

# **ENDOMETRIAL CARCINOMA**

## **A Comparative Multicentre Epidemiologic and Pathologic Study**

**Thesis**

**Submitted For Fulfillment of The Requirement of Master Degree in  
Pathology**

**By: Sara EL-Sayed Khalifa**

**M.B.B.Ch, Cairo University**

**Supervisors**

***Prof. Dr. Nevine Ismail Ramzy***

***Professor of Pathology***

***Faculty of Medicine***

***Cairo University***

***Prof. Dr. Zeinab Mohie- Eldin***

***Professor of Pathology***

***Faculty of Medicine***

***Cairo University***

***Dr. Sahar Abdel Hamid Tabak***

***Lecturer of Pathology***

***Faculty of Medicine***

***Cairo University***

***Faculty of Medicine***

***Cairo University***

**2009**

## **ABSTRACT**

This study aims at registering the incidence of endometrial carcinoma cases received by the pathology departments in El Kasr El Aini Hospital as well as the New Kasr El Aini Teaching Hospital. 64 cases were collected from both hospitals. The incidence of endometrial carcinoma in Kasr El Aini Hospital was found to be 1.25 /1000, while in New Kasr El Aini Teaching Hospital 1.23 /1000. Age ranged from 33 to 80 yrs. 52 cases (81.3%) were endometrioid type, 6 cases (9.4%) were serous adenocarcinoma, 2 cases (3.1%) were clear cell adenocarcinoma, 2 cases (3.1%) were mixed cell type, and 2 cases (3.1%) were undifferentiated carcinoma. Statistically significant results were obtained.

Key words: endometrial carcinoma

## ACKNOWLEDEMENT

*First and foremost thanks to God, the most beneficent and merciful.*

*I would like to express my sincere gratitude and deepest appreciation to Prof. Dr. Nevine Ismail Ramzy, Professor of Pathology, Faculty of Medicine, Cairo University for her generous supervision, valuable advices, constructive criticism and indispensable help throughout this work.*

*I am very much indebted to Prof. Dr. Zeinab Mohie- ELdin, Professor of Pathology, Faculty of Medicine, Cairo University for her kind supervision, great help and guidance.*

*I would like to express my sincere gratitude and appreciation to Dr. Sahar Abdel Hamid Tabak, Lecturer of Pathology, Faculty of Medicine, Cairo University for her meticulous supervision, valuable criticism and enthusiastic push.*

*The Candidate.*

# Table of Contents

<b>Introduction.....</b>	<b>1</b>
<b>Aim of The Work .....</b>	<b>3</b>
<b>Review of Literature .....</b>	<b>4</b>
<b>Material and Methods .....</b>	<b>50</b>
<b>Results .....</b>	<b>53</b>
<b>Discussion.....</b>	<b>85</b>
<b>Summary.....</b>	<b>92</b>
<b>Conclusions &amp; Recommendations .....</b>	<b>95</b>
<b>References.....</b>	<b>96</b>
<b>Arabic Summary .....</b>	<b>.....</b>

---

## LIST OF ABBREVIATION

**ASRs:** Age-standardized incidence rates.

**BMI:** Body Mass Index.

**CAH:** Complex atypical hyperplasia.

**CEA:** Carcinoembryonic antigen.

**CGIN:** Cervical glandular intraepithelial.

**CH:** Complex hyperplasia.

**CIN:** Cervical intraepithelial neoplasia.

**CT:** Computed tomography.

**D&C:** Dilation and curettage.

**EH:** Endometrial hyperplasia.

**EIC:** Endometrial intraepithelial carcinoma.

**EmGD:** Endometrial glandular dysplasia.

**EPIC:** European Prospective Investigation into Cancer and Nutrition.

**ER:** Estrogen receptor.

**ESCs:** Endometrial Serous Carcinomas.

**FIGO:** International Federation of Gynecology and Obstetrics.

**HNPCC:** Hereditary nonpolyposis colorectal cancer.

**HPV:** Human papillomavirus.

**HRT:** Hormone replacement therapy.

**IGF:** Insulin-like growth factor.

**LUS:** Lower uterine segment.

---

---

**MECC:** Middle East Cancer Consortium.

**MMR:** Mismatch repair.

**MRI:** Magnetic resonance imaging.

**MSI:** Microsatellite instability.

**NCI:** National Cancer Institute.

**NIH-AARP:** National Institutes of Health-American Association of Retired Persons.

**Nos:** Not otherwise specified.

**OS:** Overall survival.

**PAS:** periodic acid Schiff.

**PR:** Progesterone receptor.

**SAH:** Simple atypical hyperplasia.

**SCC:** Squamous cell carcinoma.

**SEER:** Surveillance, Epidemiology, and End Results program.

**SH:** Simple hyperplasia.

**SPSS:** Statistical Product for Services Solutions.

**UK:** United Kingdom.

**UPSC:** Uterine papillary serous carcinoma.

**US:** Ultrasound.

**WHO:** World Health Organization.

---

---

## LIST OF TABLES

**Table (1):** Risk factors for endometrial cancer.

**Table (2):** Clinico-pathological characteristics in Type I and Type II endometrial carcinomas.

**Table (3):** WHO classification of endometrial adenocarcinoma.

**Table (4):** FIGO architectural grading of endometrial carcinoma.

**Table (5):** Nuclear grading.

**Table (6):** Histologic differential diagnosis of villoglandular and serous carcinomas of the endometrium.

**Table (7):** Diagnostic features helpful in the distinction of microglandular carcinoma from microglandular hyperplasia in limited endometrial or endocervical curettage specimens.

**Table (8):** Clinicopathologic profiles of villoglandular and serous carcinomas of the endometrium.

**Table (9):** 1971 FIGO clinical staging system.

**Table (10):** Classification of endometrial carcinoma using TNM and International Federation of Gynecology and Obstetrics (FIGO) staging systems.

**Table (11):** Ancillary studies in the differential diagnosis of endocervical versus endometrial adenocarcinoma.

**Table (12):** Number of endometrial curettage and hysterectomy specimens.

**Table (13):** Type of specimens included in the survey.

---

---

**Table (14):** Incidence of endometrial carcinoma in Kasr El Aini Hospital and New Kasr El Aini Teaching Hospital.

**Table (15):** Comparison between incidence of endometrial carcinoma per year in Kasr El Aini Hospital and New Kasr El Aini Teaching Hospital.

**Table (16):** Age incidence in endometrial carcinoma cases.

**Table (17):** Uterine bleeding as a presenting symptom in endometrial carcinoma cases.

**Table (18):** Histopathologic types of endometrial carcinoma cases.

**Table (19):** Histologic variants of endometrioid type of endometrial carcinoma.

**Table (20):** Age incidence of endometrial carcinoma in relation to histopathologic type.

**Table (21):** FIGO architectural grade of endometrioid carcinoma.

**Table (22):** Nuclear grade of endometrioid carcinoma cases.

**Table (23):** Depth of myometrial invasion in endometrial carcinoma cases diagnosed by hysterectomy.

**Table (24):** Histopathologic types of endometrial carcinoma and depth of myometrial invasion in cases diagnosed by hysterectomy.

**Table (25):** Histopathologic types of endometrial carcinoma and myometrial invasion (invasive or not).

**Table (26):** FIGO stage of endometrial carcinoma cases diagnosed by hysterectomy.

**Table (27):** FIGO stage of endometrial carcinoma cases diagnosed by hysterectomy in relation to histopathologic type.

---



---

## LIST OF FIGURES

**Fig (1):** Endometrioid carcinoma, villoglandular variant showing long delicate papillary fronds. (H and E x100)

**Fig (2):** Endometrioid carcinoma, variant with squamous differentiation. (H and E x100)

**Fig (3):** Endometrioid carcinoma, secretory variant showing irregular shaped glands lined by rounded cells with overlapping nuclei showing subnuclear, supranuclear vacuoles and luminal secretions. (H and E x100)

**Fig (4):** Endometrioid carcinoma, secretory variant showing supranuclear vacuolization of the cells lining the malignant glands. (H and E x400)

**Fig (5):** Endometrioid carcinoma, villoglandular variant showing confluent glandular pattern in which glandular epithelium interconnects one gland with another. (H and E x100)

**Fig (6):** Endometrioid carcinoma, showing cribriform pattern. (H and E x100)

**Fig (7):** Endometrioid carcinoma, architectural grade III composed mainly of solid sheets of pleomorphic malignant cells showing nuclear atypia and mitosis. (H and E x400)

**Fig (8):** Endometrioid carcinoma showing numerous mitotic figures. (H and E x400)

**Fig (9):** Endometrioid carcinoma, secretory variant, nuclear grade I. The glands are lined by malignant cells oval elongated nuclei, fine chromatin, and small nucleoli. (H and E x400)

---

---

**Fig (10):** Endometrioid carcinoma showing cribriform pattern, nuclear grade II (the glands are lined by malignant cells showing moderate degree of anaplasia. (H and E x400)

**Fig (11):** Endometrioid carcinoma showing foam cells. (H and E x400)

**Fig (12):** Endometrioid carcinoma invading myometrial muscles. (H and E x200)

**Fig (13):** Serous adenocarcinoma showing complex, short, and dense papillae. (H and E x100)

**Fig (14):** Serous adenocarcinoma with highly pleomorphic anaplastic cuboidal cells. (H and E x200)

**Fig (15):** Serous adenocarcinoma with hobnail-shaped cells. (H and E x400)

**Fig (16):** Serous adenocarcinoma with prominent hobnail-shaped cells and exfoliated cells. (H and E x400)

**Fig (17):** Clear cell adenocarcinoma showing anaplastic cells having clear cytoplasm with areas of necrosis. (H and E x200)

**Fig (18):** Mixed adenocarcinoma composed of endometrioid and transitional component. This figure shows the transitional component. (H and E x400)

**Fig (19):** Undifferentiated carcinoma with wide areas of necrosis. (H and E x100)

**Fig (20):** Undifferentiated carcinoma. Higher magnification of the previous picture showing highly anaplastic cells with pleomorphism. (H and E x400)

---

---

## LIST OF GRAPHS

**Graph (1):** Endometrial curettage and hysterectomy specimens.

**Graph (2):** Incidence of endometrial carcinoma per year in Kasr El Aini Hospital and New Kasr El Aini Teaching Hospital.

**Graph (3):** Presence of bleeding as a presenting symptom in studied cases of endometrial carcinoma.

**Graph (4):** Histopathologic types of endometrial carcinoma cases.

**Graph (5):** Variants of endometrioid adenocarcinoma.

**Graph (6):** Architectural grade of endometrioid adenocarcinoma.

**Graph (7):** Nuclear grade of endometrioid adenocarcinoma.

**Graph (8):** Depth of invasion in endometrial carcinoma.

**Graph (9):** Endometrial carcinoma types and depth of myometrial invasion.

**Graph (10):** FIGO stage of endometrial carcinoma cases diagnosed by hysterectomy.

**Graph (11):** FIGO stage of endometrial carcinoma cases diagnosed by hysterectomy in relation to histopathologic type.

---

## INTRODUCTION

Endometrial cancer is the most common malignant tumor of the female genital tract (**Gründker *et al.*, 2008**). It is more common in western countries (**Li *et al.*, 2005**). Endometrial carcinoma is the fourth most frequent cancer among that women (**Manfredi *et al.*, 2004**).

Incidences throughout different regions of the world vary considerably. Compared to Africa and Asia having the lowest rates of incidence, Western Europe, USA and Canada are shown to have the highest incidence worldwide. Even within Europe the incidence rates are very heterogeneous (**Münstedt *et al.*, 2004**).

Among the Middle East Cancer Consortium countries (MECC), the highest rate for endometrial carcinoma was observed in Israeli Jews (13.8/100 000), followed by Cypriots (11.8/100 000), Israeli Arabs (8.7/100 000), Jordanians (5.8/100000), and Egyptians (3.5/100 000). Endometrial carcinoma incidence according to US SEER was much higher (17.6/100 000) (**Komodiki, 2006**).

The incidence of endometrial carcinoma in cancer registry performed by NCI 2003-2004 was found to be 0.69% (**Mokhtar *et al.*, 2007**).

Incidence of endometrial carcinoma is higher in women with median age 55-65 year (**Planaguma *et al.*, 2004**). It is most probably presented by postmenopausal vaginal bleeding (**Mansour *et al.*, 2007**). Postmenopausal bleeding is a significant early symptom of endometrial carcinoma (**Al Kadri *et al.*, 2004**).

The majority of cases can be divided into two different types of endometrial cancer based on clinico-pathological and molecular characteristics. Type I is associated with estrogen predominance. These tumors are of endometroid histology and develop from endometrial hyperplasia. They have good prognosis and are sensitive to endocrine

---

treatment. Type II endometrial cancers are not associated with a history of unopposed estrogens and develop from the atrophic endometrium of elderly women (**Gründker *et al.*, 2008**).

Prognosis is relatively good: relative survival at 5 years is 63–78%, though poorer survival is observed in several eastern European countries (**Coleman *et al.*, 2003**). In Europe, endometrial carcinoma is the tenth most common cause of cancer death in women (**Bray *et al.*, 2005**).

## **AIM OF THE WORK**

- Production of an accurate registry of endometrial carcinoma cases received by Kasr El Aini Hospital and comparing the incidence with number of cases received by New Kasr El Aini Teaching Hospital.
- Re evaluation of all cases histologically using the latest grading system (FIGO Grading).
- Comparing incidence of endometrial carcinoma among Egyptian patients with registries of other centers, in a trial to detect any special epidemiologic features among Egyptian patients.

## **EPIDEMIOLOGY OF ENDOMETRIAL CARCINOMA**

### **A- Incidence and Geographic Distribution**

Endometrial cancer is the most common malignant tumor of the female genital tract (**Gründker *et al.*, 2008**). It is the fourth most common malignancy in women in the developed world after breast, colorectal and lung cancer with an incidence estimated at 15–20 per 100,000 women per year. Despite the curability of endometrial cancer being high, tumors with particular morphological variants, adverse histopathological features and/or advanced stage are characterized by aggressive behavior and poor prognosis (**Ryan *et al.*, 2005**). Incidences throughout different regions of the world vary considerably. Compared to Africa and Asia having the lowest rates of incidence, Western Europe, USA and Canada are shown to have the highest incidence worldwide. Even within Europe the incidence rates are very heterogeneous. In some of these countries, e.g. Germany, endometrial carcinoma is the most common among genital carcinoma (**Münstedt *et al.*, 2004**). In North America and Europe, endometrial cancer accounts for about 8-10% of all cancer cases in women, whereas in Africa and Asia, it represents only 2-4% of cancers (**Purdie and Green, 2001**).

The incidence rates of endometrial cancer are highest in the United States and Canada and lowest in Asia and Africa, while Asian women who have migrated to the United States have an intermediate incidence. Such international variation suggests that lifestyle factors may play a major role in the aetiology of this disease (**Tao *et al.*, 2005**).

In Shanghai, China, the age-adjusted incidence of endometrial cancer increased markedly during the last years. This striking increase in the incidence of this disease in Shanghai parallel marked weight gain among women in China that has been linked, in part, to physical inactivity (**Matthews *et al.*, 2005**).