

**DIAGNOSTIC ACCURACY OF PIPELLE ENDOMETRIAL BIOPSY AS COMPARED TO HYSTERECTOMY IN ABNORMAL UTERINE BLEEDING – A TERTIARY HOSPITAL EXPERIENCE**

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**ABSTRACT**

**Background:** Endometrial sampling for histopathology is important in the assessment of abnormal uterine bleeding. To date, hysteroscopic biopsy & D&C is considered as the standard for endometrial sampling without its place in gynecology being challenged. Several office endometrial samplers like pipelle are available which are cost effective, which have better patient compliance and which gives comparable histological findings from tissue obtained by D&C or hysterectomy. This study seeks to place D&C in its historical perspective and to chart the development of pipelle for sampling the endometrial lining of the uterus. **Objectives:** 1)To compare the diagnostic ability of pipelle-endometrial biopsy comparing with hysterectomy and/or hysteroscopy specimens in abnormal uterine bleeding. 2)To assess sensitivity and specificity of pipelle in identifying focal as well as global lesions of endometrial pathology. **Results:** Histopathology report was available in all the 125 cases sampled by pipelle device. These reports were compared with gold standard hysterectomy specimen. Five samples were inadequate for opinion. There was 22.4% of hyperplasia, 8.8% of malignancy of the endometrium and 64.8% of benign conditions of the endometrium other than hyperplasia in our study group, which were all sampled by pipelle device. In the present study specificity rate of pipelle endometrial biopsy for the detection of endometrial hyperplasia and endometrial carcinoma was 100%. Sensitivity rate of pipelle endometrial biopsy for endometrial hyperplasia was 96.4% and endometrial carcinoma was 91.6%. 99.07% was the accuracy rate for endometrial hyperplasia followed by 99.16% for endometrial carcinoma. Negative predictive value was 100% for both endometrial hyperplasia as well as carcinoma. Positive predictive value was 96.4% and 91.6% for endometrial hyperplasia and carcinoma respectively

**KEY WORDS:** Abnormal uterine bleeding, Pipelle endometrial biopsy, Histopathological examination.

**INTRODUCTION**

Endometrial sampling for histopathology is important in the assessment of abnormal uterine bleeding, which is a major problem accounting for 33% of outpatient gynecological referrals.<sup>[1,2]</sup> This proportion rises to 70% in the perimenopausal and postmenopausal years.<sup>[3]</sup> Setzler & colleagues found that 18% of perimenopausal women had menorrhagia or metrorrhagia & one fifth of

these were due to premalignant or malignant disease. Endometrial hyperplasia occurs in 5-10% of patients with postmenopausal bleeding.

This study is being conducted to establish the validity of pipelle & adequacy of endometrium sampled by pipelle for histopathology. This study was carried out to determine the accuracy of pipelle sampling in the diagnosis of abnormal uterine bleeding by comparing it

with histopathology of the hysterectomy specimens taken as gold standard. This study seeks to place D&C in its historical perspective and to chart the development of pipelle for sampling the endometrial lining of the uterus.

### AIM OF THE STUDY

Aim of the present study is to evaluate the effectiveness and accuracy of pipelle comparing with hysterectomy specimens in diagnosing global as well as focal lesions of the endometrium.

### MATERIALS AND METHODS

The study material will be obtained from outpatient, patients admitted to the department of Obstetrics and

Gynaecology at AJIMS&RC, aged 35years or above who presented with abnormal uterine bleeding. Informed consent was taken from the patients to undergo pipelle endometrial biopsy as an office procedure followed by diagnostic hysteroscopy with endometrial biopsy. Patients with indication for hysterectomy following pipelle biopsy diagnosis will also be included in the study.

The duration of the study was from July 2013 to June 2015. Since there are not many such studies from India, the accurate sample size cannot be assessed. 125 cases of both pipelle and hysterectomy and/ or hysteroscopic biopsy were included in the study. We followed universal sampling method.



**Figure 1: Pipelle device.**

The samples were transported to the laboratory in 10% formalin. Samples were then subjected to gross examination, morphology recorded and processed in the automatic tissue processor for the preparation of paraffin blocks. Sections for microscopy were cut at 4-6 $\mu$  thickness and stained with hematoxylin and eosin.

### Plan for Data Analysis

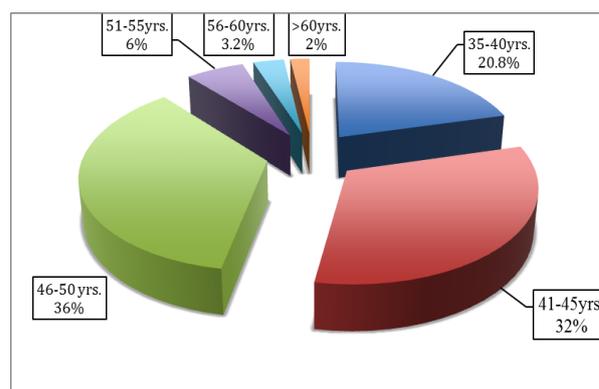
The obtained parameters were evaluated using descriptive statistical analysis. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the pipelle were calculated using 2x2 tables.

### OBSERVATIONS AND RESULTS

Total number of patients enrolled in this study was 125 patients with abnormal uterine bleeding who was scheduled for pipelle endometrial biopsy in OBG department, A.J. Institute of Medical Sciences, Mangalore, after providing informed consent to participation & after obtaining fitness for the procedure. The study was carried out between the years July 2013 – June 2015.

A detailed clinical assessment of patient was performed in the outpatient department including history, physical examination and base line investigations. Diagnostic intervention endometrial sampling by pipelle device with diagnostic reference gold standard hysterectomy. The sample was then transferred in to the 10% formalin contained bottle and sent to histopathologist for histopathology assessment. There were no association

between ease of pipelle sampling or sample adequacy with age or menopausal status.



**Figure 2: Pie chart showing age distribution of the patients presenting with abnormal uterine bleeding.**

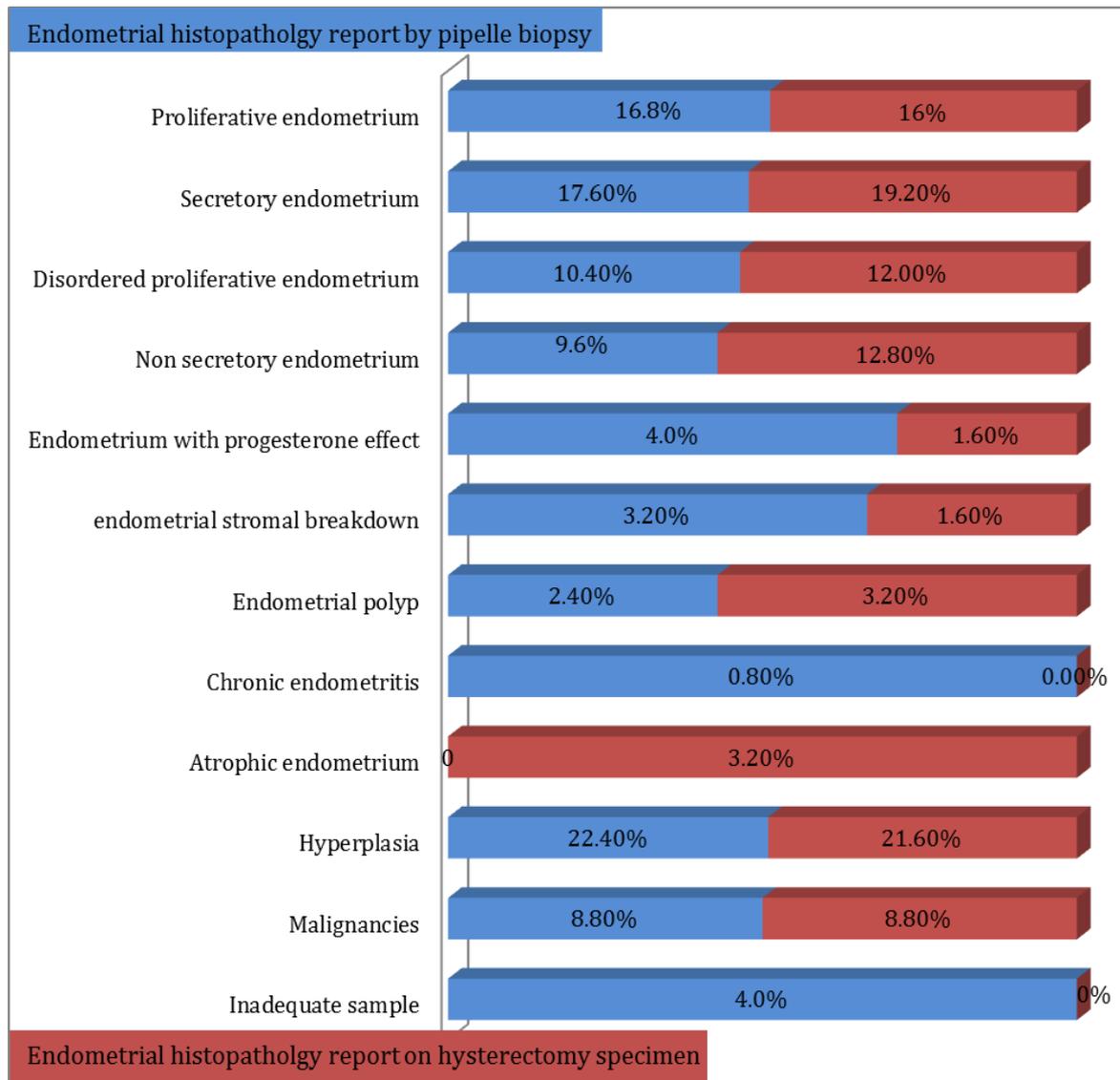
Mean age was 45.072 years with standard deviation of +/- 15 (mean +/- SD).

Out of the 125 cases, the maximum number of cases were in the age range of 46 to 50 years, which constitute about 36%, followed by 32% of cases between 41 to 45 years of age.

**Figure 3: Table showing age distribution of the patients presenting with abnormal uterine bleeding.**

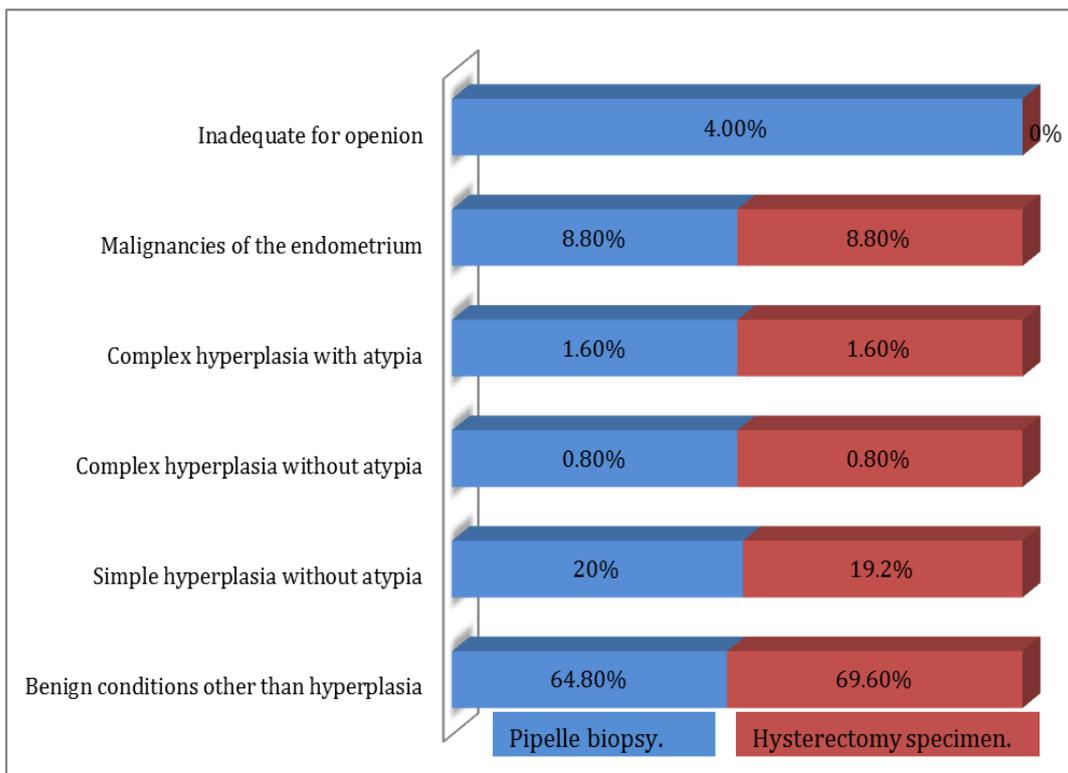
Age of the patients with abnormal uterine bleeding		
Age (years)	N=125	Percentage
35-40	26	20.8%
41-45	40	32%
46-50	45	36%
51-55	7	6%
56-60	4	3.2%
>60	3	2%
<b>Total</b>	<b>125</b>	

20.8% of the study subjects were in the age group of 35-40 years and 6% of subjects were between 51-55 years. Least number of patients was more than 60 years showing 2% followed by 3.2% of subjects between 56-60 years. Mean $\pm$ SD of the age group was 45.72 $\pm$ 8years. (As shown in figure-3).

**Figure 4: Comparison of histopathology reports for pipelle biopsy with corresponding hysterectomy.**

In the present study 22.4% of endometrial hyperplasia, 17.6% of secretory endometrium, 16.8% of proliferative endometrium, 10.4% of disordered proliferative endometrium, 9.6% of non secretory endometrium, 8.8% of malignancy, 4% of case was endometrium with

progesterone effect and 4% was inadequate for opinion by pipelle endometrial biopsy. Histopathology reports of the hysterectomy specimen were concordant with the pipelle biopsy reports. (As shown in figure- 4).



**Figure 5: Comparison of histopathology reports of the pipelle endometrial biopsy with corresponding hysterectomy.**

In the present study pipelle endometrial biopsy revealed 64.8% of benign conditions of the endometrium other than hyperplasia and corresponding hysterectomy of the same patients showed 69.6% of benign conditions of the endometrium, but in this 4% were inadequate for opinion by pipelle endometrial biopsy because of the atrophic endometrium and endometrial polyp. In case of

hyperplasia of the endometrium, maximum number of cases were simple hyperplasia of the endometrium (20%), this was concordant with hysterectomy (19.2%). In 2 cases pipelle biopsy report was complex hyperplasia with atypia, this was concordant with hysterectomy of the same patients, which also showed complex hyperplasia with atypia.

**Figure 6: Histopathology reports on hysterectomy specimen which are reported as inadequate by pipelle biopsy.**

Age (years)	No. of cases.	Percentage	Histopathology report by pipelle biopsy.	Histopathology report on hysterectomy specimen
46-50	1	(0.8%)	Inadequate	Non secretory endometrium
51-55	1	(0.8%)	Inadequate	Endometrial polyp.
56-60	2	(2.4%)	Inadequate	Non secretory endometrium
>60	1	(0.8%)	Inadequate	Atrophic endometrium.

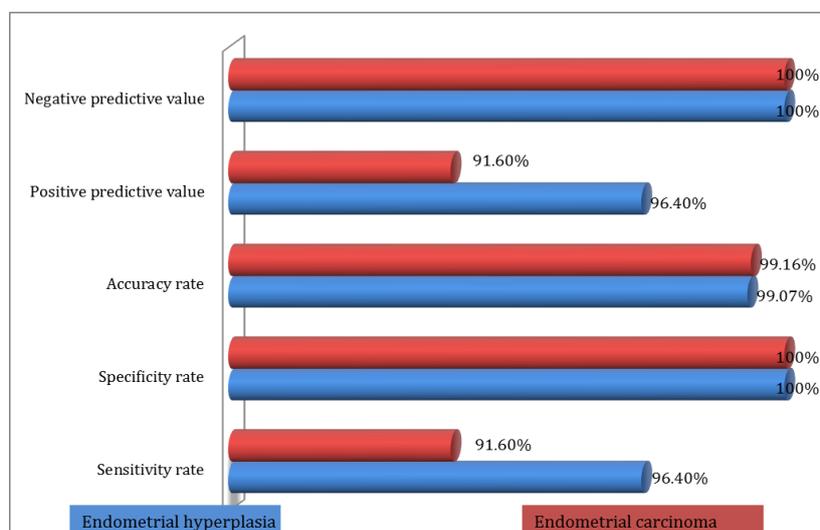
In the present study 96% of the cases the sample was adequate. Inadequate sampling has been reported in 4% of cases. In all these inadequate cases after comparing with hysterectomy specimens, we found that there was no malignancy.

**Figure 7: age distribution of the patients with malignancies of the endometrium and cervix.**

Age (years)	No of cases-11	Pipelle biopsy	Hysterectomy specimen	Percentage
40-45	3	Secretory endometrium with CIN-3 & HPV associated koilocytic atypia.	Non-keratinizing squamous cell carcinoma of the cervix-associated with CIN-3 and HPV induced koilocytic atypia.	2.4%
		Non keratinizing squamous cell carcinoma	Non keratinizing squamous cell carcinoma of the cervix infiltrating in to the endometrium	
		Endometrioid adenocarcinoma	Endometrioid adenocarcinoma	
46-50	2	Endometrioid adenocarcinoma	Endometrioid adenocarcinoma	1.6%
		Keratinizing squamous cell carcinoma	Keratinizing squamous cell carcinoma of the cervix infiltrating in to the endometrium	
51-60	1	Secretory endometrium with stromal nodule suspicious for malignency	Low grade endometrial stromal sarcoma	0.8%
61-65	3	Keratinizing squamous cell carcinoma	Keratinizing squamous cell carcinoma of the cervix infiltrating in to the endometrium	2.4%
		Endometrioid adenocarcinoma	Endometrioid adenocarcinoma	
		Keratinizing squamous cell carcinoma	Keratinizing squamous cell carcinoma of the cervix infiltrating in to the endometrium	
66-70	2	Endometrioid adenocarcinoma	Endometrioid adenocarcinoma	1.6%
		Pleomorphic sarcoma	Undifferentiated endometrial stromal sarcoma	
<b>Total</b>	<b>11</b>			<b>8.8%</b>

In the present study we are able to detect 11 cases of malignancies of the endometrium by pipelle endometrial biopsy, which constitute 8.8% out of 125 cases. All these malignancies were confirmed by hysterectomy (as

mentioned in table-2). Majority of the malignancies were detected in the perimenopausal age group that is 4<sup>th</sup> and 5<sup>th</sup> decades of life showing 4.8% of cases. (As shown in figure-7).

**Figure 8: Multiple bar chart showing validity of pipelle endometrial biopsy for endometrial hyperplasia and endometrial carcinoma.**

In the present study specificity rate of pipelle endometrial biopsy for the detection of endometrial hyperplasia and endometrial carcinoma was 100% (As mentioned in figure -8).

**Figure 9: studies have reported the success of pipelle in obtaining an adequate sample ranging from 67% to 98%.**

Study	Year	No. of Patients	Sample Adequacy(%)
<b>Present Study</b>	<b>2015</b>	<b>125</b>	<b>96</b>
Shazia Fakhar et al. <sup>[4]</sup>	2008	100	98
Fouziya Yasmin et al. <sup>[11]</sup>	2007	100	100
Abera Choudary et al. <sup>[3]</sup>	2005	350	98
Machado et al. <sup>[5]</sup>	2003	1535	83.91
Epstein et al. <sup>[6]</sup>	2001	133	84
Bakour et al. <sup>[7]</sup>	2000	248	70.20
Gordon et al. <sup>[8]</sup>	1999	100	67
Antoni et al. <sup>[9]</sup>	1997	191	75
Ben Baruch et al. <sup>[10]</sup>	1994	172	90.6
Stovall et al. <sup>[11]</sup>	1991	149	87.2

**Figure 10: Comparison of the sensitivity and specificity of the pipelle endometrial biopsy.**

Validity of PES	Present study. N=125 2015		Fouzia et al. N=100, 2007		Fakhar S et al. N=100 2008		Machao F et al. N=1535 1997-2000
	Endometrial hyperplasia	Endometrial malignancy	Endometrial hyperplasia	Endometrial malignancy	Endometrial hyperplasia	Endometrial malignancy	Endometrial malignancy
<b>Sensitivity</b>	<b>96.4%</b>	<b>91.6%</b>	100%	75%	100%	100%	84.2%
<b>Specificity</b>	<b>100%</b>	<b>100%</b>	94%	100%	100%	100%	99.1%
<b>Accuracy rate</b>	<b>99.07%</b>	<b>99.16%</b>	95%	98%	100%	100%	96.9%
<b>Positive predictive value</b>	<b>96.4%</b>	<b>91.6%</b>	84%	100%	100%	100%	94.1%
<b>Negative predictive value</b>	<b>100%</b>	<b>100%</b>	100%	98%	100%	100%	93.7%

## DISCUSSION

This observational clinical correlation diagnostic study was designed to compare the efficiency of pipelle endometrial sampling in obtaining an adequate endometrial sample for histopathological diagnosis with gold standard hysterectomy.

In our study, we found that the pipelle is a user friendly and patient friendly device. In 96% of the cases the sample was adequate. Inadequate sampling has been reported in 4% of cases. In all these inadequate cases after comparing with hysterectomy specimens, we found that there was no malignancy.

In the present study cut off limit for endometrial thickness is taken as 4-5mm. Few case data were available for correlation. The endometrial thickness was compared with the pipelle biopsy report, where ever available. Twenty cases showed endometrial thickness

with in 5mm and the corresponding pipelle biopsy were also correlating revealed non neoplastic lesions. Three cases showed endometrial thickness between 6-10mm, pipelle biopsy revealed benign lesion after confirming with hysterectomy. One case, endometrial thickness was 8mm and the pipelle biopsy revealed disordered proliferative endometrium. The number of cases available for this correlation is too less, hence statistics cannot be applied.

In the present study histopathology report was available in all the 125 cases sampled by pipelle device. The most common endometrial pathology identified was hyperplasia of the endometrium 22.4%, in which simple hyperplasia without atypia was 20%, followed by complex hyperplasia without atypia 1.6% and complex hyperplasia with atypia 0.8%. Malignancies of the endometrium was 8.8%, most common was endometrioid adenocarcinoma 4%, followed by squamous cell carcinoma of the cervix infiltrating in to

the endometrium 3.2% and 2 rare malignancy of the endometrium which includes undifferentiated endometrial stromal sarcoma by hysterectomy and corresponding pipelle was pleomorphic sarcoma (0.8%). Second rare malignancy reported by pipelle biopsy was endometrial stromal nodule suspicious for malignancy and corresponding hysterectomy showed low- grade endometrial stromal sarcoma.

In the present study, the results of pipelle endometrial sample (PES) were compared with those of hysterectomy specimen in 125 patients and in 115 patients the result were similar in both PES and hysterectomy showed the concordance of 94.4%. The use of pipelle in perimenopausal age group and postmenopausal bleeding detected endometrial carcinoma in all cases. These results are comparable to the study of Fouziya et al and Shazia et al.

The present study supports the finding that pipelle endometrial biopsy was more accurate in detecting global as compared to focal lesion such as endometrial polyp which could be diagnosed only 3 out of 4 cases, which can be considered as a limitation of pipelle sampling. Pipelle procedure was done without anesthesia as an out patient procedure. No adverse effects were found in pipelle endometrial sampling, except for mild pain, especially on the application of vulsellum, patients tolerated pipelle procedure well.

Endometrial sampling using pipelle device is an easy and safe method of getting tissue diagnosis, which can be done as an outpatient procedure. Pipelle is cost effective and has better patient compliance in addition to the added advantage of no anesthesia or other procedure complications like perforation compared to D&C.

Thus it can be considered as the first line investigation for getting an adequate endometrial sample for histology in patients with AUB with high sensitivity and specificity even for the detection of hyperplasia and malignancy.

## CONCLUSION

The pipelle sampling can be considered as a first line investigation for getting an adequate endometrial sample for histology in patients with AUB. Pipelle has high sensitivity and specificity for the detection of hyperplasia and malignancy. Pipelle is cost effective and has better patient compliance and hence can be done as an outpatient procedure. Thus Pipelle has an added advantage of no anesthesia or other procedure complications compared to D&C.

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