

# Endometrial Aspiration Cytology by Karman's Cannula with Histopathological Correlation

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**Abstract:** *Introduction:* Dilatation and curettage is the commonly used diagnostic technique to assess endometrial normalcy and pathology. Endometrial aspiration cytology on the other hand is a simple outpatient procedure without the cost of hospitalization, operation theatre & risk of anesthesia inherent in dilatation and curettage. *Objectives:* The present study was carried out to assess the sensitivity and specificity of endometrial cytology performed by using Karman's cannula compared with histopathology. *Materials & Method:* Endometrial aspiration was done using 4mm Karman's cannula in 144 cases who presented with dysfunctional uterine bleeding, postmenopausal bleed and infertility prior to dilatation and curettage. The cytological diagnosis was correlated with histopathological diagnosis. *Results:* Adequate material was obtained in 93.06% of cases on aspiration. Proliferative endometrium was the most common pattern (38.2%) observed. There was an overall 100% correlation in case of secretory endometrium, atypical hyperplasia and endometrial carcinoma and 90.9% correlation in case of proliferative endometrium between cytological and histopathological findings. The sensitivity and specificity of endometrial aspiration was 88.31% and 100% respectively. *Conclusion:* Endometrial aspiration was found to be simple, safe, cost effective, well tolerated outpatient procedure which can be offered to patients as an outpatient sampling technique.

**Keywords:** Endometrial Aspiration Cytology, Karman's Cannula, Endometrial Carcinoma

## 1. Introduction

Endometrial aspiration cytology is an effective method for ensuring endometrial normalcy, cytohormonal evaluation of the endocrine status and for diagnosing malignant and premalignant states. However direct cytological sampling and examination of the endometrium is not generally practiced, which is surprising as the endometrium is exceedingly easy to sample.<sup>[1]</sup>

Aspiration cytology is a safe, simple and reliable technique without any complication and can be used as a safe and reliable out-patient procedure with minimum discomfort to the patient.<sup>[2]</sup> Hysteroscopy directed endometrial biopsy of suspicious lesions is the gold standard investigation but is invasive, needs specialized equipment and is operator dependent.<sup>[3]</sup> It also involves the cost of hospitalization and operation theaters, bed shortages and risk of anesthesia and operative complications which can be avoided by aspiration cytology.<sup>[4]</sup>

The development of a technique for sampling the endometrium was encouraged by Papanicolaou himself, who acknowledged the inadequacy of the cervical smear for detecting endometrial pathologies. Thus, many attempts were made by authors to find out a simple and accurate method to obtain the endometrial sample. These authors concluded that endometrial aspiration technique was an acceptable and valuable method of assessing the endometrium which can be taken up as an OPD procedure.<sup>[5,6]</sup>

In this study an attempt was made to evaluate the sensitivity and specificity of endometrial aspiration cytology using a Karman's cannula taking histologic findings as gold standard.

## 2. Materials and Methods

The study was carried out for a duration of 1 year and 144 cases were sampled. Thorough clinical history and general systemic and local examination were done for each case. Informed consent of the patients was obtained before the diagnostic procedure, endometrial aspiration cytology followed by diagnostic curettage. Endometrial aspiration was performed by a plastic disposable Karman's cannula measuring 4mm by the pathologist in the gynecology theater under supervision of the gynecologist and without administering anesthesia. The cannula was inserted into the endometrial cavity and connected to 20cc disposable syringe. Negative pressure was then created by withdrawing the piston and maintained, while the mucosa was uniformly aspirated. The suction was released after aspiration and the cannula was withdrawn. After removal of the cannula, the surface was wiped to avoid contamination by cervical and vaginal cells. The material was expressed on a clean glass slide; the type of specimen aspirated is noted and then smeared. Then it was immediately fixed in a fixative (90% alcohol).

In the same sitting, immediately after aspiration, the gynecologist obtains endometrial biopsy and fixed in 10% formaldehyde. After the biopsy, the patient was observed and evaluated for vaginal bleeding at least for 15 minutes.

The cytology slides were stained by Papanicolaou stain. The specimen for histology were taken through the necessary steps and then stained with hematoxylin & eosin. The results of endometrial aspiration cytology and histopathology were compared. All data was analyzed manually, and with the help of SPSS and Excel software.

### 3. Results

Among 144 patients examined, most women were in the age group of 36-45 (41.7%), followed by 46-55 years (40.3%). There were 17.4% and 7% in <35 years and >55 years age groups respectively. 85 cases were in reproductive age group and 6 cases were postmenopausal, the rest of the cases belonged to peri menopausal age group. Only 10 samples were inadequate for opinion, of which 6 samples were mucoid and 4 samples were hemorrhagic on gross examination and 5 samples were reported as proliferative phase, 2 as simple hyperplasia, 2 as endometritis and 1 as atrophic endometrium on histopathology.

Cytological examination of 85 cases in the reproductive age group showed that 44 cases were reported as proliferative phase, 5 cases as secretory phase, 19 cases as simple hyperplasia, 1 case as complex hyperplasia, 4 cases as atypical hyperplasia, 5 cases as endometritis, 1 case as granulomatous endometritis and 3 cases as endometrial adenocarcinoma and aspirate material of 3 cases were inadequate for diagnosis.

In premenopausal and postmenopausal age group, out of 59 cases, 15 cases had proliferative phase, 2 cases belonged to secretory phase, 29 cases had endometrial hyperplasia, of which 1 case was reported as atypical hyperplasia. 2 cases were reported as endometrial adenocarcinoma and 7 cases had inadequate material for interpretation. 2 cases were reported as atrophic endometritis. The remaining 2 cases were reported as non-specific endometritis.

Proliferative endometrium was the most common pattern both on histopathology (38.19%) as well as endometrial aspiration cytology (40.97%). There was 100% cyto-histo correlation in cases of secretory endometrium, specific endometritis, atypical hyperplasia and endometrial adenocarcinoma. 90.90% cases of proliferative endometrium could be diagnosed on cytology. 5 cases were missed due to inadequacy.

The histo-cyto correlation in case of atrophic endometrium and nonspecific endometritis were 66.7% and 77.8% respectively. The diagnoses missed were due to inadequacy.

All the cases of atypical endometrial hyperplasia were correctly detected by cytology. However, 76.60% cases of simple hyperplasia could be correctly diagnosed by cytology. Endometrial aspiration cytology was unable to diagnose 11 cases of simple hyperplasia, 9 of which were reported as proliferative phase on histopathology. Other 2 cases were inadequate for reporting. Also, endometrial cytology detected only 4 out of the 12-complex hyperplasia reported on histopathology. All the misdiagnosed cases were reported as simple hyperplasia on cytology.

On cyto-diagnosis total 5 cases were reported as malignancies of which all 5 correlated well with histological diagnosis of endometrial adenocarcinoma, with correlation of 100%.

**Table 1:** Correlation of Cytological and Histological Findings

Diagnosis	Number of cases diagnosed on cytology	Number of cases proved on histology	Number of cases matched	Percentage (%) of Correlation
Proliferative Phase	59	55	50	90.90
Secretory Phase	7	7	7	100.00
Atrophic Endometrium	2	3	2	66.67
Non-Specific Endometritis	7	9	7	77.78
Specific Endometritis	1	1	1	100.00
Simple Hyperplasia	44	47	36	76.60
Complex Hyperplasia	04	12	4	33.33
Atypical Hyperplasia	5	5	5	100.00
Endometrial Carcinoma	5	5	5	100.00
TOTAL	134	144	117	-

### 4. Statistical Analysis

Out of the 134 valid cases, 66 cases were reported as cyclic or normal endometrium and 68 cases abnormal endometrium on cytology. On histopathology 57 cases were reported as cyclic endometrium and 77 cases were reported as abnormal endometrium. These data were further used for statistical analysis.

**Table 2:** Statistical Analysis in present study

Cytologic diagnosis	Histologic diagnosis		Total	P-value
	Positive	Negative		
Positive	68	0	68	<0.0001
Negative	9	57	66	
TOTAL	77	57	134	

- Sensitivity = 88.31%
- Specificity = 100%
- Positive Predicted value (P+) = 100%
- Negative Predicted value (P-) = 86.36%
- Accuracy = 93.29% (50.75% + 42.54%)

Statistical analysis of endometrial aspiration study of 134 samples showed that it has a high specificity (100%), positive (100%) and negative (86.36%) predictive values. The sensitivity of this technique was 88.31%. The accuracy of the test was 93.29% and a highly significant ( $p < 0.001$ ) statistical relation was observed between histopathology and cytopathology.

### 5. Discussion

Traditionally the standard method of assessing the endometrium has always been dilation of the cervix and curettage of the uterine cavity under general anesthesia. It accounts for a large proportion of hospital bed use and operating room time. The cost is significant and also carries the complication of anesthesia. Therefore, alternative procedures of endometrial sampling like endometrial brush,

Endocyte, Endo-pap sampler, membrane filtration method, endometrial Gravlee-jet washers, Isaacs's endometrial cell sampler, Mi-Mark Helix, lippies loop method and disposable plastic cannula were adopted. For a cytological technique to be accepted as a useful tool for endometrial screening it must first be proven to be an inexpensive, simple (can be used by any gynecologist) and painless sampling method that is able to obtain representative endometrial cells. Secondly, it must be shown that accurate interpretation of samples is possible.<sup>[7]</sup>

With this in mind, uterine aspiration cytology, an ambulatory procedure for endometrial sampling was studied. Often endometrial lesions are focal in distribution. A single strip biopsy may miss the lesion, but by application of this technique, more representative samples of endometrium can be obtained. Studies have revealed that, at times even when curettage findings have been normal, endometrial aspiration cytology has been found to be useful for diagnosing endometrial pathology.<sup>[8]</sup> Outpatient sampling of the Endometrium could complement conventional curettage and assist in patient management.

Endometrial aspiration cytology was performed using 4mm Karman's cannula in our study and we found it to be acceptable as an outpatient procedure with only mild to moderate discomfort in most of the patients. Complications like hemorrhage, infection or perforation following the procedure were also absent.

When sample adequacy of Karman's cannula was compared with other similar devices, results are on a par. Liza et al used the insemination cannula for intrauterine aspiration, with sensitivity of 81.6% and specificity of 83.3%.<sup>[9]</sup> Malik et al used insemination cannula of 0.5mm diameter for aspiration sampling reported successful sampling of 96%.<sup>[2]</sup> In 2010 Upadhyaya I. and Malla D.S. used pediatric feeding tube for sampling and reported successful sampling of 95.29%.<sup>[10]</sup> Also in 2014 Samina Ashraf and Farhat Jabeen using Karman's cannula reported an adequacy rate of 93.4%.<sup>[11]</sup>

In our experience using Karman's cannula, adequate material was obtained in 93.06% of the cases which rank well when compared with other studies. The cellular morphology was well maintained in all the smears.

The study conducted by Dowling et al using Gravlee jet washer had inadequacy rate of 27%.<sup>[12]</sup> Isaac reported the inadequacy rate of 2.5%.<sup>[13]</sup> In the study conducted by Afonso et al, using Gravlee jet washer, the inadequacy rate was 1.6% and Liza et al 2.8%.<sup>[9,14]</sup> Samina Ashraf and Farhat Jabeen using Karman's cannula reported an inadequacy rate of 6%.<sup>[11]</sup> The various causes of inadequacy of cellular fluid in endometrial aspiration cytology are due to atrophic Endometrium, cervical stenosis, difficulty in insertion, poor technique, drying artifact, etc.

In our study, aspirated material was inadequate for interpretation in 7% of cases, which is comparable to Malik et al and results of Samina Ashraf and Farhat Jabeen.<sup>[2,11]</sup> We considered that the major causes of inadequacy in our case are atrophic endometrium and technique failure.

If we consider type of aspirate, among the all 144 cases, hemorrhagic type was the most common (87.5%) and there was only one purulent aspirate which turned out to be a case of endometrial carcinoma. Hemorrhagic aspirates were found to have a high adequacy rates (96.8%) and mostly reported as cyclic endometrium (43.65%). Hemorrhagic aspirates with tissue fragment were all (11 of 144 cases) were reported as hyperplasia in 81.8% of the cases. All mucoid aspirates (4.2%) were reported inadequate on examination.

Malik et al reported hemorrhagic aspirate as the most common finding and 96% of which was cyclic endometrium, 2% as hyperplasia and 2% as inadequate. All aspirates showing hemorrhagic aspirate with tissue fragment were reported as hyperplasia. Mucoid and serous aspirates were found inadequate and purulent aspirate as adenocarcinoma.<sup>[2]</sup> In the study conducted by Samina Ashraf and Farhat Jabeen hemorrhagic aspirates were reported to have a high adequacy rate. They also reported hemorrhagic aspirate was most common and 84.2% of which was reported as cyclic endometrium. In mucoid aspirates 50% were reported as inadequate and 50% as proliferative endometrium.<sup>[11]</sup> Thus, the results are in agreement with the findings of Malik et al and Samina Ashraf and Farhat Jabeen.<sup>[2,11]</sup>

The accuracy of major cytological diagnoses in the present study when compared to methods used by other authors are presented in the table 3. A correlation of 90.90% was observed for proliferative phase similar to AMBIYE et al and Malik et al.<sup>[2,15]</sup> An accuracy of 100% was observed for secretory phase, in the present study, which is comparable to Malik et al and Upadhyaya I., Malla D.S.<sup>[2,10]</sup> Accuracy of 70.31% was observed in diagnosis of hyperplasia, including simple hyperplasia (76.70%), complex hyperplasia (33.33%) and atypical hyperplasia (100%) similar to that of Schachter et al of 77% and Malik et al (67%).<sup>[2,16]</sup>

**Table 3:** Correlation between endometrial cytology and histology in various series

Authors	Proliferative Phase	Secretory Phase	Endometrial Hyperplasia	Endometrial Carcinoma
Ambiye et al (1981)	88.00	88.0	-	-
Schachter et al (1980)	86.40	78.50	77	100
Liza et al (1990)	100.00	82.30	82.6	100
Malik et al (2008)	87.40	100.0	67	100
Upadhyaya I. and Malla D.S. (2010)	98.11	97.17	100	-
Samina Ashraf and Farhat Jabeen (2014)	96.00	90.90	96.96	-
Present Study (2014)	90.90	100.0	70.31	100

On cytology, the diagnosis of hyperplasia could be made but the type of hyperplasia was successfully interpreted only in 33.33% in case of complex hyperplasia and 76.70% in case of simple hyperplasia. Intact glandular structures with



preserved architecture if present on smear provide valuable clues to diagnosis between simple and complex hyperplasia. The use of cell block technique with cytology smear have been suggested which can provide important information about the architecture. [17] Recently Noritatsu et al published interesting results using an Endocyte sampler device. They propose new diagnostic criteria based on the composition and architecture of tissue fragments. Cell aggregates with a tube or sheet-shaped pattern were found in 97.5% of samples of normal proliferative endometrium. In Endometrial hyperplasia, cell aggregates with a dilated or branched pattern were found in 34.9% of cases. [8]

The cytological differentiation between atypical hyperplasia and endometrial adenocarcinoma was another difficulty that we faced. This issue was discussed in two sessions at the XV International Congress of Cytology, (Santiago de Chile, 2004), 'The Jiménez-Ayala Classification' was proposed by Jiménez-Ayala M which divided endometrial proliferative lesions as endometrial hyperplasia and endometrial neoplasia. Endometrial hyperplasia included both simple and complex hyperplasia and endometrial neoplasia included atypical hyperplasia and well differentiated endometrial carcinoma. [18] We strongly agree with the use of this classification.

An accuracy of 77.78% was observed when diagnosis of endometritis was made. 7 cases out of 9 when compared with histopathology. One case was diagnosed as tubercular endometritis both on histopathology and cytology with a correlation of 100%. A study by Padubidri et al showed 100% accuracy of tubercular endometritis. Triparty SN, Mahanty J. (1990), Padubidri et al and V. Malhotra (1996) found a 100% correlation in case of tuberculous endometritis. The findings of present study are in agreement the findings of these authors. [19,20,21]

The incidence of tuberculosis in India is high when compared to western countries and tubercular endometritis is considered a common cause of infertility. The combination to endometrial aspiration cytology and endometrial biopsy is recommended as an outpatient sourcing procedure in such cases where the rate of tuberculosis is high.

Atrophic Endometrium was reported in 3 cases. 2 cases diagnosed on cytology were confirmed by histopathology and a correlation of 66.67% was observed. Upadhyaya I. and Malla D.S. reported a 100% correlation, however only one case was detected in the study. Samina Ashraf and Farhat Jabeen reported 82.4% correlation in case of atrophic endometrium. In atrophic Endometrium, shedding of Endometrium is less, so some aspirates are sometimes reported inadequate for interpretation. The findings of present study are in agreement the findings of Samina Ashraf and Farhat Jabeen in case of atrophic endometrium. [10,11]

In the present study, 5 cases of malignancy were diagnosed as endometrial adenocarcinoma on cytology and were confirmed by histology. The correlation was 100%, and the results are similar to findings of other authors. [2,9,16]

The sensitivity and specificity reported in the present study by using Karman's cannula when compared to methods used by other authors is summarized in the table 4. Samina Ashraf and Farhat Jabeen in their study used the Karman's cannula with a sensitivity and specificity of 91.9% and 100%. [11] In the present study too, the Karman's cannula was used which gave a sensitivity of 83.31% and a specificity of 100%. Similar studies done by An-Foraker et al, Bistoletti et al, Liza et al and Malik et al by using different devices as the Isaac cell sampler, Endo-pap sampler and Insemination cannula with sensitivity of 81.62-96.15% and specificity of 95.5-100%. [2,9,22,23]

**Table 4:** Sensitivity and specificity in various series compared with present study

Authors	Method used for intrauterine washing	Sensitivity (%)	Specificity (%)
An-Foraker et al	Isaac cell sampler	96.15	96.85
Bistoletti et al	Endo-pap sampler	97	84
Liza et al	Insemination cannula	81.62	83.33
Malik et al	Insemination cannula	83.3	95.4
Samina Ashraf, Farhat Jabeen	Karman's cannula (4mm)	91.9	100
Present study	Karman's cannula (4mm)	83.31	100

## 6. Conclusion

Endometrial aspiration was found to be simple, safe, cost effective, well tolerated outpatient procedure in the diagnosis of abnormal and normal endometrium for patients of all ages.

While not completely replacing the conventional D&C, endometrial aspiration still has few advantages.

- It is a simple, inexpensive outpatient procedure with no complication & well tolerated by patients.
- Adequacy of material is high.
- It has got high accuracy in phasing the endometrium & assessing the cytohormonal status.
- It can also detect endometrial pathologies like endometrial hyperplasia, atrophy, atypia and malignancy even when focal in nature.

Therefore, at the end of this study, we propose that endometrial aspiration cytology can be used as a screening procedure for early detection of various endometrial diseases, thereby leading to a better prognostic outcome.

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