Original Article

Association of Obesity with Endometrial Carcinoma

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Abstract

Objectives: To assess the association of anthropometric parameters including obesity with endometrial carcinoma in our study population.

Study Design: Case control study

Place and duration of study: This study was conducted in departments of Obstetrics & Gynecology and Radiology, Combined Military Hospital, Quetta, from August 2016 to May 2018.

Methodology: The patients in cases group were new or old diagnosed cases of endometrial carcinoma and for controls, healthy participants visiting to both of these departments were selected. A total of 174 consisting of 87 cases and 87 controls were included. A structured in-person interview was conducted to collect the information regarding demographics age, parity, menstrual cycle, past medical, drug and contraceptive method used, followed by general physical, examination. Diagnostic reports, including information regarding cancer site, histology, extent of disease were obtained. The final confirmation and characterization of disease status was based upon histological report.

Results: The mean age of cases was 48.30 ± 8.50 years and the mean age of control group was 47.87 ± 8.29 years. The history of any type of cancer in first degree relative was positive in 33 (37.93%) participants among cases group and 21 (24.14%) participants in the control group. There was a positive history of using oral contraceptives in 33 (37.93%) cases and 22 (25.29%) controls. The body mass index also showed a similar positive trend for risk of endometrial carcinoma as the BMI of the woman increases. The waist to hip ratio was a more prominent indicator for risk of endometrial carcinoma with odds ratios of 1.48, 2.60 and 3.0 for increasing WHR categories respectively.

Conclusion: Overall adiposity in terms of body weight and body fat distribution that is central obesity were strongly associated with endometrial cancer risk with the latter being a stronger disease predictor.

Key Words: Endometrial carcinoma, obesity, central obesity, body mass index.

Cite this article as: Nayyar S, Khan AA, Nayyar A, Nayyar S. Association of Obesity with Endometrial Carcinoma.J. Soc. Obstet. Gynaecol. Pak. 2018; Vol 8(3):180-184.

Introduction

Endometrial carcinoma is one of the most common type of women cancers in the world like breast, lung and colon cancers. All these cancer are increasing sharply over past few decades. The incidence of endometrial cancer is also one among these cancers which is rising very sharply and its incidence has increased by 40% but due to improvement in treatment modalities its survival rate also has increased considerably upto 20-40%. The incidence of endometrial cancer is about 10 times greater in developed countries as compared to developing

Authorship Contribution: [1]Supervised the study design, sample collection and & discussion, [2,3]Literature review, Interpretation, Data analysis.

Funding Source: none

Conflict of Interest: none

Received: June 26, 2018

Accepted: Oct 11, 2018

countries of Asia and Africa. Which shows that endometrial cancer has the strong relationship with non-genetic factors like environmental factors due to westernization and changing lifestyles. The most common factors of industrialization include overweight and obesity which cause a very severe impact on health cause morbidity and mortality. Many studies have elaborated that obesity increases the chance of endometrial carcinoma by 2-5 times.[1]

In developed countries, endometrial cancer (EC) is the most common malignancy of the female genital tract. The most important and well-recognized risk factors for type 1 EC are obesity, hypertension, diabetes mellitus, sustained unopposed hyperestrogenism and adenomatous endometrial hyperplasia.[2, 3] The etiology of endometrial carcinoma has a strong relation with obesity, which increases its chance to 1.7-4.5 times. It has been reported that weight gain or increased adiposity has an association with risk of endometrial carcinoma.[4,5] Excessive and prolonged levels of estrogenic stimulation result in endometrium hyperplasia, which further progresses to endometrial adenocarcinoma. The young women with persistent anovulation and menopause are significant contributors for hyperplasia. [6]

Long-term use of exogenous estrogen for treatment of postmenopausal symptoms or due to pathological ovarian condition consisting of polycystic ovarian disease, overweight and obesity and functioning granulosa cell tumor or the coma.[7]

A variety of studies have linked endometrial cancer to obesity, primarily based on either weight or a body mass index. More recently there has been interest in adult weight gain since this largely reflects changes in body fat, and in the distribution of body fat. Of particular interest is whether fat is distributed according to male type obesity (fat predominately on the upper body, e.g., nape of the neck, shoulder, chest, abdomen), or female type obesity (fat predominately on the lower body, e.g., hips, buttocks, thighs). Male type obesity has been related to a variety of hormonal abnormalities, including decreased sex hormone-binding globulin and elevated estradiol and testosterone levels.[8] The association of fat distribution with endometrial cancer is unclear. There is a positive relationships of endometrial cancer risk with high waist-hip ratio and skinfold measurements. Studies have shown positive relationships of risk with upper body obesity as well as with central obesity.[9]

Previous literature shows that obesity is the strongest risk factor for the development of endometrial cancer due to the mechanism of increased exposure to non-opposed estrogen. Consequently, the link between obesity and endometrial cancer become stronger. In our study population, this association has not been studied comprehensively. So, this present study was planned to find out the association of anthropometric parameters like obesity with endometrial Carcinoma in our population.

Methodology

This case control study was conducted in outpatient departments of Obstetrics & Gynecology and Department of Radiology, Combined Military Hospital, Quetta, from August 2016 to May 2018. The patients in cases group were new or old diagnosed cases of endometrial carcinoma visiting to both of these departments were included and for controls healthy participants, who don't have any symptom or diagnosed endometrial carcinoma were selected. A total of 174 samples was collected consisting of 87 cases of endometrial carcinoma and 87 controls. The sample size was calculated by using WHO sample size calculator on the basis of 5% level of significance, 80% power of a test, and anticipated population proportions (incidence of obesity) 36.30% in cases and 22.58% in controls. The patients in cases group were female having age 40–79 years, with a new diagnosis of invasive endometrial cancer during the study period.

After written consent was obtained, a structured in-person interview was conducted to collect the information regarding demographics age, parity, menstrual cycle, past medical, drug and contraceptive method used, followed by general physical, systemic, per speculum and bimanual pelvic examination. Transvaginal ultrasound was performed to measure the thickness of endometrium in the follicular phase of the menstrual cycle and MRI was used to find outspread of the endometrial carcinoma by single expert radiologist observer. Diagnostic reports, including information regarding cancer site, histology, the extent of disease were obtained. The final confirmation and characterization of disease status was based upon a histological report by an expert histopathologist who reviewed all the reports.

The matching controls were selected from the same departments visiting for any other purpose. The control group was selected in the same age group as in patients of endometrial cancer in the cases group. The patients having confounding factors like uterus fibroid,

cervical polyp, ovarian cyst and genital tract malignancy were not included in the study. The comorbidities including bleeding disorders, hyperthyroidism and liver disease, which can be a cause of biasedness were also excluded from the study. BMI was calculated with formula as (weight (kg)/[height (m)]2). The BMI categories were outlined by international and national guidelines for this study: BMI less than 25.0 (normal weight); 25.0–29.9 (overweight); and BMI > 30.0 were classified as obese.

All the collected data was entered and analyzed with SPSS v. 21. Mean as standard deviation were calculated for quantitative variables and frequency with percentages were presented for qualitative variables. Odds ratio (OR) with 95% confidence interval was calculated with Binary logistic regression to find out the association of anthropometric variables with endometrial carcinoma. P-value < 0.05 was considered significant.

Results

In this case control stud a total of 174 participants were included consisting of 87 cases of endometrial carcinoma and 87 normal healthy controls. The mean age of cases was 48.30 ± 8.50 years and the mean age of control group was 47.87 ± 8.29 years. Majority of the participants (42.53%) in cases group and (47.13%) in control group had a parity of 1 to 3, followed by (32.18%) in cases and (28.74%) in control group had a parity of 3 to 5. Among cases (14.94%) and (11.49%) controls had a parity of more than 5.

The history of any type of cancer in first degree relative was positive in 33 (37.93%) participants among cases group and 21 (24.14%) participants in control group. There was a positive history of using oral contraceptives in 33 (37.93%) cases and 22 (25.29%) controls. In cases group 28 (32.18%) participants had a routine of regular physical activity and 33 (37.93%) participants in a control group had routine of regular physical activity as elaborated in table I.

The association of anthropometric characteristics was calculated with help of odds ratio (OR) for each category taking the first category as the reference category in the calculation of OR for each parameter. The body mass index also showed a similar trend for risk of endometrial carcinoma elaborating that the chance increases as the BMI of the woman increase. According to the results women with normal weight having BMI of 21-25, have a similar chance of getting endometrial cancer as compared to women having BMI of < 20 but the overweight women having BMI of 26-30 have almost double chances of endometrial cancer as compared to women having BMI of < 20. The obese women having BMI of > 30 are at great risk for endometrial carcinoma with odds ratio of 2.35 indicating a more than double chances of getting endometrial cancer as compared with women having BMI of < 20.

Table I: Distribution of demographic characteristics of the participants

Characteristics	Cases (n=87)		Controls (n=87)	
Age of participant				
Mean ± SD	48.30 ± 8.50		47.87 ± 8.29	
Parity				
0	9	10.34%	11	12.64%
1-3	37	42.53%	41	47.13%
3-5	28	32.18%	25	28.74%
> 5	13	14.94%	10	11.49%
History of cancer in first degree relatives				
Positive	33	37.93%	21	24.14%
Negative	54	62.07%	66	75.86%
History of using oral contraceptives				
Positive	19	21.84%	22	25.29%
Negative	68	78.16%	65	74.71%
Routine of regular physical activity				
Yes	28	32.18%	33	37.93%
No	59	67.82%	54	62.07%

The waist to hip ratio was a more prominent indicator for risk of endometrial carcinoma the women having a WHR of 0.76 to 0.80 have 1.48 times increased chance of endometrial cancer as compared to women having < 0.75 WHR. This risk increases to 2.60 times among the women having 0.81-0.85 WHR and this risk rises enlarges 3 times among women having a waist to hip ratio of > 0.85 as compared to women having WHR < 0.75 as elaborated in table II.

Table II: Association of anthropometric parameters with endometrial cancer

Anthropo-metric Characteristics	Control (n=87)	Cases (n=87)	Odds Ratio (OR)	95% CI for OR	
				Lower	Upper
Body Mass Index					
< 20	17	10			
21-25	18	12	**1.13**	0.39	3.30
26-30	26	29	**1.90**	0.74	4.87
> 30	26	36	**2.35**	0.93	5.96
Waist to Hip ratio					
< .75	22	11			
.76-.80	23	17	**1.48**	0.57	3.85
.81-.85	20	26	**2.60**	1.03	6.59
> .85	22	33	**3.00**	1.22	7.40

Discussion

The patterns of endometrial carcinoma are different among premenopausal and postmenopausal women

but studies have proved the association of obesity with endometrial cancer in both pre and post-menopausal women and accounts for 40% of the disease burden. Whereas previous researchers have studied the relationship between obesity and endometrial cancer among women of all ages.[10] In the early 1980s, the Cancer and Steroid Hormone study examined the relationship between oral contraceptive use and breast, ovarian, and endometrial cancers in women aged 20–54 years and a large number of patients were found to have BMI in the overweight category. This provided a base to study the relationship between overweight/obesity on the basis of BMI and endometrial cancer.[11, 12]

In this present study the mean age of cases was 48.30 ± 8.50 years and mean age of control group was 47.87 ± 8.29 years. Many patients in cases group (34.48%) and control group (37.93%) were illiterately followed by (21.84%) in cases and (18.39%) participants in the control group had education till primary level. Majority of the participants (42.53%) in cases group and (47.13%) in control group had a parity of 1 to 3, followed by (32.18%) in cases and (28.74%) in control group had a parity of 3 to 5. Among cases (14.94%) and (11.49%) controls had a parity of more than 5. The studies on the relationship of obesity with endometrial cancer are being conducted since decades. Initially in early 1970s, body fat and weight was reported as one of the major risk factor for endometrial cancer and after that many studies discovered the function of obesity to increase the chances of endometrial cancer. The overall adiposity of fat was measured on the basis of body weight and indicators of relative weight like waist circumference and waist to hip ratio. Majority of these studies have reported that overall adiposity have a significant relationship with endometrial cancer.[13] But there are few studies investigating the association of obesity with endometrial cancer have shown results of no association between obesity and endometrial cancer and many studies have elaborated a strong relationship between body fat and risk of endometrial cancer.[14] Obesity is a main cause of hyperplasia which further develop to endometrial cancer. Hyperplasia is caused by chronic inflammation due to obesity.[15] The obese women (BMI > 30) have nearly 4 times increased the incidence of endometrium hyperplasia as compared with women having normal weight (BMI < 25). Similarly, women having BMI > 40 have 13-23 times higher risk for development of hyperplasia which results in the development of adenocarcinoma.[16]

According to the results of this present study, the chance of endometrial carcinoma increases as the weight increases. The results are in accordance with previous studies which suggested that weight gain throughout adulthood, particularly during the peri-menopausal period, increases the risk of endometrial cancer. Preventing weight gain should be recommended to curtail this and other chronic diseases in women. [17, 18]

According to the results of this study body mass index showed a positive trend for risk of endometrial carcinoma elaborating that the chance increases as the BMI of the woman increase. Women with the normal weight having BMI of 21-25, have a similar chance of getting endometrial cancer as compared to women having BMI of < 20 but the overweight women having BMI of 26-30 have almost double chances of endometrial cancer as compared to women having BMI of < 20. The obese women having BMI of > 30 are at great risk for endometrial carcinoma with odds ratio of 2.35 indicating a more than double chances of getting endometrial cancer as compared with women having BMI of < 20. These results have the agreement with previous studies like in a study, the odds ratios for women with BMIs of 25–30 and >30 were 1.6 and 3.3 respectively, as compared with women having BMIs <25.[19]

The waist to hip ratio was a more prominent indicator for risk of endometrial carcinoma the women having a WHR of 0.76 to 0.80 have 1.48 times increased chance of endometrial cancer as compared to women having < 0.75 WHR. This risk increases to 2.60 times among the women having 0.81-0.85 WHR and this risk rises enlarge 3 times among women having a waist to hip ratio of > 0.85 as compared to women having WHR < 0.75. Many studies support this result and elaborated that high waist circumference is significantly related to risk of endometrial cancer independently of BMI, and the positive association has been seen for women with BMI < 25. Some studies have suggested that waist circumference is a better predictor of endometrial cancer risk, and recommended it as a more practical tool for assessment of abdominal fat along with overall adiposity indicated by BMI.[20,21]

Since there is a well-defined relationship between endometrial cancer and obesity, medical practitioners should counsel their obese endometrial cancer patients on the benefits of weight loss. A lot of data is available which shows that patients diagnosed with endometrial carcinoma have a poor quality of life and get many

comorbid diseases and among these patients, the cancer is not the main cause of death. So, it is very important that these patients should be counsel for benefits of weight loss in their disease by the gynecologic oncologists along with their regular treatment. Potential options include self-directed or supervised diet and exercise programs, medical management with insulin-sensitizing agents and/or statins, and bariatric surgery.[22]

Conclusion

Overall adiposity in terms of body weight and body fat distribution central obesity were strongly associated with endometrial cancer risk with the latter being a stronger disease predictor. The association between central obesity and endometrial cancer was more distinct. The distribution of body fat appeared to have an independent effect, with high risks associated with fat located on the trunk of the body. These findings infer a relationship of endometrial cancer risk to positive energy balance. Standardized measurements for fat distribution, along with the assessment of hormonal and other biological parameters, are also needed to assist in identifying causal mechanisms for endometrial carcinoma.

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