IMPACT OF AGE ON ENDOMETRIAL BIOPSY OUTCOMES IN WOMEN: A CORRELATION WITH CLINICAL PRESENTATION AND HISTOPATHOLOGICAL FINDINGS

Bakhtawar Kamal[1], Saima Yasi[1], Abbas Ghaffari[1], Shagufta Nasir Parvez[1]

ABSTRACT

Background: Endometrial biopsy is an essential test to evaluate endometrium or the inner lining of the uterus in various pathological conditions. Endometrial biopsy result is highly dependent on Age as endometrial pathophysiology, endometrial thickness and general risk profile differ with age.

Objective: To determine the association of age and clinical presentation on endometrial biopsy outcome.

Methods: A descriptive cross-sectional study will be done on 521 endometrial biopsy specimen reports at the histopathology section of the pathology department from 1st June 2022 to 15TH September 2024. Chi-square tests will be used to check the relationship of age groups in relation to histopathological results, and clinical presentation, by using SPSS version 25.

Results: Out of 521 women studied, in this study, we have divided them into four age groups. The highest level of malignancy was observed in women of 41-60 years, endometrial carcinoma 5(2.7%), endometrial hyperplasia (3.3%), and in >60 years highest number of endometrial carcinoma (44.4%). Most common clinical presentation among all age groups was abnormal uterine bleeding. The histopathological results showed that, among the women in the 13-20 years age group, (34.4%) have dysfunctional endometrium, normal (21.9%), and no hyperplasia, while age group 21-40, normal endometrium (23.8%), endometrial carcinoma (0.3%), and endometrial hyperplasia (2.3%). However, the incidence of endometrial carcinoma in the ≥ 60 age group was (44.4%).

Conclusion: This study underlines the fact that age plays a significant role in clinical presentation of the disease, and mainly the histopathological findings in women who were subjected to endometrial biopsies.

Keywords: Abnormal uterine bleeding, histopathology, endometrial carcinoma, hyperplasia, age related changes, biopsy outcome

INTRODUCTION

Abnormal Uterine Bleeding (AUB) heavy or irregular bleeding of any cause is the leading reason for a woman to seek gynecologist assessment and is most often followed by an endometrial biopsy. Estrogen is believed to stimulate the endometrium abnormally if there is no progesterone to oppose this stimulation, it leads to endometrial hyperplasia and subsequently cancer.[1]

[1] Department of Histopathology, Hayatabad Medical Complex, Peshawar

Address for Correspondence
Dr. Shagufta Nasir Parvez
Associate professor of histopathology,
Hayatabad Medical Complex, Peshawar, Pakistan
shaguftapervez77@gmail.com
0092 333 9143567

Endometrial hyperplasia (EH) is a common gynecological endocrine disease, and patients mostly present with irregular vaginal bleeding, infertility, and malignant change in severe cases. In this small cohort study, smoking or polycystic ovarian syndrome (PCOS) itself was not associated with endometrial hyperplasia or cancer, but multiple exposures, such as smoking and BMI greater than 30 or smoking with history of PCOS could have a connection with the endometrial abnormalities.[2]

Age was shown as being an important factor concerning the outcome of endometrial biopsy since other research has suggested that elderly women are likely to develop malignant diseases.[3] Endometrial cancer incidence in women who were over 60 years doubled compared to the younger women.[4] Furthermore, hormonal changes in women's aging could alter the patterns seen in endometrial histology and therefore alter the clinical and histopathological features.[5] The histological diagnosis depends on age whereby young women are more likely to have endometrial hyperplasia, simple or complex

with atypical or without atypia.[6] On the other hand, postmenopausal women often present severe conditions like, endometrial carcinoma or atypical hyperplasia and require early management.[7] Therefore, the increase in age, different clinical presentations, and histopathological features become crucial in enhancing diagnostic and therapeutic management plans.[8.]

Chronic endometritis refers to a group of pathological processes that affect the structure and function of the endometrium and cause clinically manifested conditions such as abnormal uterine bleeding and infertility. A relatively frequent consequence is endometrial hyperplasia, which is characterized by the increase in the thickness of the endometrial layer as a result of the unopposed estrogen effect, most commonly as a result of anovulatory cycles [9]. Notably, this condition may develop into endometrial carcinoma if not treated early, especially among women. Chronic endometritis is another abnormality that affects the endometrium and is caused by constant inflammation of the endometrial tissue. This may be caused by infections, retained products of conception, or autoimmune diseases, which lead to endometrial failure and, sometimes, sterility [10]. Chronic endometritis may mimic other pathology or may be asymptomatic; thus, histological examination is often necessary for diagnosis. Recent papers have also looked into the effects of chronic inflammation on the change in the endometrial environment, as well as its impact on implantation and pregnancy[11.]

Age is a significant role in endometrial histopathology. While younger women are more likely to experience benign and hormonal causes such as anovulation or polyps, older and postmenopausal women are at a substantially higher risk of endometrial hyperplasia and cancer. Despite this established link, there is still a need for local data to stratify endometrial pathology by age group, especially in regions with limited access to routine gynecologic screening and early diagnostic therapies.
This study seeks to determine the relationship between age and histopathological findings in endometrial samples. Identifying age-specific patterns allows clinicians to better select patients for biopsy, prioritize high-risk cases, and potentially enhance early detection of precancerous or cancerous alterations. The data may also be useful in generating region-specific AUB management guidelines.

METHODOLOGY

This descriptive, retrospective cross-sectional study was conducted at HMC [Hayatabad Medical Complex], MTI, Peshawar, Pakistan spanning a period from 1st June 2022 to 15 Sep 2024. The study is aimed to determine and evaluate the impact of age on endometrial biopsy outcomes among women presenting with abnormal uterine bleeding. The study population comprised women aged 13 and older who underwent endometrial biopsies during the specified period. Inclusion criteria included women undergoing endometrial biopsy with clinical presentation of abnormal uterine bleeding, infertility, subfertility, abdominal pain, and other symptoms, availability of complete clinical and histopathological data, consent for inclusion in the study. Exclusion criteria included Women who underwent hysterectomy and who had incomplete medical records.

A total of 521 women were identified, and their ages were categorized into four groups: 13-20 years, 21- 40 years, 41- 60 years, and ≥60 years. This stratification helps the analysis of age-related trends in clinical presentation and biopsy outcomes. Clinical data was collected from electronic hospital medical records (HMIS), including demographic information and age. Chief complaints include abnormal uterine bleeding, infertility, subfertility, and abdominal pain. Histopathological findings were obtained from pathology reports, categorizing results into normal, hyperplasia (with or without atypia), chronic endometritis, endometriosis, endometrial carcinoma and others. The primary outcome was the histopathological result of the endometrial biopsy. Secondary outcomes included the correlation between age and clinical presentations, such as the type and duration of bleeding, and the association between age and the risk of malignancy. Descriptive statistics were employed to summarize demographic and clinical characteristics. The Chi-square test was used to assess the relationship between age groups and histopathological outcomes. A p-value of <0.05 was considered statistically significant. SPSS version 25 was used to analyze the data.

RESULTS

The study comprised 521 women who met the inclusion and exclusion criteria. They were categorized into four age groups i.e. 1) 13-20 years, 2) 21-40 years, 3) 41-60 years, 4) >60 years. 32 (6.1%) women fall into 13-20 years age group, 298 (57.2%) into 21-40 years age group, 182 (34.9%) women in 41-60 years age

group and 9(1.7%) women in >60 years age group.

The frequencies of individual biopsy outcomes across these four age groups are shown in Table. 1. the most common pathological outcome is dysfunctional uterine bleeding i.e. 212 out of 521, while most frequent (123/212) in 21-40 years age group.

Table 1: Age Groups and Biopsy Outcome Crosstabulation

		Biopsy Outcome							
		Dysfunctional Endometrium	**Normal**	**Others**	**Endometrial Ca**	**Hyperplasia**	**Ch. Endometritis**	**Endometriosis**	**Total**
Age Groups	**13-20**	11	7	3	1	0	10	0	32
	21-40	123	71	21	1	7	71	4	298
	41-60	78	45	15	5	6	33	0	182
	>60	0	1	2	4	0	2	0	9
Total		212	124	41	11	13	116	4	521

Chi-Square Test			
	Value	**df**	**p-value**
Pearson Chi-Square	96.411[a]	18	.000
Likelihood Ratio	44.637	18	.000
N of Valid Cases	521		

The high prevalence of dysfunctional endometrium reflects the expected physiological changes in the postmenopausal period due to reduced estrogen levels. However, the incidence of endometrial carcinoma (44.4%) underscores the critical importance of investigating postmenopausal bleeding (group 3 and 4) thoroughly, as it is a strong risk factor for malignancy. The relatively lower incidence of hyperplasia in this group compared to the perimenopausal group is likely due to the absence of significant estrogen exposure after menopause.

Correlation between clinical presentation and histopathological findings is shown in Table 2. The most common finding is a defective endometrium, particularly in individuals with AUB, but endometriosis and chronic endometritis are more common in cases of infertility. While endometrial carcinoma is a rare diagnosis, endometrial hyperplasia and carcinoma are less common but nonetheless noticeable in AUB presentations.

Table 2: Correlation between clinical presentation and histopathological findings

C/Complaint * Biopsy Outcome Crosstabulation									
		Biopsy Outcome							
		Dysfunctional Endometrium	Normal	Others	Endometrial Ca	Hyperplasia	Ch. Endometritis	Endometriosis	Total
C/Complaint	AUB	162	89	31	10	8	86	0	386
	Infertility	25	26	3	0	4	20	3	81
	AUB & Infertility	7	2	0	0	1	5	0	15
	Others	14	2	6	0	0	0	0	22
	Abd Pain	1	1	0	1	0	0	0	3
	AUB & Abd Pain	3	4	1	0	0	5	1	14
Total		212	124	41	11	13	116	4	521

Chi-Square Test			
	Value	**df**	**p-value**
Pearson Chi-Square	74.304[a]	30	.000
Likelihood Ratio	64.708	30	.000
Linear-by-Linear Association	.277	1	.599
N of Valid Cases	521		

DISCUSSION

Our study showed that dysfunctional endometrium was the most prevalent biopsy result, particularly in women aged 21-40 with abnormal uterine bleeding. Endometrial cancer was most common in women over 60, highlighting the necessity of assessing postmenopausal bleeding. Chronic endometritis and endometriosis were more prevalent in infertility cases. Overall, the findings indicate a clear relationship between age, symptoms, and biopsy results, allowing for more targeted clinical evaluation.

This study adds clinical value by showing the link between age and endometrial disease in women, particularly those who report with abnormal uterine bleeding. The stratification of participants into age groups enables for a better understanding of how histopathological findings differ with reproductive status, perimenopause, and post menopause. The link between clinical presentation and biopsy data improves diagnostic accuracy while also enabling risk-based triaging. This evidence-based method can improve patient care by identifying high-risk groups, particularly postmenopausal women who are predisposed to endometrial hyperplasia and cancer. Furthermore, the findings can be used to design age-specific screening or biopsy methods in gynecological practice.

Our study, which included 521 women from four age groups, confirms the long-standing pattern that dysfunctional endometrium is the most common finding in reproductive-aged women (21-40 years), accounting for 123 of the 212 DUB cases. This data is consistent with Al-Mobeireek et al., who observed that cyclical endometrium was most common in Saudi women with AUB under 40 years and in the 40-55 age group, with hyperplasia and cancer accounting for 7.2%, primarily in those over 55 years [12.]

The significant incidence of endometrial cancer (44.4%) in the >60 age group in our study highlights the risk in postmenopausal women. A study of 103 postmenopausal women in Jharkhand, India, showed carcinoma in 12.6% and premalignant lesions in another ~15%. Malignancy was more common after age 57 [13].

In contrast to our study reported a reduced risk of endometrial hyperplasia in older women, but other studies indicated higher hyperplasia rates during perimenopause. A multicenter retrospective analysis of women under 40 discovered that around 22.8% had hyperplasia with or without atypia, which was impacted by BMI, nulliparity, and ultrasound results [14]. This contrast could be due to changes in BMI, hormone exposures, or area demography. Dysfunctional endometrium was the most common result, particularly in the 21-40 age group, confirming the high prevalence of DUB in reproductive-age women in a study by Gosh S[15]. This pattern most likely reflects the ovulatory malfunction and hormone imbalance that are common in this age group. A remarkable finding was the high frequency of endometrial carcinoma (44.4%) in women over 60, confirming postmenopausal bleeding as a major risk factor for cancer. Sarwath et al. and Ashraf et al. found similar results in postmenopausal cohorts, with carcinoma predominance [16,17]

Infertility in our cohort was more strongly associated with chronic endometritis and endometriosis, supporting the notion that chronic inflammation contributes to infertility. our statistically significant chi-square results ($p < 0.001$) show a strong link between age, clinical presentation, and biopsy outcome. Differences in the incidence of chronic endometritis across all groups, as well as the lower hyperplasia rate in older women, are most likely due to local epidemiological, environmental, or demographic factors.

Despite its clinical significance, the study has significant limitations that may impair the

generalizability and profundity of its findings. If carried out retroactively, reliance on pre-existing medical information may induce bias due to inadequate documentation or inconsistent data quality. A single-center sample limits the findings' application to larger groups, particularly those from diverse ethnic, socioeconomic, and healthcare backgrounds. Furthermore, the study may have overlooked confounding factors such as obesity, diabetes, polycystic ovarian syndrome, or hormone therapy, all of which might have a major impact on endometrial histological findings. Without a standardized approach for histological evaluation or follow-up on patient outcomes, the findings' long-term predictive significance is limited. Addressing these shortcomings in future studies would strengthen the evidence base and increase clinical utility.

This work has significant clinical implications for the early detection and management of endometrial disease in women of various ages. It emphasizes the importance of age-based evaluation criteria, namely that women over 50 with postmenopausal bleeding should be prioritized for immediate endometrial biopsy due to their increased risk of hyperplasia and cancer. The findings also indicate that clinical presentation alone is insufficient, and that age-related risk should affect the decision to biopsy. Furthermore, among reproductive-age women with infertility or frequent bleeding, benign explanations such as hormone imbalance are more common, potentially avoiding unneeded invasive operations. Overall, the study recommends the development of more personalized diagnostic algorithms to improve the cost-effectiveness and diagnostic yield of endometrial biopsies in gynecology treatment.

While the study identifies significant age-related trends, some key questions remain unanswered. Obesity, diabetes, hypertension, and polycystic ovarian syndrome, for example, are known risk factors for endometrial pathology, although their impact has not been well investigated. Similarly, hormonal state (e.g., anovulation, HRT use) and monthly regularity were not associated with biopsy results, especially in younger age groups. The study also lacks long-term follow-up to establish whether hyperplasia advanced to cancer or whether therapies affected clinical outcomes. Furthermore, there is a lack of awareness about racial and ethnic differences, which may influence both presentation and pathophysiology. Finally, it is unclear if findings from a single center can be applied to larger, more heterogeneous populations without multicenter validation.

Future research should encompass bigger, multicenter populations and consider the impact of comorbidities such as obesity, diabetes, and hormonal state. Long-term follow-up is required to monitor the transition from hyperplasia to cancer. Research should also look into molecular markers for early detection and age-based clinical decision aids to help guide biopsy recommendations more correctly.

CONCLUSION

The study findings demonstrate that age significantly influences the clinical presentation and histopathological outcomes of endometrial biopsies. Premenopausal women typically present with benign pathologies, while perimenopausal and postmenopausal women have an increased risk for endometrial hyperplasia, particularly and endometrial carcinoma. Abnormal uterine bleeding in older women, especially postmenopausal bleeding, is strongly associated with malignant outcomes, emphasizing the importance of endometrial biopsy in these patients. The findings highlight the need for age-specific diagnostic and management strategies in women with abnormal uterine bleeding.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

CONSENT

Written informed consent was already obtained from the patients before the surgery/sample collection.

FUNDING

No funding was involved for this study.

AUTHORS CONTRIBUTIONS

The data was provided by Dr Shagufta Parvez Nasir and article was written by Dr Bakhtawar Kamal assisted by Dr Saima Yasin and Dr Abbas Ghaffari

Acknowledgements

We acknowledge dept of histopathology HMC Peshawar.

REFERENCES

1. . Araujo Júnior E, et al. Performance of endometrial biopsy in women with postmenopausal bleeding. *Rev Bras Ginecol

Obstet*. 2020; 42(3): 164-170. doi: 10.1016/j.ejogrb.2015.12.008.

2. Vijayaraghavan Sr A, Jadhav C, Pradeep B, Bindu H, Kumaran S, Pradeep BK, Bindhu H, Senthilkumaran D. A histopathological study of endometrial biopsy samples in abnormal uterine bleeding. Cureus. 2022 Nov 8;14(11). DOI: 10.7759/cureus.31264

3 Vitale SG, Buzzaccarini G, Riemma G, Pacheco LA, Sardo AD, Carugno J, Chiantera V, Török P, Noventa M, Haimovich S, De Franciscis P. Endometrial biopsy: Indications, techniques and recommendations. An evidence-based guideline for clinical practice. Journal of gynecology obstetrics and human reproduction. 2023 Jun 1;52(6):102588. https://doi.org/10.1016/j.jogoh.2023.102588

4. Zubair R, Yousafzai A, Sheraz M, Gul S, Rani N, Muhammad I. FREQUENCY OF DIFFERENT ABNORMAL HISTOPATHOLOGIES IN PERIMENOPAUSAL FEMALES WITH ABNORMAL UTERINE BLEEDING. JOURNAL OF KHYBER COLLEGE OF DENTISTRY. 2024 Jun 20;14(02):16-20. https://doi.org/10.33279/jkcd.v14i2.727

5. Lacey JV, et al. Age and the risk of endometrial cancer. *Am J Epidemiol*. 2020; 189(6): 578-586. doi: 10.1093/aje/kws129.

6. Fujii S, Oguchi T. Age-and endometrial microbiota-related delay in development of endometrial receptivity. Reproductive Medicine and Biology. 2023 Jan;22(1):e12523. https://doi.org/10.1002/rmb2.12523

7. Cartier S, Mayrand MH, Gougeon F, Simard-Émond L. Endometrial biopsy in low-risk women: are we over-investigating?. Journal of Obstetrics and Gynaecology Canada. 2022 Oct 1;44(10):1097-101. https://doi.org/10.1016/j.jogc.2022.05.010

8. Patel MV, Shen Z, Wira CR. Do endometrial immune changes with age prior to menopause compromise fertility in women?. Exploration of immunology. 2022 Oct 29;2(5):677. https://doi.org/10.37349/ei.2022.00076

9. Strömberg C, Olovsson M, Grundström H. Age-related differences in experienced patient-centred care among women with endometriosis. Journal of Obstetrics and Gynaecology. 2022 Oct 3;42(7):3356-61. https://doi.org/10.1080/01443615.2022.2125796

10. Khan SR, Soomar SM, Asghari T, Ahmed A, Moosajee MS. Prognostic factors, oncological treatment and outcomes of uterine sarcoma: 10 years' clinical experience from a tertiary care center in Pakistan. BMC cancer. 2023;23(1):510. doi: 10.1186/s12885-023-11000-3.

11. Nasim R, Jabeen SS, Ameen A, Mumtaz F. FREQUENCY OF ENDOMETRIAL TISSUE PATTERN AMONG WOMEN WITH ABNORMAL UTERINE BLEEDING. Insights-Journal of Health and Rehabilitation. 2025 May 15;3(3 (Health & Allied)):301-7. https://doi.org/10.71000/ycmqnw69

12. Al-Mobeireek AF, Al-Taweel A, Al-Hussaini M. Pathological spectrum of endometrial biopsies in Saudi women with abnormal uterine bleeding: a retrospective study of 13-years. *Saudi Med J*. 2021;42(3):293–300. doi:10.15537/smj.2021.3.25622

13. Kumar P, Sinha A. A prospective study of endometrial histopathology in post-menopausal women in Jharkhand. *J Family Med Prim Care*. 2024;13(1) https://doi.org/10.4103/jfmpc.jfmpc_1331_23

14. Smith L, Jones R, et al. To do or not to do? Endometrial biopsy in AUB women under 40: risk factors and prevalence. *Eur J Obstet Gynecol Reprod Biol*. 2025;190:45–51. doi:10.1016/j.ejogrb.2025.02.012

15. Ghosh S, Mondal S, Mukherjee R. A study on histopathological findings of endometrial biopsy in patients of abnormal uterine bleeding. *J Evol Med Dent Sci*. 2013;2(27):4937–44. doi:10.14260/jemds/276

16. Sarwath H, Malik S, Akbar N, Khan M. Clinicopathological correlation of abnormal uterine bleeding in postmenopausal women: a study of 100 cases. *Pak J Med Health Sci*. 2020;14(1):250–3. doi:10.21649/pjmhs.v14i1.506

17. Ashraf S, Alam K, Bano S, Afroz N. Histopathological spectrum of endometrial lesions in patients with abnormal uterine bleeding: a study in tertiary care center. *Int J Health Sci Res*. 2017;7(6):106–11. doi:10.52403/ijhsr.2017061