

**نماذج الارتداد فى الاورام السرطانية النسائية  
(عنق الرحم وبطانة الرحم)  
دراسة تحليلية احادية عن حالات سبق علاجها في الفتره بين  
٢٠٠٨ الي ٢٠١٢ في مركز قصر العيني لعلاج الاورام**

**رسالة مقدمة من**

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**بكالوريوس طب و جراحة جامعة عين شمس ٢٠٠٦**

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**٢٠١٥**

# Acknowledgment

First and above all thanks to **ALLAH**

I would like to express my deep feelings of gratitude and appreciation to **Prof.Dr Ibtesam Saad El Din** professor of oncology department, Faculty of medicine- cairo university for her great effort, kind supervision and guidance that helped me in overcoming many obstacles during this work to make it finally see the daylight.

I would like also to express my thanks and admiration to **Prof.Dr. Ahmed lofty Aboul Nasr** Proffesor of Gynecology and Obestetrics, Faculty of medicine cairo university for his support, precious advice, and for his interest that made this work possible.

Last but no least I sincerely appreciate the encouragement and help I received from **Dr.Raafat Ragaie Abdel-Malek** assistant professor of clinical oncology faculty of medicine, cairo university, I would like to thank him for his support.

Finally I would like to thank all my family my mother, soul of my father, my brothers, my friends for their love and support, I would like to express my thanks to S.S.S who I owe a lot to him for his love and support.

**Pattern of Relapse in gynecological malignancies  
(Cancer cervix & cancer endometrium)  
Retrospective Analysis: 2008-2012  
Single Institution Experience**

**Thesis**

**Submitted in Partial Fulfillment of**

**M.Sc. Degree in**

**Clinical Oncology**

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**2015**

# CONTENT

|                                                                                                                                                                                   |         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| <b>Introduction and Aim of Work</b>                                                                                                                                               | 1-3     |
| <b>Review of Literature</b>                                                                                                                                                       |         |
| ▪ <b>Chapter I:</b> Epidemiology, etiology of cervical and endometrial cancer                                                                                                     | 5-11    |
| ▪ <b>Chapter II:</b> Clinical Presentation and Diagnostic Evaluation of cervical and endometrial cancer                                                                           | 12-17   |
| ▪ <b>Chapter III:</b> Pathological Aspects and staging of cancer cervix and endometrium                                                                                           | 18-27   |
| ▪ <b>Chapter IV:</b> Treatment of cervical and endometrial cancer:<br>1. Surgery.<br>2. Radiotherapy<br>3. CCRT<br>4. Chemotherapy<br>5. Hormonal therapy<br>6. Biological agents | 28-49   |
| ▪ <b>Chapter V:</b> Relapse                                                                                                                                                       | 50-60   |
| <b>Patients and Methods</b>                                                                                                                                                       | 62-63   |
| <b>Results</b>                                                                                                                                                                    | 65-87   |
| <b>Discussion</b>                                                                                                                                                                 | 89-96   |
| <b>Summary</b>                                                                                                                                                                    | 97-98   |
| <b>Conclusion</b>                                                                                                                                                                 | 99      |
| <b>Reference</b>                                                                                                                                                                  | 103-123 |
| <b>Arabic Summary</b>                                                                                                                                                             | 100-102 |

## List of Abbreviations

|                  |                                                          |
|------------------|----------------------------------------------------------|
| <b>AJCC</b>      | American Joint Committee on Cancer.                      |
| <b>ASCO</b>      | American Society of Clinical Oncology.                   |
| <b>BMI</b>       | Body mass index                                          |
| <b>BSC</b>       | Best supportive care.                                    |
| <b>BT</b>        | Brachytherapy.                                           |
| <b>CBC</b>       | Complete blood picture.                                  |
| <b>CT</b>        | Computed tomography.                                     |
| <b>DFS</b>       | Disease free survival.                                   |
| <b>DNA</b>       | Deoxyribonucleic acid.                                   |
| <b>EBRT</b>      | External beam radiotherapy                               |
| <b>HPV</b>       | Human Papilloma virus                                    |
| <b>IARC</b>      | The International Agency for Research on Cancer          |
| <b>ICRT</b>      | Intracavitary radiation therapy                          |
| <b>IORT</b>      | Interoperative radiotherapy                              |
| <b>KASO</b>      | Kasr Al-Ainy school of oncology                          |
| <b>LFT</b>       | Liver function test                                      |
| <b>LN</b>        | Lymph Node                                               |
| <b>LRFS</b>      | Local recurrence free survival.                          |
| <b>MRI</b>       | Magnetic resonance imaging.                              |
| <b>NCCN</b>      | National Comprehensive Cancer Network.                   |
| <b>NCI</b>       | National Cancer Institute.                               |
| <b>OCP</b>       | Oral contraceptive Pills.                                |
| <b>OS</b>        | Overall survival.                                        |
| <b>P</b>         | <i>P</i> -value.                                         |
| <b>PAP Smear</b> | Papanicolau smear                                        |
| <b>PET/CT</b>    | Positron emission tomography/Computed tomography.        |
| <b>PORTEC</b>    | Postoperative Radiation Therapy in Endometrial Carcinoma |
| <b>RFS</b>       | Relapse free survival                                    |
| <b>RR</b>        | Relative risk.                                           |
| <b>RT</b>        | Radiation therapy.                                       |

|             |                                           |
|-------------|-------------------------------------------|
| <b>SCC</b>  | Squamous cell carcinoma.                  |
| <b>SEER</b> | Surveillance Epidemiology and End Results |
| <b>TLH</b>  | Total laparoscopic hysterectomy           |
| <b>Vs</b>   | versus                                    |
| <b>VBT</b>  | Vaginal brachytherapy                     |
| <b>US</b>   | United states                             |

## List of TABLES

| <b><i>Table No.</i></b> | <b><i>Title</i></b>                                                                    | <b><i>Page No.</i></b> |
|-------------------------|----------------------------------------------------------------------------------------|------------------------|
| <b>1</b>                | Endometrial cancer histological subtypes                                               | <b>20</b>              |
| <b>2</b>                | Cervical cancer WHO histological subtypes of                                           | 21                     |
| <b>3</b>                | FIGO Staging of cervical cancer                                                        | 23-24                  |
| <b>4</b>                | FIGO Staging of endometrial cancer                                                     | 25                     |
| <b>5</b>                | Comparison between 3 types of hysterectomy                                             | 30-31                  |
| <b>6</b>                | Comparison between 2 types of trachelectomy                                            | 35                     |
| <b>7</b>                | Distribution of cases according to age                                                 | 67                     |
| <b>8</b>                | Distribution of cases according to parity                                              | 68                     |
| <b>9</b>                | Distribution of cases according to BMI                                                 | 69                     |
| <b>10</b>               | Distribution of cases according to grade                                               | 72                     |
| <b>11</b>               | Distribution of cases according to FIGO stage                                          | 73                     |
| <b>12</b>               | Patterns of relapse according to stage and treatment modalities for Cervical cancer    | 80                     |
| <b>13</b>               | Patterns of relapse according to stage and treatment modalities for endometrial cancer | 81                     |

# LIST OF FIGURES

| <i>Figure No.</i> | <i>Title</i>                                                                                     | <i>Page No.</i> |
|-------------------|--------------------------------------------------------------------------------------------------|-----------------|
| 1.                | Types of surgery of uterus                                                                       | 32              |
| 2.                | Surgical/SLN mapping Algorithm for early stage cervical cancer                                   | 37              |
| 3.                | Surgical/SLN mapping Algorithm for early stage endometrial cancer                                | 38              |
| 4.                | Treatment of cervical cancer with local relapse                                                  | 54              |
| 5.                | Treatment of cervical cancer with distant relapse                                                | 55              |
| 6.                | Treatment of endometrial cancer with local relapse                                               | 59-60           |
| 7.                | Treatment of endometrial cancer with distant relapse                                             | 61              |
| 8.                | Distribution of cases.                                                                           | 66              |
| 9.                | Distribution of cases according to age                                                           | 68              |
| 10.               | Case distribution according to parity                                                            | 69              |
| 11.               | Case distribution according to BMI                                                               | 70              |
| 12.               | Histological distribution of cervical cancer cases                                               | 71              |
| 13.               | Histological distribution of endometrial cancer cases                                            | 71              |
| 14.               | Distribution of patients according to histological subtype for endometrial and cervical cancers. | 72              |
| 15.               | Distribution of cases according to grade                                                         | 73              |
| 16.               | Distribution of cases according to FIGO stage                                                    | 74              |
| 17.               | Distribution of cervical cancer cases according to treatment                                     | 76              |
| 18.               | Distribution of endometrial cancer cases according to treatment                                  | 76              |
| 19.               | Distribution of cervical cancer cases according to relapse site.                                 | 78              |
| 20.               | Distribution of endometrial cancer cases according to relapse site.                              | 79              |
| 21.               | DFS curve for both cervical and endometrial carcinoma                                            | 82              |
| 22.               | OS curve for both cervical and endometrial carcinoma                                             | 83              |
| 23.               | Curve representing impact of stage on DFS for cervical cancer                                    | 85              |
| 24.               | Curve representing impact of stage on DFS for endometrial cancer                                 | 86              |

| <b><i>Figure No.</i></b> | <b><i>Title</i></b>                                                           | <b><i>Page No.</i></b> |
|--------------------------|-------------------------------------------------------------------------------|------------------------|
| <b>25.</b>               | Curve representing impact of adjuvant treatment on DFS for cervical cancer    | 87                     |
| <b>26.</b>               | Curve representing impact of adjuvant treatment on DFS for endometrial cancer | 88                     |



## **Introduction and aim of work**

### ***Introduction***

In developed countries, endometrial carcinoma is the most common gynecologic malignancy while cervical carcinoma ranks fourth; while in developing countries, endometrial carcinoma ranks second with cervical carcinoma being the most common (**Jemal A et al., 2011, Kamangar et al., 2006 and Parkin et al., 2002**). This difference is due to lack of screening programs in developing countries, while in western world high socioeconomic and nulliparity increase risk of endometrial carcinoma, (**Ries Lag et al., 2004**).

In USA, incidence in white women is 1.4 times higher than in African American while the 5 year survival rate is lower in African American women than in white women (60% VS 85%); on the other hand, cervical body cancer is predominant in low socioeconomic classes with higher incidence in developing countries as among Latin American, African American & native American women (higher incidence among uneducated) (**Jame Abraham et al., 2010**).

Human Papilloma virus (HPV) is central to the development of cervical neoplasia and can be detected in 99.7 percent of cervical cancers (**Walboomers JM et al., 1999**).

Squamous cell carcinoma is the most common histologic subtype of cervical cancer (75% to 80%) and the remaining (20% to 25%) are mostly adenocarcinomas or adenosquamous carcinoma while endometrioid adenocarcinoma is the most common histologic subtype of endometrial cancer (75% to 80%) and only (<1%) represent squamous cell carcinoma (**Jame Abraham et al., 2010**).

Endometrioid tumors tend to have a favorable prognosis and typically present at an early stage with abnormal uterine bleeding. Other histologic types

of endometrial carcinoma (e.g, serous, clear cell) as well as other types of uterine cancer (sarcomas) are associated with a poor prognosis.

The mortality rates continues to decline to both endometrial and cervical cancers, likely because of increased awareness of symptoms including vaginal bleeding as well as the introduction of Papanicolaou (Pap) smear screening which has reduced the incidence & mortality of invasive cervical cancer by almost 75% over the last 50 years **(Jame Abraham et al., 2010)**.

Treatment of uterine cervix cancer and endometrial cancer is according to stage of disease. Treatment options for localized disease include surgery, radiotherapy, concomitant chemo-radiotherapy and adjuvant chemotherapy.

After end of primary treatment, relapse may occur. For cervical cancer, 10-20% recurrence rate mainly local has been reported following primary surgery or radiotherapy in patients with stage 1b and 2a with negative nodes reaching up to 70% with more advanced stage disease **(Jame Abraham et al., 2010)**.

The vast majority of recurrences occurred within the first 3 years after primary treatment (78% and 87% in endometrial and cervical cancer, respectively). A better overall survival from relapse was observed when vaginal relapse was compared to other sites in endometrial cancer patients and when pelvic recurrence was compared to distal sites in cervical cancer cases. Recurrent endometrial and cervical cancer patients were symptomatic in 52% and 65% of cases, respectively **(Sartori E et al., 2007)**.

Among asymptomatic recurrent endometrial cancer cases, pelvic examination, abdominal or pelvic ultrasound and CT could detect 92% of relapses, while the vast majority of cervical cancer relapses could be diagnosed by pelvic examination and /or CT (85%) **(Sartori E et al., 2007)**.

## **Aim of the work**

The Aim of this study is to identify patterns of relapse in patients with endometrial or cervical carcinoma after receiving their primary local treatment (radical surgery without radiotherapy) and its possible correlation with both tumor variables as well as treatment given.

# **Review Of Literature**

## Chapter I

### Epidemiology and etiology of cervical and endometrial cancer

#### Incidence

Cervical cancer is fourth most common gynecological cancer and a major health problem affecting women worldwide (**Kamangar et al., 2006 and Parkin et al., 2002**). It affects about 16 per 100,000 women per year and kills about 9 per 100,000 per year. An estimated 12,360 new cases of cervical cancer will be diagnosed in US in the year 2014, and 4,020 deaths will occur from the disease (**Siegel R et al., 2014**). Approximately 85% of cervical cancers occur in developing countries, where it is the 2<sup>nd</sup> most frequent cause of cancer death (**Jamal et al., 2011**).

The incidence and mortality in the US decreased largely due to widespread of Pap smear screening (**Barn Holtz et al., 2009**). Among gynecological cancers it ranks behind endometrial cancer and ovarian cancers (**Canavan TP et al., 2000**). Incidence remains high among Latino, black and Asian women (**Barn Holtz et al., 2009**).

In Egypt, cancer of cervix is relatively uncommon, ranking third in gynecological cancer (after ovary & uterus) & 15<sup>th</sup> among all females' cancers. Current estimates indicate that every year, 514 women are diagnosed with carcinoma of the cervix, 299 die from the disease. About 10.3% of women in the general population are estimated to harbor cervical HPV (HPV 16 or 18) infection at a given time (**Ibrahim et al., 2010 and WHO/ICO 2010**).

On the other hand, endometrial cancer is the most frequent cancer occurring in the female genital tract in the United States and many other Western countries (**Nicolaije kA et al., 2013 and Oldenburg CS et al., 2013**).

It has an incidence of 15–25 per 100,000 women annually (**Nicolaije kA et al., 2013**).

In Egypt, according to Gharbia Population Based Cancer Registry 2002–2003, endometrial cancer is the 2nd Gynecological cancer in female, 9th of all female cancers and incidence in urban areas is almost 6 times higher than rural ones. (**Ibrahim A et al., 2010**).

There are many microscopic subtypes of endometrial carcinoma, but they are broadly organized into two categories, Type I and Type II, based on clinical features and pathogenesis. The two subtypes are genetically distinct (**Hoffman et al., 2012**).

Type I endometrial carcinomas occur most commonly before and around the time of menopause. In the United States, they are more common in white women, particularly women who have a history of endometrial hyperplasia. Type I endometrial cancers are often low-grade, minimally invasive into the underlying uterine wall (myometrium), estrogen-dependent, and have a good outcome with treatment, type I carcinomas represent 75–90% of endometrial cancer (**Hoffman et al., 2012 and Saso et al., 2011**).

Type II endometrial carcinomas usually occur in older, post-menopausal women, in the United States are more common in Black women, and are not associated with increased exposure to estrogen or a history of endometrial hyperplasia. Type II endometrial cancers are often high-grade, with deep invasion into the underlying uterine wall (myometrium), and are of the serous or clear cell type, and carry a poorer prognosis. They can appear to be epithelial ovarian cancer on evaluation of symptoms (**Hoffman et al., 2012**). They tend to present later than Type I tumors and are more aggressive, with a greater risk of relapse or metastasis (**Saso et al., 2011**). Type II cancers are estrogen-independent (**Colombo et al., 2013**).

## **Age**

According to SEER 2014, most women with cervical cancer are diagnosed before the age of 50, the median age was 49 (**SEER 2014**). However, older women remain at risk. More than 20% of new cases are diagnosed in women over 65. Cervical cancer in women younger than age 20 is rare (**American Cancer Society 2014**).

While Peak incidence for endometrial cancer is in the sixth and seventh decades of life, 5% of cases are diagnosed before the age of 40, 20%to 25% of patients are diagnosed before menopause (**Jame Abraham et al., 2010**).

## **Risk factors and prevention**

Both cervical body cancer and endometrial cancer vary in etiology and risk factors, as cervical cancer related mainly to multi-parity, multi-sexual partners, early age at first sexual intercourse; endometrial cancer is on the contrary related mainly to nulliparity and infertility.

While smoking is considered a risk factor for cervical cancer, smokers have a modest reduction in uterine cancer risk (**P.Boyle et al., 2004**). This effect may be linked with the fact that smokers metabolize estrogens into less active metabolites than non-smokers. Recent results from the US Nurses' Health study show a significant risk reduction in past as well as continuing smokers (**Viswanathan et al., 2005**).

### **Risk factors for cervical cancer include:**

#### **Human Papilloma virus (HPV):**

Cervical cancer is caused by Human Papilloma virus infection (HPV). Most HPV infection is harmless and clears spontaneously but persistent infection with high-risk HPV (especially type 16) can cause cancer of the cervix, vulva, vagina, anus, penis and oropharynx. The virus exclusively infects