

Sonographic evaluation of mullerian anomalies in women with polycystic ovaries

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ABSTRACT

Background: Mullerian anomalies are relatively common and contributing to the problems of infertility and poor pregnancy outcomes. But their molecular pathophysiology has been insufficiently studied. On the other hand, polycystic ovary syndrome (PCOS) is found in nearly 80% of women with hyperandrogenism and also in 8% - 25% of normal ones. It seems that anti-mullerian hormone (AMH) which inhibits the formation of the mullerian ducts in male increases in women with PCOS. Therefore, the aim of the study is whether PCOS is associated with mullerian anomalies. **Methods:** In this case-control study, 83 women with PCOS and 83 cases without PCOS were evaluated with transvaginal ultrasound (TVS) for the diagnosis of mullerian anomalies. The results of each group were compared with other groups. **Results:** In the PCOS patients, TVS revealed mullerian anomalies in the uterine cavity in 29 out of 83 women. Among 29 patients who had lesions in their uterine cavity, 27 cases had septate uterus and two had arcuate uterus. In the healthy women, TVS revealed 6 septate uterus and 4 arcuate uterus abnormality cases of the uterine cavity. There were significant correlation between polycystic ovary syndrome of the patients and the mullerian anomalies lesions (i.e. septate and arcuate uterus) which were seen in them. **Conclusion:** Mullerian anomalies were more common in women with PCOS and the most common anomaly was uterine septum. In fact, the present results revealed that it seemed a cause-effect relationship between the mullerian anomalies and PCO syndrome may in fact exist.

Keywords: Polycystic Ovaries Syndrome; Mullerian Anomalies; Trans-Vaginal Ultrasound; Septate Uterus; Arcuate Uterus

1. INTRODUCTION

Congenital abnormalities of the mullerian ducts are very common (7% - 10%) in the female and may be contributing to the problems such as infertility, recurrent pregnancy loss and poor pregnancy outcomes [1,2]. Also, these *congenital uterine* anomalies can raise the preterm labor, breech presentation and complications that may lead to interventions and treatments that will reduce *uterine* anomalies-related mortality. In addition, these abnormalities can produce the symptoms of dysmenorrhea and dyspareunia and even amenorrhea [1,2]. The molecular pathophysiology of these abnormalities has been insufficiently studied. However, the association with other somatic anomalies suggests genetic linkages [1].

Uterine anomalies can be organized into the following categories: uterus didelphys, unicornuate uterus, bicornuate uterus, septated uterus and arcuate uterus. In the past, full diagnosis required surgical intervention, first laparotomy and then, more recently, laparascopy. Today vaginal ultra sonography (TVS) especially three-ultrasound, sonohysterography and magnetic resonance imaging are highly accurate and surgical intervention is usually not necessary [2]. Trans-vaginal ultra sound has a high diagnostic value based on several studies [3-5]. The critical factors in determining which of the duct structures stabilize or regress are anti mullerian hormone (AMH) and testosterone that are secreted from the testes [5].

AMH is a member of the transforming growth factor- β family of glycoprotein differentiation factors. AMH is synthesized by sertoli cells of testes and is responsible

for the ipsilateral regression of the mullerian ducts [5].

In general, very small amount of AMH mRNA is present in the follicular cells of the ovary of the immature female and its production later by the granulosa cells leads to autocrine and paracrine actions in oocyte maturation and follicular development [2]. Indeed, AMH is produced by the granulosa cells of preantral and small antral follicles [6]. The serum level of AMH in women with polycystic ovary syndrome is 2 to 3 fold higher than in ovulatory women with normal appearing ovaries [7-10]. It's worth to note that, in overall, the higher level AMH in PCOS cases is not associated with hyper-androgenism [11].

Polycystic ovaries syndrome, typically, is exhibited with increased size and stromal volume of the ovaries and also increases the number of small follicles [2]. Also, the prevalence of polycystic ovaries is quite high among women with androgen excess. However, some of health subjects and even some of women using oral contraceptives also meet the ultrasonographic criteria for polycystic ovaries. PCOS is a functional disorder which in turn can be resulted in making chronic anovulation in the women caught up to it [12].

Trans-vaginal ultra sound is more accurate for detecting small follicles because of its high resolution [12]. Considering the fact that many women with polycystic ovaries syndrome are suffering from infertility problems and pregnancy outcomes are very important in these women, in this study we are going to evaluate the mullerian anomalies in women with PCOS and determine if there is an association between mullerian anomalies and polycystic ovaries.

2. METHOD AND MATERIAL

This is a case-control study that carried out in the obstetrics and gynecology ward of Imam Khomeini teaching hospitals in Ahvaz, Iran. This study was performed during February 2012 to February 2013. One hundred and sixty six women that were referred to these wards due to infertility (primary or secondary) or only pelvic pain or other gynecological complains were equally divided into PCOS and normal appearing ovaries groups. The patients were aged 18 - 45 years (mean 28.6 years). All patients were studied in the proliferative (follicular) phase.

The inclusion criteria were healthy women with 18 - 45 years old and absence of history of surgical correction for uterine anomalies and patient's agreement for participation in the study.

The presence of polycystic ovaries was determined with trans-vaginal ultrasound with MyLab™ 20 Plus ultrasound by the expert gynecologist in 2D-TVUS and all women in both group were evaluate for mullerian

anomalies. For doing this process the speculum was put in vaginal. Concomitantly, the distention was observed by transvaginal sonography and continued until the entire cavity was clearly visible. During sonohysterography the intrauterine space was evaluated and findings were recorded.

3. STATISTIC

All data are expressed as the means \pm SEM. Chi-square test and t-test were used for comparison the data of the PCOS group in versus the normal appearing ovaries groups. P-value less than 0.05 were considered as significant difference.

4. RESULTS

In polycystic ovaries syndrome group, the age range of women were between 18 and 42 years old with the average of 27.14 ± 4.65 and in control group the age range were between 20 and 45 years old with the average of 29.95 ± 6.13 . The age difference between two groups was significant statistically ($p = 0.001$, **Table 1**).

Also in PCOS group the mean BMI (body mass index) was 27.03 ± 4.65 and in non PCOS group was 25.95 ± 3.73 . Although the mean BMI of both group were in "overweight" category but the difference between two groups was significant statistically ($p = 0.044$, **Table 1**).

Both groups were not different significantly in the number of gravid and living child. However the history of abortion was higher in PCOS group (25.3% vs. 15.6%, **Table 1**).

All women were evaluated for two important symptoms of polycystic ovaries syndrome, which are oligomenorrhea and hirsutism. In PCOS group 73.5% and in non PCOS group 15.7% had oligomenorrhea that means in PCOS group oligomenorrhea was higher significantly than in non PCOS group ($p < 0.001$, **Table 1**).

Also in PCOS and non PCOS groups, hirsutism was seen in 54.2% and 12% of subjects respectively. This difference was statistically significant ($p < 0.001$, **Table 1**).

In our study mullerian anomalies were found in 29 women of PCOS group (34.9%) and 10 women of non PCOS group (12%), that means women with polycystic ovaries had a higher rate of uterine anomalies significantly than normal appearance ovaries group ($p = 0.001$, **Table 1**).

In case of kind of congenital mullerian malformation, it was found two types of mullerian anomalies included septated uterus and arcuate uterus. The septated uterus was detected in 23 women in PCOS group (27.7%) and 6 women in non PCOS group (7.2%). The difference was statistically significant ($p = 0.001$, **Table 1**). Also the arcuate uterus was found in 6 (7.2%) women with PCOS

Table 1. Baseline characteristics women who admitted to the department were comparable in the two groups.

	Groups		
	PCOS: mean \pm S.E. (%)	Non PCOS mean \pm S.E. (%)	P value
Age (years)	27.14 \pm 4.65	29.95 \pm 6.13	0.001
BMI (kg/m ²)	27.03 \pm 4.65	25.95 \pm 3.73	0.044
Gravidity	19 (57.6%)	16(48.5%)	0.97
Abortion	21 (25.3%)	13(15.6%)	0.001
Living child	62 (74.7%)	70(84.4%)	0.241
Oligomenorrhea	61 (73.5%)	13(15.7%)	0.001
Hirsutism	45 (54.2%)	10(12 %)	0.001
Mullerian anomalies	29 (34.9%)	10(12%)	0.001
Septate uterus	23 (27.7%)	6(7.2%)	0.001
Arcuate uterus	6 (7.2%)	4(4.8%)	0.514

and 4 (6.8%) women without PCOS but the difference wasn't reached to the point that became significant ($p = 0.514$, **Table 1**).

5. DISCUSSION

Mullerian anomalies are relatively common and are present in 5.5% of the unselected population, in 8% of infertile women and in 13.3% of subjects with history of miscarriages [3,13]. These anomalies are classified as uterus didelphys, unicornuate uterus, bicornuate uterus, septate uterus and arcuate uterus.

The studies about these anomalies are insufficient and also the studies about the relationship between mullerian anomalies and poly cystic ovaries are very limited [2]. Moreover, although some genetic studies implicate that the Hox and Wnt genes are essential regulators of uterine organogenesis and functional differentiation. However, Organogenesis, morphogenesis and functional differentiation of the uterus are complex and multifactorial process that are not well understood yet in the mammals [1].

In the present study, mullerian anomalies in the PCOS cases were more observed than normal appearance ovaries subjects. In keeping line with this study, Ugur *et al.* [14] was reported that the prevalence of ultrasound-defined polycystic ovaries in infertile patients with mullerian anomalies is more pronounceable when compared with women who had normal appearance ovaries and also uterine. Also they concluded that as PCOS are more prevalent in certain mullerian anomalies, an embryogenetic defect may also be involved in the etiopathogenesis of PCOS [14].

The results of the current study also show that septate uterus has a highest rate among all mullerian anomalies in the PCOS group and the difference of prevalence of

this anomaly between two groups was statistically significant. It's worth to note that the other anomalies were not seen.

Yilmaz *et al.* [15] through their retrospective clinical study was reported that a complete uterine septum and cervical duplication and a longitudinal vaginal septum and also the different degrees of endometriosis were more observed in polycystic ovaries syndrome. Therefore, they show that there is a probability of relationship between mullerian anomalies and PCOS subjects.

Also, Appelman *et al.* [16] during a case-control study conducted on 214 women with polycystic ovaries and normal ones reported that the cases with PCOS had a higher rate of mullerian anomalies than healthy women. In addition, in the polycystic ovaries syndrome subjects, the uterine anomalies were higher found in compared to non PCOS cases. Appelman *et al.* [16] was declared that there is an association between polycystic ovaries syndrome and high rate of mullerian anomalies. Although, this study in accordance of the present study however, the prevalence of these anomalies were lower when compare with the Appelman *et al.* study [16].

Therefore, with considering above information and also present study, it can be supposed that the congenital mullerian anomalies may create severe conditions in the uterus so that this problem may reduce the chance of embryo implantation. It will be possible that the close communication of anti-mullerian hormone (AMH) in one hand with mullerian anomalies and other hand with follicles in the ovarian parenchyma will cause increased the high risk of side effects of PCOS.

Also, it can be declared, with considering the result of this study and the above previous study, that it seems there is a relationship between mullerian anomalies and

PCOS.

In the current study, in the patients undergoing TVS examination, fatness has been associated with more observing of congenital mullerian malformations in the PCOS cases. Moreover, in the obese PCOS women, the rate of history abortion was high. Other studies have been able to find the side effects of obesity on the polycystic ovaries appearance outcome [17-19]. In contrast, other study has reported that the ovarian problems of females such as severe OHSS and PCO were not related to the BMI of subjects [20].

Also oligomenorrhea and hirsutism in the PCOS group were significantly higher which also could be due to hyperandrogenism in the subjects with polycystic ovaries appearance.

6. CONCLUSION

Based on the results of this study, women with the ultrasound *manifestation* of polycystic ovaries have a higher rate of mullerian anomalies and the septate uterus is the most common congenital uterus *anomalies* that are seen. Therefore, it seems there is a relationship between polycystic ovaries syndrome and mullerian anomalies especially septate uterus.

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