International Journal Dental and Medical Sciences Research
Volume 5, Issue 2, Mar - Apr 2023 pp 08-14 www.ijdmsrjournal.com ISSN: 2582-6018

Assessment of Embryo Quality in Polycystic Ovary Syndrome: Acase-Controlstudy.

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Date of Submission: 01-03-2023 Date of Acceptance: 08-03-2023

I. INTRODUCTION:

Polycystic ovarian syndrome (PCOS) is a hormonal disorder common among women of reproductive age. According to Rotterdam criteria, a woman has to have at least two of the three characteristics: clinical and/or biochemical hyperandrogenism,ovarian dysfunction, and Polycystic Ovary Morphology (PCOM)to be diagnosed as having PCOS [1]. PCOM is defined as either an ovary with 12 or more follicles, ranging in size from 2mm to 10mm, in a single plane or an ovarian volume of more than 10cc without a dominant follicle [2,3].Polycystic ovarian morphology (PCOM) and poly cystic ovary syndrome(PCOS)are very common findings in the sub-fertile population. Up to 18–25% of infertile women meet the diagnosis criteria for PCOS and the prevalence of PCO Mina symptomatic patients has been estimated to be as high as 33%[4-6].

The presence of an excessive number of follicles in PCOM is a result of disturbances infolliculogenesis which are thought to be the consequence of intra-ovarian hyperandrogenismand hyperinsulinemia [7,8].In a PCOS cases most of the oocytes are not mature, which lead to a decrease in pregnancy rates and an increase in abortion [6]. The oocyte quality is defined by factors such as ability to undergo meiotic maturation, fertilization, proper embryonic development and successful pregnancy [7]. These qualities are obtained thorough the follicular growth by the interaction of theca and granulose cells (GCs) [8]. Since follicular growth is disrupted in PCOS patients, especially during Controlled Ovarian Hyper stimulation (COH), fewer good embryos in ART cycles are a widespread problem. Various factors can affect the quality of the embryo. Therefore, we decided to evaluate the quality of embryos in PCOS patients undergoing ART cycles at our institute.

II. MATERIALS&METHODS:

Study Design:

This retrospective case-control study was performed on PCOS and non-PCOS patients referred to Institute of reproductive medicine (IRM), Madras Medical Mission Hospital. The inclusion criteria were patients with confirmed diagnosis of polycystic ovarian syndrome in PCOS group (case group) and in the non-PCOS group the patients with a tubal factor or male factor were included (control group). Exclusion criteria were patients with high Follicle Stimulating Hormone (FSH), of more than 12 IU/mL or a history of ovarian surgery, ovarian tumor, systemic diseases, endometriosis, and patients more than 38 years of age. A total of 169 patient were included in the study and they were divided into PCOS group (58 cases) and non- PCOS group (111 cases). The study was confirmed by the Ethical Committee of IRM Madras Medical Mission Hospital.

ASSESMENT OF EMBRYO QUALITY

Embryos are graded to choose them for transfer, embryos with better grades have higherchanceof implantation. Grading was done on days 2 and day 3 embryos and embryo transfer was done on day 3.

The Istanbul workshop consensusfor cleavage-stage embryos was used to grade the embryos[16]. The embryos were graded depending on the following variable.

Cell number

Embryos that have cleaved more slowly than the expected rate have a reduced implantation potential, and that embryos that have cleaved faster than the expected rate are likely to be abnormal and have a reduced implantation potential. The current expected observation for embryo development is 4 cells on Day 2 and 8 cells on Day 3[16].

Fragmentation

A fragment was defined as an extracellular membrane-bound cytoplasmic structure that is<45µm on day 2 embryo and<40 µm diameter in a Day-3 embryo. The relative degrees of fragmentation were defined as: mild (<10%); moderate (10–25%) and severe (>25%). The percent values are based on the cell equivalents [16].

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Multinucleation

It is defined as the presence of more than one nucleus in a blastomere and includesmicronuclei. Multinucleation is associated with a decreased implantation potential, and that multinucleated embryos are associated with an increased level of chromosome abnormality and, therefore, increased risk of spontaneous abortion [16].

Cell size

In embryos until the 8 celled stage the blastomeres should be of equal size. For all other cell stages, one would expect a size difference in the cells.

The grading scheme for cell size is binaryi.e., cell size is stage appropriate or not stage appropriate [16].

It was the consensus opinion that an optimal Day-2 embryo (44 ± 1 h post-insemination) would have 4 equally sized mononucleated blastomeres in a three-dimensional tetrahedral arrangement, with <10% fragmentation[16]. It was the consensus opinion that an optimal Day-3 embryo (68 ± 1 h post-insemination) would have 8 equally sized mononucleated blastomeres, with <10% fragmentation. The consensus scoring system for cleavage-stage embryos is presented in Table I[16]. The scoring format would be cell number, grade,and reason for the grade.

Table 1

Grade	Rating	Description
A	Good	• <10% fragmentation
		• Stage-specific cell size
		• No multinucleation
B	Fair	• 10–25% fragmentation
		• Stage-specific cell size for majority of cells
		• No evidence of multinucleation
C	Poor	• Severe fragmentation (>25%)
		• Cell size not stage specific
		• Evidence of multinucleation

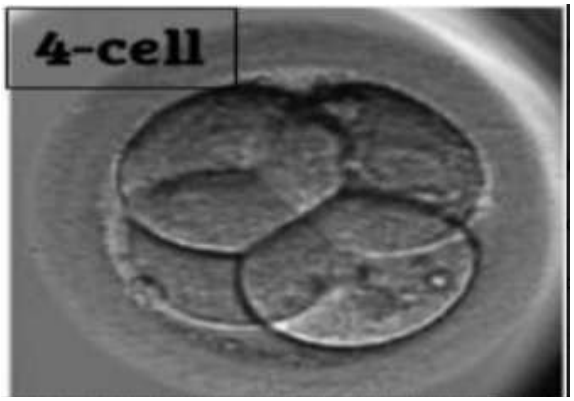

FIGURE 1: DAY 2 (4 CELLED STAGE)

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FIGURE 2: DAY 3 (8 CELLED STAGE)

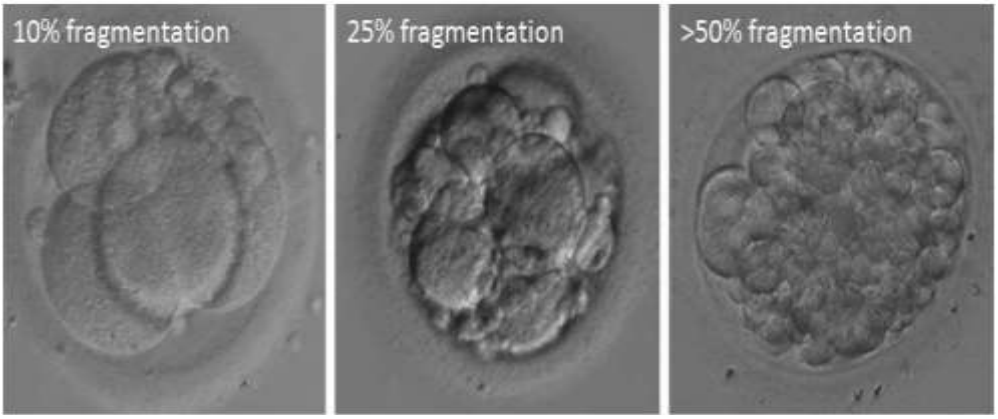

FIGURE 3 (PERCENTAGE OF FRAGMENTATION)

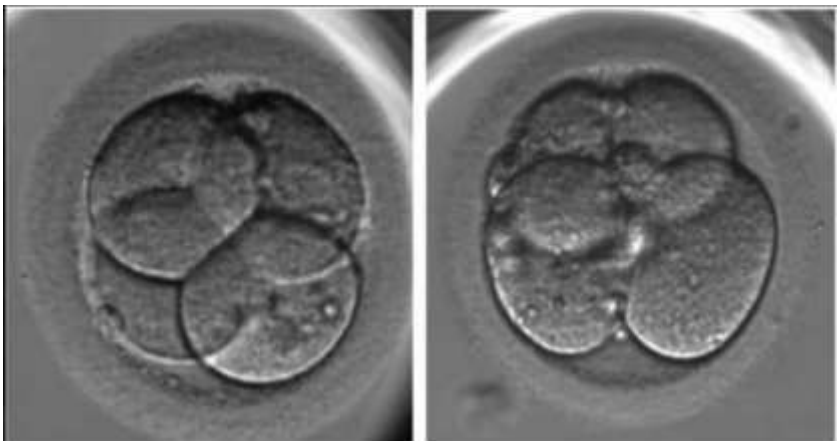

FIGURE 4(CELL SIZE: SYMMETRIC CELL SIZE, IMAGE TO THE LEFT &ASSYMETRIC CELL SIZE, IMAGE TO THE RIGHT

Statistical Analysis:

The continuous variables were expressed in Mean ± SD. An independent t-test which is a typeof inferential statistic was used to determine if there is a significant difference between themean variables of the two groups. A general linear model

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was used for the generalization ofmultiple linear regression to the case of more than one dependent variable. All the analyses were performed using SPSS software version 22(IBM) and ap-value of <0.05 was considered as statistically significant.

III. RESULTS:

Table1: Descriptive statistics in cases and controls inCasesand Controls(Grade-A, Grade-B)

	Group	N	Mean+SD	P-value
Grade-A	PCOS	58	6.09±4.46	>0.05
	Non-PCOS	111	4.96±4.75	
	Total	169	5.34±4.67	
Grade-B	PCOS	58	3.16±2.2	>0.05
	Non-PCOS	111	2.01±2.36	
	Total	169	2.4±2.36	

The interpretation of this current retrospective study a total of 169 patients were included for the statistical analysis. The samples were separated into two groups PCOS (58)-Case, and Non-PCOS(111)- Control. An independent T-test was performed to find the statistical difference between thegroups. In this study, we found that there is no significant between the cases and control-Grade-A,Grade-B(p>0.05)(Table. 1)

Table2: Distribution of group statistics using Student T-test.

	Group	N	Mean±SD
Grade-A	PCOS	58	6.09±4.46
	Non-PCOS	111	4.96±4.75
Grade-B	PCOS	58	3.15±2.2
	Non-PCOS	111	2.01±2.36
PCOS-D2-A	PCOS	25	6.96±4.97
	Non-PCOS	52	4.71±4.54
PCOS-D2-B	PCOS	25	3.2±2.51–

	Non-PCOS	52	2.17±2.16
PCOS-D3-A	PCOS	33	5.76±4
	Non-PCOS	49	5.75±4.73
PCOS-D3-B	PCOS	33	3.18±1.96
	Non-PCOS	49	2.34±2.59

In mean value of Grade-A quality embryos in PCOS and Non-PCOS was found to be 6.09±4.46 and 4.96±4.75 respectively and there is no statistically significant difference between the PCOS and the Non-PCOS group (P-value <0.05).

In mean value of Grade-B quality embryos in PCOS and Non-PCOS was found to be 3.15±2.2and 2.01±2.36 respectively and there is no statistically significant difference between the PCOS and the Non-PCOS group (P-value<0.05).

Similarly, there was no statistically significant difference between the mean value of grade A and B embryos of day 2 and day 3(cleavage stage embryos) between the PCOS and Non-PCOS group (P-value <0.05).

IV. DISCUSSION:

The current study is to examine the Embryo quality with the risk of Polycystic Ovary SyndromePCOS and Non-PCOS. Polycystic ovary syndrome is considered a multifactorial disorder withdiverse hereditary, metabolic, endocrine, and environmental abnormalities. It is well predictablethat PCOS women are more susceptible to obesity-interrelated health problems like diabetes,hypertension, cardiovascular disorders, anovulation, infertility, difficulties in onset, and adversepregnancyoutcomes.

In a study by Roshan Nikbakh et al. it was found that there was nostatistically significant difference in thenumber of embryo subtypes (A, B, C and D) and pregnancy rate between two groups (PCOS and non-PCOS). It was seen that; the higher rate of retrieved oocyte numbers in PCOS group did not guarantee the higher clinical pregnancy rate in PCOS group. What was important in increasing the pregnancy rate was the quality of retrieved oocytes and embryos, not the higher number of them. Despite the higher number of retrieved oocytes, the number of high-quality oocytes and embryos didn't differ significantly in two groups[17].

Ludwig et al. [18] and Plachot et al. [19]in their studies concluded that a lower number of 'high quality oocytes' in PCOS compared tonon-PCOS patients could be attributed to a lower fertilization rate in these cycles.

Fernandez et al. compared the quality of oocytes and embryos in PCOS and control groups and showed, although the number of retrieved oocytes in PCOS group was higher, the number of high-quality embryos was not significantly different between two groups [20].

Based on the findings of the present study, we foundthat there is no statistically significant difference in the embryo quality in women who had PCOS when compared to the non -PCOS group. Analysis of oocyte and thereby corelating it with embryo quality can give more definite results.

V. CONCLUSION:

Our study findings showed that there is no statistically significant difference in the quality of embryos (Grade-A and Grade-B)in both PCOS and non-PCOS control group.

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