



## Original Research Article

## IVF/ICSI success rate in PCOD women in fresh IVF cycle

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## ABSTRACT

**Background:** Polycystic ovary syndrome (PCOS) is a common endocrine disorder of women, which occurs in 5% to 13% in women of reproductive age. It is one of the major reason of infertility in women. Therefore, the prediction of clinical pregnancy in women with PCOS is more challenging.

**Aim:** Our aim was to investigate the IVF/ICSI outcomes in PCOD patients.

**Material and Methods:** In the present retrospective study, total of 126 women in 133 fresh IVF cycles were involved, where 42 patient were PCOD and 84 patient were non-PCOD (other factor of infertility). All the patients' medical data of age, duration of infertility, factor of infertility, AMH hormone level, number of total retrieved oocyte, matured (M2) oocytes, day 3 cleaved embryos and biochemical pregnancy rates were used for this study and data were statistically analyzed by Student T-Test.

**Result:** After statistical analysis, significantly higher AMH level, higher number of total oocyte, mature oocyte and day3 cleaved embryos were observed. The biochemical pregnancy rate was also found to be higher in PCOD patient but it was not statistically significantly.

**Conclusion:** In the present study, number of oocytes and cleaved embryos were found to significantly higher in PCOD group but biochemical pregnancy was not significant.

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## 1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder of women, which occurs in 5% to 13%<sup>1,2</sup> in women of reproductive age. PCOD characterized by a heterogeneous presentation of hyperandrogenism (increased body hair or hirsutism, acne), ovulatory dysfunction (irregular or absent periods, abnormal or absent ovulation and infertility) and increased body weight/body mass index (BMI) at the reproductive age is often associated with infertility<sup>3</sup> and clinical and metabolic disorders.<sup>4</sup> The ovaries of women with PCOS contains multiple micro-cysts often arranged like a “string of pearls” immediately below the ovarian surface (capsule), interspersed by an overgrowth of ovarian connective tissue (stroma). PCOS has its unique properties such as increased antral follicle count, serum AMH (Anti-Mullerian hormone) and LH/FSH ratio. The

low FSH concentration combined with high LH probably shows a well-preserved ovarian reserve and is associated with high pregnancy rates in IVF/ICSI cycles.<sup>5</sup> Antral follicle count evaluates by ultrasonography and the AMH level considered a diagnostic or even prognostic marker of PCOS.<sup>6</sup> AMH is a dimeric glycoprotein of the transforming growth factor- $\beta$  (TGF- $\beta$ ) family produced in the ovary by granulosa cells of pre-antral and small antral follicles of less than 4 mm diameter. AMH is considered a useful marker of ovarian reserve, and even clinical outcome of IVF.<sup>7,8</sup> PCOS Patients greater oocyte production and are more likely to experience ovarian hyperstimulation syndrome (OHSS) and miscarriages. However, the rates of pregnancy are equivalent to those in patients with other causes of infertility.<sup>9–11</sup> The prediction of clinical pregnancy in PCOS is more challenging than non-PCOS women.<sup>12</sup> Many other studies have demonstrated that oocyte quality and embryo development may be affected by PCOS. However, it is still obscure whether these deleterious effects can

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induce developmental arrest of early embryos during IVF. Therefore, the present retrospective study has been designed to evaluate the ART outcomes in PCOS IVF Patients.

## 2. Materials and Methods

The present retrospective study were conducted on PCOD and non-PCOD IVF patients from January 2017 to December 2019. Before starting IVF treatment written informed consent were obtained. A total of 142 women were involved in 147 fresh IVF cycles, where 58 patients of PCOD and 84 Patients of non-PCOD (other infertility factor). Inclusion criteria: women with age of >22 and <46 years, exclusion criteria: patients with oocyte recipient in IVF cycle.

AMH test were measured by outsourced pathological investigation laboratory using Chemiluminescence method. All PCOS cases were diagnosed by Rotterdam criteria (2004) two out of three of the following criteria: oligo- or anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries). Polycystic ovary appearance was characterized as the presence of 12 or more follicles in each ovary, each measuring 2–9 mm in diameter, and/or increased ovarian volume (>10 ml) at transvaginal ultrasonography.<sup>13</sup>

All women underwent control ovarian stimulation with FSH and pituitary suppression with an agonist long protocol consisting of oral contraceptive pretreatment with lupride-4mg/4ml 20U & 10U. The ovarian stimulations were done by using recombinant follicle stimulating hormone Follisurge (rFSH) 150U and human menopausal gonadotropins (HMG). Ovarian response was monitored with serum E2 level and transvaginal ultrasonography. The dose of rFSH and HMG was individually adjusted based on the number and size of follicles and the estradiol level. The administration of hCG triggers was decided when at least 3 follicles reached >17mm diameter. Final maturation of follicles was done by intramuscular of hCG. After 36 h of hCG administration oocyte retrieval carried out under local anesthesia using Transvaginal USG–guided ovum pickup needle. Retrieved oocyte from both ovary maintained in culture media and cumulus cell were removed after exposure to HEPES-buffered medium with hyaluronidase by gently denuding pipette. Matured metaphase II (M2) oocytes were identified and in-vitro fertilized with husband sperm or donor sperm by Intra Cytoplasmic Sperm injection (ICSI). Day 3 fertilized embryos were assessed and good quality 2-3 embryos were transferred in uterus. Luteal phase support progesterone administration was started on the day of oocyte pick-up and continuing daily until the pregnancy test. After 14 days of embryos transfer  $\beta$ -hCG test for biochemical pregnancy were performed. The  $\beta$ -hCG value more than 100mIU/mL considered as positive biochemical pregnancy.

The IVF patient's medical record data were statistical analyzed by using Student T-Test (online available Graph Pad Prism software). The P values of <0.05 were considered statistically significant. Values were expressed as mean  $\pm$  SD, unless stated otherwise (Table 1).

## 3. Results

In the present retrospective study 58 PCOD patients in 61 cycles and 84 non-PCOD patients (other factor of infertility) in 86 cycles were included. The PCOD group involved 28 patients of only PCOD factor and 14 patient of both factors (PCOD and male factor), whereas the Non- PCOD group had involved 27 patient of female factor other than PCOD, 21 patients of both factors, 25pt of male factor and 11pt of unexplained infertility. Table 1 shows the patient's characteristics of PCOS and Non-PCOD group. The results showed that the study groups were comparable in terms of female age, duration of infertility, AMH level, retrieved oocyte, mature oocyte, fertilized good quality cleaved embryos, endometrium thickness and positive biochemical pregnancy rate (%) after 14 days of embryo transfer.

After comparative analysis in between PCOD and non-PCOD group, there was no significant differences were found with patient's age ( $30.89 \pm 3.64$  vs  $30.66 \pm 4.02$ ) duration of infertility ( $6.84 \pm 3.57$  vs  $6.97 \pm 3.47$ ) and endometrium thickness ( $9.66 \pm 1.83$  vs  $9.49 \pm 1.40$ ), but significant difference (<0.05) were found for AMH level ( $7.78 \pm 3.06$  vs  $2.46 \pm 1.05$  ng/mL), total retrieved oocytes ( $13.00 \pm 5.51$  vs  $9.55 \pm 5.02$ ), mature oocytes ( $10.75 \pm 4.34$  vs  $7.76 \pm 4.24$ ) and good quality day 3 cleaved embryos ( $7.15 \pm 3.37$  vs  $5.39 \pm 2.96$ ) respectively.

The significance of embryos transferred cycles were compared by Z Score Calculator online available software (<https://www.socscistatistics.com/tests/ztest/default2.aspx>)<sup>14</sup> and found to be significantly less (<0.05) in PCOD group as compare to Non- PCOD group (81.96% vs 94.14%), whereas canceled cycles were found to be higher in PCOD group as compare to Non-PCOD group (18.03% vs 5.81%). The  $\beta$ -hCG biochemical pregnancy after fourteen days of embryo transfer was found to be higher in PCOD group (58% vs 55.55%) as compare to non- PCOD group, but it was not statistically significant.

### 3.1. Comparison between PCOD groups

The PCOD patients again categorized in two groups as for AMH level, groups 1 of PCOD patients having  $\leq 6$ ng/mL AMH level and group 2 having more than 6 ng/mL AMH. The comparative analysis of total oocyte, mature oocyte and good quality cleaved embryos were significantly less in group1 as compare to group 2 however, biochemical pregnancy rate were found to be higher but it was not statistically significant (Table 2).

**Table 1:** Analysis of PCOD and Non- PCOD characteristics

	PCOD(N=58 )	Non-PCOD (N=84)	P Value (Significance)
Male Factor	-	25(30%)	-
Female factor	39(67.2%) (Only PCOD)	27 (32%) (other than PCOD)	-
Both factor	32.7% (19)	21(25%)	-
Unexplained infertility	-	11(13%)	-
Age	30.89±3.64	30.66 ±4.02	0.732 (NS)
Duration of infertility	6.84± 3.57	6.97± 3.47	0.829 (NS)
AMH level	7.78± 3.06	2.46± 1.05	0.0001
Retrieved oocytes	13.00±5.51 (793)	9.55±5.02 (821)	0.0001
Matured oocytes	10.75 ± 4.34 (656)	7.76± 4.24 (667)	0.0001
Fertilized good quality cleaved embryos	7.15 ±3.37 (436)	5.39± 2.96(464)	0.001
Endometrium thickness	9.66± 1.83	9.49±1.40	0.549(NS)
Total cycle	61	86	-
Total Embryo transfer	50 (81.96%)	81(94.18%)	0.0195
Embryo transfer cancel cycle	11(18.03%)	5(5.81%)	0.0174
Positive Biochemical pregnancy rate (%)	29(58.00%)	45(55.55%)	0.7686 (NS)

Values are < 0.05 significantly different

**Table 2:** Analysis of Group 1 and Group 2 PCOD Patients

	Groups 1(AMH ≤6)	Groups 2 (AMH > 6)	P Value
Number of cycle	22	17	-
Age	31.59±3.80	29.24±3.09	0.045
Duration of infertility	7.00±4.32	5.56±2.12	0.215
AMH level (ng/mL)	5.37±0.92	10.31±2.12	0.0001
Total oocyte	226 (10.27±4.45)	263 (15.47±6.40)	0.004
Mature oocyte	196 (8.91±3.75)	209 (12.29±5.13)	0.022
Day3 cleaved Embryos	126 (5.73±2.29)	150 (9±3.81)	0.003
Endometrium thickness (mm)	10±2.17	9.39±1.62	0.408
Embryo transfer Cancel	2	5	0.101
Biochemical pregnancy Positive	12 (55%)	8 (47%)	0.645

Values are < 0.05 significantly different

#### 4. Discussion

Many factors such as tube blockage, endometriosis, fibroids, poor ovarian reserve etc. are mainly responsible for infertility but PCOD is one of major factor in women. Many studies have been conducted to evaluate the IVF/ICSI outcome in PCOD and non-PCOD patient<sup>11,15,16</sup> but all of them reported higher or lower success rate. Swanton et al<sup>11</sup> found that significantly increased number of retrieved oocyte and decreased rate of fertilization rate in the PCOD group as compare to non-PCOD group in first IVF or ICSI cycle however, they did not found any significance differences in clinical pregnancy rates.

In the present study significantly higher (<0.05) AMH level were observed in PCOD patient as compare to non-PCOD. This finding is consistent with studies reported by Skalba et al<sup>17</sup> and Wiweko et al<sup>18</sup> who both found significant higher AMH level in PCO patient. This may be due to increased synthesis and secretion of AMH by polycystic ovaries. Elevated serum AMH levels in

PCOS patients may also be caused by disturbances in folliculogenesis, resulting in the accumulation of excessive pre-antral and small antral follicles the high levels of follicles they have in the early stage of development.<sup>19</sup> Cessation of antral follicle development toward the dominant follicle is due to suppression of aromatase activity by AMH and by lower follicle sensitivity to FSH.<sup>20,21</sup> The meaning that patients with higher AMH levels ( $\geq 4.45$  ng/ml) have higher possibility to suffer from PCOS compared to patients with low AMH. Pellat et al<sup>22</sup> also reported that AMH production increases approximately 75 times higher in each polycystic ovarian granulosa cell.

The average number of retrieved oocyte and matured oocyte were found to be significantly ( $P < 0.05$ ) higher in PCOD group as compare to non- PCOD. Similar to our study Swanton et al.<sup>11</sup> found that significantly higher number of retrieved oocyte in PCO group in IVF or ICSI cycle. Mahajan et al<sup>23</sup> also found that the mean number of total oocytes retrieved in PCOD ( $23.03 \pm 9.9$ )

were significantly higher as compare to control group ( $10.39 \pm 6.03$ ) and mean number of matured oocytes were significantly higher ( $P < 0.05$ ) in PCOD ( $18.51 \pm 8.99$ ) than the controls ( $8.3 \pm 4.78$ ). This higher number of total oocyte retrieval and matured oocyte is probably because the AMH level in patients with PCOS is not only related to increase in the follicle pool but also increase in the production per follicle.<sup>24,25</sup> Many authors have been also reported increased level of the AMH leads to a greater number of oocytes retrieval in PCOS women.<sup>26–28</sup>

In our study fertilized good quality embryos were found to be significantly ( $P < 0.05$ ) higher in PCOD group as compare to non-PCOD. Similar to our study Heijnen et al<sup>9</sup> and Yin et al<sup>29</sup> found significantly higher fertilization rate and cleavage rate in PCOS patients in ICSI cycles. Tal et al.<sup>15</sup> also reported that PCOS women had significantly more good quality embryos. In contrast some study have demonstrated that oocyte quality and embryo development may be affected by PCOS.<sup>30</sup> However, it is still unclear whether these deleterious effects can induce developmental arrest of early embryos during IVF. Many authors reported that PCOS decreased fertilization rate and even fertilization failure.<sup>31–33</sup> The most of studies had been reported decreased fertilization in IVF cycle not in ICSI cycle. But Hwang et al<sup>34</sup> shown that decreased fertilization rate in PCOS may be due to abnormalities in zona pellucida of oocyte IVF cycle but ICSI could avert these abnormalities and increase fertilization rate.

The cycle cancellation rate in PCOD patient was found to be significantly higher in our study Likewise, Heijnen et al<sup>9</sup> and Kodama et al<sup>35</sup> also found a significantly increased cancellation rate in PCOS as compared to non PCOD (12.8% vs 4.1%) and (6% vs 1%) respectively. PCOS considered higher incidence of OHSS due to presence of polycystic ovaries.<sup>36,37</sup> The increased risk of OHSS is associated with an increased expression of vascular endothelial growth factor (VEGF) mRNA within the hypertrophic stroma of polycystic ovaries.<sup>38</sup>

The biochemical pregnancy rate of our study was found to be higher in PCOD group as compared to non-PCOD, this higher rate of pregnancy may be due availability of more oocyte but this differences was not found to be significant. Tal et al<sup>15</sup> and Esinler et al<sup>39</sup> found significantly higher success rate in PCOD patients compared to other factor of infertility (66% vs 44%).<sup>39</sup> Rocaa et al<sup>40</sup> reported that PCOS women with AMH level  $\leq 5$  ng/ml had significantly ( $P > 0.05$ ) higher likelihood of pregnancy compare to women without PCOS (53% vs 38%). These studies supported to our study that PCOD patients had more chance of IVF success than many other factors of infertility. However, Xi et al<sup>16</sup> reported lower clinical pregnancy rate in PCOS women. In our study between the PCOD groups it was found that the AMH level of group 2 ( $> 6$  ng/mL) had significantly higher number of retrieved oocytes and cleaved embryos. But, biochemical pregnancy rate was lower in group 2, although

it was not statistically significant with group 1 ( $AMH \leq 6$ ). Similarly Rocaa et al<sup>40</sup> found that, PCOS women with higher AMH levels ( $> 5$  ng/ml) had higher average number of total oocytes, but lower possibility of pregnancy were observed. They also concluded that AMH levels  $> 5$  may have a negative impact on IVF success in women with PCOS. So it is our recommendation that PCOD women with high AMH level, who got higher number of retrieved oocyte and cleaved embryos, for such type of patients freeze all strategy should be opt. So that freezed embryo can be transfer in frozen cycle that may be improve the IVF Success rate.

## 5. Conclusion

In conclusion, the present study significantly higher number of oocytes and good quality cleaved embryos were observed in PCOD group. However, the biochemical pregnancy rate was higher in PCOD group but it was not significant. The comparison between PCOD group it was found that the AMH level of more than 6 ng/mL had significantly higher number of oocytes and good quality cleaved embryos but lower biochemical pregnancy rate were found although it was not statistically significant.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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