

**Follicular Anti-Mullerian Hormone in
prediction of Intracytoplasmic sperm
injection outcome in women with
polycystic ovary syndrome**

Thesis

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Master Degree in Obstetrics and Gynecology*

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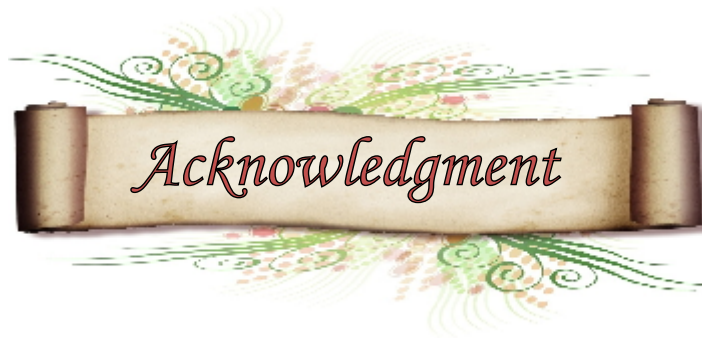
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List of Abbreviation

AA	Adrenal androgen
ACTH	Adrenocorticotrophic hormone
AES	Androgen excess society
AFC	Antral follicle count
AMH	Anti-mullerian hormone
ART	Assisted reproductive technology
BMI	Body mass index
CAH	Congenital adrenal hyperplasia
CC	Clomiphene citrate
CGH	Comparative genomic hybridization
CHD	Coronary heart disease
CNS	Central nervous system
COH	Controlled ovarian hyperstimulation
CTET	Clinical touch embryo transfer
DHEA-S	Dihydro epi androstenedione sulphate
DOPU	Day of Ovum pick up
E ₂	Estradiol
ELISA	Enzyme-Linked Immunosorbent Assay
ESHRE	European Society of Human Reproduction and Embryology
FF	Follicular fluid
FSH	Follicle stimulating hormone
GnRH	Gonadotrophin-releasing hormone
GV	Germinal vesicle
HA	Hyperandrogenemia
HCG	Human chorionic gonadotropin
HDL	High density lipoprotein
HMG	Human menopausal gonadotropin

List of Abbreviation

HOMA	Homeostatic model assessment
HRP	Heat Recovery Package
ICSI	Intracytoplasmic sperm injection
IGF- γ	Insulin growth factor γ
IR	Insulin resistance
IVF	In vitro fertilization
LDL	Low density lipoprotein
LH	Luteinizing hormone
M I	Metaphase I
M II	Metaphase II
MESA	Microsurgery epididymal sperm aspiration
MIF	Mullerian inhibiting factor
MIH	Mullerian inhibiting hormone
MIS	Mullerian inhibiting substance
NaN r	Sodium tri nitrate
NASH	Nonalcoholic steatohepatitis
NHANES	National Health and Nutrition Examination Survey
NIH	National Institutes of Health
NPV	Negative predictive value
OCs	Oral contraceptive
OD	Optical density
OPU	Ovum pick up
OR	Ovarian reserve
P B	Polar body
PCO	Polycystic ovary
PCOM	Polycystic ovarian morphology
PCOS	Polycystic ovary syndrome
PGD	Preimplantation genetic diagnosis

List of Abbreviation

PPV	Positive predictive value
PVS	Perivitelline space
PZD	Partial Zona Dissection
ROC curve	Receiver operating characteristic curve
SHBG	Sex hormone binding globulin
SPSS	Statistical package for social science
SUZI	Sub Zonal Insemination
TESE	Testicular Sperm extraction
TGF- β	Transforming growth factor- β
TMB	Tetra methyl benzidine
TVS	Trans-vaginal ultrasound
U/S	Ultrasound
UGET	Ultrasound-guided embryo transfer

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Introduction

Polycystic ovary syndrome (PCOS) is the most common cause of oligo-anovulation, infertility and hyperandrogenism in women, affecting between 5% and 10% of women of reproductive age worldwide. PCOS is characterized by an excessive number of growing follicles (2- to 3-fold that seen in normal ovaries) up to the stage of 2 to 6 mm in size (small antral follicles). In PCOS patients, the selection of one follicle from this increased pool of selectable follicles and its further maturation to a dominant follicle does not occur. The reason for this last phenomenon is unknown, although inhibition of the local effect of follicle-stimulating hormone (FSH) seems pivotal (*Arabzadeh et al., 2017*).

Anti mullerian hormone (AMH), could be involved in the abnormal folliculogenesis in PCOS. Follicular fluid (FF) and serum of PCOS women revealed increased AMH levels in studies. The increase in serum AMH levels is not only due to an increase in the number of follicles, but may also result from increased AMH production per follicle. So far, little is known about the factors that regulate AMH expression in the ovary (*Yilmaz et al., 2017*).

In the ovary, anti-Müllerian hormone (AMH) is exclusively produced by the granulosa cells from a wide range of follicles from the primary to the small antral stages of folliculogenesis in the adult rat and human. Anti-Müllerian hormone (AMH), a member of the transforming growth factor- β superfamily, it has become clear that it plays an important role in ovarian function, especially in follicle development and selection. AMH seems to inhibit the initiation of human primordial follicle growth and prevents multiple selection of a dominant follicle. In addition, it has been shown that AMH is a negative regulator of follicle growth, acting by reducing the sensitivity of follicles to FSH (*Arabzadeh et al., 2013*).

One of the main advantages of AMH measurement in IVF treatment instead of the other markers of ovarian reserve may stem from its low inter and intra-cycle variability. For this reason, AMH could be used as a menstrual cycle-independent marker of ovarian response to controlled ovarian stimulation. AMH appears to correspond well with antral follicle counts (AFCs) and ovarian response to hyperstimulation in in vitro fertilization (IVF) and to be useful for predicting ovarian response in women undergoing IVF treatment (*Nelson et al., 2014*).

It has been suggested that serum basal AMH levels represent both the quantity and quality of the ovarian follicle pool during the cycle. Lack of success in IVF, indicative of a diminished ovarian reserve, is associated with reduced serum basal AMH concentrations. In PCOS, the increase in serum basal AMH level has been shown to be closely related to the degree of menstrual disorder and with the excess in the 2 to 9 mm follicle number (FN) on ultrasonography (US). The role of AMH as a predictive factor of IVF outcomes remains a contentious subject in patients with PCOS (*Arabzadeh et al., 2017*).

Aim of the Work

The aim of this study is to assess the relationship between follicular AMH and intracytoplasmic sperm injection outcomes in patients with polycystic ovary syndrome (PCOS).

Intracytoplasmic Sperm Injection **(ICSI)**

Introduction:

ICSI exhibited least total fertilization failure rate and gave less abnormal fertilization rate with statistical significance in unexplained infertility when compared to the IVF. Therefore, applying of ICSI procedure may increase the success chance of embryo transfer and pregnancy outcomes (*Chiamchanya et al., 2008*).

In addition, ICSI may be needed for IVF treatment if polyspermy or poor fertilization occurred in a prior cycle where insemination alone was used or if preimplantation genetic diagnosis (PGD) is planned, especially for single gene defects (*Palermo et al., 1996*).

Interest in the initial types of micro-manipulation procedures, such as zona drilling and Partial Zona Dissection (PZD), evolved because of the disappointing results of standard IVF for the severe male factor patients. In these procedures, a physical opening is created in the zona pellucida by using chemical "drilling" or by making a microscopic mechanical incision. In Sub Zonal Insemination (SUZI), the micro-injection of spermatozoa

into the peri-vitelline space (between the zona pellucida and the plasma membrane), gained popularity for severe male factor infertility because typically only 3 to 4 sperms were inserted per oocyte. The high rate of polyspermy, a lethal condition involving the entrance of more than 1 sperm into the egg and a problem with PZD and SUZI, was finally overcome with ICSI, which requires the injection of only a single sperm per egg (*Lamb and Lipshultz, 2003*).

This procedure is thought to bypass some of the physiologic events, such as capacitation and the acrosome reaction, that are normally required for fertilization in-vivo. In general, ICSI has allowed couples with male factor infertility to achieve pregnancy outcomes that are comparable with those of couples with non-male factor infertility using IVF treatment (*Yao and Schust, 2002*).

Indications for ICSI:

Conventional IVF and intracytoplasmic sperm injection (ICSI) are two common techniques used to achieve fertilization. Although conventional IVF entails standard microinsemination, ICSI involves injection of a single spermatozoon into a mature oocyte. Although ICSI is indicated when a male factor for infertility exists, it is often suggested that even in cases of non-male factor infertility and unexplained infertility, fertilization can be improved (*Gozlan et al., 2007*).

Other indications of ICSI include the sole presence of spermatozoa lacking an acrosome or those that are completely immotile, as well as the use of surgically recovered epididymal or testicular sperm. Other absolute indications for ICSI are non-male factor-related and include a history of two previous fertilization failures with conventional IVF and the fertilization of oocytes before pre-implantation genetic diagnosis (*Hamberger et al., 2004*).

Polycystic ovary patients showed better global oocyte and embryo quality. However, pregnancy and live birth rates were similar to normo-ovulatory women undergoing intracytoplasmic sperm injection (ICSI) cycles when number