HORMONAL PROFILE OF THE PERITONEAL FLUID IN FEMALES WITH UNEXPLAINED INFERTILITY A COMPARATIVE STUDY

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

By

ABEER MAHMOUD EL-SAYED SULTAN
M.B.B.Ch . 1986 Ain Shams University
M.Sc. (Ob/Gyn) l993 Ain Shams University

Supervised by

Prof. Dr. HAZEM AMIN EL ZENEINY
Professor of Obstetrics and Gynaecology
Faculty of Medicine
Ain shams University

Prof. Dr. AHMED RAMY MOHAMED RAMY
Prof. of Obstetrics and Gynaecology
Faculty of Medicine
Ain Shams University

Ass. Prof. HESHAM MAHMOUD MOHAMMED HARB
Assistant Prof. of Obstetrics and Gynaecology
Faculty of Medicine
Ain Shams University

Prof. Dr. DALIA HELMI MOHAMED FARAG
Professor of Clinical Pathology
Faculty of Medicine
Ain Shams University

2005

HORMONAL PROFILE OF THE PERITONEAL FLUID IN FEMALES WITH UNEXPLAINED INFERTILITY A COMPARATIVE STUDY

A Thesis Submitted for Partial Fulfillment of M.D. Degree in Obstetrics and Gynaecology

By

ABEER MAHMOUD EL-SAYED SULTAN
M.B.B.Ch . 1986 Ain Shams University
M.Sc. (Ob/Gyn) l993 Ain Shams University

Supervised by

Prof. Dr. HAZEM AMIN EL ZENEINY
Prof. of Obstetrics and Gynaecology
Faculty of Medicine
Ain shams University

Prof. Dr. AHMED RAMY MOHAMED RAMY
Prof. of Obstetrics and Gynaecology
Faculty of Medicine
Ain Shams University

Ass. Prof. HESHAM MAHMOUD MOHAMMED HARB
Assistant Prof. of Obstetrics and Gynaecology
Faculty of Medicine
Ain Shams University

Prof. Dr. DALIA HELMI MOHAMED FARAG
Professor of Clinical Pathology
Faculty of Medicine
Ain Shams University

2005

Acknowledgement

I would like to express my deepest appreciation and extreme gratitude to Professor. Hazem Amin El Zeneiny, Professor of Obstetrics and Gynecology, Ain Shams University for his continuous supervision and valuable guidance throughout the work of this study.

I would like to express my supreme appreciation and sincere thanks to Professor Dr. Ahmed Ramy Mohamed Ramy, Professor of Gynecology and Obstetrics, Ain Shams University for his great support and continuous help.

I wish to express my deep gratitude and thanks to Dr. Hesham Mahmoud Mohamed Harb Assistant Professor of Gynecology and Obstetrics, Ain Shams University for his valuable help and continuous encouragement.

I am especially indebted to Professor Dalia Helmi Mohamed Farag, Professor of Clinical Pathology, Ain Shams University for her invaluable participation, continuous guidance and support althrough the analytical part of the study.

Finally, I would like to express my deep thanks and gratitude to all members of Endoscopy unit, Ain Shams University for their help during conduction the practical part of this study

LIST OF ABBREVIATIONS

AFS	American Fertility Society
APA	Anti-phospholipids antibody
ART	Assisted reproductive Technologies
ASABs	Antisperm Antibodies
CC	Clomiphene citrate
DNA	Deoxy-ribonucleic Acid
CI	Cervical Insemination
CL	Corpus Luteum
COH	Controlled Ovarian Hyperstimulation
DHEAS	Dihydro ethyl androstendion
DZPIAR	Disorder in Zona Pellucida-Induced Acrosome Reaction.
E	Estrogen
E2	Estradiol
ebaf	Endometrial bleeding associated factor
FF	Follicular Fluid
FFP	Follicular fluid progesterone
FSH	Follicle stimulating hormone
FSP	Fallopian Tube Sperm Perfusion
G	Granulosa cell
HA	Hyperactivation
HCG	Human chorionic gonadotropin
HSG	Hystrosalpingography
HyCoSy	Hysterosalpingo contrast Sonography
HZA	Hemizona assay
ICSI	Intracytoplasmic sperm injection
Ig	Immunoglobulin
IGF II	Insulin-like growth factor II
IgG	Immunoglobulin G
IL-1	Interleukin-1

IL-1B	Interleukin-1B
IL-6	Interleukin 6
IL-8	Interleukin-8
INF-*g*	Interferon-Gamma
IVF	In-vitro fertilization
IVF.ET	In-vitro fertilization with embryo transfer
IUI	Intra Uterine Insemination
LDL	Low density lipoprotein
LH	Lutenizing hormone
LP	Late-proliferative phase
LPC	Lysophosphatedyle choline
LPD	Luteal Phase Defect
LPS	Lipopolysaccharides
LUF	Lutenized unruptured follicle
MHC	Major histocompetability complex
MMPs	Matrix metalloproteinases
MMP2-P	Matrix metalloproteinases-2-progesteron.
MMP9	Matrix metalloproteinases-9
MP	Mid-proliferative phase
MPs	Macrophages
MRI	Magnetic resonance imaging
NK	Natural killer
NNT	Number needed to treat
OHSS	Ovarian hyper stimulation syndrome
OSCM	Oil-soluble Contrast Media
P	Progesterone
PCT	Post-coital Test
PF	Peritoneal Fluid
PFE2	Peritoneal Fluid Estradiol
PFP	Peritoneal Fluid Progesterone
PF-PRL	Peritoneal Fluid Prolactin
PFV	Peritoneal Fluid Volume

PGs	Prostaglandins
PM	Peritoneal Macrophages
POF	Premature Ovarian Failure
PRL	Prolactin
PRLR	Prolactin Receptors
RANTES	Regulated on activation, normal T cell expressed and secreted.
RIA	Radioimmunoassay
SHBG	Steroid Hormone Binding Globulin
SHG	Sonohysterography
SP	Serum Progesterone
SPA	Sperm Penetration Assay
Sprms	Selective Progesteron Receptors modulators
STAR	Steroidogenic Acute Regulatory Protein
SSG	Sonosalpingography
STC	Selective Tubal Catheterization
T	Testosterone
TIMP-l mRNA	Tissue inhibitor metalloproteinase-1 mRNA
TNFa	Tumor Necrosis Factor-alpha
TRH	Thyrotropin Releasing Hormone
U/S	Ultrasonography
VEGF	Vascular Endothelial Growth Factor
VEGF-A	Vascular Endothelial Growth Factor Antagonist
WHO	World Health Organization
WSCM	Water-soluble Contrast Media
ZP	Zona Pellucida

LIST OF CONTENTS

ITEMS	Page
INTRODUCTION	1
AIM OF THE WORK	3
REVIEW OF LITERATURE	4
- Unexplained infertility	4
- Auto antibodies in unexplained infertility	26
- Tubal abnormalities in women with unexplained infertility	35
- The role of laparoscopy in unexplained infertility	45
- The role of hysteroscopy in unexplained infertility	51
- Options for unexplained infertility	59
- Peritoneal fluid	63
- Possible mechanism by which peritoneal fluid constituent may cause infertility	74
- Steroid hormones in the peritoneal fluid	89
- The relation between steroid hormones, endometriosis and unexplained infertility	102
- Prolactin hormone	111
PATIENTS AND METHODS	120
RESULTS	126
DISCUSSION	165
SUMMARY	182
CONCLUSION	186
RECOMMENDATION	187
REFERENCES	188
ARABIC SUMMARY	-

LIST OF CONTENTS

ITEMS	Page
INTRODUCTION	1
AIM OF THE WORK	3
REVIEW OF LITERATURE	4
- Unexplained infertility	4
- Auto antibodies in unexplained infertility	26
- Tubal abnormalities in women with unexplained infertility	35
- The role of laparoscopy in unexplained infertility	45
- The role of hysteroscopy in unexplained infertility	51
- Options for unexplained infertility	59
- Peritoneal fluid	63
- Possible mechanism by which peritoneal fluid constituent may cause infertility	74
- Steroid hormones in the peritoneal fluid	89
- The relation between steroid hormones, endometriosis and unexplained infertility	102
- Prolactin hormone	111
PATIENTS AND METHODS	120
RESULTS	126
DISCUSSION	165
SUMMARY	182
CONCLUSION	186
RECOMMENDATION	187
REFERENCES	188
ARABIC SUMMARY	-

LIST OF FIGURE

Fig. No.	Title	Pages
1	Age distribution of 30 patients of unexplained infertility and 30 controls.	131
2	Age distribution of 30 patients of unexplained infertility according to their percentage of age.	133
3	Distribution of 30 patients with unexplained infertility according to their type of infertility.	135
4	Distribution of 30 patients with unexplained infertility according to the period of infertility.	137
5	Serum E2 level among patients and controls.	139
6	Peritoneal fluid E2 among patients and controls.	141
7	Serum progesterone level among patients and controls.	143
8	Peritoneal fluid progesterone among patients and controls.	145
9	Serum prolactin among patients and controls.	147
10	Peritoneal fluid prolactin among patients and controls.	149
11	Correlation coefficient of serum prolactin with peritoneal fluid prolactin among 30 patients with unexplained infertility.	150
12	Correlation coefficient of serum prolactin with peritoneal fluid prolactin among controls.	151
13	Correlation coefficient of peritoneal fluid Estrogen with peritoneal fluid prolactin among 30 patients.	152
14	Correlation coefficient of peritoneal fluid E2 and peritoneal fluid prolactin among controls.	153

15	**Correlation coefficient of serum prolactin with peritoneal fluid estrogen among 30 patients of unexplained infertility.**	**154**
16	**Correlation coefficient of serum prolactin with peritoneal fluid E2 among controls.**	**155**
17	**Correlation coefficient of serum progesterone with peritoneal fluid progesterone among 30 patients with unexplained infertility.**	**156**
18	**Correlation coefficient of serum progesterone with peritoneal fluid estrogen among 30 patients with unexplained infertility.**	**157**
19	**Correlation coefficient of serum E2 with peritoneal fluid E2 among 30 patients with unexplained infertility.**	**158**
20	**Correlation coefficient of peritoneal fluid progesterone with serum E2 among 30 patients with unexplained infertility.**	**159**
21	**Correlation coefficient of serum progesterone and peritoneal fluid progesterone among 30 patients.**	**160**
22	**Correlation coefficient of serum progesterone with serum E2 among 30 patients with unexplained infertility.**	**161**
23	**Correlation coefficient of serum prolactin with serum E2 among 30 patients with unexplained infertility.**	**162**
24	**Correlation coefficient of serum progesterone with peritoneal fluid prolactin among 30 patients with unexplained infertility.**	**163**
25	**Correlation coefficient of peritoneal fluid prolactin with peritoneal fluid progesterone among 30 patients with unexplained infertility.**	**164**

LIST OF TABLES

Table No.	Title	Pages
1	Age distribution of 30 patients of unexplained infertility and 30 controls.	130
2	Age distribution of 30 patients of unexplained infertility according to their percentage of age	132
3	Distribution of 30 patients with unexplained infertility according to their type of infertility	134
4	Distribution of 30 patients with unexplained infertility according to their period of infertility	136
5	Comparison between 30 patients of unexplained infertility and 30 controls regarding serum level of Estrogen.	138
6	Comparison between 30 patients of unexplained infertility and 30 controls regarding the level of peritoneal fluid Estrogen.	140
7	Comparison between 30 patients of unexplained infertility and 30 controls regarding serum level of Progesterone.	142
8	Comparison between 30 patients of unexplained infertility and 30 controls regarding the level of peritoneal fluid Progesterone.	144
9	Comparison between 30 patients of unexplained infertility and 30 controls regarding serum level of Prolactin.	146
10	Comparison between 30 patients of unexplained infertility and 30 controls regarding the level of peritoneal fluid Prolactin.	148

INTRODUCTION

The presence of peritoneal fluid in normal women was described by ***Novak (1922)***. Recently very high steroid hormone concentrations were detected during the luteal phase in peritoneal fluid ***(Koninckx et al., l980a).***

Peritoneal fluid is considered to be an ovarian exudate and a hormonally active ovary is the major determinant of the peritoneal secretion ***(Donnez et al., 1982),*** which is strongly supported by the higher concentrations of ovarian steroid hormones in that fluid than in plasma.

The peritoneal environment has been recognized as a dynamic zone of gamete interaction that may be of relevance in early study of sperm and oocyte transport, fertilization and early embryo cleavage ***(Oral et al., 1996).***

Further exploration of this compartment with better understanding of normal and abnormal events in this pelvic microenvironment rationales for novel treatment modalities ***(Kim and Hornstein, 1997).***

For about three out of four couples with problems of conceiving (75%), discussion with a doctor and/or medical tests will show what is preventing pregnancy, while other couples who have not been able to conceive naturally, are said to have unexplained infertility ***(Randolph and Jr, 2000).***

Unexplained infertility does not mean there is no physical explanation for the infertility, but just that medical tests have not identified any specific problem ***(Cahill and Wardle, 2002).***

The laparoscope is one of the greatest developments in gynecologic instrumentation. It is indicated as the last test in the evaluation of infertility when the medical history and routine investigations directs the attention to a pelvic factor as the cause of unexplained infertility ***(Speroff et al., 2005).***

Utilization of laparoscopic procedures in evaluating patients with unexplained infertility could be expanded to sampling peritoneal fluid in this group of patients. Studying levels of steroid hormones in the peritoneal fluid could prove helpful in the direction of attempting to throw light on the overt basic etiologic factors behind unexplained infertility in a subgroup of these patients.