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Study of Isolated polycystic ovarian morphology in Egypt

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Abstract: Background: The review of literature showed that PCOM represents 16-25% of apparently normal women, it is also called isolated polycystic ovarian Morphology (PCOM) and it is found to be an intermediate subclinical androgenic ovarian dysfunction, so there is a risk of development of PCOS in the future. **Objectives:** To detect the prevalence of isolated polycystic ovarian morphology (PCOM) in eumenorrheic women without hyperandrogenism, attending Mansoura University Hospital (MUH) (tertiary hospiltal in Egypt). **Subjects and methods:** An observational prospective study was conducted on 156 eumenorrhiec, nonhyperandrogenic women. Cases were presented with vaginal discharge, seeking for fertility, postcoital bleeding etc. These cases were subdivided into 2 groups; 20 women with Isolated PCOM group and other group included 136 women without isolated PCOM. All the cases underwent full history taking, full examination and trans-vaginal ultrasonography. **Results:** The prevalence of isolated PCOM was 12.8% among the included women in the study (20 of 156 cases). The prevalence of isolated PCOM decreased with increasing age in comparison with non PCOM group (P-value=0.13). Body mass index was significantly increased in isolated PCOM (P-value= 0.003). Premature pubarche was significantly increased in patients with isolated PCOM (P-value= 0.001). Infertility was significantly more evident in patients with isolated PCOM (P-value= 0.001). Positive family history of PCOS and DM was significantly increased in these patients (P-value <0.001,0.001, respectively). **Conclusion:** Isolated PCOM is prevalent in 12.8% among eumenorrhiec women without hyperandrogenism attending MUH which is more associated with obese, prematurepubarche, young age and positive family history of PCOS & DM. **Recommendatons:** Further multicentric studies of isolated polycystic ovarian morphology with larger numbers are recommended.

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Key word: Isolated PCOM, Hyperandrogenism, Infertility, Polycystic Ovary Syndrome

1. Introduction

Polycystic ovarian morphology (PCOM), one of the diagnostic criteria for polycystic ovary syndrome (PCOS), is defined according to Rotterdam criteria 2003 by consensus criteria in adults as an ovary with a volume of >10.0 mL by a simplified formula or a small antral follicle (2–9 mm diameter) count of ≥12 per ovary. However, it became apparent that these criteria were problematic for young adults, especially since the latest high-definition vaginal imaging techniques show that small antral follicle counts up to 24 are normal but it was found that the sensitivity of the measurement was compromised. PCOM is considered a pre-PCOS state, a normal morphological variant in adolescence, and a possible complication in high responders to controlled ovarian hyperstimulation **[1 & 2 & 3]**.

The aim of this research was to study the prevalence of polycystic ovarian morphology (PCOM) in eumenorrheic women without hyperandrogenism, attending Mansoura University Hospital, Egypt.

2. Methods:

Ethical consideration approval was acquired by the health facility Ethics Committee and written knowledgeable consent was taken to all of the enrolled subjects. A an observational prospective study was conducted on 156 women and they were subdivided into 2 groups; isolated PCOM group included 20 women with PCOM and other group included 136 women without isolated PCOM.

Patients were recruited from the gynecology out-patient clinic in Mansoura University hospital within the period from June 2018 to June 2019.

Inclusion criteria included; all women have regular menstruation (21-35 days in length and 3-7 days in duration of menses), no hyperandrogenism. Exclusion criteria included; patients unable or refusing to provide consent, pregnant females, women

using hormonal contraceptives, fertility medications and/or valproate (Epilepsy medication), hyperandrogenism (clinical picture of hyperandrogenemia and menstrual disturbance).

All the included cases underwent full history taking including; name, age, residence, age of pubarche, medical history and family history of PCOS and diabetes mellitus, full examination including assessment of weight, height and body mass index (BMI), presence of hirsutism, acne and alopecia in addition to trans-vaginal ultrasonography.

Data were analyzed using statistical package of social science program (SPSS) for windows version 22 (SPSS Inc. Chicago, IL, USA). All statistical analyses were based on two-sided hypothesis tests with a significance level of $P < 0.05$.

3. Results

The prevalence of isolated PCOM was 12.8% among the included women according to Rotterdam criteria (Figure 1). In the present study the prevalence of isolated PCOM decreased with increasing age in comparison with the non PCOM group (P-value=0.13). Body mass index was significantly increased in isolated PCOM (P-value= 0.003). Premature pubarche was significantly increased (45%) in patients with isolated PCOM (P-value= 0.001). Infertility was significantly evident (60%) in patients with isolated PCOM (P-value= 0.001) (Table 1). Positive family history of PCOS and DM represented 95% and 80% (respectively) of isolated PCOM in our study which was significant in these patients (P-value<0.001). Ovarian follicle count, follicular size, ovarian volume, peripheral follicular distribution and central stromal density were significantly (P-value= 0.001, 0.001, 0.001, 0.001, 0.001, respectively) (Table 2). Multivirate analysis revealed that family history of obesity in patient's mothers, BMI of patients, family history of PCOS & DM and Ovarian volume were significant predictors of isolated PCOM (Table 3).

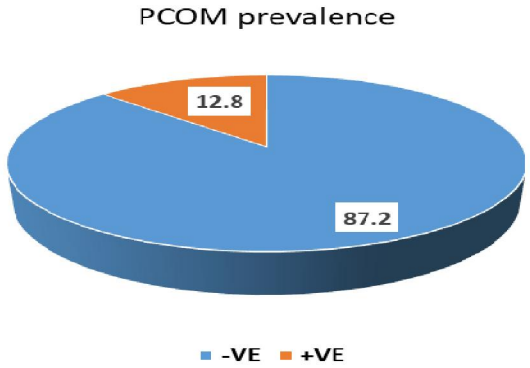

Figure 1: The prevalence of isolated PCOM according to Rotterdam criteria 2003 among the studied sample

Table (1): Comparison between isolated PCOM group and without isolated PCOM women group regarding different parameters

		Without PCOM women (n=136)	With PCOM (n=20)	Test of significance
Age/years	18-28	41(30.1)	10(50.0)	χ^2=4.15 p=0.13
	28-38	39(28.7)	6(30.0)	
	38-51	56(41.2)	4(20.0)	
Pubarche age/years	≥8 years	136(100.0)	11(55.0)	χ^2=64.95 p<0.001*
	<8 years	0(0.0)	9(45.0)	
BMI of patients (Kg/m2)		27.78±3.28	30.32±4.49	t=3.07 p=0.003*
Infertility		26(19.1)	12(60.0)	χ^2=15.82 p<0.001*
Family history of PCOS -ve +ve		 94(69.1) 42(30.9)	 1(5.0) 19(95.0)	 χ^2=30.1 p<0.001*
Family history of DM -ve +ve		 118(86.8) 18(13.2)	 4(20.0) 16(80.0)	 χ^2=45.59 P<0.001*

N: Number, P: p value for comparing between the groups, SD: Standard deviation, T-test: Student t-test, X^2: Chi square test

Table (2): Comparison between isolated PCOM & without isolated PCOM group regarding different ultrasound findings

		Without PCOM (n=136)	With PCOM (n=20)	significance
Ovarian follicle count Mean ± SD		5.80±1.25	13.2±0.89	t=25.57 p<0.001*
Follicular size	2-5 mm	36(26.5)	14(70.0)	χ^2=23.64 p<0.001*
	3-7 mm	22(16.2)	6(30.0)	
	5-10 mm	78(57.4)	0(0.0)	
Ovarian volume Mean ± SD		7.03±2.09	13.11±0.78	t=12.83 p<0.001*
Follicular distribution	Peripheral	1	20(100.0)	FET P<0.001*
	Random	135(93.3)	0(0.0)	
Stromal density	Normal	135(99.3)	0(0.0)	FET P<0.001*
	Central density	1(0.7)	20(100.0)	

χ^2: Chi-Square test, ET: Fischer exact test, MC: Monte Carlo test, * statistically significant (p<0.05), t: Student t test, *: Statistically significant at p < 0.05, P: p value for comparing between the groups, SD: Standard deviation

Table (3): Associators (Predictors) of isolated PCOM among studied cases (Multivariate analysis)

	β	p	AOR (95%CI)
Pubarche age/years	23.72	0.99	Undefined
Family history of obesity in patient's others	3.15	<0.001*	23.28(4.78-113.49)
BMI of patients (Kg/m^2)	1.09	0.02*	1.33(1.08-4.35)
Family history of PCOS	3.2	0.002*	6.78(1.34-9.96)
Family history of DM	4.1	0.003*	3.24(2.67-7.73)
Ovarian volume	0.72	0.002*	2.06(1.30-3.29)
Overall % predicted=87.2%			

CI: Confidence interval, AOR: Adjusted Odds ratio

4. Discussion

In the present study [figure 1] we found the prevalence of isolated polycystic ovarian morphology among women included in the present study was 12.8%. Previously the prevalence of which has been estimated as high as 33% in asymptomatic patients **[3] [4]**. Using the Rotterdam criteria we found a 12.2% incidence of PCO which is lower than the incidence of 19-33% in western population, and 32-45% in African populations **[5]**. That difference in the prevalence of PCOM among studies might be caused by limited number of the studied cases, and the difference among the studied population.

In the present study [Table 1] we found that prevalence of isolated PCOM decreased with increasing age. Previously it was demonstrated that the parameters used to document PCOM, both ovarian volume and follicle number, decrease with increasing age **[6]**. This can be explained as the age-related decline in female reproductive function due to the reduction of the ovarian follicle pool has been well established in normal women **[7]**.

In the present study [Table 1], premature pubarche was significantly increased in patients with isolated polycystic ovarian morphology. It is unclear whether the relationship of prematurepubarche and risk of PCOS is predicated on increased androgen production by the adrenal glands, a collective increase in circulating androgens (adrenal plus ovarian), or greater androgen bioactivity. A mechanism for the morphogenesis of the polycystic ovary has not yet been established, although a role for androgen excess on follicle growth and development has been suggested from ovarian morphology in hyperandrogenic women with congenital adrenal hyperplasia and androgen-producing ovarian tumours **[8]**. Other research found a link between in utero exposure to maternal obesity and gestational diabetes mellitus (GDM) and metabolic processing of the female offspring, presented as early onset of pubarche according to Associations Between Maternal Pregravid Obesity and Gestational Diabetes and the Timing of Pubarche in Daughters. Adrenarche was clinically diagnosed by pubarche, including the presence of pubic and axillary hair, apocrine body odor, and acne **[9].**

Excluding other pathogenic causes of androgen excess were critical. Such disorders involve late onset

or non-classical congenital adrenal hyperplasia (NCAH), three hereditary conditions including familial male-limited precocious puberty, androgen-producing tumors in the gonads or adrenal glands, and exogenous androgen exposure **[10]** So Premature adrenarche is a diagnosis of exclusion **[11].**

In the present study [Table 1], infertility was evident in 60% of patients with isolated PCOM. Previously it was reported that the prevalence of PCO generally is up to 34% of women attending fertility clinics **[12]**. This can be explained as polycystic ovarian morphology is characterized by a significantly enlarged cohort of early-growing and recruitable follicles. This excessive follicle number is linked to disturbances in folliculogenesis, which are thought to be the consequence of intraovarian hyperandrogenism **[13]**. The cohort of growing follicles during controlled ovarian hyperstimulation (COH) is frequently heterogeneous in size, with mature, intermediate, and small follicles. In addition, the number and quality of mature oocytes has been proposed as being poor **[14]**; Other evidence indicated that oocyte competency in PCOM patients could be compromised due to inadequate interaction between cumulus cells and oocytes **[15]**. Due to the distorted quality of the oocyte there is lack of fertilization capability of the ovum causing infertility **[16]**.

According to **Toselli S.** and his colleagues at 2014 BMI of females in Egypt in years 2011-2012 was 41.6% for obesity (BMI>30) **[17].** In the present study [Table 1], BMI was significantly increased among women with isolated PCOM, the percentage of obese women was significantly increased (65%) in isolated PCOM women than women without isolated PCOM (28.7%) also we found that BMI was a significant predictor for isolated PCOM. This increase in our results could be explained by the significant correlation between obesity and isolated PCOM and the high risk of developing the syndrome in this specific group of population. **Wijeyaratne and his colleagues** showed in his study that 69.2% of overweight/obese patients had polycystic ovary morphology **[18]**. **Esmaeilzadeh and his colleagues** in their study concluded that the overweight/obese women were at an increased risk of sonographic view of polycystic ovarian diseases **[19]**.

In the present study [Table 2], ovarian follicle count among patients with isolated PCOM was 13.2±0.89. In agreement with **Lujan and his colleagues** who suggested that a significantly higher threshold than 12 is needed to adequately discriminate between polycystic and normal ovaries **[20]**.

In our study [Table 2], 100% of patients with isolated polycytic ovaries showed typical peripheral follicle distribution in agreement with **Ali and his colleagues** showed that 93.3% of patients with polycytic ovaries showed typical peripheral follicle distribution. Historically, the peripheral distribution of follicles has been considered a hallmark of polycystic ovaries. The classic “string of pearls” appearance is embedded in the medical Imaging literature and remains highly remarked upon in radiological reports confirming the presence of polycystic ovarian morphology **[21]**.

In the present study [Table 2], ovarian volume was 13.11±0.78 in patients with isolated polycytic ovaries. Since 2003, both a lower threshold of 7 cm^3 and a higher threshold of 13 cm^3**[22]** have been proposed as being more appropriate thresholds for polycystic ovarian morphology.

In the present study [Table2], central ovarian density was found in 100% of patients with isolated polycystic ovaries. Stromal hypertrophy is characterized by an increased component of the ovarian central part, which seems to be rather hyperechoic. Stromal hypertrophy is highly specific of PCO. However, in the absence of a precise quantification, the stromal hypertrophy is a subjective sign. The estimation of stromal hyperechogenicity is also highly subjective, mainly because it depends on the settings of the ultrasound machine **[23]**. However, **Buckett and his colleagues** found no difference in the stromal echogenicity between women with PCOS and women with normal ovaries **[24]**. The conclusion is that the subjective impression of increased stromal echogenicity is due both to increased stromal volume alongside reduced echogenicity of the multiple follicles **[23]**.

It has been suggested that vascular endothelial growth factor (VEGF) has a part in the maintenance of perifollicular blood flow and recent evidence shows a positive correlation between VEGF and ovarian stromal blood flow velocities in women with ultrasound-diagnosed polycystic ovaries and PCOS. This increased vascularity, possibly mediated by VEGF, is, therefore, probably responsible for the formation of increased stroma and the ultimate phenotype associated with PCOS that is stromal echogenicity **[25]**.

Positive family history of PCOS and DM represented 95% and 80% (respectively) of isolated PCOM in our study [Table 1] which was found to be significant in these patients. Controversy, Lerchbaum E and her colleagues found in 2014 that positive family history of PCOS and DM were prevalent in 21.4 and 36.8% of PCOS women respectively [**26**]. This can be explained that our study was on a special category of PCOS (isolated PCOM) but the other study was on PCOS with all its phenotypes.

In 2018, Helena and her colleagues suggested that hyperandrogenism could be assessed by clinical examination relative to biochemical investigations

because of its low cost and valuability. In the other hand they suggested that biochemical investigations of hyperandrogenism was very useful for diagnosis of PCOS in adolescent and women demonstrating minimal to no features of clinical hyperandrogenism. So, biochemical investigations can be used for follow up of isolated PCOM cases [**27**]**.** In addition, There was a contraversary in diagnosis of PCOM with AMH because of the lack of standardization and appropriate cutoffs for the different assays available **[28],** even though another data suggested that such measurements, when accurately quantified, might predict ovarian follicle counts both in patients with PCOS and in healthy women **[29].**

Conclusion

Polycystic Ovarian Morphology in eumenorrheic women without hyperandrogenism (Isolated PCOM) is prevalent in 12.8% in MUH and more associated with obese, premature pubarche, young age and positive family history of Poly Cystic Ovarian Syndrome and Diabetes Milletus.

It's recommend that:

1) Strict Follow up study of isolated PCOM to assess the risk of developing PCOS.

2) Multicenteric studies are recommended for more investigations of isolated PCOM as a subtle PCOS.

References

1. Jeong JY, Kim MK, Lee I, Yun J, Won YB, Yun BH, Seo SK, Cho S, Choi YS, Lee BS. Polycystic ovarian morphology is associated with primary dysmenorrhea in young Korean women. Obstet Gynecol Sci. 2019;62(5):329-334.
2. Kenigsberg LE, Agarwal C, Sin S, et al. Clinical utility of magnetic resonance imaging and ultrasonography for diagnosis of polycystic ovary syndrome in adolescent girls. Fertil Steril 2015;104:1302e9. e4.
3. Kim YJ, Ku SY, Jee BC, Suh CS, Kim SH, Choi YM, Kim JG, Moon SY. A comparative study on the outcomes of in vitro fertilization between women with polycystic ovary syndrome and those with sonographic polycystic ovary-only in GnRH antagonist cycles. Arch Gynecol Obstet. 2010; 282(2):199-205.
4. March WA, Moore VM, Willson KJ, Phillips DIW, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010;25:544–51.
5. Ogueh O, Zini M, Williams S, Ighere J. African Journal of Reproductive Health March 2014; 18(1): 161.
6. Kim H-J, Adams JM, Gudmundsson JA, Arason G, Pau CT, Welt CK. Polycystic ovary morphology: age-based ultrasound criteria. Fertility and Sterility VOL. 2017;108(3):548-553.
7. Ford JH. (2017) Androgens Regulate Human Female Reproductive Ageing and Meiotic Fidelity. J Rep Endo Infert 2: 12.
8. Shayya R, Chang RJ. Reproductive endocrinology of adolescent polycystic ovary syndrome. The gynaecological and reproductive health problems of puberty and adolescence. 2010; 117 (2):150-155.
9. Voutilainen R, Jääskeläinen J. Premature adrenarche: etiology, clinical findings, and consequences. J Steroid Biochem Mol Biol. 2015;145:226-236. doi:10.1016/j. jsbmb. 2014.06.004.
10. Utriainen P, Laakso S, Liimatta J, Jääskeläinen J, Voutilainen R. Premature adrenarche – a common condition with variable presentation. Horm Res Paediatr. 2015;83:221-231.
11. Novello, L., & Speiser, P. W. (2018). *Premature Adrenarche. Pediatric Annals, 47(1), e7–e11.*
12. Wendy A. March, Melissa J. Whitrow, Michael J. Davies, Renae C. Fernandez & Vivienne M. Moore. Postnatal depression in a community-based study of women with polycystic ovary syndrome. Nordic Federation of Societies of Obstetrics and Gynecology, Acta Obstetricia et Gynecologica Scandinavica97(2018) 838–844.
13. Decanter C. Oocyte Quality in PCOS. Infertility in Women with Polycystic Ovary Syndrome 2017; pp 31-39.
14. Qiao J, Feng HL. Extra- and intra-ovarian factors in polycystic ovary syndrome: impact on oocyte maturation and embryo developmental competence. Hum Reprod Update 2010;17:17–33.
15. Kwon H, Choi DH, Bae JH, Kim JH, Kim YS. mRNA expression pattern of insulin-like growth factor components of granulosa cells and cumulus cells in women with and without polycystic ovary syndrome according to oocyte maturity. Fertil Steril 2010;94:2417–20.
16. B. Wirleitner J. Okhowat L. Vištejnová M. Králíčková M. Karlíková P. Vanderzwalmen F. Ectors L. Hradecký M. Schuff M. Murtinger. Relationship between follicular volume and oocyte competence, blastocyst development and live - birth rate: optimal follicle size for oocyte retrieval. Ultrasound Obstet Gynecol2018;51: 118 – 125.

17. Toselli S, Gualdi-Russo E, Boulos DN, Anwar WA, Lakhoua C, Jaouadi I, Khyatti M, Hemminki K. Prevalence of overweight and obesity in adults from North Africa. Eur J Public Health. 2014 Aug;24Suppl 1:31-9.
18. Wijeyaratne CN, Balen AH, Belchetz PE. Polycystic ovary syndrome and its relevance to women from south Asia. Ceylon Medical Journal. 2014;47(1):22-6.
19. Esmaeilzadeh S, Andarieh MG, Ghadimi R, Delavar MA. Body Mass Index and Gonadotropin Hormones (LH & FSH) Associate With Clinical Symptoms Among Women With Polycystic Ovary Syndrome Global Journal of Health Science; Vol. 2015;7(2).
20. Lujan E, Chizen R, Peppin K, Dhir A, Pierson A. Assessment of ultrasonographic features of polycystic ovaries is associated with modest levels of inter-observer agreement. J Ovarian Res 2009;2:6.
21. Ali HI, Elsadawy ME, Khater NH. Ultrasound assessment of polycystic ovaries: Ovarian volume and morphology; which is more accurate in making the diagnosis?! The Egyptian Journal of Radiology and Nuclear Medicine (2016) 47, 347–350.
22. Köşüş N1, Köşüş A, Turhan NÖ, Kamalak Z. Do threshold values of ovarian volume and follicle number for diagnosing polycystic ovarian syndrome in Turkish women differ from western countries? Eur J Obstet Gynecol Reprod Biol. 2011 Feb;154(2):177-81.
23. Dewailly D, Pigny P, Soudan B, Catteau-Jonard S, Decanter C, Poncelet E, Duhamel A. Reconciling the definitions of polycystic ovary syndrome: the ovarian follicle number and serum anti-Mullerian hormone concentrations aggregate with the markers of hyperandrogenism. J Clin Endocrinol Metab. 2010;95: 4399–405.
24. Buckett W.M., Bouzayen R., Watkin K.L., Tulandi T., Tan S.L. Ovarian stromal echogenicity in women with normal and polycystic ovaries *Hum Reprod* 1999; 14: 618-621.
25. Mayank D, Ujjaliya K, Kaushik A. Assessment of the Best Predictor for Diagnosis of Polycystic Ovarian Disease in Color Doppler Study of Ovarian Artery Sudeept. International Journal of Scientific Study. 2019; (6):12:154-162.
26. Lerchbaum E, Schwetz V, et al. and others. Influence of a positive family history of both type 2 diabetes and PCOS on metabolic and endocrine parameters in a large cohort of PCOS women: a clinical study. European Journal of Endocrinology. 2014;170, 727–739.
27. Helena J, Misso M, Costello M, Dokras A, Laven J, Moran L, Piltonen T and Norman R. International evidence based guideline for the assessment and management of polycystic ovary syndrome. Copyright Monash University, Melbourne Australia 2018.
28. Casadei L, Madrigale A, Puca F, Manicuti C, Emidi E, Piccione E, Dewailly D. The role of serum anti-Müllerian hormone (AMH) in the hormonal diagnosis of polycystic ovary syndrome. Gynecol Endocrinol. 2013 Jun; 29(6):545-50.
29. Christiansen SC, Eilertsen TB, Vanky E, Carlsen SM. Does AMH Reflect Follicle Number Similarly in Women with and without PCOS? *PLoS One*. 2016 Jan 22;11(1):e0146739.

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