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A survey on the frequency of polycystic ovary morphology (PCOM) in infertile patients with septate and arcuate uterine anomalies: a cross-sectional study

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Polycystic ovarian syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age. Previous research has highlighted a potential link between PCOS and Müllerian anomalies. The present cross-sectional study aimed to evaluate the prevalence of polycystic ovary morphology (PCOM) in infertile patients with uterine anomalies (septate and arcuate uterine), attending the Royan Research Institute in Tehran, Iran, between January 2021 and December 2022. A total of 884 infertile women who underwent 3D-hysterosonography at the Institute were included in the study. The participants were divided into two groups: 127 women with uterine anomalies and 757 women without. Data was collected from the participants' medical records. The results showed that the frequency of PCOM was significantly higher in women with uterine anomalies (40.9%, 52 women) compared to those without such anomalies (14.7%, 111 women) ($p = 0.0001$). A higher prevalence of PCOM in women with uterine anomalies highlights the need for targeted screening within this population and underscores the importance of integrated diagnostic approaches.

Keywords Uterine abnormalities, Polycystic ovary morphology (PCOM), Septate uterine, Arcuate uterine, Polycystic ovarian syndrome (PCOS)

Abbreviations

APGAR	APGAR score is a quick test performed on a newborn at 1 and 5 minutes after birth and includes the examination of Appearance, Grimace, Activity, and Respiration
ASRM	American Society for Reproductive Medicine

One of the common endocrine system disorders that affects women of reproductive age is polycystic ovary syndrome (PCOS)[1]. Numerous studies have established a link between PCOS and Müllerian abnormalities such as septate uterus and arcuate uterus[2–5]. The prevalence of PCOS varies between 4% and 21%, depending on the specific diagnostic criteria used[1]. The 2023 International Evidence-based Guideline[6] for the assessment and management of PCOS recommends diagnosing the condition based on the 2018 International Evidence-based Guideline criteria, which build upon the 2003 Rotterdam criteria. Diagnosis requires the presence of two out of the following three criteria: ovulatory dysfunction, clinical or biochemical signs of hyperandrogenism, and polycystic ovary morphology (PCOM). PCOM is defined as having at least one ovary with a follicle number per ovary (FNPO) ≥ 20 or an ovarian volume ≥ 10 mL, or follicle number per section (FNPS) ≥ 10 in at least one ovary in adult.

Alternatively, anti-Müllerian hormone (AMH) levels can be used instead of ultrasound in adults. When ovulatory dysfunction and hyperandrogenism are present, the diagnosis can be made without the need for

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ultrasound or AMH. In adolescents, both ovulatory dysfunction and hyperandrogenism are required for diagnosis, and ultrasound or AMH is not recommended due to their low specificity[6].

The etiology of PCOS is multifactorial, including genetic, environmental, and trans-generational influences[7]. Women with PCOS frequently experience metabolic dysfunction and obesity[8]. It has been suggested that women with PCOS, regardless of ovulatory status, should be considered as having a diminished capacity for reproduction[9]. PCOS can lead to changes in various reproductive processes in women. One possible mechanism contributing to infertility in PCOS is impaired oocyte competence[10]. Experimental and clinical evidence suggests that women with PCOS have distinct endometrial structures compared to healthy controls, resulting in reduced endometrial receptivity[11]. However, it is important to note that there is insufficient evidence to support interventional strategies aimed at improving endometrial receptivity in women with PCOS, which limits their clinical application[12].

Women diagnosed with PCOS are at a significantly higher risk of pregnancy complications, including multiple gestations, pregnancy-induced hypertension (PIH), pre-eclampsia (PE), gestational diabetes mellitus, and preterm birth, compared to a control group[13]. Additionally, women with PCOS have higher rates of miscarriage, an increased risk of ovarian hyperstimulation syndrome (OHSS), and lower APGAR scores in infants conceived through assisted reproduction technology (ART)[14].

Müllerian ducts serve as embryological precursors of the female reproductive tract, which consists of the fallopian tubes, uterus, cervix, and superior segment of the vagina[15,16]. The development of the female reproductive system involves a series of mechanism within the Müllerian duct system, including differentiation, migration, fusion, and canalization[17]. Müllerian duct anomalies occur when there is abnormal development of the Müllerian ducts[15,16]. The American Society for Reproductive Medicine (ASRM) classification (2021) categorizes Müllerian anomalies into 9 groups: Müllerian agenesis, cervical agenesis, unicornuate uterus, uterus didelphys, bicornuate uterus, septate uterine, longitudinal vaginal septum, transverse vaginal septum, and complex anomalies[18]. Women with uterine anomalies have a higher incidence of miscarriage, preterm birth, and fetal growth restriction[19,20]. Studies show that up to 7% of women in the general population and 18% of women with recurrent miscarriages may have uterine abnormalities[21].

A significant proportion of women with uterine abnormalities have been found to also have polycystic ovaries, which can contribute to further infertility[21]. Given the emotional and financial challenges that infertility treatments present to both patients and society, understanding the relationship between polycystic ovaries and uterine anomalies is crucial. This knowledge can help prevent unnecessary expenditures and time loss by allowing for more targeted and efficient treatment strategies.

This study aimed to estimate the prevalence of polycystic ovary morphology (PCOM) in infertile patients with uterine abnormalities, specifically septate and arcuate uterine anomalies. Any reference to uterine abnormalities in this article pertains exclusively to these two types.

Methods

This retrospective cross-sectional study was conducted on the total of 884 infertile women who were referred to the Royan Research Institute in Tehran (Iran) for 3D-hysterosonography between January 2021 and December 2022. The participants were divided into two groups based on the presence or absence of uterine abnormalities.

The required information, including demographic data (age) and obstetric and gynecological history (type, cause, and duration of infertility, as well as PCOM), was extracted from the patients' medical records.

The eligibility criteria for participation in the study were as follows, women of reproductive age (20–48 years), without: systemic diseases, a history of previous uterine surgery or ovarian cysts, hormonal drug use, or the presence of uterine leiomyoma, polyps, or uterine cavity adhesions. The exclusion criterion was any defect in the patients' medical records.

PCOM was diagnosed based on the Rotterdam criteria and confirmed through ultrasound, with the presence of an ovarian volume > 10 mL or 12 or more follicles measuring 2–9 mm in size. In this study, we utilized the Rotterdam criteria for diagnosing PCOM, as these criteria have not yet been disproven and serve as the foundation for PCOM diagnosis at our institution.

Uterine anomalies were diagnosed using 3D-hysterosonography and classified according to the ASRM (2021) classification[18]. According to this classification, a septate uterus is characterized by the presence of an endometrial septum (length > 1 cm) measured from the bicornual line, with the leading edge of the septum forming an angle < 90°. An arcuate uterus is defined by an endometrial indentation (length ≤ 1.0 cm), while a normal uterus is identified by the absence of any indentation.

The sampling method used was convenient and based on availability.

Initially, a total of 897 infertile women were included in the study. However, 13 women were found to have unicornuate, T-shaped, bicornuate, or didelphys uteri and were subsequently excluded from the study. Ultimately, the research was carried out on 884 women: 127 women in the infertility group with uterine abnormalities and 757 women in the infertility group with a normal uterine.

The distribution of variables was tested by the Kolmogorov-Smirnov's test. Student's t-test was used for variables with a normal distribution. The comparison of proportions was carried out using the Chi-square test. Continuous variables are presented as mean ± standard deviation (M ± SD), and categorical variable are presented as numbers (percentages). P-value < 0.05 was considered significant. All the statistical analyses were performed using the SPSS software (SPSS ver. 20; SPSS Inc., Delaware).

The research was approved by the Ethics Committee of Royan Institute (IR.ACECR.ROYAN.REC.1402.124). All procedures complied with the Helsinki Declaration of 1964 and its subsequent amendments, as well as the ethical guidelines established by the Regional Research Committee. Due to the retrospective nature of the study, the Ethics Committee of Royan Institute waived the requirement for informed consent.

		Frequency	Percent
With anomaly	Arcuate uterine ≤ 1 cm	112	12.7
	Septate uterine > 1 cm	15	1.7
Without anomaly		757	85.6
Total		884	100.0

Table 1. Distribution of anomalies in the studied women (n: 884).

Variables	Anomaly	Mean (*n*)		Standard Deviation (%)	*p*-value
Age (years)	Yes	35.64		5.47	
	No	36.84		5.24	0.019
Duration of infertility (years)	Yes	6.24		4.35	
	No	5.72		3.61	0.145
Type of infertility	Yes	Primary	99	78%	0.116
		Secondary	28	22%	
	No	Primary	539	71.2%	
		Secondary	218	28.8%	
Cause of infertility	Yes	Male	30	23.6%	0.002
		Female	65	51.2%	
		Male & Female	15	11.8%	
		Unexplained	17	13.4%	
	No	Male	279	36.9%	
		Female	264	34.9%	
		Male & Female	80	10.6%	
		Unexplained	134	17.7%	

Table 2. Demographic and clinical characteristics of the studied women (n: 884). The data are presented as means ± SD or n (%). P-values were obtained by independent sample t-test and Chi-square test (statistical differences at 0.05).

			Anomaly		p-value
			Yes	No	
PCOM history	No	n	75	646	
		%	59.1%	85.3%	0.0001
	Yes	n	52	111	
		%	40.9%	14.7%	

Table 3. PCOM frequency in the studied women (n: 884).

Results

Initially, the study included 897 infertile women, of whom 6 (0.66%) had a unicornuate uterus, 3 (0.33%) had a bicornuate uterus, 3 (0.33%) had a T-shaped uterus, and 1 (0.11%) had a didelphys uterus. Consequently, these 13 women (1.44%) were excluded from the study. Ultimately, 884 infertile women participated in the study, including 127 (14.4%) with uterine anomalies and 757 (85.6%) without uterine anomalies. The distribution of uterine anomalies was as follows: 112 women (88.1%) had an arcuate uterus (septum length ≤ 1 cm), while 15 women (11.9%) had a septate uterus (septum length > 1 cm) (Table 1).

As presented in Table 2, the mean age of women with uterine anomalies was 35.64 ± 5.47 years, while the mean age of those without anomalies was 36.84 ± 5.24 years ($p = 0.019$). The mean duration of infertility was 6.24 ± 3.61 years for women with uterine anomalies and 5.72 ± 3.61 years for those without anomalies. Of the participants, 99 women (78%) with uterine anomalies and 539 women (71.2%) without uterine anomalies reported primary infertility. Among women with uterine anomalies, female factors were the most common cause of infertility (65 out of 127; 51.2%), whereas in women without uterine anomalies, the most common cause was male factors (279 out of 757; 36.9%) ($p = 0.002$).

The data revealed a significant difference in the frequency of PCOM history between patients with and without uterine anomalies ($p = 0.0001$) (Table 3). Table 4 presents the depth of the fundal indentation of the uterine cavity (length of concavity) in women with uterine anomalies, categorized by PCOM history. The

PCOM		N	Mean	Std. Deviation	95% Confidence Interval for Mean		Minimum	Maximum	p-value
					Lower bound	Upper bound			
Length of concavity	No	72	7.25	3.67	6.39	8.11	3	27	
	Yes	50	7.10	3.90	5.99	8.21	3	20	0.829

Table 4. Depth of fundal indentation of uterine cavity (concavity measurements) in women with anomalies (n: 112) according to PCOM history. The data are presented as means ± SD. P-values were obtained by independent sample t test (statistical differences at 0.05).

measured depth of fundal indentation of uterine cavity in patients with and without PCOM was 7.10 ± 3.90 and 7.25 ± 3.67, respectively ($p = 0.829$).

Discussion

In the present study, the prevalence of PCOM in infertile patients with uterine anomalies at Royan Institute was significantly higher than in those without uterine anomalies. Similar differences have also been observed in previous studies. For example, in a large study involving over 3,000 infertile patients, 57 (8%) of 710 infertile patients with PCOS and 74 (3%) of 2,323 infertile patients without PCOS were found to have uterine anomalies[3]. Another study found a higher proportion of PCOS in patients with a septate uterus (31.9%) compared to women with a normal hysteroscopy (24.0%)[22]. Similarly, in a study of 49 patients diagnosed with PCOS, 15 patients (31%) were found to have uterine anomalies[2]. The results of another study revealed that uterine abnormalities were present in nearly one-third ($n = 149$, 31.4%) of 409 patients with diagnosed PCOS[4]. Additionally, a study of 83 patients with PCOS found that 29 (34.9%) had uterine anomalies[23]. Similarly, another study showed that the percentage of patients with a normal uterine cavity in the PCOS group (51%) was significantly lower than that in the control group (77%)[24].

The studies mentioned above assessed the frequency of uterine anomalies in women with PCOS, while the current research focused on the frequency of PCOM in women with uterine abnormalities. This difference in focus explains the discrepancy in findings between the previous and current studies. The presence of uterine anomalies in the women can be attributed to abnormalities in the processes of combination, canalization, and resorption of the septum during the development of the Müllerian ducts[15]. Anti-Müllerian hormone (AMH) undeniably plays a crucial role in the deterioration of Müllerian ducts in the initial stages of life. There is a possibility that the strong interaction between AMH and Müllerian anomalies[25] as well as its interaction with follicles in the ovarian parenchyma, may increase the likelihood of PCOS/PCOM side effects. Furthermore, based on the findings of this study and previous research, there appears to be an association between Müllerian abnormalities and PCOS/PCOM[25,28].

The present study found that the mean length of fundal indentation in PCOM patients with uterine anomalies was 7.10 ± 3.90, while it was 7.25 ± 3.67 in non-PCOM patients with uterine anomalies. However, this difference was not statistically significant between the two groups. In contrast, another study reported that women with PCOS had more acute indentation angles and deeper uterine cavity indentations compared to women without PCOS[26]. This discrepancy could be attributed to our focus on PCOM in women with uterine abnormalities, rather than uterine anomalies in women with PCOS.

Our findings indicated that the prevalence of uterine anomalies in infertile women was 14.4%. In comparison, a study evaluating infertile women reported a frequency of uterine anomalies at 8.13%[27], while another study found Müllerian anomalies in 4.4% of infertile women[28]. These findings suggest that the prevalence of uterine anomalies in infertile women may be higher than previously reported. This highlights the need for thorough evaluation of uterine abnormalities, as they may impact infertility treatment outcomes.

The smaller sample size of women with uterine anomalies (n: 127) compared to those without (n: 757) may limit the ability to generalize the findings, especially since uterine anomalies are less common. Additionally, the study is limited by its focus on infertile women, meaning the findings may not reflect the prevalence of PCOM in women with Müllerian malformations in the general population. Women with Müllerian abnormalities who do not have PCOM may not experience infertility[28]. Furthermore, since Müllerian anomalies are rare and often undetected due to being asymptomatic, conducting an epidemiological study on these anomalies is challenging.

A key strength of this study is its large sample size. Additionally, to the best of our knowledge, this is the first study to assess the prevalence of PCOM in infertile women with uterine anomalies in our region.

It is recommended that ovarian morphology in women with uterine abnormalities be carefully considered, particularly when assessing the presence of PCOM. Early diagnosis in these women can help reduce both time and financial costs in their treatment interventions.

Conclusion

According to the results of the present research, women with uterine anomalies (septate and arcuate) have a higher prevalence of PCOM compared to those without uterine anomalies. Clinically, understanding the association between uterine abnormalities and PCOM can aid in improving infertility management. It is therefore recommended that infertility treatment providers pay careful attention to this aspect when developing and delivering treatment plans.

Data availability

The datasets used and/or analyzed during the current study are available upon reasonable request from the corresponding author , Dr. Firoozeh Ahmadi (Dr.Ahmadi1390@gmail.com).

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Author contributions

S.I. collected and assembled data and A.N. drafted the manuscript and S.V. and F.N. statistically analyzed the data and M.M. The individuals involved in this research were part of her patient cohort, all of whom received care and consultation from her, and were subsequently directed to our facility, F.A. organized and reviewed all ultrasound measurements and was involved in revising the manuscript.

Declarations

Competing interests
The authors declare no competing interests.

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