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## COMPARATIVE EVALUATION OF BIOPSY METHODS IN PRE- AND POSTMENOPAUSAL WOMEN WITH ENDOMETRIAL PATHOLOGY

The study aimed to evaluate the effectiveness of the methods by comparing the histological results obtained using two endometrial sampling methods (endometrial aspiration biopsy using Pipelle and traditional dilatation and curettage) with the histological results of the hysterectomy sample. In total 57 women, both pre- and postmenopausal, who were experiencing abnormal uterine bleeding and postmenopausal bleeding, were examined using two techniques for obtaining endometrial samples. Among the 57 women, 41 experienced perimenopausal uterine bleeding, while 16 presented with postmenopausal uterine bleeding. During the ultrasound examination, endometrial polyps were detected in 19.3 % of cases, uterine fibroids in 73.7 %, and signs of adenomyosis in 35.1 % of patients. In terms of sensitivity, Pipelle biopsy, dilatation, and curettage demonstrated detection rates of 30.8 % and 61.5 %, respectively, for identifying endometrial polyps. For cases of endometrial hyperplasia without atypia, these figures were 89.7 %, and 84.6 %, respectively. Notably, both methods exhibited 100 % sensitivity in diagnosing atypical hyperplasia.

**Key words:** dilatation and curettage, perimenopausal bleeding, Pipelle biopsy, endometrial polyps, endometrial hyperplasia.

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## ПОРІВНЯЛЬНА ОЦІНКА МЕТОДІВ БІОПСІЇ У ЖІНОК ІЗ ПАТОЛОГІЄЮ ЕНДОМЕТРІЇ У ПРЕ- І ПОСТМЕНОПАУЗАЛЬНОМУ ВІСІ

Метою дослідження була оцінка ефективності методів біопсії шляхом порівняння гістологічних результатів, отриманих з використанням двох методів забору ендометрію (аспіраційна біопсія ендометрію (пайпель-біопсія) та традиційна дилатація та вишкрібання)), з гістологічними результатами зразка гістеректомії. Усього було обстежено 57 жінок як у пре-, так і постменопаузі, у яких спостерігалися аномальні маткові кровотечі та постменопаузальні кровотечі, з використанням двох методів отримання зразків ендометрію. Серед 57 жінок 41 відчувала перименопаузальні маткові кровотечі, а 16 – постменопаузальні маткові кровотечі. При ультразвуковому дослідженні у 19,3 % випадків були виявлені поліпи ендометрію, у 73,7 % – міома матки та у 35,1 % пацієток – ознаки аденоміозу. З точки зору чутливості, пайпель-біопсія, дилатація та вишкрібання продемонстрували показники виявлення 30,8 % та 61,5 % відповідно для виявлення ендометріальних поліпів. Для випадків гіперплазії ендометрію без атипії ці показники становили 89,7 % та 84,6 % відповідно. Примітно, що обидва методи продемонстрували 100 % чутливість у діагностиці атипової гіперплазії.

**Ключові слова:** дилатація та вишкрібання, перименопаузальна кровотеча, пайпель-біопсія, ендометріальні поліпи, ендометріальна гіперплазія.

Endometrial hyperplasia is a prevalent type of endometrial pathology, mainly observed in pre- and postmenopausal women. Understanding the significance of early detection becomes more apparent, considering the increased risk of endometrial cancer during this age range [6, 10, 11].

To confirm the diagnosis of endometrial pathologies, it is necessary to evaluate endometrial tissue histopathologically [5]. There are various methods for obtaining endometrial samples for histopathological assessment. The most common are aspiration biopsy, dilatation and curettage, and the hysteroscopic method.

Endometrial aspiration biopsy using Pipelle does not require cervical dilatation, anesthesia is not necessary during the procedure, and can be easily performed on an outpatient basis. However, it is less sensitive to local processes [4, 8, 9].

Dilatation and curettage are invasive inpatient procedures performed under general anesthesia. Sampling all parts of the endometrial layer with this method allows a complete histological evaluation [3].

If alternative treatments fail, a hysterectomy stands as the final recourse for addressing abnormal uterine bleeding, irrespective of the presumed underlying cause. The recommended approaches for conducting the surgery are the vaginal or laparoscopic methods, with laparotomy seldom being necessary [1, 7].

**The purpose** of the study was to evaluate the efficacy of the methods by comparing the histological results obtained using two endometrial sampling methods (endometrial aspiration biopsy using Pipelle and traditional dilatation and curettage) with the histological results of the hysterectomy sample.

**Materials and methods.** This comparative study was performed at the Department of Obstetrics and Gynecology at Azerbaijan Medical University, focusing on patients experiencing uterine bleeding. The

study occurred between 2018 and 2021 and was based in a hospital setting. The study involved 57 women who were experiencing abnormal uterine bleeding. Among these women, 41 were in the premenopausal phase, and 16 were in the postmenopausal stage. Patients aged above 40 years were included in our study. Patients with cervical stenosis, bleeding disorders, a history of hormonal intake or intrauterine contraceptive device (IUCD), and lower genital tract infections were excluded from the study. Each woman included in the study first underwent an ultrasound examination. Then, endometrial samples were obtained using a combination of Pipelle biopsy and dilatation and curettage in the hospital.

Patients were provided information and guidance for each procedure, and a written consent was obtained. Clinical and anamnestic data, patients' complaints, and concomitant diseases were studied, and a gynecological examination was performed. After a detailed history and examination, transvaginal ultrasound was performed. The procedures were performed under general anesthesia in an inpatient setting. Biopsy methods were performed in hospital conditions under general anesthesia. The Pipelle biopsy was conducted initially in every patient, followed by dilatation and curettage. Firstly, without dilating the cervical canal, the Pipelle was inserted into the uterine cavity, and a sample of the endometrium was taken by performing back-and-forth and rotation movements. The sample was collected in a container containing formalin, and the container was numbered. Subsequently, dilatation and curettage were performed, and scraped endometrial tissue was collected and numbered in a second container. Both samples were sent for pathohistological examination.

Despite the histopathological results showing the absence of atypical processes in the majority of patients, a decision was made to perform a total laparoscopic hysterectomy for all individuals, considering the recurring complaint of abnormal bleeding and concurrent gynecological pathologies such as uterine fibroids and adenomyosis. All patients in the study underwent total laparoscopic hysterectomy at the scheduled time, and surgical specimens were sent for histopathological analysis.

Statistical analysis was performed using Cohen's Kappa statistic. We also used discrepant analysis to assess the data, wherein we calculated the sensitivity, specificity, positive predictive value, and negative predictive value of the biopsy techniques. This assessment involved comparing these techniques to the histological findings from excised tissues in patients undergoing hysterectomy.

**Results of the study and their discussion.** The mean age of patients was  $51.8 \pm 0.8$  years. The median body mass index (BMI) was  $29.5 \pm 0.5$  kg/m<sup>2</sup> (95 % CI 21.2–41.02). Among 57 women, 41 women presented with perimenopausal bleeding, and 16 women presented with post-menopausal bleeding. We noticed that postmenopausal women have a higher incidence of extragenital diseases such as obesity, diabetes, and hypertension than premenopausal women (Table 1).

Table 1

**Demographic and clinical variables of the study group**

Age (years, mean $\pm$ SD)	51.8 $\pm$ 0.8
Age < 55 (%)	41 (71.9 %)
Age $\geq$ 55 (%)	16 (28.1 %)
Menorrhagia (%)	30 (52.6 %)
Menometrorrhagia (%)	11 (19.3 %)
Postmenopausal bleeding (%)	16 (28.1 %)
BMI (kg/ m <sup>2</sup> )	29.5 $\pm$ 0.5
Obesity (%)	24 (42.1 %)
Diabetes (%)	8 (14.0 %)
Hypertension (%)	14 (28.1 %)

The mean thickness of the endometrium was  $12.5 \pm 0.8$  mm. During the ultrasound examination, endometrial polyps were detected in 19.3 % of cases, uterine fibroids in 73.7 %, and signs of adenomyosis in 35.1 % of patients. Out of 11 patients with endometrial polyps, 6 patients also had uterine fibroids, and 2 patients had adenomyosis at the same time.

Histological findings from both Pipelle biopsy and dilatation and curettage indicated that the predominant pathology among patients was endometrial hyperplasia without atypia, with atypical hyperplasia being less prevalent. The distribution of pathologies is illustrated in Fig. 1.

Patients underwent total laparoscopic hysterectomy due to recurrent abnormal uterine bleeding, multiple myomas, adenomyosis, and unresponsiveness to prior treatments. The distribution of various pathologies based on the results of histopathological analyses of total laparoscopic hysterectomy specimens is presented in Fig. 2.

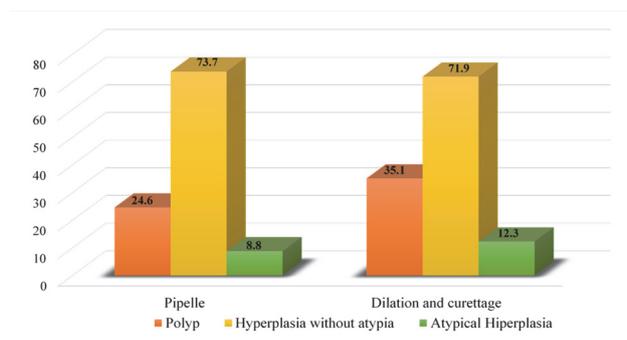


Fig. 1. Endometrial histopathology report by Pipelle, dilatation and curettage.

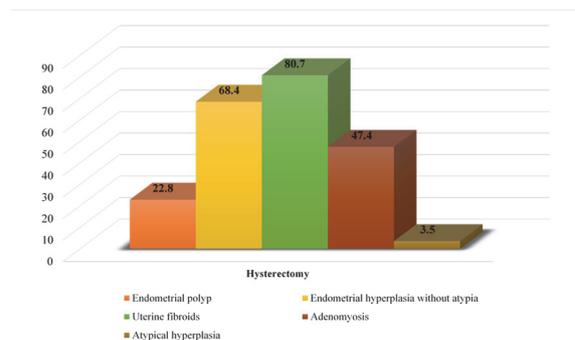


Fig. 2. Pathologic findings on the analysis of total laparoscopic hysterectomy specimens.

The majority of these results are attributed to uterine fibroids (80.7 %), with a significant presence of endometrial hyperplasia without atypia (68.4 %). Table 2 displays the Kappa coefficient, sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of Pipelle biopsy and dilatation and curettage for the detection of endometrial polyps, endometrial hyperplasia with and without atypia.

Table 2

**Kappa statistic results, sensitivity, specificity, PPV, NPV for endometrial polyps, endometrial hyperplasia with and without atypia**

Biopsy method	Kappa	P-value	Sn (%)	Sp (%)	PPV (%)	NPV (%)
Endometrial polyps						
Pipelle biopsy	0.078±0.139	0.554	30.8±12.8	77.3±6.3	28.6±12.1	79.1±6.2
Dilatation and curettage	0.288 ±0.131	0.023	61.5±13.5	72.7±6.7	40.0±11.0	86.5±5.6
Endometrial hyperplasia without atypia						
Pipelle biopsy	0.532±0.123	<0.001	89.7±4.9	61.1±11.5	83.3±5.8	73.3±11.4
Dilatation and curettage	0.414±0.131	0.002	84.6±5.8	55.6±11.7	80.5±6.2	62.5±12.1
Endometrial hyperplasia with atypia						
Pipelle biopsy	0.549±0.226	<0.001	100.0	94.5±3.1	40.0±21.9	100.0
Dilatation and curettage	0.412±0.203	<0.001	100.0	90.9±3.9	28.6±17.1	100.0

Notes: Sn – Sensitivity. Sp – Specificity. PPV – Positive Predictive Value. NPV – Negative Predictive Value.

The results indicate that when comparing the two methods for detecting endometrial polyps, the sensitivity of Pipelle biopsy is notably lower than that of the other method. This distinction is evident in other statistical indices as well.

As depicted in the table, the statistical indicators for Pipelle biopsy and dilatation and curettage in detecting endometrial hyperplasia without atypia are closely aligned with each other. There is a remarkably high sensitivity (100.0 %) of the methods employed in the study for diagnosing atypical hyperplasia. Additionally, other indices also demonstrate notably high values.

The evaluation of peri- and postmenopausal bleeding relies significantly on endometrial sampling for histopathology. Traditionally, dilatation and curettage have been the established method for assessing the endometrium. General anesthesia is necessary for this procedure, which carries potential complications such as uterine perforation, hemorrhage, and infection [3, 4]. Patients who suffer from abnormal uterine bleeding (AUB) or postmenopausal bleeding frequently encounter waiting periods for medical appointments, preoperative assessments and uterine curettage. This places a burden on the healthcare system, causing delays in diagnosis and treatment. Pipelle biopsy may be regarded as more efficient since it can be performed on an outpatient basis without anesthesia. Furthermore, while Pipelle biopsy may not exhibit flawless accuracy for localized endometrial lesions such as polyps, it has demonstrated high accuracy in detecting endometrial cancer [2, 8].

In our study, changes in the endometrium (thickness, structure) and endometrial polyps, as well as various localized myomas and adenomyosis, were detected during ultrasound examination in pre- and postmenopausal patients complaining of abnormal uterine bleeding. These findings show that endometrial pathologies were not the only cause of uterine bleeding complaints. Nevertheless, considering the high risk of endometrial cancer in patients in this age group, we decided to perform a biopsy.

Based on the histopathological findings in our study, endometrial hyperplasia without atypia was observed as the most frequent condition, while atypical hyperplasia was identified as the least common. The results indicate that the sensitivity of dilatation and curettage in detecting endometrial polyps was high, whereas the sensitivity of Pipelle biopsy was comparatively lower. This implies that Pipelle biopsy may not be a more dependable method for detecting endometrial polyps. On the other hand, Pipelle biopsy and diagnostic curettage showed similar success rates in diagnosing hyperplasia without atypia, demonstrating relatively high sensitivity.

A total of 3.5 % of patients were found to have atypical hyperplasia. It is worth noting that the small number of patients with atypical hyperplasia limits the accuracy of sensitivity assessment for both methods. However, based on the available data, both methods displayed statistically high sensitivity in diagnosing atypical hyperplasia.

Considering the ease of performing Pipelle biopsy in any medical institution and its informative nature, the study concludes that it is appropriate to utilize it as a screening method for diagnosing endometrial pathologies. This suggests that Pipelle biopsy can serve as a valuable tool in evaluating patients with suspected endometrial abnormalities.

It is important to consider the strengths and limitations of this study. The strengths include comparing multiple biopsy methods, a significant sample size, and a histopathological assessment of the collected samples. However, the study could benefit from a larger sample size, particularly in evaluating atypical hyperplasia. Additionally, further research could explore each method's cost-efficiency and patient acceptability, along with their respective complication rates.

### Conclusion

This comparative evaluation provides valuable evidence on the efficacy of different biopsy methods for diagnosing endometrial pathology in pre- and postmenopausal women. The findings suggest that Pipelle biopsy can be a convenient screening method for identifying various endometrial pathologies. Our research findings along with other performed studies, Pipelle biopsy demonstrates a high diagnostic accuracy in various endometrial pathologies, except for endometrial polyps. The results of this study contribute to the existing body of knowledge and can guide clinical decision-making in evaluating patients with endometrial abnormalities.

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## DYNAMICS OF CLINICAL AND PSYCHOPATHOLOGICAL CHARACTERISTICS IN PATIENTS WITH NEGATIVE SYMPTOMS OF SCHIZOPHRENIA

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In the study 252 patients with negative symptoms of schizophrenia were examined: 83 patients with a first psychotic episode, 88 patients with schizophrenia in a state of exacerbation, and 81 patients with schizophrenia in a state of remission. The study of the clinical-psychopathological structure of patients with negative symptoms in schizophrenia at different stages of the disease included the analysis of the distribution of patients according to the severity of forms, the type of course and manifestations of schizophrenia, the duration and progression of the disease, the number of relapses, hospitalizations and the duration of episodes, and the presence of leading symptom complexes in the examined patients.

**Key words:** patients with schizophrenia, negative symptoms, clinical characteristics, clinical and anamnestic analysis, first psychotic episode, schizophrenia in a state of exacerbation, schizophrenia in a state of remission.

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## ДИНАМІКА КЛІНІКО-ПСИХОПАТОЛОГІЧНИХ ХАРАКТЕРИСТИК У ПАЦІЄНТІВ З НЕГАТИВНИМИ СИМПТОМАМИ ПРИ ШИЗОФРЕНІЇ

У дослідженні взяли участь 252 пацієнта з негативною симптоматикою при шизофренії: 83 пацієнта з першим психотичним епізодом, 88 пацієнтів з шизофренією в стані загострення та 81 пацієнт з шизофренією у стані ремісії. Вивчення клініко-психопатологічної структури у пацієнтів з негативними симптомами при шизофренії на різних етапах захворювання включало в себе аналіз розподілу пацієнтів за вираженістю форм, типом перебігу та проявів шизофренії, тривалістю і прогресивністю захворювання, кількістю рецидивів, госпіталізацій та тривалістю епізодів та наявністю провідних симптомокомплексів у досліджуваних.

**Ключові слова:** хворі на шизофренію, негативні симптоми, клінічні характеристики, клініко-анамнестичний аналіз, перший психотичний епізод, шизофренія у стані загострення, шизофренія у стані ремісії.

*The work is a fragment of the research project "To study patterns and factors of variability of clinical-psychological and psychophysiological characteristics of patients with depressive disorders in conditions of subsensory perception", state registration No. 0121U110685.*

The prevalence of schizophrenia in the world is from 0.3 to 1.4 % [9]. Negative symptoms (NS) are considered as core psychopathological or core symptoms in schizophrenia [2, 9]. Current epidemiological data on the prevalence of negative disorders indicate that these disorders are registered in 90 % of patients with schizophrenia [4]. For around 20–30 % of these patients, several characteristic domains of NS are manifested, that indicate an increased risk of chronicity of symptoms and an unfavorable outcome of the disease [5]. Most often, NS are not recognized, and primary NS do not respond or respond poorly to available types of therapy [7].

Schizophrenia, which occurs especially with negative disorders, entails serious financial costs for patients, their relatives, and the economy as a whole, making the disease one of the "most expensive" mental disorders [5, 6]. Since NS are associated with adverse functioning and outcome of schizophrenia, their recognition, correct assessment and treatment are extremely important [11]. However, the process of developing innovative treatment methods has been quite slow until now, and NS still represent an unsolved problem in the treatment of people suffering from schizophrenia [7, 11]. The clinical-psychopathological analysis of the NS structure and severity in patients with schizophrenia is essential for the diagnosis of the disease and is also directly related to treatment and rehabilitation. Therefore, the investigation of the peculiarities of clinical and anamnestic characteristics in patients with NS in schizophrenia is relevant and determines the purpose of this study.

**The purpose** of the study was to determine the features of clinical and anamnestic data in patients with schizophrenia for establishing determinants associated with negative symptoms at different stages of the pathological process development.

**Material and methods.** The study was carried out on the basis of SI the Institute of Neurology, Psychiatry and Narcology at the National Academy of Medical Sciences of Ukraine. In this study, 252 patients with NS in schizophrenia totally were examined, including 83 patients with the first psychotic