Correlation Between Body Mass Index and ICSI Outcome in Women With PCOS

Thesis

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By

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List of Abbreviations

Abbrev.	Full-term
AES	: Androgen Excess Society
AFC	:Antral follicle counts
AMH	: Anti Mullerian hormone
ART	: Assisted-reproductive technique
ASRM	: American Society for Reproductive Medicine
BMI	: Body mass index
CHR	**:** Center for human reproduction
ESHRE	: European society for human reproduction and Embryology
ET	: Embryo transfer
FSH	: Follicle-stimulating hormone
GnRH	: Gonadotropin releasing hormone
GWAS	:Genome-wide association studies
hCG	: Human chorionic gonadotropin
ICSI	: Intracytoplasmic sperm injection
IR	**:** Insulin resistance
IVF	: In-vitro fertilization
LH	: Luteinizing hormone
MRHD	: Maximum Recommended Human Dose
NIH	:National Institutes of Health
OHSS	: Ovarian hyperstimulation syndrome
OPKS	:ovulation predictorkits
PCOS	: Polycystic ovarian syndrome
TSH	: Thyroid-stimulating hormone
TV	: Transvaginal
U/S	: Ultrasound

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1. INTRODUCTION

The Polycystic ovary syndrome (PCOS) is a common abnormality of young women of reproductive age associated with menstrual dysfunction, infertility, hyperandrogenism, and insulin resistance. Previous studies have reported a variable prevalence of gonadotropin secretory abnormalities, including elevated baseline LH and LH to FSH ratio in 35–90% of patients with PCOS ***(Rebar et al., 2015).***

Observations suggest that prospective assessment of the quality of decidualization response in the endometrium may be an important tool for predicting the likelihood of successful implantation and pregnancy outcome. Since its introduction into the clinic, ultrasound has been used widely to assess uterine features such as endometrial thickness, endometrial pattern and that may be predictive of pregnancy, especially in the context of assisted reproductive technology ***(Taylor et al., 2006).***

Patients with polycystic ovarian syndrome (PCOS), commonly present with irregular ovulation and menstruation, elevated testosterone levels, which can lead to an over abundance of body hair, and multiple small cysts within the ovaries. Women with PCOS are generally successful at achieving pregnancy, either naturally or through assisted reproduction such as ovulation induction and in vitro fertilization (IVF). Women with PCOS tend to have an increased number of eggs preparing to be released from

the ovary, as well as increased levels of anti-Müllerian hormone, which is produced by growing eggs and is thought to reflect ovarian reserve, or the number of eggs a woman has remaining. Therefore, it has been hypothesized that PCOS is associated with an increase in ovarian reserve. As fertility declines after the age of 40 in all women, a larger ovarian reserve may be associated with a longer fertile period in women with PCOS ***(Suleena Kansal Kalra, 2013).***

In a non-PCOS population, BMI is known to affect in vitro fertilization (IVF) outcomes. Although weight reduction improves fertility in PCOS patients attempting spontaneous conception, studies of PCOS patients to date do not fully evaluate the impact of a range of BMIs on IVF outcomes. One study quantified the negative impact of morbid obesity on pregnancy outcomes in agroup of women with PCOS, although lean-only PCOS population was not included for comparison. **In 2011, Marquard** found that obesity and PCOS were both independently associated with smaller oocyte diameter among 8 obese and 5 non obese PCOS patients, although only patients undergoing intracytoplasmic sperm injection (ICSI) were included. Norway study evaluated 100 cycles from 56 PCOS patients categorized by insulin-resistance status, which did not correlate completely with BMI. Those findings showed that insulin resistance was associated with a lower oocyte count and increased follicle stimulating hormone (FSH) requirement; however, the data analysis controlled for body weight ***(Fedorcsak et al., 2001).***

2. AIM/ OBJECTIVES

The aim of this study is to correlate between body mass index and gonadotrophin secretions in PCOS patients and their effect on clinical pregnancy in ICSI cycles.

Hypothesis

In women with history of PCOS who are going to have ICSI, body mass index and gonadotrophin secretions may affect the success of ICSI outcome.

Research Question

In women with history of PCOS who are going to have ICSI. Does body mass index and gonadotrophin secretions affect the success of ICSI outcome?

Outcomes

Primary outcomes:

To correlate between body mass index and gonadotropin secretions in PCOS patients and their effect on ICSI outcome clinical pregnancy in ICSI cycles.

Secondary outcomes:

Clinical ICSI outcomes included:

(1) Ovarian hyper stimulation syndrome.

(2) Miscarriage.

(3) Number of gonadotrophin ampules.

(4) Duration of induction of ovulation.

3. METHODOLOGY:

Patients and Methods

Study Design

Retrospective cohort trial

Study Setting:

Assisted Reproductive Technology unit at Maternity Hospital - Ain Shams University.

Population of the study:

A total of 100 women with history of PCOS and infertility enrolled in the study will be divided into two groups:

- Group A (N=50): women with BMI $\geq$ 30 kg/m^2
- Group B (N=50): women with BMI < 30 kg/m^2

-Inclusion criteria for both groups will be:

Cases of PCO syndrome according to Rotterdam criteria:

PCOS could be diagnosed, after the exclusion of related disorders, by two of the following three features:

(1) Oligo- or anovulation,

(2) Clinical and/or biochemical signs of hyperandrogenism, or

(3) Polycystic ovaries by ultrasound features.

-Exclusion criteria will be:

(1) Women who had previous pregnancy or ICSI Failure.

(2) Female age < 20 and > 35 years.

(3) Using any oral contraceptive pills.

(4) Using oral hypoglycemic drug.

(5) Any uterine abnormality.

Research Methodology

All participants will be subjected to the following:

A) Detailed medical history including:

- Personal history.
- Menstrual history.
- Past and obstetric history.

B) Physical examination:

- Complete physical examination was recorded including anthropometric measurements body mass index [BMI] in kg/m2, Waist circumference in cm Waist-hip ratio

C)Laboratory investigations:

Routine investigations including:

- Hormonal profile LH/FSH ratio.

D)Induction of ovulation:

- On day 3 of spontaneous cycles, all patients will have basal hormonal profile (FSH, LH, E2, TSH and prolactin).
- Transvaginal (TV) ultrasound (U/S) on day 3 of non-stimulated cycles will be done by transvaginal probe of 5-9 MHZ. Any patient found to have uterine abnormalities will be excluded.
- Ovarian hyper stimulation protocol will be held according to a long GnRH agonist protocol starting from midluteal phase by daily subcutaneous injection of triptoreline acetate (Decapeptyl 0.05 mg, Ferring Pharmaceutical, Kid, Germany). Then on day 3 of next cycle ovarian hyper stimulation will be started by daily injection of HMG (Menogon 75 lU/amp "Ferring Pharmceutical, Kid, Germany "or Merional 75 IU/amp" IBSA, Switzerland"). The starting dose of gonadotropines will be prescribed according to the age and body weight of the subjects, then the dose will be adjusted according to the ovarian response that will be assessed by transvaginal folliculometry which will be started on cycle day six.
- According to the ovarian response, every other day TV U/S will be performed and at the moment when the leading follicle reaches 16mm, daily TV U/S will be performed till the largest follicle reach a diameter of >18mm.

- HCG (Choriomon 10,000 lU/amp. "IBSA, Switzerland") will be administered for triggering ovulation.

E) Ovum pick up:

- 34-36 hours after HCG injection, the transducer will be connected to the ultrasound system. The direction of the guide beam will be checked. The puncturing needle will be connected to an aspiration apparatus attached by a fixation ring to the front and rear ends of the vaginal transducer, thereby defining the direction of puncture corresponding to the guide beam on the ultrasound image.
- The aspiration will be checked using test tubes. The uterus, both ovaries and iliac vessels will be identified by the visualization in both planes. The distance between the upper pole of the vagina and the ovary will be closely evaluated (care will be taken to avoid intestinal or vascular interposition).
- Depth localization of the closest accessible follicle (distance from the upper vaginal pole to the center of the follicle) will be done. Needle will be pushed forcefully to the center of the follicle (Aspiration pressure 90-100mmHg).

F) ICSI:

- Intracytoplasmic sperm injection will be performed on metaphase II oocytes using the direct penetration