CONCENTRATION OF VASCULAR ENDOTHELIAL GROWTH FACTOR IN FOLLICULAR FLUID IN RELATION TO DIAMETER, MATURITY OF OOCYTES AND FERTILIZATION RATE IN PATIENTS UNDERGOING INVITRO FERTILIZATION

THESIS

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By

SHAIMAA MOHAMMED THABET

M.B.; B.Ch., 2004 Faculty of Medicine, Cairo University Resident of obstetrics and gynecology Hawamdia hospital

Supervised By

DR. MOSTAFA MAHMOUD ASEM

Professor of Gynecology and Obstetrics Faculty of Medicine, Cairo University

DR. AMAL SHOHAYEB AHMED

Professor of Gynecology and Obstetrics Faculty of Medicine, Cairo University

> Faculty of Medicine Cairo University 2014

جامعه القاهره و دليه المسلم الدراسات العليا

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المعتدن الداغلي

بسم الله الرحمن الرحيم

"قالوا سبحانك لا علما لنا الا ما علمتنا انك أنت العليم الحكيم"

صدق الله العظيم سورة البقرة الآية ٣٢

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LIST OF ABBREVIATIONS

AFC Antral follicle count.

AMH Anti mullirian hormone.

ART Assisted Reproductive Technology.

Cb2 Cabergoline

COH Controlled ovarian hyperstimulation.

DA Dopamine agonists.

E2 Estradiol.

ECM Extracellular matrix.

EGF Epidermal growth factor

eNOS Endothelial nitric oxide synthase.

ET Embryo transfer.
FF Follicular fluid.

FGF Fibroblast growth factor.

FLK Fetal liver kinase.

FSH Follicular stimulating hormone.

GC Granulosa cell.

GnRH | Gonadotropin releasing hormones.

GV Germinal vesicle.

HSA Human serum albumin.

HCG Human chorionic gonadotropin.

HLA Human leucocytic antigen.

HMG Human memopausal gonadotropin.

ICM Inner cell mass.

ICSI Intracytoplasmic sperm injection.

IVF In vitro fertilization.IVM In vitro maturation.LH Luteinizing hormone.

LMWH Low molecular weight heparin.

LPS Luteal phase support.

MCES The mean cumulative embryo score.

MPR Multiple pregnancy rates.

NIVF Natural cycle IVF.

NRP1 Neuropillin 1.

NSAIDs Non-steroidal anti-inflammatory drugs.
OHSS Ovarian hyperstimulation syndrome.

OPU Ovum Pick Up.

PAF Platelets activating factor.

PCO Polycystic ovary.

PCR Polymerase chain reaction.

PGD Preimplantation genetic diagnosis.

PN Pronuclei.

PR Pregnancy rate.

RCTs Randomized controlled trials.

RIF Recurrent implantation failure.

SART Society for Assisted Reproductive Technology.

SBT Single Blastocyst Transfer.

SEET Stimulation endometrium embryo transfer.

SET Single embryo transfer.

SVEGFR Soluble VEGF receptor.

tPA Tissue type plasminogen activator.

UPA Urokinase type plasminogen activator.

VEGF Vascular endothelial growth factor.

VP Vascular permeability.

XO Crossing over.ZP Zona Pellucida.

ABSTRACT

From this study we can conclude that locally produced growth factor, such as VEGF has significant important modulatory role in follicular growth and development by angiogenesis. Our study demonstrated that VEGF concentration in FF is positively correlated with follicular diameter and volume of FF r-0.885 (p-value 0.0001). HS VEGF is the major regulator of ovarian angiogenesis and may play a modulator role in the functional activity of GCs and follicular growth. Local production of VEGF may be important for mediating the GC-theca cell interaction required for antral follicle development. VEGF is associated with higher fertilization rate of mature oocytes. oocytes with positive fertilization had higher VEGF concentration (357.7±176.1) than negative fertilized oocytes 351.8±229.2 (p-value, 918) NS.

KEYWORDS:

Vascular endothelial growth factor Follicular fluid Oocytes and fertilization In vitro fertilization



INTRODUCTION

The development of an ovarian follicle from a small preantral follicle to a large preovulatory follicle, ovulation, and the formation of a corpus luteum (CL) after ovulation are key processes in the female reproductive cycle. These physiological processes are accompanied by marked changes in vasculature of the ovary (Kanzaki H., et al., 1982).

The ovary is distinctive in that it is a site of active angiogenesis, and the development of follicular microvasculature is regulated by angiogenic factors in the ovary (**Robinson RS.**, et al., **2009**)

A number of mediators induce angiogenesis, including members of the fibroblast growth factor (FGF) family, vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), tumor necrosis factor (TNF)-α, and members of the chemokine family (Yancopoulos GD., et al., 2000).

Substances participating in angiogenesis are often secreted or transported into the follicular fluid (FF), and several factors detected in human FF are suggested to play roles in the human ovary (**Kawano Y.**, *et al.*, **2003**).

The VEGF acts as a key angiogenic factor in the regulation of ovarian vascularization; vascular endothelial growth factor is a 46-kDa disulfide-linked homodimeric glycoprotein that stimulates vascular endothelial cell proliferation, migration, organization into tubules, and permeability (**Ferrara N.**, *et al.*, **1998**).

All types of VEGF are produced by GCs, predominantly VEGF121 and VEGF165. The VEGF121 and VEGF165 promote the proliferation of vascular endothelial cells and permeabilization of blood vessels (**Kamat BR.**, *et al.*, **1995**).

It is produced by the theca interna and granulosa cells (GCs) in the human ovary in the preovulatory phase.

In view of pleiotropic functions of VEGF, we hypothesized that this angiogenic factor was involved in the development of human ovarian follicles. In this study, we will measure the concentrations of VEGF in individual human preovulatory follicles and related them to follicular diameter and volume to clarify the role of these molecules in folliculogenesis and assess relation between concentration of VEGF and maturity of oocyte and fertilization rate.

AIM OF THE WORK

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Aim of this work is to examine the relationship between VEGF concentration in FF and diameter of mature oocytes and fertilization rate in patients undergoing IVF.