbirth, and neonatal outcomes in women with different phenotypes of polycystic ovary syndrome and healthy women: a prospective cohort study. Gynecol Endocrinol. 2020; 36(1): 61–65, doi: 10.1080/09513590.2019.1631278, indexed in Pubmed: 31264483.

9. Valdimarsdottir R, Wikström AK, Kallak TK, et al. Pregnancy outcome in women with polycystic ovary syndrome in relation to second-trimester testosterone levels. Reprod Biomed Online. 2021; 42(1): 217–225, doi: 10.1016/j.rbmo.2020.09.019, indexed in Pubmed: 33077357.
10. Christ JP, Gunning MN, Meun C, et al. Pre-conception characteristics predict obstetrical and neonatal outcomes in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2019; 104(3): 809–818, doi: 10.1210/jc.2018-01787, indexed in Pubmed: 30590587.
11. Xia H, Zhang R, Sun X, et al. Risk factors for preeclampsia in infertile Chinese women with polycystic ovary syndrome: A prospective cohort study. J Clin Hypertens (Greenwich). 2017; 19(5): 504–509, doi: 10.1111/jch.12957, indexed in Pubmed: 28026098.
12. ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol. 2019; 133(1): 1, doi: 10.1097/AOG.0000000000003018, indexed in Pubmed: 30575675.
13. Mack LR, Tomich PG. Gestational diabetes: diagnosis, classification, and clinical care. Obstet Gynecol Clin North Am. 2017; 44(2): 207–217, doi: 10.1016/j.ogc.2017.02.002, indexed in Pubmed: 28499531.
14. Appanna G, Kallis Y. An update on the management of cholestatic liver diseases. Clin Med (Lond). 2020; 20(5): 513–516, doi: 10.7861/clinmed.2020-0697, indexed in Pubmed: 32934048.
15. O'Gorman N, Wright D, Syngelaki A, et al. Competing risks model in screening for preeclampsia by maternal factors and biomarkers at 11-13 weeks gestation. Am J Obstet Gynecol. 2016; 214(1): 103.e1–103.e12, doi: 10.1016/j.ajog.2015.08.034, indexed in Pubmed: 26297382.
16. Committee Opinion Summary No. 638: First-Trimester Risk Assessment for Early-Onset Preeclampsia. Obstet Gynecol. 2015; 126(3): e25–e27, doi: 10.1097/01.AOG.0000471175.95314.42, indexed in Pubmed: 26287782.
17. Poon LCY, Kametas NA, Valencia C, et al. Hypertensive disorders in pregnancy: screening by systolic diastolic and mean arterial pressure at 11-13 weeks. Hypertens Pregnancy. 2011; 30(1): 93–107, doi: 10.3109/10641955.2010.484086, indexed in Pubmed: 20818956.
18. Sotiriadis A, Hernandez-Andrade E, da Silva Costa F, et al. ISUOG CSC Pre-eclampsia Task Force. ISUOG Practice Guidelines: role of ultrasound in screening for and follow-up of pre-eclampsia. Ultrasound Obstet Gynecol. 2019; 53(1): 7–22, doi: 10.1002/uog.20105, indexed in Pubmed: 30320479.
19. Joham AE, Palomba S, Hart R. Polycystic ovary syndrome, obesity, and pregnancy. Semin Reprod Med. 2016; 34(2): 93–101, doi: 10.1055/s-0035-1571195, indexed in Pubmed: 26854709.
20. Joham AE, Boyle JA, Zoungas S, et al. Hypertension in Reproductive-Aged Women With Polycystic Ovary Syndrome and Association With Obesity. Am J Hypertens. 2015; 28(7): 847–851, doi: 10.1093/ajh/hpu251, indexed in Pubmed: 25542625.
21. Chen MJ, Yang WS, Yang JH, et al. Relationship between androgen levels and blood pressure in young women with polycystic ovary syndrome. Hypertension. 2007; 49(6): 1442–1447, doi: 10.1161/HYPERTENSIONAHA.106.083972, indexed in Pubmed: 17389259.
22. Quan A, Chakravarty S, Chen JK, et al. Androgens augment proximal tubule transport. Am J Physiol Renal Physiol. 2004; 287(3): F452–F459, doi: 10.1152/ajprenal.00188.2003, indexed in Pubmed: 15100096.
23. Koster MPH, de Wilde MA, Veltman-Verhulst SM, et al. Placental characteristics in women with polycystic ovary syndrome. Hum Reprod. 2015; 30(12): 2829–2837, doi: 10.1093/humrep/dev265, indexed in Pubmed: 26498178.
24. Palomba S, Russo T, Falbo A, et al. Macroscopic and microscopic findings of the placenta in women with polycystic ovary syndrome. Hum Reprod. 2013; 28(10): 2838–2847, doi: 10.1093/humrep/det250, indexed in Pubmed: 23756703.
25. Naver KV, Grinsted J, Larsen SO, et al. Increased risk of preterm delivery and pre-eclampsia in women with polycystic ovary syndrome and hyperandrogenaemia. BJOG. 2014; 121(5): 575–581, doi: 10.1111/1471-0528.12558, indexed in Pubmed: 24418062.
26. Chen JQ, Wang D, Liu B, et al. Department of Disease Control Ministry of Health, PR China. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci. 2004; 17 Suppl(5): 1–36, indexed in Pubmed: 15807475.
27. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. Clin Epidemiol. 2013; 6: 1–13, doi: 10.2147/CLEP.S37559, indexed in Pubmed: 24379699.
28. Ganie MA, Marwaha RK, Dhingra A, et al. Observation of phenotypic variation among Indian women with polycystic ovary syndrome (PCOS) from Delhi and Srinagar. Gynecol Endocrinol. 2016; 32(7): 566–570, doi: 10.3109/09513590.2016.1141879, indexed in Pubmed: 26878496.
29. Lønnebotn M, Natvig GK, Benediktsdóttir B, et al. Polycystic ovary syndrome, body mass index and hypertensive disorders in pregnancy. Pregnancy Hypertens. 2018; 11: 32–37, doi: 10.1016/j.preghy.2017.12.006, indexed in Pubmed: 29523270.
30. Bahri Khomami M, Joham AE, Boyle JA, et al. Increased maternal pregnancy complications in polycystic ovary syndrome appear to be independent of obesity-A systematic review, meta-analysis, and meta-regression. Obes Rev. 2019; 20(5): 659–674, doi: 10.1111/obr.12829, indexed in Pubmed: 30674081.
31. de Mouzon J, Goossens V, Bhattacharya S, et al. Assisted reproductive technology in Europe, 2007: results generated from European registers by ESHRE. Human Reproduction. 2012; 27(4): 954–966, doi: 10.1093/humrep/des023.
32. Schieve LA, Cohen B, Nannini A, et al. Massachusetts Consortium for Assisted Reproductive Technology Epidemiologic Research (MCARTER). A population-based study of maternal and perinatal outcomes associated with assisted reproductive technology in Massachusetts. Matern Child Health J. 2007; 11(6): 517–525, doi: 10.1007/s10995-007-0202-7, indexed in Pubmed: 17345154.
33. Pandey S, Shetty A, Hamilton M, et al. Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis. Hum Reprod Update. 2012; 18(5): 485–503, doi: 10.1093/humupd/dms018, indexed in Pubmed: 22611174.
34. Carbillon L, Gronier H, Cedrin-Durnerin I, et al. The impact of ovulation induction and ovarian stimulation on the risk of pregnancy-induced hypertension and on neonatal outcomes: A case/control study. Eur J Obstet Gynecol Reprod Biol. 2017; 217: 137–143, doi: 10.1016/j.ejogrb.2017.08.032, indexed in Pubmed: 28898686.
35. Liu Q, Wang J, Xu Q, et al. A retrospective cohort study of obstetric complications and birth outcomes in women with polycystic ovarian syndrome. J Obstet Gynaecol. 2022; 42(4): 574–579, doi: 10.1080/01443615.2021.1931066, indexed in Pubmed: 34392796.