

Journal of Pharmaceutical Advanced Research**(An International Multidisciplinary Peer Review Open Access monthly Journal)**Available online at: www.jpardonline.com**A review of Pregnancy complications associated with Polycystic Ovary Syndrome****Reeja Jiji**

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Received: 16.05.2022

Revised: 08.06.2022

Accepted: 16.06.2022

Published: 30.06.2022

ABSTRACT:

Polycystic ovary syndrome (PCOS) is a heterogeneous disease in women between thirteen to forty years of reproductive age. Globally, prevalence estimates of PCOS range from 2.2% to 26%. In India, experts claim that about 10% of women are affected by PCOS. Women with PCOS usually experience pregnancy complications like gestational diabetes, gestational hypertension, preeclampsia, preterm birth, and cesarean delivery. Pregnancy complications like spontaneous abortions, gestational diabetes, hypertensive disorders of pregnancy, fetal complications such as low birth weight, need for NICU (neonatal intensive care unit) and lower APGAR (appearance, pulse, grimace, activity, respiration) were more associated with PCOS. The impact of these on a woman's quality of life may result in psychological distress that threatens her feminine identity. This review briefly focuses on the prevalence of pregnant women with PCOS, pregnancy complications associated with PCOS, and the health-related quality of pregnant women with PCOS.

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INTRODUCTION:

Polycystic ovary syndrome in the present generation is a very common reproductive disorder and the prevalence is on the rise. According to Rotterdam ESHRE/ ASRM in the year 2003, PCOS is characterized by a combination of infrequent or absence of monthly periods, clinical or endocrine signs of increased androgen levels, and polycystic ovaries. The term PCOS was first described by Stein and Levinthal^[1]. The World Health Organization (WHO) estimates that around 3.4 % of women were affected by PCOS worldwide in 2012^[2]. Irregular menstrual periods, abnormal hair growth, facial acne, and obesity can occur in women with PCOS. Together with the physical disturbances, many mental problems are also related to PCOS^[3]. Currently, the

Keywords: Gestational hypertension, Preeclampsia, Caesarean delivery, Preterm delivery, Low birth weight.

reason behind PCOS is not known. However, there are associations with excess insulin, low-grade inflammation, and genetics ¹⁴. In women with PCOS, hormone imbalance will occur: they usually have a higher level of androgens and may have a lower level of estrogen ¹⁵. Women with PCOS have an increase in the frequency of gonadotrophin-releasing hormone (GnRH) pulses. Shorter pulses preferentially promote the production of luteinizing hormone (LH) and result in a decrease in the production of follicle-stimulating hormone (FSH). Increased LH levels stimulate ovarian theca cells to produce androgenic hormones (Testosterone, androstenedione, and dehydroepiandrosterone) and an irregular or absent menstrual cycle. Besides this decreased level of FSH relative to LH, the ovarian granulosa cells cannot aromatize the androgen into estrogen. As a result, there is less estrogen available, no LH surge, and ovulation may not be able to occur. Typically, progesterone is released from the corpus luteum following ovulation. Progesterone acts to reduce GnRH pulsation. In PCOS, anovulation or oligoovulation causes a drop in circulating progesterone and an increase in GnRH pulsation. Some studies have identified the roles of the regulatory genes of the cytochrome P450 (CYP)11A, FST, IVSR, 3-HSDL, and CYP 17 enzymes in association with PCOS. Genetic studies have identified an association between PCOS and disordered insulin metabolism and hyperinsulinemia. Hyperinsulinaemia is secondary both to insulin resistance at the periphery and to abnormal pancreatic cell function. Insulin resistance affects 50 to 70 % of women with PCOS. Increased insulin levels may have gonadotrophin (LH) accelerating effects on ovarian function. Insulin helps to regulate ovary function, and the ovaries respond to excess insulin by producing androgen. Hyperinsulinaemia also suppresses the generation of carrier protein sex hormone-binding globulin (SHBG), which in turn increases androgenicity. Hyperandrogenism, a clinical hallmark of PCOS, can cause inhibition of follicular development, microcyst formation in the ovaries, anovulation, and menstrual irregularity. High levels of androgen and high insulin levels can affect the menstrual cycle and prevent ovulation ¹⁶. After successfully passing the first trimester, women with PCOS commonly encounter later pregnancy complications like gestational diabetes (GDM), pregnancy-induced hypertension (PIH), preeclampsia, preterm delivery, the birth of small for age (SGA), and cesarean delivery ¹⁷.

The Barker hypothesis explains that the fetal nutrition and endocrine environment affect the developing neuroendocrine systems leading to long-term health hazards. The low fertility in these women makes it a must-have for them to have reproduction assistance like ovulation induction or IVF, putting them at the risk of developing multiple gestations ¹¹. Therefore, this review briefly focuses on the prevalence of pregnant women with PCOS, pregnancy complications associated with PCOS, and the health-related quality of pregnant women with PCOS.

Diabetes mellitus-insulin resistance is the main feature of both obese and lean PCOS. It occurs in 70 to 95 % of people with obese PCOS and 30 to 75 % of people with lean PCOS. This leads to an increased risk of developing type-2 diabetes and cardiovascular disorders. Dyslipidaemia-an increased level of insulin is also responsible for dyslipidemia and for elevated levels of plasminogen activator inhibitor-1 (PAI-1) in patients with PCOS. It is a risk factor for intravascular thrombosis. Endometrial Cancer-endometrial hyperplasia and endometrial cancer are possible as a result of excessive uterine lining accumulation and a lack of progesterone, which results in prolonged stimulation of uterine cells by estrogen ¹⁶.

Polycystic ovary syndrome:

Polycystic ovary syndrome (PCOS) is one of the endocrine disorders in women between 13 to 40 years of reproductive age, and in a recent study, its prevalence was found to be 25.6 % (Table 1) ^{11,8}.

Table 1. Distribution of subjects based on prevalence rate in South India.

Prevalence	No of cases	Percent
PCOS	128	25.6
Non-PCOS	372	74.4
Total	500	100.0

Both insulin resistance and hyperandrogenism have a task in inhibiting breastfeeding in terms of pathophysiology. Obesity may additionally play a role in inhibiting breastfeeding in PCOS ¹⁷. Gestational hypertensive disorders are the leading causes of maternal morbidity and mortality, affecting 3 to 10 % of all pregnancies, including a subset of pregnancies resulting in preeclampsia, and contributing to 16 % of maternal deaths in developed nations. Two large meta-analyses found a two- to the four-fold increased rate of pregnancy-induced hypertension (PIH) as well as

preeclampsia in women with PCOS. Hypertensive disease in pregnancy (HDP) occurs in 8 % of PCOS pregnancies. It includes pregnancy-induced hypertension), defined as new-onset hypertension in pregnancy after 20 weeks of gestation, and preeclampsia, defined as PIH (pregnancy-induced hypertension) with the presence of abnormal quantities of protein within the urine. There’s an inconsistent association between PCOS and HDP. GDM (gestational diabetes mellitus) complicates 40 to 50 % of PCOS pregnancies. In pregnancy, it intervenes when pancreatic β cells become unable to beat insulin resistance. Early

pregnancy loss (EPL) occurs in 30 to 50 % of PCOS women, compared with 10 to 15 % of normal women. The explanation for EPL (early pregnancy loss) in PCOS women is elevated testosterone, which downregulates the expression of HOXA10 (Homeobox A10-protein coding gene), thereby decreasing uterine receptivity and implantation. Preterm birth complicates 6 to 15 % of pregnancies in PCOS women. Preeclampsia itself could be a risk factor for preterm deliveries ¹⁸. The complications related to PCOS are not just confined to reduced fertility but also include pregnancy complications (Table 2 and 3; Fig 1) ¹⁶.

Table 2. Distribution of subjects based on pregnancy outcome.

Pregnancy complications	Non-PCOS		PCOS		Chi-square test	
	NO:	%	NO:	%	Chi-Square Value	p-value
Spontaneous Abortions	16	4.30	58	45.31	127.03	<0.001*
Gestational Diabetes	7	1.88	60	46.88	166.13	<0.001*
Gestational Hypertension	16	4.30	72	56.25	177.21	<0.001*
Preterm Labour	1	0.27	19	14.84	52.68	<0.001*

Table 3. Distribution of subjects based on caesarean rate.

Group	NO:	%	Chi-Square test	
			Chi-Square value	p-value
Normal women	29	22.66	115.27	<0.001*
PCOS women	65	80.24		

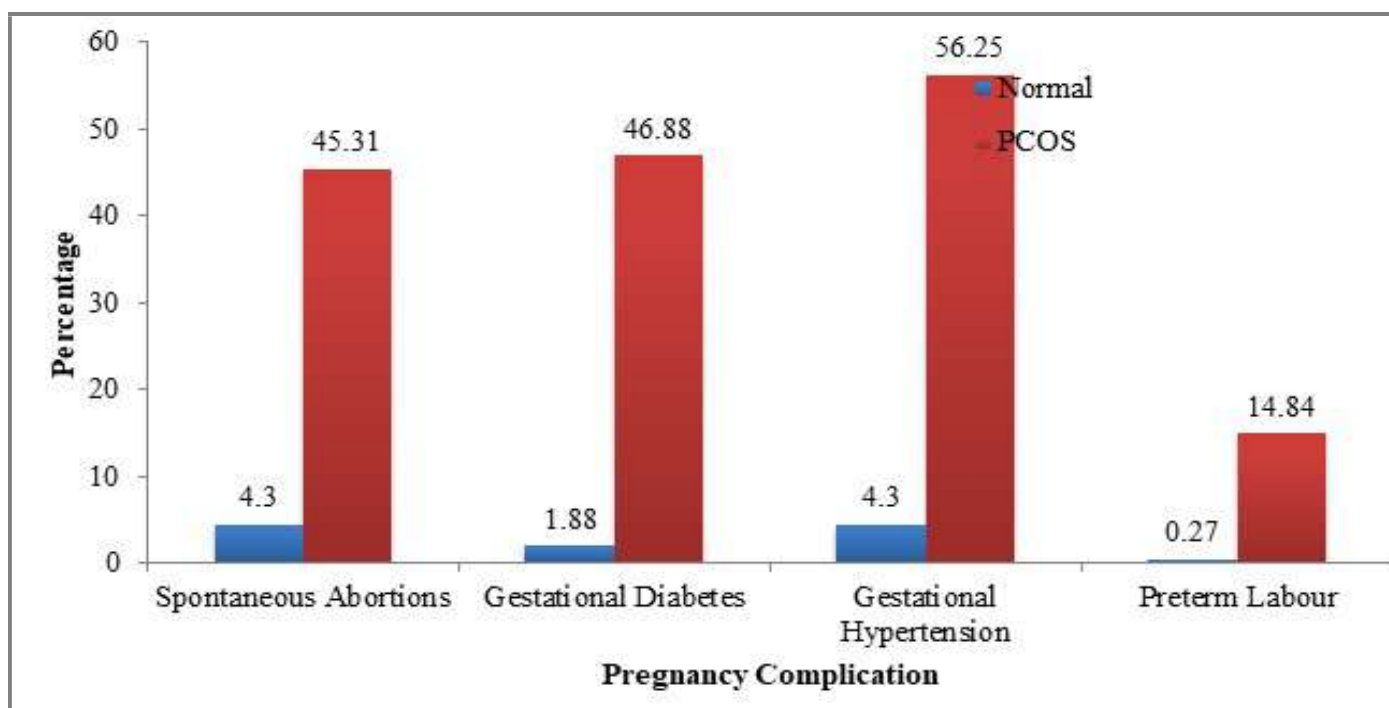


Fig 1. Distribution of subjects based on pregnancy complications.

Hence, routine screening for blood glucose abnormalities, obesity, and infrequent menstrual periods is to be managed enthusiastically in adulthood. Routine antenatal screening and early diagnosis of GDM and hypertensive disorders can provide a much better fetal and maternal outcome^[9]. Management of PCOS includes education on health conditions, healthy lifestyle interventions (diet, exercise), and therapeutic interventions targeting its symptoms^[10]. Many women with PCOS need insulin sensitising agents because they have positive effects on insulin resistance, menstrual irregularities, anovulation, and hirsutism. Metformin and clomiphene, alone or together, are used for ovulation induction. Hyperandrogenism can also be treated with insulin-sensitizing agents, oral contraceptives, spironolactone, and topical eflornithine^[11]. Recently, the use of Metformin (Biguanide), which is a category B drug according to the FDA, during pregnancy has become increasingly popular (absence of teratogenic effects supported by animal data)^[12,13]. The use of metformin is safe during pregnancy since it doesn't cross the placenta, and is safe to take while breastfeeding the child. Trace amounts of the medication can be detected in breast milk, but it won't harm or affect the infant's growth and development^[13]. Obesity worsens both the symptomatology and endocrine profile, and so obese women (BMI 30 kg/m²) should therefore be encouraged to reduce weight. The menstrual irregularity- The easiest way to control the menstrual cycle is the use of a low dose combined oral contraceptive preparation. Birth control pills work by correcting the hormone imbalance, lowering the level of testosterone, regulating menstrual periods, and lowering the risk of endometrial cancer. Surgical removal is not required for these noncancerous cysts. The surgical treatment option available for infertility is laparoscopic ovarian drilling. Regular medical follow-up is required for girls with PCOS. She should test her blood sugar once a year or have a glucose challenge test (oral glucose tolerance test) every few years^[7]. Despite all the available medications, lifestyle changes are the main therapy that improves all parameters of PCOS without the potential side effects of medication^[14]. PCOS appears to be bi-directionally associated with obesity. Women with PCOS have a higher body mass index (BMI) and greater weight gain compared with women without PCOS. A higher body mass index (BMI) decreases the breastfeeding rate^[15]. It's found that DHEAS

(Dehydroepiandrosterone sulfate) levels at gestational weeks 32 and 36 show a weak negative correlation with breastfeeding at one and three months postpartum^[16]. Evidence suggests that low Apgar scores at 5 min are more common in babies born to women with PCOS^[17]. The impact of these on a woman's quality of life may result in psychological distress that threatens her feminine identity (Table 3 to 8).

Typically, PCOS treatment focuses on symptom relief. Hence, effective treatment can reduce the burden of those symptoms as well as the associated psychological disturbances and thus improve health-related quality of life (HRQoL)^[6,18]. Pregnant women with PCOS are more likely to have a C-section because of the pregnancy complications associated with PCOS, such as pregnancy-induced high blood pressure (Table 3)^[6]. Pregnancy complications could influence long-term maternal health independently of the presence of cardiovascular and metabolic disease in mothers with PCOS. In fact, many data suggest that pregnancy-related disorders such as PIH, PE, or GDM are associated with an increased risk of development of type 2 DM as well as future maternal cardiovascular disease and mortality. It is not possible to exclude that the underlying risk factors that lead to pregnancy complications may also lead to long-term health problems. In particular, patients with A more metabolically disturbed PCOS phenotype could have an increased risk of obstetric or neonatal complications^[8]. PCOS women are at an increased risk of adverse pregnancy and birth outcomes and need increased surveillance during pregnancy and parturition. Despite the growing incidence of this syndrome, limited research has been done to review its severity. One of the most challenging aspects of PCOS is its ambiguous diagnostic criteria and also the vast complexity of its characteristics. In the future, more research is required for the prevention as well as the successful treatment modalities for this syndrome^[19,20].

CONCLUSION:

Polycystic Ovary Syndrome (PCOS) is a complex, poorly understood, and underdiagnosed endocrine disorder in women. This review provides the prevalence rate of 25.6% and HRQOL of pregnant PCOS women. PCOS women have a low HRQoL while considering factors like menstrual problems, body hair problems, fertility problems, emotional disturbances, and weight problems. The complications associated with PCOS are not just confined to reduced fertility but also pregnancy

Table 4. Distribution of subjects based on menstrual problems.

Factor	Items	Frequency		Chi-Square test	
		With PCOS	Without PCOS	Chi-Square value	p-value
Menstrual problems	Irregular menstrual periods	104	24	279.74	<0.001*
	Menstrual periods with clots	50	10	119.32	<0.001*
	Heavy menstrual bleeding	61	15	140.60	<0.001*
	Menstrual cramps	50	28	71.93	<0.001*
	Abdominal bloating	7	6	5.59	0.02*

Table 5. Distribution of subjects based on body hair problems.

Factor	Items	Frequency		Chi-Square test	
		With PCOS	Without PCOS	Chi-Square value	p-value
Body hair	Growth of hair on the abdomen	49	19	89.19	<0.001*
	Growth of visible hair on the face	83	19	209.27	<0.001*
	Growth of hair on upper arms or upper legs	28	8	55.45	<0.001*
	Male type of balding or frontal hair loss	12	2	27.33	<0.001*

Table 6. Distribution of subjects based on fertility problems.

Factor	Items	Frequency		Chi-Square test	
		With PCOS	Without PCOS	Chi-Square value	p-value
Fertility problems	Fear of infertility	80	16	207.92	<0.001*
	Feeling difficulty conceive	42	8	99.48	<0.001*
	Abortion	63	17	141.26	<0.001*
	Do not feel sexy because of excessive hair growth	12	0	35.73	<0.001*
	Do not feel sexy because of overweight	7	5	6.92	0.009*

Table 7. Distribution of subjects based on emotional disturbances.

Factor	Items	Frequency		Chi-Square test	
		With PCOS	Without PCOS	Chi-Square value	p-value
Emotions	Angry	62	23	120.51	<0.001*
	Anxiety	49	15	100.08	<0.001*
	Sleeplessness	64	31	107.43	<0.001*
	Depression	78	20	186.56	<0.001*
	Fear / worried	44	13	89.91	<0.001*
	Feeling weak	32	34	20.91	<0.001*

Table 8. Distribution of subjects based on weight problems.

Factor	Items	Frequency		Chi-Square test	
		With PCOS	Without PCOS	Chi-Square value	p-value
Weight	Unusual weight gain	74	41	117.73	<0.001*
	Frustrating with losing weight	8	6	7.52	0.006*
	Trouble dealing with weight	30	7	64.58	<0.001*
	Difficulties staying at ideal weight	37	11	73.89	<0.001*

complications like spontaneous abortions, gestational diabetes, hypertensive disorders of pregnancy, and fetal complications like low birth weight, need for NICU care, and lower APGAR. Pregnant women with PCOS are more likely to have a C-section because of the pregnancy complications associated with PCOS, such as pregnancy-induced high blood pressure. Studies have identified that maternal and neonatal complications are associated with PCOS. The complications associated with pregnancy, such as spontaneous abortions, gestational diabetes, hypertensive disorder in pregnancy, preterm birth, and the need for NICU care for infants, are much higher in women with PCOS. Overall, proper care should be provided for PCOS women during their pregnancy period, as early diagnosis of PCOS can provide a better fetal and maternal outcome.

ACKNOWLEDGMENT:

I would like to express my gratitude to Dr. A. P. Basavarajappa (Principal), Dr. G. L. Prabhushankar (HOD), and Dr. Sruthi Viswanathan (Asst. Prof.), Department of Pharmacy Practice, Bapuji Pharmacy College, Davangere for their continuous support and encouragement.

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Conflict of Interest: None

Source of Funding: Nil

Paper Citation: Jiji R. A review of Pregnancy complications associated with Polycystic Ovary Syndrome. J Pharm Adv Res, 2022; 5(6): 1552-1558.