

**MEASUREMENT OF UTERINE ARTERY BLOOD FLOW,
SUB-ENDOMETRIAL BLOOD FLOW, ENDOMETRIAL
THICKNESS AND PATTERN BY 2D DOPPLER
ULTRASOUND ON THE DAY OF HCG INJECTION AS A
METHOD OF PREDICTING PREGNANCY IN ICSI
PROGRAM**

Thesis

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By

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ABSTRACT

Aim of the work:

To evaluate the role of endometrial thickness, pattern and sub-endometrial blood flows measured by 2D power Doppler ultrasound to predict pregnancy during IVF/ICSI treatment.

Patients and methods:

This was a prospective clinical study. A total of 70 infertile women were recruited from the Assisted Reproduction Technology unit of Ain Shams University Maternity Hospital during the period from September 2015 to April 2016. Women with male factor, tubal factor, ovarian factor and unexplained infertility were included in the study.

Results:

The mean age was 28.5 years and the mean duration of infertility is 6.1 years. Fifty eight (82.9%) patients had primary infertility and twelve (17.1%) had secondary infertility. The mean endometrial thickness was 11.9 mm. Sixty two women had triphasic pattern (88.6%), four women had isoechoic pattern (5.7%) and four had hyperechoic pattern (5.7%). On evaluating the sub-endometrial blood flow; the mean PI is 1.03, the mean RI is 0.63 and the mean S/D ratio is 2.51. The mean uterine a. PI is 2.18, the mean RI is 0.89, and the mean S/D ratio is 8.29. Overall, 32 (45.7%) patients conceived and in these women the endometrial pattern was triphasic and the mean sub-

endometrial PI was 0.96, and those were the statistically significant parameters.

Conclusion:

Endometrial pattern and sub-endometrial PI measured on the day of HCG injection have value in judging endometrial receptivity and predict the final outcome of IVF/ ICSI- ET. Other ultrasound and Doppler parameters did not differ between pregnant and non-pregnant patients in IVF/ICSI cycles, so they cannot predict the likelihood of pregnancy in stimulated cycles of IVF/ICSI.

KEYWORDS

Doppler;

Endometrial thickness;

Endometrial pattern;

Endometrial receptivity;

Endometrial blood flow;

In-vitro fertilization;

Intracytoplasmic sperm injection.

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List of Abbreviations

2D-TVUS	Two - dimensional transvaginal ultrasound
ACE	Association of Clinical Embryologists
AH	Assisted hatching
ART	Assisted Reproductive Technology
ASRM	American Society for Reproductive Medicine
BFS	British Fertility Society
BMI	Body mass index
CBAVD	Congenital bilateral absence of vas deferens
CC	Clomiphene citrate
COH	Controlled ovarian hyperstimulation
DET	Double embryo transfer
EE	Endometrial epithelium
EnP	Endometrial pattern
EnT	Endometrial thickness
eSET	Elective single embryo transfer
ET	Embryo transfer
FSH	Follicle stimulating hormone
GnRH	Gonadotropin-releasing hormone
GnRHa	Gonadotrophin - releasing hormone agonist
GnRH-ant	Gonadotrophin - releasing hormone antagonist

HB-EGF	Heparin-binding epidermal growth factor-like growth factor
HCG	Human Chorionic Gonadotropin
HFEA	Human Fertilisation and Embryology Authority
HIV	Human Immunodeficiency Virus
HMG	Human Menopausal Gonadotropin
HMG	Human menopausal gonadotropin
ICM	Inner cell mass
ICSI	Intracytoplasmic sperm injection
IGFBP-1	Insulin-like growth factor binding protein-1
IVF	In vitro fertilization
IVM	In vitro maturation
JZ	Junctional zone
LH	Luteinizing hormone
LIF	Leukemia Inhibitory Factor
MBR	Multiple birth rate
MDAs	Mullerian duct anomalies
NICE	National Institute for Health and Care Excellence
OAT	Oligoasthenoteratospermia
OHSS	Ovarian hyperstimulation syndrome
OPU	Ovum pick-up
OS	Ovarian stimulation
PAF	Platelet-activating factor

PAI	Plasminogen activator inhibitor
PDGF	Platelet-derived growth factor
PGD	Preimplantation genetic diagnosis
PI	Pulsatility index
PIF	Prolactin-inhibiting factor
PLCζ	Phospholipase C zeta
PR	Pregnancy rate
PRF	Pulse repetition frequency
PSV	Peak systolic velocity
RI	Resistance index
RIF	Recurrent implantation failure
ROC	Receiver operating characteristic
S/D	Systolic/Diastolic ratio
SART	Society for Assisted Reproductive Technology
SD	Standard deviation
TE	Trophoectoderm
TGF-β	Transforming Growth Factor beta
TNF-α	Tumor Necrosis Factor alpha
TSH	Thyroid-Stimulating Hormone
TVUS	Trans-vaginal ultrasound
USSR	Uterine scoring system for reproduction
VEGF	Vascular endothelial growth factor

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INTRODUCTION

In the menstrual cycle, the endometrium has no adhesive qualities until the implantation window phase, during which for a very short time, the endometrium allows the implantation of gestational sacs. This feature is referred to as endometrial receptivity. Endometrial receptivity has, for a long time, been the major focus in the field of assisted reproduction because the synchronous changes of the endometrium with embryonic development are the basis for embryonic implantation (*Wang et al., 2010*).

Favorable maternal conditions and embryo quality are important for successful implantation. Problems that can originate from the host environment include abnormal uterine anatomy, maternal medical conditions, and a non-receptive endometrium; all can have adverse effects on the cross-communication between the embryo and the endometrium. The endometrium is critical for successful implantation through interaction with the embryo. Endometrial embryo interactions can be altered if the embryo is defective, which can result from either paternal sperm factors or oocyte abnormalities (*Kim et al., 2014*).

To increase advantageous endometrial-embryo interactions, the endometrium must become thicker, with richer vascularity. Endometrial blood flow reflects uterine receptivity because the endometrium is the site of embryonic implantation (*Merce et al., 2008*). During in vitro fertilization (IVF) and embryo transfer (IVF-ET)

cycles, implantation is a major determinant of success or failure. Up to two-thirds of implantation failures are estimated to be caused by defects in endometrial receptivity (*Achache and Revel, 2006*).

Implantation failure remains an unsolved problem in reproductive medicine and is considered as a major cause of unexplained infertility in otherwise healthy couples. Indeed, the average implantation rate in IVF is around 25% (*de los Santos et al., 2003*). It is well established that embryos cannot implant in a poorly matured endometrium, and this may be responsible for low implantation rates with transfer of “good quality” embryos (*Aghajanova et al., 2008*).

Endometrial receptivity plays a key role in the establishment of a successful pregnancy, and its impairment may limit the success of assisted reproductive technologies. Histological, morphological, and functional aspects of the endometrium were investigated in order to establish a test to assess endometrial receptivity and consequently to better predict pregnancy outcomes (*Cakmak and Taylor, 2012*). Efforts have been made to evaluate endometrial receptivity in endometrial and sub-endometrial blood supplies, especially during intrauterine insemination and IVF-ET cycles (*Revel, 2012*). Past studies related to endometrial receptivity were mainly focused on histopathological investigation of the endometrium, presented as endometrial dating by "Noyes et al, 1975" dating (*Noyes et al., 1975*) or investigation of the receptors for estrogen, progesterone

and other known factors related to endometrial receptivity. However, the diagnostic methods used for the above studies were invasive and a waste of time, and entailed intrauterine biopsy were not accepted by patients, because they were worried about subsequent miscarriage, and thus lost their value in guiding the assessment of endometrial receptivity, in those who wanted to be pregnant in this cycle (*Wang et al., 2010*).

Ultrasound examination of the endometrium is a commonly used non-invasive method to assess endometrial receptivity during IVF treatment. A good blood supply towards the endometrium is usually considered to be an essential requirement for implantation and therefore assessment of endometrial blood flow in IVF treatment has attracted a lot of attention in recent years (*Ng et al., 2007*). Ultrasonographic examination is routinely performed in ART treatment because of accurate evaluation and noninvasive detection. Following the periodic stimulation of ovarian hormone, the changes in endometrial structure during the menstrual cycle can be identified easily by ultrasound examination (*Killick, 2007*).

Ultrasound parameters including endometrial thickness, endometrial pattern, endometrial volume, Doppler study of uterine arteries and endometrial blood flow have been used to assess endometrial receptivity during IVF treatment. Assessment of endometrial blood flow adds a physiological dimension to the anatomical ultrasound parameters. However, conflicting results are