## Original Article

# Study of demographic and risk factors in endometrial cancer at Al-Zahra hospital from 2007-2009

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#### **ABSTRACT**

*Objective:* To determine demographic status and risk factors in endometrial cancer among patients with this cancer.

**Methodology:** A case control study has been carried out on 53 patients with endometrial cancer and 303 patients with other endometrial disease that they refer to Al-Zahra Hospital of Tabriz between 2007-2009. Demographic data such of both groups of patients were evaluated.

**Results:** There were significant correlations between postmenopausal status (OR:13.37), hypertension (OR:2.7), Diabetes (OR:5.02), Diabetes & hypertension (OR:5.84) and infertility (OR:5.04) with endometrial cancer. There was no correlation between familial histories of urogenital cancer with endometrial cancer. There was no significant association between job and low income with endometrial cancer.

**Conclusion:** We conclude that age, obesity, hypertension, diabetes, postmenopausal status, and infertility are associated with a modestly increased risk for endometrial cancer. Diabetes is significant markers of risk for endometrial cancer, especially among the hypertensive women. Lower education was associated with endometrial cancer.

KEY WORD: Socioeconomic status, Risk factor, Endometrial cancer.

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## INTRODUCTION

Uterus cancer is the most common reproductive system cancer in British females and every year 3500 new cases are being reported. Endometrial cancer is the fourth common cancer after breast, lung and intestine cancers and the eighth cause of death due to malignancy in females. <sup>1,2</sup> In the recent years the prevalence of this cancer has increased. Although in the previous years the prevalence of this disease was high in developed and rich countries, the epidemiologic trend is changing due to the increase

in risk factors such as obesity, hypertension, diabetes and in developing countries.

Endometrial cancer is the cancer of menopause period however 25% of its presentation is observed before menopause and 5% before the age of 40.<sup>1,3</sup> At the time being the reason causing uterus cancer is not precisely known, but genetic and environmental factors have been proved to be influential.

Considering the individual, social and nutritional differences between Asian and non-Asian countries, the low number of studies carried out on endometrial cancer no related study was carried out in Tabriz, patients' cases being incomplete regarding the variables needed for this research, social status and endometrial cancer risk factors in the recently diagnosed patients, this research was designed aiming at determining socio-individual status and risk factors in patients with endometrial cancer.

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# **METHODOLOGY**

In a cross sectional case-control study carried out on the patients with endometrial cancer (casegroup) in the oncology ward of Alzahra Hospital in 2008 – 2009, patients with and the history of cancer

were selected and evaluated. Three hundred three females referred to the Alzahra gynecology clinic who had curettage and had no endometrial, cervical or ovarian cancers were randomly selected as the control group. Endometrial biopsy was performed by either Pipelle out patiently or a fine no 0 currette under general anesthesia. Required socio-individual data including age, weight, age at marriage, number of term deliveries, age at the first delivery, age at that last delivery, menarche age, menopause age, the duration between the last delivery and endometrial cancer emergence, education, occupation and income status were collected.

The risk factors studied in this study were as following: obesity, nulliparity, delayed menopause (after the age of 52), infertility, history of medical diseases (hypertension, diabetes and hypothyroidism), and familial history of cancer and estrogen administration without progesterone. Obtained data were analyzed using SPSS 16 software. To perform descriptive analysis, descriptive analysis approaches (mean & standard deviation) and to perform analytic analysis, the test of means comparison (t-test), Chi-square test, & odd's ratio were used in case and control groups. P<0.05 was considered significant. *Findings:* In the case group, 49 cases (92.45%) had no income and in four cases (7.5%), the income level was higher than 300,000 Tomans per month. In the control group income level of 291 cases was zero and for 12 cases it was higher than 300,000 Tomans per month. Chi-square test results revealed no significant difference between two groups regarding income (X2= 30.1, df = 2, p = 0.202). The results obtained from this test also revealed no significant difference between the patients of two groups regarding income (X2=31.2, df = 2, p= 0.315).

In the case group, 37 patients (69.8%) were older than 50 years and in the control group, 67 patients (22.11%) were older than 50 years. Age over 50 years increases the risk of endometrial cancer 1.2 times (: 23.1 OR, (234.0-064.0)=CI, p= 0.001). Nulliparity also increases the risk of endometrial cancer seven times (Odds ratio = 57.7, CI 95% = 72.16, p<0.001). Overallin 26 people (49.05%) of the patients with endometrial cancer the number of the pregnancies lasting more than five months was zero or one and or two. In 27 people (50.9%) the number of the pregnancies more than five months was three or more. In the control group, in 106 people (34.9%) the number of the pregnancies more than five months was zero or one and or 2. In 197 people (65.01%) the number of the pregnancies more than five months was three or more. (CI 95% = 1-31.0, Odds ratio = 559.0, x2 = 29.38, df=1, p=0.037).

Based on the above mentioned findings, it can be concluded that the number of pregnancies more than five months less than three times increases the risk of endometrial cancer by 50%. Term delivery number equal or more than three has a protective effect of 45% against endometrial cancer. Eight people (22.22%) of the case group patients and 25 people (8.71%) of the control group patients had a last delivery age of more than 40 years and delivery age more than 40 years increased the risk of endometrial cancer 2.9 times (CI 95%= 26.7-23.1, Odds ratio 994.2,p= 0.019).

Menopause was another valuable evaluated in this study. Findings revealed that menopause increases the risk of endometrial cancer by 13.3%. (CI 95%= 97.25-8.6, Odds ratio= 37.13, X2= 58.4,df=4,p> 0.001). 15 people (28.3%) of the case group patients and 188 people (63.04%) of the control group patients had a history of OCP consumption and OCP consumption reduced the risk of endometrial cancer by 76%. (CI 95%= 45.0-127.0, Odds ratio= 24.0, p<0.001). In the case group except for two people, no familial history of reproductive organs cancer was found in the patients with endometrial cancer. In the control group only four cases had a positive familial history.

In eight people (15.09%) of the case group patients and 13(4.2%) of the control group patients the familial history of other organs cancer was positive and familial history of cancer increased the risk of endometrial cancer 3.9 times (CI 95%= 10.10-51.1, Odds ratio= 96.3, p= 0.001). Infertility increased the risk of endometrial cancer five times. Diabetes and diabetes associated with hypertension increased the risk of endometrial cancer 5 and 5.8 times respectively.

Finally the influential factors on pathogenicity of endometrial cancer were reevaluated using logistic regression model and the results are presented in Table-I. The results obtained from the analysis revealed that although analyses obtained from chisquare report significant difference in nine cases

Table-I: Determine endometrial cancer risk factors at the bale of logistic regression model.

Risk Factors	P_Value
Menopause	<0.001
Nulliparity	< 0.001
Age over than 50 years	0.004
Delivery age more than 40 years	0.438
Familial history of non reproductive organs cancer	0.200
HTN	0.855
Diabetes	0.404
Diabetes and HTN	0.403
Infertility	0.882

regarding the prevalence of risk factors in both groups, in this model there were only three significant differences which were introduced as endometrial cancer risk factors. Nulliparity and menopause are the most important major risk factors of endometrial cancer followed by age over 50 in our study.

#### **DISCUSSION**

The mean age of the patients with endometrial cancer was 56 years in this study which was significantly higher compared to control group. 69.8% of patients with endometrial cancer were in the age range of more than 50 years which was in accordance with our study, in the study of Lapinska the mean age of patients with endometrial cancer was also 58.9 years and 71.79% of the patients were in the menopause age<sup>4</sup>. In most studies, like the present study, endometrial cancer is mostly seen in the females older than 50 years old and its risk increases by age. In our study also age more than 50 years increased the risk of endometrial cancer 1.2 times.

In our study, the mean weight of the patients with endometrial cancer was significantly more in the patients of control group. BMI is considered a risk factor in many cancers including endometrial cancer in different studies. 4-6 Hankinson and Shoff hypothesized that increase in estrogen in obese patients increases the risk of endometrial cancer.<sup>4,5</sup> Some studies however has questioned this relation and suggested the need for further studies.<sup>7,8</sup> One very minute point which has been ignored in these studies is that the recent weight gain and increase in BMI are more valuable than the present BMI of patients. Weiderpass has emphasized this issue in his study.8 According to the findings of Weiderpass, the risk of endometrial cancer emergence in overweight (BMI = 99.29 -28) females is 5.1 times and in obese females (BMI= 30-33.99) it is three times more than normal people. In the present study weight less than 80 kg decreases the risk of endometrial cancer by 51%. In some studies, the relation between obesity and endometrial cancer has been explained by hormonal changes. Obesity in adults is in relation with ovarian cycle and therefore it is explainable.8,9

In the present study there was a significant relation between nulliparity and the prevalence of endometrial cancer and nulliparity increased the risk of endometrial cancer seven times and in the similar studies nulliparity increased the endometrial cancer risk 2 to 3 times compared to multiparity.<sup>4</sup>

In our study, pregnancies more than five months had a 45% protective effect against endometrial cancer. However in the previous studies, no proof

was found to confirm these two factors being risk factors. Some researchers however believe that this factor can be one of the influential factors in increasing endometrial cancer emergence.<sup>4</sup>

Age at the first delivery was below 30 in our study except for two cases in control group which is different from the results of the study of Hinkula et al. <sup>10</sup> In their study the risk of endometrial cancer was less in the patients with first pregnancy age of over 30 compared to the patients with the first pregnancy age of less than 30. As it was already mentioned in the findings part, the menopause mean age was not significantly different in two groups whereas menarche mean age was significantly less in the case group.

Hinkula et al also found no significant relation between early menarche and the emergence of endometrial cancer but they believed that the history of irregular menstruations increases the risk of endometrial cancer due to the effect of non-ovulation cycles.<sup>10</sup>

In the present study, OCP consumption decreases the risk of endometrial cancer by 76%. In the study of Dossus et al OCP consumption also decreased the risk of endometrial cancer by 35% and OCP consumption of more than 10 years decreased the risk by 42%. In the present article the mean OCP consumption was less in the patient group compared to the control group however the difference was not significant.<sup>11</sup>

In our study, the prevalence of endometrial cancer was significantly more in menopausal females compared to non-menopausal females. The menopause increases the risk of endometrial cancer 13 times and in most studies menopause specially delayed menopause are considered risk factors in the emergence of endometrial cancer.<sup>7</sup> Although in most studies smoking is considered a protective factor against the endometrial cancer, in our study none of the patients smoked. It should also born in mind that smoking is uncommon among Iranian females and therefore this can be considered as a confounding factor.

Another interesting point is that however in most studies endometrial cancer prevalence is higher in the females with positive reproductive organs cancer history<sup>7</sup>, in our study no significant relation was found between two groups in this regard. On the other hand a significant positive relation was found between the familial history of cancer in other organs and emergence of endometrial cancer in this study. Positive familial history of other cancers increased the risk of endometrial cancer 3.9 times which was not observed in the previous studies.

In our study, there was a significant relation between endometrial cancer and hypertension as hypertension increased the risk of endometrial cancer 2.7 times. In the study of La vecchia et al. hypertension associated with obesity increased the risk of endometrial cancer 1.4 times and sole hypertension had no effect on the increasing risk of cancer emergence.<sup>8</sup>

In our study also diabetes was an independent risk factor in increasing endometrial cancer risk and increased endometrial cancer risk five times. Diabetes associated with hypertension also increased the risk of endometrial cancel 5.8 times. Weiderpass et al reported a higher endometrial cancer risk in the patients with diabetes type I compared to the patients with diabetes type IIs whereas Kjeruff reported that diabetes type II increased the risk of endometrial cancer.<sup>12</sup>

Similar to the findings of our study, the relation between diabetes and endometrial cancer have been proved in most epidemiologic studies. Weiderpass believes that diabetes obviously increases the risk of endometrial cancer so that even after balancing BMI, its effects linger on (CI 95%= 3.2-2.1) (9, OR= 1.7). Berek gynecology states that diabetes increases the risk of endometrial cancer 1.3-2.8 times. Other diseases such as hypertension and hypothyroidism were associated with endometrial cancer but their relation was not significant.2 Therefore further studies emphasizing these risk factors are required. According to the findings of our study, infertility is considered a risk factor for endometrial cancer (OR=5) which is in accordance with the previous studies.<sup>7</sup> In the evaluation of the relations between endometrial cancer and social educational status of the patients, in the case group the educational status was significantly lower than control group and the relation between endometrial cancer and family income level was also significant.

It is said that the difference in the prevalence of some diseases especially cancers in different societies and races is due to the differences in socioeconomical goals in different societies. Krieger et al believe that no effective measures can be taken to prevent the effect of socio-economic factors are being ignored in the emergence of cancers.<sup>13</sup> In the study of Kjerulff et al, females with income levels higher than moderate were at a lower risk of having endometrial cancer compared to the poor and the degree and severity of the disease was significantly lower. This can be due to the early reference of the patients with enough income and their point of view regarding the deceased and diagnostic and therapeutic interventions.<sup>14</sup>

Kjerulff and Pokras, in their study, announced that income level of all the patients with endometrial cancer and hysterectomy was below normal level. Although the findings of this study are different from the similar studies regarding income level of patients with endometrial cancer, it should be considered that there is the possibility that the patients have not been honest and have been reluctant to reveal the truth. Nulliparity and menopause are the most important major risk factors of endometrial cancer followed by age over 50 in our study.

## **CONCLUSION**

According to the findings of the present study, age over 50, obesity, early menstruation, menopause, hypertension especially associated with diabetes, infertility and positive familial history of the cancer of other organs are the risk factors in the emergence of endometrial cancer. No significant relation was found between familial history of reproductive organs cancer and hypothyroidism. The prevalence of endometrial cancer was significantly higher in the females with lower educational levels, however no significant relation was found between endometrial cancer and income level.

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