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ORIGINAL ARTICLE

Accuracy of Pipelle Endometrial Samplingin comparison to D&C in women with abnormal uterine bleeding: A comparative analysis of all samples vsonly adequate samples by Pipelle

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ABSTRACT

Background: The Pipelle endometrial sample biopsy (PESB) is considered the most convenient, non - invasive method for endometrial sampling. The abnormal uterine bleeding has many causes and consequences in women. The exact causes are described by histology of sample through D&C. The accuracy of PESB is under observation in different settings and a lot of work is further required.
Aim: To see the accuracy of PESBin comparison to D&C for morphological findings among women with abnormal uterine bleeding.
Study design: Cross--sectional analytical study.
Place and duration of study: Gyne OPD & Histopathology Departments, Shaikh Zayed Hospital, Lahore during 1st May 2019 to 8th December 2019.
Methodology: Two hundred and thirty five adult women with AUB recommended for D&C and with Pipelle endometrial sample were included. Those with endometrial thickness less than 4mm, having fibroids, with pelvic inflammatory disease, or clotting factor disorders were excluded. Pipelle endometrial sample was taken in GyneOPD and were examined at Histopathology Department. Data were managed through SPSS-20.
Results: 80.0% had adequate Pipelle samples and Pipelle inadequate as negative were considered for comparison the accuracy of Pipelle for proliferative endometrium and secretory endometrium were lower (90.6% vs 100.0%) and (93.6% vs 100.0%) as compared to only 188 adequate samples considered; by considering D&C as gold standard. Accuracies for Hyperplasia, and chronic endomitritis were little higher for all cases and for carcinoma the accuracy was 100.0% in either case.
Conclusion: Pipelle endometrial sampling can be considered an effective method for endometrial sampling with an accuracy of more than 90.0% for each of the endometrial morphology.
Keywords: Abnormal uterine bleeding, Pipelle endometrial biopsy, Diagnostic accuracy

INTRODUCTION

An optimal endometrial sampling (ES) technique should be minimally invasive, pain free, efficient, less labor intensive and cheap. It should offer an adequate and a high quality sample for histopathological examination without severe complications[1]. Various invasive and non - invasive techniques are performed to collect endometrial tissue sample for diagnosing endometrial abnormalities in women with AUB. These ES techniques can be categorized into three main types i.e. dilatation and curettage (D&C), aspiration methods and hysteroscopy[2].

The D&C technique is widely considered as the gold standard method to obtain endometrial tissue sample for diagnosing the endometrial pathologies. But, the requirement of hospital admission, anesthesia and relatively higher cost have made D&C endometrial sampling technique less favorable.[3] It has also been reported that the D&C method is associated with certain risks such as infection, perforation and anesthesia related complications[4]. Furthermore, less than half of the uterine cavity can be evaluated in ~ 60% of D&C procedures that may give false negative results[5].

On the other hand, the aspiration techniques or office sampling procedures with good patient acceptability are easier to perform and comparatively cheaper. For these reasons, the aspiration techniques are becoming more popular. A number of office endometrial biopsy devices such as the Pipelle, the Vabra aspirator, the Endorette, the Novak, the Tis-u- Trap, the Tao Brush, etc are being used to obtain endometrial tissue sample[6]. These devices are used in outpatient department without any anesthesia and at a comparatively lower cost[7].

The AUB is reported to be the most frequently observed symptom of endometrial pathologies[8], therefore women with AUB, especially post - menopausal women, should be screened for these endometrial pathologies[9].

The Pipelle aspirator is the most studied device in the literature. It is 23.5mm long and has a polypropylene sheath of outer diameter 3.1mm. When the inner plunger is withdrawn, negative pressure gradient is created for suction.[10]It can be used without hospital admission, general anesthesia and cervical dilatation. It is less expensive, minimally invasive and easy to perform outpatient procedure for diagnosing endometrial pathologies in patients with AUB[11]. Under strict aseptic conditions, the Pipelle is inserted into the uterine cavity and the endometrial tissue sample is collected. However, it is well known that the Pipelle sample 4.2% of the endometrial surface area.[12]So it seems that the Pipelle ES obtain inadequate tissue sample or may miss focal endometrial pathologies. Also, it may involve minor complications such as some patients may report mild abdominal pain along with some vaginal spots for a short duration after the procedure[13].

The diagnostic accuracy of the Pipelle ES, under investigation in this study, is comparable to the D&C, but has got the added advantage of being a cost-effective, minimally invasive and patient-friendly procedure. Compared to the D&C, the patients undergoing the Pipelle ES, not only avoid the side effects and complications associated with general anesthesia, have a lower risk of infection and a shorter duration of hospital stay. The findings of this study underscore the potential benefit of the Pipelle ES to the patients and the gynecologists, but also helps economize on healthcare resources.

MATERIAL AND METHODS

This cross-sectional analytical study was conducted at the Department of Histopathology in collaboration with Department of Gynecology of Shaikh Zayed Hospital Lahore Pakistan from 1st May 2019 to 8th December 2019. This study is a part of larger study[8] with a sample size of 235. The methods of sampling, Inclusion and exclusion criteria, descriptive statistics and endometrial morphologies of 188 adequate samples through Pipelle are given in that study[8]. Data were managed through SPSS version 20. The diagnostic measures like sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, PPV, NPV and accuracy along prevalence of each pathology were reported by using percentages with 95% confidence interval. The qualitative variables such as type of various pathologies were presented as n(%).

RESULTS

Majority was of age ≤ 30 years and the average age of patients was 33.1±10.8 years. While for those 188 (80.0%) with adequate Pipelle sample had an average age of 34.0±11.0 years. Only

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12/235 (5.1%) were nulliparous and 8 of them were among group with inadequate samples. The mean uterus thickness was 6.8±1.2 mm and 183/235 (77.9%) had bulky uterus. There were 144/188 (76.6%) with bulky uterus among those with adequate samples, indicating 39/235 (16.6%) Pipelle samples missed the pathology for bulky uterus.

The major problem, the cases were reported, was menorrhagia; 111/235 vs 96/188, followed by polymenorrhagia; 55/235 vs 35/188, metrorrhagia; 44/235 vs 36/188, postmenopausal bleeding; 18/235 vs 16/188 and irregular bleeding; 11/235 vs 9/188. This mentioned also that most inadequate samples were of those women with polymenorrhagia. The two cases with others, i.e. Chronic cervicitis with focal squamous metaplasia and infaracted decidual tissue with chorioicvilli were not included in analysis. The Pipelle missed 22/90 of the Proliferative endometrium, 1/8 of the Atrophic endometrium, 15/90 secretory endometrium, 8/31 of chronic endomitritis, while wrongly identified 1/68 Secretory and 3/68 of chronic Endomitritis as proliferative endometrium.Similarly one chronic Endomitritis was labeled as Atrophic endometrium, 2 wrongly identified as hyperplasia without atypia and 4 as hyperplasia without atypia (Table 1).

When these 47 cases with inadequate sample through Pipelle were considered negative and diagnostic measures were estimated for Pipelle for each pathology the sensitivity for three types of endometrium, i.e. Proliferative, Atrophic and Secretory were 75.6%, 87.5% and 83.3% respectively, while the specificities for all three types were 100.0%. The lowest sensitivity was estimated for chronic Endomitritis, which was 74.2(55.4 - 88.1)%. The sensitivity and specificity were both 100.0% for malignancy (Table 2).

When only those 188 cases were considered for analysis, which had adequate Pipelle sample, Pipelle missed only 7 chronic Endomitritis cases. The wrong labeling of hyperplasia without atypia and with atypia was done for 2 and 4 cases respectively. Here sensitivity for each of the morphology was 100.0% except chronic Endomitritis which was 76.7(57.7 – 90.1) and the specificities for hyperplasia without atypia was 98.9% and with atypia was 97.9%, while for all other morphologies were 100% (Table 3, 4).

When the accuracy of Pipelle was estimated for all 235 cases and compared to 188 cases, it was observed that the proliferative endometrium and Secretory endometrium had much lower accuracy for all samples, i.e. (90.6% vs 100%) and (93.6% vs 100%) respectively. For atrophic endometrium, hyperplasia without atypia and with atypia and chronic Endomitritis both were comparable with just a little higher percentages. For carcinoma the accuracy was 100.0% for 235 samples as well as for 188 sample. (Fig. 1).

Figure 1 : Accuracy of Pipelle biopsy for all 235 cases in comparison to 188 cases with adequate sample (n=235)

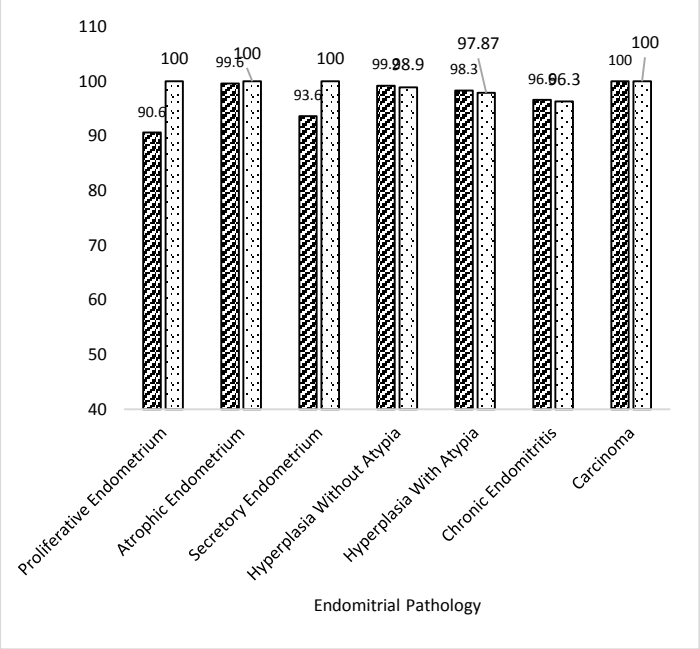

Table 1: Distribution of all 235 cases by Pipelle, taking Dilation and curettage as gold standard

		Dilation and curettage (D&C)													
		Proliferative Endometrium		Atrophic Endometrium		Secretory Endometrium		Hyperplasia Without Atypia		Hyperplasia With Atypia		Chronic Endomitritis		Carcinoma	
Pipelle		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Proliferative	Yes	**68**	**0**	0	68	1	67	0	68	0	68	3	65	0	68
Endometrium	No	**22**	**145**	8	159	89	78	3	164	2	165	28	139	6	161
Atrophic	Yes	0	7	**7**	**0**	0	7	0	7	0	7	1	6	0	7
Endometrium	No	90	138	**1**	**227**	90	138	3	225	2	226	30	198	6	222
Secretory	Yes	1	74	0	75	**75**	**0**	0	75	0	75	0	75	0	75
endometrium	No	89	71	8	152	**15**	**145**	3	157	2	158	31	129	6	154
Hyperplasia	Yes	0	5	0	5	0	5	**3**	**2**	0	5	2	3	0	5
Without Atypia	No	90	140	8	222	90	140	**0**	**230**	2	228	29	201	6	224
Endo Hyp With	Yes	0	6	0	6	0	6	0	6	**2**	**4**	4	2	0	6
Atypia	No	90	139	8	221	90	139	3	226	**0**	**229**	27	202	6	223
Chronic	Yes	3	20	1	22	0	23	0	23	0	23	**23**	**0**	0	23
Endomitritis	No	87	125	7	205	90	122	3	209	2	210	**8**	**204**	6	206
Carcinoma	Yes	0	6	0	6	0	6	0	6	0	6	0	6	**6**	**0**
	No	90	139	8	221	90	139	3	226	2	227	31	198	**0**	**229**

Note: the highlighted cells present the 2 x 2 tables of finding for all cases by two methods

Table 2: Diagnostic measures for Pipelle biopsy by taking D&C as gold standard (n=235)

	Proliferative Endometrium	Atrophic endometrium	Secretory endometrium	Hyperplasia Without atypia	Hyperplasia With atypia	Chronic Endomitritis	Carcinoma
Sensitivity	75.6 (65.4 - 84.0)	87.5 (47.4 - 99.7)	83.3 (74.0 - 90.4)	100.0 (29.2 - 100.0)	100.0 (15.8 - 100.0)	74.2 (55.4 - 88.1)	100.0 (54.1 - 100.0)
Specificity	100.0 (97.5 - 100.0)	100.0 (98.4 - 100.0)	100.0 (97.5 - 100.0)	99.1 (96.9 - 99.9)	98.3 (95.7 - 99.5)	100.0 (98.2 - 100.0)	100.0 (98.4 - 100.0)
Positive LR				116.0 (29.2 - 461.1)	58.3 (22.1 - 153.9)		
Negative LR	0.24(0.17 - 0.35)	0.12(0.02 - 0.78)	0.17(0.11 - 0.26)	0	0	0.26(0.14 - 0.47)	0
Disease prevalence	38.3(32.1 - 44.8)	3.4(1.5 - 6.6)	38.3(32.1 - 44.8)	1.3(0.3 - 3.7)	0.85(0.1 - 3.0)	13.2(9.1 - 18.2)	2.6 (0.94 - 5.5)
PPV	100.0	100.0	100.0	60.0(27.4 - 85.6)	33.3(15.9 - 56.9)	100.0	100.0
NPV	86.8(82.1 - 90.5)	99.6(97.3 - 99.9)	90.6(85.9 - 93.9)	100.0	100.0()	96.2(93.4 - 97.9)	100.0
Accuracy	90.6 (86.2 - 94.0)	99.6 (97.7 - 100.0)	93.6 (89.7 - 96.4)	99.2 (97.0 - 99.9)	98.3 (95.7 - 99.5)	96.6 (93.4 - 98.5)	100.0 (98.4 - 100.0)

()*: No estimate was possible, LR: Likelihood ratio, PPV: Positive predictive value, NPV: Negative predictive value*

Table 3 Distribution of 188 adequate sample cases by Pipelle, taking D&Cas gold standard

Pipelle		Dilation and curettage (D&C)													
		Proliferative Endometrium		Atrophic Endometrium		Secretory Endometrium		Hyperplasia Without Atypia		Hyperplasia With Atypia		Chronic Endomitritis		Carcinoma	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Proliferative Endometrium	Yes	**68**	**0**	0	68	1	67	0	68	0	68	3	65	0	68
	No	**0**	**120**	7	113	74	46	3	117	2	118	27	93	6	114
Atrophic Endometrium	Yes	0	7	**7**	**0**	0	7	0	7	0	7	1	6	0	7
	No	68	113	**0**	**181**	75	106	3	178	2	179	29	152	6	175
Secretory endometrium	Yes	1	74	0	75	**75**	**0**	0	75	0	75	0	75	0	75
	No	67	46	7	106	**0**	**113**	3	110	2	111	30	83	6	107
Hyperplasia Without Atypia	Yes	0	5	0	5	0	5	**3**	**2**	0	5	2	3	0	5
	No	68	115	7	176	75	108	**0**	**183**	2	181	28	155	6	177
Hyperplasia With Atypia	Yes	0	6	0	6	0	6	0	6	**2**	**4**	4	2	0	6
	No	68	114	7	175	75	107	3	179	**0**	**182**	26	156	6	176
Chronic Endomitritis	Yes	3	20	1	22	0	23	0	23	0	23	**23**	**0**	0	23
	No	65	100	6	159	75	90	3	162	2	163	**7**	**158**	6	159
Carcinoma	Yes	0	6	0	6	0	6	0	6	0	6	0	6	**6**	**0**
	No	68	114	7	175	75	107	3	179	2	180	30	152	**0**	**182**

Note: the highlighted cells present the 2 x 2 tables of finding for all cases by two methods

Table 4: Diagnostic measures for Pipelle biopsy by taking D&C as gold standard (n=188)

	Proliferative Endometrium	Atrophic endometrium	Secretory endometrium	Hyperplasia Without atypia	Hyperplasia With atypia	Chronic Endomitritis	Carcinoma
Sensitivity	100.0 (94.7 - 100.0)	100.0 (59.0 - 100.0)	100.0 (95.2 - 100.0)	100.0 (29.2 - 100.0)	100.0 (15.8 - 100.0)	76.7 (57.7 - 90.1)	100.0 (54.1 - 100.0)
Specificity	100.0 (97.0 - 100.0)	100.0 (98.0 - 100.0)	100.0 (96.8 - 100.0)	98.9 (96.1 - 99.9)	97.9 (94.6 - 99.4)	100.0 (97.7 - 100.0)	100.0 (98.0 - 100.0)
Positive LR				92.5 (23.3 - 367.1)	46.5 (17.6 - 122.6)		
Negative LR	0	0	0	0	0	0.23 (0.12 - 0.45)	0
Disease prevalence	36.2 (29.3 - 43.5)	3.7 (1.5 - 7.5)	39. 9 (32.8 - 47.3)	1.6 (0.3 - 4.6)	1.06 (0.1 - 3.8)	16.0 (11.0 - 22.0)	3.2 (1.2 - 6.8)
PPV	100.0	100.0	100.0	60.0 (27.4 - 85.6)	33.3 (15.9 - 56.9)	100.0	100.0
NPV	100.0	100.0	100.0	100.0	100.0	95.8 (92.2 - 97.7)	100.0
Accuracy	100.0 (98.1 - 100.0)	100.0 (98.1 - 100.0)	100.0 (98.1 - 100.0)	98.9 (96.2 - 99.9)	97.87 (94.6 - 99.4)	96.3 (92.5 - 98.5)	100.0 (98.1 - 100.0)

(): *No estimate was possible, LR: Likelihood ratio, PPV: Positive predictive value, NPV: Negative predictive value*

DISCUSSION

The descriptive of this study are already discussed in the earlier article[8] and the primary objective of this study was to study the diagnostic accuracy of the Pipelle endometrial sampling taking D&C as a gold standard. For this particular purpose the diagnostic power of Pipelle biopsy was studied under two conditions. One was, to include all cases undergone Pipelle sampling as well as D&C and considering inadequate samples as not able to find the pathology. The second condition was to consider only those 188(80.0%) cases which had adequate sample[8].

Under condition one, i.e. (n=235), in this study the Pipelle missed 22/90 (24.4%) of the Proliferative endometrium, 1/8 (12.5%) of the Atrophic endometrium, 15/90 (16.7%) ofsecretory endometrium, 8/31(25.8%) of chronic endomitritis and in total 47(20.0%) were missed. There were fewwrongly identified cases as well, which included 1/68 (1.5%)Secretory and 3/68 (4.4%) of chronic Endomitritis as proliferative endometrium. Similarly one chronic Endomitritis was labeled as Atrophic endometrium. The most numbers mislabeled by Pipelle sample were 2/5(40.0%) wrongly identified as hyperplasia without atypia and 4/6(66.7%) as hyperplasia with atypia, while not having that particular condition. This condition is not discussed in articles as most of the articles only consider the samples when Pipelle produces adequate endometrial sample[12,14,15].

Under second condition (n=188), when the Pipelle contained the endometrial sample. In this comparison the Pipelle only missed 7/30 (23.3%) of the chronic Endomitritis while all other pathologies in comparison to D&C sample, including malignancy were accurately detected by the Pipelle sample. The mislabeling of 2 and 4 out of 5 and 6 still were there for Pipelle biopsy sample. There were also many cases with multiple pathologies, being identified by either both or one of the method. This condition is comparable with the study conducted by Abdelazimetal[12] which Pipelle correctly identified all pathologies except chronic endomitritis. However this study has a much higher rate 23.3% missed sample as compared to 1/8 (12.5%) in that study. The second condition produced sensitivity of 100% for all pathologies except chronic endomitritis which had 76.7% which coordinates with other studies[14,15], The difference is for endomitritis which was 88.9% in other study[12].

The positive predictive value for hyperplasia without atypia was reported to be (42.9–100.0) by the recent study[14], which in present study is reported to be 60.0(27.4–85.6). Similarly the positive predictive value for hyperplasia with atypia was reported to be (33.3–100.0) by the same study[14] and in our study this range was estimated (15.9–56.9) with lower range. The study by Abdelazimetal[12], however reported all diagnostic measures as 100.0% for hyperplasia, not segregating with and without atypia.

This study further elaborates what differences the diagnostic measures take, when inadequate samples (which are declared inadequate by pathologists in the lab) are included for calculating the diagnostic measures (not a common practice). It is reported that the (n=235) condition produced accuracy for proliferative endometrium as 90.6%, which is much lower than the accuracy measured for (n=188) which was 100.0%. Similarly the difference was reported in accuracyof secretory endometrium, which was (93.6% vs 100%). The accuracy of atrophic endometrium was 0.4% lower in condition-2, while all other pathologies including hyperplasia, and Endomitritis had a little higher accuracy by 0.3%, 0.3% and 0.4%. The accuracy of carcinoma was same under both conditions.

These above readings suggest that, if the missed cases are included in the analysis for diagnostic measure accuracy goes down significantly, specifically for pathologies with higher

prevalence as in this study it is 38.3% for the proliferative and secretory endometrium, each.

CONCLUSION

Papillary sample is an accurate measure for pathologies taking D&C as gold standard and the adequacy of Pipelle sample plays an important role in diagnostic measures, so the sampling expertise needed to be improved significantly.

Conflict of interest: Nil

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