بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / حسام الدين محمد مغربي

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات : لا يوجد

Follicular Fluid Leptin as a Marker for Pregnancy Outcomes in Women in General Subfertility Population Undergoing IVF/ICSI Treatment

Thesis

Submitted for Partial Fulfillment of M.D. Degree in Obstetrics and Gynecology

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Ahmed Mohamed Salah Koura

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List of Abbreviations

Abb.	Full term
AMH	Anti-Müllerian hormone
ARC	Arcuate nucleus
ART	Assisted reproduction technology
ASAs	Anti-sperm antibodies
BMI	Body mass index
CC	Clomiphene citrate
CNS	Central nervous system
COH	Controlled ovarian hyperstimulation
ET	Embryo transfer
FF	Follicular fluid
FSH	Follicle-stimulating hormone
GIFT	Gamete intrafallopian transfer
GnRH	Gonadotrophin releasing hormone
GnRHa	Gonadotropin releasing hormone agonist
HOXA-10	Homeobox A10
HPG	Hypothalamic–pituitary–gonadal
HyCoSy	Hysterosalpingography or Hysterosalpingo-Contrast-Sonography
ICSI	Intracytoplasmic Sperm Injection
IGFI	Insulin-like growth factor I
IL-6	Interleukin-6
IM	Intramuscular
IMC	Integrated morphology-cleavage
IUI	Intrauterine insemination
IVF	In vitro fertilization
IVF-ICSI	IVF with intracytoplasmic sperm injection
JAK	Janus kinase
LepR	Leptin receptor
LH	Luteinizing hormone
LPD	Luteal phase defect
LPS	Luteal phase support
MESA	Microsurgical epididmal sperm aspiration
NSAIDs	Non-steroidal anti-inflammatory drugs
OHSS	Ovarian hyperstimulation syndrome

List of Abbreviations cont...

Abb.	Full term
PAI	Plasminogen activator inhibitor
PGD	Preimplantation genetic diagnosis
PR	Pregnancy rate
PZD	Partial zonal dissection
ROS	Reactive oxygen species
SPSS	Statistical Package for Social Sciences
SUZI	Sub-zonal insemination
TESE	Testicular sperm extraction
TET	Tubal embryo transfer
TNF-α	Tumor necrosis factor-alpha
TTF	Total fertilization failure
UI	Unexplained infertility
WHO	World Health Organization
ZIFT	Zygote intrafallopian transfer
ZP	Zona pellicuda

PROTOCOL

PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF M.D. DEGREE

Title of the Protocol: Follicular fluid leptin as a marker for pregnancy outcomes in women in general subfertility population undergoing IVF/ICSI treatment

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What is already known on this subject? AND

What does this study add?

Leptin is a key regulator and stimulator of the hypothalamic-pituitary-gonadal axis, through its direct action on the CNS leading to the regulation of gonadotrophin releasing hormone (GnRH) secretion in the hypothalamus, In some studies it has been suggested that low concentrations of follicular fluid and serum leptin is associated with an increased pregnancy rate and this study will try illustrate the relationship between concentration of follicular fluid leptin and pregnancy outcome.

1. INTRODUCTION/ REVIEW

Infertility has been always considered as one of the most important serious and costy health issues in different societies. Various studies have already been performed to discover the causes of infertility; among them high leptin level has been considered as one of the important and effective factors in several studies ***(Kamyabi and Gholamalizade, 2015).***

Leptin has been shown to control energy homeostasis and food intake and exert many actions on female reproductive function ***(Catteau et al., 2016).***

Leptin is a hormone secreted mainly by the adipocytes that regulates energy homeostasis by promoting energy expenditure and inhibiting food intake with an essential role in the regulation of body weight. It acts on the reproductive axis at different sites, with stimulatory effects at the hypothalamo-pituitary level and inhibitory interactions at the gonads. Leptin also plays an important role in fetal growth and development and influences placental functions including implantation, placental angiogenesis, nutrient transport and immunomodulation ***(Al-Aqbi et al., 2020).***

Leptin has a permissive role in the secretion of gonadotrophins and gonadotrophin-releasing hormone ***(Barash et al., 1996),*** but the episodic pulses of leptin and LH are independently regulated ***(SirPetermann et al., 1999).*** Other studies have illustrated leptin's importance in the onset of puberty and its relationship with gonadotrophins and other hormones ***(Garcia-Mayor et al., 1997).*** Leptin and its receptors are expressed in the blastocyst and endometrium indicating the importance of leptin in the implantation process ***(Dos Santos et al., 2015).***

During the menstrual cycle leptin levels increase in the follicular phase and decline in the luteal phase ***(Hardie et al. 1997),*** suggesting a disproportional influence of estradiol elevation on leptin secretion ***(Mannuci et al. 1998, Riad-Gabriel et al. 1998).*** During IVF cycles, serum leptin rises in response to exogenous follicle-stimulating hormone (FSH) administration ***(Butzow et al. 1999).***

Leptin membrane receptors have been demonstrated in the ovarian granulosa and theca cells. Within these cells leptin reduces steroid production by antagonizing insulin-like growth factor I(IGFI) ***(Llaneza-Suarez et al.,2014).***

Leptin promotes the proliferation and survival of trophoblast cells by an autocrine action and an anti-apoptotic effect. The positive effect of HCG on leptin gene expression in placenta was reported ***(Catteau et al., 2016).*** Leptin also has an important role during the first stage of pregnancy by modulating proliferation, protein synthesis, invasion and apoptosis in placenta cells ***(Perez et al., 2018).***

In some studies it has been suggested that low concentrations of follicular fluid and serum leptin is associated with an increased pregnancy rate ***(Mantzoros et al., 2000)*** and high levels of serum and follicular fluids leptin are associated with low pregnancy rates ***(Anifandis et al., 2005a).*** Low concentrations of leptin in follicular fluids are positively

associated with embryo quality, implantation rate and pregnancy rate ***(Anifandis et al., 2005b).***

In the setting of obesity, however, leptin resistance ensues, and higher body fat is correlated with circulating levels ***(Al-Aqbi et al., 2020).***

Some investigators have suggested that leptin might exert a double role in regulation of reproduction. They showed that when leptin level is lower than normal, it can exert a negative effect on endocrine system, regulating reproduction, While when leptin level is higher than normal, it negatively affects normal function of ovary and fetus development ***(Kamyabi and Gholamalizade, 2015).***

2. AIM/ OBJECTIVES

The aim of this study is to investigate the correlation of follicular fluid leptin concentrations and IVF/ICSI success in the form of clinical pregnancy.

Research question:

In women with infertility undergoing IVF/ ICSI, does high follicular fluid leptin concentration have a role in decreasing the clinical pregnancy rate?

Research hypothesis (Alternate hypothesis):

In women with infertility undergoing IVF/ICSI, high follicular fluid leptin concentration is associated with decrease in clinical pregnancy rate.

Primary outcome:

Clinical pregnancy rate by positive pregnancy test done 2 weeks after embryo transfer followed by transvaginal U/S examination done 2 weeks after positive pregnancy test to confirm the presence of intrauterine healthy gestational sac(s).

Secondary outcomes:

1- Dose of gonadotrophins used during COH.

2- Ovarian Stimulation days.

3- Level of serum Estradiol (E2) at day of HCG trigger.

4- Number of oocytes retrieved at OPU day.

5- Quality of retrieved oocytes.

6- Fertilization rate.

7- Embryo Quality and grading.

8- Correlation between follicular fluid leptin and Serum AMH level.

3. METHODOLOGY:

Patients and Methods/ Subjects and Methods/ Material and Methods

- **Type of Study:** A Prospective Observational Cohort Study (Study of a diagnostic test).
- **Study Setting:** Assisted reproductive technology unit of Ain Shams University Maternity hospital after approval of the research ethical committee.
- **Study time:** The study will be done starting from June 2020 for one year ending in June 2021.
- **Study Population:**

  - *Inclusion Criteria:*

1. Women in reproductive age; 20 to 40 years.
2. Medically free.
3. BMI less than 30.