# INCIDENCE OF ENDOMETRIAL HYPERPLASIA IN 100 CASES PRESENTING WITH POLYMENORRHAGIA/MENORRHAGIA IN PERIMENUPAUSAL WOMEN

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**Background:** To study the Incidence of endometrial hyperplasia in perimenupausal women presenting with polymenorrhagia/menorrhagia. This observational study was conducted at Gynae 'B' unit of Khyber Teaching Hospital Peshawar from January 2000 to December 2001. **Methods**: One hundred consecutive patients who presented at Gynaecology OPD with Polymenorrhagia/ Menorrhagia were registered and incidence of endometrial hyperplasia evaluated in them. All women were above 45 years of age. Post-menopausal bleeding cases were excluded from the study. **Results:** Out of 100 patients, 15 patients were found to have endometrial hyperplasia, 10 patients (66.6%) simple cystic hyperplasia, 3 patients (20.0%) had adenomotous hyperplasia, 2 patients (13.3%) had atypical hyperplasia, 8 patients (53.3%) with menorrhagia, 1 (6.6%) with polymenorrhagia, and 6 patients (40.0%) with polymenorrhoea. Duration of symptoms was from 4 months to 1 year. Thirteen (86.6%) patients were treated medically, 5 patients (33.33%) needed surgical treatment following medical treatment, 2 patients (13.3%) underwent Total Abdominal Hysterectomy (TAH) and Bilateral Salpingo-oophorectomy (BSO) who were 51–53 years of age with atypical hyperplasia. **Conclusion:** endometrial hyperplasia is a pre-malignant condition; if treated in time, incidence can be reduced and early treatment can increase life expectancy and quality in women over age of 45 years.

**Keyword**: Menorrhagia, Polymenorrhagia, Endometrial hyperplasia, Transvaginal Ultrasound, TVS

## INTRODUCTION

Hyperplasia is the increase in size of an organ or tissue due to increase in no. of its specialized cells. Endometrium is capable of marked hyperplasia as a response to stimulus of prolonged and unopposed oestrogen classification of endometrial hyperplasia.[1] Simple or cystic hyperplasia is a benign proliferation of endometrial glands that are irregular and dilated but do not display back to back crowding or cellular atypia. Complex adenomatous hyperplasia is a proliferation of endometrial glands with irregular outline architectural complexity and back to back crowding but no atypia.

Atypical hyperplasia is a varying degrees of nuclear atypia and loss of polarity fond in both simple and complex hyperplastic lesion. Incidence of hyperplasia in a study by Wentz[2] in curettage specimen was:

- Cystic hyperplasia 5.1%
- Adenomatous hyperplasia 2.6%
- Atypical hyperplasia 1.3%

Endometrial hyperplasia is a precursor of endometrial carcinoma, the most common malignancy of female reproductive tract. It accounts for 6% of new female cases and 3% of female cancer deaths.[1] Besides endometrial hyperplasia prominent risk factors for endometrial carcinoma are unopposed oestrogen therapy, obesity, diabetes early menarche and late menopause.[2]

The 3 grades of endometrial hyperplasia are simple (cystic), adenomatous (complex) and atypical hyperplasia. Endometrial hyperplasia in most of the cases is idiopathic. It may be due to anovulation at extreme of age.[3]

The role of exogenous oestrogen in inducing endometrial hyperplasia in a well-known recent prospective study showed that 10% of women developed adenomatous hyperplasia every year. Tamoxifen used for breast cancer, due to its weak oestrogenic effect can induce endometrial hyperplasia. Niwa *et al*[4] conducted a study on mice to see the effects of Tamoxifen on endometrium. The results showed increased incidence of pre-neoplastic lesions of the endometrium. Oestrogen secreting ovarian tumours, may be the occasional cause of endometrial hyperplasia.[5]

Clinical presentation at perimenopausal age is usually abnormal uterine bleeding. The three pathological types of endometrial hyperplasia are simple in which there is cystic dilatation of glands; adenomatous hyperplasia when glands have very irregular outline showing marked structural complexity; and atypical hyperplasia is characterised by glands showing nuclear atypia with abnormal mitotic figures. Association with concomitant endometrial cancer, ovarian cancer, and progression of hyperplasia to cancer should be kept in mind while dealing with these patients.

In atypical hyperplasia, co-existent carcinomas range from 25 to 50%.[6] The risk of progression to endometrial cancer ranges from 22.6 to 88.9%.[7]

Malignant transformation occurs in 15%, 24%, and 45% of mild moderate and sever atypical

hyperplasia respectively.[8] Certain animal data support the hypothesis that oestrogen can be carcinogenic for endometrium but human data are less certain. The best representation of these are based on data by Sommers[9] which illustrate endometrial polyps progressing to cystic hyperplasia and then to adenomatous under the influence of oestrogen.

## PATIENTS AND METHODS

Study was conducted from January 2000 to December 2001. One hundred patients of more than 45 years age presenting with Menorrhagia/ Polymenorrhagia were studied. Postmenopausal bleeding cases were excluded from the study.

All patients were seen in out door clinic. A detailed history was taken. Inquiry about bleeding disorder, liver and thyroid dysfunction was also made to exclude these causes of menorrhagia. Drug history especially of oestrogen and Tamoxifen was taken and none was found using these drugs. There was no family history of ovarian or endometrial carcinoma in all patients.

After taking history, patients were examined thoroughly. Examination included general physical, systemic and pelvic examination. Per rectum examination was done in all patients. Routine investigations including blood group and Rh-factor, random blood sugar, urine routine analysis and special investigation, transvaginal ultrasound (TVS) was done to see for endometrial thickness and ovarian enlargement. Diagnostic curettage preferably in the second half of the cycle was done and histopathology of the specimens done.

## RESULTS

Age of the patients ranged from 45–53 years (Table-1). All patients with adenomatous and atypical hyperplasia were having irregular periods showing the severity of disease. Pattern of bleeding in patients having cystic endometrial hyperplasia was mainly Menorrhagia/polymenorrhagia (Table-2).

Duration of symptoms were from 4 months to 1 year. Cystic hyperplasia found to be the commonest of all. Endometrial thickening was significant in diagnosis of endometrial hyperplasia. (Table-3).

Ten (66.6%) patients had endometrial thickness more then 10 mm (Table-5). Hypertension and diabetes, were found common in patients having adenomatous hyperplasia (Table-6). Medical treatment was also found effective in patients having simple or cystic hyperplasia. Medical followed by surgical treatment was needed in a few patients while direct TAH+BSO was done in patients above the age of 51 years (Table-7).

**Table-1: Age groups of the patients having endometrial hyperplasia (n=15)**

| Age Groups | Number | Percentage |
|---|---|---|
| 45–48 years | 10 | 66.66 |
| 49–50 years | 3 | 20.0 |
| 51–53 years | 2 | 13.3 |

**Table-2: Pattern of bleeding in patients having endometrial hyperplasia (n=15)**

| Pattern of Bleeding | Number | Percentage |
|---|---|---|
| Menorrhagia | 8 | 53.33 |
| Polymenorrhagia | 1 | 6.6 |
| Polymenorrhoea | 6 | 40.0 |

**Table-3: Duration of symptoms (n=15)**

| Duration of Symptoms | Number | Percentage |
|---|---|---|
| 4 – 8 months | 10 | 66.6 |
| 8 – 12 months | 4 | 26.6 |
| > 1 years | 1 | 6.6 |

**Table–4: Type of endometrial hyperplasia**

| | Number | Percentage |
|---|---|---|
| Cystic Hyperplasia | 10 | 66.6 |
| Adenomatous Hyperplasia | 3 | 20.0 |
| Atypical Hyperplasia | 2 | 13.33 |

**Table-5: Endometrial thickness on transvaginal ultrasound**

| | Number | Percentage |
|---|---|---|
| 5 – 6 mm | 2 | 13.33 |
| 7 – 8 mm | 3 | 20.0 |
| > 10 mm | 10 | 66.66 |

**Table-6: Associated disease with endometrial hyperplasisa**

| | Number | Percentage |
|---|---|---|
| Hypertension | 3 | 20 |
| Diabetes | 2 | 13.3 |
| Thyroid disease | 0 | 0 |
| Liver disorder | 0 | 0 |

**Table-7: Type of management**

| Treatment | Number | Percentage |
|---|---|---|
| Medical | 13 | 86.6 |
| Medical followed by surgical | 5 | 33.33 |
| Direct surgical | 2 | 13.3 |

## DISCUSSION

Endometrial hyperplasia is common in perimenopausal women causing symptoms of irregular or prolonged bleeding due to anovulatory cycles in majority of cases. Heavy bleeding is secondary to sustained level of oestrogens. The overgrowth not only affects glands and stroma but there is also abnormal vascularisation. Bleeding is prolong and excessive because of massive tissue available for bleeding and random break down of tissue resulting in exposure of vascular channels. There is no vasoconstrictive rhythmicity, no tight coiling of spiral vessels and no collapse to induce stasis. The healing effect of oestrogen is brief and vicious cycle of bleeding reoccurs. In a study by Horbelt *et al*[10] ultra structure of microvasculature in human endometrium was studied. Their results showed microvasculature with

morphologic disorder with altered, extracellular matrix and wide spread cell death. For detection of complex hyperplasia or lesion beyond it in endometrial cytology it is important to observe for papillary clusters.

Naheed Moghal[11] performed diagnostic curettage in cases presenting with abnormal uterine bleeding. Out of 114 patients with intra uterine abnormal uterine pathology, 51 patients were having endometrial hyperplasia. Forty-two patients having simple or adenomatous and 7 atypical hyperplasia, majority of the patients were in age group 41–50 years. Fayaz S[12] has studied causes of Gynaecological hysterectomies and in her study incidence of endometrial hyperplasia was 4.68%. Jalil R[13] correlated the indications of abdominal hysterectomy with histopahological findings in her reports preoperative diagnosis, by D&C of endometrial hyperplasia was 14.42%. Fouzia Adil[14] conducted a 2 years study and performed D&C in excessive and abnormal uterine bleeding. Incidence of cystic hyperplasia, was 32.8% and adenomatous hyperplasia was 8.8%. In our study, the commonest among endometrial hyperplasia was cystic hyperplasia (66.6%).

In most of the patients with cystic hyperplasia bleeding is heavy but cycle is regular, while the pattern of bleeding is irregular in complex and atypical hyperplasia showing the severity of disease. In our study, 80% of patients with cystic hyperplasia had menorrhagia only.

In most of the patients with cystic hyperplasia the condition resolves within short period of time. In our study 69.2% resolved while 30.8% persisted as such after repeat D&C at 12 weeks interval. Progression of pathology was not seen in any case. In a study by Terakawa *et al*[15] 51 patients with endometrial hyperplasia were followed for 6 months, with repeated endometrial biopsy monthly for 3 months and at the end of 6 months. In 69% histology became normal. Their findings are consistent with our study. Terakawa *et al* found the lesion to persist in 17% of simple, 25% complex, 80% with complex atypical in 17% of simple, 25% complex, 80% with complex atypical. In our study lesion persisted in 20% of cystic hyperplasia cases and in 333.3% in complex hyperplasia. Terakawa *et al* observed that in 3 patients with cystic hyperplasia lesion progressed to atypical hyperplasia by the end of follow up. In our study no one progressed.

Endometrial thickness had no particular value regarding diagnosis of endometrial hyperplasia as 2 patients out of 15 were having endometrial thickness 5–6 mm. A study performed by Bakos[17] showed that transvaginal ultrasound is as effective as D&C in women with irregular bleeding. Doppler endovaginal ultrasonography could detect 76% of endometrial abnormalities.[18] Although hysteroscopy has revolutionised the management of Dysfunctional Uterine Bleeding (DUB), D&C remains the 'gold standard'. Perhaps hysteroscopy could be diagnostic aid to D&C rather than a complete replacement. Dilatation and Curettage is a day care procedure, easy, cheep, and no special personnel are required although it needs a senior person for proper assessment. Hysteroscopy cannot properly differentiate between various types of endometrial hyperplasia. The hysteroscopist should always proceed under assumption that every hyperplasia can harbour deep foci of atypical hyperplasia or early invasive carcinoma Ben Yehuda *et al*.[19] Three hundred and seventy-three patients between 1991–1995 were included in his study. In 61 patients having endometrial hyperplasia by diagnostic D&C the hysteroscopic impression of hyperplasia was in only 32 patients indicating that hysteroscopy did not improve upon the sensitivity of D&C in detecting endometrial hyperplasia.

Ho *et al*[20] conducted a study from Jan 1991–Dec 1994. Twenty-nine patients in their study had endometrial hyperplasia with atypia and 87 were without atypia. Incidence of endometrial carcinoma was 27.6% in those with atypia and 3.4% in those without atypia. Gucer *et al*[21] studies surgical specimen of 214 patients, operated for endometrial cancer 43% had concomitant endometrial hyperplasia. In our study, no patient had concomitant endometrial carcinoma, probably due to less number of patients in the study.

When endometrial hyperplasia is diagnosed the women should be investigated for endometrial or ovarian cancer, and to look for any endogenous source of oestrogen, investigations should include hysteroscopy to see endometrial and endocervical cavities.

Management options are to stop exogenous and remove oestrogen producing ovarian tumour if found. Medical and surgical treatment depends upon the severity of pathological condition, and the patient's age and her wishes for further children.

Short-term use of Gonadotrophin releasing hormone analogue is being in use for endometrial hyperplasia. Colacurci *et al*[22] used short-term (3 months) therapy with Gonadotrophin releasing hormone analogue to premenopausal women. They showed long, symptoms free period, and low incidence of side effects.

Six published cases were collected by Gimpelson[23] to establish a link between the development of endometrial cancer and endometrial ablation. That study observed that pre-existing endometrial hyperplasia is a common cause of endometrial carcinoma. Endometrial ablation which could cure DUB is not an ideal management for endometrial hyperplasia rather a contraindication.

## CONCLUSION

The commonest cause of DUB at perimenopause is anovulatory cycles. Among endometrial hyperplasias, cystic hyperplasia is the commonest. Transvaginal

sonography is not very helpful in diagnosis of endometrial hyperplasia and D&C still remains the 'gold standard' for its diagnosis.

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