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Comparison of cytomorphology and frozen section of endometrial aspiration with histopathology in abnormal uterine bleeding

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Abstract
Background: Endometrial aspiration cytology is the latest available modality for the study of endometrial diseases. A large range of diseases like atypia's, malignancies, and infective changes can be diagnosed using a cytological examination.
Aim and Objectives: To assess the adequacy of the aspirate of endometrium for cytological examination and correlating the diagnosing efficiency with frozen section and histopathology.
Methods: A cross sectional study was conducted at department of pathology, tertiary care health center in Pondicherry. Endometrial aspiration and Curettage were done in 58 perimenopausal women with abnormal uterine bleeding. Endometrial aspiration sample were subjected for cytological examination by Papanicolaou staining and May- Grunewald- Gimesa staining, frozen section and histopathology examination with Hematoxalin & Eosin staining. Diagnostic accuracy was compared with gold standard histopathological examination. Sensitivity, specificity and predictive values were calculated.
Results: Among 58 participants, the mean age was 45.02 ± 4.12 years. Majority (63.79%) of the participants had menorrhagia. High cellularity was seen in 58.62%. Sheets were the most commonly observed pattern on cytology (65.52%). The cytological diagnosis of simple hyperplasia had sensitivity of 100% and specificity was 94.44% in predicting HPE diagnosis. The frozen section of simple hyperplasia had sensitivity of 100% in predicting HPE diagnosis.
Conclusion: Endometrial aspiration cytology and frozen section are useful and minimally invasive techniques that can be utilized for the diagnosis of endometrial pathologies at par with the efficiency of histopathological examination.

Keywords: Cytomorphology, frozen section, histopathology, abnormal uterine bleeding, Karman's cannula, Perimenopausal women

Introduction
Bleeding from the uterus that is abnormal in volume, regularity or timing is defined as abnormal uterine bleeding [1]. Abnormal uterine bleeding occurs in 14 to 25% of the reproductive age group women [2]. Endometrium is subjected to constant changes due to influence of hormones and proliferative changes; malignancies are prone to occur. Traditional method used for the assessment of the endometrial status was dilatation and curettage. It is an invasive procedure that needs anesthetic block and is time consuming to perform. The post procedure recovery time is considerably long. With recent advancements, more noninvasive or minimally invasive techniques are available for assessment of endometrium [3]. One such technique is endometrial aspiration. It can be done in both premenopausal and postmenopausal women [4]. It is thought to be the effective and safest method for histopathological (HPE) assessment of the endometrium. A wide variety of lesions such as atypias, inflammatory changes, carcinoma and infectious conditions can be detected by this method. This technique can be repeated overtime and follow-up of high-risk cases can be done for checking the development of malignancy. Women on hormone replacement therapy can be followed up as they are at risk of developing endometrial carcinoma [5, 6]. Papanicolaou and Marchetil were the ones who first discovered endometrial aspiration. They utilized a metal cannula inserted into the uterus to aspirate the endometrium for diagnosis of cancer lesions. The first ever cannula was development in the year 1943 by Cary. Various other devices such as endometrial brush, endo pap sampler, and disposable plastic cannula were used [7, 2].

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Karman's plastic cannula is being used for the aspiration that can be done in the outpatient settings. This procedure can avoid admissions and morbidity caused due to invasive procedures [8, 9, 6].

As per previous studies, endometrial aspiration is as efficient as D and C in diagnosing atypias and carcinomas [10-12]. A study done by Ankur et al. [13] has compared the diagnostic accuracy of endometrial aspiration against dilatation and curettage. The study was done among 100 women with AUB. The authors concluded that aspiration cytology is efficient and minimally invase compared to HPE. Literature is available for the efficiency of cytology, whereas it has been hypothesized that frozen section of the aspirate can give similar result in short duration and technicality. Even though previous literature states the advantage, being an effective, inexpensive method endometrial aspiration cytology and frozen section s has not obtained the acceptance of clinicians. Hence, this study was undertaken with aim to compare the efficiency of frozen section, cytology with that of histopathological examination in diagnosing the endometrial diseases.

Materials and Methods

A cross sectional study was done at Department of pathology in a Tertiary care health center, during the period of three years from July 2013 to June 2016 with primary objective to study the diagnostic efficacy of cytomorphology and frozen section with Histopathological examination and secondary objective to compare the predictability of these methods in diagnosing endometrial diseases. Institutional ethical committee approval was obtained. Informed written consent of the participants was obtained and confidentiality maintained. Study participants attending tertiary care hospital where selected based on inclusion and exclusion criteria. Convenient sampling technique was followed. A total of 58 subjects were studied. Sample size was calculated assuming the proportion of hyperplasia in HPE diagnosis as 22.1% as per the study by Kaur N et al., [14] The other parameters considered for sample size calculation were 12% absolute precision and 95% confidence level. An infinite population correction was applied. The following formula was used for sample size calculation [15].

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where n = Sample size, Z= Z statistic for a level of confidence, P = Expected prevalence of proportion (If the expected prevalence is 22.1%, then P= 0.221), and d = Precision (If the precision is 12%, then d=0.12). The required number of subjects as per the above-mentioned calculation was 46. To account for a non-participation rate of about 20% (10 subjects), it was decided to sample about 58 subjects in to the study. Those patients with clinical diagnosis of AUB were recruited into the study. Patients having acute inflammatory disorders of genital tract, cervical malignancy and pregnancy were excluded from the study and the study included patients above 40 years of age with menorrhagia, polymenorrhoea and post-menopausal bleeding who required D&C as recommended by the Gynecologist. As per a standardized protocol, thorough history was taken, physical examination, laboratory investigations were done. The study protocol was explained to the patient and after informed consent was obtained. Those consented participants were subjected to endometrial aspiration cytology followed by curettage. As per the hospital protocol under strict aseptic precautions, endometrial aspiration was done and curettage was performed either in the OPD or in the operating theater, before dilatation and curettage. A 4mm Karman's cannula was introduced into the endometrial cavity with a 20cc sterile disposable syringe attached to it. A slow suction force was given through the syringe and vacuum was created. This force sucks in the endometrial tissue into the syringe as an aspirate. Aspirated material divided into two parts and first portion subjected for frozen section with H& E staining, with second portion of the aspirated material a smear was prepared on a clean glass slide and air dried. Fixation of the smear was done using methanol. These were stained with May-Grunewald-Giemsa stain. Some of the smears were immediately fixed in 95% ethyl alcohol and then stained with Papanicolaou stain. The adequacy of the cytology smears was assessed using Bistoletti and Hjerpe criteria. 10 to 20 endometrial fragments were considered adequate. Following this, all patients were subjected to routine D and C. the tissue sample obtained was formalin fixed and paraffin blocks were made for routine histopathological examination. Hematoxylin and eosin (H and E) staining was done. Using five microns cut slices. Finally, the diagnosis obtained through cytology, histopathology and frozen section were all compared using appropriate statistical tests.

Statistical Methods

Cytological diagnosis, HPE diagnosis and frozen section were considered as primary outcome variable. Demographic parameter like age, clinical parameter like presenting complaints, clinical diagnosis, cellularity, pattern, cytoplasm, nuclearize, nuclei atypias, chromatin, nucleoli, mitosis, stroma, secretary activity, infectious cells, bare nuclei, vascularity, necrosis and b/g were considered as Primary explanatory variable. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. HPE diagnosis was considered as gold standard. Diagnosis and frozen section were considered as screening test. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening test along with their 95% CI were presented. Reliability of the screening test was assessed by kappa statistic along with its 95% CI and p Value.P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis. A total of 58 subjects were included in the final analysis.

Results

The mean age was 45.02 ± 4.12(ranged 40 to 55 years) in the study population. Among the study population, majority (63.79%) participants had menorrhagia. Out of 58 subjects, 30(51.72%) had dysfunctional uterine bleeding. 20subjects (34.48%) had fibroid and 6 subjects (10.34%) had adenomyosis. Among the study population, 34(58.62%) participants had high cellularity, 5(8.62%) had low cellularity and 19(32.76%) people had moderate cellularity. Majority (65.52%) of the subjects had sheets, the followed by 24.14% people had papillaroid ad 5.17% people had small clusters. (Table 1)

Table 1: Summary of demographic and comorbidities of the participants (N=58)

Parameter	Summary
Age**(mean±SD) (in years)**	45.02 ± 4.12 (range 40 to 55)
Menorrhagia	37(63.79%)
Menorrhagia associated with dysmenorrhoea	16(27.59%)
Amenorrhea	3(5.17%)
Postmenopausal bleeding	2(3.45%)
Clinical Diagnosis	
Dysfunctional Uterine Bleeding	30(51.72%)
Fibroid	20(34.48%)
Adenomyosis	6(10.34%)
Endometrial polyp	1(1.72%)
Hyperplasia	1(1.72%)
Cellularity	
High cellularity	34(58.62%)
Low cellularity	5(8.62%)
Moderate cellularity	19(32.76%)
Pattern	
Sheets	38(65.52%)
Papillaroid	14(24.14%)
Small clusters	3(5.17%)
Dyscohesive clusters	2(3.45%)
Clusters	1(1.72%)
Cytoplasm	
Abundant	16(27.59%)
Moderate cellularity	11(18.97%)
Scanty	31(53.45%)
Nuclearize	
Anisonucleosis	29(50.00%)
Normal nuclei	26(44.83%)
Macronucleoli	3(5.17%)
Nuclei atypia	3(5.17%)
Chromatin	
Granular chromatin	37(63.79%)
Fine granular chromatin	18(31.03%)
Coarse granular chromatin	3(5.17%)
Nucleoli	6(10.34%)
Mitosis	3(5.17%)
Stroma	
Scanty	26(44.83%)
Abundant	17(29.31%)
Moderate cellularity	15(25.86%)
Sec.Activity	20(34.48%)
Inf.Cells	21(36.21%)
Barenuclei	49(84.48%)
Vascularity	
High vascularity	31(53.45%)
Low vascularity	13(22.41%)
Moderate vascularity	14(24.14%)
Necrosis	5(8.62%)
B/G	
Haemorrhage	40(68.97%)
Absent	12(20.69%)
Cytolysis	4(6.90%)
Nuclear debris	2(3.45%)

Among the people with diagnosis, majority 41.38% of the subjects had simple hyperplasia. Among the people with HPE diagnosis, majority 37.93% of the subjects had simple hyperplasia. Majority 39.7% of the subjects had frozen section of simple hyperplasia (Table 2)

Table 2: Summary of cytological diagnosis, HPE diagnosis and frozen section parameters (N=58)

Parameter	Summary
Diagnosis	
Simple Hyperplasia	24(41.38%)
Secretory Phase endometrium	21(36.2%)

Shedding Endometrium	5(8.62%)
Endometritis	4(6.90%)
Adenocarcinoma	2(3.45%)
Atypical hyperplasia	1(1.72%)
Decidual Reaction	1(1.72%)
HPEdiagnosis	
Simple Hyperplasia	22(37.93%)
Secretory Phase endometrium	21(36.21%)
Endometritis	5(8.62%)
Shedding Endometrium	4(6.90%)
Decidual Reaction	1(1.72%)
Adenocarcinoma	2(3.45%)
Atypical hyperplasia	1(1.72%)
Endometrial polyp	1(1.72%)
Pill Endometrium	1(1.72%)
Frozen section	
Simple Hyperplasia	23(39.7%)
Secretory Phase endometrium	22(37.9%)
Endometritis	5(8.62%)
Shedding Endometrium	5(8.62%)
Adeno carcinoma	2(3.45%)
Atypical hyperplasia	1(1.72%)

Among the people with HPE diagnosis of simple hyperplasia group, 22 (100%) people had diagnosis simple hyperplasia by cytology. Among the people with HPE diagnosis of Secretory Phase endometrium group,20 (95.24%) people had diagnosis Secretory Phase endometrium by cytology also. Among the people with HPE diagnosis of shedding endometrium group, 2 (50%) people had diagnosis shedding endometrium by cytology. (Table 3)

Table 3: Comparison of cytological diagnosis with HPE diagnosis (N=58)

Simple Hyperplasia	**Simple Hyperplasia**		P value
	Yes (N=22)	No (N=36)	
Yes	22 (100%)	2 (5.56%)	*
No	0 (0%)	34 (94.44%)	
Secretory Phase endometrium	Secretory Phase endometrium		
	Yes (N=21)	No (N=37)	
Yes	20 (95.24%)	0 (0%)	*
No	1 (4.76%)	37 (100%)	
Shedding endometrium	Shedding endometrium		
	Yes (N=4)	No (N=54)	
Yes	2 (50%)	3 (5.56%)	0.002
No	2 (50%)	51 (94.44%)	
Endometritis	Endometritis		
	Yes (N=5)	No (N=53)	
Yes	4 (80%)	0 (0%)	*
No	1 (20%)	53 (100%)	
Carcinoma	Carcinoma		
	Yes (N=2)	No (N=56)	
Yes	2 (100%)	0 (0%)	*
No	0 (0%)	56 (100%)	
Atypical Hyperplasia	Atypical Hyperplasia		
	Yes (N=1)	No (N=57)	
Yes	1 (100%)	0 (0%)	*
No	0 (0%)	57 (100%)	
Decidual Reaction	Decidual Reaction		
	Yes (N=1)	No (N=57)	
Yes	0 (0%)	1 (1.75%)	*
No	1 (100%)	56 (98.25%)	

* No statistical test was applied-due to 0 subjects in the cell

The cytological diagnosis of simple hyperplasia had sensitivity of 100% in predicting HPE diagnosis. Specificity was 94.44%, positive predictive value was 91.67%, negative predictive value was 100% and the total diagnostic accuracy was 96.55%. The cytological diagnosis of secretory Phase endometrium had sensitivity of 95.24%in predicting HPE diagnosis. Specificity was 100.00%, positive predictive value was 100.00%, negative predictive value was 97.37% and the total diagnostic accuracy was 98.28%. (Table 4)

Table 4: Predictive validity of cytological diagnosis in predicting HPE diagnosis (N=58)

Parameter	Diagnosis	HPE diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Simple Hyperplasia	24	22	100.00%	94.44%	91.67%	100.00%	96.55%
Secretory Phase endometrium	20	21	95.24%	100.00%	100.00%	97.37%	98.28%
Shedding endometrium	5	4	50.00%	94.44%	40.00%	96.23%	91.38%
Endometritis	4	5	80.00%	100.00%	100.00%	98.15%	98.28%
Adenocarcinoma	2	2	100.00%	100.00%	100.00%	100.00%	100.00%
Atypical hyperplasia	1	1	100.00%	100.00%	100.00%	100.00%	100.00%
Decidual Reaction	1	1	0.00%	98.25%	0.00%	98.25%	96.55%

Among the people with HPE diagnosis of simple hyperplasia group,22 (100%) people had frozen section diagnosis of simple hyperplasia. People with HPE diagnosis of Secretory Phase endometrium group,21 (100%) people had frozen section diagnosis of Secretory Phase endometrium. (Table 5)

Table 5: Comparison of frozen section diagnosis with HPE diagnosis (N=58)

Simple Hyperplasia	Simple Hyperplasia		P value
	Yes (N=22)	No (N=36)	
Yes	22 (100%)	1 (2.78%)	*
No	0 (0%)	35 (97.22%)	
Secretory Phase endometrium	Secretory Phase endometrium		
	Yes (N=21)	No (N=37)	
Yes	21 (100%)	1 (2.7%)	*
No	0 (0%)	36 (97.3%)	
Endometritis	Endometritis		
	Yes (N=5)	No (N=53)	
Yes	5 (100%)	0 (0%)	*
No	0 (0%)	53 (100%)	
Shedding endometrium	Shedding endometrium		
	Yes (N=5)	No (N=53)	
Yes	4 (80%)	0 (0%)	*
No	1 (20%)	53 (100%)	
Carcinoma	Carcinoma		
	Yes (N=2)	No (N=56)	
Yes	2 (100%)	0 (0%)	*
No	0 (0%)	56 (100%)	
Atypical Hyperplasia	Atypical Hyperplasia		
	Yes (N=1)	No (N=57)	
Yes	1 (100%)	0 (0%)	*
No	0 (0%)	57 (100%)	

* No statistical test was applied-due to 0 subjects in the cell

The frozen section diagnosis of simple hyperplasia had sensitivity of 100%in predicting HPE diagnosis. Specificity was 97.22%, positive predictive value was 95.65%, negative predictive value was 100% and the total diagnostic accuracy was 98.28%. The frozen section diagnosis of secretory Phase endometrium had sensitivity of 100.00%in predicting HPE diagnosis. Specificity was 97.30%, positive predictive value was 95.45%, negative predictive value was 100.00%and the total diagnostic accuracy was 98.28%. (Table 6)

Table 6: Predictive validity of frozen section diagnosis in predicting HPE diagnosis (N=58)

Parameter	Frozen section	HPE diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Simple Hyperplasia	23	22	100.00%	97.22%	95.65%	100.00%	98.28%
Secretory Phase endometrium	22	21	100.00%	97.30%	95.45%	100.00%	98.28%
Endometritis	5	5	100.00%	100.00%	100.00%	100.00%	100.00%
Shedding Endometrium	5	4	100.00%	98.15%	80.00%	100.00%	98.28%
Adenocarcinoma	2	2	100.00%	100.00%	100.00%	100.00%	100.00%
Atypical hyperplasia	1	1	100.00%	100.00%	100.00%	100.00%	100.00%

Discussion

A cross sectional study was done among 58 subjects with complaints of abnormal uterine bleeding. They were subjected to endometrial aspiration using Karman's cannula followed by dilatation and curettage. The aspirate sample was subjected to cytology and frozen section study and the tissue from dilatation and curettage to histopathological examination. In this current study, it was observed that

frozen section and cytological examination had diagnostic accuracy at par with histopathological examination. This creates evidence for minimally invasive procedures that can be used for the early diagnosis of endometrial changes.

In absence of effective screening programs and wide usage of invasive procedures have led to delay in the diagnosis of endometrial carcinomas [16]. Researchers are still concentrating on early diagnosis of endometrial malignant diseases, especially its precancerous lesion.

The age range of the study participants was 45.02 ± 4.12. it was comparable to the mean age of 44 years in the study done by Liza *et al*. [17]. The most common age group of presentation I this study was perimenopausal similar to other study [10]. The most common presenting complaint was menorrhagia this was similar to the observations by Kaur *et al*. [14]. In this study the endometrial aspirate adequacy was assessed based on the presence of endometrial tissue or cells. A total of 10 to 20 endometrial cell fragments were taken as an adequate aspirate. Based on these criteria all the samples in this study were adequate. In this study there was good correlation between the histopathological and cytomorphological group. This findings was similar to the study by Hemalatha *et al*. were 95% correlation was observed by the researchers [18]. Diagnostic efficacy of cytology with histopathological examination was 100 percentage in adenocarcinoma and atypical hyperplasia, similar findings were observed in previous literature [19, 20]. Endometrial aspiration using Karman's cannula proves effective in diagnosing various endometrial pathology. However, it is limited in cases of cervical stenosis, bladder and uterine prolapse and in cases of endometrial atrophy [21, 22]. The percentage accuracy of cytology in diagnosing simple hyperplasia was 96.55% and by frozen section was 98.28%. This was comparable with the studies by Kyroudi *et al*. [23], Segadal *et al*. [24] and 100% in diagnosing malignancy in malignancy both by cytology and frozen section. This was similar to study by Papaefthimiou *et al*. in which the accuracy was 98.7%.

Hence, Endometrial aspiration cytology and frozen section has clearly a valuable role in the preliminary evaluation of women presenting with abnormal uterine bleeding.

Conclusion
Based on the evidence from this study, endometrial aspiration cytology and frozen section can be utilized as a minimally invasive procedure for the assessment of abnormal uterine bleeding in women. With a good cytology setup and proper interpretation can diagnose the endometrial pathologies similar to histopathological examination. These being minimally invasive can be used as an outpatient procedure thereby preventing anesthetic complications and morbidity. These procedures can improve the early detection of endometrial malignancies and enable timely appropriate treatment.

Declarations
Conflict of interests: The authors declare no conflicts of interest.

References
1. Tehranian A, Rezaii N, Mohit M, Eslami B, Arab M, Asgari Z. Evaluation of women presenting with postcoital bleeding by cytology and colposcopy. Int J Gynaecol Obstet Off organ Int Fed Gynaecol Obstet 2009;105(1):18-20.
2. Ozdemir S, Celik C, Gezginç K, Kıreşi D, Esen H. Evaluation of endometrial thickness with transvaginal ultrasonography and histopathology in premenopausal women with abnormal vaginal bleeding. Arch Gynecol Obstet 2010;282(4):395-9.
3. Kaliyamoorthy S, Gandhi R. A Study to Determine the Diagnostic Accuracy of Endometrial aspiration Cytology with Histopathological Correlation at Rural Tertiary Health Care Hospital. Ann Pathol Lab Med. 2018;5(11)(A):916-22.
4. Malik R, Agarwal R, Tandon P. Cytological assessment of endometrial washings obtained with an insemination cannula and its histological correlation. Journal of Cytology 2008;25(4):128-132.
5. Fraser IS, Langham S, Uhl-Hochgraeber K. Health-related quality of life and economic burden of abnormal uterine bleeding. Expert Review of Obstetrics and Gynecology 2009;4(2):179-89.
6. Jadhav MV, Phatke AS, Kadgi NV, Rane SR, Kulkarni KK. Endometrial aspiration cytology in gynecological disorders. J Cytol 2016;33(1):13-6.
7. Garcia F, Barker B, Davis J, Shelton T, Harrigill K, Schalk N *et al*. Thin-layer cytology and histopathology in the evaluation of abnormal uterine bleeding. J Reprod Med 2003;48(11):882-8.
8. Isaac JH, Ross FH jr. Cytologic evaluation of endometrium in women with post-menopausal bleeding. Am J Obs Gynecol 1978;131(4):410-5.
9. Dharan M. Utility of cell block preparation in endometrial aspiration cytology: A report of 4 cases. Acta Cytol 2010;54(5):893-7.
10. Meena J Bhardwaj V. Evaluation of endometrial aspiration cytology in diagnosis of normal and abnormal endometrium and its correlation with histopathology. J Adv Res Biol Sci 2013;5(4):366-9.
11. Kaur N, Chahal JS, Bandlish U, Kaul R, Mardi K, Kaur H. Correlation between cytological and histopathological examination of the endometrium in abnormal uterine bleeding. J Cytol. 2014;31(3):144–8.
12. Koss, Leopoland G, Melamed, Myron R. Diagnostic cytology & its histopathologic basis. Edn Philadelphia: Lippincott Williams & Wilkins 2005;5:2.
13. Nama A, Kochar S, Suthar N, Kumar A, Solanki K. Accuracy of Karman endometrial aspiration in comparison to conventional D and C in women with AUB at tertiary care hospital in North West Rajasthan. J Fam Med Prim Care 2020;9(7):3496-3501.
14. Kaur N, Chahal JS, Bandlish U, Kaul R, Mardi K, Kaur H. Correlation between cytological and histopathological examination of the endometrium in abnormal uterine bleeding. J Cytol 2014;31(3):144-8.
15. Betty R. Kirkwood and Jonathan A. C. Sterne. Essential medical statistics. Edn 1, John Wiley & Sons 2010.
16. Sorosky JI. Endometrial cancer. Obs Gynecol.

2012;120(2-1):383-97.

17. Liza S, Ramesh Kumar K, Lillian S. Value of endometrial aspiration cytology in assessing endometrial status in symptomatic Peri and postmenopausal women. Indian J Cancer 1999;36(1):57-61.

18. Hemalatha AN, Pai MR, Raghuveer CV. Endometrial aspiration cytology in dysfunctional uterine bleeding. Indian J Pathol Microbiol 2006;49(2):214-7.

19. Shu YJ IFI. Cytopathology of the Endometrium-Correlation with Histopathology. New York McGraw Hill 1992,26-161.

20. Meisels A, Jolicoeur C. Criteria for the cytologic assessment of hyperplasias in endometrial samples obtained by the Endopap Endometrial Sampler. Acta Cytol 1985;29(3):297-302.

21. Fakhar S, Saeed G, Khan AH, Alam AY. Validity of pipelle endometrial sampling in patients with abnormal uterine bleeding. Ann Saudi Med 2008;28(3):188-91.

22. Gordon SJ, Westgate J. The incidence and Management of Failed Pipelle Sampling in a general outpatient clinic. Aust New Zeal J Obs Gynaecol 1999;39(1):115-8.

23. Kyroudi A, Paefthimiou M, Symiakaki H, Mentzelopoulou P, Voulgaris Z KP. Increasing diagnostic accuracy with a cell block preparation from thin-layer endometrial cytology: a feasibility study. Acta Cytol 2006;5((1):63-9.

24. Segadal E, Iversen OE UM. Comparison of cytological "jet-wash" specimens and histology in endometrial carcinoma. J Clin Pathol 1980;33(7):688-90.