



## A Review on Risk Factors, Staging and Survival Rates of Endometrial Cancer in Both Black and White Women in Infertility Patients in USA

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### ABSTRACT

This article is focused mainly on risk factors, staging and survival rates of endometrial cancer in infertility patients in both black and white women in United States. These risk factors split into two groups such as exogenous & endogenous. Exogenous mainly (fertility treatment clomiphene, tamoxifen, human chorionic gonadotropins, human menopausal Gonadotropins & Birth control pills, intra uterine devices) These factors which increase the concentrations of unopposed estrogen for a short period of time but successful leads to fertility, long-term leads to endometrial cancer, and endogenous risk factors include mainly (Poly cystic ovary syndrome, Obesity, Diabetes, and Hypertension) these risk factors in infertility women may lead to increased unopposed estrogen in the body may lead to development of endometrial cancer over a period of time. It is the commonest reproductive cancer. Our objective was to assess association between exogenous and endogenous risk factors, in infertility patients staging and survival rates in infertility patients which leads to an endometrial cancer. It is estimated that by 2030, endometrial cancer will become the 6th most common cancer overall, and the 3rd most common among women. In addition, five year survival after an EC diagnosis is lower for black women when compared to white women at every stage of diagnosis. "Early detection leads to early prevention".

### Key words:

Endometrial cancer, infertility patients, endogenous risk, exogenous risk Factors, staging, survival rates.

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### INTRODUCTION

In United States every year estimated cancer cases were 1,735,350, and estimated cancer deaths were 609,640, out of that Endometrial estimated cases were more than 63,230 and estimated deaths are 11,350. Endometrial cancer is the most commonest cancer in women. Data from the Surveillance, Epidemiology and End Results program report the age-adjusted incidence rate of EC is lower among black women than white women (24.8 and 26.3 cases per 100,000 women, respectively). Infertility is a most common woman health problem currently affecting up to 10% of reproductive age groups in United States. How infertility is going to be a leading cause to endometrial cancer and differentiate between black and white women. Black women are significantly different with regard to socioeconomic position and marital status. They have a higher prevalence of some risk factors for infertility such as uterine fibroids and excess weight. Out of 100 people only 5% people are diagnosed under the age of 40 years, and over 70% of people are nulliparous at diagnosis<sup>1-3</sup>. An even larger proportion of premenopausal women are diagnosed with complex atypical hyperplasia, a known precursor of endometrial carcinoma<sup>4</sup>.

Overall, this evidence suggests that there are major differences between black women and white women seeking care for infertility. However, whether these differences are present and contribute to increased infertility in black women in the general population is unknown. Endometrium is the inner layer of uterus. It is highly vascularized. The Endometrium is divided into two layers, the stratum functionalis lines the uterine cavity

and sloughs off during menstruation. The deeper layer the stratum basalis is permanent and gives rise to new stratum functionalis after each menstruation<sup>1</sup>. Thus, exploring factors associated with EC may provide insight regarding racial differences that potentially impact incidence and ultimately, survival. Black women have a higher proportion of non-endometrioid tumors, such as serous or clear cell cancers, which may be less hormonally-dependent. The aim of this study was to compare the risk factors for endometrial cancer in black and white women in infertility patients. After a woman is diagnosed with endometrial cancer, doctors will describe staging. Staging describes the amount of cancer in the body<sup>2-4</sup>. The 5-year survival rate is the percentage of people who live at least 5 years after being diagnosed with cancer.

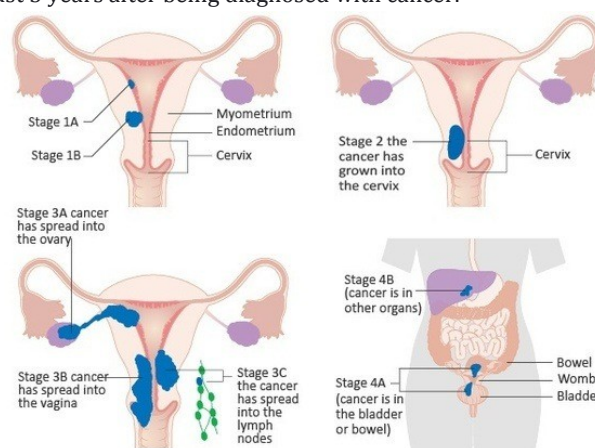


Fig 01: Types of Endometrial cancer Stages

Staging:Table: 1

STAGE	STAGE GROUPING	FIGO STAGE	STAGE DESCRIPTION
I	T1 N0 M0	I	The cancer is growing within in the body of the uterus .it may grow in to the glands of the cervix(TI). No spread to nearby lymph node(N0) No Metastasis(M0)
IA	T1a N0 M0	IA	The cancer is in the endometrium and spread to the myometrium(T1a) No spread to near by lymph node. No Metastasis
IB	T1b N0 M0	1B	Cancer spreads from endometrium to myometrium. But it doesn't spread to body of uterus(T1b) No spread to nearby lymph node(N0) No Metastasis(M0)
II	T2 N0 M0	II	The cancer spreads outside of the uterus.(T2) No spread to nearby lymph node(N0) No metastasis(M0)
III	T3 N0 M0	III	Cancer spread to outside of the uterus(T3) No spread to near by lymph node(N0) No metastasis(M0)
IIIA	T3a N0 M0	IIIA	Cancer spreads to the outer surface of uterus and also spreads to the fallopian tubes.(T3a) No spread to the near by lymph node(N0) No metastasis(M0)
IIIB	T3b N0 M0	IIIB	cancer spreads to the vagina or parametrium.(T3b) No spread to the near by lymph node(N0) No metastasis(M0)
IIIC1	T1-T3 N1,N1 mi,or N1a M0	IIIC1	Cancer growing to the body of uterus, spreads to the nearby tissues(T1-T3). Spread to pelvic lymph node(N1or N1mi orN1a). No metastasis.(M0)
IIIC2	T1-T3 N2,N2mi or N2a	IIIC2	Cancer spreads to the body of uterus, spreads to nearby tissues(T1-

	M0		T3). spreads to para aortic lymph nodes(N2,N2 mi,orN2a) no metastasis(M0)
IVA	T4 ANY N M0	IVA	Cancer spreads to the inner lining of rectum and urinary bladder(T4). It may or may not spread to the nearby lymph node (ANY N). No metastasis(M0)
IVB	ANY T ANY N M1	IVB	The cancer be any size(ANY T) it may or may not be spreads to nearby lymph node(ANY N) It spreads to groin nearby lymphnode, it spreads to organs away from uterus to other organs such as liver, lung, or bones(M1)

## METHODS

The analysis was done according to PRISMA guidelines. A literature search was performed using Medline, Embase, and the Cochrane Library and Google Scholar databases for comparative studies until 2017 to investigate a clinical significance of risk factors of endometrial cancer in infertility patients .the following search headings were used fertility agents,infertility,female,endometrial cancer, neoplasms, clomiphene, tamoxifen,hCG, hMG ,intrauterine devices, birth control pills,diabetes,pcos,obesity,hypertension. Using these strategies study was comparing endogenous risk factors and exogenous risk factors causing an endometrial cancer in infertility patients in both and black and white women.

## POLY CYSTIC OVARY SYNDROME

Pcos on long term risk mainly associated with endometrial cancer. PCOS leads to an ovulation which characterizes the syndrome is considered to be the main mechanism responsible for continual unopposed secretion of estrogen's where estrogen receptors are present on endometrium and consequent increase in growth stimulating factor which leads to progressive changes from benign proliferation to atypical hyperplasia which leads to adenocarcinoma risk of an endometrial carcinoma5-8. Endometrial hyperplasia may be a precursor to adenocarcinoma. In women with PCOS intervals between menstruations of more than three months may be associated with endometrial hyperplasia and later carcinoma9, 10.

## OBESITY

Healthy weight BMI is 18.5-24.9.overweight BMI IS >25, obese is >30 .obesity people are more risk for causing an endometrial cancer in both black and white women. Adipose tissue is the primary site for the conversion of adrenal androstenedione to oestrone,which in turn leads to low levels of sex hormone binding globulins which leads greater bioavailability of estrogen .which leads to progressive changes from endometrial hyperplasia to endometrial carcinoma.

## DIABETES

Independent of obesity, the presence of a defect in insulin action which amplifies LH stimulated androgen secretion from thecal cells, has been well established. Insulin binding sites are present in endometrium which stimulates insulin and insulin like growth factors are raised in PCOS. Hyperandrogenism and hyperinsulinemia may increase the potential for neoplastic change in the endometrium <sup>11</sup>. It is reported that more than 20% of obese women with PCOS will have impaired glucose tolerance after the age of 30. Evidence demonstrates that the prevalence of type 2 diabetes in women diagnosed with PCOS is 7 times higher than controls. Insulin resistance combined with abdominal obesity is thought to account for the higher prevalence of type 2 diabetes in PCOS. However, the risk of developing type 2 diabetes is also increased in non-obese women with PCOS <sup>12, 13</sup>. Thus PCOS is an independent risk factor for type 2 diabetes in middle age. The majority of women under 45 with type 2 diabetes are also diagnosed with PCOS. Diabetes causes more risk of endometrial cancer in black women when compared to white.

## CARDIOVASCULAR DISEASE AND HYPERTENSION

There are two mechanisms by which insulin resistance in PCOS contributes significantly to higher incidence of cardiovascular disease in these women. One mechanism is the direct atherogenic action and the other mechanism is the adverse effect of the lipoprotein profile <sup>14</sup>. Women with PCOS are seen to have more extensive coronary artery disease by angiography. Impaired glucose tolerance and diabetes caused by PCOS are known risk factors for cardiovascular disease. The lipoprotein profile in women with polycystic ovaries is significantly distorted. They usually have high concentrations of serum triglycerides and total and low-density lipoprotein cholesterol <sup>15</sup>. On the other hand the levels of high density lipoprotein (HDL) and particularly HDL2 subfraction are suppressed <sup>16, 17</sup>. In addition serum plasminogen activator inhibitor-I concentrations are also elevated. The last could lead to impaired fibrinolysis and thus affect directly vascular tissue causing changes associated with coronary heart disease. The evidence is thus mounting that there is indeed an increased risk for women with PCOS of developing cardiovascular disease.

Regarding hypertension there to be a direct relationship between insulin plasma levels and blood pressure <sup>18,19</sup>. The prevalence of treated hypertension is three times higher in women with PCOS between the ages of 40-59 years in comparison with controls. The incidence of preeclampsia in obese women with PCOS conceiving compared to the general pregnant population is 4 times higher. It seems that significant risk factors for developing atherosclerotic conditions, hypertension and myocardial infarction, are present at an earlier age than women without PCOS <sup>20</sup>.

## CLOMIPHENE CITRATE (CC)

The incidence of endometrial cancer after intake of this drug in United States was estimated as 0.44% (13 of 2974) in the CC. Data was collected from end result and surveillance program.

## TAMOXIFENE

Tamoxifen causes estimated chances of getting of endometrial cancer is 0.66% (35 of 5257) leads to 2-3 fold increase risk of hyperplasia and subsequent increase the risk of endometrial

cancer. Any abnormal vaginal bleeding, discharge, staining or spotting should be investigated. Clomiphene citrate and human menopausal gonadotropins (CC + hMG)

The incidence of endometrial cancer was 0.20% (14 of 7023) in the CC + hMG group. Human menopausal gonadotropin (hMG). The incidence of endometrial cancer was 0.07% (5 of 6861) in the hMG.

## Birth control pills:

These pills on long-term use may increase estrogen level in the body which may lead to progressive changes from atypical hyperplasia to carcinoma. Only 5% of people are more chance of getting endometrial cancer people who are using contraceptive pills. These are very less chance of causing an endometrial cancer.

## Inclusion criteria and exclusion criteria:

All comparative studies of exogenous and endogenous risk factors in infertility patients in black and white women patient groups reporting incidence rates and prevalence rates of endometrial cancer outcomes are included. The term 'fertility treatment' refers here specifically to patients who were administered fertility drugs to induce multiple folliculogenesis, also known as superovulation. Those studies not reporting endometrial cancer incidence either at all or separately in both the exogenous and endogenous risk factors were excluded. Other reproductive tract cancers including the cervix were excluded from our analysis.

## RESULTS

Based on various studies we have concluded that white women have a higher incidence of endometrial cancer than black women. Their mortality is higher, based on ethnicity and race. Estimated percentage of occurring endometrial cancer up to 2017 is blacks 24.8% and whites is 26.3%. Overall incidence rates are 25.6% and overall estimated death rates are 4.6%. But in black women estimated death rates are 8.1% and white women death rates are 4.2%. Because black women diagnosed with less favourable histologies and more poorly differentiated tumours when compared to white. PCOS, diabetes, obesity all important risk factors increasing a woman's probability for endometrial cancer 5-10 times compared with patients without risk factors. There is evidence to support higher incidence in westernized populations. A number of studies have shown that diets high in fat and low in complex carbohydrates and fiber increase a woman's risk of endometrial cancer. Large body mass and obesity in particular cases women at increased risk of endometrial cancer. Obese women have higher endogenous oestrogens than lean women. For each 5kg weight gain the risk for developing endometrial cancer increases by 21%. Prevention of endometrial cancer requires early detection and diagnosis of atypical hyperplasia. The most important predictor of outcome and survival in women with endometrial cancer is tumour stage. Stage I disease is limited to the uterus corpus without involvement of serosa. With 5 years survival rates of 75%. In stage II the uterus is involved and disease extends to the cervix and survival is 69%. In stage III cancer spreads to the body of uterus and survival rates are 47%. In stage IV cancer spreads to regional or distant metastasis and disease has spread the outside of uterus and survival rates are 15%.

## DISCUSSION AND CONCLUSION

This review analysis offers the first estimates of risk associated with EC in black women for common risk factors. The prevalence of these risk factors vary by race in the US population. Obesity is the strongest risk factor for EC among all women examined in this study. A potentially modifiable risk factor, obesity is linked with a number of cancers, but the strongest association is with EC. The previously reported relative risk of 1.6 per 5 kg/m<sup>2</sup> incremental increase is similar to the 3-fold increase among both black and white women we reported between women who were obese and those of normal weight. Overweight women are also at increased risk of EC, although the effect size is more modest. The racial disparity in obesity prevalence between black and white women has been widely reported. With a greater proportion of black women classified as obese, one would expect to see higher incidence of endometrial cancer among black women, as has been reported when the higher prevalence of hysterectomies is accounted for in the black population. Similar to our findings, the association between type II diabetes and EC has been reported in various studies. Reporting an approximate 2-fold increase in risk, Prevalence of type II diabetes continues to rise in the United States, and remains relatively higher among black women. The prevalence of childlessness increased more rapidly among black women than among white women during this time period (30% increase among blacks compared to 11% in whites). PCOS is other major risk factor for causing an endometrial cancer majorly predispose in black women compared to white women. Short term fertility treatment leads less risk of endometrial cancer compared to long term treatment. There is less usage of these drugs among black and white women so there is less risk of an endometrial cancer. Oral contraceptives usage is also very less among black so there is less chance of causing an endometrial cancer. Conclusion: Risk factors of an endometrial cancer in black and white women in infertility patients. In infertility patients compared to exogenous, endogenous risk factors are major chances of an occurring an endometrial carcinoma especially in black women more chances of causing an endometrial cancer. So "early detection leads to early prevention". So if we find in an early stages of cancer so we can go with an alternative treatment. In final stage hysterectomy is only option. Finally in endometrial carcinoma death is only option. So preventive measures should be taken. By 2030, endometrial cancer will become the 6th most common cancer overall, and the 3rd most common among women.

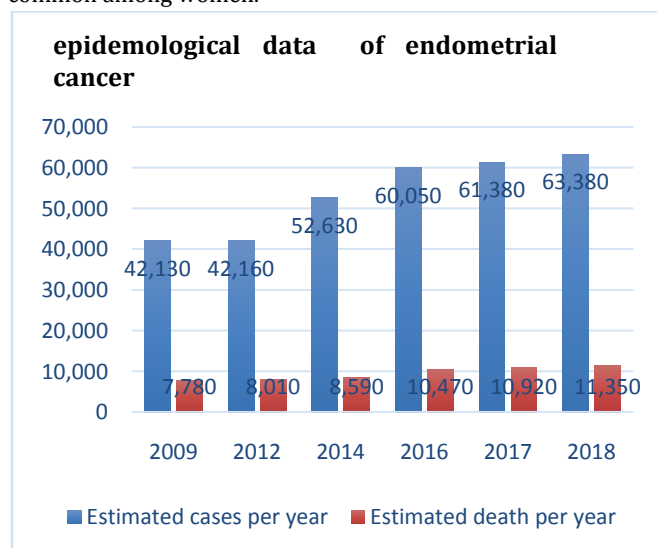


Fig 02: epidemiological data of endometrial cancer

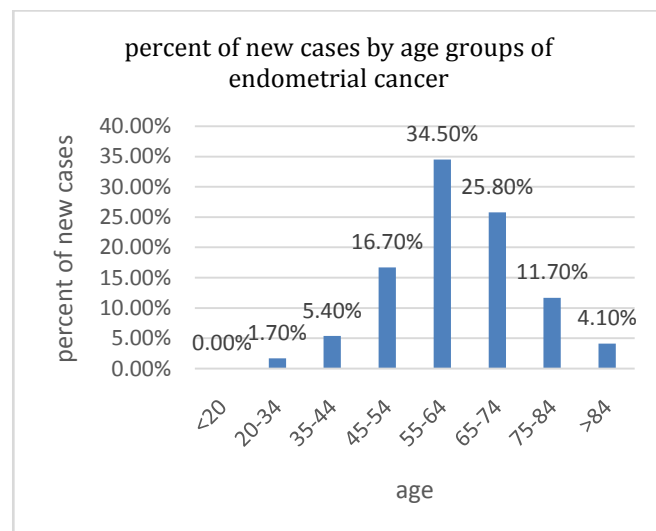


Fig 02: percent of new cases by age groups of endometrial cancer

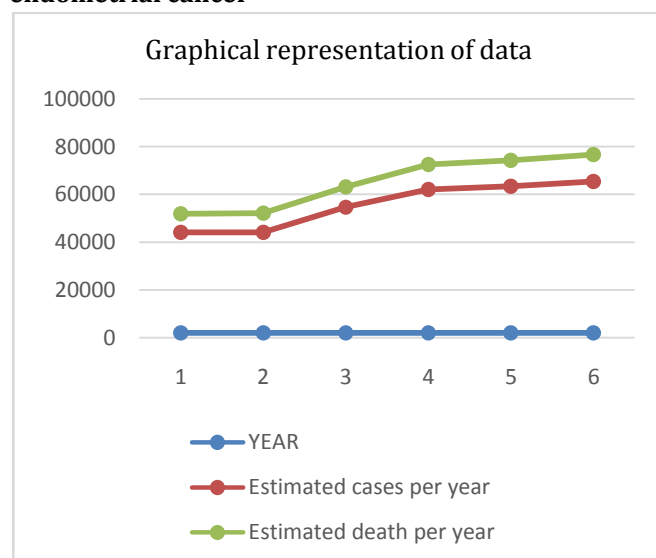


Fig 02: Graphical representation of data

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