# Effect of Body mass index and Age on the Outcome of PCOS Infertile Patients Undergoing Intracytoplasmic Sperm Injection

A Thesis

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✍ **Aya Mohammad Elsayed**

# List of Contents

# List of Abbreviations

| Abbr. | Full-term |
|---|---|
| **AFC** | **:** Antral follicle count |
| **AMH** | **:** Anti-Müllerian hormone |
| **ART** | **:** Assisted reproduction technology |
| **ASRM** | **:** American Society of Reproductive Medicine |
| **BMI** | **:** Body mass index |
| **CVD** | **:** Cardiovascular disease |
| **CVS** | **:** Chorionic villus sampling |
| **DCI** | **:** D-chiro-inositol |
| **DE** | **:** Donated oocytes |
| **DNA** | **:** Deoxyribonucleic acid |
| **ET** | **:** Embryo transfer |
| **FSH** | **:** Follicle-stimulating hormone |
| **FAI** | **:** Free androgen index |
| **GnRH** | **:** Gonadotropin-releasing hormone |
| **HA** | **:** Hyperandrogenic anovulation |
| **HDL** | **:** High density lipoprotein |
| **ICSI** | **:** Intracytoplasmic sperm injection |
| **IPG** | **:** Inositol phosphoglycans |
| **IVF** | **:** In vitro fertilization |
| **LDL** | **:** Low density lipoprotein |
| **LH** | **:** Luteinizing hormone |

**MYO** : Myo-inositol

**NIH** : National Institutes of Health

**OCP** : Oral contraceptive pills

**OHSS** : Ovarian hyperstimulation syndrome

**PCOS** : Polycystic ovary syndrome

**SART** : Society for Assisted Reproductive Technology

**SD** : Standard deviation

**SE** : Self-oocytes

**SHBG** : Sex hormone-binding globulin

**SPSS** : Statistical package for social science

**TESE** : Testicular sperm extraction

**TZD** : Thiazolidinediones

**VE** : Vitrified/frozen embryos

**WHO** : World Health Organization

# List of Tables

# List of Figures

# Introduction

There are potential numerous causes of female infertility which should be approached systematically to help identifying them in patients, one of them is the Polycystic ovary syndrome ***(Brassard et al., 2008).***

Polycystic ovary syndrome (PCOS) is a common endocrinopathy typified by oligovulation or anovulation, signs of androgen excess and multiple small ovarian cysts ***(Williams gynecology 2nd edition).***

Signs and symptoms of PCOS include menstrual dysfunction which may range from amenorrhea to oligo-menorrhea to episodes of menometrorrhagia with anemia, acne, excess body and facial hair ***(Azziz, 2003)***. Also PCOS could be associated with type 2 DM ***(Schneider, 2006)***, obesity ***(Talbott, 1995)***, mood disorders ***(Deeks, 2010)***, PCOS also accounts for 80 to 90 percent of cases with infertility secondary to anovulation ***(Adams, 1986)***.

While there are a number of definitions of PCOS, the Rotterdam consensus is the most widely accepted across Europe, Asia and Australia and was the definition used for the guideline. It encompasses the National Institutes of Health definition, which generally describes women with a more severe form of PCOS and requires the presence of both hyper-androgenism and

oligo/anovulation. The Rotterdam Criteria require the presence of two of the following: oligo/anovulation, hyperandrogenism or polycystic ovaries on ultrasound ***(Rotterdam ESHRE/ASRM, 2004).***

During ovarian follicular development, primordial follicles are recruited into a group of growing follicles, from which one antral follicle is selected to ovulate. These events require coordinated reproductive, metabolic and intraovarian interactions. In PCOS, ovarian hyperandrogenism, hyper-insulinemia from insulin resistance and altered intraovarian paracrine signaling can disrupt follicle growth. The consequent follicular arrest in PCOS is accompanied by menstrual irregularity, anovulatory subfertility and the accumulation of small antral follicles within the periphery of the ovary, giving it a polycystic morphology ***(Jonard et al., 2003).***

Management of infertility in polycystic ovary syndrome includes lifestyle modification including weight loss as well as assisted reproductive technology such as ovulation induction by clomiphene citrate or Aromatase inhibitors, oocyte release triggering and surgery as laparoscopic ovarian drilling ***(Consensus on infertility treatment related to polycystic ovary syndrome, 2013).***

The literature contains different opinions about the role of body mass index (BMI) in IVF -cycles. A study by Loveland

et al. demonstrated that implantation rates and pregnancy rates decrease with increasing BMI ***(Loveland et al., 2001).*** In 2006, Dechaud et al. showed that obesity does not have any adverse impact on IVF ***(Dechaud et al., 2006)***

In 2014, Bailey et al. investigated the effect of BMI on the characteristics and outcomes of IVF cycles in PCOS and found lower clinical pregnancy rates in an obese PCOS group than in a lean group and a lower rate of ovarian hyper-stimulation syndrome (OHSS) in the obese group.

Among women without ovulation abnormalities, fertility throughout reproductive life is largely determined by age. Age-related female infertility is primarily a result of decreasing ovarian reserve ***(Ahmed et al., 1994).***

After the age of 35 years, the serum level of follicle-stimulating hormone (FSH) begins to increase, the serum level of inhibin B decreases slightly, and the serum estradiol (E2) level remains unchanged ***(Klein et al., 1996).*** The serum levels of FSH and inhibin B are known endocrine markers of ovarian aging ***(de Vet et al., 2002)***.

The serum anti-Müllerian hormone (AMH) concentration also demonstrates age-related decreases in women without ovulation abnormalities ***(van Rooij et al., 2002).***

Furthermore, the serum AMH level is correlated with the ovarian response in patients with a normal FSH level undergoing in vitro fertilization (IVF**) *(Seifer et al., 2007).***

As a woman ages, the ovarian follicles are depleted and the ovary develops a poorer response to exogenous gonadotropin ***(***Faddy***, 2000).***

***Müberra Namlı Kalem et al*** also published a paper in this subject Dec 2015. His objective from the study was to investigate age-related variations and the effect of body mass index (BMI) on in vitro fertilization (IVF) outcomes.

# Aim of the Work

The purpose of this study was to evaluate the effect of BMI and age on the outcome of PCOS infertile patients undergoing intracytoplasmic sperm injection (ICSI).

# Chapter (1)
# Polycystic Ovary syndrome

Polycystic Ovary Syndrome (PCOS), also referred to as hyperandrogenic anovulation (HA), or Stein–Leventhal syndrome, is one of the most common endocrine system disorders that affect women in their reproductive age of unknown etiology, with a prevalence ranging from 8.7 to 17.8% in women of reproductive age ***(Zueff et al., 2012).***

Evidence suggests that PCOS phenotype may vary widely and is most commonly observed in the post-pubertal period ***(Spritzer, 2014).*** Despite a diversity of phenotypes, women with PCOS are characterized by polycystic ovaries, chronic anovulation, hyperandrogenism and gonadotropin abnormalities ***(Azziz, 2016).***

In addition to the characteristics that are inherent in PCOS, it is a common occurrence of metabolic and hormonal abnormalities associated with obesity, type 2 *diabetes mellitus* and dyslipidemia. A combination of these characteristics lead to metabolic syndrome ***(Costa et al., 2010).***

The variety of metabolic disturbances in PCOS may be related to a higher risk of developing cardiovascular disease. This fact may explain a predisposition to arterial hypertension in women suffering from the syndrome ***(Rocha et al., 2010).***

Although the association between changes in arterial blood pressure and PCOS has still not been fully elucidated, the increased risk of hypertensive state may be explained by insulin resistance and hyperandrogenism, even when adjusted for age, body mass index and other anthropometric parameters ***(Palomba et al., 2015).***

The study of PCOS is one of the most important topics in female reproductive endocrinology, subject that has the experience of our research group with studies in rats in persistent estrus mimicking state of chronic anovulation. Although the syndrome has been widely investigated, its definition and pathophysiological aspects are still highly controversial ***(Chen et al., 2007).***

- ***Epidemiology:***

Systematic screening of women according to the National Institutes of Health (NIH) diagnostic criteria estimated that 4–10% of women of reproductive age suffer from PCOS ***(Azziz et al., 2004).***

Although it was previously considered as a disorder of adult women, recent evidence suggests that PCOS is a lifelong syndrome, manifesting since prenatal age. In fact, according to the Rotterdam diagnostic criteria, the prevalence of PCOS in adolescents varies between a minimum of 3% and a maximum