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PolyCystic Ovary Syndrome and Spontaneous Abortion

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ABSTRACT

Background: In sexually active women, PolyCystic Ovary Syndrome (PCOS) is the most prevalent endocrine metabolic condition.

Aim of the work: To discover the relationship between abortion and polycystic ovary syndrome.

Patients and methods: The research was conducted at the obstetrics and gynecology department's outpatient clinic, Al-Azhar University Hospitals within six months started from 1st December 2019 till 1st June 2020.

Results: there was significantly increase in the incidence of abortion in PCOS group (group A) compared to non PCOS group (group B) (p= 0.041).

Conclusion: our research reveals that PCOS has a greater impact on the risk of spontaneous abortion in pregnant women than previously thought. This could be attributed to the high prevalence of obesity in their population. Women having PCOS are more likely to have an unfavorable pregnancy and birth outcome, and may require more monitoring through pregnancy and parturition.

Keywords: *Polycystic ovary syndrome; Abortion; birth outcomes; pregnancy.*

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INTRODUCTION

Despite the fact that Stein and Leventhal (1935) were the first to identify polycystic ovarian syndrome (PCOS), it was initially discovered in 1721 by Antonio Vallinsneri, an Italian scientist, who noticed larger-than-normal ovaries in young peasant women who were infertile and obese.[1]

An ovulatory infertility is caused by PCOS, which is the most frequent source of an ovulatory infertility in the globe. In addition to a low rate of conception, early pregnancy loss is much greater (30-60%) than in the general population.[2]

The cause of this illness is unclear. Because of its negative impact on the implantation environment and endometrial function, hyperinsulinemic resistance was identified as a risk factor for early abortion. By raising androgen concentration and approaching ovulation, the disease is exacerbated by hyperinsulinemic resistance.[3]

PCOS is the most prevalent endocrine metabolic disorder in women of reproductive age. PCOS is at this time divided into four phenotypes: 1) hyperandrogenism + oligo-anovulation + polycystic ovarian morphology; 2) hyperandrogenism + oligo-anovulation; 3) hyperandrogenism + polycystic ovarian morphology; and 4) oligo-anovulation + polycystic ovarian morphology.[4]

Pathophysiological anomalies in gonadotropin secretion and action, steroidogenesis, ovarian folliculogenesis, insulin secretion and action, and adipose tissue activity have all been associated to PCOS, among many other things. Hypertension, dyslipidemia, vascular diseases, vascular thrombosis, and possibly cardiovascular events; glucose intolerance and type 2 diabetes; metabolic syndrome and hepatic steatosis; hypertension, dyslipidemia, cerebrovascular accidents, vascular thrombosis, and cardiovascular events; Subfertility and obstetric issues are more prevalent in women with PCOS, as are hypotension, dyslipidemia, vascular thrombosis, cerebrovascular accidents, and possibly cardiovascular events (such as early abortion, gestational diabetes mellitus, Pregnancy induced hypertension, Preeclampsia, and large for Gestational Age).[4]

At least 1 ovary with an ovarian volume greater than 10 cm3 (or 10 mL) or a greater number of antral follicles (those visible as cysts in the ovarian cortex measuring 2–9 mm in diameter) is considered polycystic ovarian shape. The exact number of antral follicles needed to diagnosis polycystic ovarian morphology is now at least 18, if not more, with today's high-frequency T.V. ultrasonography probes.[5]

Humans have a high rate of spontaneous abortion. Up to 75% of fertilised ova and at least 15% of clinically recognised pregnancies never make it to term. The majority of spontaneous losses happen

early; approximately half happen before or shortly after a missed menstrual period, and the majority of the remaining losses happen before 8 to 10 weeks of gestation.[6]

During the first or early second trimester, spontaneous abortion occurs in 10–15 percent of clinically diagnosed pregnancies. Pregnancy loss before the 20th week of pregnancy is commonly referred to as miscarriage.[5]

Many early abortions are known to be caused by genetic abnormalities, with 35–75 percent revealing chromosomal abnormalities on karyotyping.[3]

Maternal age and a history of recurrent miscarriages are other factors connected to abortion (defined as two or more such outcomes in previous pregnancies), as well as maternal infections like Toxoplasma gondii and rubella.[7]

Ant phospholipid antibodies and factor V Leiden are also associated to spontaneous miscarriage, as are poorly managed maternal insulin-dependent diabetes and thyroid autoimmunity.[8]

Also other endocrinal factors may play a role as PCOS, thyroid dysfunction, cushing syndrome and hyperprolactinemia [7]

Abortion is known as ending a pregnancy before the 24-week mark. Approximately 10% to 15% of all result of pregnancies in a first-trimester spontaneous abortion.[9]

Spontaneous abortion is an abortion that occurs accidently while early abortion is pregnancy failure during first 12 weaks of gestation.[8]

Abortion may be complicated by bleeding which may be prolonged or severe or even hemorrhagic shock, also may be complicated by infection leading to septic shock, DIC, pelvic abscess, tubal adhesions and asherman s syndrome, in addition to big psychic trauma especially with PG or even after a long time of infertility.[9]

The aim of this study was to discover if there was a link between abortion and polycystic ovary syndrome.

PATIENTS AND METHODS

The study was place at Al-Azhar University Hospitals' obstetrics and gynecology department's outpatient clinic for six months, starting on December 1, 2019 and ending on June 1, 2020.

Type of study and study population: This prospective case-control study included 50 married female within reproductive age 20 – 45 years. We divided the patients into 2 groups: **Group A:** PCOS cases aiming to get pregnant. **Group B:** Non PCOS cases aiming to get pregnant.

Inclusion Criteria for study group: Female within reproductive age 20 – 45 years, married and female with polycystic ovary syndrome aiming to get pregnant.

Exclusion Criteria for groups:: Patints with Thyroid disorders, patients with luteal phase defect, patients with genetic defects, patients with history of induced abortion, consanguinity, uterine anomalies, patient age less than 20 year or more than 45 year and virgin

Methods: patients were subjected to:

Complete history taking: personal history including: Name, Age, marital state, address. Menstrual history: including age of Menarche, menstrual disruption, dysmenorrhea, related symptoms, history Parity, obstetric history, present history: of chronic diseases and medication, past history of HTN, DM, family history of any disease, history of allergy to any medication, surgical history of operation, laparoscopic interference, treatment of hirsutism by Laser.

Examination:

General examination: Vital signs (Temperature, Heart rate, Blood pressure, Respiratory rate), **Signs of** (Pallor, Cyanosis, Jaundice, oedema and Lymph node enlargement) and **Chest and heart examination**

Abdominal examination for exclusion of HSM, ascites, fundal level if pregnant more than 12 weeks GA: Examine the patient's belly for scars, abdominal distension, Caput medusa, striae (stretch marks), and hernias, all of which might indicate gastrointestinal disease. Light probing of the abdomen and thorough palpation of the abdomen are two types of abdominal palpation. Abdominal percussion: Percuss the liver and percuss the spleen. Abdominal auscultation: Assess bowel sounds by auscultating at least two positions on the abdomen: tinkling bowel sounds, normal bowel sounds and absent bowel sounds. Basic developmental evaluation, symmetry, hair quality and growth distribution, skin anomalies, swelling, ulcerations, growths such as external genital warts (EGW) or tumor's, rashes, lacerations, piercings, bruises, and discharge are all part of the vulvar examination. Examine the region around the vaginal canal: The hymenal ring can be seen by slightly separating the labia minora. The vaginal walls, especially those towards the back, relax when light pressure is applied to the bulbocavernosus muscle, making speculum insertion easier. During examination of the urethral, the urethral aperture, the Skene glands, any discharge, soreness or erythema, and any eversion or prolapse of the meatus are all examined. Contour, erosion, os form (patulous, parous, scarred, nonparous), discharge, lacerations, polyps, neoplasias, and lesions, as well as discharge, lacerations, polyps, neoplasias, and lesions, should all be checked on the cervix (eg, warts). The cervix of a pregnant woman may be purple in colour.

Laboratory investigation: Complete blood picture (CBC): hemoglobin concentration (Hb %), white blood cells (WBCs), red blood cells (RBCs), platelet count, progesterone, LH, Estrogen E2, testosterone and fasting and postprandial blood sugar

We followed up the two groups to know incidence of those continue their pregnancy and others which undergo abortion during first 12 weeks of gestational age

Ethical Consideration: The study protocol had been submitted to Al-Azhar University's Institutional Review Board for approval, each participant had given informed verbal permission, and confidentiality and personal privacy had been protected at all stages of the study.

Data management and Statistical Analysis: The information gathered during the history, basic clinical examination, laboratory tests, and outcome measures was coded, entered, and analysed in Microsoft Excel. The Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software was used to analyse the data. Per the nature of data, qualitative data is represented as a number and a percentage, whereas quantitative data is represented as a mean and standard deviation ± SD. To determine the significance of differences, the following tests were employed Mann-Whitney testing, and T test ;., correlation by Pearson's correlation or Spearman's . For significant results, the P value was set at<0.001 for very significant result & <0.05 for significant results.

RESULTS

		Group (A) (PCOS cases) (n = 50)		Group (B) (Non PCOS cases) (n = 50)		Test value	P-value	Sig.
		n	%	n	%			
Age (years)	**Mean± SD**	30.84± 8.06		30.4± 6.7		T=0.210	0.835	NS
	Median (IQR)	30.0 (24.0 - 38.0)		29.0 (25.0 - 36.0)				
	Range	20.0 - 45.0		20.0 - 45.0				
Residence	**Rural**	26	52.0%	22	44.0%	X^2= 0. 321	0.571	NS
	Urban	24	48.0%	28	56.0%			
Weight (Kg)	**Mean± SD**	72.04± 9.83		68.8± 8.6		T=1.227	0.226	NS
	Median (IQR)	73.0 (64.0 - 81.0)		70.0 (62.0 - 75.0)				
	Range	58.0 - 87.0		56.0 - 84.0				
Height (cm)	**Mean± SD**	170.12± 7.51		169.56 6.58		T=0.280	0.780	NS
	Median (IQR)	171.0 (164.0 - 175.0)		169.0 (165.0 - 174.0)				
	Range	157.0 - 182.0		157.0 - 181.0				
BMI (Kg/ m^2)	**Mean± SD**	24.93 3.35		23.96 2.88		T=1.095	0.279	NS
	Median (IQR)	24.39 (22.53 - 27.10)		23.57 (21.89 - 26.17)				
	Range	19.84 - 32.74		19.84 - 30.12				

p less than or equal 0.05 is deemed statistically important, p≤0.01 is regarded as high notable imbortant SD= standard deviation, IQR= Interquartile range, BMI= Body mass index

-Comparison between groups done by Student T test and Chi- Square test

Table 1: Socio-demographic characteristics among the studied groups

Table (1) shows socio-demographic characteristics among the two studied groups. The variation between PCO and non-PCO groups was not statically important regarding age (p= 0.835) and residence (p= 1.00). Also, Weight variance among the two groups was not wide variation (p= 0.226), height (p= 0.780) and BMI (p= 0.279).

		Group (A) (PCOS cases) (n = 50)		Group (B) (Non PCOS cases) (n = 50)		Test value	P-value	Sig.
		n	%	n	%			
SBP	**Mean± SD**	116.80± 7.48		116.0± 6.45		Z_{MWU} = 0.278	0.781	NS
	Median (IQR)	120 (110.0 - 120.0)		120.0 (110.0 - 120.0)				
	Range	110.0 - 130.0		110.0 - 130.0				
DBP	**Mean± SD**	74.80± 5.10		74.40± 5.83		Z_{MWU} = 0.144	0.885	NS
	Median (IQR)	70.0 (70.0 - 80.0)		70.0 (70.0 - 80.0)				
	Range	70.0 - 80.0		60.0 - 80.0				
Pulse	**Mean± SD**	72.80± 8.02		73.28± 9.51		Z_{MWU} = 0.097	0.923	NS
	Median (IQR)	71.0 (67.0 - 80.0)		69.0 (65.0 - 82.0)				
	Range	60.0 - 86.0		60.0 - 86.0				
Temperature	**Mean± SD**	36.53± 0.30		36.52± 0.32		Z_{MWU} = 0.088	0.930	NS
	Median (IQR)	36.5 (36.3 - 36.8)		36.5 (36.2 - 36.8)				
	Range	36.0 - 37.0		36.1 - 37.0				
Respiratory rate	**Mean± SD**	13.88± 1.48		14.08± 1.35		Z_{MWU} = 0.537	0.592	NS
	Median (IQR)	14.0 (12.0 - 15.0)		14.0 (13.0 - 15.0)				
	Range	12.0 - 16.0		12.0 - 16.0				

Table 2: General examination done for the study groups

Table (2) illustrates general examination done for the study groups. On comparison of systolic and diastolic blood pressure between PCO and non PCO groups, there was no notable variation (P = 0.781 & 0.885 respectively). In addition, between the two groups, there was no important change in pulse (p=0.923), temperature (p=0.088) and respiratory rate (p= 0.537).

		Group (A) (PCOS cases) (n = 50)		Group (B) (Non PCOS cases) (n = 50)		Test value	P-value	Sig.
		n	%	n	%			
Ovarian volume	**Mean± SD**	13.6± 1.5		7.2± 0.7		z_{MWU} = 6.067	**<0.001**	**HS**
	Median (IQR)	13.7 (12.9 - 14.8)		7.1 (6.6 - 7.6)				
	Range	10.1 - 15.8		5.8 - 8.2				
FSSP	**Mean± SD**	13.3± 1.3		6.5± 0.4		z_{MWU} = 6.068	**<0.001**	**HS**
	Median (IQR)	13.0 (12.4 - 14.0)		6.5 (6.2 - 6.8)				
	Range	10.9 - 16.3		5.6 - 7.3				
FNPO	**Mean± SD**	29.8± 5.6		9.9± 1.6		z_{MWU} = 6.065	**<0.001**	**HS**
	Median (IQR)	30.4 (26.0 - 33.4)		10.0 (8.9 - 11.0)				
	Range	19.8 - 41.1		6.5 - 12.5				

Table 3: Distribution of ultrasonic findings amongst the study groups

Table (3) the distribution of ultrasonic findings among the study groups was depicted in this table. In both groups, the median values of ovarian volume, FSSP, and FNPO were comparable. The results demonstrate that the PCOS group (group A) had considerably larger ovarian volume, FSSP, and FNPO than the non-PCOS group (group B).

		Group (A) (PCOS cases) (n = 50)		Group (B) (Non PCOS cases) (n = 50)		Test value	P-value	Sig.
		n	%	n	%			
LH	**Mean± SD**	11.0± 1.3		4.1± 0.5		z_{MWU} = 6.072	**<0.001**	**HS**
	Median (IQR)	11.0 (10.6 - 11.4)		4.1 (4.0 - 4.2)				
	Range	8.1 - 13.2		2.7 - 5.5				
Testosterone	**Mean± SD**	1.8± 0.2		1.2± 0.4		z_{MWU} = 5.236	**<0.001**	**HS**
	Median (IQR)	1.8 (1.7 - 2.0)		1.2 (1.0 - 1.5)				
	Range	1.4 - 2.2		0.4 - 1.8				
Estrogen (E2)	**Mean± SD**	29.34± 1.56		27.58± 0.42		z_{MWU} = 4.832	**<0.001**	**HS**
	Median (IQR)	28.85 (28.12 - 30.80)		27.59 (27.24 - 27.75)				
	Range	27.32 - 32.27		26.88 - 28.38				

Table 4: Distribution of laboratory results among the study groups

Table (4) represents the variation of test findings among the study groups. The median values of LH, testosterone and E2 were comparable in the two groups. The results show that LH, In the PCOS group (group A), testosterone and E2 levels were considerably greater than in the non-PCOS group (group B).

		Group (A) (PCOS cases) (n = 50)		Group (B) (Non PCOS cases) (n = 50)		Test value	P-value	Sig.
		n	%	n	%			
Abortion	**Absent**	24	48.0%	38	76.0%	X^2= 4.16	**0.041**	**S**
	Present	26	52.0%	12	24.0%			

Table 5: Distribution of abortion among the studied groups

As shown in table (5), there was significantly increase in the incidence of abortion in PCOS group (group A) compared to non PCOS group (group B) (p= 0.041).

DISCUSSION

Polycystic ovary syndrome is a complicated endocrinopathy. Regarding to the Rotterdam principles, 2 of the 3 requirements should be achieved in order to diagnose PCOS: persistent anovulation, clinical and/or biochemical evidence of hyperandrogenism, and polycystic ovaries.[10]

After being endorsed by the Endocrine Society Clinical Practice Guideline for diagnosing PCOS, the Rotterdam criteria have been commonly distributed utilized PCOS diagnostic model globally.[10]

Maternal age, controlled ovarian hyperstimulation regimen, cycle type, and PCOS status may all influence the miscarriage rate.[11]

As a result, this research looked at the relationship between abortion and polycystic ovary syndrome.

This case –control study was carried out on 100 female cases that attended outpatient clinic of obstetrics and gynecology department of Al-Azhar University Hospitals.

They were split into two groups: group A included PCOS cases aiming to get pregnant and group B included non PCOS cases aiming to get pregnant.

Socio-demographic characteristics among the two our studied groups showed no important variations between PCO and non PCO groups regarding age, residence, weight, height and BMI which indicate good matching between groups.

There was no statistically notable change in gravidity, parity, or the incidence of abortion between PCO and non-PCO groups, according to the

current study's participants. None of the studied females in PCO and non PCO groups had DM. 4 (8%) females in in PCO group and 6 (12%) females in non PCO group were hypertensive with no important change between the 2 groups regarding hypertension.

Regarding ultrasonic findings among the current study groups, the results showed that PCOs group had higher mean ovarian volume (13.6± 1.5) than no PCOs group (7.2± 0.7) (p<0.001).
In the current study, PCOs group had higher mean FSSP (13.3± 1.3) than no PCOs group (6.5± 4.0) (p<0.001). PCOs group had higher mean FNPO (29.8± 5.6) than no PCOs group (9.9± 1.6) (p<0.001). PCOS group had higher mean of LH, testosterone and E2 compared to non PCOS group (p<0.001).
This is in agreement with study in which the mean ovarian volume for the NO women was 7.15 ± 2.14 cm^3 and for PCOS patients was 13.56 ± 3.52 cm^3, P<0.0001. The average maximum FSSP was greater in PCOS patients (13.3 ± 3.21) than in NO women (6.5 ± 1.43), P<0.0001. The mean FNPO was also greater in PCOS patients (29.80 ± 11.53) than in NO women (9.89 ± 3.59, P<0.0001).[12]
Several investigations have also discovered that higher LH or the LH/follicle stimulating hormone (FSH) ratio, as well as abnormally high androstenedione and/or testosterone levels, are all endocrinological results associated with PCOS.[13]
The impact of basal luteinizing hormone (bLH) in PCOS on spontaneous abortions patients was studied in two studies including 1329 participants with continuous data. According to the findings of these studies, LH may raise the risk of miscarriage in PCOS patients.[14]
In this study, abortion rates have risen at a statistically significant rate in PCOS group (52%) compared to non PCOS group (24%) (p= 0.041).
PCOS women are concerned about early pregnancy loss (EPL), also referred as first-trimester miscarriage. PCOS women are affected by EPL in 30 to 50 percent of the time, compared to 10 to 15percent of normal women. [13] Treatment with ovulation-inducing medications is related to a greater incidence of spontaneous EPL when compared to the prevalence in the regularly ovulating, naturally conceiving population. [15]
The current study's findings support prior findings that the risk of spontaneous abortion rises with increased BMI in both PCOS and non-PCOS women [16] and without.[17]
Our study has higher rate than **Ibrahem et al.,** [18] study in which the early pregnancy rate of failure in our sample was 5 (10 percent) out of 50 patients**.**
Similar to our result **Galiano et al.**, [19] study found that 21 patients (42 %) out of 50 patients) was the incidence of abortion in PCOS group.
According to **Zeng et al.,** [21] insulin resistances put women at risk for PCOS and hyperandrogenism. They are frequently exposed to an unfavourable hormonal environment, which might disrupt pregnancy and implantation.
From 40 observational studies with a diverse demographic, a large and comprehensive quantitative metanalysis comprised 17,816 PCOS-positive pregnancies and 123,756 PCOS-negative pregnancies. PCOS is associated to a significant incidence of miscarriage during pregnancy, according to the findings of a meta-analysis.[21]
Another meta-analysis indicated that 3196 women with PCOS and 21 934 women without PCOS miscarried in 21 studies. Miscarriage was more common in PCOS women. (OR: 1.59, 95% CI: 1.11-2.28). [22]
According to another study, in developed countries, PCOS is the most common cause of anovulatory infertility. [23] and most commonly identified abnormality among women who have repeated miscarriages.[24]
Obesity, hyperinsulinemia, IR, hyperandrogenemia, hyperhomocysteinemia, high levels of plasminogen activator inhibitor-1 factor, poor endometrial receptivity, and higher rates of luteinizing hormone are all possible causes of spontaneous foetal loss in women with PCOS (LH).[25]
The rate of embryo implantation and medical pregnancy was found to be lesser. [26]
The level of miscarriage in the 1st trimester was observed to be substantially greater. [27] Late in the pregnancy, complications were also more common, and the live birth rate in PCOS individuals was observed to be much lower. [26]
Previous research comparing the rate of early pregnancy loss in PCOS and non-PCOS women failed to account for embryo aneuploidy, This is largely acknowledged as the most critical factor in early miscarriage.[28]

This study has some limitations. No history of treatment was reported which can affect the rate of occurrence of spontaneous abortion. Multiple factors contribute to recurrent pregnancy loss, and endocrine disruption is one of one of those.

CONCLUSION

In conclusion, our research reveals that PCOS has a greater impact on the risk of spontaneous abortion in pregnant women than previously thought. This could be attributed to the high incidence of obesity in their population. PCOS women are more likely to get an unfavourable pregnancy and birth outcome, and may need further monitoring throughout pregnancy and delivery.

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