Original Article

Study of the Efficacy of Pipelle Biopsy Technique to Diagnose Endometrial Diseases in Abnormal Uterine Bleeding

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Abstract

Background: Pipelle biopsy is ideal for obtaining endometrial sample in outpatient department. It samples only 4% of the endometrial surface and has sensitivity up to 97%. A positive biopsy can avoid inconvenience to a patient, but a nonspecific finding should be interpreted with caution. Thus, the objectives of this study were to analyze the efficacy of pipelle biopsy by adequacy of the sample obtained and also to establish the reliability by comparing the histopathology report obtained by pipelle biopsy with that of the hysterectomy specimen. **Materials and Methods:** A prospective study conducted at a tertiary care hospital on 104 women with abnormal uterine bleeding (AUB). They were scheduled for pipelle endometrial sampling before hysterectomy. The sensitivity, specificity, negative and positive predictive values, and accuracy of pipelle biopsy in diagnosing various endometrial pathologies were analyzed. The validity of pipelle biopsy was studied for endometrial hyperplasia and carcinoma and their statistical significance was tested. **Results:** The overall concordance rate was 63.8%. The sensitivity, specificity, positive and negative predictive values, and accuracy of pipelle biopsy for endometrial hyperplasia was 64.2%, 88.8%, 94.1%, 85.5%, and 47.3% and for endometrial carcinoma was 75%, 100%, 100%, 97.9%, and 98%, respectively. The *P* value for endometrial hyperplasia and carcinoma was 0.001 (statistically significant). **Conclusion:** Pipelle biopsy is valuable in diagnosing endometrial pathology of AUB cases. It has very high sensitivity and specificity for endometrial malignancies. A hysteroscopic dilatation and curettage is required for definitive diagnosis in cases of polyps and focal endometrial lesions.

Keywords: *Abnormal uterine bleeding, endometrial carcinoma, endometrial hyperplasia, hysterectomy, pipelle biopsy*

Introduction

Abnormal uterine bleeding (AUB) includes any disturbance in the regularity, frequency, duration or volume of menstrual flow, and nonmenstrual disturbance of any cause.[1] About 9%–30% of the reproductive age group women have menstrual irregularities requiring medical evaluation.[2] This proportion rises up to 70% in peri and postmenopausal women. It also accounts for two-thirds cases of hysterectomy. Dilatation and Curettage (D and C) under general anesthesia has long been the gold standard for the assessment of AUB. The need for hospital admission, general anesthesia, and the cost has made it less favorable.[3]

Recently, office procedures which are quick, safe, and inexpensive such as pipelle biopsy device, Vabra and Z sampler have superseded this technique with good patient acceptability.[4] Pipelle is a flexible polypropylene device which works using a suction mechanism. It can be inserted into the cervical canal without dilatation making it an ideal outpatient endometrial biopsy procedure.[3] There are very few studies that have analyzed the efficacy of pipelle biopsy or validated

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this method of endometrial sampling against the gold standard histopathological diagnosis from hysterectomy specimens.

Thus, the aim of our study was to analyze the efficacy of pipelle biopsy in terms of adequacy of the sample and to establish its reliability by comparing the histopathology report obtained by pipelle biopsy with that of hysterectomy specimen for diagnosing endometrial diseases in all cases of AUB.

Materials and Methods

This was a prospective study conducted at Ramaiah Medical College & Hospitals, a tertiary care hospital in South India on 104 women with AUB in the age group of 34–74 years. Informed written consent from all the patients and ethical committee approval from our institution were obtained. Data were collected on a pro forma that included history, clinical examination, pap smear, and laboratory investigations. Ultrasonography (USG) was done before endometrial sampling in all the cases; findings were considered abnormal in cases with the endometrial thickness (ET) >5 mm in postmenopausal women, ET >12 mm in pre- and peri-menopausal women and those with focal endometrial lesions like polyp. All patients were subjected to pipelle endometrial sampling (PES) before hysterectomy. Exclusion criteria included patients with pelvic inflammatory disease, pregnancy-related bleeding, and acute vaginal infections.

Method of sample collection

With the patient in dorsal position, the cervix was held with vulsellum during insertion of the pipelle sampler into the cervix. The pipelle endometrial sample was collected under aseptic precautions through the undilated cervix without anesthesia. On reaching the uterine fundus, the piston was withdrawn to create negative pressure. Endometrial tissue was aspirated from all the uterine walls, and the sample was sent in a container with ten percent formaldehyde for histopathological examination (HPE) to the Department of Pathology in the same Institution. Hysterectomy was done on a later date. Both the specimens were reported by the same pathologist.

Statistical analysis

The data were analyzed using statistical software version SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc. The descriptive statistics of clinical features, USG findings, and endometrial histopathology obtained by pipelle biopsy and hysterectomy were presented in terms of frequency and percentage. The variables such as age and duration were summarized in terms of the median with inter-quartile range since the data were not normally distributed. The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy of pipelle biopsy in diagnosing various endometrial pathologies were analyzed. The validity of pipelle biopsy was studied for endometrial hyperplasia and carcinoma and their statistical significance was tested using McNemars test. Value of $P < 0.05$ was considered statistically significant.

Results

Majority (25%) of the patients were in the age group of 46–50 years ($n = 26$). The median age of the study group was 47 years. Maximum number ($n = 50$) of AUB patients were of parity two (48.08%). About 79.8% ($n = 83$) of the study population had symptoms up to 1 year and the median duration of symptoms was 6 months.

In this study, 73.07% ($n = 76$) presented with chronic AUB, while 26.9% ($n = 28$) presented with acute AUB. The most common symptom was heavy menstrual bleed (HMB) seen in 87 cases (83.6%) followed by postmenopausal bleed (PMB) in 17 (16.3%) and intermenstrual bleed (IMB) in eight (7.7%) cases. The patients who had IMB also had HMB. Table 1 shows the analysis of patients with PMB and their USG findings. In the 16.35% ($n = 17$) who presented with PMB, the most common endometrial lesion was adenocarcinoma ($n = 6$, 35.3%), followed by complex endometrial hyperplasia with atypia ($n = 2$, 11.8%). The percentage of scanty tissue obtained was high

Table 1: Analysis of patients with postmenopausal bleed and study of ultrasonography features

Endometrial HPE on pipelle biopsy	*n* (%) (*n*=17; 16.35%)	USG ET (mm)
Adenocarcinoma	6 (35.3)	>5
Complex endometrial hyperplasia with atypia	2 (11.8)	>5
SEH	1 (5.8)	>5
Proliferative endometrium	1 (5.8)	5
Atrophic endometrium	1 (5.8)	3
Scanty tissue	6 (35.3)	Atrophic endometrium (2) - <5
Hysterectomy HPE of these scanty samples		All others (4) - >5
SEH - 1		
Proliferative endometrium - 1		
Endometrial polyp - 2		
Atrophic endometrium - 2		

USG: Ultrasonography, HPE: Histopathological examination, ET: Endometrial thickness

(*n* = 6, 35.3%) in this population due to continuous bleed per vagina (P/V), focal endometrial lesion, and atrophic endometrial tissue. Out of the 114 USG findings in total, the most common uterine pathology was fibroid seen in 27.2% (*n* = 31) followed by thickened endometrium in 21.05% (*n* = 24), adenomyosis in 14.9% (*n* = 17), and endometrial polyp in 7.89% (*n* = 9) of the cases.

There were 63 cases who underwent prior medical therapy, of which 74.6% (*n* = 47) were treated with oral and injectable progesterone therapy, 19.05% (*n* = 12) were treated with anti-fibrinolytic, 3.2% (*n* = 2) were treated with progesterone intrauterine device and another 3.2% (*n* = 2) were treated with oral contraceptives in view of AUB. All of them who underwent medical treatment previously, had relapse of symptoms and hence underwent hysterectomy. Comorbidities were seen in 43.3% (*n* = 45) of the study population. Of which, hypothyroidism was observed in 24.4% (*n* = 11) of these patients. Anemia was observed in 20.2% (*n* = 21) of the entire study population due to chronic blood loss with every menstrual cycle.

The study findings are tabulated as follows:

Table 2 shows the summary of the pipelle biopsy procedure. Among the 23 (22.1%) patients in whom inadequate samples were obtained, seven had continuous P/V, three patients were in the early proliferative phase, four patients had an enlarged uterus with difficult negotiation of the pipelle device into the uterine cavity, five had endometrial polyp and four had atrophic endometrium. Table 3 compares the histopathological reports of Pipelle biopsy and hysterectomy. The total number of pipelle endometrial histopathology in this study constituted to 106 as there were two patients who had two interpretations in their HPE report: proliferative endometrium and stromal sarcoma in one patient and the other with simple endometrial hyperplasia (SEH) and focal secretory endometrium. The total number of hysterectomy HPE report constituted to 122 because the 17 cases of polyp also had associated endometrial HPE and one case had SEH associated with stromal sarcoma. The most common finding on both pipelle biopsy and hysterectomy HPE was proliferative endometrium. Out of the 75 patients with an associated myometrial lesion diagnosed after hysterectomy, 46 (61.3%) patients were found to have adenomyosis and 29 (38.7%) patients were found to have leiomyoma. As shown in Table 4, there were 38 discordant cases on comparing the endometrial HPE reports of pipelle biopsy and hysterectomy with a discordance rate of 36.5%. The discordance in four cases of secretory endometrium and proliferative endometrium was because these cases had pipelle biopsy and hysterectomy done in different phase of menstrual cycle due to delayed hospital admission for surgery. One case of simple hyperplasia was diagnosed with proliferative endometrium in pipelle biopsy. There was an over detection of six cases of proliferative endometrium and two cases of secretory endometrium as SEH by pipelle biopsy. Two cases of endometrial adenocarcinoma were diagnosed with complex endometrial hyperplasia with atypia in pipelle biopsy. In 23 patients, scanty tissue was obtained in pipelle biopsy which actually contributed to seven cases of proliferative endometrium, four cases of secretory endometrium, two cases of SEH, one case of complex endometrial hyperplasia, five cases of endometrial polyp, and four cases of atrophic endometrium on hysterectomy HPE. Table 5 depicts the statistical analysis of endometrial pathologies in which pipelle biopsy had an accuracy of 88.5% in detecting simple hyperplasia, 99.04% in complex hyperplasia, 98.07% in complex hyperplasia with atypia, 98% in adenocarcinoma, 99.04% in stromal sarcoma, and 95.2% in detecting atrophic endometrium. Pipelle biopsy did not detect any of the polyps. Table 6 shows the validity of pipelle biopsy in diagnosing endometrial hyperplasia and carcinoma. The value of *P* = 0.001 was statistically highly significant for both endometrial hyperplasia and carcinoma.

Table 2: Summary of the pipelle biopsy procedure

Findings	*n* (%)
Total number of patients under the study	104
Successful entry into the endometrial cavity	104 (100)
Difficult negotiation of the pipelle device into the uterine cavity	4 (3.8)
No sample obtained	Nil
Material adequate for histological analysis	81 (77.9)
Material inadequate for histological analysis	23 (22.1)

Table 3: Comparison of histopathological reports of pipelle biopsy and hysterectomy

Histopathological report	Pipelle biopsy (*n*=106), *n* (%)	Hysterectomy (*n*=122), *n* (%)
Proliferative endometrium	32 (30.2)	48 (39.3)
Secretory endometrium	20 (18.9)	23 (18.9)
Simple hyperplasia	14 (13.5)	10 (8.2)
Complex hyperplasia	2 (1.9)	3 (2.5)
Complex hyperplasia with atypia	3 (2.8)	1 (0.8)
Adenocarcinoma	6 (5.7)	8 (6.6)
Atrophic endometrium	5 (4.7)	10 (8.2)
Adenomatous polyp	-	13 (10.7)
Leiomyomatous polyp	-	4 (3.3)
Stromal sarcoma	1 (0.9)	2 (1.6)
Scanty tissue	23 (21.7)	-
Total	106 (100)	122 (100)

Table 4: Pipelle histopathological examination report not comparable to hysterectomy histopathological examination report

Endometrial HPE report on pipelle biopsy	Total, *n* (%) (*n*=38; 36.5%)	Hysterectomy HPE report, *n* (%)
Proliferative endometrium	2 (5.3)	SEH - 1 (50)
		Secretory - 1 (50)
Secretory endometrium	3 (7.9)	Proliferative - 3 (100)
SEH	8 (21.05)	Proliferative - 6 (75)
		Secretory - 2 (25)
Complex endometrial hyperplasia with atypia	2 (5.3)	Adenocarcinoma - 2 (100)
Scanty tissue	23 (60.5)	Proliferative endometrium - 7 (30.4)
		Secretory endometrium - 4 (17.4)
		SEH - 2 (8.7)
		Complex endometrial hyperplasia - 1 (4.3)
		Endometrial polyp - 5 (21.7)
		Atrophic endometrium - 4 (17.4)

HPE: Histopathological examination, SEH: Simple endometrial hyperplasia

Table 5: Statistical analysis of endometrial pathologies obtained by pipelle biopsy

HPE report	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Simple hyperplasia	60	91.5	42.9	95.5	88.5
Complex hyperplasia	66.6	100	100	99.02	99.04
Complex hyperplasia with atypia	100	98.06	33.3	100	98.07
Adenomatous polyp	-	100	-	87.5	-
Leiomyomatous polyp	-	100	-	96.1	-
Adenocarcinoma	75	100	100	97.9	98
Stromal sarcoma	50	100	100	99.03	99.04
Atrophic endometrium	50	100	100	94.9	95.2

HPE: Histopathological examination, NPV: Negative predictive value, PPV: Positive predictive value

Table 6: Validity of pipelle endometrial sampling for endometrial hyperplasia and endometrial carcinoma

Validity of PES	Endometrial hyperplasia (%)	Endometrial carcinoma (%)
Sensitivity rate	64.2	75
Specificity rate	88.8	100
Accuracy rate	47.3	98
PPV	94.1	100
NPV	85.5	97.9
P	0.001	0.001

PES: Pipelle endometrial sampling, NPV: Negative predictive value, PPV: Positive predictive value

Discussion

AUB accounts to 33% of patients attending the gynecology clinic and two-third cases of hysterectomy.[5] Three decades ago a blind D and C was considered as the gold standard procedure for the diagnosis of AUB. However in ten to 25% of cases D and C alone can miss the diagnosis of an existing endometrial pathology. It can be associated with uterine perforation in 0.6%–1.3% of cases, infection in 0.3%–0.5% of the cases, unexpected hemorrhage in 0.4% of the cases, also associated with the complications of general anesthesia and the need for the prolonged hospital admission.[6] This led to the discovery of office biopsy procedures like pipelle biopsy device which is simple, quick, inexpensive, and safe with good patient acceptability. The most common symptom in the present study was heavy menstrual bleeding in 83.6%, followed by postmenopausal bleeding in 16.3%. HMB was the most common symptom in most of the other studies also. This was followed by IMB in other studies. However, the second-most common symptom in our study was postmenopausal bleeding which was 16.3% and comparable to a study conducted by Rasheed and Yasmeen where PMB was 5% and the second-most common symptom.[7] The number of PMB cases in our study (16.35%) was comparable to 17.14% of PMB cases obtained in the study by Abdelazim *et al*.[8]

The number of inadequate endometrial samples obtained in our study accounted to 22.1% (n = 23), with an adequacy rate of 77.9% (n = 81), which was comparable to a study conducted by Tanriverdi *et al*. where the inadequacy rate was 22.8%, and the adequacy rate was 77.2%.[4] Thus, pipelle is an effective device in obtaining adequate samples without anesthesia. Table 7 compares the accuracy of pipelle biopsy in diagnosing endometrial pathologies as observed in our study with that of a study

Table 7: Comparison of accuracy of pipelle biopsy in diagnosing endometrial pathologies

Endometrial HPE	Accuracy in present study (*n*=104) (%)	Accuracy in Edessy *et al*.[9] study (*n*=100) (%)
Benign histology	64.7	68.7
Hyperplasia without atypia	61.5	77.9
Hyperplasia with atypia	98.07	69.2
Atrophic endometrium	50	61.35
Endometrial polyp	Nil	16
Endometrial carcinoma	98	71.2
Uterine sarcoma	50	38.7

HPE: Histopathological examination

conducted by Mahmoud Edessy *et al*.[9] Our study was 98.07% accurate in diagnosing hyperplasia with atypia and 98% accurate in diagnosing carcinoma compared to 69.2% and 71.2%, respectively, in the other study. Compared to a 16% accuracy rate for polyps in the other study we had no polyps detected by pipelle in our study. However, the authors of the other study concluded that hysteroscopy is the gold standard to accurately detect focal uterine pathologies where pipelle will be an inadequate device.

Coming to the reliability of the pipelle device, the validity of PES obtained in our study with respect to hyperplasia and endometrial carcinoma were compared with a study by Yasmin *et al*.[2] The results were completely comparable for endometrial carcinoma whereas it was not comparable for endometrial hyperplasia. Our study had sensitivity, specificity, PPV, NPV and accuracy of 64.2%, 88.8%, 94.1%, 85.5%, and 47.3%, respectively, for hyperplasia whereas the other study had 100% sensitivity, 94% specificity, 84% PPV, 100% NPV, and 95% accuracy. The low sensitivity and accuracy rates in our study were attributed to the over detection of proliferative and secretory endometrium as endometrial hyperplasia by pipelle biopsy. The study proved that pipelle had 75% sensitivity, 100% specificity, 100% PPV and 97.9% NPV, and 98% accuracy in diagnosing endometrial carcinoma as in the study by Yasmin *et al*. which showed 75% sensitivity, 100% specificity, 100% PPV and 98% NPV, and 98% accuracy.[2] The sensitivity of pipelle biopsy for endometrial hyperplasia in our study of 64.2% was comparable to a study conducted by Demirkiran *et al*. which had a sensitivity of 67% for endometrial hyperplasia.[10] Thus, it can be inferred from the above findings that pipelle is an effective device in diagnosing endometrial carcinoma, but in case of hyperplasia pipelle is more useful in ruling out than in diagnosing these lesions due to high NPV, high specificity and low sensitivity. The overall concordance rate between pipelle biopsy and hysterectomy in the study was 63.8% which was comparable to a study conducted by Demirkiran *et al*. in which the concordance rate was 67%.[10] This proves that pipelle is a valuable device in the diagnosis of endometrial pathologies with high accuracy in the diagnosis of endometrial malignancies. Those cases diagnosed as hyperplasia on pipelle biopsy and all those patients who had persistent symptoms despite pipelle biopsy revealing benign histology would require a hysteroscopic D and C to confirm the diagnosis and to overcome the low accuracy rates. Those cases diagnosed with complex atypical hyperplasia would require a repeat biopsy to rule out focal malignant changes. In view of pipelle biopsy being a safe, inexpensive, outpatient procedure requiring no anesthesia, and less expertise, it would be the most cost-effective biopsy procedure with better diagnostic efficacy for all cases of AUB.

Conclusion

In the present study, we were able to obtain 77.9% of adequate samples by pipelle biopsy. It had a high accuracy rate in diagnosing the benign endometrial pathologies and carcinoma. In terms of validating the use of pipelle biopsy for the diagnosis of endometrial hyperplasia, it had high specificity, positive and NPVs though the sensitivity was relatively low. Hence, we can conclude that pipelle is a valuable device for the diagnosis of endometrial pathologies with the highest efficacy in ruling out endometrial hyperplasia and diagnosing carcinoma. We need to be aware of the higher rates of false positives in case of hyperplasia though the specificity is still high in these cases. A positive biopsy is always diagnostic, but a negative biopsy does not rule out endometrial lesions, and further evaluation is required in cases with recurrent and persistent symptoms. An additional hysteroscopic D and C is required for definitive diagnosis in cases of polyps and focal endometrial lesions.

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Conflicts of interest

There are no conflicts of interest.

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