

Comparative study of pipelle device versus conventional dilatation and curettage for endometrial sampling in diagnosis of endometrial pathology causing abnormal uterine bleeding or infertility in women > 25 years of age

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Abstract

Background: Abnormal Uterine bleeding (AUB) is a cause of significant healthcare burden for the women, common methods for endometrial assessment are USG, hysteroscopy, D&C, however multiple newer outpatient method are becoming popular due to their ease of application and cost effectiveness. Present study was aimed to compare the diagnostic accuracy and histopathological success of Pipelle verses conventional curettage in diagnosing endometrial pathology in AUB cases.

Material and Methods: Present study was single-center, Prospective and comparative single blind study, conducted women aged ≥ 25 years, with complaints of abnormal uterine bleeding with or without infertility. Initially, endometrial sample was collected by pipelle sampler in the outpatient department followed by endometrial biopsy by curettage under general anesthesia.

Results: Out of 106 patient's majority were from 40-60 years age group, had 2 or more parity. Majority had abnormal uterine bleeding alone (77.36%), infertility alone (10.37%) & infertility with abnormal uterine bleeding (12.26%). Common USG findings were endometrial polyp (19.81%), fibroid uterus (10.38%), adenomyosis (3.77%), cystic endometrium (3.77%) and Thickened Endometrium (1.89%). In women with AUB & infertility the sensitivity of pipelle in picking up the endometrial pathology was 100% as compared to D&C and specificity was 99.02%. The negative predictive value was 100% and Positive predictive value was 80%. In the premenopausal women the sensitivity, specificity, NPV & PPV are all 100% for Pipelle sample as compared to curettage. In the postmenopausal women, specificity & PPV was 100%, however sensitivity was 66% and NPV was 95.2%.

Conclusion: In women with AUB & infertility the sensitivity of pipelle in picking up the endometrial pathology was 100% as compared to D&C and specificity was 99.02%. The negative predictive value was 100% and Positive predictive value was 80%.

Keywords: AUB, infertility, pipelle biopsy, dilatation & curettage, endometrial sample, endometrial assessment

Introduction

Abnormal Uterine bleeding (AUB) is a cause of significant healthcare burden for the women, their families and society as a whole. Women who are obese, with history of anovulatory cycles, nulliparous or with family history of cancer are at higher risk ^[1, 2]. Therefore endometrial biopsy should be considered for high risk women and all post-menopausal women. The common methods for endometrial assessment are USG, hysteroscopy, D&C, however multiple newer outpatient method are becoming popular due to their ease of application and cost effectiveness ^[3].

Currently outpatient endometrial biopsy, "Pipelle" has replaced D&C as the first line diagnostic test in the evaluation of endometrium, and has shown similar accuracy to curettage. Hysteroscopy and directed biopsy is another procedure being increasingly used for evaluation of endometrium ^[4, 5]. This is suitable for high resource setting and may not be feasible in all of our health care facilities.

Our study is a prospective single blind study to compare the diagnostic accuracy and histopathological success of pipelle verses conventional curettage in diagnosing endometrial pathology in AUB and in cases with infertility, as an outpatient procedure to reduce the cost of procedure.

Material and Methods

Present study was single-center, Prospective and comparative single blind study, conducted in department of OBGY at Apollo Hospital Jubilee Hills Hyderabad, Telengana, India. Study duration was of One year with effect from 15th April 2014-20th April 2015. Study was approved by institutional ethical committee.

Inclusion criteria

- Women aged ≥ 25 years, with complaints of abnormal uterine bleeding with or without infertility.

Exclusion criteria

- Pregnancy or pregnancy related bleeding.
- Unmarried adolescent girl.
- Endometrial thickness < 4 mm on ultrasound scans.
- Stenosed cervix, pelvic inflammatory disease

Counseling regarding both the procedures & patients were included in the study after informed consent. A detailed clinical assessment was done. Consisting of history taking (Detailed menstrual, medical and family history, presence of post coital, inter menstrual or post-menopausal bleeding, associated dysmenorrhea or premenstrual symptoms, history of intake of hormones, contraceptive pills or device, history of iron therapy or blood transfusion), general examination (Vitals, Weight / BMI, Thyroid examination, Breast examination, Abdominal examination) & detailed gynaecological examination (local Inspection of vulva, vagina, cervix, anus and urethra, bimanual examination of uterus and adnexal structures, per rectal examination if bleeding from rectum is suspected, PAP smear & Cervical cultures for sexually transmitted infection). Laboratory investigations (Complete Blood Picture, Thyroid profile, Serum creatinine, Blood sugar, Prolactin) and

Ultrasonography were done.

Initially, endometrial sample was collected by pipelle sampler in the outpatient department. These (pipelle) endometrial samples were labeled (coded) by numbers. These patients then underwent dilatation & curettage and endometrial biopsy. In the operation theatre endometrial biopsy was obtained by curettage under general anesthesia. The curettage sample was sent to Histopathology department.

The results were compared in terms of sensitivity and specificity of pipelle as compared to curettage, which was the gold standard. Additionally the positive predictive and negative predictive value was also calculated. Statistical analysis was done using descriptive statistics. The histopathology findings of pipelle biopsy were compared against the histopathology of curettage sample (gold standard) and the sensitivity and specificity was calculated. This was also done for the entire study sample as well as for the subgroups mentioned above. The positive predictive value and negative predictive value was also calculated in all these groups.

Results

106 patients were included, 40-60 years as the most common age group (45.28%) & mean age was 44.5 ± 11.98 years. 60% of the patients had 2 or more parity & 19.81% (21) were nulliparous women. Common co-morbidities noted were hypertension (20.76%), diabetes (14.15%) & hypothyroidism (16.04%).

Table 1: General characteristics

Characteristics	Frequency	Percent
Age (Years)		
25 – 40	45	42.46%
40 – 60	48	45.28%
> 60	13	12.26%
Parity		
0	21	19.81%
1	14	13.21%
2	48	45.28%
3	14	13.21%
≥ 4	9	8.49%
Co-morbidities		
Hypertension	22	20.76%
Diabetes Mellites	15	14.15%
Hypothyroidism	17	16.04%
Hypertension + Diabetes Mellites	11	10.38%
Hypertension + Hypothyroidism	4	3.77%
Diabetes Mellites + Hypothyroidism	2	1.89%

In present study population, 35 (33.02%) women had irregular menstrual cycle and 14 (13.21%) had regular cycles. 28 (26.41%) presented with heavy menstrual bleeding. Post menopausal bleeding was seen in 29 (27.36%) of women. In this study population 30.19% (32) women had dysmenorrhea, whereas 7.55% (8) had post coital bleeding.

Table 2: Menstrual history & complaints

Menstrual History	Frequency	Percent
Regular	14	13.21%
Irregular	35	33.02%
Heavy	28	26.41%

Menopausal	29	27.36%
Associated complaints	Present	Percent
Dysmenorrhea	32	30.19%
Post Coital Bleeding	8	7.55%
Only AUB	66	62.60%

Out of 106 women included in this study, 82 (77.36%) women presented with abnormal uterine bleeding alone while 11 (10.37%) women had infertility alone at their presentation. 13 (12.26%) women who had infertility also had abnormal uterine bleeding at the time of their presentation. AUB was present in 95 women (89.62%) (66 Premenopausal & 29 postmenopausal) whereas 11 women (10.38%) had no menstrual abnormality and in these women endometrium was analysed for infertility presentation.

Table 3: Analysis of indications for endometrial evaluation

Indication for endometrial analysis	Present	Percent
AUB alone	82	77.36%
Infertility alone	11	10.37%
Infertility + AUB	13	12.26%
Abnormal Uterine Bleeding	95	89.62%
Premenopausal	66	
Postmenopausal	29	

Out of 106 women 64 (60.38%) women had normal findings on ultra-sonography. Common findings were endometrial polyp (19.81%), fibroid uterus (10.38%), adenomyosis (3.77%), cystic endometrium (3.77%) and Thickened Endometrium (1.89%). Out of 106 women 65 (61.32%) women had Endometrial Thickness less than or equal 10mm and 41 (38.68%) women had more than 10mm.

Table 4: Ultrasound findings (N=106)

Ultrasound Findings	Frequency	Percent
Normal	64	60.38%
Endometrial Polyp	21	19.81%
Fibroid	11	10.38%
Adenomyosis	4	3.77%
Cystic Endometrium	4	3.77%
Thickened Endometrium	2	1.89%
Endometrial thickness		
≤ 10 mm	65	61.32%
>10 mm	41	38.68%

Out of 106-women included in the study, histopathology was reported as benign in 102 (96.23%) and malignant in 4 (3.77%) women. The curettage reported 102 (95.28%) as benign and 5 (4, 72%) as malignant. Equal numbers 52 (49.06%) and 3 (2.83%) women were reported as proliferative and disordered proliferative respectively on histopathological examination for both pipelle and curettage. 19 women (17.2%) were reported as secretory endometrium on pipelle biopsy as compared to 15 (14.15%) in curettage group. Benign endometrial polyp was only reported in 2 (1.89%) in pipelle group as compared to 14 (13.21%) in the curettage group. 2 (1.89%) and 1 (0.94%) was reported as atrophic in pipelle and curettage group respectively. Scanty endometrium was seen in 10 (9.43%) women in pipelle group while the same was seen in 9 (8.49%) women in curettage group. In the pipelle group simple hyperplasia was reported in 11(10.38%) and complex hyperplasia in 3 (2.83%) while curettage group had 5 (4.72%) and complex hyperplasia in 2 (1.89%) women.

Endometrial malignancy was reported in 4 (3.77%) women in pipelle group whereas the same was reported in 5 (4.72%) in curettage group.

Table 5: Histopathological results of Pipelle and curettage biopsy (N=106)

Factor	Pipelle Biopsy		Endometrial Curettage	
	Frequency	Percent	Frequency	Percent
Proliferative	52	49.06%	52	49.06%
Secretory	19	17.92%	15	14.15%
Simple Hyperplasia	11	10.38%	5	4.72%
Scanty	10	9.43%	9	8.49%
Adenocarcinoma	3	2.83%	5	4.72%
Disordered Proliferative	3	2.83%	3	2.83%
Complex Hyperplasia	3	2.83%	2	1.89%
Benign Endometrial Polyp	2	1.89%	14	13.21%
Atrophic	2	1.89%	1	0.94%
Stromal Sarcoma	1	0.94%	0	0.00%

When we compared the histopathology report of all the women in this study, 101 women had concurrent report of benign pathology and 4 women had concurrent report in the malignant group. The sensitivity was 100% while the specificity was 99.02%. The positive predictive value is 80% and the negative predictive value is 100%.

Table 6: Comparison of results of the two groups

Curettage	Pipelle		Total
	Benign	Malignant	
Benign	101	0	101
Malignant	1	4	5
Total	102	4	106

20 women had concurrent finding of benign endometrium in both pipelle and curettage group, while 1 case that was reported as malignant in curettage group, was reported as benign in pipelle group. 2 cases had concurrent finding of malignancy both on pipelle and curettage analysis. The sensitivity was 95.24% while the specificity was 66.67%. The positive predictive value is 95.24% and the negative predictive value is 66.67%.

Table 7: Comparison of Pipelle results with curettage results in infertility group

Curettage	Pipelle		Total
	Benign	Malignant	
Benign	20	1	21
Malignant	1	2	3
Total	21	3	24

In women with AUB & infertility the sensitivity of pipelle in picking up the endometrial pathology was 100% as compared to D&C and specificity was 99.02%. The negative predictive value was 100% and Positive predictive value was 80%. In the premenopausal women the sensitivity, specificity, NPV & PPV are all 100% for Pipelle sample as compared to curettage. In the postmenopausal women, specificity & PPV was 100%, however sensitivity was 66% and NPV was 95.2%. In women with endometrial thickness <10mm, the sensitivity, specificity, NPV & PPV are all 100% for Pipelle sample as compared to curettage. In women were endometrial thickness was ≥ 10 mm, specificity & PPV was 100%, however sensitivity was 60% and NPV was 97.44%. This could be the fact that Pipelle is less

sensitive in picking up endometrial polyp and women with endometrial thickness >10mm often have a polyp as underlying pathology. For cases presenting with infertility, Pipelle was 95% sensitive with a PPV of 95%. The NPV and specificity in these cases was 66.67%.

Table 8: Overall sensitivity of pipelle

Status	Sensitivity	Specificity	PPV	NPV
Overall	100%	99.02%	80%	100%
Premenopausal group	100%	100%	100%	100%
Post-menopausal group	66%	100%	100%	95.24%
Endometrial thickness <10mm	100%	100%	100%	100%
≥10mm	60%	100%	100%	97.44%
Infertility	95.24%	66.67%	95.24%	66.67%

Discussion

Although D&C is the gold standard method of sampling the endometrium; Pipelle biopsy is becoming a convenient and acceptable outpatient method. This shift in popularity is mainly because pipelle is minimally invasive outpatient procedure and it is less expensive and less time-consuming procedure as compared with D&C.

In cases of AUB, the goal of endometrial evaluation is twofold. First, is to exclude any premalignant hyperplasia or malignancy. Second, is to distinguish between AUB due to anatomic pathology like (polyps, myomas, adenomyosis, hyperplasias, and even carcinoma) from AUB without anatomic pathology (bleeding secondary to dysfunctional oligo-anovulatory cycles in premenopausal women and atrophic changes in postmenopausal women). Once these two-major categories are differentiated, therapy can be instituted correctly [6, 7].

In present study, 40-60 years was the most common age group (45.28%), which was comparable with the result published by Rauf *et al.*, [8] where the mean age of the patients in this was also 46.3 ± 4.45 years ACOG9 recommends that endometrial assessment should be done to exclude cancer in any woman older than 35 years especially who is suspected of having anovulatory uterine bleeding.”

The first concern about the endometrial sampling techniques is to obtain sufficient material. A meta-analysis by Dijkhuizen FP *et al.*, [10] revealed a failure rate of 10.4% for pipelle while Clark *et al.*, [11] reported a mean failure rate of 8% for pipelle in a review. Scientific data show that the sampling rate of pipelle biopsy is acceptable. Obtaining sufficient tissue for a histologic diagnosis is a problem for D&C as well. In a study published by Barut *et al.*, [12] insufficient tissue rate of D&C was found as 6.5% and 49% in premenopausal and postmenopausal women, respectively. In our study, out of 106, the pipelle and curettage reported as scanty in 10 (9.43%) women and 9 (8.49%) women respectively. On doing a sub group analysis of women presenting with infertility (24), both pipelle and curettage group had one report of scanty tissue.

Looking at the overall result of 106 women in our series and comparing their histopathology report, 101 women had concurrent report of benign pathology and 4 women had concurrent report in the malignant group. The sensitivity was 100% while the specificity was 99.02%. The positive predictive value is 80% and the negative predictive value is 100% in our study. In our study population, 52 (49.06%) and 3 (2.83%) women were reported as proliferative and disordered proliferative respectively on histopathology examination for both pipelle and curettage. That means that the proliferative and disordered proliferative report was concurrent in both the pipelle and curettage specimens. Which indicates that there was 100% concordance reporting for these conditions. All other reports had similar numbers but not complete concordance. In his series, Faut *et al.*, [13] reported that the general concordance

between pipelle and D&C was 84%. However, there was concordance rate of 95% in patients with hyperplasia and atypia.

Mechado,^[14] reviewed 1535 reports of endometrial biopsies taken in outpatient using the Cornier Pipelle, in pre and postmenopausal patients with abnormal vaginal bleeding, to establish the accuracy of endometrial biopsy with the Pipelle in the diagnosis of endometrial cancer and atypical endometrial hyperplasia. The Pipelle was 84.2% sensitive, 99.1% specific, 96.9% accurate, with 94.1% PPV and 93.7% NPV for detection of endometrial carcinoma and atypical hyperplasia. Our series demonstrates a 100% negative predictive value. A high NPV in both the above studies points to the fact that endometrial biopsy taken with the Pipelle is an accurate method for diagnosis of endometrial cancer and its precursor atypical hyperplasia.

The meta-analysis by Dijkhuijen *et al.*,^[10] concluded that the endometrial biopsy with the Pipelle was superior to other endometrial techniques in detecting endometrial carcinoma and atypical hyperplasia in pre- and postmenopausal women. In their study, the Pipelle had 88.9% sensitivity, 99.2% NPV. It had 60% sensitivity, 89.6% NPV and it was 98.6% accurate for diagnosing endometrial polyps. In their study, in spite of the low sensitivity of the Pipelle device for diagnosing endometritis and endometrial polyps (88.9% and 60%; respectively), it had a high negative predictive value (99.2% and 89.6%; respectively) and high accuracy (99.3% & 98.6%; respectively).

In the study by Yang GC *et al.*,^[15] the size and type of tumor and its location within the uterine cavity influenced the detection of cancer by Pipelle. This device could miss adenocarcinoma or a leiomyosarcoma in a polyp. Pipelle can miss focal cancers. Therefore a negative biopsy by Pipelle in a symptomatic patient must be followed by a fractional curettage or hysteroscopic guided biopsy under anesthesia.

Leng X,^[16] studied a total of 200 patients for outcomes of Pipelle biopsy. The specimen satisfaction rate of Pipelle was 93.0%; its pathological accuracy was 85.0% (in these 200 cases. There was no significant difference between two kinds of endometrial sampling ($P > 0.05$). Thus concluding that Pipelle could obtain satisfactory samples used for histological diagnosis in normal endometrium, simple hyperplasia, complex hyperplasia, atypical hyperplasia and endometrial cancer disease. Since its pathological accuracy is so close to the diagnostic curettage; this method may be used as a routine screening tool of endometrial diseases

The combined use of office endometrial sampling and transvaginal ultrasonography has been advocated in the evaluation of abnormal uterine bleeding by De Kroon CD *et al.*,^[17]. All women in our series had USG evaluation of the pelvis before the endometrial biopsy. The USG evaluation aimed at diagnosing the anatomical problems along with measurement of the endometrial lining thickness. Out of 106 women, 64 (60.38%) women had normal findings on ultrasonography. These were the cases, which would otherwise be classified as Dysfunctional Uterine Bleeding. Since this terminology is not described in the FIGO PALM-COEIN classification, we evaluated their endometrium to look for any endometrial pathology. When the bleeding cycle is regular; the most likely source is a big endometrial cavity with a simply increased endometrial surface area. However it is mandatory to rule out disordered, hyperplastic or malignant conditions of endometrium.

Also, we must understand that transvaginal ultrasonography is not without limitations. It has interobserver variations, as it is a technical procedure. A reliable endometrial echo may not always be feasible. Previous surgery, presence of leiomyoma, obesity, and adenomyosis can alter the ability to find a reliable endometrial echo.

Advantages of Pipelle over conventional curettage were Outpatient procedure, does not require prior cervical dilation or anesthesia or hospitalization, no cross contamination, minimal post procedure discomfort or bleeding, less cost & has less incidence of uterine perforation 0.1-0.2% as compared to 0.3-2.6% in Dilation and Curettage.

The limitation of our study is that it is not a Randomised Clinical Trial and our study was small as it included only 106 cases. We recommend that in future studies a greater number of infertility cases should be included as this is an important reason for outpatient endometrial assessment. However the strength of our study is that it was single blinded study where the pathologist was not aware that the pipelle and curettage sample was of the same patient. All samples were collected by the same investigator and all Pipelle samples were analyzed by the same pathologist.

Conclusion

In women with AUB & infertility the sensitivity of pipelle in picking up the endometrial pathology was 100% as compared to D&C and specificity was 99.02%. The negative predictive value was 100% and Positive predictive value was 80%. Pipelle is a simple technique to obtain the endometrial sample for evaluation in cases of abnormal uterine bleeding and infertility in outpatient department without the need of operation theatre & anaesthesia. Hence a good method for endometrial assessment in low resource setting.

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