

# **The role of subendometrial microvascularization and uterine artery blood flow changes in IUD-induced side effects**

A THESIS

SUBMITTED FOR PARTIAL FULFILLMENT OF MD DEGREE  
IN OBSTETRICS AND GYNECOLOGY

**By**

**Marwa Radwan Abbass Shahin**

M.B., B.Ch – Ain Shams University – 2001

M.Sc. Obstetrics and Gynecology – Ain Shams University – 2007

Specialist of Obstetrics and Gynecology– El Galaa Teaching Hospital

**Under Supervision of**

**Prof. Dr. Mohamed Alaa Mohy El-Din EL-Ghannam**

*Professor* and Head of the Department Of obstetrics and gynecology

Faculty of medicine

Ain-Shams University

**Prof. Tamer Ahmed El-Refaie**

Assistant Professor in obstetrics and gynecology

Faculty of medicine

Ain-Shams University

**Ain Shams University – Cairo**

**2015**

## *Acknowledgement*

*First and foremost, I Thank **Allah** who granted me the strength to accomplish this work,*

*Words do fail to express my deepest gratitude and appreciation to **Prof. Dr. Mohamed Alaa Mohy El-Din EL-Ghannam**, Professor and Head of the Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his generous supervision, keen interest, excellent guidance and powerful support. I really consider myself very fortunate that I worked under his generous supervision.*

*Words can never express my deep gratitude and sincere consideration to **Dr. Tamer Ahmed El-Refaie**, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his valuable instructions and meticulous advices.*

*My deepest thanks and appreciation go to **Prof. Dr. Karim Ahmed Wahba**, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his valuable instructions, kind support, meticulous advices and expert touches.*

*I would like to express my deepest thanks and sincere gratitude to **Prof. Adel Shafik Salah El-Din**, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his continuous guidance and instructions. His effort is most truly appreciated. Without his keen guidance, it would have never been possible to accomplish this work,*

*I would also like to truly thank each and every person who gave me a hand in accomplishing this work especially my kind subjects who were so cooperative till the end of the study.*

*Last but not least, my true affection and love goes to all my family members, who were, and will always be, by my side and without whom I would have never been able to accomplish this work. Their love, patience and support are most appreciated.*

***Marwa Radwan Shahin***

# List of Contents

Title	Page
<i>List of abbreviations .....</i>	
<i>List of tables.....</i>	
<i>List of figures .....</i>	
<i>Protocol .....</i>	
• <b>Introduction .....</b>	<b>1</b>
• <b>Aim of the Work.....</b>	<b>4</b>
• <b>Review of literature:</b>	
- The endometrium .....	5
- Doppler Ultrasound.....	14
- Intrauterine Device.....	33
• <b>Patients and Methods.....</b>	<b>49</b>
• <b>Results .....</b>	<b>55</b>
• <b>Discussion.....</b>	<b>78</b>
• <b>Summary .....</b>	<b>90</b>
• <b>Conclusion and Recommendations .....</b>	<b>94</b>
• <b>References.....</b>	<b>96</b>
• <b>Arabic Summary.....</b>	<b>--</b>

## List of Abbreviations

°	Degree
<b>BMI</b>	Body Mass Index
<b>cm</b>	centimeter
<b>dB</b>	Decibels
<b>ECM</b>	Extracellular Matrix
<b>EnSCs</b>	Endometrial Stem Cells
<b>FI</b>	Flow Index
<b>Hz</b>	Hertz
<b>IUD</b>	Intrauterine Device
<b>IVF</b>	In-Vitro Fertilization
<b>kHz</b>	kiloHertz
<b>LNG</b>	Levonorgestrel
<b>LNG-14 IUD</b>	Skyla® IUD
<b>LNG-20 IUD</b>	Mirena® IUD
<b>mcg</b>	microgram
<b>mg</b>	milligram
<b>MHz</b>	Megahertz
<b>mm</b>	millimeter
<b>MMP</b>	Matrix Metalloproteinase
<b>MSCs</b>	Endometrial Mesenchymal Stem Cells
<b>PDE</b>	Power Doppler Energy
<b>PI</b>	Pulsatility Index
<b>PID</b>	Pelvic Inflammatory Disease
<b>PIF</b>	Fourier Pulsatility Index
<b>PPI</b>	Peak To Peak Pulsatility Index
<b>PZT</b>	Lead Zirconate Titante
<b>RI</b>	Resistive Index
<b>S/D</b>	Systolic/Diastolic Ratio
<b>SD</b>	Standard Deviation
<b>TAMV</b>	Time Averaged Maximum Velocity
<b>VFI</b>	Vascularization Flow Index
<b>VI</b>	Vascularization Index



## List of Tables

<b>Number</b>	<b>Title</b>	<b>Page</b>
Table(1):	Demographic Data of Included Women.	55
Table(2):	Initial Mid luteal Endometrial Thickness and Subendometrial Vascular RI and PI in Included Women.	58
Table(3):	Post-Insertion Mid-luteal Endometrial Thickness and Subendometrial Vascular RI and PI in Included Women.	58
Table(4):	Difference between Initial and Post-Insertion Mid-luteal Endometrial Thickness and Subendometrial Vascular RI and PI in Included Women.	59
Table(5):	Subendometrial RI and PI $\Delta$ Percentage in Included Women.	62
Table(6):	IUCD-related Side Effects in Included Women.	63
Table(7):	Difference between Groups regarding Demographic Data.	65
Table(8):	Difference between Groups regarding Initial Sonographic Parameters.	67

## List of Tables (cont.)

<b>Number</b>	<b>Title</b>	<b>Page</b>
Table(9):	Difference between Groups regarding Post-Insertion Sonographic Parameters.	69
Table(10):	Difference between Groups regarding Subendometrial RI and PI $\Delta$ Percentages.	71
Table(11):	Difference between Groups regarding PDE Category of Subendometrial blood flow.	73
Table(12):	Association between Measured Variables and IUCD-related Side Effects.	74
Table(13):	Association between IUCD-related Side Effects and PDE Category of Subendometrial blood flow.	75



## List of Figures

<b>Number</b>	<b>Title</b>	<b>Page</b>
Figure (1):	The Endometrium.	6
Figure (2)	Normal secretory phase endometrium.	7
Figure (3):	Menstrual endometrium.	8
Figure (4):	The relevance of menstrual physiology.	13
Figure (5):	Waveform type C.	21
Figure (6):	Waveform type A.	21
Figure (7):	Waveform type B.	22
Figure (8):	Waveform type 0.	22
Figure (9):	Placement of intrauterine devices (IUDs).	34
Figure (10):	Bar-Chart showing Age Distribution in Included Women.	56
Figure (11):	Bar-Chart showing Parity Distribution in Included Women.	56
Figure (12):	Bar-Chart showing Weight Distribution in Included Women.	57

## List of Figures (Cont.)

Number	Title	Page
Figure (13):	Bar-Chart showing BMI Distribution in Included Women.	57
Figure (14):	Box-Plot Chart showing Difference between Initial and Post-Insertion Mid-luteal Endometrial Thickness in Included Women	60
Figure (15):	Box-Plot Chart showing Difference between Initial and Post-Insertion Mid-luteal Subendometrial Vascular RI in Included Women.	60
Figure (16):	Box-Plot Chart showing Difference between Initial and Post-Insertion Mid-luteal Subendometrial Vascular PI in Included Women	61
Figure (17):	Box-Plot Chart showing Subendometrial RI and PI $\Delta$ Percentage in Included Women	62
Figure (18):	Pie-Chart showing Categories Subendometrial RI and PI $\Delta$ Percentage in Included Women.	63
Figure (19):	Bar-Chart showing IUCD-related Side Effects in Included Women.	64
Figure (20):	Box-Plot Chart showing Difference between Groups regarding Age.	65

## List of Figures (Cont.)

<b>Number</b>	<b>Title</b>	<b>Page</b>
Figure (21):	Box-Plot Chart showing Difference between Groups regarding weight.	66
Figure (22):	Box-Plot Chart showing Difference between Groups regarding BMI.	66
Figure (23):	Box-Plot Chart showing Difference between Groups regarding Initial endometrial thickness.	67
Figure (24):	Box-Plot Chart showing Difference between Groups regarding Initial Subendometrial RI.	68
Figure (25):	Box-Plot Chart showing Difference between Groups regarding Initial Subendometrial PI	68
Figure (26):	Box-Plot Chart showing Difference between Groups regarding Post-Insertion Endometrial Thickness.	70
Figure (27):	Box-Plot Chart showing Difference between Groups regarding Post-Insertion Subendometrial RI.	70
Figure (28):	Box-Plot Chart showing Difference between Groups regarding Post-Insertion Subendometrial PI.	71

## List of Figures (Cont.)

Number	Title	Page
Figure (29):	Box-Plot Chart showing Difference between Groups regarding Subendometrial RI $\Delta$ Percentages.	72
Figure (30):	Box-Plot Chart showing Difference between Groups regarding Subendometrial PI $\Delta$ Percentages.	72
Figure (31):	Bar-Chart showing Difference between Groups regarding PDE Category of Subendometrial blood flow.	73
Figure (32):	Bar-Chart showing Association between IUCD-related Pain and PDE Category of Subendometrial blood flow.	75
Figure (33):	Bar-Chart showing Association between IUCD-related Bleeding and PDE Category of Subendometrial blood flow.	76
Figure (34):	Bar-Chart showing Association between IUCD-related pain and PDE Category of Subendometrial blood flow.	76
Figure (35):	Bar-Chart showing Association between Severe IUCD-related Side Effects and PDE Category of Subendometrial blood flow.	77

# **The role of subendometrial microvascularization and uterine artery blood flow changes in IUD-induced side effects**

A PROTOCOL OF THESIS  
SUBMITTED FOR PARTIAL FULFILLMENT OF MD DEGREE  
IN OBSTETRICS AND GYNECOLOGY

**By**

**Marwa Radwan Abbass Shahin**

M.B., B.Ch – Ain Shams University – 2001

M.Sc. Obstetrics and Gynecology – Ain Shams University – 2007

Specialist of Obstetrics and Gynecology– Galaa Teaching Hospital

**Under Supervision of**

**Prof. Dr. Mohamed Alaa Mohy El-Din EL-Ghannam**

*Professor Of obstetrics and gynecology*

*Faculty of medicine*

*Ain-Shams University*

**Dr. Tamer Ahmed El-Refaie**

*Lecturer in obstetrics and gynecology*

*Faculty of medicine*

*Ain-Shams University*

**Ain Shams University – Cairo**

**2010**

## INTRODUCTION

Intrauterine devices (IUDs) are one of the world's most popular methods of reversible birth control. The IUD is a foreign body that is placed in the uterine cavity to prevent pregnancy. Most types of IUDs have a plastic T-shaped frame that is wrapped with copper and/or copper bands. The contraceptive effects of IUDs may be due to a sterile inflammatory reaction in the endometrial cavity which interferes with sperm function, so that fertilization is less likely to occur. IUDs also interfere with implantation but the extent to which this contributes to their contraceptive action is unknown. An IUD is usually used for 3-5 years because it increases the risk of PID with longer duration of use (*Kalmantis et al., 2009*).

Copper intrauterine devices (IUDs), first marketed in the early 1970s, represent an important contraceptive option for 150 million women worldwide. The method is safe, rapidly reversible, inexpensive, highly effective, long-acting and non-hormonal; these attributes make it unique and desirable for many users (*Sivin, 2007*).

During 5 years of IUD use, pregnancy occurs in less than 2 per 100 insertions. Bleeding and pain are the most common

reasons for removal rates of 10% in the first year and up to 50% within 5 years. In nulliparous women rates of expulsion and removal for bleeding and/or pain are higher than in parous women. Effective use of IUDs for up to 10 years has the same pregnancy rate as tubal interruption. Thus, the IUD may be an alternative to female sterilization, especially in younger women who are more likely to experience regret after sterilization (*ESHRE, 2008*). Infection risk is a relative contraindication to fitting any woman with an IUD, it is only present for a few weeks after insertion and probably arises from an undiagnosed cervical infection at the time of insertion. The risk of developing PID following IUD insertion is less than 1% when the risk of sexually transmitted disease is low, as in women who are in a stable, monogamous relationship (*Grimes et al., 2007*).

However, increased bleeding and pain cause up to 10% of users to have the device removed within the first year; still higher percentages tolerate some level of these side effects yet retain use of the method (*Hubacher et al., 2006*). In one study, 67% of women using the TCu380A complained about menstrual side effects within the first year of use. Anecdotal information accumulated from clinicians and some published information suggests that side effects from the copper IUD decrease over time (*Suvisaari and Lahteenmaki, 1996*).