Original Research Article

Efficacy of endometrial aspiration cytology in diagnosis of endometrial pathologies in a tertiary care centre

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Abstract

Introduction: Endometrial pathologies contribute significantly to increased morbidity and mortality in females, and still tend to remain undiagnosed till later stages. Endometrial cytology is one of the most powerful and reliable investigations in detection of various endometrial pathologies, including hyperplasia, malignancies and can be used as an early evaluative modality on routine basis.

Objectives: The present study was aimed at assessing the diagnostic efficacy of endometrial aspirate cytology in the diagnosis of various endometrial pathologies in terms of accuracy, sensitivity and specificity etc., considering histopathology as standard . It also involved the study of various morphological patterns ranging across the spectrum of endometrial pathology by aspiration cytology .

Material and methods: Using Karmann's cannula, endometrial aspirate sample was obtained in 106 patients from gynaecology out-patient department and the smears were stained using papanicolaou stain. The findings of cytology were correlated with histopathology.

Results: The present study comprises 106 patients. 102 out of 106 samples for cytology were adequate with an overall diagnostic accuracy of 95.1% , a sensitivity of 93.2%, specificity of 97.7%, with 98.2% positive predictive value and 91.3% negative predictive value.

Conclusion: Endometrial aspiration cytology is an easy to perform, minimally invasive, safe and cheaper procedure for diagnosing endometrial pathologies. Its results are fairly acceptable with good cyto-histopathological correlation and hence can be used for screening of endometrial pathologies and malignancies.

Keywords: Endometrial aspiration cytology, histopathology, Karmann's cannula, dilatation and currettage

Introduction

Globally, endometrial diseases are being ranked among the most common gynaecological disorders that affect women. These range from hyperplasias to malignancies contributing significantly to increased mortality and morbidity. Most young women of reproductive age present more commonly with changes associated with hormonal imbalance. However, older women of peri and postmenopausal age group present commonly with endometrial hyperplasia and endometrial carcinoma. Many of these lesions can be diagnosed by endometrial sampling.[1]

Reports state that endometrial carcinoma is the most common gynaecological malignancy in developed countries and 2nd most common gynaecological malignancy in developing countries after cervical carcinoma.[1]

Endometrial cytopathology is a powerful test for the detection of a variety of benign lesions ranging from inflammatory changes to atypias. It can be used for the cytohormonal evaluation of patients and for screening of malignancy.[2]

Till date, endometrial biopsy or curettage has remained the diagnostic investigation for endometrial lesions. Dilatation and curettage (D & C) has for long been considered "the gold standard" in the diagnosis of endometrial pathology.[3] However, this invasive procedure requires hospitalization and poses a risk to the patient from anaesthesia, surgical trauma, and acquired infections.[4] The cost is significant and carries the complications of anaesthesia. Hence, it is not suitable to use it for mass screening of patients for endometrial carcinoma.[5]

Even though cervical cancer is historically more common than endometrial cancer, pap screening is gradually decreasing its incidence, whereas the number of patients of endometrial cancer is still high . [6] The early detection of endometrial cancer is important for the improvement of the long term survival rate of patients.[7] So, there is a need for a screening procedure to detect endometrial premalignant and early malignant lesions.[8]

The routine Pap smear is not adequate for the detection of endometrial cancer as the rate of positivity is only 50%.The development of a technique for the sampling of endometrium was encouraged by Papanicolaou, who acknowledged the inadequacy of cervical smears for detecting endometrial pathologies. Papanicolaou and Marchetli described the 'sample aspiration method' in the diagnosis of cancer and other conditions of the uterus, which involved the use of a metal cannula developed by Cary in 1943.[9] The cells of aspiration show better morphology and more yield than exfoliated endometrial cells found in cervico-vaginal/pap smears.

For these reasons, there is a need for a simple, accurate and good outpatient department (OPD) procedure as an alternative to D & C. Endometrial aspiration cytology (EAC) can be used as a safe, minimally invasive, cheaper and reliable OPD procedure with minimum discomfort to the patient.[10] It is does not require anaesthesia or admission, thus seems to have more patient acceptability.

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Our main purpose was to study the various patterns of endometrial pathologies using aspiration cytology and to assess the utility of endometrial aspirate cytology in the diagnosis of these lesions considering histopathology as standard.

Material and Methods

The present study was conducted in the department of pathology of our institute during the period from December 2016 to October 2018.

It was a prospective observational study, consisting of cytological evaluation of 106 cases suspected to have endometrial pathology by the clinicians. The endometrial aspiration samples were received in the Pathology department from Gynaecology OPD. The relevant and required information pertaining to the study was collected. The smears made from the aspirates were studied and the diagnostic efficacy of aspirate cytology was assessed using the sensitivity, specificity and predictive values considering histopathological evaluation as a gold standard.

Inclusion criteria

Women in reproductive and peri-menopausal age group presenting with symptoms like menorrhagia, intermenstrual bleed/ spotting and cases of dysfunctional uterine bleeding,

per vaginal bleeding in post-menopausal women.

Exclusion criteria

Endometrial sepsis, pelvic inflammatory disease, recent abortions, suspected ectopic pregnancy confirmed by means of ultrasonography.

Procedure

After written informed consent, the patients were subjected to endometrial aspiration using a plastic disposable 4mm Karman's cannula was inserted into the endometrial cavity and a 20cc disposable syringe before biopsy or currettage. The material was put on a clean glass slide, smeared & immediately fixed in a fixative and then stained by Papanicolaou stain.[11]

The stained smears were then used for the study and later on compared with histopathological findings of the corresponding patients, the samples for which were received in the department of pathology in the form of endometrial biopsy, curettage or hysterectomy specimens. These samples were processed and stained with Haematoxylin and Eosin stain.

The cytologic criteria used for diagnosing and assessment of the endometrial aspirates were as given by Bistolleti and Hjerpe et.al.[12], Foraker et al.[13], and Meisels et al.[14]

Results

Out of 106 endometrial aspirates 102 i.e. 96.2% aspirates were adequate while 4 i.e. 3.8% were inadequate. All 106 samples received for histopathological examination were adequate in the study

Table 1: Adequacy of the material in endometrial aspiration & histopathology

	Smears from endometrial aspiration		Biopsy/hysterectomy specimen for histopathological examination	
	No. of cases	**Percentage**	**No. of cases**	**Percentage**
Adequate	102	96.2%	106	100%
Inadequate	4	3.8%	Nil	0%
Total	106	100%	106	100%

It was found that, maximum, i.e. 47 patients were in reproductive age group, 43 in peri-menopausal and 16 in post-menopausal age group.

Table 2: Cytological diagnosis of cases

Cytological Diagnosis	No. of Cases	Percentage
Proliferative endometrium	39	36.8
Secretory endometrium	7	6.6
Atrophic endometrium	5	4.7
Endometritis	3	2.8
Simple hyperplasia	25	23.6
Complex hyperplasia	25	23.6
Atypical hyperplasia	4	3.8
Malignancy	3	2.8
Inadequate	4	3.8
Total	106	100

Endometrial aspirate cytology lead to diagnosis of proliferative endometrium in maximum females i.e. 39 while in 7 cases endometrium were diagnosed to be secretory. 5 females had atrophic endometrium, 3 had endometritis and 25 had simple hyperplasia. Complex hyperplasia was noted in 4 cases, atypical hyperplasia in 16 and malignant cytological diagnosis was in 3 females while 4 aspirate samples were found inadequate .

In the study 55 females presented with menorrhagia, 7 had menometrorrhagia, 9 had metrorrhagia while 4 had oligomenorrhea. Polymenorrhea was observed in 15 females . These mainly belonged to reproductive and perimenopausal group . Rest 16 females presented with post-menopausal bleeding.

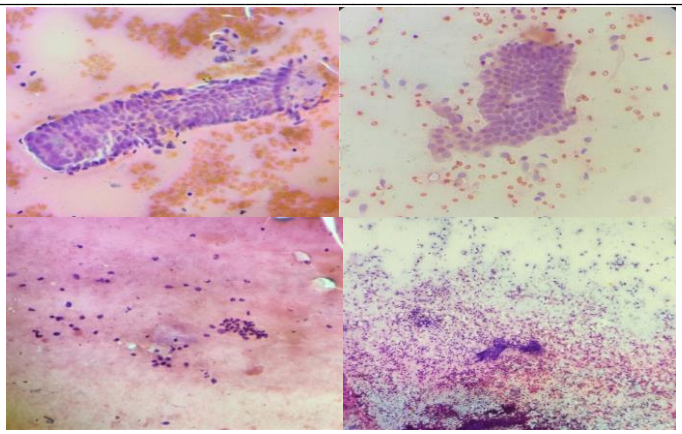

Fig 1: Various patterns of endometrium- a-Proliferative endometrium, b -Secretory endometrium, c-Atrophic endometrium (Pap,40x), d-Endometritis on cytology (Pap, 10 x)

Out of 39 cases reported as proliferative endometrium cytologically, 36 correlated well with histopathological diagnosis, 2 turned out to be simple hyperplasia and one as disordered proliferative endometrium. 7 smears were labelled as secretory endometrium cytologically. Out of them, 6 were confirmed being the same on histopathology. One case was diagnosed as Arias-Stella Reaction on histopathology. All cases labelled as endometritis, atrophic endometrium, and malignancy on cytology, were labelled as the same on histopathological examination.

Cytological diagnosis of 25 cases was given as simple hyperplasia. Histopathological diagnosis was the same in 22, whereas remaining 3 turned out to be complex hyperplasia, atypical hyperplasia and proliferative endometrium. Cytologically, 4 cases were diagnosed as complex hyperplasia and 16 cases as atypical hyperplasia, all of which, correlated well with histopathological diagnosis.(Table 3)

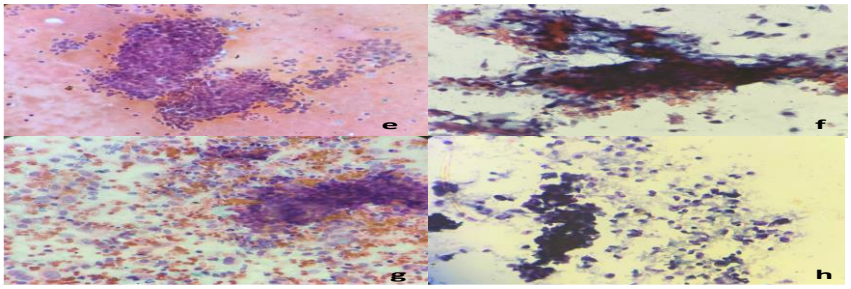

Fig 2: Endometrial hyperplasia & malignant endometrium: e-Simple hyperplasia , f-Complex hyperplasia, g-Atypical hyperplasia , h-Endometrial malignancy on cytology (Pap , 40x)

Table 3: Relation of Cytological diagnosis to histopathological diagnosis

Histopathological Diagnosis	Cytological diagnosis									Total
	Proliferative endometrium	Secretory endometrium	Endometritis	Atrophic endometrium	Simple hyperplasia	Complex hyperplasia	Atypical hyperplasia	Malignancy	Inadequate	
Proliferative endometrium	36				1				1	38
Secretory endometrium		6								6
Disordered proliferative endometrium	1									1
Endometritis			3							3
Arias-Stella Reaction		1								1
Atrophic endometrium				5					1	6
Simple Hyperplasia	2				22				2	26
Complex hyperplasia					1	4				5
Atypical hyperplasia					1		16			17
Malignancy								3		3
Total	39	7	3	5	25	4	16	3	4	106

The percentage correlation of cytological and histopathological diagnosis for proliferative endometrium was 94.7% and that for secretory endometrium was 100%. There was 100% correlation in cases of endometritis and malignancy. Correlation for atrophic endometrium was 83.3%, that for Simple hyperplasia was 84.6%, complex had 80% correlation & that for atypical hyperplasia, it was 94.1%.

Table 4: Correlation of cytological finding with histological findings

	Cytological Diagnosis	Histopathological Diagnosis	Number of cases matched	% Correlation
Proliferative endometrium	39	38	36	94.7%
Secretory endometrium	7	6	6	100%
Endometritis	3	3	3	100%
Atrophic endometrium	5	6	5	83.3%
Simple hyperplasia	25	26	22	84.6%
Complex hyperplasia	4	5	4	80%
Atypical hyperplasia	16	17	16	94.1%
Malignant	3	3	3	100%

Cytological aspirate was able to correctly diagnose 93.2% patients compared to histopathological findings while it missed 6.8% patient. 2.3% samples were wrongly given positive finding. There was 93.2% sensitivity, 97.7% specificity, 98.2% positive predictive value and 91.3% negative predictive value and with 95.1% accuracy.

Thus from all the above data, it is clear that the endometrial aspirate cytology using Karman's cannula had an adequacy of 96.2%, with an overall diagnostic accuracy of 95.1% in diagnosing endometrial pathologies. Majority of the cases of hyperplasias and malignancies were evidenced in peri and post-menopausal age groups, indicating the need of routine, practically feasible, easily applicable and reliable diagnostic test for screening of malignancy in this age group. There was good cyto-histopathological correlation with an overall sensitivity and specificity of 89-100% in all types of normal and abnormal endometrial patterns. Eventhough, EAC was unable to comment on the type of malignancy, none of the malignancy was missed by cytology.

Discussion

In the present study, a detailed cytological analysis of the endometrial samples was done based on cytomorphological parameters as described by Bistolleti and Hjerpe et.al. [12], Foraker et al. [13], Meisels et al. [14] These parameters helped to diagnose different benign, hyperplastic and malignant conditions, in coherence with studies by Malik et al[2] and K. Shashikala et al.[15] These findings were further validated by histopathological correlation.

39 were diagnosed as proliferative endometrium which showed glandular cells having uniform round nuclei and evenly distributed nuclear chromatin, with thin rim of cytoplasm arranged cohesively, in monolayered sheets or in tubules, having honeycomb pattern. The cells were lacking cytoplasmic vacuoles, which was helpful in distinguishing it from secretory endometrium. (Fig.1-a). Out of 39 cases, 36 were proved histopathologically, 2 turned out to be simple hyperplasia which may be due to the fact that simple hyperplasia represents exaggerated pattern of proliferative phase, which was seen missing in these samples and 1 as disordered proliferative endometrium. It was not possible to differentiate between proliferative and disordered proliferative endometrium cytologically. Out of the 2 extra cases which were diagnosed as proliferative on histology, one was given as simple hyperplasia, which may have been confused because of slightly hypercellular smear with few tightly packed cell clusters in this case and the other one was having inadequate material on aspiration, which may be due to technical failure.

7 were diagnosed as secretory phase endometrium owing to the their appearance which showed cells with round or oval nuclei, finely granular chromatin, and larger quantity of cytoplasm showing vacuolations and well defined borders, arranged in single layered sheets with no overlapping. The nucleo-cytoplasmic ratio is lower than that of proliferative phase with greater spacing of nuclei that leads to impression of loosely packed appearance of the sheets.(Fig.1-b) Cytology had detected all 6 cases diagnosed as secretory by histology. The remaining one was reported as Arias-Stella reaction on histopathology and was difficult to differentiate from secretory endometrium cytologically.

5 were reported as atrophic endometrium, which were showing lesser number of cell clusters with cells having smaller nuclei compared to proliferative and secretory. The cellular components were not as numerous as active endometrium.(Fig.1-c). All the 5 cases reported as atrophic on cytology proved to be the same on histopathology. One extra case, which was diagnosed as atrophic on histopathology, was inadequate cytologically, maybe due to sparce glands in the atrophic endometrium.

3 cases were labelled as endometritis cytologically, which were showing endometrial cell clusters, benign in nature, admixed with numerous inflammatory cells, predominantly consisting of lymphocytes and plasma cells. (Fig.1-d). All 3 cases were proved on histology. One of them was labelled as granulomatous endometritis, both cytologically and histopathologically and was showing background having admixture of lymphocytes and occasional aggregates of epitheloid cells. Later on, AFB was performed and turned out to be tubercular endometritis.

25 cases were diagnosed as simple hyperplasia cytologically, which were showing increased cellularity compared to proliferative endometrium with cells arranged in small and large groups, sheets, and tight clusters with cell cohesion, nuclei showing mild to moderate anisonucleosis, fine granulation, even chromatin and scant cytoplasm (Fig.2-e).Out of 25 cases, 22 were confirmed on histopathology. Of the remaining 3, one was reported as proliferative, one as complex hyperplasia and one as atypical hyperplasia on histopathology. Out of the 4 extra cases diagnosed as simple hyperplasia on histopathology, 2 were labelled as proliferative endometrium, and 2 were inadequate cytologically for opinion, maybe due to some technical failure.

Cytologically, 4 cases were labelled as complex hyperplasia, which were showing many cell clusters having branching glandular structures with marked increase in cellularity and pilling up of cells with crowding and overlapping of nuclei. Few of the cells were having prominent nucleoli with enlargement of nuclei (Fig.2-f). All 4 cases were proved to be the same histologically. One extra case was diagnosed as complex hyperplasia on histopathology, which was labelled as simple hyperplasia cytologically, this maybe be due to the fact that changes of complex hyperplasia maybe focal.

16 cases were diagnosed as atypical hyperplasia on cytology. These were the hypercellular smears having marked crowding and overlapping of nuclei with cells having increased nucleo-cytoplasmic ratio. Cellular atypia was notable. Majority of the cells were having prominent nucleoli (Fig.2-g). All the 16 were proved histopathologically.

3 cases were diagnosed as malignant cytologically. They were showing cells with marked anisonucleiosis, with extreme variation in cell size and shape, loss of nuclear polarity, prominent nucleoli, hyperchromasia or increased granularity of nuclear chromatin. The cells were found dispersed, singly scattered and few in small and large clusters.(Fig.2-h). All 3 cases turned out to be malignant on histopathology, 2 being endometrioid type of adenocarcinoma and one was diagnosed as malignant mixed mullerian tumour. Cytologically, it was not possible to detect the type of malignancy. But still, an accurate interpretation was done on cytology regarding the malignant nature of the cells.

Out of 106 endometrial aspirates 102 i.e. 96.2% aspirates were adequate while 4 i.e 3.8% were inadequate. These results are concordant with Hemalatha et al [10] and K. Shashikala et al. [15], Ashraf S and Jabeen F[16] , Jyoti B. Saikia and Adity Sharma[17], and Handa et al[18] who also used Karman's cannula for obtaining the aspirate.

Table 5: Adequacy of material in various studies

	Adequacy of material (%)
Hemalatha et al. [10]	95
Ashraf S, Jabeen F. [16]	93.4
K. Shashikala et al. [15]	92
Jyoti S., Adity S[17]	93.06
Handa et al.[18]	89
Present study	**96.2**

In the present study, it was found that there was 94.7 % correlation for proliferative endometrium similar to Jyoti Saikia and Adity Sharma[17]. and Liza et al[19].

Percentage correlation of 100 % was observed for secretory endometrium in the present study, which is similar to studies by Malik et al.[2] and Jyoti Saikia and Adity Sharma[17]. Hyperplasia showed 87.5 % correlation, which is comparable to that of Liza et al.[19] , Schachter et al.[20] ,and Vennila M . et al.[21]

Table 6: Percentage correlation between cytology and histology in various studies

	Present study	Schachter et al[20]	Liza et al.[19]	Malik et al.[2]	Jyoti Saikia & Adity Sharma[17]	Vennila M . et al.[21]
Proliferative endometrium	**94.7**	86.4	100	87.4	90.90	100
Secretory endometrium	**100**	78.5	82.3	100	100	92.3
Endometrial hyperplasia	**87.5**	77	82.6	67	70.31	77
Malignancy	**100**	100	100	100	100	83.3

In the present study, Karman's cannula was used for obtaining endometrial aspirate and the sensitivity observed was 93.2% and specificity was 97.7% .This is in coherence with Shashikala et al.[15] who also used Karman's cannula and observed sensivity of 93 % and specificity of 85.7 %. Similar observations were also noted by Bistoletti et al.[12], Favre et al.[5], Malik et al.[2], and Foraker et al[13] who used Endo-pap sampler, Gravlee jet washer, Insemination cannula, and Isaac cell sampler respectively for obtaining endometrial aspirate.

Table 7: Comparison of sensitivity and specificity in various studies

	Technique	Sensitivity(%)	Specificity(%)
Bistoletti et al.[12]	Endo-pap sampler	97	84
Shashikala et al.[15]	Karman's cannula	93	85.7
Favre et al.[5]	Gravlee jet washer	88.1	98.6
Malik et al.[2]	Insemination cannula	83.3	95.4
Foraker et al.[13]	Isaac cell sampler	96.15	96.85
Present study	Karman's cannula	93.2	97.7

Thus from above data, we can comment that the adequacy of sample by Karman's cannula is 9.2% which appreciable. The sensitivity and specificity by different instruments almost similar thus, type of instrument used did not affect the outcome much. We preferred the use of Karman's cannula because of its easy availability, patient acceptability because of minimal discomfort to the patient and cheaper cost.

In the present study, the accuracy of endometrial aspirate cytology in diagnosing abnormal endometrium was found to be 95.1 %. This is comparable with diagnostic accuracies of Jadhav et al.[22] and Jyoti Saikia and Adity Sharma[17] who obtained accuracy of 90.4 % and 93.29 % respectively. The sensitivity and specificity of aspirate cytology for endometrial malignancy was found to be 100 % and 100 % respectively, which is comparable to findings of Kaur et al.[23] who observed a sensitivity of 100 % and specificity of 96.51 %, also Handa et al.[18] observed a sensitivity of 100 % and specificity of 96.51 %.

Thus the results of the cytological examination in terms of sensitivity, specificity and diagnostic accuracies in detection of malignancies and the pre-malignant conditions such as atypical hyperplasias, were satisfactory. Even though the further categorisation was difficult on cytology, it can be effectively used as a screening procedure in order to detect the pre-malignant and malignant lesions of endometrium at an early stage.

Conclusion

Endometrial aspiration cytology was found to be an easy, safe, comparatively cheaper and minimally invasive out-patient procedure for diagnosing endometrial pathologies, carried out without any need of anaesthesia. The Karman's cannula used in the study was a good and effective alternative to other expensive devices used for aspiration, and had good patient acceptability.

On cytology, it was possible to diagnose majority of the patterns ranging across the morphologic spectrum of endometrial pathologies, including normal phases of endometrium.

The percentage correlation of aspirate cytology with respect to histopathology was found to be 100% in cases of endometritis, secretory endometrium and malignancies. For other endometrial findings, it ranged from 80-100%. The results of the cytological examination in terms of sensitivity, specificity and diagnostic accuracies in detection of malignancies and the pre-malignant conditions such as atypical hyperplasias, were satisfactory. Even though the further categorisation was difficult on cytology, it can be effectively used as a screening procedure in order to detect the pre-malignant and malignant lesions of endometrium at an early stage.

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