

## A Comparative Evaluation of the Three Different Methods of Endometrial Sampling in the Diagnosis of Perimenopausal Bleeding: A cross sectional study

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**Abstract:** Abnormal uterine bleeding (AUB) is a common cause for a woman of all ages to consult their gynaecologists. One-third of patients attending the Gynaecology OPD present with complaints of AUB. The present study was proposed to obtain the endometrial sampling by three different techniques: 1. endometrial cytology using the nasogastric tube 2. Endometrial aspiration biopsy using the pipelle, 3. conventional dilatation and curettage and to evaluate the effectiveness of this three different process in obtaining satisfactory samples for endometrial evaluation by pathologists. The study of available literature shows that all the three different processes of endometrial sampling have not been evaluated to each other. A total of 200 patients with the indication of perimenstrual bleeding were estimated. Each woman was subjected to the three different methods of endometrial sampling (endometrial aspiration cytology using the nasogastric tube, pipelle aspiration biopsy and dilatation and curettage). Endometrial aspiration cytology was able to diagnose benign pathology in 44% cases and premalignant pathologies in 19% cases. Endometrial aspiration cytology was failed to detect pathology in 37% cases. It was failed to detect any malignancy. Pipelle biopsy showed benign pathologies in 49% cases, premalignant pathology in 45% cases and carcinoma in 2% cases. Endometrial sample was found to be inadequate in 4% cases. On the other hand, dilatation and curettage diagnosed benign pathologies in 50% cases, premalignant pathologies in 44% cases and carcinoma in 2% cases. Inadequate sample was found in 4% cases. Results of the present study suggest that accuracy for endometrial diagnosis of pipelle biopsy was equal to dilatation and curettage method of endometrial sampling. Pipelle biopsy has very high accuracy of 99% in detecting premalignant and malignant pathologies of endometrium. However, pipelle biopsy and dilatation and curettage method are equally effective in diagnosing endometrial pathologies. Comparing to dilatation and curettage method pipelle biopsy of endometrium takes shorter time and preserves stromal architecture better. We emphasise that pipelle biopsy should be used for the endometrial diagnosis in perimenopausal bleeding as it is less painful as well as rapid along with that it is cost effective.

**Keywords:** Endometrial aspiratory cytology, pipelle biopsy, dilatation and curettage, perimenopausal bleeding.

### INTRODUCTION

Abnormal uterine bleeding (AUB) is a common cause for a woman of all ages to consult their gynaecologists. One-third of patients attending the Gynaecology OPD present with complaints of AUB [1]. This proportion rise to 70% in the pre-menopausal and post-menopausal age group [2]. Perimenopausal bleeding is associated with unbalanced and reducing ovarian function. An increasing variability of the menstrual pattern is observed as women approach menopause. So, the detection of underlying endometrial pathology is particularly very challenging in this age group [3].

The AUB in women aged 40 and older, especially in peri and post-menopausal age group requires exclusive assessment, to exclude atypical endometrial hyperplasia and carcinoma[3-5]. Less than one percent of endometrial carcinomas occur under thirty-five years of age and six percent in those forty-five years or less[6].

An endometrial pathology (polypi, submucous myomas, endometrial hyperplasia and endometrial carcinoma) should always be suspected besides systemic, iatrogenic and hormonal causes and

evaluation is mandatory [7]. The earlier the diagnosis of endometrial carcinoma is made, the better the survival rate. The presentation of the disease is usually by abnormal vaginal bleeding. The analysis consists of well-established techniques ranging from clinical examination to the transvaginal scan, traditional dilatation and curettage, endometrial aspiration cytology, and office-based endometrial biopsy [8].

To diagnose benign and malignant pathology endometrial biopsy in women with perimenopausal bleeding should be performed, so that the required treatment can be designed [8,9].

Various methods of endometrial sampling are used in practice including invasive and non-invasive technique at either an inpatient or outpatient basis. Hence, the present study was proposed to obtain the endometrial sampling by three different techniques: 1. endometrial cytology using the nasogastric tube 2. endometrial aspiration biopsy using the pipelle, 3. conventional dilatation and curettage and to evaluate the effectiveness of this three different processes in obtaining satisfactory samples for endometrial evaluation by pathologists. The study of available literature shows that all the three different processes of endometrial sampling have not been evaluated to each other.

**MATERIALS AND METHODS**

This comparative cross-sectional study was carried out in the Department of Obstetrics and Gynaecology, Teerthanker Mahaveer medical college and hospital Moradabad from March 2016 to April 2018. Institutional Ethical Committee approval was obtained and a total of 200 patients with the indication of perimenstrual bleeding were estimated. Each woman was subjected to the three different methods of endometrial sampling (endometrial aspiration cytology using the nasogastric tube, pipelle aspiration biopsy and dilatation and curettage). Patients aged above 40 years were included in our study. Exclusion criteria: Patients with adenomyosis, cervical stenosis, bleeding disorders,

history of hormonal intake or IUCD, and lower genital tract infections were excluded from the study.

Informed written consent was taken from the patients who were counselled about all three procedures. Patients were asked to evacuate their bladder before pelvic ultrasound was performed after taking their detailed history and examination. With the patient in dorsal position, Sim’s speculum was inserted into the vagina to retract the posterior vaginal wall, and anterior lip of cervix was held with vulsellum. Without anaesthesia or analgesia, first of all, an infant nasogastric tube no. ten was introduced into the endometrial cavity. With the help of syringe five millilitres of normal saline was injected, followed by suction of uterine cavity material through a nasogastric tube using the syringe. In a bottle containing normal saline material aspirated was collected. This sample was labeled as A, Secondly, the pipelle was put into uterine cavity without performing cervical dilatation and then withdrawn outside by rotatory movements to get a sample which was collected in a bottle including formalin and was labeled as sample B. The pipelle biopsy was followed by standard dilatation and curettage procedure and sample was collected in bottle containing formalin and labeled as sample C. All three samples were observed by a pathologist for cytohistopathology assessment.

**STATISTICAL ANALYSIS**

Data analysis was performed by using IBM Statistical Package for the Social Sciences (SPSS) software version 21.0. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and diagnostic accuracy were calculated taking the result of dilatation and curettage method as the reference

**RESULTS**

Table 1 shows that 46% of women with perimenopausal bleeding belonged to 41 to 45 years age group. Whereas rest of the 34% and 11% women were from 46 to 50 years and 51 to 55 years age group respectively. Among two hundred women 18 females were presented with post-menopausal bleeding.

**Table-1: Distribution of patients according to age**

| Age (Years) | Number of patients | Percentage (%) |
|-------------|--------------------|----------------|
| 41 – 45     | 92                 | 46%            |
| 46 – 50     | 68                 | 34%            |
| 51 – 55     | 22                 | 11%            |
| 56 – 60     | 12                 | 6%             |
| 61 – 65     | 6                  | 3%             |
| Total       | 200                | 100%           |

In table 2 benign cytomorphology was recorded in 42% and endometrial hyperplasia was

observed in 19%. Further, smear was inadequate for the diagnosis in 37% perimenopausal women.

**Table-2: Endometrial aspiratory cytology**

| Endometrial aspiratory cytology      | Number of patients | Percentage (%) |
|--------------------------------------|--------------------|----------------|
| Endometrial hyperplasia              | 84                 | 42%            |
| Benign cytomorphology                | 38                 | 17%            |
| Disordered proliferative hyperplasia | 2                  | 4%             |
| Inflammatory smear                   | 2                  | 4%             |
| Inadequate                           | 74                 | 37%            |
| Total                                | 200                | 100%           |

Table 3 shows that pipelle biopsy and dilatation and curettage method recorded almost similar diagnosis for simple hyperplasia without atypia (28%), secretory endometrium (19%), irregular endometrium (5%), complex hyperplasia without atypia (9%), and

complex hyperplasia with atypia (9%). However, diagnosis was different for simple hyperplasia with atypia and complex hyperplasia with atypia by both methods. Two cases of carcinoma were detected by both methods.

**Table-3: Endometrial histopathology by pipelle biopsy and D&C**

| Endometrial histopathology           | Pipelle biopsy     |                | D&C                |                |
|--------------------------------------|--------------------|----------------|--------------------|----------------|
|                                      | Number of patients | Percentage (%) | Number of patients | Percentage (%) |
| Simple hyperplasia without atypia    | 56                 | 28%            | 56                 | 28%            |
| Secretory endometrium                | 38                 | 19%            | 36                 | 18%            |
| Irregular endometrium                | 10                 | 5%             | 10                 | 5%             |
| Complex hyperplasia without atypia   | 18                 | 9%             | 18                 | 9%             |
| Disordered proliferative endometrium | 18                 | 9%             | 16                 | 9%             |
| Simple hyperplasia with atypia       | 10                 | 5%             | 10                 | 5%             |
| Complex hyperplasia with atypia      | 6                  | 3%             | 6                  | 3%             |
| Inadequate                           | 8                  | 4%             | 8                  | 4%             |
| Carcinoma                            | 4                  | 2%             | 4                  | 2%             |
| Proliferative endometrium            | 32                 | 16%            | 36                 | 18%            |
| Total                                | 200                | 100%           | 200                | 100%           |

Results shows that 37% of endometrial samples were found to be inadequate by endometrial aspiration cytology method while 4% of sample were

found inadequate by both pipelle and dilatation and curettage methods (Table 4).

**Table-4: Adequacy of endometrial sample by all three methods**

| Endometrial sampling            | Adequate (n=200)   |                | Inadequate (n=200) |                |
|---------------------------------|--------------------|----------------|--------------------|----------------|
|                                 | Number of patients | Percentage (%) | Number of patients | Percentage (%) |
| Endometrial aspiratory cytology | 126                | 63%            | 74                 | 37%            |
| Pipelle biopsy                  | 192                | 96%            | 8                  | 4%             |
| Dilatation and curettage        | 192                | 96%            | 8                  | 4%             |

Endometrial aspiration cytology was able to diagnose benign pathology in 44% cases and premalignant pathologies in 19% cases. Endometrial aspiration cytology was failed to detect pathology in 37% cases. It was failed to detect any malignancy. Pipelle biopsy showed benign pathologies in 49% cases, premalignant pathology in 45% cases and carcinoma in 2% cases. Endometrial sample was found to be inadequate in 4% cases. On the other hand, dilatation and curettage diagnosed benign pathologies in 50% cases, premalignant pathologies in 44% cases and carcinoma in 2% cases. Inadequate sample was found in 4% cases.

**DISCUSSION**

Perimenopausal bleeding is now considered as separate entity from menopause. Perimenopausal years are transitional year during which various emotional, psychological, menstrual and ovulatory cycle changes occurs years before menopause[10]. Endothelial sampling is among one of the important diagnostic tools for perimenopausal bleeding. Dilatation and curettage was considered as standard procedure for the diagnosis of endometrial pathology. However, general anaesthesia is required for the dilatation and curettage; moreover, various complications like uterine infection, haemorrhage and proliferation [4, 7, 11].

**Table-5: Correlation of endometrial diagnosis by all three methods.**

| Endometrial Pathology  | Endometrial aspiratory cytology |                | Pipelle biopsy     |                | Dilatation and curettage |                |
|------------------------|---------------------------------|----------------|--------------------|----------------|--------------------------|----------------|
|                        | Number of patients              | Percentage (%) | Number of patients | Percentage (%) | Number of patients       | Percentage (%) |
| Benign Pathology       | 88                              | 44%            | 98                 | 49%            | 100                      | 50%            |
| Premalignant Pathology | 38                              | 19%            | 90%                | 45%            | 88                       | 44%            |
| Carcinoma              | 0                               | 0%             | 4                  | 2%             | 4                        | 2%             |
| Inadequate             | 74                              | 37%            | 8                  | 4%             | 8                        | 4%             |

Results of the present study showed that 80% of females with perimenopausal bleeding belonged to 40 to 50 years age group. These findings are consistent with the observations of previous study of Bhosle *et al.* They recorded 78.6% of female with perimenopausal bleeding belonged to 40 to 50 years age group in a retrospective study on 112 perimenopausal women.

This higher incidence of perimenopausal bleeding in 40 to 50 years age group women seems to be due variation of female hormone due to menopausal approaches. Endometrial growth is decreased due to low level of oestrogen due to increased resistance of gonadotropic hormones caused by decline in number of ovarian follicles[12].

Further, results of the current study revealed that commonest pathology involved in perimenopausal bleeding was simple hyperplasia without atypia in 28% patients followed by secretory endometrium and proliferative endometrium. The incidence of endometrial carcinoma was recorded only in 4 women of the study group belonging to 51 to 60 years age group ie postmenopausal age group.

These findings are in agreement to the previous studies of Sarwar *et al.* [13] and Muzzafar *et al.* [14] Sarwar *et al.* [13] observed 30% of patients had endometrial hyperplasia as endometrial pathology in women with abnormal uterine bleeding. Moreover they recorded incidence of carcinoma in 2% women among their study population of 50 females with abnormal uterine bleeding. Similarly, Muzzafar *et al.* [14] reported that endometrial hyperplasia (24.7%) was the commonest pathological factor in female suffering with profuse menstrual bleeding. In addition they recorded incidence of heavy bleeding was more common in 41 to 50 years age group. Various other studies of Baral R *et al.* [15] Khare A *et al.* [16] and Doraiswami S *et al.* [17]. recorded similar frequency of endometrial pathology in perimenopausal bleeding women.

This endometrial hyperplasia which is a commonest diagnosis among the present study population seems to be due to anovulatory cycles during perimenopausal periods which in turn lead to prolonged or excessive bleeding[18]. Further, heavy bleeding in

perimenopausal women may be due to constantly increased level of oestrogens[19].

Histopathological evaluation of the endometrium is essential in women suffering with perimenopausal bleeding as malignancy may be involved in pathology of perimenopausal bleeding patients [14-16]. Further, results of the current study revealed that endometrial aspiratory cytology was not able to detect endometrial hyperplasia in 14% whereas it was failed to diagnose benign endometrial pathologies in 20% women with perimenopausal bleeding.

Endometrial aspiratory cytology was unable to detect pathogenesis in six women out of eighteen women with post-menopausal bleeding. Moreover, two cases of proliferative endometrium and two cases of endometrial hyperplasia were missed in women with post-menopausal bleeding. In one case of post-menopausal bleeding where both pipelle biopsy and dilatation and curettage reported sample to be inadequate, cytology could detect benign pathology in that patient. This is the only instance where endometrial cytology has proved to be superior to other two methods of sampling. However, endometrial aspiratory cytology was failed to diagnosis of malignancy in four patients.

Current study recorded that both methods pipelle biopsy and dilatation and curettage showed 96% of adequacy. Of the four inadequate endometrial samples obtained by pipelle biopsy, two were from women with perimenopausal bleeding where in one woman, cytology reported endometrial hyperplasia and dilatation and curettage method reported inactive endometrium. In the other woman, dilatation and curettage method reported proliferative endometrium which was missed by other two methods of sampling. Rest two inadequate samples were from women with postmenopausal bleeding of whom all the three methods of endometrial sampling were insufficient in one woman and in the other woman benign pathology was detected on endometrial aspiration cytology.

Four endometrial samples were found inadequate for diagnosis in dilatation and curettage. Out

of these four samples one case was of simple hyperplasia with atypia, another one was of disordered proliferative endometrium. Both of these cases were detected by pipelle endometrial sampling. However, rest of the two cases belonged to post-menopausal women out of which one case was not diagnosed by all the three methods implicated in the study whereas, one case of benign pathology was diagnosed only by endometrial aspiratory cytology.

Further, there is very little information about adequate or inadequate specimen in literature. Present study recorded inadequate endometrium samples in 4% perimenopausal bleeding women. These findings are very similar to the findings of the Baral R *et al.* [15] Jairajpuri ZS *et al.* [18] and Shams G [19] as they recorded inadequate samples in 8%, 2.6% and 2% respectively in women with perimenopausal bleeding.

This substandard reports in the current study may be due to stroma and large haemorrhagic area in endometrium of perimenopausal bleeding women especially post-menopausal women [17]. In addition, these inadequate endometrial samples in post-menopausal women may be due to decrease of oestrogen causes atrophy of endometrium [14].

Findings of the current study showed that premalignant and malignant endometrial pathologies were detected by endometrial aspiration cytology with 59% accuracy. These findings are in agreement with previous studies of Malik R *et al.* [20] and Hemalatha AN *et al.* [21].

Further, pipelle endometrial biopsy recorded 100% sensitivity and 98.15% specificity for the diagnosis of premalignant and malignant pathologies. These findings are very similar to the findings of the earlier study of Fakhar S *et al.* [8] and Bunyavejchevin S *et al.* [22] Fakhar S *et al.* [8] reported 100% sensitivity and specificity for detecting malignancy whereas, Bunyavejchevin S *et al.* [22] recorded 87.5% sensitivity and specificity for malignancy.

## CONCLUSION

Findings of the current study showed that pipelle biopsy and dilatation and curettage had sample adequacy for 96% of cases while endometrial aspiration cytology had sample adequacy of 63%.

Further, results of the present study suggest that accuracy for endometrial diagnosis of pipelle biopsy was equal to dilatation and curettage method of endometrial sampling. Pipelle biopsy has very high accuracy of 99% in detecting premalignant and malignant pathologies of endometrium. However, pipelle biopsy and dilatation and curettage method are equally effective in diagnosing endometrial pathologies. Comparing to dilatation and curettage method pipelle biopsy of endometrium takes shorter time and preserves

stromal architecture better. We emphasise that pipelle biopsy should be used for the endometrial diagnosis in perimenopausal bleeding as it is less painful as well as rapid along with that it is cost effective. Moreover, anesthesia or cervical dilatations are not required for pipelle biopsy method. Nonetheless, studies on larger population are required to establish an ideal screening procedure in low perimenopausal bleeding women.

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