

ORIGINAL RESEARCH

Triad of obesity, hypertension and diabetes in endometrial cancer-do we really need to worry?¹Dr. Ramandeep, ²Dr. Ravinder Ravi, ³Dr. Deeksha Sharma, ⁴Dr. Parveen Rajora^{1,2}Junior Resident, ³Senior Resident, ⁴Professor, Department of Obstetrics and Gynaecology, GGSMCH, Faridkot, Punjab, India**Corresponding author**

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Abstract

Introduction: Endometrial cancer is the most common malignancy of women in developed countries, and its incidence is rising among pre- and postmenopausal women. The major risk factor for endometrial carcinoma (EC) is the presence of a clinical scenario associated with an excess of endogenous or exogenous estrogen without adequate opposition by a progestin. Obesity, a global health problem, has been identified as the most important risk factor for hypertension and diabetes. Obese persons have a significantly higher risk of hypertension and type 2 diabetes. Many studies have shown that common pathophysiology is shared by diabetes and hypertension which has direct link with obesity.

Material and method: This is a prospective study done at Guru Gobind Singh Medical college and Hospital, Faridkot from June 2019 to June 2021. A total of 70 patients with biopsy proven endometrial carcinoma were enrolled in this study.

Results: In this study, it is found that maximum women having carcinoma endometrium belongs to mean age of 54.52±9.57 years. About 88.57% were having history of postmenopausal bleeding. BMI is more than 30 in 60% of subjects. 24.2% women had hypertension, 21.4% had triad of hypertension, diabetes and obesity, 20% had diabetes and 17.7% had both diabetes and hypertension.

Conclusion: Obesity, diabetes and hypertension are the metabolic triad of endometrial cancer. The results of this study strongly suggest that the metabolic syndrome and its individual components (BMI, glucose and triglyceride concentrations, and hypertension) are important contributors in the development of endometrial carcinoma.

Keywords: Endometrial carcinoma, diabetes mellitus, hypertension, obesity.

Introduction

Endometrial cancer is the most common malignancy of women in developed countries, and its incidence is rising among pre- and postmenopausal women. Over 90 percent of uterine cancers are endometrial, originating in the epithelium; most of the remainder are mesenchymal, originating in the myometrial muscle or, less commonly, the endometrial stroma (1). The major risk factor for endometrial carcinoma (EC) is the presence of a clinical scenario associated with an excess of endogenous or exogenous estrogen without adequate opposition by a progestin (2). Endometrial cancer is more common in postmenopausal women than in premenopausal women. It was concluded that the risk of endometrial cancer is positively correlated with older age, early menarche and late menopause, obesity, family history of endometrial cancer (especially among close relatives), radiation exposure, and

infertility particularly in the presence of Polycystic Ovarian Syndrome. Lynch syndrome (hereditary nonpolyposis colon cancer) is a genetic risk factor; pathogenesis in these cases is a germline mutation in one of the DNA mismatch. Long-term use of unopposed estrogens for hormone replacement therapy also increases the risk of endometrial cancer(3). Caucasians have a higher incidence of endometrial cancer than African or Asian women.

Obesity, a global health problem, has been identified as the most important risk factor for hypertension and diabetes .The incidence of endometrial cancer is increasing due to prevalence of obesity, increased prevalence of diabetes and changes in reproductive behaviour (eg, nulliparity)(4).Obese persons have a significantly higher risk of hypertension and type 2 diabetes mellitus. Fatty tissue in women who are overweight produces additional estrogen, a sex hormone that can increase the risk of uterine cancer. About 70% of uterine cancer cases are linked to obesity. Hypertension increases the risk of carcinoma by blocking apoptosis. Hypertension inturn causes insulin resistance & hyperinsulinemia. Hyperinsulinemia, insulin resistance, hormonal disturbances, release of inflammatory mediators in Diabetes mellitus and Hypertension are the most important pathways that are responsible for endometrial carcinogenesis. Hyperinsulinemia and IGF-1 have pro-proliferative and anti-apoptotic action on endometrial cells(5).

Obesity, Hypertension and Diabetes mellitus are also known as ‘triple syndrome of endometrial cancer’ or ‘metabolic triad of endometrial cancer’.Under this background this study was done to find out correlation of this triad Hypertension , diabetes and obesity in causing endometrial carcinoma.

Aims and Objectives

To find out association between endometrial cancer and diabetes,hypertension and obesity.

Material and Method

This is a prospective study done at Guru Gobind Singh Medical College and Hospital, Faridkot from June 2019 to June 2021. A total of 70 patients with biopsy proven endometrial carcinoma were enrolled in the study. The patients were well informed about the study procedure and written informed consent was taken. A thorough history, clinical examination and biochemical investigations done and their corelation with hypertension, obesity , and diabetes documented.

Statistical Analysis

IBM SPSS. Statistics Windows, Version 20.0. (Armonk, NY: IBM Corp) was used for statistical analysis Descriptive statistics like mean and percentages were used for analysis.

Results

Table 1:

Age (years)	Frequency	Percentage
26-40	2	2.85%
41-55	26	37.14%
56-70	30	42.85%
71-85	12	17.14%
Total	70	100%
Mean±SD	54.52±9.57	
Median	58.00	
Range	26-85	

Table 1 showed the age distribution of subjects. Maximum subjects were in 56-70 years of age group and the mean age was 54.52±9.57 years.so most of the patients were of perimenopausal and postmenopausal age group.

Table 2: History of Post-Menopausal Bleeding

Post-Menopausal Bleeding	Frequency	Percentage
Absent	8	11.4%
<1 Month	10	14.42%
1-6 Months	34	48.57%
7-12 Months	15	21.42%
>12 Months	3	4.28%
Total	70	100%

Out of 70, 34 patients had postmenopausal bleeding since 1-6 months while 3 patients had bleeding since around 1 year as shown in the following table 2. Significantly 88.57% presented with chief complaint of post menopausal bleeding.

Table 3: Co-Morbidity association

Co-Morbidity	Patients	Percentage
Hypertension	17	24.2%
Diabetes Mellitus	14	20%
Diabetes Mellitus + Hypertension	12	17.7%
Diabetes Mellitus + Hypertension + HypoTH	1	1.42%
Hypertension + HypoTH	2	2.85%
Breathlessness + Hypertension	15	21.42%
Breathlessness	5	7.14%
Cleft Lip	1	1.42%
None	3	4.28%
Total	70	100%

Table 3 showed the associated comorbidities. Approximately 24.2% subjects had hypertension followed by 20% subjects having diabetes mellitus, and 17.7% having both diabetes mellitus and hypertension.

Table 4a): Weight (kg)

Weight (kg)	Frequency	Percentage
45-64	9	12.85%
65-84	44	62.85%
85-104	17	24.28%
Total	70	100%
Mean±SD	78.45±7.81	
Median	81.00	
Range	45-102	

(b): Height (mtr)

Height (mtr)	Frequency	Percentage
1.26-1.40	4	5.7%
1.41-1.55	24	34.28%
1.56-1.70	39	55.71%
≥1.71	3	4.2%
Total	70	100%
Mean±SD	1.66±0.09	
Median	1.59	
Range	1.28-1.73	

(c): BMI

BMI	Frequency	Percentage
Underweight (<18.5)	0	0%
Normal (18.5-24.9)	9	12.85%
Overweight (25.0-29.9)	18	25.71%
Obese (≥ 30)	42	60%
Total	70	100%
Mean \pm SD	32.38 \pm 3.08	
Median	32.00	
Range	24.40-39.00	

Table 4 showed the weight, height and BMI of the subjects. Mean weight was 78.45 \pm 7.81 kg, mean height was 1.66 \pm 0.09 meters, Mean BMI was 32.38 \pm 3.08 kg/m². 25.71% subjects were having BMI more than 25 and 60% were having BMI more than 30 indicating total of 85.71% were of above normal range of ideal body weight .

Table 5: Random Blood Sugar (RBS)(mg%)

Random Blood Sugar (mg%)	Frequency	Percentage
<90	12	17.14%
90-120	26	37.14%
121-200	13	18%
≥ 201	19	27.14%
Total	70	100%
Mean \pm SD	159.58 \pm 91.79	
Median	118.00	
Range	70-442	

Table 5 showed the random blood sugar(mg%). The mean random blood sugar was 159.58 \pm 91.79(mg%). 32 patients were diabetics out of 70 making it 45% which is quite a significant figure.

Table 6: Endometrial Biopsy Report

Endometrial Biopsy Report	Frequency	Percentage
Endometroid CA,	46	65.71%
Adenocarcinoma, Moderately differentiated	9	12.85%
Adenocarcinoma- Poorly Differentiated	4	5.7%
Adenocarcinoma Endometrium, Well Differentiated	3	4.24%
Poorly Differentiated Carcinoma with Areas of Necrosis	2	2.8%
Poorly Differentiated Carcinoma with Foci of Cartilaginous Differentiation	1	1.42%
Clear Cell Carcinoma Poorly Differentiated	1	1.42%
Endometrial Adenocarcinoma+ Squamous Cell Differentiation	2	2.8%
Endometrium Malignant Pathology	1	1.42%
S/O Malignant Tumor Exhibiting Morphology of Endometroid Adenocarcinoma	1	1.42%
Total	70	100%

Table 6 showed the endometrial biopsy report. It showed that 65.71% subjects had endometrial CA, in their biopsy, 12.85% subjects showed Adenocarcinoma, Moderately differentiated endometrium. We have taken all biopsy confirmed endometrial carcinoma cases only.

Discussion

The results of our study indicates that there is high correlation between Hypertension, Obesity and Diabetes mellitus with endometrial carcinoma. The risk increases with increase in number of these metabolic manifestations. There occurs association between these conditions(6). Obesity is associated to endometrial cancer because of increased levels of serum estrogens. Hyperinsulinemia and IGF-1 causes pro-proliferative action on endometrial cells and also increase estrogen levels of body. Hypertension increases endometrial carcinoma risk but its mechanism is still unclear(7).

In our study, it was found that mean age of affected women was 54.52±9.5 years. In a study conducted by Sunanda Bharatnur et al mean age found out was 55.19±6.7 years(8). Mean age at presentation was 59.83 years in a study conducted by Jeenu babu et al(9).

In our study, majority women 88.57%(n=62) were having history of post menopausal bleeding. Similar findings were seen in a study conducted by Megan et al that post menopausal bleeding occurs in approximately 90% of women with endometrial cancer(10). This indicates that in women presenting with post menopausal bleeding, possibility of carcinoma endometrium could be kept in mind.

Our study shows that among 70 women with endometrial carcinoma 12.85%(n=9) had normal BMI, 25.71%(n=18) were overweight whereas 60%(n=42) were obese. This result corresponds with the results observed by Begum SA et al. Their results shows distribution of BMI(body mass index) of 50 women having endometrial carcinoma, only 4% (n=2) normal BMI, 36% (n=18) overweight, 60% (n=30) obese. Another 50 healthy women without endometrial carcinoma presented with 4% (n=2) underweight, 70% (n=35) normal weight, 14% (n=7) overweight and only 12% (n=6) were obese(11).

Our study concluded that association of Diabetes mellitus alone with carcinoma endometrium is 20%(n=14) and association of hypertension alone is 24.2%(n=17). Association between Diabetes mellitus+Hypertension is 17.7%(n=12). In a study conducted Wijaya et al, the association between diabetes mellitus and/or hypertension with endometrial cancer was showed in 66.4 % patients(12). Women with diabetes mellitus and hypertension are at increased risk for endometrial cancer.

Conclusion

Obesity, diabetes, hypertension are the triad of endometrial cancer. By multiple endocrine and inflammatory mechanisms, there occurs correlation between carcinoma endometrium and obesity, diabetes mellitus and hypertension. Strengthening public awareness about changing lifestyle and maintaining healthy weight, early diagnosis and treatment of hypertension and diabetes mellitus can decrease morbidity and mortality due to endometrial cancer.

References

1. Sagnic, S. Obesity and Endometrial Cancer. Role of Obesity in Human Health and Disease [Internet]. London: IntechOpen; 2021 [cited 2022 Dec 09]. Available from: <https://www.intechopen.com/chapters/78609> doi: 10.5772/intechopen.99827
2. Lukanova, A, Circulating levels of sex steroid hormones and risk of endometrial cancer in postmenopausal women. *Int J Cancer*, 2004;108(3):425-32.
3. Ewertz M, Schou G, Boice JD Jr. The joint effect of risk factors on endometrial cancer. *Eur J Cancer Clin Oncol*. 1988;24:189-94.
4. Constantine GD, Kessler G, Graham S, Goldstein SR. Increased Incidence of Endometrial Cancer Following the Women's Health Initiative: An Assessment of Risk Factors. *J Womens Health*. 2019;28(2):237-43.
5. Njoku K, Agnew HJ, Crosbie EJ. Impact of Type 2 Diabetes Mellitus on Endometrial Cancer Survival: A Prospective Database Analysis. *Front Oncol*. 2022;12:899262.

6. Bjørge T, Stocks T, Lukanova A, Tretli S, Selmer R, Manjer J, Rapp K, et al. Metabolic syndrome and endometrial carcinoma. *Am J Epidemiol.* 2010;171(8):892-902.
7. Rosato V, Zucchetto A, Bosetti C, Dal Maso L, Montella M, Pelucchi C, et al. Metabolic syndrome and endometrial cancer risk. *Ann Oncol.* 2011;22(4):884-9.
8. Bharatnur S, Kustagi P, Krishnamohan D. Endometrial Carcinoma in a Young Woman: "30 is Not Immune". *J ObstetGynaecol India.* 2011;61(6):686-8.
9. Babu J, Pulinilkunnathil RG, Kumar BR. An epidemiological assessment of endometrial carcinoma including demographics and histopathological correlation, from a tertiary care teaching hospital in south India. *J Evid Based Med Healthc.* 2021;8(30):2751-56.
10. Clarke MA, Long BJ, Del Mar Morillo A, Arbyn M, Bakkum-Gamez JN, ET AL. Association of Endometrial Cancer Risk With Postmenopausal Bleeding in Women: A Systematic Review and Meta-analysis. *JAMA Intern Med.* 2018;178(9):1210-22.
11. Begum SA, Mahmud T, Amatullah M. Association of Endometrial Carcinoma with Obesity and Diabetes Mellitus. *Bangladesh Med Res Counc Bull.* 2020;46:120-7.
12. Wijaya CF, Martaadisoebrata D. Diabetes Mellitus and Hypertension are Risk Factor for Endometrial Cancer. *Indones J Obstet Gynecol.* 2012;36(3):140-3.