

# Clinicopathological correlation of endometrial aspiration cytology in women with infertility

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## Abstract

**Background:** Infertility is a common problem for which the couple seeks gynecological consultation. Endometrial aspiration cytology (EAC) has emerged as a minimally invasive and cost-effective diagnostic procedure for assessing the endometrial status of these patients that can aid in the high-burden and resource-limited settings.

**Aims:** The study was conducted to evaluate the utility of EAC in women with infertility, and the cytological diagnosis was correlated with the histopathology.

**Materials and Methods:** A total of 50 patients presenting with infertility were subjected to EAC using a 5F infant feeding tube attached to 20 cc disposable syringe; later, they also underwent endometrial dilation and curettage. The cytology smears were evaluated for architectural and cytomorphological features. The cytological diagnoses henceforth made were compared with the histopathological diagnosis to calculate sensitivity, specificity, and diagnostic accuracy of EAC.

**Results:** EAC showed a sample adequacy of 80% viz a viz 90% for histopathology. EAC showed a specificity and sensitivity of 97.3% and 100% for assessing the endometrial status in infertility. There was a good overall agreement between cytological and histopathological diagnosis ( $P$  value-0.60).

**Conclusions:** EAC is an effective and minimally invasive procedure for the primary investigation of women with infertility.

**Keywords:** Endometrial aspiration cytology, histopathology, infertility, ovulation

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## INTRODUCTION

Infertility is a common problem for which gynecological consultation is needed and induces considerable stress in the life of the couple as they have to go through an exhaustive list of investigations including endometrial biopsy. Thus, there is a need for an accurate, rapid, cheap, safe, and simple procedure to detect ovulation in these patients. Dilatation and curettage used for this purpose is

expensive, time-consuming, painful, requires anesthesia, and hospitalization. For these reasons, there is a need for a simple, accurate, and good outpatient department (OPD) procedure as an alternative to D and C. Endometrial aspiration cytology (EAC) can be used as a safe, minimally invasive, and reliable OPD procedure with minimum discomfort to the patient to monitor the status of the endometrium<sup>[1]</sup> in relation to menstrual cycle which may

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be ovulatory or anovulatory. In this view, we thought it worthwhile to study its diagnostic utility of EAC in evaluating the endometrium of infertile patients.

## MATERIALS AND METHODS

A total of 50 cases of primary and secondary infertility attending gynecology and obstetrics OPD were evaluated. We followed a well-set protocol for selecting our patients. A detailed history with special reference to associated medical disease, menstrual disorders, and obstetrical abnormalities was noted. Only patients with normal menstrual flow and cycles were included in this study. Patients on steroidal contraceptives were not included in the study.

The procedure was well-explained to the patients, and their consent was taken. Under all aseptic conditions, endometrial aspiration was carried out in the OPD or in the operation theater before curettage. Endometrial aspiration obtained using a 5F infant feeding tube attached to 20 cc disposable syringe and curettings obtained by blunt end endometrial curette. Endometrial aspiration material was smeared directly onto three clean glass slides. Two air-dried smears were stained using Giemsa stain. One of the slides was immediately fixed in 95% ethyl alcohol and then stained with Papanicolaou stain.

Subsequently, all the patients were subjected to D and C, and then, the curettings were fixed in 10% formalin. After tissue processing, sections were obtained and stained with hematoxylin and eosin stain. Finally, cytological and histopathological results were compared.

The cytomorphological criteria used in various conditions of the endometrium were as given by An-Foraker *et al.*,<sup>[2]</sup> Shu and Ikle,<sup>[3]</sup> and Meisels and Jolicœur<sup>[4]</sup> The factors of inadequacy were followed as stated by Veneti *et al.*<sup>[5]</sup> that the reason of histologically and cytologically inadequate material could be old age, uncooperation by the patient, or technical errors. The study of composition, architecture, and growth pattern of the large tissue fragments in the cytological samples from the endometrium was done and evaluated using criteria given by Skaarland<sup>[6]</sup> and Yanoh *et al.*<sup>[7]</sup>

## RESULTS

The age of the patient with both primary and secondary infertility ranged between 20 and 40 years. The maximum number of patients belonged to the age group of 20–30 years. The duration of infertility ranged from 1 to 18 years for primary infertility patients and 1–16 for secondary infertility patients.

The maximum number of cases was of primary infertility (74%), followed by secondary infertility which accounted for 26% of cases.

Aspirated material from endometrium was adequate in 80% of cases. Inadequate material was either due to scant cellularity, poor preservation, or presence of mucoid material only. Inadequacy in biopsy material (six cases) was either due to a small biopsy or blood clot only.

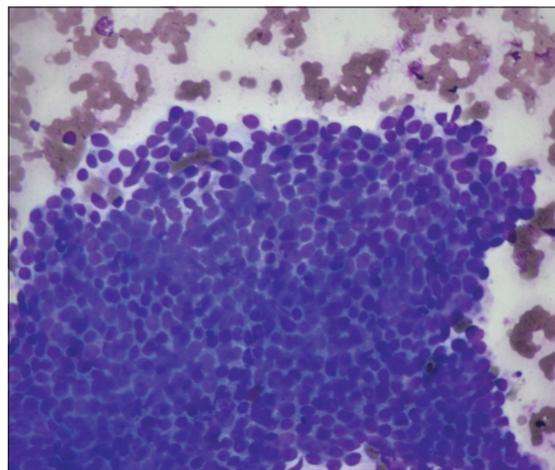
## Cytological findings

Proliferative phase endometrium was characterized by intact tubular glands and glandular cells in monolayered sheets revealing tight cohesion, uniform, round, or oval nuclei, evenly distributed nuclear chromatin, scanty cytoplasm with distinct cell borders [Figure 1]. Stromal cells vary from dense and spindly to fusiform to oval. Oval nuclei are more common in the mid and late proliferative phase.

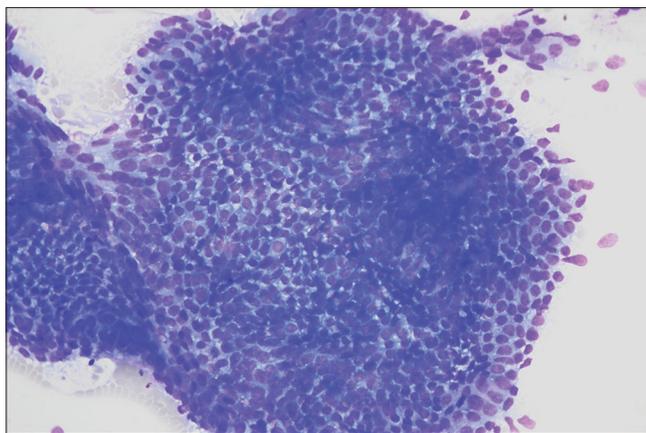
Secretory phase endometrium showed loose monolayered sheets of cells with uniform round or oval nuclei, finely granular chromatin, more abundant cytoplasm showing vacuolations, and well-defined borders. Nuclei are more widely separated from one another [Figure 2]. Stromal cells showed oval to plump nuclei.

In the anovulatory cycle, the aspiration smears revealed clusters of endometrial cells with features of proliferative glands in a dirty background of degenerated cells, stromal cells, bare nuclei, inflammatory cells (neutrophils and lymphocytes), mucinous secretions, and red blood cells [Figure 3].

Cases of menstrual endometrium revealed clusters of degenerated endometrial glandular and stromal cells along



**Figure 1:** Smear from proliferative phase showing dense sheets; monolayered sheets of endometrial cells revealing tight cohesion, uniform, round to ova oval nuclei, scanty cytoplasm with distinct cell borders (Giemsa, ×400)



**Figure 2:** Secretory phase showing a flat honeycomb sheet of epithelial cells with a round-to-oval nucleus and more abundant vacuolated cytoplasm (Giemsa,  $\times 400$ )

with inflammatory cells, fibrin, and residual vessels with adherent plump stromal cells.

Single case of endometritis was characterized by endometrial glandular and stromal fragments and histiocytic cell clusters with neutrophils, eosinophils, lymphocytes, and plasma cell infiltration. Single case of tuberculous endometritis revealed epithelioid cell granulomas, caseous necrosis, and Langhans giant cells.

Endometrial patterns obtained on EAC were correlated with histological findings obtained on endometrial biopsy [Table 1]. There was a perfect 100% cytohistological correlation in cases reported as proliferative endometrium, nonspecific endometritis, tuberculous endometritis, and hypersecretory phase. One case reported as irregular shedding in aspiration smears was diagnosed as secretory phase in histology. Cytohistological findings correlated in 92.29% of cases of secretory endometrium. About 92.3% of cases of anovulatory cycles showed cytohistological correlation. Five cases reported as menstrual phase on histopathology but none could be diagnosed by aspiration.

One case which was reported as irregular shedding endometrium on aspiration cytology was diagnosed as secretory phase endometrium with fragments of isthmic tissue in histopathology that mimicked proliferative endometrial cells in aspiration smears. Five cases diagnosed as menstrual phase endometrium on histopathology were reported either as hemorrhagic aspirate or as blood-mixed scant cellular material in EAC.

Statistical analysis of EAC findings revealed 100% sensitivity, 97.3% specificity, 66.7% positive predictive value, and 100% negative predictive value. EAC has a high diagnostic accuracy of 97.5% with  $P$  value of 0.60.

## DISCUSSION

The significance of the detection of ovulation is immense in infertility workup. The study of the endometrium is used as an adjunct to the monitoring of the efficacy of treatment for ovulatory failure, in the confirmation and typing of endometrial hyperplasia in the woman with persistent anovulatory cycles, for the diagnosis of genital tuberculosis and as a means of culturing the *Mycobacterium* for antibiotic sensitivity testing.

Very few studies have been done in the past to evaluate cytomorphological features of endometrium using EAC in infertility cases. In the present study, cytomorphological and histopathological features of endometrium were studied in 50 patients of infertility. Among these, 74% of cases were of primary infertility and 26% were of secondary infertility. This type of infertility incidence is comparable to the study done by Malhotra<sup>[8]</sup> who reported 62% primary infertility and 38% secondary infertility cases. Another study done by Shrivastava and Dekate<sup>[9]</sup> reported 83% and 17% cases of primary and secondary infertility, respectively. In the present study, 82% of cases of infertility were in the age group of 20–30 years. This age incidence is comparable to that reported by Shrivastava and Dekate<sup>[9]</sup> who found a maximum number of infertility cases in the age group of 20–25 years.

The present study evaluated the efficacy of EAC in comparison with histopathology in patients of infertility. The results showed a good agreement between EAC and histopathology. Adequacy of the representative sample is an important factor limiting the utility of EAC. In the present study, a sample adequacy of 80% was achieved using No. 5 infant feeding tube and 20cc disposable syringe that involves a simple and cost-effective technique. Different studies, using different techniques/devices for endometrial sample collection, have yielded variable adequacy rates ranging from 59% to 100%.<sup>[10–13]</sup> Some of these include insemination cannula, Karman cannula, intra-cath cannula, Isaac's cell sampler, and pistol aspirator. However, the difference in methodology did not affect the sensitivity and specificity of the cytological results that remained between 68.2%–97% and 79%–100%, respectively.<sup>[10]</sup> Adequate material was obtained in 80% of cases by endometrial aspiration in our study which is comparable to 88% adequate material in endometrial aspiration using pediatric cannula by Malhotra<sup>[12]</sup> and 81% adequacy reported by Shrivastava SS *et al.*<sup>[9]</sup>

**Table 1: Comparison of endometrial patterns obtained on endometrial aspiration cytology and histopathology**

Endometrial pattern	Number of cases diagnosed by aspiration cytology	Number of cases diagnosed by histopathology	Percentage correlation
Proliferative phase	11	11	100
Proliferative phase with breakdown (anovulatory cycle)	6	7	92.3
Secretory phase	19	18	92.29
Menstrual phase	0	5	00
Irregular shedding	1	0	00
Hypersecretory phase	1	1	100
Nonspecific endometritis	1	1	100
Tuberculous endometritis	1	1	100

In the present study, 15% of cases were reported as anovulatory cycle in endometrial aspiration. This number is less in comparison to 32% anovulatory cycle reported by Shrivastava and Dekate. Proliferative endometrium was reported in 42.5% cases and secretory endometrium in 47.5% of cases in the present study. Shrivastava and Dekate reported 32% cases in the proliferative phase and 68% cases in the secretory phase. The number of secretory phase endometrium is less in the present study, although the number of proliferative phase endometrium is comparable. In the present study, there was 100% cytology and histopathology correlation for proliferative phase endometrium which is comparable to 90% correlation reported by Malhotra<sup>[8]</sup> and is much higher than 75% reported by Shrivastava and Dekate.<sup>[9]</sup>

Cytology and histopathology correlation of 94.73% was reported for secretory phase endometrium in the present study, which is comparable to 92.67% correlation reported by Malhotra<sup>[8]</sup> and is higher than 80.9% reported by Shrivastava and Dekate.<sup>[9]</sup>

Although one of the most common causes of infertility in our scenario, only one case of tuberculous endometritis was reported in the present study; Malhotra<sup>[8]</sup> also reported one case of tuberculous endometritis in a similar study.

In the present study, no case of endometrial hyperplasia was reported. The reason may be the younger age group of the patients studied. Malhotra<sup>[8]</sup> reported a single case of endometrial hyperplasia in their study.

Shrivastava and Dekate<sup>[9]</sup> reported 100% sensitivity and 73.36% specificity of EAC for evaluating different endometrial conditions. In the present study, the specificity of the procedure was 97.3%, whereas sensitivity was 100%, which is comparable to the findings of Shrivastava and Dekate.<sup>[9]</sup>

Thus, according to the results of our study, EAC has high sensitivity and specificity in the evaluation of endometrium

in infertility. Shrivastava and Dekate<sup>[9]</sup> also concluded that coupled with vaginal cytology and cervical mucus studies, EAC can be used as a noninvasive technique to document ovulation/anovulation. Similarly, Malhotra<sup>[8]</sup> also concluded that EAC can be used as the first investigation in infertility and when deemed necessary can be supplemented by endometrial biopsy.

## CONCLUSIONS

Endometrial aspiration using No. 5 infant feeding tube with attached 20cc syringe is an accurate, quick, inexpensive, convenient, and a one-time method, which can be repeated in successive cycles without any patient discomfort in infertility workup.

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## Conflicts of interest

There are no conflicts of interest.

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Mardi and Rao: Endometrial aspiration cytology in infertility

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