

Assessment of the Predictability of Pipelle Biopsy in Detecting Endometrial Pathology

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Abstract

Objective: To assess the predictability of pipelle biopsy in detecting endometrial pathology in patients with heavy menstrual bleeding and its verification by uterine histopathology at hysterectomy.

Methods: A validation study inclusive of 50 patients, aged 35-55 years, sampled through convenience sampling technique, diagnosed with abnormal uterine bleeding and belonging to the peri-menopausal age group was carried out in obstetrics and gynaecology department Karachi, from January 2015 to June 2015. The patients included in the research investigation, were scheduled for hysterectomy, and got their endometrial sampling done through pipelle technique. The data collected were then sent for histopathology analysis. The final findings of histopathology were then verified by means of histopathology report. Patients having previous experience of D&C within the last four weeks or with uterus size greater than sixteen weeks were excluded. Inferential analysis was performed using Wilcoxon signed sum rank test. Kappa analysis was also done to measure the degree of agreement between pipelle and histopathological outcomes.

Result: The results of the study showed the mean age of sample as 45.94 ± 7.92 years. Medical history for the sample has been shown and revealed that 14% of the sample had menopause. KAPPA analysis was conducted to compare the degrees of acknowledgement for histopathology and pipelle outcomes. The analysis showed that there was a 76.6% positive agreement observed in between the two techniques, with p-value results significant (<0.01). The study reported 14% cases of proliferative endometrium, while 4% cases of endometrial hyperplasia and 4% cases of endometritis and endometrial polyps have been diagnosed in the given sample.

Conclusion: The results of the study has shown that pipelle biopsy is a significant methodology used to assess the endometrial pathology among the patients with heavy menstrual bleeding, as verified by histopathology reports after assessment through hysterectomy.

Keywords: Biopsy, endometrial hyperplasia, endometritis, hysterectomy.

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Introduction

It is critical to screen those women at risk of endometrial carcinoma or its precursor (hyperplasia)¹. Corrective diagnosis influences employment

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of appropriate treatment strategies. Although endometrial cytology should not be recommended to screen endometrial diseases, it may be used as an alternative diagnostic tool when hysteroscopic biopsies for endometrial sampling are not needed². Previously, gynaecologist had been engaged at reducing the uncertainties and cost associated to dilation and curettage (D&C) via its consumption as an effective outpatient procedure. For instance, the endometrial sample was firstly obtained by Moriche in 1882 through a catheter, followed by endometrial biopsies which are under outpatient practice, since

1935³. During the process of endometrial biopsies, a metal cannula is inserted that has a syringe attached to it that assist in the process of suction. Nevertheless, this process induces immense cramps among patients during removal of endometrial tissue. Later on, methodologies like vabra aspiration and pipelle De-Cornier came into inception⁴. However, among all the aforementioned endometrial sampling methodologies, pipelle De-Cornier has gained admiration, mainly due to its implication. It has a 3.1 mm diameter tube, semi-rigid in nature and inclusive of a side opening and can be inserted successfully without dilatation of cervical canal. It is an alternative to traditional D&C which is considered safer and quicker⁵. It also has a high sensitivity and specificity for diagnosing endometrial pathologies and endometrial carcinoma⁶. Currently, endometrial biopsy namely pipelle biopsy has substituted D&C, for critical examination of anomalous uterine bleeding. Both the techniques can be used in the assessment of bleeding, however, pipelle biopsy is safe and cost effective⁷, and is also reported to have higher efficacy⁸. Empirically it has been revealed that women around the age of 40 years are expected to have endometrial examination as a precautionary measure. This is because 9% of women with endometrial carcinoma are younger than 44 years of age, while 20% are between 45-54 years of age⁹, to assess the predictability of pipelle biopsy in detecting endometrial pathology in patients with heavy menstrual bleeding, and its verification by uterine histopathology at hysterectomy.

Subjects and Methods

The current validation study was structured on the quantitative research methodology and was conducted for the duration of six months (January 2015 to June 2015). Using the sensitivity of pipelle biopsy to be 100% for group 1 and 75% for group 2 from an earlier study⁷, with 90% power and 100% confidence interval, the sample size calculated was 48 patients. Non-probability sampling strategy was adopted for the study. Convenience sampling technique was chosen as the researcher had time and budgetary constraints. Patients aged 35-55 years were part of the research. These patients were scheduled for hysterectomy procedure in order to assess heavy menstrual bleeding. Patients having previous experience of D&C within the last four

weeks were excluded from the research. If the patients had uterus size greater than sixteen weeks, they were excluded.

The data was collected from a sample of 50 patients acquiring outpatient services in the gynaecology and obstetrics unit 1, these women belong to the menopausal age bracket i.e. 35-55 years old, with their hysterectomy scheduled. Pipelle was used to obtain endometrial sample in these women. The primary data collected was then sent for histopathology analysis. The final findings of histopathology were then verified by means of histopathology report. Histo-pathologist further affirmed the results of the study.

The primary data was entered into SPSS version 23 and statistical treatment of the data was performed. Descriptive statistics were presented in the form of frequency distribution and percentages for the categorical variables namely; medical history, marital status, examination, contraceptive history, etc. For the continuous variables as duration of menstrual cycle, blood examinations and age, the data was represented in the form of mean and standard deviations. Wilcoxon signed sum rank test was used to compare the differences of menstrual history before and after six months, and contraceptive history before and after three months. Kappa analysis was done to measure the degree of agreement between pipelle and histopathological outcomes. P-values less than 0.05 were considered significant.

Results

In the present study there were fifty patients having mean age 45.94 ± 7.92 years, marriage duration 27 ± 10.98 years, parity 5.51 ± 2.95 , last delivery since 13.17 ± 7.96 years before and age of menarche 12.96 ± 1.34 .

Medical history of patients revealed that 14% sample had menopause, 38.8% had hypertension, 16% were diabetic, 4% were asthmatic, 4% were having ischemic heart disease, 6% had endocrine disorder, 56% reported for the drugs consumption, 34% were obese, 24% had surgery in the past, 38% had family history for diabetes/hypertension/IHD and 94% had presenting illness.

Table 1 reports the comparison of menstrual history before and after six months. Results showed that the mean duration of cycle was 4.72 ± 1.65 before 6/12 and it was 10.01 ± 4.27 after 6/12. There were significant changes observed for duration of cycle, rhythm, flow, IMB, dysmenorrhea, and dyspareunia with p-value less than 0.05 for before and after 6/12 menstrual history.

Table 1. Comparison of Menstrual History before and after 6/12

Characteristics		Before 6/12		After 6/12		p-value
		n	%	n	%	
Duration of Cycle	Mean, SD	4.72	1.65	10.01	4.27	<0.01*
Rhythm	Regular	49	98.0	11	22.0	<0.01*
	Irregular	1	2.0	39	78.0	
Flow	Heavy	3	6.0	49	98.0	<0.01*
	Normal	45	90.0	0	0.0	
	Scanty	2	4.0	1	2.0	
IMB	Yes	0	0.0	8	16.0	<0.01*
	No	50	100.0	42	84.0	
Dysmenorrhea	Yes	3	6.0	35	70.0	<0.01*
	No	47	94.0	15	30.0	
P.C.B	Yes	0	0.0	3	6.0	0.083
	No	50	100.0	47	94.0	
Dyspareunia	Yes	2	4.0	11	22.0	<0.01*
	No	48	96.0	39	78.0	

*p<0.05 was considered significant using Wilcoxon Sum Ranked test

The examination of studied patients further showed that 90% of women had anaemia, 2% had jaundice, 6% had oedema, 6% had clubbing, 4% had koilonychia, and 34% of them had thyroid (Fig 1).

Research has further reported that the average SBP was 118.98 ± 14.76 , mean DBP was 77.09 ± 9.67 , average pulse was 85.96 ± 6.64 , average temperature was 98 F, the mean R.R was 18.18 ± 1.02 , mean haemoglobin was 9.1 ± 2.4 , mean WBCS were 9947.4 ± 7552.38 , the platelets were 240.88 ± 80.9 and RBS were 120.8 ± 49.82 .

Table 2 reports that the results of KAPPA analysis. To compare the degree of agreement of pipelle and histopathological outcomes, results showed that there was 76.6% positive agreement observed between these two techniques with significant p-value less than 0.01. There were 14% cases

of proliferative endometrium diagnosed commonly from pipelle and histopathological reports, 38% cases of secretory endometrium diagnosed commonly from both technique, 4% cases of endometrial hyperplasia without atypia, 4% cases of endometritis and 4% cases of endometrial polyp were commonly diagnosed from both techniques.

Table 2. Comparison of Pipelle and Histopathology Report Findings (n=50)

Findings	Pipelle (Histopathology)		Histopathology report		Common Findings of Pipelle & Histopathology	
	N	%	n	%	N	%
Proliferative Endometrium	91	8.0	91	8.0	7	14
Secretory Endometrium	22	44.0	20	40.0	19	38
Endometrial Hyperplasia without atypia	2	4.0	3	6.0	2	4
Endometrial Hyperplasia with atypia	2	4.0	0	0.0	-	-
Endometritis	3	6.0	2	4.0	2	4
Endometrial Polyp	3	6.0	5	10.0	2	4
Adenocarcinoma	4	8.0	4	8.0	4	8
Endometrial Adenocarcinoma	2	4.0	2	4.0	2	4
Papillary Serous Carcinoma	1	2.0	1	2.0	1	2
Proliferative Endometrium & Endometrial Polyp	0	0.0	1	2.0	-	-
Secretory Endometrium & Endometritis	2	4.0	2	4.0	2	4
Secretory Endometrium & Endometrial Polyp	0	0.0	1	2.0	-	-

Kappa Measure of Agreement 76.6% with p-value <0.01

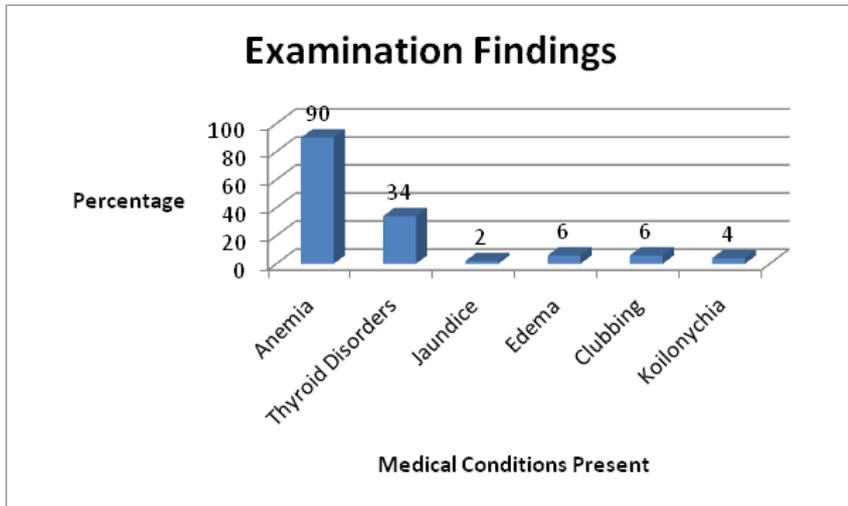


Fig 1. Examination Findings (n=50)

8% cases of adenocarcinoma, 4% cases of endometrial adenocarcinoma, 2% cases of papillary serous carcinoma and 4% cases of secretory endometrium & endometritis were also commonly diagnosed from pipelle and histopathology reports.

Discussion

Women having endometrial cancer experience vaginal discharge or bleeding in majority of cases. The women that are young; have failed in their medical management, or have polycystic ovarian syndrome or obesity may also experience symptoms of heavy menstrual bleeding¹⁰. Abnormal uterine bleeding can vary from mild to life threatening if not recognized and treated promptly¹¹. Pipelle biopsy preserves stromal architecture better and takes shorter time compared to dilatation and curettage. Hence, it is a highly useful screening procedure¹². Currently, considerable literature is available that recommends the gynaecologist while they diagnose the women experiencing endometrial cancer or hyperplasia on curettage or biopsy, however, research on pipelle implications in Pakistani healthcare setting is limited in context¹³⁻¹⁵. Therefore, the current research investigation was aimed at assessing the endometrial sample in women experiencing abnormal uterine bleeding, however, with the consumption of pipelle technique and comparing it to the conventional D&C technique.

Evidence has shown that preoperative endometrial sampling is a prevailing indicator of endometrial cancer histology and assists in understanding the disease recurrence and risk of spread of cancer¹⁶.

Pipelle biopsy has many implications in the endometrial sampling and literature has shown considerable evidence of pipelle methodology role in revealing endometrial pathology^{6,7,17}. However, the literature on Pakistani samples is limited in context. No 1 et al. in 2011 reported the adequacy of pipelle specimen to be 92% and reported a significant correlation of histopathological findings of pipelle endometrial biopsy with histopathological findings of hysterectomy. Moreover, the sensitivity of pipelle biopsy was found to be 93.4%, specificity to be 100%, positive predictive value to be 100% whereas negative predictive value was estimated to be 20%⁷. Seto et al. projected pipelle endometrial tissue sampling predictive value, while assessing the presence of endometrial polyp¹⁷. In the sample of 195 women that were scheduled hysterectomy or polypectomy and diagnosed with polyp, were reviewed in the study. The study compared the histology of the samples with consequent final hysteroscopic biopsies and reviewed by two pathologist (gynaecological). The study sample revealed 162 women as premenopausal, while 33 of them were postmenopausal. Seto et al. in 2016, affirmed that abnormal endometrial uterine bleeding is the commonest marker for endometrial sampling by pipelle. Moreover, the positive predictor value was shown as 53.7% for premenopausal women and 72.7% for the women that were postmenopausal¹⁷. The results of the aforementioned study support the results of current research investigation. The histopathology sample has shown that 9 patients were experiencing proliferation of endometrium, 2 patients with endometrial hyperplasia without atypia and 2 patients with endometrial hyperplasia with atypia.

Abnormal uterine bleeding is deemed to have a clinical condition that occurs among women during their menarche to menopausal stages (15-20%). It has been argued that the women that are experiencing uterine bleeding, menstrual irregularities and infertility are having a strong association to thyroid dysfunction¹⁷. Byna and colleagues in 2017, conducted an examination of thyroid dysfunction in

perimenopausal women, aged 35-55 years that were experiencing abnormal uterine bleeding. Their study results reported 7 patients diagnosed with hyperthyroidism and 12 patients having hypothyroidism. Out of the total 19 women of the sample having thyroid dysfunction revealed 42% of the women having abnormal menstrual bleeding and 31.57% experiencing polymenorrhagia¹⁸. In the current study, out of the sample of 50 patients, there is 34% of the sample experiencing thyroid dysfunction.

For the assessment of abnormal uterine bleeding, endometrial biopsy assists the gynaecologist in diagnosing endometrial carcinoma and at the same time inhibiting any redundant radical surgery²⁰. Abdel Azim Aboelezz and Abdul Kareem in 2013 compared conventional D&C and contemporary Pipelle endometrial sampling in abnormal uterine bleeding patients¹⁹. They showed that even the low sensitivity of Pipelle device was successful in diagnosing endometrial polyp (60%) and endometritis (88.9%). The results of their study revealed a negatively higher predictive value for endometritis (99.2%) and endometrial polyp (89.6%). The high accuracy was revealed as 99.3% for endometritis and 98.6% for endometrial polyps¹⁹. The results of Abdel Azim Aboelezz and Abdul Kareem in 2013, supports the results of current study. The pipelle technique among the sample of Abbasi Shaheed Hospital patients, assisted in diagnosing secretory endometrial polyp (n=3). However, the research sample did not find any women experiencing secretory endometrium and endometrial polyp.

Different types of methods are used for endometrial sampling; non-invasive and invasive on outpatient or inpatient basis^{20,21}. One of the commonly used invasive inpatient methodological approach is D&C that is performed under general anaesthesia. On the contrary, Pipelle biopsy technique is applied as a non-invasive outpatient method, which is deemed appropriate, revealing 98% adequate sample. The adequacy of the sample increases as the thickness of endometrial tissue increases²², though in cases of focal endometrial pathologies, it provides limited diagnostic accuracy²³.

Empirically, research scholars have argued that pipelle is acceptable and accurate specifically for outpatient sampling in comparison to D&C²⁴.

Abdel Azim Aboelezz Abdul Kareem in 2013, professed that pipelle is a better approach than D&C, as the results of the study showed 100% specificity, 100% sensitivity and likewise, 100% predictive values using the pipelle technique for diagnosing endometrial carcinoma and endometrial hyperplasia (without or with atypia)¹⁹.

Sanam M et al. in 2015 reported a high agreement and cohesion coefficient between curettage and pipelle on the issue of sampling adequacy, histopathology finding (except atrophic endometrium), low failure rate, duration of sampling and cost²⁴. In the given context, use of technology with a high sensitivity to detect abnormal uterine bleeding can enable a physician to make correct decisions²⁵.

Conclusion

Endometrial examination is crucial for women having abnormal uterine bleeding for their early diagnosis and prompt treatment. Endometrial pathology can be examined by means of both D&C and pipelle technique. The study results showed that pipelle biopsy is a reliable technique for the diagnosis and prediction of endometrial pathologies and carcinoma. In light of the study findings, it is recommended that for diagnosis of endometrial pathologies and carcinoma, Pipelle biopsy should be used as a routine screening tool for peri-menopausal women.

Conflict of Interest

Authors have no conflict of interests and no grant/funding from any organisation.

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