Evaluation of Maternal and Fetal Complications in Pregnant Women with Polycystic Ovary Syndrome (PCOS) with Severe and Mild Phenotype

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Article Info

ABSTRACT

Background & Objective: An essential issue in obstetrics is the prevalence of maternal and fetal complications in pregnant women with polycystic ovary syndrome (PCOS). The purpose of the present study was to investigate the prevalence of pregnancy complications among various phenotypes of pregnant women with PCOS.

Materials & Methods: In the current study, the pregnancy period of 143 women with PCOS who were referred to the Babylon teaching hospital in Iraq in 2021 was analyzed based on their medical records. These women were separated into two groups based on their PCOS-related clinical symptoms. People in the first group possessed a severe phenotype, while those in the second group possessed a mild phenotype. SPSS version 23 was utilized for comparing maternal and fetal complications during pregnancy and for data analysis.

Results: Regarding maternal and fetal complications, there was a significant difference between the two groups regarding low birth weight (LBW) (P<0.05). In this study, there was no statistically significant difference between PCOS phenotypes and the incidence of gestational diabetes, preterm birth, or spontaneous abortion (P>0.05). In conclusion, women with a more severe phenotype are more likely to give birth to babies with low birth weight (LBW) (approximately 1.9 times).

Conclusion: In clinical considerations of pregnant women with PCOS, it appears necessary to consider the disease's phenotype as one of the factors influencing fetal outcomes.

Keywords: Pregnant Women, Polycystic Ovary Syndrome, Maternal-Fetal, Low Birth Weight

Introduction

Physiological changes in the secretion and general functioning of the endocrine glands are so influential in the reproduction process that even the smallest change in hormone levels can have a significant impact on fertility. Pregnancy can affect the normal function of endocrine glands, while endocrine diseases can also affect pregnancy. Polycystic ovary syndrome (PCOS) is a form of hyperandrogenism in the ovaries (1). The ovary's disruption of androgen production is evident during puberty, but its origins can be traced back to childhood or even the fetal period. PCOS affects 6-8% of women of reproductive age and is responsible for approximately 75% of infertility caused by a lack of ovulation (2). In addition to infertility, PCOS is linked with insulin resistance, hyperinsulinemia, hyperandrogenism, and other features of the metabolic syndrome, as well as a higher risk for developing diabetes (3). Most sufferers experience menstrual disorders, excessive facial hair growth, acne, weight gain, and infertility (4, 5).

In addition to causing fertility issues, PCOS is known to be the underlying cause of breast cancer and reproductive cancers (including endometrial and ovarian tumors). Women with PCOS are more likely to develop metabolic syndrome (6). Also, hyperandrogenism, which is caused by endocrine changes such as increased androgen production and abnormal estrogen secretion, occurs in these patients and is regarded as one of the most prominent symptoms of PCOS. Obesity and PCOS-related reproductive disorders are two important cancer risk factors, including ovarian cancer. Therefore, PCOS can be...
proposed as a suspect factor in ovarian cancer risk increase. In addition, the disorder of sex hormones, weight gain, and obesity are major risk factors for the onset and progression of breast cancer (7).

PCOS is recognized as the underlying cause of various reproductive system cancers, including endometrial, ovarian, and breast cancers. Genetic factors, insulin resistance, obesity, and environmental and chemical pollution play a role in developing this disease (8). This syndrome is characterized by a low menstrual frequency and skin diseases caused by androgens, such as acne and hirsutism. This condition is currently classified as a multiple disorder. This symptom has been observed in approximately fifty percent of them. 41% of patients diagnosed with this syndrome are obese (9).

Although some drug interventions are used to control the symptoms of polycystic ovary syndrome, no approved drug has been reported to treat polycystic ovary syndrome despite the efforts of researchers from around the world. In addition to lifestyle modification, specialists also prescribe antiandrogens and metformin. As non-pharmacological therapeutic interventions, all types of interventions related to exercise and physical activity, diet, acupressure, and food supplements have been studied to date, according to the findings of review studies. Several of them have reported an improvement in hormonal levels and metabolic markers (10).

PCOS is difficult to diagnose due to its heterogeneous nature and possible patient condition changes (11). Currently, the most prevalent diagnostic criteria are the 2003 agreement-based Rotterdam criteria. This method requires the presence of two of the three conditions (hyperandrogenism, chronic anovulation, and sonographic pattern of polycystic ovaries) (12). In addition, women with PCOS have lower FSH, SHBG, and high-density lipoproteins than healthy individuals (13).

PCOS can manifest with any or all symptoms: menstrual disorder, infertility, hirsutism, acne, and alopecia (14). 40% of the treatment cost burden in the United States health care system in 2004 was attributable to them (15). Consequently, its investigation, prevention, and management are crucial, particularly in PCOS patients with insulin resistance (16). Insulin resistance is a condition in which the biological effect of insulin, regardless of concentration, is diminished. In addition, insulin resistance is caused by decreasing the sensitivity of target tissues to the insulin hormone. Insulin resistance is the most well-known contributor to polycystic ovary syndrome's pathogenesis (17, 18).

Phenotypes include a) menstrual disorders, clinical-laboratory hyperandrogenism, and ovaries with multiple cysts on ultrasound view (PCOM); b) menstrual disorders, clinical-laboratory hyperandrogenism without multiple ovarian cysts; c) clinical-laboratory hyperandrogenism and ovaries with multiple cysts without menstrual disorders; and d) menstrual disorders, ovaries with multiple cysts and no laboratory clinical hyperandrogenism (19, 20).

In PCOS patients, the elevated serum estrogen level and its direct effect on endometrial tissue, as well as changes in the concentration of ovarian steroid hormones and growth factors, create a potential environment for the development of estrogen-dependent tumors (21). Consequently, PCOS is not only a risk factor for endometrial cancer, but also for other estrogen-dependent tumors of the reproductive tract with steroid hormone receptors, such as breast and ovarian cancers. The majority of epidemiological studies to date have confirmed this association. If the concentration of androgen in the peripheral blood is directly related to the development of breast cancer, it is anticipated that an increase in the incidence of breast cancer will be observed in diseases such as PCOS, in which women experience hyperandrogenism, irregular menstruation, and infertility issues. PCOS is the most prevalent cause of excessive androgen production in anovulatory women and is considered a breast cancer risk factor. Despite extensive epidemiological studies in this field, the existence of a correlation between PCOS and breast cancer has not yet been established (22).

New research indicates that PCOS is characterized by low levels of chronic inflammation, progression of metabolic abnormalities, and ovarian dysfunction. Currently, PCOS is recognized as an inflammatory condition. New research focuses on the connection between hyperandrogenism and inflammation in PCOS patients. Recent research suggests that an inflammatory diet may strongly induce hyperandrogenism in PCOS patients (23).

According to research, patients are more likely to experience pregnancy complications than those without the condition (24). In addition to increasing the likelihood of infertility in these women, this syndrome also increases the likelihood of complications during pregnancy (both fetal and maternal) (25). In addition, the prevalence of low birth weight in these women's infants is greater than that of unaffected women (26).

Considering that PCOS is a common, heterogeneous and hereditary disorder that affects women throughout their lives; examining its various aspects is particularly important. Therefore, the necessity of early diagnosis and long-term management is quite clear and can help control this syndrome and also prevent its long-term consequences such as maternal and fetal complications in pregnant women. So far, limited studies have been conducted in the mentioned field, which sometimes have conflicting results. Examining complications for women with severe and mild PCOS is one of the innovations of this study.
Methods

The current comparative study is based on the data of patients referred to the Babylon educational hospital in Iraq with the diagnosis of PCOS beginning in 2021; the College approved the study by Medicine's ethics committee. The disease was diagnosed by a gynecologist and obstetrician based on the Rotterdam diagnostic criteria, which required the presence of at least two of the three Rotterdam conference-defined characteristics.

Among 382 women with polycystic ovary syndrome diagnosed with PCOS prior to pregnancy, 143 were included in the current study. Inclusion criteria included age over 18 years, the absence of diabetes and hyperthyroidism, an interest in participating in a research study, and a history of at least one spontaneous pregnancy (without medication) in women. Also excluded from the study were women with a bad past history of obstetrics, including stillbirth, prolonged labor, and frequent pregnancy loss. Since the study was only done on clients of a medical center in 2021 and had considered things like a bad history of midwifery and people's choice to participate in the research, the sample size has been reduced. In order to comply with ethical considerations, all aspects of the research were explained in detail to each patient before its initiation. In addition, patients were assured that their identities would remain private. Next, demographic, anthropometric, fertility, and disease history information, as well as the results of biochemical and hormonal tests and ultrasound results, were compiled in the patient's file.

In the present study, PCOS was diagnosed based on the Rotterdam definition's characteristics and the presence of two of its three characteristics. These characteristics include oligoovulation, clinical or biochemical hyperandrogenism, the detection of polycystic ovaries via ultrasound, or an ovarian volume more significant than 10 milliliters. According to the characteristics of the Rotterdam definition of polycystic ovary syndrome, the participants in the current study were divided into two groups. Patient information records were accessed through Iraq's Health System. The first group (A) had all three characteristics of anovulatory hypogonadism, hyperandrogenism, and multiple ovarian cysts on sonography, or they had only two characteristics of anovulatory hypogonadism and increased androgens either clinically or in the laboratory. The second group (B) had oligoovulation with PCOM or hyperandrogenism, either clinical or clinical, with PCOM. The diagnosis of PCOM was determined based on the ultrasound results sheet attached to the patient's medical records. In these reports, the diagnosis of PCOM was based on one of the following criteria: a) the presence of a rosary-like pattern of cysts in the ovary, or b) the volume of the ovary exceeding ten cubic mm. Without ovarian ultrasound results, the participant was excluded from the study. In this study, group A represented the most severe form of PCOS.

According to the Ferriman-Gallwey score (1961) attached to the patient's file, information regarding clinical hyperandrogenism was determined, and the final score was determined based on the parameters (27). During the patient's initial visit, a specialist collected the parameters mentioned above, including terminal hair and thickness in defined points or the diagnosis of clinical hyperandrogenism.

The complications of pregnancy were divided into two categories: maternal and neonatal. In addition to spontaneous abortion and ectopic pregnancy, maternal complications include gestational diabetes, placental abruption, and preeclampsia. Neonatal complications such as low birth weight (LBW) (less than 2,500 g), high birth weight (more than 4,000 g), stillbirth, and preterm birth (before 37 weeks of gestation) were taken into account. A specialist physician administered a questionnaire regarding maternal and neonatal complications to patients referred to the hospital based on their self-reporting of pregnancy complications.

Comparing and analyzing maternal and fetal complications between the two groups using SPSS statistical software (version 23, IBM, USA). First, the Kolmogorov-Smirnov test was used to determine the normality of the quantitative data distribution and utilized descriptive information about quantitative variables with normal distribution in the form of mean and standard deviation indices and non-normal data ranging from the 25th to 75th quartiles.

Results

In the current study, 143 women aged 20 to 45 with polycystic ovary syndrome participated. At the time of their clinic visit, the mean age of study participants was 33.73±5.49 years, while the mean ages of marriage and first pregnancy were 21.83±3.65 and 25.36±4.19 years, respectively. Table 1 presents the demographic characteristics of the studied population by the group. Group B had the highest incidence of PCOS phenotype among participants (61.47%). The Ferriman-Gallwey score demonstrated a statistically significant difference between the two groups (P<0.05). Notably, in addition to clinical criteria, laboratory values were evaluated within the groups but were not presented due to the volume of data.
Table 1. Demographic characteristics and hormonal indicators of women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD*</th>
<th>Group A</th>
<th>Group B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>33.93 ± 5.62</td>
<td>32.84 ± 5.18</td>
<td>0.087</td>
</tr>
<tr>
<td>Age of marriage</td>
<td></td>
<td>21.91 ± 3.84</td>
<td>21.47 ± 3.79</td>
<td>0.164</td>
</tr>
<tr>
<td>Age of first pregnancy</td>
<td></td>
<td>26.14 ± 4.65</td>
<td>24.73 ± 4.27</td>
<td>0.524</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>1.62 ± 0.34</td>
<td>1.54 ± 0.29</td>
<td>0.406</td>
<td></td>
</tr>
<tr>
<td>Number of births</td>
<td>1.38 ± 0.24</td>
<td>1.26 ± 0.18</td>
<td>0.117</td>
<td></td>
</tr>
<tr>
<td>Ferriman-Gallwey score</td>
<td>8</td>
<td>5</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td>28.43 ± 4.18</td>
<td>29.13 ± 4.37</td>
<td>0.183</td>
</tr>
</tbody>
</table>

*SD= Standard deviation

Demographic characteristics and hormonal indicators of women are shown in Table 2. The average number of pregnancies in women with a history of LBW was significantly greater than in those without a history of LBW (P<0.05). In addition, the age of marriage and the age of first pregnancy were older among women with PCOS who had a history of spontaneous abortion than those without such a history. Therefore, their weight, BMI, waist circumference, and wrist circumference were significantly lower than those of women without a history of abortion (P<0.05).

In examining maternal and neonatal complications between the two study groups, spontaneous abortion was the most prevalent complication observed among the women in the present study. Its prevalence did not differ significantly between the two groups (P>0.05). However, the rate of low-birth-weight babies and the prevalence of premature birth were higher in group A than in group B, and the difference was statistically significant (P<0.05).

Table 2. Demographic characteristics and hormonal indicators of women

<table>
<thead>
<tr>
<th>Effect</th>
<th>Number (Percentage)</th>
<th>Group A</th>
<th>Group B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous abortion</td>
<td>26 (42.6%)</td>
<td>26 (42.6%)</td>
<td>32 (39%)</td>
<td>0.148</td>
</tr>
<tr>
<td>LBW</td>
<td>17 (27.9%)</td>
<td>17 (27.9%)</td>
<td>11 (13.4%)</td>
<td>0.026</td>
</tr>
<tr>
<td>High baby weight</td>
<td>6 (9.8%)</td>
<td>6 (9.8%)</td>
<td>5 (6.1%)</td>
<td>0.249</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>8 (13.1%)</td>
<td>8 (13.1%)</td>
<td>13 (15.9%)</td>
<td>0.273</td>
</tr>
<tr>
<td>Hypertension of pregnancy</td>
<td>14 (23%)</td>
<td>14 (23%)</td>
<td>18 (22%)</td>
<td>0.491</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>9 (14.8%)</td>
<td>9 (14.8%)</td>
<td>4 (4.9%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>4 (6.6%)</td>
<td>4 (6.6%)</td>
<td>5 (6.1%)</td>
<td>0.312</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>3 (4.9%)</td>
<td>3 (4.9%)</td>
<td>5 (6.1%)</td>
<td>0.245</td>
</tr>
</tbody>
</table>

With greater precision, several parameters were then adjusted to examine the effects of LBW and preterm birth (dependent variables). In the logistic regression model, the mentioned parameters, including age at pregnancy, BMI, number of pregnancies, and investigated groups (independent variables), were performed individually and simultaneously. The adjusted results indicated that LBW remained significant (P<0.05), whereas preterm birth showed no significant difference between the two groups (P>0.05). According to the findings, the odds ratio for low birth weight in group A relative to group B was 1.9. The outcomes are shown in Tables 3 and 4.

Table 3. Results of logistic regression analysis for LBW

<table>
<thead>
<tr>
<th>Effect</th>
<th>Variable</th>
<th>Odds ratio</th>
<th>Confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW</td>
<td>Age of first pregnancy</td>
<td>0.94</td>
<td>0.82-1.08</td>
<td>0.243</td>
</tr>
</tbody>
</table>
Table 4. Results of logistic regression analysis for preterm delivery

<table>
<thead>
<tr>
<th>Effect</th>
<th>Variable</th>
<th>Odds ratio</th>
<th>Confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm delivery</td>
<td>Age of first pregnancy</td>
<td>0.96</td>
<td>0.86-1.06</td>
<td>0.319</td>
</tr>
<tr>
<td></td>
<td>Number of pregnancies</td>
<td>1.01</td>
<td>0.92-1.14</td>
<td>0.264</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>1.24</td>
<td>1.16-1.30</td>
<td>0.172</td>
</tr>
<tr>
<td>Group</td>
<td>Group A</td>
<td>1.4</td>
<td>1.1-1.7</td>
<td>0.113</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Discussion

This study's results indicated a statistically significant difference (P<0.05) between the likelihood of neonatal complications and the PCOS phenotypes. In the present study, the odds ratio for low birth weight as one of the neonatal complications in group A was 1.90 times that of group B. In addition, regardless of PCOS phenotype, the LBW rate was higher in women with PCOS who had a higher age of marriage, gestational age, and the number of pregnancies on average. In addition, the rate of spontaneous abortion in women with PCOS (regardless of phenotype) who had a smaller waist circumference and BMI was significantly higher than in women with a smaller BMI, wrist size, and waist circumference (P<0.05). However, the results of this study revealed that spontaneous abortion rates do not differ significantly between PCOS phenotypes.

PCOS has been associated with an increased risk of LBW in numerous studies, and studies have demonstrated that LBW is one of the fertility complications in women with PCOS. Therefore, women with PCOS deliver infants with a lower birth weight than expected for their gestational age (28). The results demonstrated that PCOS patients have an elevated risk of LBW. This risk is associated with an increased risk of low birth weight in the more severe disease phenotype (group A) compared to the new phenotypes defined at the Rotterdam conference (29). Notably, some researchers did not observe a difference in LBW among the various phenotypes of polycystic ovary syndrome (30, 31). This discrepancy between the findings of different studies is likely due to the small sample sizes and study designs of the various studies, and it requires further investigation. However, it appears that the type of disease phenotype should be considered in preventing low birth weight infants born to PCOS mothers with a more severe disease phenotype (group A) of polycystic ovary syndrome.

Before adjusting for other factors, the preterm birth rate in group A was significantly higher than in group B in this study (P<0.05). After adjusting for age at conception and the number of births, these influential factors remained significant. Nevertheless, after adjusting for the number of births, its significance disappeared. In this study, spontaneous abortion (40.8%) and low birth weight (20.65%) were the most, regardless of phenotype. The reported rate of spontaneous abortion in the average population is 15%, making it the most common pregnancy complication, and its incidence decreases with increasing gestational age (32). Diverse studies have yielded contradictory results regarding spontaneous abortion in PCOS patients (33). So, in some studies, researchers did not observe an increase in the rate of abortion among PCOS-affected women compared to unaffected women (34). In contrast, several studies reported a high prevalence of spontaneous abortion among PCOS-affected women (35).

Determining the karyotype of aborted fetuses from women with PCOS reveals that the karyotype is normal, indicating that other factors cause spontaneous abortion in women with PCOS. Multiple studies have demonstrated the role of increased serum androgens in reducing the maturation of endometrial cells and, as a result, increasing recurrent miscarriage in women with PCOS and women without PCOS. They experience recurrent miscarriages (36). The effect of increasing age at conception and multiple pregnancies on the prevalence of spontaneous abortion among women with PCOS, regardless of their phenotype, was another finding of the present study. In women without PCOS, increasing age at first pregnancy and multiple pregnancies also increase the number of miscarriages.
In the present study, the BMI of PCOS patients with a history of abortion was significantly lower than that of PCOS patients without a history of abortion (37). Women with PCOS who are underweight and have a low BMI are more likely to experience spontaneous abortions than unaffected women. Low maternal weight and BMI are associated with an increased risk of preterm birth in women without PCOS. Consistent with the present study's findings, other studies indicate that thin women with PCOS are more susceptible to miscarriage than obese women with insulin resistance (38). It appears that the low BMI of mothers causes abortions by interfering with fetal development. Hormonal changes are another prominent mechanism related to low BMI in mothers with increased abortion rates. This issue, caused by the weight loss of pregnant mothers, harms hormone regulation and is directly associated with maternal malnutrition.

Limitations of this Study

Patients referred to a specific city's treatment center were one of the current study's limitations. In addition, due to the low prevalence of certain pregnancy complications, the current study lacked the statistical power to compare complications with low prevalence, and investigating complications with low prevalence requires a larger sample size with various phenotypes. In addition, because the information regarding the hormones and biochemistry of the study subjects was extracted from the patient's files, some information was incomplete and could not be analyzed. Due to this study's retrospective nature, it was impossible to compare weight and BMI during pregnancy; however, BMI status was accounted for in the regression analysis.

Conclusion

Similarities in demographics and endometriosis-associated symptoms among the Australian and non-Australian women with endometriosis were identified.

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Conflict of Interest

The authors of the article have no conflict of interest.

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