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RESEARCH ARTICLE

POST MENOPAUSAL BLEEDING PATTERNS IN PREDICTION OF ENDOMETRIAL CARCINOMA

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Abstract

Objective: To determine the demographic profile, patterns of bleeding and histopathological patterns of endometrial biopsy in women presenting with postmenopausal bleeding.
Study Design: Descriptive cross-sectional study.
Place and Duration of Study: Department of Obstetrics and Gynaecology, CAIMS, Karimnagar from October 2020 to April 2022.
Material and Methods: This descriptive cross-sectional study included women of any parity and age >45 years who had spontaneous cessation of menstruation for the last one year and who presented with abnormal uterine bleeding. Premenopausal women, drug or irradiation induced, or iatrogenic menopause cases were excluded. All patients were admitted, transvaginal ultrasound done (cut off endometrial thickness >4mm) and subjected to dilatation and curettage under anesthesia and endometrial biopsies obtained. Samples were sent for histopathology and followed.
Results: A total of 70 women were included. Commonest age group was 61-70 years, and was seen in 38 (54.3%) women, followed by the 52-60 years age group where 18 (25.7%) subjects were observed. Mean age was 62 ± 2.54 years. Twenty-four (35%) women were hypertensive while Type 2 Diabetes Mellitus (T2DM) was seen in 14 (20%). forty (57%) women complained of streaks of blood on the sanitary pad, and in 56 (80%) (P=0.032) there were recurrent episodes. Forty-eight (68.57%) women were multiparous. Atrophic endometrium was the most common benign histopathological pattern, seen in 18 (26%) followed by 16 (23%) chronic endometritis. Endometrial carcinoma was seen in 16 (23%). (p=0.041)
Conclusion: Postmenopausal bleeding is an alarming symptom and should be thoroughly investigated with transvaginal ultrasound followed by endometrial biopsy for timely diagnosis and treatment.

Introduction:-

Menopause is defined as the last menstrual period after a minimum of one year's amen-orrhoea. There is no mutual consensus for deciding the appropriate interval of amenorrhoea which will precede an episode of vaginal bleeding due to the anovulatory cycles that precedes menopause. It is estimated that 1-25% and on the average 10% women who present to the clinicians with postmenopausal bleeding will be ultimately diagnosed with endometrial

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carcinoma. Endometrial atrophy is the most common cause amongst the postmenopausal women. Endometrial polyps and hyperplasia are other common causes.

Endometrial cancer is the most diagnosed reproductive tract malignancy and is the fourth most common cancer among women, superseded by cancers of breast, lung and colorectal origin. Although it is responsible for causation of 6% of female malignancies, its ease of diagnosis and timely therapy makes it responsible for only 3% of malignancy related deaths. There are two types of endometrial carcinomas, type I is secondary to unopposed estrogen induced endometrial hyperplasia and type II are serous or clear cell origin, are independent of estrogen stimulation and have relatively poor prognosis. Recent data shows that type I comprises 90% and type II comprises 10% of endometrial malignancies.

For women receiving hormone replacement therapy, the pattern of bleeding depends on the type of gonadal steroids, especially the progestogens. Breakthrough bleeding occurs in women taking estrogen alone or both estrogen and progestogens. Fifty percent of women on hormone replacement therapy (HRT) experience breakthrough bleeding. In women with uterus, systemic estrogens of HRT increase the risk of endometrial carcinomas, even after its use is stopped.

For postmenopausal women not taking HRT, risk of endometrial carcinoma is 4.9% to 11.5%. Risk factors for endometrial carcinoma are obesity, hypertension and hypoestrogenism (exogenous or endogenous). Early menarche, late menopause and nulliparity due to high frequency of anovulatory cycles are also a risk factor. Hereditary nonpolyposis colorectal cancer is a rare risk factor with relatives of an affected family member having 50% risk of endometrial cancer.

Transvaginal ultrasonography is used to measure thickness of endometrium. This should be thinner in post-menopausal women (<4mm) not receiving HRT. This is by convention a double thickness in mid sagittal view called Endometrial Echo Complex (EEC). In general, thicker EECs are associated with a greater risk of endometrial lesions. Sampling of endometrium can be accomplished by devices for office use like pipelle, suction catheter, by dilatation and curettage, or under hysteroscopic guidance. Any method of sampling the endometrium will certainly miss a proportion of endometrial carcinoma.

The aim of our study is to conduct a hospital-based survey to determine the risk factors for endometrial carcinoma, its incidence and histopathological assessment.

Patients And Methods:-

This descriptive cross-sectional study was conducted at Gynaecology and Obstetrics Department of Chalmeda Anandrao Institute of Medical sciences from October 2020 to April 2022. All postmenopausal women irrespective of parity, who presented with vaginal bleeding of any amount, were included in the study. Menopause was considered a period of spontaneous amenorrhoea of one year. Premenopausal women, those having premature menopause, iatrogenic menopause, irradiation, or drug induced menopause or with incidental finding of increased endometrial thickness on ultrasound were excluded from the study. Sample size was calculated by using WHO sample size calculator and non-probability convenience sampling technique was adopted for this study.

Approval from the hospital ethical committee was obtained. Written informed consent was taken from all patients after explaining to them the purpose of study. Patients were recruited from outpatient department (OPD), detailed history was taken regarding age, parity, time since menopause, number of episodes of vaginal bleeding whether single or recurrent, amount of bleeding whether spotting, streak of blood on sanitary pad or fully soaked pad. Associated vaginal discharge, abdominal mass or history of weight gain or loss was also inquired. Drug history with special emphasis on intake of anticoagulants or antiplatelets, Tamoxifen and HRT was also taken. Diabetes, hypertension and any hepatic disorders were recorded as part of past medical history.

Thorough general physical examination including body mass index and blood pressure was recorded. Abdominal, bimanual pelvic and speculum examination was performed to evaluate uterus and cervix and smears obtained. Baseline investigations, bleeding and clotting profile, ECG and chest x-ray were performed from hospital laboratory and radiology department. Transvaginal ultrasound was done to evaluate the uterus for endometrial thickness with a cut off at 4mm. Anesthesia fitness was confirmed from the anesthetist and examination under anesthesia (EUA) was done after written informed consent. Dilatation and curettage were performed. Specimens were sent for

histopathology. Patients are discharged on the same day. Her histopathology reports and cervical smear results were followed in the OPD.

Table I:- Demographic characteristics (n=70).

Demographic variable		**Frequency**	**Percentage**
Age	45- 51 years	10	14%
	52- 60 years	18	25.70%
	61- 70 years	38	54.30%
	>70 years	4	5.70%
Parity	Nulliparous	22	31.40%
	Multiparous	48	68.57%
Diabetes	Yes	14	20%
	No	56	80%
Hypertension	Yes	24	34%
	No	46	66%

Table II:- Patterns of postmenopausal bleeding (n=70).

	Frequency	**Percentage**
Spotting	16	23%
Light	40	57%
Heavy	14	20%
Frequency of Bleeding		
Single Episode	14	20%
Recurrent Episodes	56	80%

Table III:- Etiology of postmenopausal bleeding based on histopathological reports (n=70).

Histopathological Report	**Frequency**	**Percentage**
Benign Disorders		
Atrophic Endometrium	18	26%
Chronic Endometritis	16	23%
Polyps	8	11.4%
Proliferative Endometrium	2	2.8%
Premalignant/Malignant Disorders		
Endometrial Carcinoma	16	23%
Atypical Endometrial Hyperplasia	10	14%
Cervical Carcinoma	2	2.8%

Data collected and analyzed in SPSS version 20.0. Mean and standard deviation calculated for numerical data and frequencies and percentages calculated for categorical variables. All data presented in the form of tables.

Results:-

A total of 70 women were recruited into the study. Four age groups were created, and subjects allocated into each group. Ten (14%) subjects were between 45-51 years old, 18 (25.7%) women were 52-60 years old, 38 (54.3%) were 61-70 years and 4 (5.7%) were more than 70 years old. Mean age was 62 ± 2.54 years.

Fourteen (20%) women had diabetes and 24 (35%) were hypertensive. Twelve (31.4%) women were nulliparous and 48 (68.57%) were multiparous (table-I).

Forty (57%) women complained of a streak of blood on the pad when asked about the amount of bleeding. Sixteen (23%) said it was mere spotting and in 14 (20%), it was heavy bleeding with soaking of full sanitary pad. Fourteen (20%) subjects had a single episode of per vaginal bleeding and 56 (80%) had this complaint multiple times before they sought medical advice (table-II). (P= 0.032)

Amongst the etiology, benign causes were more common when histopathological reports were reviewed. Atrophic endometrium was the most common, being seen in 18 (26%) subjects, followed by chronic endometritis in 16 (23%), polyp in 8 (11.4%) and proliferative endometrium in 2 (2.8%) cases. Amongst the premalignant and malignant etiologies, endometrial carcinoma was seen in 16 (23%), atypical endometrial hyperplasia in 10 (14%) and cervical carcinoma was seen in 2 (2.8%) cases of postmenopausal bleeding. (P=0.041)

In our study those who were diagnosed with endometrial carcinoma were found to have recurrent episodes or moderate to heavy bleeding and, 44 (63%) subjects had time period of less than 10 years between menopause and initiation of postmenopausal bleeding, but the risk of malignancy increased with increasing interval between menopause and development of symptoms.

Discussion:-

The main objective in managing a patient with postmenopausal bleeding is to exclude malignancy. Although 80-90% of patients presenting with this complaint had benign etiology, premalignant and malignant causes must be ruled out.

The commonest age group seen in our study was 61-70 years age, with mean age being 62 ± 2.54 years. Our result correlates with the study done by Burbos et al where the mean age was 64 years and the studies done by Davis et al by Von Doorn et al in terms of common age group. Regarding parity, 68.57% of our patients were multiparous. Nulliparity has been considered to be a risk factor for endometrial carcinoma not because of itself but due to the anovulatory cycles in infertile subjects. In a study done by Kothapally et al at Andhra Pradesh, India, it was concluded that most of the women with postmenopausal bleeding with ultimate histopathological findings of endometrial carcinoma were multiparous.

Diabetes was co-morbidity in 20% of our studied population. Burbos et al reported the figure around 17% and Visser et al reported it as 12.9%, whereas it was present in 54.5% of women studied by Fatima et al at Khyber Teaching Hospital, Peshawar. Food with high carbohydrate contents, hyperinsulinemia, resistance to insulin and high levels of insulin like growth factors are related to division of endometrial cells thus leading to endometrial carcinoma. Hypertension was seen in 35% of cases in our study. This is in accordance with different national and international studies where figures of 34.4% and 27.3%.

Most of our patients (57%) were presented with a light episode of vaginal bleeding. This amount of bleeding was reported by 55% of subjects in a study done at Norwich, UK in 2010, whereas frequency was reported as recurrent in the same study in 76% cases, close to our study (80%).

Table IV:- Comparison of my study with other studies.

Study	Endometrial Carcinoma cases %	p-value
Gullet at	22.20%	0.002
Gen lo	13.20%	<0.001
Keirs etal	15.80%	<0.05
weiderpas etal	9.40%	0.03
feldman etal	15.00%	0.01
Burbos etal	13.40%	0.017
Karlsson etal	10.00%	0.021
Jillaniketal	8.00%	0.01
Present Study	23.00%	0.003

In this table among all studies, most of women who developed endometrial carcinoma had recurrent episodes of post-menopausal bleeding.

Regarding the histopathological reports of these patients, we observed that 26% of our cases had atrophic endometrium, followed by chronic endometritis in 23% cases. Different authors have reported similar findings in their studies. The reason might be that the very weak and fragile support of blood vessels which is provided by stromal tissue leads to hemorrhages and ulcerations in mucosal lining and may also lead to infection (endometritis). Polyps were seen in 11.4% of cases in our study, which contrasts with the study by Fatima et al where they reported

26% cases of postmenopausal bleeding due to polyps. Banfa et al reported close figures to ours whereas it was high in a study conducted by Ghoubara et al in 2018.

In the premalignant and malignant etiologies, atypical endometrial hyperplasia was seen in 14% cases. Brand et al reported similar results and it has been suggested that atypical endometrial hyperplasia is indeed a troublesome finding as it precedes the development of endometrial carcinoma or may be harboring it at that time. Endometrial carcinoma was seen in 23% of our study population, whereas it was responsible for causation of postmenopausal bleeding in 16% subjects in the study conducted by Jillani et al and 11% in study conducted by Ghazi et al. These are relatively lower figures compared to ours. Yousaf et al in their study at Lady Willingdon Hospital, Lahore have reported 30.5% incidence of endometrial carcinoma in patients presenting with postmenopausal bleeding. The commonest type of endometrial carcinoma seen in our study was endometrioid type (80%) which is close to that seen by Fatima et al in their study (81.8%) but contrary was seen in a study done in 2018 at Ankara, Turkey where only 10% women were found to have endometrioid type of carcinomas28.

Considering the limitations in our study like small sample size, hospital-basedsurvey and lack of follow up by some patients, the results, however, cannot be generalized for the whole population.

Conclusion:-

In our study those who were diagnosed with endometrial carcinoma were found to have recurrent episodes or moderate to heavy bleeding and subjects with more than 10 years gap after menopause had more risk of carcinoma and the most common histopathological types in benign disorders are Atrophic endometrium followed by Chronic endometritis followed by polyps followed by proliferative endometrium and in premalignant and malignant disorders endometrial carcinoma followed by atypical endometrial hyperplasia followed by cervical carcinoma were seen.

Postmenopausal bleeding is an alarming symptom and should be thoroughly investigated with transvaginal ultrasound followed by endometrial biopsy for timely diagnosis and treatment.

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