Original Article

Effect of Body Mass Index on the Biochemical Outcome after Fresh Embryo Transfer in Women with and without Polycystic Ovary Syndrome (PCOS)

[1]Surleen Kaur, [2]Irsad Ahamad, [3]M. Gouri Devi, [4]Rita Singh

[1,2,4]Division of Molecular Endocrinology and Reproduction, Department of Zoology, University of Delhi, Delhi, India

[2]IVF Department, Gouri Hospital, Ridge IVF Pvt. Ltd., Delhi, India

Abstract

Aim: To evaluate the influence of body mass index (BMI) on the biochemical outcome of fresh embryo transfer in women with and without polycystic ovary syndrome (PCOS).

Methodology: A retrospective study on biochemical outcome after fresh embryo transfer was done for a total of 230 patients with a diagnosis of PCOS and 556 non-PCOS women who were undergoing IVF due to male infertility or tubal factor. PCOS as well as non-PCOS women were categorised based on their BMI. Total oocytes retrieved, average oocytes, mature oocytes, average mature oocytes, mature oocyte rate, fertilization Rate, total ETs and positive biochemical outcome were compared among BMI categories.

Result: Among the 230 patients with a diagnosis of PCOS, 62 had BMI ≤ 24 and 168 had BMI ≥ 25. Among the 556 non-PCOS women, 220 had BMI ≤ 24 and 336 had BMI ≥ 25. The age of women with PCOS and without PCOS in all the groups was not significantly different. The average number of oocyte retrieved and matured were higher in PCOS group, however, the rate of fertilization was lower in PCOS group than in non-PCOS group and was independent of BMI. The percentage of negative biochemical outcome was comparable between the PCOS and non-PCOS group with BMI≤ 24. However, percentage of the positive biochemical outcome was significant less in PCOS women than the non-PCOS women with BMI ≥ 25 (25.57% vs. 42.25%).

Conclusion: The present study show an increase in percentage of negative biochemical outcome in women with PCOS with BMI ≥ 25 after fresh embryo transfer than in the non-PCOS group. However, the rate of oocyte maturation was not significantly different.

Keywords: Polycystic ovary syndrome, infertility, pregnancy loss, assisted reproductive technology, embryo transfer, oocyte matu

INTRODUCTION

Polycystic ovary syndrome (PCOS), the most common endocrine disorder, has negative impact on the child bearing potential of these women. Most women with PCOS (73% of the cases) have anovulatory infertility [1]. Women with PCOS have higher risk of adverse pregnancy outcome [1-2]. Assisted reproductive technology (ART) has revolutionised infertility treatment for the management of subfertility in PCOS women, helping many couples who previously suffered from mental stress due to problems in having successful pregnancy [3-4]. One of the several applications of *in vitro* fertilization (IVF) techniques for increasing the chances of conception in women with PCOS is the use of fresh and frozen embryo transfer. This is important for women with PCOS who had failed pregnancy after ovarian stimulation or who do not ovulate in response to repeated ovarian stimulation or have tubal or male factor infertility [3, 5]. Women with PCOS have higher number of oocytes retrieved during each IVF cycle with similar or lower fertilization rate, however, they have lower rate of pregnancy than healthy women [2, 6].

The response to gonadotropin therapy and the success of ART in both PCOS and non-PCOS women is impacted by age, obesity, and ovarian reserve [5-7]. The ovarian hyperstimulation (COH) protocol to be used in women with

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***Address for correspondence:** Rita Singh, Division of Molecular Endocrinology and Reproduction, Department of Zoology, University of Delhi, Delhi, India. Email: ritas@zoology.du.ac.in

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PCOS depends on several factors in addition to the inherent hormonal imbalance. PCOS women suffer a higher risk of ovarian hyperstimulation syndrome (OHSS) than non-PCOS while undergoing IVF treatment. Choosing an optimal controlled protocol for COH is important and therefore, women with PCOS would require optimal combination of gonadotropins and the ovulatory dose of human chorionic gonadotropin (hCG) injection or the gonadotropin-releasing hormone agonist (GnRH-a) trigger to get high-quality follicles [5-7]. Long protocol is one of the common regimens for ovarian stimulation in women with PCOS. Previous studies from India and abroad have shown that 35-65% of women with PCOS are obese and have insulin resistance [8]. Furthermore, the prevalence of obesity has been increasing all over the world especially in PCOS women. For Indian women, BMI ≤ 23 is taken as normal [9]. Obesity is a significant factor that may influence the outcomes of IVF after fresh embryo transfer in these women.

Several international studies have reported data on the relationships between PCOS, BMI, and the outcomes of IVF/intracytoplasmic sperm injection (ICSI). The success rate of IVF gets impacted by high BMI in women with or without PCOS [11-13]. A few retrospective studies reported the adverse effect of abnormal BMI on the ovarian response and there was increased rate of miscarriage even in non-PCOS women. To date, there have been few studies on the association of BMI and IVF outcomes after fresh embryo transfer in Indian women with PCOS. Therefore, we designed this retrospective study to evaluate the association of BMI on biochemical outcome after fresh embryo transfer [14-15]. We examined the positive biochemical outcome after fresh embryo transfer in women with and without PCOS undergoing IVF therapy and ICSI.

MATERIALS AND METHODS

STUDY POPULATION

Following the approval by institutional ethics committees, women with PCOS who were undergoing IVF from 2014 to 2020 were selected based on BMI criteria. Polycystic ovary syndrome was diagnosed as per the Rotterdam criteria of 2003, women had menstrual disturbance and hyperandrogenism or polycystic ovary on ultrasonography, and exclusion of other causes of hyperandrogenism and ovulation dysfunction as described earlier [8]. The details of the subjects contributing to this study are given in Table 1 and Table 2. The inclusion and exclusion criteria for the subjects were as in our earlier studies [8].

STUDY PROCEDURE

A retrospective study on biochemical outcome after fresh embryo transfer was done for a total of 230 patients with a diagnosis of PCOS and 556 non-PCOS women who were undergoing IVF/ICSI. As far as biochemical outcome after assisted conception is concerned, this end point was reported in the medical records of most of the PCOS patients. PCOS as well as non-PCOS women were categorised based on their BMI. A GnRH Agonist/antagonist protocol was used for ovarian stimulation in all patients. Patients who were assigned to fresh embryo transfer underwent a transfer of up to two day-3 embryos. Luteal phase support with progesterone began on the day of oocyte retrieval and continued to the day of pregnancy test. Total oocytes retrieved, average oocytes, mature oocytes, average mature oocytes, mature oocyte rate, fertilization Rate, total ETs and positive biochemical outcome were compared among BMI categories. Different parameters were calculated as per formula: biochemical outcome or Pregnancy Rate (PR) = Number of βhCG positive pregnancies/Total number of transfers; Fertilization Rate for ICSI (FR) = Total number of normal fertilized zygotes on Day1/Total number of MIIs injected; Fertilization Rate for IVF (FR) = Total number of normal fertilized zygotes on Day1/Total number of MIIs inseminated.

STATISTICAL ANALYSIS

Continuous variables were represented as mean ± SD for normally distributed variables; differences in these variables were compared by Student t test or Mann-Whitney nonparametric tests. A two-sided P value of <.05 was considered to be statistically significant in all tests. All analyses were performed with the use of R software.

RESULTS

Baseline characteristics of study subjects (women with and without PCOS) are listed in Table 1 and 2 based on 2 categories of BMI. Among the 230 patients with a diagnosis of PCOS, 62 had BMI ≤ 24 and 168 had BMI ≥ 25 (Table 1). Among the 556 non-PCOS women, 220 had BMI ≤ 24 and 336 had BMI ≥ 25 (Table 2). The age and BMI of women with PCOS and without PCOS in BMI ≤ 24 groups were not significantly different (Age, P=0.901; BMI, P=0.857). The age and BMI of women with PCOS and without PCOS in BMI ≥ 25 group was not significantly different (Age, P=0.131; BMI, P=0.06). The two groups based on BMI have significant difference in BMI (P≤0.01, Table 1 and Table 2).

Table 1: Basic characteristics of women with and without PCOS with BMI ≤ 24

Cases BMI ≤ 24	Total Cases	AGE[#]	BMI[$]
PCOS	62	34.48±4.26	21.58±1.74
Non PCOS	220	34.56±4.40	21.63±1.62

[#]P=0.901; [$]P=0.857

Table 2: Basic Characteristics of women with and without PCOS with BMI ≥ 25

Cases BMI ≥ 25	Total Cases	AGE[#]	BMI[$]
PCOS	168	34.73±4.2	28.47±4.43
Non PCOS	336	34.11±4.48	27.70±3.77

[#] P=0.131; [$]P=0.06

Oocyte retrieval the total oocyte retrieved from women with PCOS were more than the non-PCOS group. The average number of oocyte retrieved (19.96±8.55) was significantly higher in PCOS group than non-PCOS group (9.05±5.53,

P<0.01), in normal BMI group (BMI ≤ 24, Table 3). The average number of oocyte retrieved (19.50±9.22) was also significantly higher in PCOS women than non-PCOS women (8.71±5.51, P<0.01) in higher BMI group (BMI ≥ 25, Table 4).

Rate of oocyte maturation the average number of matured oocytes (16.13±7.26) was significantly higher in women with PCOS than without PCOS (6.90±4.45, P<0.01) in normal BMI group (BMI ≤ 24, Table 3). The average number of matured oocyte (15.56±7.79) was significantly higher in women with PCOS than without PCOS (6.71±4.30, P<0.01), in higher BMI group (BMI ≥ 25, Table 4).

Rate of fertilization the rate of fertilization was significantly lower in PCOS group than in non-PCOS group and was independent of BMI (Table 3 and Table 4, P<0.05).

Positive biochemical outcome the positive biochemical outcome (%) was comparable between the PCOS and non-PCOS group with BMI≤24 (Table 3). However, positive biochemical outcome was significantly lower in PCOS women with BMI ≥ 25 than the non-PCOS group in this BMI category (28.57% vs. 41.25%, P<0.01, Table 4). Positive biochemical outcome was significantly lower in PCOS women with BMI ≥ 25 than PCOS women with BMI ≤ 24 (28.57% vs. 58.33%, P<0.01, Table 3 and Table 4). Women without PCOS but with BMI ≥ 25 had significantly less percentage positive biochemical outcome (41.25 % vs. 60.0%, P<0.01, Table 3 and Table 4).

Table 3: The number of oocyte retrieved, mature oocyte, fertilization rate and embryo transfer in women with and without PCOS with BMI ≤24

Cases BMI ≤ 23	Oocytes Retrieved	Average Oocytes Retrieved	Mature Oocytes	Average Mature Oocytes	Mature Oocyte rate (%)	Total Fertilization	Fertilization Rate (%)	Total ETs (%)	Positive Biochemical Outcome (%)
PCOS	1238	19.96±8.55*	1000	16.13±7.26*	80.78	774	77.40*	12 (1.55*)	58.33
Non-PCOS	1992	9.05±5.53	1518	6.9±4.45	76.20	1249	82.27	90 (7.20)	60.0

*P<0.01

Table 4: The number of oocyte retrieved, mature oocyte, fertilization rate and embryo transfer in women with and without PCOS with BMI ≥25

Cases BMI ≥ 25	Oocytes Retrieved	Average Oocytes Retrieved	Mature Oocytes	Average Mature Oocytes	Mature Oocyte rate (%)	Total Fertilization	Fertilization Rate (%)	Total ETs (%)	Positive Biochemical Outcome (%)
PCOS	3276	19.5±9.22*	2615	15.56±7.79*	79.82	2117	80.91	28 (1.32*)	28.57*
Non-PCOS	2928	8.71±5.51	2255	6.71±4.30	77.02	1881	83.30	143 (7.3)	41.25*

*P<0.01

DISCUSSION

The findings of the present study show that BMI has an impact on the success of fresh embryo transfer especially in PCOS women. BMI higher than the normal range for the Indian women (BMI ≥ 25) was associated with lower biochemical outcome after fresh embryo transfer than the PCOS women with normal BMI, non-PCOS women with either normal or higher range of BMI. Although, the number of oocytes retrieved was higher in PCOS, the fertilization rate was lower than non-PCOS women in both the categories of BMI. Previous studies have reported that an optimal BMI is required for reproductive function in women with or without PCOS. There is an increased risk of anovulatory infertility in overweight/obese women and this may be due to the alterations in endocrine, adipokine, and metabolic milieu of follicles which ultimately is essential for follicle growth, embryo development, and implantation [16-17]. PCOS women undergoing IVF with fresh or frozen embryo transfer have an increased risk of implantation failure and chances of having large-for-gestational age birthweight of the infant [18]. Insulin resistance and preconception glucose intolerance in women with PCOS adversely impact the success of Pregnancy [19-20].

PCOS and maternal obesity affect the size of the oocyte and the oocytes may be smaller in size than the oocytes retrieved from healthy women [11]. Previous studies have shown that obesity impacts the blastocyst formation rate negatively [12]. The most crucial step in IVF is the quality assessment of the oocytes and embryos. An accurate and non-invasive strategy for quality assessment of fresh embryos before transfer remains a major challenge for the success of conception. The initial rise in βhCG indicates the positive biochemical outcome however, it may end up in biochemical pregnancy where the hCG levels go down slowly and there is no conception [21-22]. There are reports which show that the female obesity increases the risk of miscarriage of euploid embryo. Some studies have shown that the pregnancy rates are significantly affected by abnormally high BMI [16-19], whereas certain other studies show no such effect on clinical pregnancy rate [23]. However, the outcome of *in vitro* fertilization may be adverse in obese women with good quality embryo [24]. This present study clearly indicates an association of higher BMI and negative biochemical outcome of fresh embryo transfer in women with PCOS more than the non-PCOS women with BMI ≥ 25.

CONCLUSION

In women with or without PCOS with BMI ≥ 25, fresh embryo transfer resulted in an increased percentage of negative biochemical outcome. The average number of oocyte retrieved and matured were higher in PCOS group,

however, the rate of fertilization was significantly lower in PCOS group than in non-PCOS group in a group with BMI≤24, however, the rate of oocyte maturation was not significantly different in these two groups**.** Women with BMI ≤24. PCOS and non-PCOS, had no difference in the percentage of negative biochemical outcome.

Limitations the study has its own limitations where several women with PCOS withdrew from study and the biochemical outcome was taken as an end point. The protocols used for ovarian stimulation had slight variation in gonadotropin doses dependent on the phenotype of the PCOS i.e. with or without insulin resistance or obesity. This is an observational study and the effect BMI reduction on the biochemical outcome of fresh embryo transfer could not be studied. The selection bias may be there due to the age limit and there is a possibility that one or more confounding factors, rather than BMI itself, were responsible for the observed differences in outcome.

Future scope a prospective study is required to find an association the live births and BMI after fresh embryo transfer in PCOS women and for better prediction of the success of fresh embryo transfer after reduction of body weight.

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ETHICAL CLEARANCE

The study had conducted after getting appropriate consent from the patients and the study was reviewed and approved by Ethical Board of Gouri hospital, Ridge IVF and University of Delhi. The patients/participants provided their informed consent to participate in this study.

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Conflicts of interest Nil.

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