Retrospective Analysis of Hysteroscopic and Histopathologic Diagnosis in Egyptian Women Presented with Abnormal Uterine Bleeding

Thesis

Submitted for Partial Fulfillment of Master Degree
Of Pathology

By

Naema Mohamed Almabrouk *M.B.B.Ch.*

Under Supervision of

Prof. Dr. Amira Khalifa Ismail

Professor of Pathology
Faculty of medicine Ain - Shams University

Prof. Dr. Magda Mohamed Abdulsalam

Professor of Pathology

Faculty of Medicine Ain - Shams University

Dr. Rola Mohamed Farid

Assistant Professor of Pathology Faculty of Medicine - Ain - Shams University

Faculty of Medicine
Ain - Shams University
2017



سورة التوبة الآية (١٠٥)

Aeknowledgment |

- After all my thanks to Allah for helping me to complete this work and forever, I would like to express my gratidude to Prof. Dr. Amira Khalifa Ismail, Professor of Pathology, Ain shams University for her great support and her encouragement.
- Dery special thanks to **Dr. Magda Mohamed**Abdulsalam, Professor of Pathology, Ain shams

 University for her valuable time and effort in reviewing this work and her useful advice till the last word of this work.
- I am also grateful to **Dr. Rola Mohamed Farid**, Assistant Professor of Pathology, Ain shams University for her proper advice and tender care.
- I can not forget to offer many thanks to my mother, father and my husband for their support until I finish this work.
- Finally, I would like to thank all staff members in the pathology department, Ain shams University and Early Cancer Detection Unit, Maternity Hospital, for their kind care throughout this work.

A Maema Mohamed



Contents

Subjects	Page
List of Abbreviation	I
List of Tables	III
List of Figures	V
Introduction	1
Aim of the work	3
Review of literature	4
Materials and Methods	73
Results	77
Discussion	104
Summary and conclusion	117
References	122
Arabic summary	

List of Abbreviations

APTT : Activated partial thromboplastin time

AUB : Abnormal uterine bleeding

BhCG : Beta human chorionic gonadotropin

CBC : Complete blood count

CK20 : Cytokinase 20

CK7 : Cytokeratin 7

CT : Computerized tomography

CTNNB1 : Catenin beta

EIN-Endometrial: Endometrial intra-epithelial neoplasia

intra

EMZ : Endometrial myometrial zone

ER : Estrogen receptor

ESGE : European Society of Gynecological Endoscopy

FIGO : International Federation of Gynecology and

Obstetrics

FSH : Follicle stimulating hormone

KRAS-V : -Kirsten rat sarcoma viral oncogene homolog

LFT: Liver function test

LH : Leutinizing hormone

MMPs : Matrix metallo-proteinases

MRI : Magnetic resonance imaging---

P16 : Proteinase inhibitor

PAX2 : Paired-Box containing

PI3K-AKT: Phosphatidylinositol 3-kinase

PIK3 CA : Phosphatidylinositol-3-kinase, Catalytic, Alpha

E List of Abbreviations &

polypeptide

PT : prothrombin time

PTEN: Phosphate and tensin homolog

PTT : Partial thromboplastin time

RIDIA : AT-rich interactive domain containing protein

1A

S.Ferritin : Serum ferritin

S.Iron : Serum iron

SIS : Saline infusion sonography

TIBC: Total iron binding capacity

TP53- : Tumor protein

TSH : Thyroid stimulating hormone

TVUS : Trans-vaginal ultrasonography

Von Willebrand: Von Willebrand factor antigen

factor Ag

WHO : World Health Organization

List of Tables

Tables	Title	Page
No.	Tiue	
1	WHO classification of endometrial	43
	hyperplasias	
2	TNM staging of endometrial cancer	53
3	Age and obstetric history of patients	78
4	Clinical presentation	79
5	Prevalence of different hystroscopic	81
	findings:	
6	Prevalence of different pathologic results	82
7	Validity of hysteroscopy for diagnosis of	84
	endometrial polyp	
8	Pathology of endometrial polyps which	86
	diagnosed by hysteroscopy	
9	Validity of hysteroscopy for diagnosis of	87
	Leiomyoma:	
10	Histopathological diagnoses of leiomyoma	88
11	Validity of hysteroscopy for diagnosis of	89
	endometrial hyperplasia	
12	Histopathological diagnoses of endometrial	90
	hyperplasia	
13	Distribution of endometrial hyperplasia	91

🕏 List of Tables 🗷

Tables	T:410	Page
No.	Title	No.
14	Validity of hysteroscopy for diagnosis of	93
	endometrial malignancy	
15	Histopathology of abnormal polypoid tissue	94
16	Hysteroscopic appearance of malignancy	95
17	Distribution of uterine malignancy	96
	according to histopathologic types	
18	Distribution of cases of endometrioid	97
	adenocarcinoma according to grading	
19	Histopathology of congested endometrium	98
20	Histopathology of atrophic (thin)	98
	endometrium	
21	Histopathology of endometrium with no	99
	gross pathology	

List of Figures

Figures No.	Title	Page No.
1	Clinical Presentation.	79
2	Prevalence of different hystroscopic findings	81
	munigs	
3	Prevalence of different pathologic results	83
4	Distribution of endometrial hyperplasia	92
5	Hysteroscopic appearance of malignancy	95
6	Histopathological types of malignancy	96
7	Grading of endometrioid adenocarcinoma	97
8	Chronic non-specific endometritis.	100
9	Disordered proliferative endometrium.	100
10	Endometrial polyp	101
11	Simple endometrial hyperplasia	101
12	Complex atypical endometrial hyperplasia	102
13	Endometrioid adenocarcinoma	102
14	Clear cell carcinoma	103

Introduction

Hysteroscopy is an endoscopic procedure by which the uterine cavity can be visualized directly (*Clark et al.*, 2002).

It helps in evaluation of endometrial cavity that is before could be only reached by dilation and curettage (brooks and Serden, 1988 and Vallie et al., 1988).

Hysteroscopy is the best way for exploration of endometrium in cases of abnormal uterine bleeding (*Garuti* et al., 2001), which defined as any bleeding, its amount, duration or frequency is increased for individual patient.

This bleeding is the main cause for more than one third of gynecologic consultations and about two thirds of hysterectomies (*Hillard*, 2005).

In predicting endometrial histopathology, *Garuti et al.*, *2001* have estimated that the sensitivity of hysteroscopy is 94.2 % and the specificity is 88.8 %. The incidence of focal uterine lesions in patients with abnormal uterine bleeding is about 74%.

Accordingly to that hysteroscopy accompanied by endometrial biopsy is the best way for evolution of causes of this bleeding (*Pal et al.*, 1997 and Garuti et al., 2001).

Previous studies clarify the implication of hysteroscopy in diagnosis and management of benign premalignant and malignant uterine bleeding (*Nagele et al.*, 1996, Gubbini et al., 1998, Serden et al., 2000, Gold stein et al., 2001 and Williams et al., 2002).

Clark et al., 2002 and Lasmar et al., (2006) have diagnosis estimated that the which depends on hysteroscopy visualization is highly accurate for endometrial cancer but it is moderately accurate for other endometrial diseases however. a combination hysteroscopy and directed biopsy has estimated to be the gold standard for diagnosis of endometrial diseases (Bender et al., 2002).

Aim of work

- To estimate the prevalence of hysteroscopic findings and histopathology diagnosis in patients presented with abnormal uterine bleeding.
- To explore the value of hysteroscopy and directed biopsy in: the diagnosis of causes of abnormal uterine bleeding.

Review of literature

Anatomy and Histology of the Uterus

The uterus is a hollow, pear-shaped, thick-walled muscular organ, suspended by ligaments and is located in the mid-sagittal plane of the pelvis. It measures about 7.5cm in length, 5cm in breadth at its upper part, 2.5cm in thickness and weighs 30-40gm (*Kadasne*, 2009).

The uterus is divided into the body and the cervix. The part of the body which lies superior to a line passing between the points of insertion of uterine tubes is called the fundus. The two lateral parts associated with fallopian tubes are called the cornua. The part connecting the body and the cervix is called the isthmus (*Rosai*, 2011).

The body of the uterus is related anteriorly to uterovesical pouch and the superior surface of the urinary bladder. It is related posteriorly to the rectouterine pouch (pouch of Douglas) and ileum coils or sigmoid colon inside it. The lateral aspects of the uterus are related to the broad ligaments, uterine artery and veins (*Snell*, 2012).

The uterus receives its blood supply from the uterine artery which is a branch from internal iliac artery, and ovarian artery which is branch from the abdominal aorta. The venous drainage is through the uterine and ovarian veins which terminates in internal iliac vein. Lymphatic drainage of the uterus ends in internal iliac and para-aortic lymph nodes. The nerve supply of the uterus is via sympathetic and parasympathetic nerves of the inferior hypogastric plexuses (*Darke*, 2008).

Histologically, the uterine wall consists of three layers; perimetrium, myometrium, and endometrium.

Perimetrium is a serosal layer of connective tissue, covers the uterus and adheres to most of the body and fundus.

Myometrium consists of smooth muscle bundles separated by connective tissue in which blood vessels, nerves, and lymphatics are present. The muscle bundles are arranged in three poorly defined layers. The external layer fibers are arranged longitudinally parallel to long axis of the uterus. The internal layer bundles are arranged longitudinally and in circular manner. In the middle layer, the bundles are arrayed in different directions. At uterine contraction, all muscle layers act together to expel the contents of the uterine cavity (*Vasudeva and Mishra*, 2011).

Endometrium is formed of mucosa and stroma. The mucosa is a simple columnar epithelium, and the stroma is a highly cellular connective tissue. The epithelium is of two cell types; ciliated and secretory cells. The differentiation between these two types is by the presence of basal bodies in the ciliated cell type (*Ross and Pawlina*, 2010). The stroma is formed of type iii collagen fibers, and fibroblasts. It contains tubular uterine glands that extends and divides near the myometrium (*Mescher*, 2010).

Functionally, the endometrium is divided in to two zones or layers; functional layer, and basal layer.

The functional layer is the outer layer, which sloughed off during menstruation. It is subdivided into the compactum and the spongiousm toward the basal layer. The basal layer is the inner layer adjacent to the myometrium. It is not sloughed off during menstruation and it act as regenerator for sloughed functional layer (*Rosai*, 2011).

The endometrium undergoes cyclic changes and is divided into three phases; proliferative, secretory, and menstrual phase.