

## ORIGINAL ARTICLE

## ASSOCIATED RISK FACTORS OF PREGNANCY WITH GESTATIONAL HYPERTENSION IN POLYCYSTIC OVARIAN SYNDROME WOMAN

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## ABSTRACT

The present study intends to identify the factors of the risk of pregnancy with associated gestational hypertension and polycystic ovarian syndrome compared with normal pregnancy. The retrospective case-control study was conducted under the Obstetric Department of Maternity and Children Hospital (MCH) Sakaka, Aljouf Saudi Arabia, between January 2020 to December 2021 including target participants of 192 pregnant women. To identify the risk factors of pregnancy with associated gestational hypertension and polycystic ovarian syndrome by the method of logistic regressions. Analysis of data on a total of 192 pregnant women divided into 54 pregnant women associated with gestational hypertension and polycystic ovarian syndrome as a case group and 138 normal pregnant women in a control group. We identified risk factors such as body mass index, family history of hypertension and gestational hypertension, history of pregnancy complications, and history of use of the contraceptive pill, which was significantly found in the case group compared to controls ( $p < 0.05$ ). Meanwhile, the family history of diabetes and multiple pregnancies has no significance between them ( $p > 0.05$ ). The logistic regression of Age  $\geq 28y$  (OR2.047, 95 %CI1.122 ~ 3.209), BMI  $\geq 24$  kg/m<sup>2</sup> (OR1.465, 95 %CI1.070 ~ 2.014), family history of hypertension (OR2.131, 95 %CI1.095 ~ 3.047), the history of pregnancy complication (OR2.439, 95 %CI1.271 ~ 4.091), history of use contraceptive pills (OR3.810, 95 %CI1.174 ~ 6.106), family history of GH (OR1.938, 95 %CI1.015 ~ 2.777) were present in a case group that considered at ( $p < 0.05$ ). In PCOS women, the risk of gestational hypertension is comparatively high. These risk factors are decreased by definitive preconception treatment for polycystic ovarian syndrome in order to prevent gestational hypertension from developing early.

**Keywords:** Pregnancy, Gestational hypertension, Polycystic ovary syndrome

## INTRODUCTION

Polycystic ovarian syndrome (PCOS) is an endocrine disorder and is common in a woman of the reproductive-age group. Abnormal menstruation, hirsutism, hyperandrogenism, and as well infertility are generally presented in PCOS women <sup>1</sup>. Although PCOS woman has adverse effects on her later life physiologically and metabolisms diseases like venous thromboembolism, diabetes Mellitus, and cardiovascular disease <sup>2,3</sup>.

The differentiation of PCOS women is following excessive androgen levels, disturbers of ovulation, and polycystic in ovaries by Rotterdam criteria and ultrasound measurement <sup>4,5</sup>. Globally accounted for 5% to 10% of PCOS women. It was previously shown that 88% of PCOS women had obesity, which elevated their levels of hyperandrogenism and other clinical features when compared to non-obese women <sup>6,7</sup>. (Al-Dubai et al., 2011)<sup>4</sup> has shown that majority of the respondents acknowledged genetic or family history as able to contribute to the possibility of getting breast cancers evidenced by 88%, followed by smoking (65%), consumption of alcohol (56.8%) and prolonged exposure to radiation (67.2%).

The control of PCOS is guided by early prevention and definite management which are currently

focused on medical research as a top priority because of its unidentified pathogenesis. Gestational hypertension is a common hypertensive disorder in pregnancy state due to obscures its pathogenesis. Meanwhile, the adverse effect of gestational hypertension (GH) is increased maternal and fetal morbidity and mortality <sup>8</sup>. The study has detected high blood pressure in pregnancy makes failure multiorgan and preconception obesity capable of changing blood viscosity that denotes to development of hypertensive disorder including gestation hypertension <sup>9</sup>. A survey data from Sweden suggested pregnancy-induced hypertension including gestational hypertension estimated increases in the case of PCOS patients <sup>10</sup>. Therefore, our present study identifies the risk factors of pregnancy-associated gestational hypertension in a woman with PCOS and compared them with normal pregnant women.

## METHODS

We designed an approved retrospective case-control study by the research ethics committee of Jouf University. Our data was gathered from the records files of Maternity and Children Hospital (MCH) Sakaka, Aljouf Saudi Arabia.

**Patients’ information (Case)**

A total of 192 pregnant women were enrolled and divided into case and control groups, among 54 gestational hypertension women with PCOS who were well diagnosed with PCOS and under treatment in this hospital and conceived during the study period from January 2020 to December 2021. We selected them during visits for antenatal care in the hospital, the criteria for inclusion such as gestational hypertension and PCOS which are diagnosed by Rotterdam criteria (anovulation or rare ovulation, hyperandrogenic clinical features, hyperandrogenemia, and as well as polycystic changes in the ovary). The laboratory reports and ultrasound findings reveal the confirmation of PCOS. However, any previous history of any tumor, a blood disorder, immune disease, chronic hypertension, taking infertility treatment were excluded from our study. As well the diagnosed gestational hypertension defined as systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg occurs after 20 weeks of pregnancy first time in the current pregnancy with a negative proteinuria report which subsequently converses after 12 weeks of the pregnancy.

**Control group**

One hundred thirty-eight women with gestation around 22 to 28 weeks, were naturally conceived and not detected any complications of their pregnancy during their antenatal follow-up. The fulfilled criteria of normal pregnancy included a single fetus and no other abnormality that assessment by ultrasound. The data of the control group were collected during the same study period.

**Collection of data**

We gathered the available data from record files undergoing the antenatal follow-up in our hospital. The ultrasound report assists the normal intrauterine pregnancy, gestational week, and fetal condition assessment. The investigation reports included routine blood, urine, liver, and kidney function tests. we reviewed the clinical feature and medical record data of pregnant women with gestational hypertension and PCOS (Case) including details about age, BMI, multiple pregnancies, history of contraceptive pill use, family history of diabetes, family history of hypertension, and as well as family history of gestational hypertension. In addition, we record similar data for the control group.

**Statistical analysis**

The software SPSS 23.0 was used to analyze the data. The expression of weight data with t-test and mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ),  $\chi^2$  test, with frequency (%) was applied for data count. To identify the independent risk factors of gestational hypertension in PCOS women, the univariate analysis (for logistic regression) of variables was performed using software that was statistically significant at P 0.05.

**RESULTS**

of 192 pregnant women who participated, among one hundred thirty-eight and fifty-four pregnancies without and with gestational hypertension and PCOS respectively, have been conducted in our study and reviewed their essential medical records and evaluated available associated risk factors for developing gestational hypertension in PCOS women. Table 1 represented the hormonal and ultrasound support for diagnosed PCOS in a woman.

**Table 1: Hormone assay and Ultrasound study of PCOS Patients**

Items	Frequency	Percentage (%)
<b>Hormonal study</b>		
Serum LH (mIU/ml)		
Raised (>14.7)	29	53.70
Normal (1.1-14.7)	25	46.29
Serum FSH (mIU/ml)		
Low (<2.8)	5	9.25
Normal (2.8-21.0)	49	90.74
Serum prolactin (ng/ml)		
Raised (>25.0)	10	18.51
Normal (1.9-25.0)	44	81.48
Serum TSH (mIU/ml)		
Raised (>4.0)	12	22.22
Normal 0.4-4.0	42	77.77
Androstenedione (nmol/L)		
Mean 13.0+5.0	54	100
<b>Ultrasonography of the ovary</b>		
Detected of PCO	54	100

**Ultrasound finding**

A total of 54 pregnant women with gestational hypertension and PCOS, previously routine ultrasound scans in the prepregnant state to detect the ovarian volume and number of follicles. The diagnosis of PCOS is based on the number of follicles, at least 12 or more follicles, and their range between 2-9 mm in diameter with a minimum 10ml volume of each ovary 8. Due to some limitations and technical errors, our study has a deficiency of imaging plates. Meanwhile, a previous study detected by ultrasound which is represented as evidence in figure 1 with reference 8.

Table 2. shows the associated risk factors of cases compared to control groups. We found a higher significant association between BMI, age, family history of hypertension, history of complications during pregnancy, family history of gestational hypertension, and history of use of contraceptive pills as  $29.80 \pm 8.12$ ,  $24.98 \pm 2.05$ ,  $70.37\%$ ,  $55.55\%$ ,  $59.25\%$ , and  $44.44\%$  respectively to the control group and considered at  $p < 0.05$ ). Conversely, no significance was found between multiple pregnancies and a family history of diabetes  $20.37\%$  and  $22.22\%$  respectively.



**Figure 1. Transabdominal ultrasound is shown (A) A normal ovary image. (B) Right ovary image with PCOS (calculated ovarian volume 13 mL) C. Right ovary PCOS with obese (ovarian volume 17 mL) 8**

The identified associated risk factors were applied for the multivariate logistic regression process that is represented in table 3.%.

Analysis of risk factors by logistic regression Table 4 represented the analyzed data of age  $\geq 28$ years (OR 2.047, 95 %CI1.122 ~ 3.209), BMI  $\geq 24$

kg/m<sup>2</sup> (OR1.465, 95 %CI1.070 ~ 2.014), family history of hypertension (OR 2.131, 95 %CI1.097 ~ 3.048), the history of pregnancy complication (OR 2.439, 95 %CI1.271 ~ 4.091), history of contraceptive pills use(OR3.810, 95 %CI1.174 ~ 6.106) and family history of GH(OR1.938, 95 %CI1.015 ~ 2.777) which considered at ( $p < 0.05$ ).

**Table 2: The baseline characteristics of case and control groups.**

Factors	Case (n=54)	Control (n=138)	t/x <sup>2</sup>	P
Age(y)	29.80 ± 8.12	25. 04 ± 7.45	1.758	0.025
BMI (kg/m <sup>2</sup> )	24.98 ± 2.05	22.90 ± 1.91	1.026	0.022
Family history of hypertension	38(70.37 %)	26(18.84 %)	1.293	0.037
Family history of gestational hypertension	32(59.25 %)	24(17.39 %)	1.204	0.008
Family history of diabetes	12(22.22 %)	28(20.28 %)	1.748	0.096
Multiple pregnancies	11(20.37 %)	27(19.56%)	1.815	0.071
The history of pregnancy complications	30(55.55 %)	14(11.59 %)	1.610	0.019
The history of contraceptive pill use	24(44.44)	24(7.24)	1.034	0.001

Table 3: The factors used in multivariate logistic

Factors	Variables	Assignment
GH with PCOS woman (case)	Y	yes = 1, no = 2
Age(y)	X <sub>1</sub>	≥ 28 = 1, < 28 = 2
BMI (kg/m <sup>2</sup> )	X <sub>2</sub>	≥ 24 = 1, < 24 = 2
Family history of hypertension	X <sub>3</sub>	yes = 1, no = 2
The history of pregnancy complications	X <sub>4</sub>	yes = 1, no = 2
The history of contraceptive pill use	X <sub>5</sub>	yes = 1, no = 2
Family history of gestational hypertension	X <sub>6</sub>	yes = 1, no = 2

Table 4: Analysis of logistic regression over the risk factors of women with gestational hypertension and PCOS

Variables	B	Wald	OR	95 %CI	P
Age ≥ 28y	0.159	12.128	2.047	1.122 - 3.209	0.043
BMI ≥ 24	0.123	7.197	1.465	1.070 - 2.014	0.026
Family history of hypertension	0.103	18.120	2.131	1.097 - 3.048	0.027
History of contraceptive pill use	0.127	16.172	3.810	1.174 - 6.106	0.025
The history of pregnancy complications	0.189	3.095	2.439	1.271 - 4.091	0.020
Family history of gestational hypertension	0.117	9.106	1.938	1.015 - 2.777	0.044

**DISCUSSION**

To our knowledge, we first evaluated the associated risk factors of gestational hypertension in PCOS women based on a hospital retrospective case-control study in Aljouf, Saudi Arabia. Several studies reported that PCOS cases steadily increased from nearly 3% to 9% in India, China, and Sri Lanka. 3,10. There was concern that PCOS is capable of progressing to adverse effects on gestation like hypertensive disorder, preeclampsia, or gestational hypertension <sup>11</sup>.

Currently, many studies have published a meta-analysis of PCOS and analyzed data showing a dramatically increased risk for the development of gestational hypertension during pregnancy; thus, PCOS is considered a risk factor for gestational hypertension <sup>12,13,14</sup>. Our data was analyzed based on one hospital because there was

no available second Maternity and Children Hospital in Sakaka. All patients referred to MCH from the surrounding primary healthcare centers in the Aljouf region. In the present study, a total of 192 pregnant women were studied, among 138 and 54 pregnant women without and with gestational hypertension associated with PCOS as case and control groups, respectively. Although 54 pregnant women with gestational hypertension and PCOS were already diagnosed and treated at the same hospital, the ultrasound scan is routinely done during the preconception period for follow-up on the condition of the PCOS. Because of some technical errors, our study has a deficiency in the image plate. Several published research papers focused on ultrasound images, and the present study included their images with reference. However, the present study identified some associated risk factors with gestational hypertension in PCOS women compared to the

control group, with 28.12% of the case group having an age and BMI of  $29.80 \pm 8.12$  and  $24.98 \pm 2.05$  respectively, higher compared to the control group. Obesity is likely to have an adverse effect on the outcomes of pregnancy in PCOS women compared to a normal pregnant woman. Our data showed that 70.37%, 59.25%, 55.55%, and 44.44% with a family history of hypertension, a family history of gestational hypertension, a history of complicated pregnancy, and a history of use of contraceptive pills are respectively significantly higher than the control group that similarly reported to other studies<sup>15,16</sup>. Additionally, it has been reported that the contraceptive pill consequently raises blood pressure due to estrogen which enhances sodium and water retention<sup>8</sup>. Therefore, the present study determined that PCOS in pregnant women subsequently developed gestational hypertension. Our study supported age, obesity, family history of hypertension, and family history of gestational hypertension as associated risk factors for PCOS women to develop gestational hypertension.

## CONCLUSION

We determined that age  $\geq 28$  years, BMI  $\geq 24$ , family history of hypertension, history of pregnancy complications, history of contraceptive pill use, and family history of gestational hypertension act as associated risk factors for the development of gestational hypertension in a PCOS woman. Hence, it is initially suggested that the prevention and definite treatment of polycystic ovarian syndrome in preconception enhance and reduce the risk of developing gestational hypertension.

## Limitation

The present study has a deficiency in including the imaging pale due to a technical computerized error. In addition, data are collected from only one hospital in Sakaka, Aljuf. There was only one Maternity and Children Hospital (MCH) available in Sakak, Aljuf. In the future, we have a plan to further study a large number of PCOS patients in different hospitals in different cities in Saudi Arabia and conduct research only based on imaging modalities.

## Conflict of interest

The authors declare no potential conflict of interest.

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