

Diagnostic efficacy endometrial aspiration cytology in gynecological pathology

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Abstract

Introduction: Endometrial aspiration cytology is a diagnostic modality for studying cyto-harmonal changes and for evaluating endometrial pathology ranging from inflammatory changes, hyperplasia and endometrial malignancies.

Aims: To assess the diagnostic accuracy of endometrial aspiration technique and to compare the cyto-morphology of aspirated smears with histopathology.

Materials and Method: Endometrial aspiration was performed using Karman's cannula in 100 cases who presented with abnormal uterine bleed, infertility and postmenopausal bleed. The endometrial specimens obtained by D& C were processed and evaluated histologically. The endometrial aspirated smears were correlated with histopathology findings for diagnostic accuracy.

Results: The study cases included 48 patients in reproductive age group and 52 patients in the perimenopausal and postmenopausal age groups. The diagnostic accuracy on cytology was 90% when compared to histology. The smears were inadequate for reporting in eight cases. The sensitivity of endometrial cytology was 93% and specificity was 85.7%.

Conclusions: Endometrial aspiration technique with Karman's cannula is convenient, simple, safe and less invasive procedure. The endometrial aspiration cytology proved to be effective diagnostic modality in the interpretation of normal and abnormal endometrium. The present study emphasizes the need for early screening to diagnose pre-invasive lesions and endometrial malignancies in peri-menopausal and post-menopausal patients.

Keywords: Endometrial aspiration cytology, Cyclic endometrium, Endometrial malignancy, Karman's cannula.

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Introduction

Endometrial aspiration technique is less invasive efficient diagnostic procedure for screening the endometrial status and for diagnosing gynecological disorders when compared to endometrial biopsy or curettage. In 1943 Cary developed a metal cannula for the aspiration technique and the method was described by Papaniculou and Marchetti. The aspiration techniques are less popular due to unsatisfactory smears and difficulty in interpretation by pathologist.^(1,2,3) Endometrial aspiration does not require cervical dilatation or anesthesia. It is a safe, simple and reliable technique without any complication and can be used as a out-patient procedure with minimum discomfort to the patient.^(2,3)

Materials and Method

The present study was conducted for 2yrs at M.V.J Medical College and Research hospital, Hoskote, Bangalore in the department of pathology and obstetrics and gynecology. The study included 100 cases in the reproductive, menopausal and postmenopausal age groups, who presented with complaints of abnormal uterine bleeding, infertility and post-menopausal bleeding. Thorough clinical history, general brief systemic and local examination was done for each case. Consent of the patient was obtained before the diagnostic procedures.

Endometrial aspiration was done using a plastic disposable Karman's cannula measuring 4mm. This was inserted into the endometrial cavity and connected to 20cc disposable syringe. Negative pressure was created and maintained, while the entire mucosa was uniformly aspirated. The material is squirted on a clean glass slide and smeared and immediately fixed in a fixative and then stained by Papaniculou stain.

After endometrial aspiration, diagnostic dilatation and curettage was done for histopathological study. The smears of endometrial aspiration cytology were compared with histopathology. Patients diagnosed with acute inflammatory disorders of the Genital tract, Pregnancy and with gross evidence of cervical malignancy were excluded.

The criteria for assessment of endometrium on cytology was based on the studies done by Bistolletti and Hjerpe et.al and Koss, diagnostic cytology.^(4,5,6,7)

Adequacy of samples: Except in women with complete atrophy of endometrium (usually past the age of 55), the smears should contain at least five or six clusters of endometrial epithelial cells to be judged as adequate.

Proliferative phase: The epithelial cells are arranged in flat monolayer sheets (honeycomb pattern). The size of the cells varies from 45 μ to 75 μ . The nuclei of the epithelial cells are closely packed with smooth contours and dispersed chromatin. Mitoses of normal configuration may be seen. (Fig. 1).

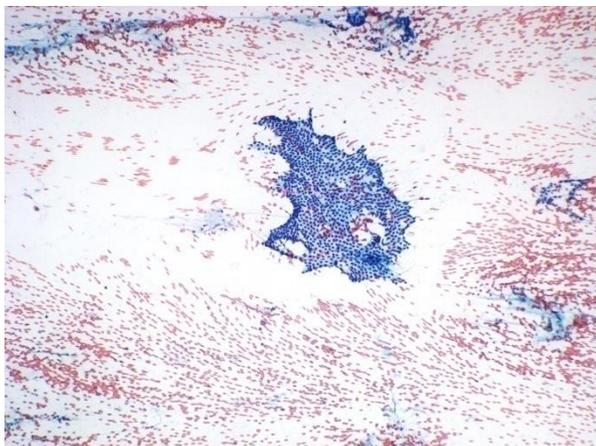
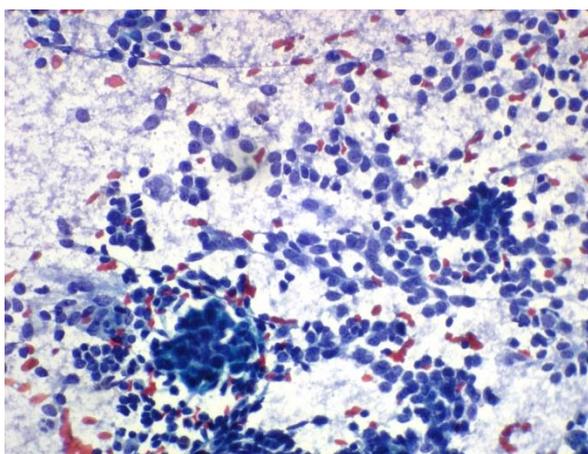


Fig. 1: Cytology –PAP Stain- Secretory Phase

Secretory Phase: The epithelial cells are arranged in clusters or sheets. In early secretory phase, the epithelial cells are larger due to increased volume of cytoplasm, often vacuolated. In late secretory phase the endometrial cells occur in thick clusters sometimes in tubular or glandular configuration. Some nuclei are small, shrunken and give a burnt out appearance. The background is hemorrhagic with neutrophils,(Fig. 2)



**Fig. 2: Cytology- PAP Stain-Proliferative Phase
X400**

Honeycomb pattern, X400

Menstrual phase: The endometrial cells appear exhausted with scanty cytoplasm. Single normal cells are seen. They appear necrotic and degenerated. In the background hemorrhage, inflammatory cells and cellular debris are present.

Atrophic endometrium: Seen in postmenopausal women with endometrial atrophy. The number of clusters of epithelial cells is small, limited to three or four clusters. The epithelial cells and their nuclei are smaller than those in proliferative or secretory endometrium. The stromal cells are sparse. Mono or multinucleated macrophages are observed.

Endometrial Hyperplasia: Endometrial samples in hyperplasia are rich in cells and cell clusters.

Criteria for cytological assessment of hyperplasia (Meisels-1985)⁽³⁾

1. Glandular cells in sheets and clusters along with stromal cells
2. Prominent nucleoli
3. Anisonucleosis
4. Granular chromatin

Simple hyperplasia: There is increase in cellularity, with cells in sheets and tight clusters. The cells are round with scanty cytoplasm mild to moderate anisonucleosis, fine granulation and even chromatin.

Complex hyperplasia: Smears are cellular with many clusters. Piling up of cells with crowding and overlapping of nuclei with mild pleomorphism, fine granular chromatin with prominent nucleoli in a few cells are seen.

Atypical hyperplasia: Smears are hypercellular with glandular cells in clusters and papillary fronds. Individual cells exhibit increased nuclear cytoplasmic ratio, granular chromatin and nuclear crowding, disturbed nuclear polarity and presence of nucleoli.

Endometritis:^(8,13)

Non-specific Endometritis: Smears showed few clusters of endometrial cells infiltrated with numerous inflammatory cells. 2 cases were reported as endometritis on cytology.

Tubercular endometritis: The smear shows sheets and clusters of endometrial cells. The cells show mild atypical changes with epitheloid cells and chronic inflammatory cells. Langerhan's giant cells and granular eosinophilic material, suggestive of caseation may be seen.

Endometrial Adenocarcinoma: Dyscohesive and three-dimensional clusters are seen with anisonucleosis. Loss of nuclear polarity, hyperchromasia, macronuclei, increased nuclear chromatin granularity and abnormal mitotic figures. The cancer cells may be dispersed or occur singly or may form clusters, that are either flat or multilayered, the latter of papillary configuration.

Results

Endometrial aspiration was done in a total of 100 patients presenting with various gynecological complaints and infertility. The relevant clinical history and findings were noted. Following endometrial aspiration D & C was done in 75 patients, whereas in 25 patients hysterectomy was done (2 Cases of Carcinoma, 1 atypical hyperplasia, 1 complex and 5 simple hyperplasia). Findings on Cytology and histopathology were studied and documented.

Among 100 patients studied 48 cases belonged to reproductive age group, 25 cases in postmenopausal and the rest belonged to peri-menopausal age group. Patients presented with symptoms of menorrhagia (52), Polymenorrhea (20). These patients belonged to reproductive and premenopausal age group, the age of

who ranged from 25-55yrs. Out of 2 malignancies, one presented with post menopausal bleeding and the other with menorrhagia. Of the 100 cases studied a clinical diagnosis of DUB was made in 65 cases and infertility in 6 cases.

Cytological Analysis: Endometrial aspirate was satisfactory only in 95 patients due to endometrial atrophy and technical failure. Although inadequate sample was obtained on aspiration, endometrial yield was sufficient on curettage, (Table 1).

Table 1: Cytology Findings

Cytology	No. of Cases	Percentage
Proliferative phase	50	50%
Secretory phase	25	25%
Simple hyperplasia	5	5%
Complex hyperplasia	1	1%
Atypical hyperplasia	1	1%
Endometritis:		

Non specific	2	2%
Specific	1	1%
Atrophic	5	5%
Malignancies	2	2%
Inadequate	8	8%
Total	100	

Cytology of 48 cases in reproductive age group showed 33 cases in proliferative phase, 9 cases in secretory phase, 3 cases with simple hyperplasia and 3 cases were inadequate for diagnosis.

In perimenopausal and postmenopausal age group, 13 out of 52 cases were in proliferative phase, 27 cases in secretory phase, 2 cases had endometrial hyperplasia, of which 1 case was diagnosed as atypical hyperplasia, 2 cases as endometrial adenocarcinoma and 5 cases were inadequate for interpretation. 3 cases were reported as non-specific endometritis of which 1 case was confirmed as tubercular endometritis.

Table 2: Correlation of cytological and histological findings

Cytological Findings	No. of Cases	Histological Findings	
		Consistence	Inconsistent
Proliferative phase	50	44	6
Secretory phase	25	24	1
Simple hyperplasia	5	3	2
Complex hyperplasia	1	1	-
Atypical hyperplasia	1	1	-
Endometritis	3	3	-
Endometrial Carcinoma	2	2	-
Metastatic Carcinoma	-	-	-
Atrophic Endometrium	5	3	2
Inadequate samples	8	-	-

Table 3: Accuracy of aspiration cytology diagnosis in relation to histopathology

Diagnosis	No. of cases diagnosed on cytology	No. of cases proved on histology	Percentage
Proliferative phase	50	44	88%
Secretory phase	25	24	92%
Simple hyperplasia	5	3	60%
Complex hyperplasia	1	1	100%
Atypical hyperplasia	1	1	100%
Endometritis	3	3	100%
Endometrial Carcinoma	2	2	100%
Metastatic Carcinoma	-	-	-
Atrophic Endometrium	5	3	60%
Inadequate samples	8	-	-
Total	100		87%

The endometrial aspiration cytology results were correlated with histopathological findings. Out of 50 cases reported as proliferative phase on cytology in the reproductive age group, 44 cases correlated well with histopathology, giving accuracy of 88%, other 6 cases were diagnosed on histopathology as simple hyperplasia (2 cases), 2 cases showing both proliferative and secretory endometrium due to hormonal therapy and early secretory phase (2 cases). 25 aspirated smears were reported as secretory phase, of which 24 were confirmed on histopathology, giving 92% accuracy and the misinterpreted case showed proliferative phase on histopathology. 7 cases were reported as endometrial hyperplasia, of which 5 cases were confirmed by histology, 3 cases were reported as simple hyperplasia, and 1 case was reported as complex hyperplasia, the other as atypical hyperplasia. The 2 cases, which did not correlate with histology, were reported as proliferative phase. The accuracy for simple hyperplasia was 50% and atypical hyperplasia was 100%. All 3 cases of endometritis, including 1 case of tubercular endometritis correlated well with the histopathological findings, (Table 2).

The diagnostic accuracy in different lesions ranged from 60-100%. The procedure had sensitivity of 93 % and specificity of 85.7% as compared to Malik et al.(Table 3).

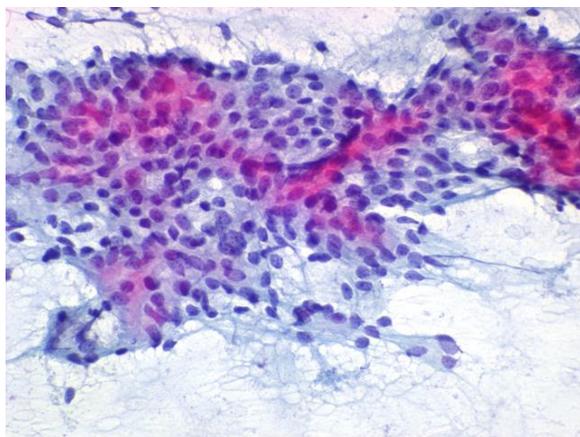


Fig. 3: Cytology: PAP Stain, Complex hyperplasia - X400

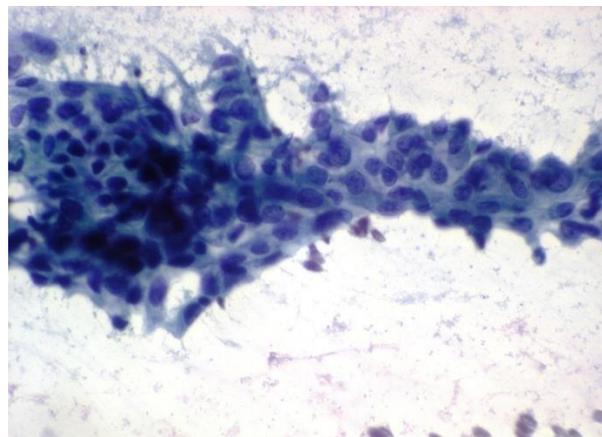


Fig. 4: Cytology: PAPStain, Atypical Hyperplasia- X400

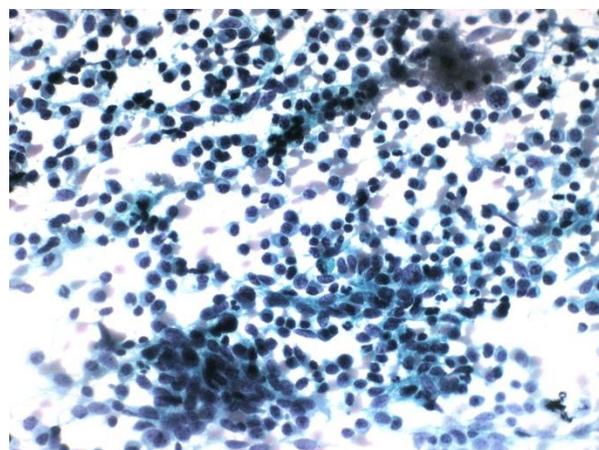


Fig. 5: Cytology: PAP Stain-Endometritis, X400

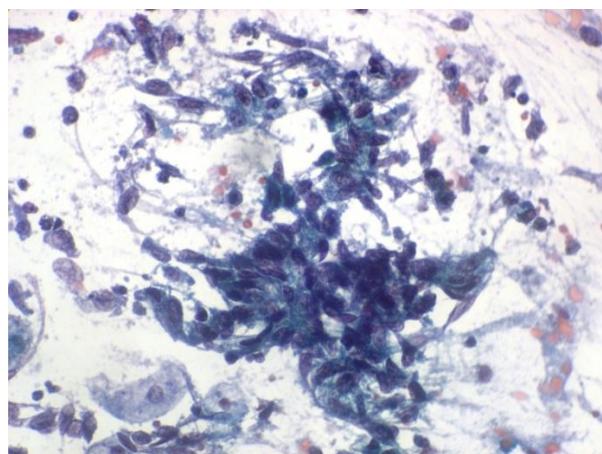


Fig. 6: Cytology: PAP Stain –Endometrial Adenocarcinoma, X400

Discussion

Diagnostic dilatation and curettage is a commonly performed Gynecological surgery. It requires hospitalization, anesthesia and cost is significant. Some complications are faced by the patients. For these reasons, various endometrial sampling techniques with

endometrial brush, membrane filtration method, endometrial Gravlee- jet washers, Isaacs's endometrial cell sampler, Mi-Mark Helix, lippies loop method, Endocyte, Endo-pap sampler, disposable plastic cannula, Vabra aspirator have been used.⁽⁷⁾

Uterine aspiration curettage under negative pressure has been reported to give excellent endometrial specimens both for cytology and histological examination. The curettage has failure rate of 12-29%. With experience, a cytopathologist can make an accurate diagnosis on aspiration cytology.

In the present study, 20cc syringe (disposable) with 4mm Karman's cannula was used for endometrial aspiration. This is easy technique, an outpatient procedure with only mild to moderate discomfort in most of the patients. The procedure was rapid, taking around two minutes, and technically was just like inserting an IUCD. There was no hemorrhage, infection or perforation following the procedure and also risk of anesthesia was not there. Aspiration cytology was done in 100 patients, the age ranged from 20-60yrs. This was followed by Dilation and curettage in 75 cases. In remaining 25 cases hysterectomy was done. Cytology smears and histopathology sections were compared and correlated.

A variety of direct endometrial sampling techniques, which are modifications of Cary's original method, have been tried with varying degrees of

success over last few decades. In studies of Liza et al., the insemination cannula used for intrauterine aspiration, had sensitivity of 81.6% and specificity of 83.3% (in 1999). Recently, Malik et al. used insemination cannula of 0.5mm diameter for aspiration sampling, in 2008 with successful sampling of 96%.⁽⁹⁾

The adequacy of the samples for cytology was 92% in the study. Inadequate samples for interpretation were 8% of cases, which was comparable to Malik et al. The causes being atrophic endometrium and technical failure.

The diagnostic accuracy of endometrial aspirates was 100% for malignancies, endometritis and atypical hyperplasias. 92% for secretory phase, 88% for proliferative phase and 72.2% for endometrial hyperplasia, similar to that of Schachter et al of 77%. The cytological appearances of simple hyperplasia represent an exaggeration of the appearance of proliferative phase and features may be due to response of the endometrium to exogenous estrogen administration. On cytology the degree of hyperplasia is difficult to interpret. Slight nuclear enlargement and the presence of small nucleoli may indicate hyperplasia. The cytological pattern of atypical hyperplasia and endometrial adenocarcinoma is difficult to differentiate. The background of these smears show aggregates of nuclear debris, leucocytes and degenerated tumor cells.^(10,11,12)

Table 4: Inadequacy rates and various causes of inadequacy encountered in different studies

Sl. No.	Authors	Technique used	Inadequacy	Causes
1.	Dowling et al	Gravlee jet washer	27%	Atrophic endometrium
2.	Isaacs et al	Isaac Endometrial sampler	2.5%	Drying artifact, failure of insertion
3.	Rich art et al	Gravlee Jet washer	9.6%	Cervical stenosis
4.	Liza et al (1999)	Insemination cannula	2.8%	Post menopausal age
5.	Hemalath et al (2006)	M.R. Syringe	05%	Atrophic endometrium
6.	Malik et al	Insemination cannula	6.6%	Atrophic endometrium, Technique failure
7	Present study	Karman's cannula (4mm)	8%	Atrophic endometrium, Technique failure

Dilation & Curettage followed endometrial aspiration in 75 cases. In remaining 25 cases, hysterectomy was done. These hysterectomy patients included prolapse, leiomyoma, and malignancies. Majority of the age group belonged to 25– 45yrs. The commonest presenting complaint in this study was menorrhagia in 45% of cases.

In the present study, proliferative phase had 88% correlation with histology which is similar to studies of Ambiyé et al and Malik et al. The accuracy of secretory phase(92%) observed in the present study, was comparable to Malik, et al. In the present study, accuracy of 73%(72) was observed in diagnosis of hyperplasia, including simple hyperplasia, complex and atypical hyperplasia. (50% simple hyperplasia, 100% for Atypical hyperplasia), similar to that of Schachter et al of 77%. There is always a tendency to over diagnose simple hyperplasia on cytology. The cytological appearances of simple hyperplasia represent an exaggeration of the appearance of proliferative phase. The features may be due to response of the endometrium to exogenous estrogen administration.

On cytology the diagnosis of hyperplasia could be made but the degree of hyperplasia is difficult to interpret. Slight nuclear enlargement and the presence of small nucleoli may indicate hyperplasia. The cytological pattern of atypical hyperplasia and endometrial adenocarcinoma is difficult to differentiate. Hence the diagnostic criteria of well- differentiated lesion are very subtle.^(11,12,14)

In the present study 2 cases were showing, both proliferative and secretory phase on aspiration smears. Both the cases had received hormone therapy earlier, and they correlated well with histology. 3 cases were reported as endometritis on aspiration cytology and all of them including a case of tubercular endometritis

were confirmed by histopathology giving an accuracy of 100%. The present study showed 100% accuracy to Padubidri et al for the diagnosis of tubercular endometritis.⁽¹³⁾

In the present study, 2 cases of malignancy were diagnosed as endometrial adenocarcinoma on cytology and were confirmed by histology. The accuracy was 100%, giving a correlation of 100% similar to the study of Malik et al.^(2,3)

The sensitivity and specificity obtained by all methods were 68.2-97% and 79-100% and the sensitivity and specificity in the present study using Karman's cannula (4mm) is 93% and 85.7% respectively.

Table 5: Sensitivity and specificity of various techniques

Sl. No.	Authors	Method used for intrauterine washing	Sensitivity %	Specificity %
1.	An- Foraker et al	Isaac cell sampler	96.15	96.85
2.	Bistoletti et al	Endo-pap sampler	97	84
3.	Liza et al	Insemination cannula	81.62	83.33
4.	Malik et al	Insemination cannula	83.3	95.4
5.	Present study	Karman's cannula (4mm)	93	85.7

Conclusion

Endometrial aspiration is a well-tolerated safe simple outpatient procedure. It is a cheap and efficient diagnostic technique for reporting endometrium of patients of all ages. It is an efficient technique for screening postmenopausal patients in diagnosing uterine as well as extra-uterine metastatic malignancies. The Karman's cannula used in this study is inexpensive and alternate endometrial sampling method. This study suggests that endometrial aspiration cytology gives good correlation with histopathology, having high sensitivity and specificity.

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