

DIAGNOSTIC ADEQUACY AND HISTOLOGICAL OUTCOME OF PIPELLE ENDOMETRIAL BIOPSIES

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ABSTRACT

Objective: To assess diagnostic adequacy and histological outcome in pipelle endometrial biopsies of the patients presenting with abnormal uterine bleeding.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Histopathology department, Army Medical College Rawalpindi, from Jan to Dec 2018.

Methodology: A total of 220 cases, which presented with abnormal uterine bleeding and underwent endometrial pipelle biopsy were included in the study. The biopsies were evaluated in terms of material adequacy and histopathological outcome. Cases with bleeding due to complications of pregnancy, cervical pathologies and lower genital tract infections were excluded. Statistical analysis was done using SPSS version 22.

Results: Out of 220 pipelle biopsies, 65 (29.54%) were inadequate for assessment while 155 (70.45%) were adequate to make a definitive diagnosis on histological examination. Among the diagnostic samples, chronic endometritis was the most common pattern observed, seen in 70 cases (45.16%). Other histological patterns included proliferative endometrium (29.03%), secretory endometrium (9.03%), exogenous hormone effect (7.10%), endometrial hyperplasia (3.87%), atrophic endometrium (4.51%) and endometrial carcinoma (1.29%).

Conclusion: Pipelle biopsy is not as successful in our setup as it is in the developed countries. This technique can be used as an initial procedure in patients with abnormal uterine bleeding, however, in patients with high risk of malignancy where pipelle biopsy is inadequate, dilation and curettage is recommended instead of repeating pipelle biopsy to get adequate material for a definite diagnosis.

Keywords: Abnormal uterine bleeding, Endometrial pathology, Pipelle endometrial biopsy, Sample adequacy.

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INTRODUCTION

Abnormal uterine bleeding (AUB) is a term used for uterine bleeding that differs from normal menstrual bleeding in regularity, duration, frequency, or volume, in the absence of pregnancy¹. It is a common cause of referral to the gynaecology clinic, and the problem has a significant impact on the health status and quality of life of women². Up to one-third of women experience AUB in their life, with higher incidence occurring around menarche and perimenopausal years³. It is a concern for women worldwide but common etiologies vary from region to region. The underlying causes according to International Federation of Gynaecology and Obstetrics (FIGO) can be

classified based on the acronym PALM-COEIN (Polyps, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory disorders, Endometrial causes, Iatrogenic and Not classified)⁴.

Histopathological examination of endometrium remains the mainstay in the evaluation of AUB in women since endometrium is the most easily sampled tissue. This is especially important in women presenting with postmenopausal bleeding being at higher risk of endometrial carcinoma. Traditionally, Dilatation and Curettage (D & C) has been the method of choice for sampling endometrial tissue in women with AUB. However, the associated hospitalization, general anesthesia, postoperative pain, increased risk of perforation and infections limit its use as a screening method for endometrial pathologies⁵. At present,

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other minimally invasive, less expensive and more rapidly performed procedures have superseded this technique^{6,7}.

One of the most widely used outpatient procedures is pipelle endometrial sampling. High patient acceptability and diagnostic efficacy of the procedure has been reported by many studies⁸. The Pipelle biopsy instrument is a 3mm diameter flexible cannula that aspirates a sample of tissue through suction as it sweeps across the endometrial surface and is small enough making cervical dilation unnecessary. Because no anesthesia is needed, it may be used readily in a private office setting and is better tolerated by patients. Despite being able to sample only a small proportion of the endometrial surface, pipelle has sensitivity and specificity comparable to dilation and curettage for global uterine lesions provided that the sample is adequate⁹.

With the advent of outpatient sampling techniques including pipelle, pathologists are faced with increasing number of samples that are inadequate or unassessable containing little or no endometrial tissue¹⁰. This necessitates repeat biopsy, hysteroscopy or even D & C in high risk women. There is scant data about pipelle biopsy in terms of sample adequacy in Pakistan¹¹. However, international studies show that its adequacy is comparable to D&C and superior to other outpatient methods¹².

The objective of study was to assess diagnostic adequacy and histological outcome in pipelle endometrial biopsy obtained from patients with AUB in our set up, and its comparison with studies from other parts of the world.

METHODOLOGY

This descriptive cross-sectional study was conducted at histopathology department of Army medical college, Rawalpindi and comprised data of pipelle biopsy cases, from Jan to Dec 2018. After getting clearance from institutional ethics committee, 220 pipelle endometrial biopsies were selected by non-probability convenience sampling technique.

Pipelle biopsies of pre and post-menopausal women, presented with abnormal uterine bleeding were included in the study. Cases with bleeding due to pregnancy and its complications, cervical pathologies and lower genital tract infections were excluded. Relevant clinical history and demographic details of patients were noted from the medical records. The biopsies received were assessed for diagnostic adequacy and histological outcome by consultant histo-pathologist. Samples containing no endometrial tissue or very scanty endometrial fragments suboptimal for assessment were considered inadequate. Intact tissue fragments containing both endometrial glands and stroma sufficient for definitive diagnosis were categorized as adequate. Data was entered on proforma designed to record all information including patient and operator details, sample adequacy with gross and microscopic features. The samples, which contained only blood, fibrin or debris were considered inadequate. Very scanty endometrial fragments, on which no diagnosis could be made were called suboptimal and were also considered inadequate. Statistical analysis was done using SPSS version 22. For qualitative variables, percentage was calculated, while mean and standard deviation (SD) was calculated for quantitative variables. Descriptive statistics were used to describe the results.

RESULTS

A total of 220 pipelle biopsies were analyzed in the study. The mean age of study population was 42.61 ± 10.57 years. Majority of patients were within the age group of 41-50 years, followed by 31-40 years. Age distribution of cases is shown in table-I.

Table-I: Age wise distribution of cases in the study.

Age groups	n (%)
20 - 30	34 (15.45)
31 - 40	60 (27.27)
41 - 50	93 (42.27)
> 50	33 (15.00)

Out of 220 pipelle endometrial biopsies, 65 (29.54%) were inadequate and 155 (70.45%) were

adequate to make a definitive diagnosis on histological examination. Adequacy of material is shown in table-II.

Table-II: Adequacy of endometrial pipellebiopsies.

Endometrial Pipelle Biopsies	n (%)
Adequate	155 (70.45)
Inadequate	65 (29.54)

Table-III: Histological findings in pipelle endometrial biopsies.

Histopathological Finding	n (%)
Chronic Endometritis	70 (45.16)
Proliferative Endometrium	45 (29.03)
Secretory Endometrium	14 (9.03)
Exogenous Hormone Effects	11 (7.10)
Endometrial Hyperplasia	6 (3.87)
Atrophic Endometrium	7 (4.51)
Endometrial Carcinoma	2 (1.29)

Among the inadequate samples, 40 biopsies (61.53%) contained no endometrial tissue at all. The samples obtained consisted of blood, fibrin or tissue derived from the cervix instead of endometrium. Rest of the 25 (38.46%) inadequate biopsies contained scanty endometrial fragments suboptimal for histological assessment and diagnosis.

Among the histological results of diagnostically adequate samples, chronic endometritis was the most common histological pattern seen in 70 (45.16%) cases, followed by proliferative endometrium in 45 (29.03%) cases, endometrial hyperplasia in 6 (3.87%) biopsies, while endometrial carcinoma was observed in 2 (1.29%) cases. Histological patterns observed in adequate pipelle endometrial biopsies samples are summarized in table-III.

DISCUSSION

Endometrial biopsy is widely employed in setting of AUB as a diagnostic tool, primarily used to exclude any non-neoplastic, pre-malignant or malignant condition. Most cases of AUB are non-neoplastic or benign and can be offered office-based treatment thus avoiding unnecessary radical surgery. Recently, pipelle endometrial biopsy has emerged as a cost-effective technique with minimal complications compared to the tra-

ditional dilation and curettage. Pipelle biopsy has the advantage of being very convenient for the clinician as well as the patient. However, the material yielded by this technique presents a diagnostic challenge to the pathologist, who is expected to make a diagnosis based on histological examination of small amount of endometrial tissue often compromised by scanty nature of tissue. At present, there are no objective criteria to determine what represents an adequate endometrial sample. A sample is judged as adequate when a specific diagnosis can be given with confidence, based on microscopic examination of the specimen obtained. Despite wide utilization of pipelle biopsy, only a few studies have assessed sampling adequacy of the procedure in our setup.

Adequacy of pipelle biopsy specimen in this study (70.45%) is much lower than previously reported rate of adequate sampling from studies conducted elsewhere in Pakistan. In a 2005 study by Abeeraetal¹³, adequate samples were obtained in 96% of the pipelle biopsies performed. Higher proportion of adequacy could be due to double sampling technique used in the study. In a study by Shams¹⁴, sufficient samples were obtained in 94.88% of the cases. A study conducted by Fakhar *et al*¹⁵ quoted 98% adequacy rate. In a local comparative study⁶, diagnostic adequacy and acceptability of pipelle biopsy was compared to sample obtained by dilation and curettage, which showed 98% specimen satisfaction rateafter exclusion of women with atrophied endometrium on ultrasound. Another study showed 96.82% adequacy of endometrial specimen obtained thorough pipelle biopsy in patients of AUB¹⁶. The proficiency of operator collecting the endometrial samples can be interpreted as one of the possible influences on adequacy rates noted in the aforementioned studies. This study however, utilizes the data compiled from the pathology reports of samples collected by various providers, each with a different level of training.

A few studies have been conducted in other Asian countries. In a study conducted in Iran by Sanam and Majid⁷, 84.6% of the endometrial biopsies were sufficient for pathological diagnosis. A

study in India recorded 96% adequate samples¹⁷. Another study reported sampling failure rate of 7% while rest of the 93% biopsies were diagnostic¹⁸. Similarly, a study comparing dilation and curettage with pipelle reported 94% sampling sufficiency¹⁹. All the above mentioned studies showed better success rate of obtaining a representative endometrial sample compared to this study. This is partly due to consideration of specific age groups and endometrial thickness on ultrasonography as inclusion criteria in most of the studies, thus excluding the cases with atrophic endometrium which otherwise would decrease the likelihood of adequate sampling.

A systemic review of relevant literature from 1984 to 2016 reported variable rate of pipelle sampling adequacy ranging from 67% to 98%¹². The heterogeneity among participant characteristics in different studies with wide ranging inclusion criteria maybe responsible for significant differences in sample sufficiency. Individual international studies have reported variable efficacy of pipelle biopsy in terms of diagnostic adequacy. An audit carried out in New Zealand demonstrated adequacy of 67%, which is comparable to our findings. This study revealed that in-training residents are more likely to retrieve non-diagnostic samples hence indicating that one of the factors influencing sample adequacy is expertise of the operator performing the procedure²⁰. A study conducted in Poland assessing effectiveness of pipelle in endometrial sampling showed 83.01% biopsies with representative sampled material²¹. In another study in Turkey, 97.9% of the biopsies were adequate²². An American study exploring pipelle biopsy failure and its associated factors reported adequate samples in 77.11% of the patients who underwent the procedure. Factors found to have significant association with failed sampling were postmenopausal patients, history of previous biopsy failure, and biopsy performed by a non-physician provider²³.

An additional aim of this study was to determine common histological patterns seen in women with abnormal uterine bleeding. Most endometrial pathologies picked up on pipelle were ben-

ign. Among 155 diagnostically adequate specimens, chronic endometritis was the most common histological finding accounting for 45.16% of the cases. This is in contrast with the figure of 13% reported in a recent study from Karachi¹¹. Other studies also reveal a significantly lower frequency^{6,13,24}. The variation maybe due to prolonged labor, pelvic procedures, poor hygiene and lower socioeconomic status prevalent in our setup, all of which increase the risk of chronic endometritis.

Proliferative and secretory phase endometrium were seen in 29.03% and 9.03% of the cases, respectively. They were reported to be the predominant histological pattern in most other studies^{6,7,13,15,24}. In a study by Tahir *et al*, proliferative phase endometrium was the most common histological outcome seen in 52.5% cases¹¹. Another study reported secretory phase endometrium to be the most frequently observed pattern accounting for 41.12% endometrial samples²⁵.

Endometrial hyperplasia was seen in 3.87% of the cases. This is lower than its frequency reported in previous studies^{6,13}. In our study, there were only 2 cases reporting malignant histology accounting for 1.29% of the biopsies. This is in agreement with 2% reported by Fakhar *et al*¹⁵ but is relatively less frequent when compared to other studies^{7,16}. Other patterns observed in our study were endometrium showing exogenous hormone effects (7.10%) and atrophic endometrium (4.51%). Endometrial polyps are also a common cause of AUB, but none were picked up on pipelle biopsy. This may be due to focal nature of the pathology.

LIMITATION OF STUDY

The major limitation of our study was that it relied on data from the cases received in the laboratory due to which detailed clinical history and information on sonographic endometrial thickness could not be collected for all patients. Some of these factors are reported to be important predictors of inadequate sampling¹⁰.

RECOMMENDATION

To improve clinical usefulness of pipelle biopsy, close liaison between pathologist and gynaecologist

cologists important. Pertinent's clinical information including the endometrial thickness should be conveyed to the pathologist. Gynecologists performing pipelle endometrial biopsy would benefit from hands-on training and experience. Double sampling technique may also improve the chances of obtaining an adequate sample. To reduce frequency of inadequate samples, further studies should focus on collecting data to identify factors associated with pipelle biopsy failure.

CONCLUSION

Pipelle biopsy though being non-diagnostic in a significant number of cases can be used as a screening tool in patients presenting with AUB. In patients who are at high risk and in which pipelle biopsy is inadequate at first instance, it is better to do D&C for making a definite diagnosis instead of repeating pipelle biopsy.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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