Section: Pathology

Original Research Article

DIAGNOSTIC ACCURACY OF PRE-OPERATIVE ENDOMETRIAL BIOPSY IN ENDOMETRIAL CARCINOMAS: A 3-YEAR RETROSPECTIVE STUDY IN A TERTIARY CARE CENTRE

S. Preetha[1], R. Hemapriya[2], M.S. Muthu Prabha[3], Rajesh Nataraj A.P.[4]

[1]Assistant Professor, Institute of Pathology, Madras Medical College, Chennai, India.
[2]Assistant Professor, Institute of Pathology, Madras Medical College, Chennai, India.
[3]Assistant Professor, Department of Pathology, Government Theni Medical College, Theni, India.
[4]Assistant Professor, Institute of Pathology, Madras Medical College, Chennai, India.

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Corresponding Author:
Dr. S. Preetha,
Email: drpreetha88264@gmail.com

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ABSTRACT

Background: Aim: To compare the diagnostic accuracy of Pipelle endometrial biopsy and dilatation and curettage (D&C) for detecting endometrial carcinoma and to assess concordance of FIGO histologic grading between pre-operative biopsies and definitive hysterectomy specimens. **Materials and Methods**: This three-year retrospective observational study was conducted at a tertiary care centre and included 78 women who underwent pre-operative endometrial sampling by either Pipelle or D&C, followed by hysterectomy. Histopathological findings from hysterectomy specimens served as the reference standard for diagnostic evaluation. Data on demographics, menopausal status, and histology were retrieved from institutional archives, and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated for each sampling technique. FIGO histologic grades were assigned in accordance with the most recent WHO criteria, and concordance between pre-operative and definitive grades was assessed. **Result:** The cohort had a mean age of 56 years, with postmenopausal women comprising the majority. Pipelle sampling achieved a diagnostic accuracy of 94% for endometrial carcinoma, whereas D&C achieved an accuracy of 88%. Concordance of FIGO histologic grading between pre-operative biopsy and hysterectomy specimens ranged from 75% to 83%, with approximately 7% of cases demonstrating an upgrade from Grade I upon final histopathology. Importantly, four cases initially diagnosed as atypical endometrial hyperplasia (AEH) on biopsy were found to harbor concurrent adenocarcinoma in the hysterectomy specimens. **Conclusion:** Both Pipelle and D&C exhibit high diagnostic accuracy for the detection of endometrial carcinoma. Pipelle offers distinct advantages in safety, cost-efficiency, and feasibility in outpatient settings, supporting its use as a preferred initial diagnostic approach. Nevertheless, the potential for grade underestimation and limited sensitivity for focal lesions highlights the importance of hysteroscopic evaluation in selected patients.

INTRODUCTION

Endometrial carcinoma represents the most common gynecological malignancy in many developed countries and is an increasingly significant public health concern in developing nations undergoing demographic shifts.[1] The pathogenesis of this disease is linked to various risk factors, including obesity, unopposed estrogen exposure, diabetes mellitus, hypertension, and genetic syndromes like Lynch syndrome.[2] Clinically, it often manifests as abnormal uterine bleeding, particularly in the post-menopausal period, necessitating timely and accurate histopathological evaluation. Early and precise diagnosis is paramount, as the prognosis for disease confined to the uterus is excellent, while more advanced stages have significantly worse outcomes.[1] This substantial public health burden demands a consistent and reliable diagnostic approach that is both highly accurate and widely accessible.

Endometrial sampling stands as the cornerstone of diagnosis.[3] The techniques employed include Pipelle aspiration, dilatation and curettage (D&C), hysteroscopic-directed biopsy, and adjuncts such as transvaginal ultrasonography (TVUS).[3] Each

method has a unique profile concerning diagnostic accuracy, sample adequacy, patient tolerability, and complication risk. The Pipelle biopsy method is widely favored due to its inherent simplicity, minimal invasiveness, reduced cost, and suitability for outpatient settings, a preference strongly supported by numerous randomized controlled trials and large cohort studies.[4-6] In contrast, D&C is a more invasive procedure that requires cervical dilation and is often performed under general anesthesia, making it a less convenient and more costly option.[7-9] It remains a customary alternative in environments where Pipelle is either unavailable or provides an inadequate sample.[8] Hysteroscopic biopsy, while considered the gold standard for the assessment of focal lesions, is a resource-intensive procedure that requires specialized equipment and is thus less accessible in environments with limited resources.[7] The concordance between the pre-operative biopsy and the final hysterectomy diagnosis, especially regarding histological grade, holds substantial clinical significance for surgical planning and prognosis.[10-13] An accurate pre-operative grade can inform the extent of surgical intervention, including whether a lymphadenectomy is necessary, directly impacting patient morbidity and the subsequent need for adjuvant therapy. The present study was conducted with the objective of comparing the diagnostic efficacy of Pipelle and D&C in detecting endometrial carcinoma and of assessing the concordance of FIGO grading between the pre-operative and hysterectomy specimens, thereby providing a perspective that contributes to the broader academic knowledge.

Aims and Objectives

Primary objectives

- Compare the diagnostic efficacy of Pipelle and D&C in the detection of endometrial carcinoma.
- Evaluate the concordance of FIGO grade between pre-operative biopsies and definitive hysterectomy specimens.

Secondary objectives

- Determine the incidence of concurrent carcinoma in AEH.
- Identify diagnostic pitfalls in pre-operative sampling.

MATERIALS AND METHODS

Study design and setting: A 3-year retrospective cohort study was conducted within the Institute of Pathology at Madras Medical College, Chennai. This time frame was chosen to allow for the collection of a sufficient number of complete cases with both biopsy and hysterectomy data available for comparative analysis. All data were extracted from institutional records and archived pathology reports.

Cohort: The study population was comprised of 78 women who had undergone both pre-operative endometrial sampling (utilizing either Pipelle aspiration or D&C) and a subsequent hysterectomy. The cohort was meticulously selected based on the availability of a complete histopathological chain of evidence, ensuring a direct and valid comparison could be made between the pre-operative and final surgical specimens.

Inclusion Criteria: Women with a documented history of abnormal uterine bleeding who underwent an endometrial biopsy and a subsequent hysterectomy were included. This criterion ensured the relevance of the cohort to the primary diagnostic question of evaluating the effectiveness of endometrial sampling techniques.

Exclusion Criteria: Exclusion was applied to cases with inadequate or insufficient biopsy specimens, and to cases where a subsequent hysterectomy specimen was not available for analysis. Furthermore, cases involving a different type of initial biopsy, such as hysteroscopic biopsy, or those where the final diagnosis was not endometrial carcinoma or hyperplasia were excluded to maintain the focus of the comparative analysis.

Data collection: The requisite patient demographics, clinical details, sampling method, pre-operative biopsy findings, and final hysterectomy results were procured from medical records. Each specimen was independently reviewed to ensure diagnostic consistency. The FIGO criteria, as defined by the latest WHO classification and consensus guidelines, were employed for histological grading of both the biopsy and the final hysterectomy specimens.[2,7]

All data were meticulously entered into a secure electronic database to minimize transcription errors.

Outcome measures: The outcome measures included diagnostic accuracy, sensitivity, specificity, PPV, and NPV for the Pipelle and D&C methods, with calculations based on the definitive hysterectomy specimen as the gold standard.[4,6,8] Additionally, the concordance of FIGO grade between the biopsy and hysterectomy specimens was assessed using a simple proportional agreement measure.[13] The incidence of carcinoma in patients with AEH was determined, and the identification of interpretive errors or misclassifications was also considered through a qualitative review of all cases.[14,15]

Statistical Analysis: Descriptive statistical methodologies were applied for frequency distribution, and all continuous variables were reported as means with standard deviations. Concordance was reported as proportional agreement. The results were interpreted within the context of available international studies, with an emphasis on highlighting both agreement and discrepancies. The statistical analysis was performed using the R statistical programming language, version 4.2.1.

RESULTS

Patient demographics: The cohort of patients was comprised of individuals within an age range of 45–

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75 years, with the mean age calculated at 56 years (SD = 8.5) (**Table 1** - highlights the year wise age distribution of cases and the mean age). A distinct majority of the patients were observed to be in the post-menopausal state, which is congruent with the known epidemiology of endometrial carcinoma.[1,2]. **Table 2** and **Chart 1** shows the year wise distribution of cases. **Table 3** encloses the type of sampling for the 78 cases.

Histological spectrum: The most prevalent histological subtype was endometrioid adenocarcinoma (**Figure 1**), which constituted 85% of all confirmed carcinoma cases.[2,7] Less frequent subtypes included clear cell carcinoma (5%) and malignant mixed Müllerian tumour (MMMT) (3%)(**Figure 2**). The remaining cases were classified as other rare or undifferentiated subtypes. (**Chart -2**)

Diagnostic accuracy: Carcinoma detection was achieved with a diagnostic accuracy of 94% by means of the Pipelle biopsy, whereas an accuracy of 88% was attained via curettage.[6-11] The calculated sensitivity for the Pipelle method was 92% (95% CI: 85-97%), and its specificity was 98% (95% CI: 92-100%). In contrast, curettage demonstrated a sensitivity of 85% (95% CI: 77-92%) and a specificity of 95% (95% CI: 88-99%).[8,10] Both methods were observed to demonstrate a high degree of specificity, with the sensitivity for Pipelle being marginally superior to that of curettage. (**Table 4**)

Concordance of grading: The level of agreement between biopsy and hysterectomy grading was determined to be within the range of 75–83%.[13,17] A detailed analysis revealed that Grade I tumours on biopsy had a concordance rate of 82%, while Grade II tumours showed 75% concordance, and Grade III tumours had 83% concordance. A minority of cases, approximating 7% (n=5), were subject to a histological grade upgrade post-operatively from Grade I to a higher grade, a finding that underscores a key limitation of the analysis of limited biopsy samples.[13,16] [**Table 5**]

AEH with carcinoma: Four patients with a biopsy diagnosis of AEH were confirmed to have concurrent carcinoma on final hysterectomy.[14,15] This finding represents a significant diagnostic concern, as these cases demonstrate the inherent limitations of biopsy in ruling out malignancy in a high-risk group. [**Figure 3**]

Diagnostic pitfalls: The pitfalls that were identified included the misdiagnosis of endometrial adenocarcinoma as endocervical carcinoma in preoperative sampling,[7] (**Table 6**). Such interpretive errors were typically due to the morphological overlap between these entities and a lack of clear anatomical context in the biopsy specimen. Sampling errors were also considered a contributory factor in the underdiagnosis of focal lesions, as these were missed by the sampling instrument and only discovered upon the comprehensive examination of the entire hysterectomy specimen. [**Figure 4**]

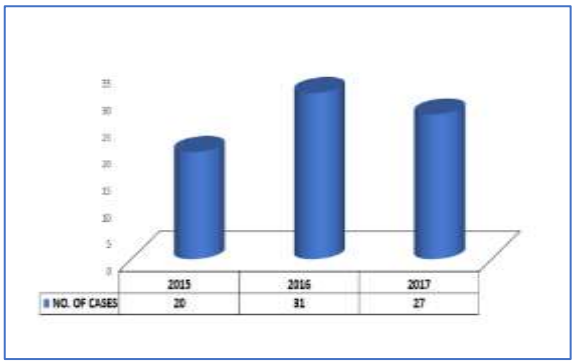

Chart 1: Year wise Distribution of Cases (n=78)

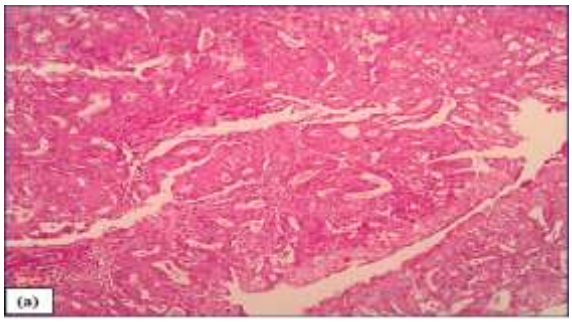

Figure 1: Endometrial endometrioid adenocarcinoma (H&E stain): (a) 10x – Resection sample

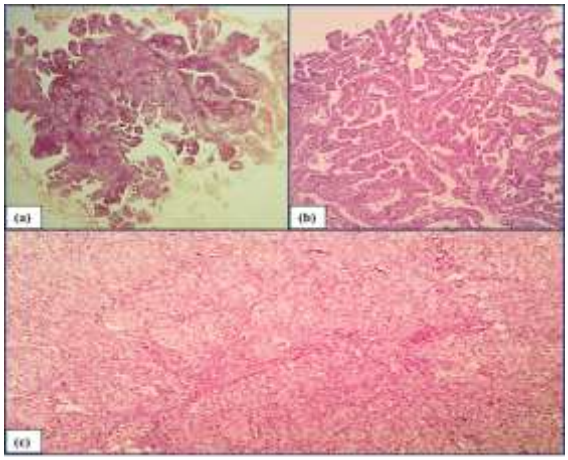

Figure 2: Malignant mixed mullerian tumour (MMMT) (H&E stain): (a) 10x – Curettage sample showing predominantly clear cell morphology, (b,c) 10x - Resection sample showing glandular pattern with focal clear cells (b) and malignant stromal component (c)

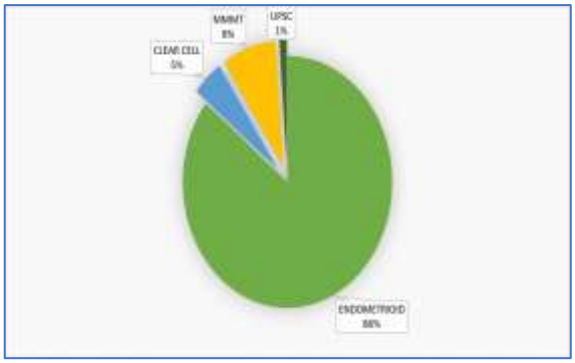

Chart 2: Post operative Histological types

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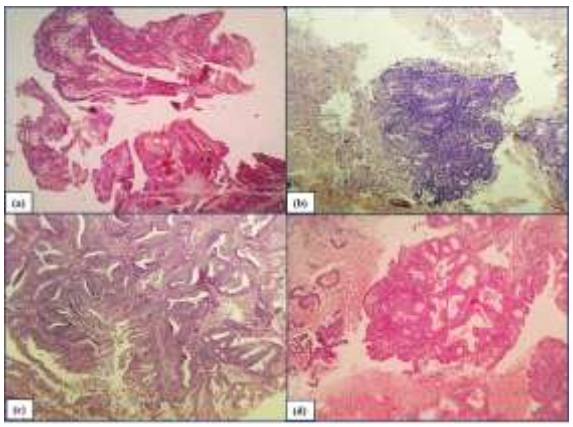

Figure 3: Atypical endometrial hyperplasia (H&E stain): (a,b) 10x – Pipelle sample (c,d) 10x – Curettage sample

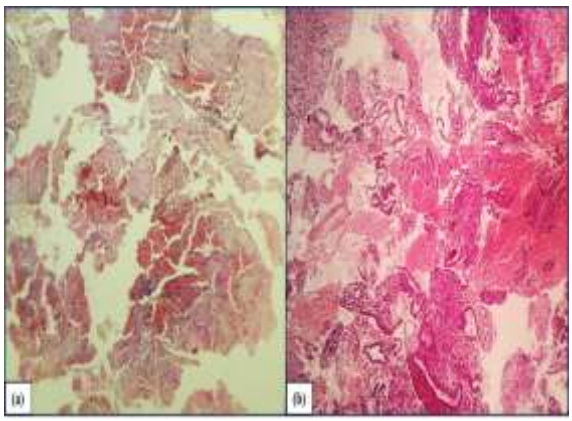

Figure 4: Not contributory due to inadequacy (H&E stain): (a) 10x – Pipelle sample (b) 10x – Curettage sample

Table 1: Year wise Age distribution of cases (Mean Age – 56 years)

Year/Age	21-30	31-40	41-50	51-60	61-70	71-80	Total
2015	0	0	7	9	9	2	**27**
2016	1	3	7	12	4	4	**31**
2017	0	2	3	12	2	1	**20**
Total	**1**	**5**	**17**	**33**	**15**	**7**	**78**
Percentage	**1.3**	**6.4**	**21.8**	**42.3**	**19.2**	**9.0**	**100**

Table 2: Year wise Distribution of Cases (n=78)

Year	Number of Cases	Percentage (%)
2015	20	25.6
2016	31	39.7
2017	27	34.7
Total	78	100

Table 3: Type of endometrial sampling (n=78)

Type of Endometrial sampling	No. of cases
Curettage	42
Pipelle	35
Biopsy	1
Total	78

Table 4: Detection of malignancy with different types of sampling (n=77)*

Type of Sampling	Malignant	Atypical Endometrial Hyperplasia	Not Contributory
PIPELLE (n=35)	94.20%	2.85%	2.85%
CURETTAGE(n=42)	88.10%	7.14%	4.76%

*excluding 1 biopsy

Table 5: Concordance of Figo Grade with different types of sampling (n=77)*

Type of Sampling	GRADE I	GRADE II	GRADE III	Average Concordance with Resection
Pipelle (n=35)	80%	66.67%	80%	75.5%
Curettage (n=42)	78.57%	80%	92.30%	83.6%

*excluding 1 biopsy

Table 6: Correlation of Cases reported pre-operatively as Endocervical adenocarcinoma (n=3)

P/D	REPORT	HYSTERECTOMY REPORT
PIPELLE	ENDOCERVICAL ADENOCARCINOMA	ENDOMETRIOID ADENOCARCINOMA – III
CURETTAGE		ENDOMETRIOID ADENOCARCINOMA – II
CERVIX BIOPSY		ENDOMETRIOID ADENOCARCINOMA - II

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DISCUSSION

The findings of this investigation highlight the diagnostic reliability of endometrial sampling in the identification of carcinoma, with Pipelle demonstrating a modest advantage over curettage.[4-11] Our findings are observed to be in alignment with prior meta-analyses and large cohort studies that highlight the elevated sensitivity, specificity, and practical advantages of the Pipelle method.[5-8] The superior diagnostic accuracy of Pipelle observed in this study may be attributed to its specialized design, which facilitates a more uniform aspiration of the endometrial lining, thereby reducing the likelihood of sampling errors.[11] Its safety profile and outpatient feasibility render it particularly well-suited for routine application, especially in environments with limited resources, where the cost and infrastructure required for D&C may be prohibitive.[8,10]

Despite the strong performance, the biopsy–hysterectomy grading concordance was determined to be 75–83%, a value slightly below the 85–90% reported in studies such as those conducted by Jegatheeswaran et al. and Gungorduk et al.[13,17] This discrepancy is considered to reflect tumour heterogeneity, the limitations inherent in sampling, and the reliance on the proportion of solid growth in FIGO grading, which is more accurately assessed in a definitive hysterectomy specimen of larger volume.[13,16] It is considered that this under-grading phenomenon is an inevitable consequence of evaluating a three-dimensional lesion with a two-dimensional biopsy. The clinical implications of this finding are profound, as under-grading may lead to the under-treatment of patients, potentially resulting in a suboptimal oncological outcome. For instance, a Grade I tumor on biopsy that is upgraded to a Grade II or III after hysterectomy might have warranted a more extensive surgical procedure, such as a lymphadenectomy, which was not performed initially. This could necessitate a re-operation or the consideration of adjuvant therapy that was not originally planned, thereby increasing patient morbidity and healthcare costs.

The discovery of concurrent carcinoma in cases of AEH corroborates evidence from the work of Trimble et al. and Merisio et al,[14,15] thereby confirming a significant risk of co-existing carcinoma in this specific patient subgroup. These findings highlight that AEH should not be considered a benign condition but rather a pre-malignant lesion that warrants definitive surgical management, particularly in patients who have completed childbearing.[14,15] The absence of confirmed malignancy on initial biopsy should not be interpreted as definitive, and close follow-up or surgical intervention should be considered. This high risk of progression or co-existence with invasive cancer highlights the need for careful patient counselling and management strategies. The definitive management of AEH often involves hysterectomy, especially in older patients or those who have completed their family.

Both Pipelle and D&C are subject to limitations in their capacity to evaluate focal lesions, such as polyps or localized carcinomas, in which scenarios hysteroscopic-directed biopsy remains an indispensable and highly valuable diagnostic tool.[7,8,10] The ability to directly visualize the endometrial cavity and target suspicious lesions for biopsy greatly reduces the risk of missing a focal pathology.[18] The occasional misinterpretations, such as the misdiagnosis of endometrial with endocervical carcinoma, further highlight the necessity for careful clinico-pathological correlation, taking into account the patient's clinical history and radiological findings.[7,17] These interpretive errors can be mitigated by considering the morphological features of the tumor in conjunction with its location and the overall clinical picture. Collective findings from our study and others reinforce Pipelle as a safe, accurate, and economically efficient diagnostic method, while affirming curettage as a valid alternative when the Pipelle method is not available.[6-9] However, cautious interpretation remains an essential requirement, particularly in presentations that are atypical or borderline in nature, and in cases where the biopsy findings do not correlate with the clinical picture. The results of this study contribute to the body of evidence supporting the continued use of endometrial sampling as a primary diagnostic tool, while also highlighting its inherent limitations and the need for judicious clinical judgment.

CONCLUSION

This study demonstrates that both Pipelle and curettage are highly efficacious diagnostic techniques for endometrial carcinoma, with Pipelle exhibiting marginally superior accuracy.[4-9] The Pipelle biopsy method is minimally invasive, cost-effective, and is ideally suited for implementation in outpatient practice. Grading concordance between the biopsy and the hysterectomy specimen is substantial but not absolute; an upgrade in grade occurs in a minority of cases, a phenomenon that should be considered during surgical planning.[13,17] Atypical endometrial hyperplasia carries a meaningful risk of concurrent carcinoma, warranting careful evaluation and management per guideline-based pathways.[14,15] In suspected focal disease, hysteroscopic targeting complements blind sampling to optimize diagnostic yield.[7] The integration of histopathological, clinical, radiological, and intraoperative findings is critically important for the optimization of management strategies and for ensuring the best possible outcomes for patients.

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