Ratio of Estrogen to Number of Follicles ≥14mm on Day of Trigger as a Prognostic Tool for In Vitro Fertilization Cycles

Thesis

Submitted for partial fulfillment of Master Degree in

Obstetrics and Gynecology

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2017

نسبة هرمون الاستروجين الى عدد البويضات اكثر من ١٤ مم كاداه تشخيصية فى دورات الحقن المجهري

رسالة

توطئة للحصول علي درجة الماجستير في النساء والتوليد

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٢٠١٧

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgement

First and foremost thanks to ALLAH, the Most Merciful.

I would first like to thank my thesis supervisors **Prof. Sherif Abd El-Khalik Akl** Professor of Obstetrics and Gynecology at Faculty of Medicine - Ain Shams University , **Dr. Sherif Hanafi Hussien** Assistant professor of obstetrics and gynecology at faculty of medicine - Ain Shams University and **Dr. Ahmed Mohamed El Kotb** Lecturer in Obstetrics and Gynecology at faculty of Medicine – Ain Shams University The door to their offices was always open whenever I ran into a trouble spot or had a question about my research or writing. They consistently allowed this paper to be my own work, but steered me in the right the direction whenever they thought I needed it.

I would also like to thank the expert who was involved in the validation survey for this research project **Dr. Azza Awad** the director of embryology lab at El-Demirdash hospital – Ain Shams University. Without her passionate participation and input, the validation survey could not have been successfully conducted.

Finally, I must express my very profound gratitude to my parents and to my wife for providing me with unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them. Thank you..

Contents

List of Abbreviations

AMH	Anti Mullerin Hormone
ART	Assisted Reproductive Technic
ATPase	Adenosine Tri Phosphatase
BMI	Body Mass Index
CBAVD	congenital bilateral absence of the vas deference
COH	Controlled Ovarian Hyper stimulation
CRF	Chronic Renal Failure
E2	Estradiol
ET	Embryo Transfer
FSH	Follicular Stimulating Hormone
GnRH	Gonadotropin Releasing Hormone
GV	germinal vesicle
GYN	Gynecology
HCG	Human Chorionic Gonadotropin
HOS	hypo-osmotic swelling
HSG	Histro Salpengo Graphy
ICSI	*Intra cytoplasmic Sperm Injection*
IU	International Unit
IVF	In Vetro Fertilization
LH	Luteinizing Hormone
MIF	Mullerian Inhibitory Factors

MII	Metaphase 2
MIS	Mullerian Inhibitory Substances
OB	Obstetrics
OHSS	Ovarian Hyper Stimulation Syndrome
PCC	premature chromosomal condensation
PCOS	Poly cystic Ovarian Syndrome
PGD	pre-implantation genetic diagnosis
ROSI	round spermatid injection
ROSNI	Round spermatid nucleus injection
SD	Stranded Deviation
T.B	Tuberculosis
TEM	transmission electron microscopy
TSH	Thyroid Stimulating Hormone
WHO	World Health Organization

List of Tables

List of Figures

Abstract

Background: infertility is usually described as the inability of a couple to conceive after one year of unprotected intercourse. Infertility is a major health problem affecting about 10-20% of couples.

Aim: it was to determine the cut-off value for E_2/Number of follicles and E2/Number of M2 oocytes at an approximately equivalent sensitivity and specificity as a predictor for pregnancy after intra cytoplasmic sperm injection (ICSI).

Patients and Methods: this study was a Cohort study, conducted at Ain-Shams University El-Demerdash Hospital, IVF Center, from September 2016 till June 2017. We studied 82 cases and inclusion criteria included age range from 20-40 years old and sub fertile women undergoing long agonist protocol ICSI cycles. Exclusion criteria included severe male factor infertility and previous history of documented poor response resulting in mature oocyte <3 oocytes, the presence of a uterine pathology, recurrent pregnancy loss (≥3 previous miscarriages) and previous implantation failure (≥3 previous failed).

Results: there is significantly higher clinical pregnancy rate in patients <36 years old (39.3%) over those had 36-40 years old (9.5%) (P=0.011). Also there is significant difference between pregnancy rate at E2/M2 oocytes number ratio groups (P=0.049). The pregnancy rate was the least in E2/M2 oocytes number ratio between (195.10-254.75) pregnancy rate was 5.9% and the pregnancy rate was the highest in E2/M2 oocytes number ratio (>=254.76) (pregnancy rate 44.4%) but there is no significant difference between pregnancy rates at E2/follicular Number Ratio quartiles (P=0.336).

Conclusion: age is an important determinant of IVF success. There is a significantly higher clinical pregnancy rate in patients <36 years old over those from 36-40 years old, estradiol per mature follicle and retrieved oocytes do have an impact. Pregnancy rate is better when E2/M2 oocyte ratio is more than 254.76 pg/ml. In contrast, E2/Follicular number ratio dose not correlate with the outcome of the IVF cycles.

Keywords: E2/follicular number ratio, E2/M2 Oocyte ratio, IVF, ICSI, Prediction of success

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A protocol of Thesis
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Introduction

In IVF cycles the main priorities are to obtain a sufficient number of mature oocytes, quality embryos and finally obtain a pregnancy. Prediction of IVF outcome has focused clinical research for many years. Many tests have been suggested to predict the probability of pregnancy in IVF cycles, such as FSH and estradiol on the third day of the cycle, FSH levels after treatment with clomiphene, levels of inhibin A and inhibin B, number of ovarian antral follicles, antimullerian hormone and the influence of women age *(Ficicioglu et al., 2006; Carrera-Rotllan et al., 2007)*.

The relationship of follicle number to the outcome of in vitro fertilization (IVF) is universally acknowledged. However, attempts to relate the number of preovulatory follicles to outcome in ovulation induction (OI), intrauterine insemination (IUI) cycles have produced mixed results *(Dickey et al., 2001)*.

The serum estradiol (E2) concentration is used to evaluate follicle maturation. This measurement is essential to predict the timing of ovulation when treating infertility patients. As the date of ovulation approaches, the E2 level changes dynamically day-by-day, particularly in natural cycle *in vitro* fertilization (IVF). In pre-menopausal women, E2 is mainly secreted by granulosa cells in the follicles. As these cells divide and proliferate within a

follicle, increasing in number as the follicle grows, the E2 level also increases. Thus, the E2 concentration is a good index of follicular maturation *(Rothman et al., 2011; Segawa et al., 2015)*.

The success of in vitro fertilization (IVF) depends on controlled ovarian hyperstimulation resulting in multi-follicular response. The follicles contain granulosa cells which secrete hormone estradiol (E2). Serum estradiol (E2) plays an important role in oocytes/follicular maturation and preparation of the uterus for implantation *(Anifandis et al., 2005)*. Controversy surrounds the role of total estradiol value as well as estradiol/follicle ratio (E2/fol) and estradiol/oocytes (E2/O) ratio in relation to IVF outcome *(Mittal et al., 2014)*.

In a systemic published review, correlating total serum estradiol with IVF outcome, two studies (1,286 patients) showed decreased probability of pregnancy with high serum estradiol, while in five studies (1,875 patients), no detrimental effect of high serum E2 was seen on pregnancy rate. In two studies (191 patients), increased probability of pregnancy was seen with higher serum estradiol levels *(Kosmas et al., 2004)*.

Loumaye and colleagues studied the ratio of estradiol (E2) level on the day of human chorionic gonadotropin (hCG) administration to the number of oocytes retrieved (E2/oocyte ratio) in patients undergoing the long GnRH-

agonist suppressive protocol. They found that the E2/oocyte ratio is a strong index for the success of an IVF cycle, with the highest pregnancy rate observed in patients with E2/oocyte ratio of 70–140 pg/ml *(Loumaye et al., 1997)*.

Yang and associates showed that patients undergoing the flare GnRH agonist protocol with an elevated E2/oocyte ratio demonstrated lower pregnancy and implantation rates *(Yang et al., 2001)*. Accordingly, another study showed that lower E2/oocyte ratio predicts higher pregnancy rate during an IVF cycle in elderly patients aged 43–45 years *(Orvieto et al., 2004)*.

This study aiming to determine the cut-off value for E_2/Number of follicles >14 at day of triggering at an approximately equivalent sensitivity and specificity as a predictor for pregnancy after intra cytoplasmic sperm injection (ICSI).

Aim of the work

The aim of this study determines the cut-off value for E_2/Number of follicles and E2/Number of M2 oocytes at an approximately equivalent sensitivity and specificity as a predictor for pregnancy after intra cytoplasmic sperm injection (ICSI).

Research question

Q: In women undergoing ICSI Can E_2/Number of follicles and E2/Number of M2oocytes predict pregnancy outcome?

Research hypothesis:

In women undergoing ICSI, E_2/Number of follicles >14 and E2/Number of M2 oocytes at day of trigger may predict pregnancy outcome.