Study of Endometrial Aspiration Cytology and Its Correlation with HPE in Cases of Dub

Authors
Dr PS. Shangreihow¹, Dr Nameirakpam Somananda², Dr Soreingam Kasar³, Dr Th. Digel Singh⁴, Dr Ng. Indrakumar Singh⁵
¹,²,³Post Graduate Trainee, Dept. of Obs. & Gynae, JNIMS, Imphal Manipur
⁴Associate Professor, Dept. of Obs. & Gynae, JNIMS, Imphal Manipur
⁵Professor, Dept. of Obs. & Gynae, JNIMS, Imphal Manipur

Abstract

**Background:** Endometrial aspiration cytology has long been undermined, but has now emerged as a powerful yet cost effective tool for diagnosing DUB in resource limited settings.

**Purpose:** The current study compares the accuracy of EAC with HPE as gold standard in diagnosis of DUB in women. It also determines the various morphologic patterns of endometrium in DUB.

**Methods:** 70 women diagnosed as DUB were subjected to endometrial aspiration with 4mm Karman’s cannula and MR syringe prior to D&C and HPE sampling. Data was compiled & analysed with SPSS 18 package. Patients were analysed based on socioeconomic, clinical parameters; cytological diagnosis was compared against HPE diagnosis based on sensitivity, specificity, diagnostic accuracy.

**Result:** EAC showed a sampling adequacy of 90%. The commonest lesion detected was proliferative endometrium followed by secretory endometrium and hyperplasia without atypia. Sensitivity for detecting proliferative endometrium was 100%, specificity 89.2% and accuracy of 89.2% against gold standard HPE. Sensitivity for detecting secretory endometrium was 100%, specificity 92.8% and accuracy was 88.5%. Sensitivity and specificity of detecting hyperplasia by aspiration cytology was 64% and 100% respectively. Accuracy was 90%. Sensitivity of aspiration cytology in detecting adenocarcinoma was 50% and specificity was 100% in this study with Accuracy of detection being 97% in this study.

**Conclusion:** Endometrial aspiration is an effective, useful and a minimally invasive procedure comparing with gold standard HPE.

Background
Defined as abnormal bleeding from the uterus in the absence of any organic pathology of the genital tract, DUB is one of the most frequently encountered conditions in the gynecological practice and accounts for approximately 10% of all new patients. Endometrial interpretation is valuable not only to find the etiology of DUB but also to rule out any organic cause for abnormal uterine bleeding. Exfoliative cytology has a unique place in the study of female genital tract lesions. Endometrial aspiration study has attempted to overcome the intrinsic weakness of vaginal and cervical smears in diagnosis of endometrial pathology. This study attempts to bust the myth of utter inadequacy of EAC as a first line, cost effective, painless, minimally invasive diagnostic tool for diagnosing DUB compared to
gold standard HPE studies, which albeit being marginally more accurate is laborious and costly.

**Aims of the Present Study**
The current study aims to evaluate the efficacy of endometrial aspiration cytology vs D&C in the diagnosis of dysfunctional uterine bleeding by correlating with histopathology. Additionally, we try to determine the various morphologic patterns of endometrium in DUB.

**Materials and Method**
70 cases of clinically diagnosed DUB at Dept of OBGYN at JNIMS, a tertiary care centre, with their informed consent, were recruited in our cross sectional study from September 2017 to March 2019. Endometrial aspiration with 4mm diameter Karman’s cannula and MR syringe prior to D&C/Hysterectomy for HPE study was done. Various variables like age, address, religion, symptoms, parity, haemoglobin, USG finding, cytology finding, HPE finding were entered in Microsoft excel 2019. Data were checked for consistency and accurateness. Data was analysed using SPSS 18 and were tabulated in mean and percentages. Sensitivity, specificity and accuracy was calculated for each method.

**Results and Discussion**
Our study shows majority of the patients were in the age group 40-50 years (50%) followed by 30-40 years (42.9%) and >50 years in 7.1% of cases (mean age of 42.5 ± 6.3 years) with anaemia in 70% of cases. In the study by Patil P et al, 80% of women belonged to age group of 40 - 49 years which is in concordance with this study. It was comparable to the mean age (44 years) of 51 patients selected for the study by Liza et al².

![Figure 1: Distribution of the respondents by symptoms](image)

Prolonged menstruation was the commonest symptom in 57% of cases; followed by heavy menstrual bleeding (48.6%), spotting (24.2%), dysmenorrhoea (17.1%) and intermenstrual bleeding (12.8%). Same was observed in the study by Devi LS et al³.

The following table elucidates the commonest endometrial patterns in some other contemporary studies.
Table: Table showing commonest endometrial findings in some studies:

| Studies           | Commonest Endometrial patterns | Percentage |
|-------------------|-------------------------------|------------|
| Rao et al         | Proliferative endometrium     | 43%        |
| Tripathy et al    | Secretory endometrium         | 45%        |
| Hemaalatha et al  | Secretory endometrium         | 54%        |
| Morse et al       | Proliferative endometrium     | 50%        |
| Perween et al     | Proliferative endometrium     | 46.15%     |
| Present study     | Proliferative endometrium     | 34%        |

Figure 2: Distribution of the respondents by BMI

80% of cases were of normal BMI, followed by overweight (BMI: 25-29.9) in 14.2% of cases and obese in 5.8% (BMI>30) as shown above. Pre aspiration Speculum examination & USG screen were done in all patients. In USG, bulky uterus was found in 55.7% of cases followed by thickened endometrium in 27.1% of cases, and 17.2% had no aberrant find. On cervical speculum examination half of them were healthy, erosion in 28.6%, cervicitis in 28.6% and enlarged cervix in 7.1%.

Table 1: Distribution of the respondents by cytology and histopathologic finding:

| Finding                              | Cytology n(%) | HPE n(%) | Consistent | Inconsistent |
|--------------------------------------|---------------|----------|------------|-------------|
| Proliferative endometrium            | 29(41.4)      | 24(34.2) | 24         | 5           |
| Secretary endometrium                | 15(21.4)      | 14(20.0) | 14         | 1           |
| Mixed (irregular)                    | 10(14.2)      | 12(17.1) | 10         | 2           |
| Endometrial hyperplasia without atypia| 9(12.8)      | 14(20.0) | 9          | 5           |
| Adenocarcinoma                       | 2(2.1)        | 4(4.2)   | 2          | 2           |
| Inadequate                           | 5(7.3)        | 2(2.1)   | 2          | 3           |
| Total                                | 70 (100.0)    | 70 (100.0)| -         | -           |

In cytology, 29 were diagnosed as proliferative vs 24 in HPE study, 15 were secretory vs 14 on HPE, 10 were mixed as compared to 12 by HPE, 9 were hyperplasia vs 14 by HPE and adenocarcinoma in 6 cases vs 4 cases by HPE. 7 cases (8%) had inadequate sample.

Below we break down each endometrial picture, and compare accuracy of EAC with gold standard HPE study.
Table 2: Distribution of the respondents by cytology and histopathologic finding

| Cytology       | HPE (gold standard) | Fisher exact test |
|----------------|---------------------|------------------|
|                | Proliferative n(%)  | Non proliferative n(%) | Total N(%) |
| Proliferative  | 24 (100.0)          | 5 (10.8)          | 29 (41.4)   |
| Non proliferative | 0 (0.0)            | 41 (89.2)         | 41 (58.6)   |
| Total          | 24 (100.0)          | 46 (100.0)        | 70 (100.0)  |

In cytology, 29 were proliferative but the gold standard HPE diagnosed 24, so 5 cases (3.4%) were false positive. Calculated sensitivity for detecting proliferative endometrium was 100%, specificity was 89.2% and accuracy was 89.2% against gold standard HPE. In the study by Kaur et al9 similar finding was noted as HPE diagnosed 20 out of 23 cases detected by cytology with a sensitivity of 100%, specificity of 96% and accuracy of 96.84%. Similar finding was noted in the study by Patel P et al58 and Handa U et al10. Thirty-four of 38 cases diagnosed as proliferative cytologically matched with their corresponding histopathology in the study by Baxi SN et al11.

Table 3: Distribution of the respondents by cytology and histopathologic finding

| Cytology       | HPE (gold standard) | Fisher exact test |
|----------------|---------------------|------------------|
|                | Secretory n(%)      | Non secretory n(%) | Total N(%) |
| Secretory      | 14 (100.0)          | 1 (1.8)           | 15 (21.4)   |
| Non secretory  | 0 (0.0)             | 55 (98.2)         | 41 (78.6)   |
| Total          | 14 (100.0)          | 56 (100.0)        | 70 (100.0)  |

In case of secretory endometrium, 15 were diagnosed by cytology but HPE diagnosed only 14, with a false positivity of 6.6%. Sensitivity for detecting secretory endometrium was 100%, specificity was 92.8% and accuracy was 88.5%. In the study by Kaur et al9, it was noted that cytology could diagnosed 16 out of 17 cases detected by HPE with a sensitivity of 94.4%, specificity of 100% and accuracy of 98.9%.

Table 4: Distribution of the respondents by cytology and histopathologic finding for malignancy

| Cytology       | HPE (gold standard) | Fisher exact test |
|----------------|---------------------|------------------|
|                | Adenocarcinoma      | No cancer        | Value:35.8 df-1 |
| Adenocarcinoma | 2 (50.0)            | 0 (0.0)          | p-0.002         |
| No cancer      | 2 (50.0)            | 66 (100.0)       |                 |
| Total          | 4 (100.0)           | 66 (100.0)       |                 |

Unfortunately, Cytology could diagnose 2 out of 4 cases of adenocarcinoma (50%) and so 2 cases were missed. Sensitivity of aspiration cytology of detecting adenocarcinoma was 50% and specificity was 100% in this study. In the study by Byrne AJ12 for cytolgical diagnosis of endometrial cancer using endocyte endometrial sampler, they found that sensitivity was 90% which was a bit higher from this study and specificity was 100% which is same with this study. Liza et al2 study had a sensitivity of 81.63% and specificity of 83.3%. Cytologic sampling demonstrated a sensitivity of 78%, specificity of 96%,and positive predictive value of 78% and a negative predictive value of 96% for detection of endometrial abnormalities.13 Accuracy of detection adenocarcinoma by aspiration cytology was 97% in this study.
Similar finding was noted in the study by Robert R where accuracy of diagnosis by endometrial smear was 92.6%, by curettage was 98% and when both were used together accuracy was 100%. This was also noted in the study by Anderson et al where there was excellent correlation of 96% between endometrial biopsies and curettage. Cytologic smears diagnostic accuracy of 93% was observed in the study by Sagar et al. Accuracy of 100% was observed in Chakravarthty in detecting adenocarcinoma.

**Table 5: Distribution of the respondents by cytology and histopathologic finding for hyperplasia**

| Cytology       | HPE (gold standard) | Fisher exact test |
|----------------|---------------------|------------------|
|                | Hyperplasia n(%)    | No hyperplasia n(%) | Value |
| Hyperplasia    | 9 (64.0)            | 0 (0.0)           | -47.2 df-1 p-0.000 |
| No hyperplasia | 5 (36.0)            | 54 (100.0)        |     |
| Total          | 14 (100.0)          | 54 (100.0)        |     |

Cytology could detect only 64% of hyperplasia and 36% were missed, also statistically significant. Regarding accuracy of hyperplasia it was 90% and this finding was similar to the finding by Chakravarthty study which they got 87.5% of accuracy.

Average correlation between aspiration cytology and histopathology in this study was 93%. A brief comparative table ascribing correlation between EAC and HPE in some studies are delineated below:

**Table 6: Comparative table of EAC vs HPE correlation in some studies:**

| Studies done     | %correlation |
|------------------|--------------|
| Tripathy et al   | 97%          |
| Hemalatha et al  | 94%          |
| Rao et al        | 78%          |
| Polson et al     | 78%          |
| Present study    | 93%          |

Aspiration yield 7 cases (8%) with inadequate sample. This finding was almost similar to the finding by Sagar et al where cytological smears were inadequate in 10.4% cases. Inadequacy of sample of 14% and 12.5% was observed in the study by Polson et al and Chakravarthty respectively. So, sample adequacy was found in around 90%.

**Conclusion**

One of the major difficulties encountered in the cytological study of the endometrium has been related to the inability to obtain a satisfactory and representative cellular sample consistently. Over the years, different authors opined that endometrial aspiration techniques was acceptable and valuable method of assessing the endometrium as an minimally invasive, almost painless and less time intensive OPD procedure. Our study corroborates this fact and proves beyond doubt that EAC faithfully mirrors the Endometrial findings in DUB as shown by gold standard HPE diagnosis.

**Limitations of the Present Study**

An added aspect which could have been studied is the diagnostic accuracy of EAC with different techniques of endometrial sampling; it could have provided a fruitful solution to ongoing efforts in bettering the EAC outcomes. Additionally, the statistical significance and applicability of any study can be magnified if a bigger pool or sample size, as is the case with our study too.

**Conflict of Interest**

The author(s) declare no conflict of interest, nor any affiliations or association of any entities or organization with financial motive and investment in this present study.

**References**

1. Patil P, Venigalla S, Kumar MLH, Raju
K. A Comparative Evaluation of the Three Different Methods of Endometrial Sampling in the Diagnosis of Perimenopausal Bleeding. J clin Gynae & obstet 2014;3(4):133-7.

2. Liza SR, Rameshkumar K, Sr. Lilian. Value of endometrial aspiration cytology in assessing endometrial status in symptomatic peri and postmenopausal women. Indian J of Cancer 1999;36:57-61.

3. Devi LS, Singh MR, Singh LR, Debnath K. The histological and histochemical study of endometrium in dysfunctional uterine bleeding. J Med Soc 2012;26:167-70.

4. Rao SS, SavithriC, Lalithakumari B, Venkataratnam G. Endometrial aspiration cytology in dysfunctional uterine bleeding. J of Obst & Gyn of India 1986;36(3):334-7.

5. Tripathy SN, Mahan J. Place of aspiration cytology in dysfunction uterine bleeding. J Indian Med Assoc 1990 Sep;88(9):247-8.

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

7. Morse AR, Ellice RM, Anderson MC. Aspiration cytology versus histology in the assessment of the endometrium of women attending a menopause clinic. Br J of Obstet & Gynaecol 1981;88:421-5.

8. Noyes RW, Hertig AT, Rock J. Dating the endometrial biopsy. Fertil Steril 1950;1:3-25.

9. Kaur NT, 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):144-9.

10. Handa U, Bansal C, Aggarwal P, Huria A, Mohan H. Diagnostic Utility of Endometrial Aspiration Cytology in Women with Abnormal Uterine Bleeding. J Midlife Health 2018 Jul-Sep;9(3):140-4.

11. Baxi SN, Panchal NS. Histopathology-like categories based on endometrial imprint cytology in dysfunctional uterine bleeding. J Cytol 2015 Apr-Jun;32(2):96–101.

12. Byrne AJ. Endocyte endometrial smears in the cytodiagnosis of endometrial carcinoma. ActaCytol 1990;34:373-81.

13. 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):882-88.

14. Robert R. Endometrial aspiration smears in diagnosis of malignancy of uterine corpus. Am J Obst Gynecol 1963 Dec 1;87(1):921-5.

15. Anderson MG, Eaton CJ, Galinkim LJ, Newton CW, Haines JP. Miller NF. The cytologic diagnosis of endometrial adenocarcinoma. Am J Obstet Gynecol 1976;125:376-83.

16. Sagar S, Prakash P, Goyal U. A histocytologic study of endometrium by aspiration technique. J of Obst & Gyn of India 1980;26(1):626-9.

17. Chakravarthi A. Diagnostic efficacy of endometrial cytology. Obstet Gynecol 1986;134:147-51.

18. Polson DW, Morse A, Beard RW. An alternative to the diagnostic dilatation and curettage- endometrial cytology. Br Med J 1984 Mar;288(6422):981-3.