ORIGINAL RESEARCH PAPER
Volume-8 | Issue-9 | September - 2019 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

RISK FACTORS ASSOCIATED WITH ABNORMAL UTERINE BLEEDING AMONG PRE AND POSTMENOPAUSAL WOMEN.

Obstetrics & Gynaecology

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ABSTRACT

A diagnostic procedure is needed to rule out hyperplasia or cancer if the patient is symptomatic or has abnormal cytology. Diagnosis of endometrial hyperplasia is usually made by sampling the endometrial cavity with an endometrial biopsy in the office or dilation and curettage in the operating room. Tissue sampling should be performed in women with risk factors who present with symptoms of abnormal vaginal bleeding or discharge. This includes women older than 35 years with abnormal bleeding, women younger than 35 years with bleeding and risk factors, women with persistent bleeding, and women with unopposed estrogen replacement therapy. 100 women in the premenopausal and postmenopausal age with abnormal uterine bleeding were subjected to transvaginal ultrasound and endometrial sampling. Obesity was an independent and significant risk factor for endometrial hyperplasia and carcinoma. The risk of endometrial hyperplasia increased in premenopausal women with anovulatory cycles which was statistically significant.Prior anovulatory cycles among postmenopausal women was a significant risk factor.

KEYWORDS

Menstruation, Perimenopause, Endometrial carcinoma,Obesity.

INTRODUCTION:

Normal menstruation is defined as bleeding from secretory endometrium associated with ovulatory cycles, not exceeding a length of five days. Any bleedingnot fulfilling these criteria is referred to as abnormal uterine bleeding (1). Surgical management of dysfunctional bleeding can be considered in patients with completed families where medical management has failed to solve the problem. Perimenopause During this phase the majority of patients will experience anovulatory excessive bleeding due to ovarian oocyte depletion. However, since the more serious forms of organic pathology occur more commonly in this age group than in younger patients, great care should be taken to exclude such disorders. This will include performing endometrial sampling and endo and ecto cervical cytology. The main concern in premenopausal and post menopausal bleeding is that the bleeding could be the only external manifestation of a hidden serious pathology such as endometrial carcinoma. Also, endometrial hyperplasia which is a fore runner of endometrial carcinoma is a common finding in women with perimenopausal bleeding.

Abnormal uterine bleeding (AUB) is the cause of roughly one-third of all visits to the gynecologist among premenopausal women and more than 70% of office visits among peri- and postmenopausal women. Abnormal uterine bleeding includes both dysfunctional uterinebleeding and bleeding from structural causes. Dysfunctional bleedingcan be anovulatory, which is characterized by irregularu npredictable bleeding, or ovulatory, which is charact erizedby heavy but regular periods (ie, menorrhagia)(2).The abnormal bleeding can be caused by a wide variety of disorders.It may represent a normal physiological state, and observation alone may be warranted. Alternatively, the bleeding can be a sign of a serious underlying condition necessitating aggressive treatment that could include a major procedure (3-5). This study proposes to correlate the finding of the twodiagnostic modalities used in the evaluation of women with premenopausal and postmenopausal bleeding namely trans vaginal sonogram and histo pathological examination and the various risk factors that were associated in women with abnormal uterine bleeding. Our aim is to study the role of tranvaginal ultrasound and endometrial sampling in the diagnosis risk factors associated and causes of abnormal uterine bleeding in premenopausal and postmenopausal women

MATERIALAND METHODS:

This is a prospective observational study carried out on women who presented with abnormal uterine bleeding, this study included 100 women of premenopausal and postmenopausal age group in department of obstetrics and gynaecology.

100 women in the premenopausal and postmenopausal age with abnormal uterine bleeding were subjected to transvaginal ultrasound and endometrial sampling.

Inclusion Criteria:

Age above 40 years,Women with Abnormal uterine bleeding,Not on any Hormone replacement therapy

Exclusion Criteria :

Cancer cervix and other benign pathological lesions of cervix,Patients with blood dyscrasias,Proven genital malignancy,Pregnancy complications,

All these patients were adequately counselled and their informed consent obtained and detailed history was elicited and a thorough general, abdominal and pelvic examination and other relevant investigations were performed and all were subjected to transvaginal sonography prior to endometrial sampling. The scan was performed with the patient in a supine position. The transducer was introduced into the posterior vaginal fornix. The uterus was scanned in long axis and coronal views with special emphasis on endometrium.

RESULTS:

Among premenopausal women, endometrial hyperplasia(67%) was seen with peak increase in the age group between 51-60 yrs which was statistically significant with P value of 0.037.χ^2 Value=6.604, df=2, p Value= 0.037 (Significant)

Among the postmenopausal women,endometrial hyperplasia(25%) and endometrial cancer(25%) were seen with peak incidence in age group of > 60 yrs. In the age group between 51-60 yrs the incidence of endometrial hyperplasia and carcinoma was 12% and 16% respectively.

Among premenopausal women who were obese, 53 % had endometrial hyperplasia. In women with normal BMI, 61.1% had normalhistopathology (either proliferative or secretory endometrium). Among the postmenopausal women who were obese, 22% had endometrial carcinoma and in those who were overweight,20% had endometrial carcinoma.A vast majority of them 83% with normal BMI had benign endometrial pathology.

In the premenopausal women,44% of primiparous women had endometrial hyperplasia whereas among the multiparous the incidence was 33%.In the postmenopausal women,who were multiparous 20 % had endometrial carcinoma and in primiparous women 33% had endometrial hyperplasia.

Table No: 1. Relationship between Age and HPE in premenopausal women (N=60)

Age in years	HPE			Total No. (%)
	Normal No. (%)	Benign No. (%)	Hyperplasia No. (%)	

41-50 Yrs	29 (56.9%)	7 (13.7%)	15 (29.4%)	51 (100%)
51-60 Yrs	1 (11.1%)	2 (22.2%)	6 (66.7%)	9 (100%)
Total	30 (50%)	9 (15%)	21 (35%)	60 (100%)

Table No: 2. Relationship between Age and HPE in postmen opausal women (N=39)

Age in Years	HPE				Total No. (%)
	Normal No. (%)	Benign No. (%)	Endometrial hyperplasia No.(%)	Cancer No. (%)	
41-50 Yrs	0 (.0%)	2 (100%)	0 (.0%)	0 (.0%)	2 (100%)
51-60 Yrs	7 (28%)	11 (44%)	3 (12%)	4 (16%)	25 (100%)
>60 Yrs	0 (.0%)	6 (50%)	3 (25%)	3 (25%)	12 (100%)
Total	7 (17.9%)	19 (48.7%)	6 (15.4%)	7 (17.9%)	39 (100%)

Table No: 3. Relationship between BMI and HPE of Premen opausal women (N=60)

BMI	HPE			Total No. (%)
	Normal No. (%)	Benign No. (%)	Hyperplasia No. (%)	
Normal	11 (61.1%)	3 (16.7%)	4 (22.2%)	18 (100%)
overweight	14 (56%)	3 (12%)	8 (32%)	25 (100%)
Obese	5 (29.4%)	3 (17.6%)	9 (52.9%)	17 (100%)
Total	30 (50%)	9 (15%)	21 (35%)	60 (100%)

Table No: 4. Relationship between BMI and HPE of Postmeno pausal women (N=39)

BMI	HPE				Total No. (%)
	Normal No. (%)	Benign No. (%)	Hyperplasia No. (%)	Cancer No. (%)	
Normal	0 (.0%)	5 (83.3%)	1 (16.7%)	0 (.0%)	6 (100%)
overweight	2 (20%)	5 (50%)	1 (10%)	2 (20%)	10 (100%)
obese	5 (21.7%)	9 (39.1%)	4 (17.4%)	5 (21.7%)	23 (100%)
Total	7 (17.9%)	19 (48.7%)	6 (15.4%)	7 (17.9%)	39 (100%)

Table No: 5. Relationship between parity and HPE in premenop ausal women (N=60)

Parity	HPE			Total No. (%)
	Normal No. (%)	Benign No. (%)	Hyperplasia No. (%)	
one child	5 (55.6%)	0 (.0%)	4 (44.4%)	9 (100%)
Multiparous	25 (49%)	9 (17.6%)	17 (33.3%)	51 (100%)
Total	30 (50%)	9 (15%)	21 (35%)	60 (100%)

DISCUSSION:

A prospective observational study, done in 100 women with abnormal uterine bleeding in premenopausal and postmenopausal age group and the role of transvaginal ultrasound and endometrial sampling was studied. In my study,among the premenopausal women the peak occurence of AUB was observed in the age group between 40-50 yrs and in the postmenopausal women it was between 50-60 yrs. In a study conducted at United Kingdom at the gynaecological oncology centre between February 2006 to may 2009 which included 3047 postmenopausal women with bleeding ,the rate of PMB during their study period also had peaked at 55-59 yrs of age, and the peak incidence of endometrial cancer was seen at more than 60yrs and declined with increasing age which correlated well with my study (6).

Majority of them were multiparous in the premenopausal group,but endometrial hyperplasia was 44% among primiparous women whereas among the multiparous it was 33%. In this study, we observed that the risks of both simple and complex hyperplasia with and without atypia decreased in proportion to the number of deliveries, at least among women younger than age 50 years. This finding contradicts that of the one previous study on the etiology of endometrial hyperplasia that examined an association with parity (7).

Obesity is a significant risk factor for endometrial cancer as there is endogenous estrogen production, adipose tissue is rich in aromatase enzyme system that converts androstenedione to estrone, which is directly converted into estradiol.In addition protein binding of estrogens in blood is lower in obese women, so the amount of bioavailable estradiol in such women is higher than would be expected from peripheral conversion of androstenedione to estrone alone. In my study, among the postmenopausal women 60% were obese and 62.5% had anovulatory cycles, 40% had endometrial hyperplasia and cancer and 75% had associated comorbidities like diabetes and hypertension thereby increasing the risk for endometrial cancer. In the Multiethnic Cohort Study, done in 50,376 women to know the association between body size and endometrial cancer risk and potential effect modification of other risk factors. During 10.3 years of follow-up, 463 endometrial cancer cases were identified. The highest risk associated with BMI gain was observed among nulliparous women and postmenopausal women who never used hormone therapy. In conclusion, adult obesity and increase in adiposity are risk factors for endometrial cancer; and the risk associated with these factors may vary across racial/ethnic groups(8).

Chronic anovulation can lead to irregular bleeding, prolonged unopposed estrogen stimulation of the endometrium, and increased risk of endometrial cancer. Causes include polycystic ovary syndrome, uncontrolled diabetes mellitus, thyroid dysfunction, hyperprolactinemia, and use of antipsychotics or antiepileptics.Terms commonly associated with anovulatory bleeding include amenorrhea (absence of periods for more than three cycles), oligomenorrhea (menses occurring at intervals of more than 35 days), metrorrhagia (menses at irregular intervals with excessive bleeding or lasting more than seven days), and dysfunctional uterine bleeding (anovulatory bleeding in which underlying etiologies have been ruled out). Recurrent anovulation causes an increased risk of endometrial cancer (9-10). About 14 percent of premenopausal women with recurrent anovulatory cycles develop endometrial cancer or its precursor, hyperplasia with atypia. ACOG recommends endometrial tissue assessment to rule out cancer in adolescents and in women younger than 35 years with prolonged unopposed estrogen stimulation, women 35 years or older with suspected anovulatory bleeding, and women unresponsive to medical therapy.

Among the postmenopausal women, a majority 67%(26) of them had benign endometrial pathology, of which 45%(19)had benign endometrial polyp and only one case was accurately diagnosed as polyp by tranvaginal USG. In a study done by Timmermans A et al women with postmenopausal bleeding in whom carcinoma has been ruled out, measurement of endometrial thickness with TVUS is not useful in the diagnosis of endometrial polyps (11).

However in women who are at high risk for endometrial cancer (obese, diabetic, with cycle irregularity, and diagnosed to have polycystic ovarian disease) the initial evaluation should include tranvaginal ultrasound and endometrial biopsy.Tranvaginal ultrasound is a useful diagnostic tool not only for diagnosis of endometrial pathology but also myometrial diseases and adenexal evaluation.Post-menopausal women with abnormal uterine bleeding must be offered endometrial biopsy. The main aim of endometrial biopsy is not only to identify cause of abnormal uterine bleeding, but also to exclude malignancy.

CONCLUSION:

In women with postmenopausal bleeding the peak occurrence was observed in age group between 50-60 yrs and the risk of endometrial cancer increased with advancing age. The association of parity with endometrial cancer have found an inverse relation between risk and number of births. Obesity was an independent and significant risk factor for endometrial hyperplasia and carcinoma. The risk of endometrial hyperplasia increased in premenopausal women with anovulatory cycles which was statistically significant.Prior anovulatory cycles among postmenopausal women was a significant

risk factor. To conclude,TUVS is a useful adjunct to endometrial biopsy for evaluating abnormal uterine bleeding and selecting patients for additional testing.

Transvaginal sonogram is a simple, non-invasive convenient way to indirectlyvisualize the endometrial cavity.The vaginal probe examination if incorporated into the gynaecology office setting and when combined with bimanual pelvic examination can enhance our anatomic diagnosis.Transvaginal sonography is useful as a first step diagnostic procedure in the evaluation of premenopausal and postmenopausal bleeding.When combined with endometrial biopsy it can supplement the shortcomings of endometrial biopsy.This study proves that this diagnostic tool correlates well with the histopathology findings.It appears that the ultrasonogram will continue to take the role of a stethoscope for the gynaecologist, to see the lining of the uterine cavity and the information obtained seems worthwhile.

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