OVARIAN RESERVE IN PELVIC ENDOMETRIOSIS

A thesis Submitted for fulfillment of
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By

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بسم الله الرحمن الرحيم

الْحَمْدُ لِلّهِ الَّذِي هَدَانَا لِهَذَا وَمَا كُنَّا
لِنَهْتَدِيَ لَوْلا أَنْ هَدَانَا اللّهُ

صدق الله العظيم

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Ibrahim Zewail

DEDICATION

TO MY

MOTHER,

FATHER

AND MY

FAMILY

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List of Abbreviations

AFC	antral follicle count
AFS	American fertility society
AMF	Anti Mullerian factor
AMH	Anti-Mullerian hormone
ART	Assisted reproductive technique
ASRM	American society of reproductive medicine
BMD	Bone marrow density
BMI	Body mass index
CA 19.9	Cancer antigen 19.9
CA-125	Cancer antigen-125
CCCT	Clomiphene citrate challenge test
CD2	Cycle day 2
CDC	Centers for Disease Control
COCP	Combined oral contraceptive pills
COH	Controlled ovarian hyperstimulation
COX-2	Cyclooxygenase type 2
CRF	Case record form
D&C	Dilatation and curettage
DMPA	Depot medroxyprogesterone acetate
DNA	Deoxy nucleic acid
DVD	Digital Versatile/Video Disc
E_2	Estradiol
EFI	Endometriosis fertility index
EFORT	Exogenous FSH ovarian reserve test
ELISA	Enzyme linked immunosorbent assay
FSH	Follicle stimulating hormone
GA	General anasthesia
GAST	Gonadotropin releasing hormone agonist stimulation test
GnRH	Gonadotrophin releasing hormone
GnRHa	Gonadotrophin releasing hormone analogue
hCG	Human chorionic gonadotrophin
HSG	hysterosalpingeogram
ICSI	Intracytoplasmic sperm injection
IL	Interleukin
IVF	In vitro fertilization
LFS	Least function score
LH	Luteinizing hormone
LNG-IUS	Levonorgestrel releasing intrauterine

	contraceptive device
MFD	mean follicular diameter
MIS	Mullerian inhibiting substance
MRI	Magnetic resonance imaging
NK	Natural killer
NSAIDs	Nonsteroidal antiinflammatory drugs
OCPs	Oral contraceptive pills
ORTs	Ovarian reserve tests
PCOS	Polycystic ovarian syndrome
PGE_2	Prostaglandin E_2
PP 14	Placental protein 14
PR	Pregnancy rate
PRL	Prolactin
PSV	Peak systolic velocity
rASRM	revised American society of reproductive medicine
RCTs	Randomized controlled trials
SD	Standard deviation
TCDD	Tetrachlorodibenzo-p-dioxin
TMB	tetramethylbenzidine
TNF	Tumor necrosis factor
TSH	Thyroid stimulating hormone
TVS	Transvaginal sonography
VEGF	Vascular endothelial growth factor
VOCAL	Virtual organ computer-aided analysis

Introduction

Introduction:

Endometriosis is characterised by the presence, outside the endometrial cavity, of tissue that is morphologically and biologically similar to normal endometrium. This ectopic endometrial tissue responds to ovarian hormones undergoing cyclical changes similar to those seen in eutopic endometrium. The cyclical bleeding from endometriotic deposits appears to contribute to the induction of an inflammatory reaction and fibrous adhesion formation, and in the case of deep ovarian implants, leads to the formation of endometriomas or chocolate cysts ***(Caroline et al., 2007a).***The current prevalence of endometriosis is estimated to be up to 10% ***(Vigano et al., 2004).*** The incidence has not increased in the last 30 years and remains at 2.37–2.49 per 1000 women per year, equating to an approximate prevalence of 6–8% ***(Hummelshoj et al., 2006).***

The main clinical symptoms of endometriosis are infertility, dysmenorrhoea, dyspareunia, dyschezia and chronic pelvic pain (defined as pain of greater than 6 months duration and not cyclical in nature)***(Treloar et al., 2005a).***The gold standard for diagnosing endometriosis in the abdomen and pelvis is the visual identification of characteristic lesions at laparoscopy. In one study, this means of diagnosis was shown to be 97% sensitive and 77% specific ***(Buchweitz et al., 2003).*** During laparoscopy of the pelvis, a scoring system is often used to assess the severity of the disease. The most commonly used is the American Society of Reproductive Medicine system (rASRM score) which grades endometriosis as minimal

(stage 1), mild (stage 2), moderate (stage 3) and severe (stage 4) ***(Chapron et al., 2003a).***

Although many hypotheses exist to explain the condition between endometriosis and infertility, the precise mechanisms by which endometriosis leads to infertility remain unclear. While more extensive endometriosis may simply impair fertility by mechanical means, hypotheses concerning subtler forms of endometriosis have suggested that infertility is impaired due to disruption of ovum transport, interference with hormone support, ovulation dysfunction, detrimental effects on gametes and/or reduced granulosa cell steroidogenesis ***(Toya et al., 2000).***

Reduced granulose cell steroidogenesis has also been noted with diminished ovarian reserve ***(Toya et al., 2000).*** To evaluate the ovarian follicular status, classically, early follicular phase serum FSH, inhibin B, and E_2 levels have been measured. However, the usefulness of those measurements and its clinical utility is limited ***(Broekmans et al., 2006).*** In addition, the assessment of the number of antral follicles by ultrasonography may predict the number of retrieved oocytes after controlled ovarian hyperstimulation (COH) ***(Hendriks et al., 2005a).***

Anti-Mullerian hormone (AMH) is produced by small, early antral follicles and was strongly connected to the number of small antral follicles than FSH, E_2, and even inhibin B levels ***(Fanchin et al., 2003a).*** In vivo and in vitro studies

showed that AMH has an inhibitory effect on primordial follicle recruitment and it decreases the sensitivity of follicles for the FSH-dependent selection for dominance. Besides its functional role in the ovary, serum AMH level serves as an excellent candidate marker of ovarian reserve ***(Visser et al., 2006).*** In addition, AMH is a marker for ovarian reserve and, as previously demonstrated, a better predictor of the number of early antral follicles as FSH, inhibin B, E_2, and LH ***(Eldar-Geva et al., 2005).***

Patients with minimal/mild endometriosis present a decreased serum AMH level. In addition, the follicular cohort in those patients was heterogeneous compared to infertile patients with tubal obstruction. This finding may be associated with poorer results in terms of COH. Our data is the first direct evidence showing an important role of endometriosis in the follicular status and ovarian reserve, which could explain the subfertility in this group of patients ***(Lemos et al., 2008).***

The association of elevated cycle day 3 E_2 and/or FSH levels with stage III/IV endometriosis, suggesting a reduction in ovarian reserve, is an important consideration in the management of infertility patients with endometriosis ***(Hock et al., 2001).***The laparoscopic excision of ovarian endometriotic cysts is associated with a statistically significant reduction in ovarian reserve, which is partly a consequence of the damage to the ovarian vascular system ***(Li et al., 2009).***

Aim of Work