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# THE ROLE OF OFFICE HYSTEROSCOPY IN THE DIAGNOSIS OF ENDOMETRIAL HYPERPLASIA: A CROSS SECTIONAL STUDY FROM CENTRAL INDIA.

Gynaecology

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## ABSTRACT

Introduction: The role of office hysteroscopy in the evaluation of endometrium in cases with abnormal uterine bleeding (AUB) has advantage of being a day care procedure without need for anaesthesia. Ultrasonographic evaluation of endometrial thickness is essential in evaluation of AUB. Hence, the combination of ultrasound and modern office hysteroscopy can be used in comprehensive assessment of endometrial pathology. Office hysteroscopy can be a preferred tool for clinicians which can not only diagnose but also treat menstrual disorders in a one-stop clinic. Materials and methods: This cross sectional study was undertaken in a tertiary care centre in central India from February 2016 to October 2017 after institute ethical committee approval. In this study 124 women with AUB were evaluated after informed consent. Pre-operative ultrasonography was performed to record the endometrial thickness followed by office hysteroscopy. Endometrial tissue was sent for histopathological study. Results: Majority of the patients i.e 60 (48.38%) had secretory endometrium. We got 2 cases of endometrial cancer, 21 cases with simple hyperplasia without atypia and 3 cases with simple hyperplasia with atypia. Office hysteroscopy had a sensitivity of 92.3%, specificity of 66.3%, positive predictive value (PPV) of 42.11%, negative predictive value (NPV) of 97.01% and diagnostic accuracy of 71.77% in diagnosing endometrial hyperplasia. The best cut off of the endometrial thickness for the prediction of endometrial hyperplasia was found to be 10.88 mm. Conclusion: Office hysteroscopy has a very high sensitivity and negative predictive value in diagnosing endometrial hyperplasia.

## KEYWORDS

Hysteroscopy, Endometrial Hyperplasia, Ultrasonography.

## INTRODUCTION:

Presently, endometrial cancer (EC) is the most common pelvic malignancy in women of developed countries and the second most common pelvic malignancy in women of developing countries with a prevalence of about 7%.[1] Most of these cancers are adenocarcinoma arising from endometrium. Around 90% of these cancers present with abnormal uterine bleeding (AUB) with 75% diagnosed in stage 1.[1] A precursor of this malignancy is endometrial hyperplasia (EH).[2] This preneoplastic lesion of endometrium presents with features of AUB. From adolescent to menopause, AUB is very common in women and includes heavy menstrual bleeding (HMB), irregular or intermenstrual bleeding (IMB) and postmenopausal bleeding (PMB). PMB and persistent IMB are very common symptoms of suspected endometrial cancer and cervical cancer. EH is diagnosed by histopathological examination of endometrial tissue and is considered as the goldstandard . The results of two meta-analyses have clearly shown the satisfactory sensitivity and specificity of an endometrial biopsy in the diagnosis of endometrial cancer in women with AUB.[7,8] But choosing a correct method of biopsy is very important. Biopsy with aspiration is good, when there is global endometrial pathology, but blind pipelle biopsy can be false negative in women with focal lesions. Bettocchi et al found that 50% of intrauterine lesions were missed when a D&C was performed alone when compared with hysteroscopy.[6] Kolhe S. has mentioned in a recent publication that, procedure of D&C has now become obsolete and is no longer acceptable as the standard of care for endometrial assessment unless it is used concomitantly with hysteroscopy.[5] Various studies have shown that office hysteroscopy is feasible without the use of anaesthesia because it is well tolerated among patients, reducing risks and costs.[21,22]

In hysteroscopy, hyperplastic endometrium demonstrates typical changes. Hysteroscopy helps in diagnosing focal changes of endometrial hyperplasia or cancer thereby allowing a guided biopsy, which may otherwise get missed in blind aspiration biopsy or dilatation and curettage (D&C). Office hysteroscopy is an endoscopic technique to visualize endometrial cavity where a smaller diameter (2-3mm) scope is used which can be negotiated into the endometrial cavity without dilatation and hence without any need for anaesthesia. Ultrasonography of pelvis is routinely performed for patients suffering from AUB. Majority of the cases of EH or endometrial cancer show thickened endometrium in ultrasonography (USG). Hence the combination of USG and office hysteroscopy allows thorough evaluation of uterine cavity in an outpatient setting, particularly in those with intrauterine pathology. The aim of this study is to determine the diagnostic performance of office hysteroscopy in the diagnosis of EH.

## MATERIALS AND METHODS:

This cross sectional study was undertaken in a tertiary care centre in central India from February 2016 to October 2017 after taking approval from institute ethical committee. A total of 124 consecutive parous women who attended gynecology outpatient department (OPD) of our hospital and who fulfilled the inclusion criteria were included after informed consent. Women having the following criteria were included in the study: 1. All parous women suffering from AUB 2. All cases of PMB. Women with following criteria were excluded from the study: 1. Nulliparous women, 2. Already diagnosed cases of EH and EC, 3.USG suggestive of focal or diffuse endometrial growth or myometrial invasion suggestive of frank EC, 4. Those suffering from active pelvic inflammatory diseases and 5. Those on progestin therapy. Objective of the study was to assess the diagnostic performance of hysteroscopy in the diagnosis of various types of EH. A detailed history was taken and physical examination was performed in each case. Before hysteroscopy, all patients underwent transvaginal sonography (TVS) and uterine anatomy was

recorded along with endometrial thickness.

Office hysteroscopy was performed using normal saline as liquid distension medium and was video assisted. A 2.9mm sheath hysteroscope (Proffice 333 by Promis) with 30 degree lens and continuous flow of normal saline was used. Since office hysteroscope was used, no cervical dilatation was required. During the procedure, 5 patients experienced mild discomfort or pain and 26 patients experienced vaginal spotting or mild bleeding. But they were self limiting and no active interventions were required. No major complications occured.

Hysteroscopic classification was based on previously reported criteria.[3] Hysteroscopic diagnosis of EH was based on the detection of one or more of the following findings: (1) Focal or extensive, polypoid or papillary unevenly thickened endometrium, showing or not showing irregular vascular network; (2) Crowded or irregularly spaced gland openings; (3) Dilatation of endometrial glands in a thickened endometrium; (4) Hyperplasia within polyp was diagnosed when these features were found within an endometrial polyp. All those patients having one or more of the above hysteroscopic pictures are considered as diseased(suggestive of EH or EC) and those having any other type of hysteroscopic findings were considered as non-diseased. A normal hysteroscopic endometrial cavity is shown in Figure.1 and hysteroscopic picture showing unevenly thickened papillary endometrium suggestive of endometrial hyperplasia is shown in Figure.2. Hysteroscopic guided biopsy was taken when features suggestive of endometrial hyperplasia were seen and random endometrial biopsy from fundus was taken if it was normal looking. All the biopsy specimens were sent for histopathological examination. Histopathologic findings were classified according to Buckley and Fox .[4]

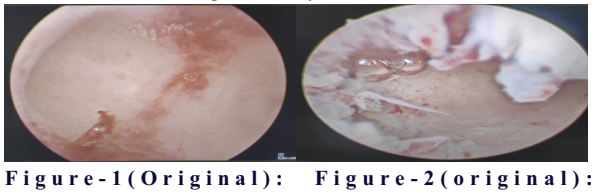

**Figure-1(Original): Hysteroscopic picture showing normal endometrial cavity**

**Figure-2(original): Hysteroscopic picture showing unevenly thickened papillary endometrium**

**RESULTS:**

Statistical analysis was done using SPSS software version 16. The sensitivity, specificity, negative predictive value and positive predictive value of hysteroscopy as a diagnostic tool for endometrial hyperplasia were calculated. All continuous data were summarized as mean & standard deviation (SD). The categorical data were expressed as frequency (as percentages), which were compared using Chi-Square test. A p value less than 0.05 was considered statistically significant. Overall, the mean age for the patients was 41.96 (±8.24) while mean age for diseased and non-diseased women was 41.96 (±7.4) and 42.65 (±8.2), respectively. Ten patients (8%) had postmenopausal bleeding and the rest presented as AUB. Distribution of various histopathological findings is mentioned in Table 1. Majority of the patients (48.38%) had secretory endometrium. We got 2 cases of endometrial cancer, 21 cases of simple hyperplasia without atypia and 3 cases of simple hyperplasia with atypia. There was no case of complex hyperplasia.

**Table-1:** Histopathological Results

| Histopathologicaldiagnosis | Percentage |
|---|---|
| Simplehyperplasiawithoutatypia | 16.93%(N=21) |
| Simplehyperplasiawithatypia | 2.4%(N=3) |
| Secretoryendometrium | 48.38%(N=60) |
| Proliferativeendometrium | 16.12%(N=20) |
| Inactiveendometrium | 8.06%(N=09) |
| Endometrialpolyp | 0.80%(N=01) |
| Partialmole | 0.80%(N=01) |
| Endometrialtuberculosis | 0.80%(N=01) |
| Disorderedproliferativeendometrium | 4.83%(N=6) |
| Endometrial cancer | 1.61%(N=02) |

Table 2 shows different hysteroscopic findings and their histopathological outcomes. As it is mentioned in the table that one patient can show one or more number of hysteroscopic abnormalities. Hence it is found that majority of the patients diagnosed to have endometrial hyperplasia without atypia had either one or more of the findings like, polypoidal endometrium or focal endometrial thickening or hypervascular endometrium or extensive endometrial thickening in hysteroscopy. Similarly the patients diagnosed to have simple hyperplasia with atypia or endometrial cancer had either one or more of the findings like polypoidal endometrium or hypervascular endometrium or glandular overcrowding in hysteroscopy.

**Table-2: Histopathological Results (hpr) And Their Hysteroscopic Findings**

| | HPR | HV | Polypoidal | GO | Polyp | FET | EET | MV | WE | AE | SMF | FA | NE | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | SHWA | 5 | 6 | 2 | 1 | 6 | 4 | 2 | 0 | 1 | 0 | 0 | 2 | 29 |
| 2 | SE | 1 | 3 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 2 | 0 | 44 | 54 |
| 3 | PE | 0 | 2 | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 19 | 26 |
| 4 | IE | 1 | 1 | 1 | 0 | 0 | 2 | 2 | 1 | 0 | 0 | 1 | 2 | 11 |
| 5 | Polyp | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 01 |
| 6 | Partialmole | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 01 |
| 7 | E.TB | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 01 |
| 8 | DPE | 0 | 1 | 0 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 2 | 07 |
| 9 | Cancer | 2 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 05 |
| 10 | SHA | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 04 |
| | Total | 11 | 16 | 08 | 03 | 10 | 12 | 05 | 01 | 01 | 02 | | 69 | |

N.B: One patient may show one or multiple patterns of endometrial hyperplasia. Hence the total numbers in the table donot indicate the total number of patients , rather total number of hysteroscopic findings.

SHWA = Simple hyperplasia without atypia, SE = Secretory endometrium, PE = Proliferative endometrium, IE = Inactive endometrium, E.TB =Endometrial tuberculosis, DPE = Disordered proliferative endometrium, SHA = Simple hyperplasia with atypia, HV = Hyper Vascular, GO = Glandular Over crowding, FET = Focal endometrial thickening, EET = Extensive endometrial thickening, MV = Mosaic vascularity, WE = Wavy endometrium, AE = Atrophic endometrium, SMF = Submucous fibroid, FA = Filmsy adhesions, NE = Normal endometrium

As depicted in Table 3, a total of 26 patients (20.96 %) out of 124 had histologically confirmed endometrial hyperplasia (19.33%) or cancer (1.6%). Here out of 57 patients with hysteroscopic features suggestive of endometrial hyperplasia, only 24 had histologically confirmed hyperplasia or malignancy and similarly out of 67 patients with hysteroscopic features not suggestive of endometrial hyperplasia, only 2 had histologically confirmed hyperplasia or malignancy. Office hysteroscopy had a sensitivity of 92.3%, specificity of 66.3%, positive predictive value (PPV) of 42.11%, negative predictive value (NPV) of 97.01% and diagnostic accuracy of 71.77% in diagnosing endometrial hyperplasia (Table 3).

**Table 3. Diagnostic Value Of Office Hysteroscopy**

| Hysteroscopic endometrial hyperplasia | Histopathological Results | | TOTAL | | |
|---|---|---|---|---|---|
| | Diseased | Non diseased | | Sensitivity (true positive) | 92.3% |
| Positive | 24 | 33 | 57 | | |
| Negative | 2 | 65 | 67 | Specificity (true negative) | 66.3% |
| TOTAL | 26 | 98 | 124 | | |
| | | | | PPV | 42.11% |

| | | |
|---|---|---|
| | NPV | 97.01% |
| | Diagnostic accuracy | 71.77% |

N.B: Diseased (Those having either hyperplasia or cancer in histopathology), Non diseased (rest of the histopathological findings)

The role of endometrial thickness as measured in TVS in the prediction of EH was analysed as a secondary outcome of our study. The best cut-off that maximized (sensitivity + specificity) the detection of EH was 10.8mm as illustrated in the receiver operating characteristic curve (ROC) (Figure.3). At this count, the sensitivity was 0.833 and specificity was 0.561 (1 – specificity = 0.439). Area under the curve (AUC) is 0.786 (SE = 0.046, 95% CI = 0.697 to 0.876) and it is highly significant (p<0.001).

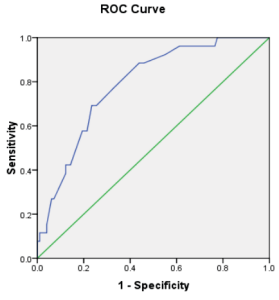


Figure 3 (original). ROC curve showing cut off value of endometrial thickness as measured by ultrasonogaraphy to predict endometrial hyperplasia (The best cut-off that maximizes (sensitivity + specificity) for the detection of endometrial hyperplasia is 10.8mm with area under the curve (AUC) is 0.786. At this count, the sensitivity is 0.833 and specificity is 0.561 (1 – specificity = 0.439.)

## DISCUSSION:

Endometrial hyperplasia (EH), a precursor of endometrial cancer (EC), needs to be detected early so as to prevent the development of cancer. There are several techniques available to obtain an endometrial sample for histology, such as simple aspiration (pipelle biopsy), blind dilatation and curettage (D&C) and hysteroscopic guided biopsy. Among various diagnostic techniques to diagnose EH, office hysteroscopy presents several advantages. It can be carried out as an out-patient procedure. It is less invasive, involves low cost and hysteroscopic directed biopsy for focal lesions can be obtained.

So far as the diagnostic accuracy of a screening technique is concerned, a positive test result is more accurate for ruling in disease than a negative test result for ruling it out. Hence screening techniques with high sensitivity and high negative predictive value are useful in diagnosing majority of the diseases. Various sensitivity rates have been reported in literature, ranging from 16% to 98%.[10] Our study shows a sensitivity of 92.3%, specificity of 66.3%, positive predictive value (PPV) of 42.11%, negative predictive value (NPV) of 97.01% and diagnostic accuracy of 71.77%. Hence our study shows a high sensitivity and high negative predictive value. A systematic review which included 65 studies and 26,346 patients on the accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia, found the sensitivity and specificity of 78.0% and 95.8%, respectively.[9] In another study with 4,054 participants, hysteroscopic viewwas validatedwith histology in cases of endometrial hyperplasia and cancer in patients with abnormal uterine bleeding. In endometrial hyperplasia, sensitivity of the hysteroscopic view was 56.3% (95% CI 52.2–60.2%), specificity was 89.1% (95% CI 88.0–90.1%), PPV was 48.0% (95% CI 44.3–51.7%), NPV was 92.0% (95% CI 90.1–92.9%), and accuracy was 72.7% (95% CI 70.7–74.7%); and in endometrial cancer, the sensitivity of the hysteroscopic view was 80.0% (95% CI 71.1–87.2%), specificity was 99.5% (95% CI 99.2–99.7%), PPV was 81.5% (95% CI 72.7–88.5%), NPV was 99.5% (95% CI 99.2–99.7%), and accuracy was 89.8% (95% CI, 85.9–93.6%).[20] In another study a hysteroscopic evaluation in 1500 women suffering from AUB was done where the investigators have recognised endometrium as functional, dysfunctional, atrophic, endometritis, polyps, hyperplasia and carcinoma with highaccuracy i.e. sensitivity, specificity, NPV, and PPV of 94.2%, 88.8%, 96.3%, and 83.1%, respectively, in predicting normal or abnormal histopathology of endometrium.[18] Similarly in a recent publication the investigators have shown a very high efficacy of office hysteroscopy in predicting normal and abnormal endometrial pathology based on their gross hysteroscopic patterns (starry sky for atrophic endometrium, strawberry appearance for secretory endometrium, tongue shaped growth for endometrial polyp, pebble stone appearance for myomatous polyp, polypoidal appearance for simple hyperplasia and cerebroid appearance for carcinoma).[19] Our study favours office hysteroscopy as a screening tool for endometrial hyperplasia or cancer owing to its high sensitivity. But a low specificity (66.3%) and low positive predictive value (42.11%) in our study findings indicates that we over-diagnosed hyperplasia. This can be due to performance of the procedure in different phases of the menstrual cycle owing to constraints of poor compliance or adherence to medical advice and attrition to follow up visits. This is a limitation of our study. Similar results like ours have been reported by Loverro G et el.[11] Variable screening results has been seen across different studies and these differences can be due to the different hysteroscopic criteria used to define normal endometrium and hyperplasia and also the different tissue sampling modalities. [3,11,12,13]

In hysteroscopy, EH appears as overdevelopment of the endometrial mucosa with increased glandular openings, polypoidal changes of the endometrium, cystic dilatations, increased vascularity etc. We got a higher sensitivity in diagnosis of endometrial hyperplasia, by following the above criteria mentioned in methodology. In this way, an improvement of hysteroscopic sensitivity to foresee hyperplasia might be achieved. Hence the correct diagnosis of EH should be considered as a goal of any early detection strategy and office hysteroscopy is a very effective procedure for achieving this goal.

In our study group we have found the prevalence of EH and EC as 19.33% and 1.6% respectively. Giannella et al have shown that the prevalence of EH and EC in their study population was 3.7% and 1.3% respectively. They have done endometrial sampling either by Vabra endometrial sampling or targeted biopsy. A study reported from India where they have done dilatation and curettage has shown the prevalence of EH and EC as 4.4% and 0.7% respectively. A high prevalence of EH and EC among our patients can be attributed to use of office hysteroscopy only, which clearly shows the superiority of the procedure.

In the present study as the secondary outcome, we have shown the relevance of endometrial thickness (ET) measured in ultrasonography (USG) before hysteroscopy in predicting EH/EC. The cut off of endometrial thickness for the diagnosis of endometrial hyperplasia or endometrial cancer is found to be 10.88 mm from the ROC with area under curve of 0.786. Wise M.R et al and Giannella L et al have shown in their study that the cut off of ET in USG for the diagnosis of EH/EC is 11 mm in premenopausal patients having AUB.[14,15] In the present study this cut off is calculated taking both premenopausal and postmenopausal women together. In our study group 10 patients belong to postmenopausal category. Various other studies have also shown the important role of endometrial thickness as determined by USG for the diagnosis of EH/EC. [16,17]

One of the limitation of our study is that we have not calculated the sample size. Another limitation of our study was that we have done the procedure either in the secretory or proliferative phase of the endometrium owing to the availability of the patient . Further studies can be performed with larger number of patients to validate our results.

## CONCLUSION:

Office hysteroscopy is advantageous in the evaluation of premalignant lesions of endometrium since it permits a global evaluation of endometrium and helps in taking directed biopsy from suspicious areas. It has other advantages like low cost, early recovery, no anaesthesia-related complications, and decreased time commitment for patients and physicians as well. Since there is no ideal screening technique for detection of endometrial cancer, detection of endometrial hyperplasia by office hysteroscopy can be a suitable screening technique. Similarly USG measurement of ET serves as a good predictor of EH.

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