

Frequency of Positive Endometrial Pipelle Biopsies in for Detection of Endometrial Carcinoma in Patients of Civil Hospital with Abnormal Uterine Bleeding

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ABSTRACT

Aim: The objective of this study was to determine frequency of positive endometrial biopsies in pre and post menopausal patients with abnormal uterine bleeding for detection of endometrial carcinoma

Study design: Cross-sectional study

Settings: Gynecological outpatient department Civil Hospital Bahawalpur.

Methods: Pre and post-menopausal women between 35-70 years with abnormal uterine bleeding fulfilling inclusion and exclusion criteria were selected for the study. After detailed history and examination, informed consent, pipelle endometrial biopsy was taken. Biopsy of each patient was labeled and sent to the histopathology department of Bahawal Victoria Hospital Bahawalpur for histopathology. The biopsy was deemed as positive if it detects endometrial carcinoma on histopathology and vice versa. Data was analyzed by using SPSS version 10. Descriptive statistics were used to analyze the data.

Results: Among 126 patients, majority (38.09%) were in age group 35-45 years and were multipara. 58.73% patients were post-menopausal and menorrhagia was the most frequent presenting complaint. Amount of tissue obtained on curetting with Pipelle was adequate in 96.82% of cases. The most frequent histopathology finding on pipelle endometrial sampling was secretory endometrium i.e. in 38.88% of cases. Endometrial biopsy for carcinoma was positive in only 5.55% of cases.

Conclusion: Pipelle biopsy is definitely a useful and cost-effective method. It can reduce the number of D &Cs performed in the operating theatre. The accuracy of the Pipelle is higher in postmenopausal women compared with premenopausal women.

Key words: Abnormal uterine bleeding, pipelle endometrial biopsy, endometrial carcinoma,

INTRODUCTION

Endometrial sampling for histopathology is important in the assessment of abnormal uterine bleeding, which a major problem is accounting for 33% of outpatient gynaecological referrals^{1,2}. Its causes include a wide spectrum of diseases and it accounts for most hysterectomies and nearly all endometrial ablative procedures. In the premenopausal period, many women with endometrial carcinoma will present with intermenstrual bleeding, but one third will present heavy periods only^{3,4}.

Abnormal perimenopausal or postmenopausal bleeding is associated with endometrial carcinoma in approximately 10% of cases^{5,6}. In 18–40% women benign focal lesions, such as endometrial polyps and fibroids, are common⁷. With regard to endometrial carcinoma, the significance of abnormal bleeding depends quite strikingly on demographic factors. If there is postmenopausal bleeding endometrial carcinoma is of particular concern. Abnormal bleeding in a premenopausal woman is, however, not a symptom of immediate concern with respect to cancer, because there are a number of potential

physiological explanations, and also because the incidence of uterine cancer under 40 years of age is very low⁸. It has been calculated that 3000–4000 women under 40 years with abnormal bleeding would have to be evaluated to detect one case of endometrial cancer⁸. This has implications for decisions regarding evaluation of AUB.

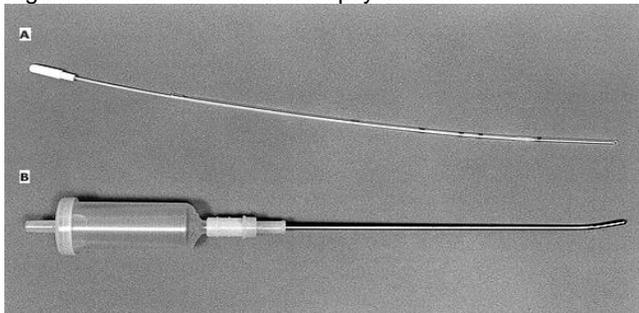
While endometrial cancer can occur in women in their twenties, the vast majority of cases occur in women over 45 years of age. The incidence rises steeply from about age 45 years to about 55 years and remains at the same high rate thereafter. Abnormal uterine bleeding in women older than 35 years and certainly in menopausal patients mandates evaluation, mainly to exclude cancer and hyperplasia⁹. Dilatation and curettage (D&C) is the gold standard for endometrial sampling, but in 60% of cases, less than half of the uterine cavity is curetted, with added risk of general anaesthesia, infection and perforation. This has led to the advent of new and simple methods for endometrial sampling. Various devices are on the market nowadays, including the pipelle curette (Endocurette, Midvale, Utah, and

USA). The safety and acceptability of this device has been reported in various studies. The pipelle device can be used on an outpatient basis and is cost effective compared D&C¹.

The Pipelle technique has shown to have high sensitivity in the detection of both endometrial cancer and atypical hyperplasia¹⁰. It has advantage of taking biopsy on the first visit of patient therapy waiting time for early diagnosis of malignancy can be reduced¹¹. With endometrial pipelle biopsy the detection rate of endometrial cancer in post menopausal women was 99.6% & 91% in the pre menopausal women when global disease is present. The detection rate for atypical hyperplasia was 88% and specificity was 98-100%¹². Pipelle had a sensitivity, specificity, positive predictive value and negative predictive value of 100% for diagnosing endometrial carcinoma, hyperplasia and secretory endometrium. The pipelle is a safe device for getting an adequate endometrial sample for histology, with a high sensitivity and specificity for detection of hyperplasia and malignancy¹.

This study will tell us the magnitude of the problem in our population which will help us to modify future planning and strategy regarding the management of endometrial carcinoma. This study will not only add in national data but also comparable with international studies.

Figure 1: Office endometrial biopsy instruments



(A) Pipelle endometrial suction curette. (B) Vabra aspirator.

PATIENTS AND METHODS

During Six months period i.e. from 20-03-2013 to 19-9-2013, pre and post-menopausal women between 35-70 years with abnormal uterine bleeding presented to gynaecology out patient department of Civil Hospital Bahawalpur were included in the study. Patients with post-menopausal women taking hormone replacement therapy and women taking oral contraceptive pills or tamoxifen were excluded. Pregnant as well as hypertensive and diabetic patients were also excluded. Approval from the hospital ethical committee was sought.

After detailed history and examination, informed consent for pipelle endometrial biopsy was by the consultant gynaecologist following thorough counseling with the patient and her husband relative. The patient was shifted to the biopsy room and pipelle endometrial biopsy was taken and stored in formaline solution. Pipelle is a disposable polypropylene sheath with an inner plunger and is used for blind endometrial biopsy. The whole procedure was done as an outpatient procedure by a consultant gynaecologist having minimum five year experience by a standard protocol. Biopsy of each patient was labeled and sent to the histopathology department of Bahawal Victoria Hospital Bahawalpur for histopathology by a consultant histopathologist. The biopsy was deemed as positive if it detects endometrial carcinoma on histopathology and vice versa. All the patient's demographic data and result of biopsy in terms of negative and positive biopsy was recorded in pre-designed proforma.

Data was analyzed by using SPSS version 10. Descriptive statistics were used to analyze the data. Quantitative variables like age, parity and amount of abnormal uterine bleeding were calculated by taking mean and standard deviation. Qualitative variables which were the outcome variables i.e. endometrial biopsy for carcinoma (positive, negative) were calculated by taking frequencies and percentages.

Confounding factors like age, parity and amount of abnormal uterine bleeding were controlled by stratification to observe an outcome.

RESULTS

During six month study period i.e. from 20-03-2013 to 19-9-2013, 126 patients were selected who fulfilled the inclusion and exclusion criteria. Among 126 patients, majority (38.09%) were in age group 35-45 years. The age group 46-55 was next in line. Analysis of parity distribution showed that majority of women were multipara (52.37%) i.e. Parity ≥ 2 . Only 4.76% of cases were nullipara. Among 126 patients, majority (58.73%) were post-menopausal. Menorrhagia was the most frequent presenting complaint i.e. in 69.04% of cases i.e. majority was having blood loss more than 80 ml per cycle. Intermenstrual and postcoital bleeding was reported in 21.42% and 9.52% of cases respectively. Amount of tissue obtained on samples with Pipelle was adequate in 96.82% of cases, while it was inadequate in only 3.17% of cases. The most frequent histopathology finding on pipelle endometrial sampling was secretory endometrium i.e. in 38.88% of cases. Proliferative endometrium was the second most frequent finding among 126 cases. Endometrial biopsy for carcinoma was positive in only 5.55% of cases. Among 126 patients, majority (38.09%) were

in age group 35-45 years. Analysis of parity distribution showed that majority of women were multipara (52.37%) i.e. Parity ≥ 2 . Among 126 patients, majority (58.73%) were post-menopausal. Menorrhagia was the most frequent presenting complaint i.e. in 69.04% of cases. Amount of tissue obtained on curetting with Pipelle was adequate in 96.82% of cases. Among 126 cases, majority was having blood loss more than 80 ml per cycle. The most frequent histopathology finding on pipelle endometrial sampling was secretory endometrium i.e. in 38.88% of cases. Highest frequency was in multipara, age group 66-70 years and having blood loss <80 ml

Table 1: Age wise distribution of patients (n=126)

Age group (in years)	=n	%age
35-45	48	38.09
46-55	41	32.53
56-60	27	21.42
61-65	7	5.55
66-70	3	2.38

Table 2: Parity wise distribution of cases (n=126)

Parity	=n	%age
P0 (Nullipara)	6	4.76
P1	28	22.22
P2	31	24.60
P3 or more	35	27.77

Table 3: Menopausal status (n=126)

Menopausal status	=n	%age
Pre-menopausal	52	41.26
Post-menopausal	74	58.73

Table 4: Bleeding Pattern (n=126)

Bleeding Pattern	=n	%age
Intermenstrual bleeding	27	21.42%
Postcoital bleeding	12	9.52%
Menorrhagia	87	69.04%

Table 5: Amount of Endometrial Curetting with Pipelle (n=126)

Amount of Tissue Obtained	=n	%age
Adequate	122	96.82
Inadequate	4	3.17

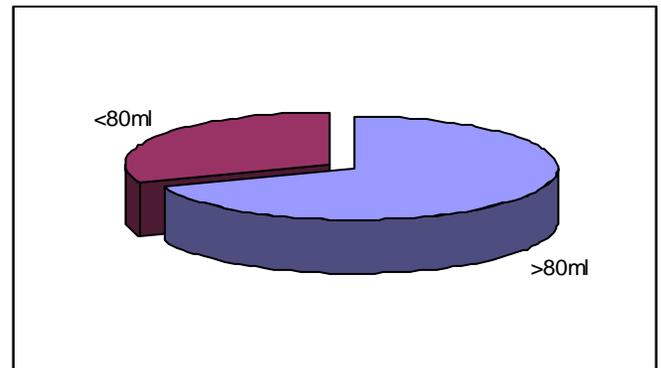
Table 6: Histopathology findings on pipelle endometrial sampling (n=126)

Histopathology	Pipelle H/P	%age
Secretory endometrium	49	38.88
Proliferative endometrium	44	34.92
Atrophic Endometrium	6	4.76
Endometritis	9	7.14
Adenomatous hyperplasia	7	5.55
Atypical hyperplasia	4	3.17
Carcinoma endometrium	7	5.55

Table 7: Frequency of positive endometrial pipelle biopsies (n=126)

Confounding variables	=n	+ve cases	%age
Maternal age in years			
35-45	48	0	0
46-55	41	1	2.43
56-60	27	3	11.11
61-65	7	2	28.57
66-70	3	1	33.33
Parity			
P0 (Nullipara)	6	0	0
P1	28	1	3.57
P2	31	3	9.67
P4 or more	35	3	8.57
Amount of bleeding			
<80 ml	39	3	7.69%
>80 ml	87	4	4.59%

Figure 2: Amount of abnormal uterine bleeding (n=126)



DISCUSSION

Endometrial tissue sampling is one of the most common diagnostic procedure in gynaecology and the primary indication, by far, are in the assessment of woman with abnormal uterine bleeding^{1,13}

Previously, the gold standard method for sampling the endometrium was dilatation and curettage (D&C) under general anaesthesia. Currently, outpatient endometrial biopsy has replaced D&C as the first line diagnostic test in the evaluation of abnormal uterine bleeding as both have been shown to have similar accuracy¹⁴⁻¹⁵. The objective of this study was to determine frequency of positive endometrial biopsies in pre and post menopausal patients with abnormal uterine bleeding for detection of endometrial carcinoma.

The analysis of histopathology reports of endometrial curettage revealed secretory endometrium in 38.88% of cases, proliferative endometrium in 34.92% of cases, atrophic endometrium in 4.76% of cases, adenomatous hyperplasia and carcinoma endometrium was

reported in 5.55% of cases. Endometritis was reported in 7.14% of cases (Table 6)

In a previous study conducted in Pakistan, proliferative endometrium was reported in 33%, cystic hyperplasia in 25% of cases. Cystic hyperplasia and proliferative endometrium were found in menorrhagic women over 40 years of age¹⁶. The results of present study also corresponds with another study from Pakistan, where on analyzing the histopathology results of the samples 34% were showing proliferative endometrium¹³. This indicates an ovulation to be the leading cause of abnormal vaginal bleeding. The second most common pattern was mild cystic hyperplasia (21%)¹³.

Proliferative phase endometrium was reported in 42% by Sheetal et al¹⁷. However it is lower than that (42% V/S 54%) reported by FakharS et al¹. Secretary phase endometrium was found in 38.88% of cases in our study. It is higher than that reported by others 14%¹⁸

Literature reports quite variable incidence of endometrial hyperplasia. Silander found it to be 6.66%¹⁹. Wentz and Behnamfar et al report it as 9% and 10.9% in their studies^{13,18}. However Jyotsana¹⁵⁸ report an incidence of 21% and 22.66%. A rather high incidence of 26% and 28.3% was reported by Sheth²¹ and AnuradhaPanda²².

Comparison of results of this study with others as stated above indicates that histopathological pattern of endometrium in patients with abnormal uterine bleeding is quite variable regardless of age, parity, and ethnicity. Although the incidence of endometrial hyperplasia is grossly variable, yet incidence of endometrial carcinoma is smaller in all sited studies. So important finding seems to be endometrial hyperplasia with its attendant risk of progression to carcinoma and further studies are required to address and explore course of progression of hyperplasia to carcinoma.

Pipelle also had high diagnostic sensitivity, specificity and negative predictive value (100%, 98% and 100%, respectively) for hyperplasia with atypia, and low sensitivity (57%) and positive predictive value (57%), but high specificity (97%) and negative predictive value (97%) for endometritis. Similarly, for proliferative endometrium, the pipelle technique had values of 94% and 93% for sensitivity and specificity, respectively¹. The sensitivity of PES in diagnosing hyperplasia is 100%, specificity 94%, accuracy 95%, positive predictive value 84% and negative predictive value was 100%¹¹.

In the present study, endometrial biopsy for carcinoma was positive in only 5.55% of cases (Table 6&7), but disagrees with other where carcinoma endometrium was reported in 11.1%²³. In a study conducted by Sultana N, Median age was 55 years.

Bleeding per vaginum was the commonest feature and endometrioidadenocarcinoma was the commonest histological type²⁷.

In the present study one case of carcinoma endometrium was reported in the pre-menopausal group and six cases were reported in the post-menopausal group. Almost similar results were observed in the other study conducted in Pakistan where Adenoicarcinoma was found in a single premenopausal women of 48 years¹⁶.

The detection rate for endometrial carcinoma was higher in postmenopausal women compared with premenopausal women in other study. In both postmenopausal and premenopausal women, the Pipelle was the best device, with detection rates of 99.6% and 91%, respectively²⁸.

The results of endometrial biopsies have been shown to be compatible with histopathological findings of hysterectomy specimen in 39(93%) cases¹³. The sensitivity of PES in diagnosing carcinoma endometrium is 75%, specificity 100%, accuracy 98% with positive predictive value 100% and negative predictive value was 98%¹¹. In another local study the sensitivity of PES in the detection of endometrial hyperplasia and carcinoma is 100% and 77% respectively¹¹. These results are similar to the study of Stocxet al²⁹ who showed that sensitivity of Pipe-le ranged from 83-96% in the detection of endometrial carcinoma.

Specificity of PES in the detection of endometrial hyperplasia/carcinoma was 94% and 100% in the PES with AUB and PMB. This is comparable to the study of Bunyamejchevin et al and Dijkhuizen et al who showed specificity of PES upto 100% and 98% respectively in the detection of endometrial carcinoma in PMB²⁸, Positive predictive value for endometrial hyperplasia/carcinoma is 84% and 100% respectively. Negative predictive value for endometrial hyperplasia/carcinoma was 100% to 98%. Similar results have been reported by Macahado et al who reported PPV 94.1% and NPP 93.7%³⁰

A substantial number of traditional diagnostic curettage can be substituted by pipelleaspiration, which is an inexpensive outpatient procedure³¹. All 6 cases of endometrial cancer were diagnosed on pipelle biopsy¹³². Batool et al studied 76 cases of PMB with Pipelle biopsies and all cases of Adenocarcinoma were identified³².

One can easily speculate that by looking at various aspects of this study that Pipelle is attractive, convenient, quite reliable instrument for endometrial sampling. With the results in this study one can easily rely upon this endometrial sampling technique.

CONCLUSION

Pipelle biopsy is definitely a useful and cost effective method. It is convenient to the patients and physicians. It can reduce the number of D&Cs performed in the operating theatre. It is useful in obese and high risk patients with minimum chances of perforation of uterus due to its soft flexible tip. It has advantage of taking biopsy on the first visit of patient thereby waiting time for early diagnosis of malignancy can be reduced. The availability of modern technique in this region is the necessity of time in order to improve facilities for diagnosis and management. So, one can easily rely upon this sampling technique in outpatient settings. However, hysteroscopic examination of high risk patients is emphasized as certain lesions in the endometrium can be missed on PES or even on thorough traditional D&C.

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