Original Article

Spectrum of Histopathological Findings of Endometrial Carcinoma among Women with Postmenopausal Bleeding

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Abstract

Objective: To determine the different histopathological findings in endometrial carcinoma biopsies received with a history of postmenopausal bleeding.

Methodology: This cross-sectional study was conducted at department of Pathology and Microbiology, LUMHS, Hyderabad/Jamshoro, from March 2023 to August 2023. Overall 138 endometrial or uterine biopsy specimens were collected from women over 45 years of age with endometrial carcinoma and a clinical history of postmenopausal bleeding were incorporated. The specimens were processed and grossed according to Rosai and Ackerman's surgical pathology guidelines, followed by formalin fixation, paraffin embedding, and H&E staining. Data regarding histopathological diagnosis were recorded analysis was carried out using SPSS version 22.

Results: Overall mean age of women was 56.32+8.55 years. Endometrioid carcinoma was found most common histopathological finding among (85.5%) of the cases, followed by serous carcinoma (6.5%) and moderately differentiated SCC (4.3%), clear cell carcinoma and endometrial stromal sarcoma were each seen in 1.4% of cases, and malignant mixed Müllerian tumor only (0.7%). Endometrioid carcinoma was the most frequent diagnosis across all age groups, specifically in the 51–60 years (33.3%) and 45–50 years (31.9%) groups, (p = 0.946).

Conclusion: Endometrioid carcinoma being the most common diagnosis of malignancy among women with PMB, indicating timely histopathological evaluation for early detection and management of malignancies in PMB cases is very important.

Key words: PMB, Histopathology, Endometrial cancer.

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Introduction

The postmenopausal bleeding (PMB), namely uterine bleeding occurring after 12 consecutive months of amenorrhea among women not receiving hormone replacement therapy (HRT), is an alarming clinical symptom that suggests thorough evaluation.[1,2] It affects approximately 4% to 11% of postmenopausal women and can often have a benign cause, while among most cases it represents the sole presenting sign of endometrial carcinoma (EC).[2] EC is the most common gynecological malignancy in the developed world and continues to increase in both incidence and mortality rate, a trend endorsed largely to increasing rates of obesity, nutritional factors, physical inactivity, medical conditions like hormone therapy, infertility, late menopause, nulliparity, metabolic syndrome, diabetes, and smoking as important risk factors for EC.[3,4] It principally affects postmenopausal women, typically occurring in the sixth and seventh decades of life of a women,[5] with suspected age at diagnosis ranging between 55 and 70 years in series mostly. Whereas rates in developing countries have historically been lower than in populations of the in high-income nations,[6] EC remains an important cause of gynecological cancer morbidity across South Asia, and

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its accurate regional burden is likely underestimated due to access variable to diagnostic services and histopathological capability.

PMB is widely established as the cardinal presenting symptom of EC, with around 90% of women subsequently diagnosed with the disease reporting abnormal uterine bleeding earlier to the diagnosis.[7]

Nevertheless, the PMB is not specific to malignancy; it may also arise from a broad spectrum of benign situations, including atrophy of endometrium, polyps, and changes of hyperplasia, making histopathological confirmation importance for correct diagnosis and suitable management.[7] For such reason, the current diagnostic pathways combine transvaginal sonographic evaluation of endometrial thickness with sampling of endometrium, whether by the biopsy, curettage, or hysteroscopic-guided tissue retrieval, to consistently distinguish malignant from benign causes of bleeding in this population.[8]

Histologically, EC has usually been classified according to the Bokhman dualistic model into Type I tumors, which are estrogen-dependent, mainly of endometrioid or mucinous morphologically, and generally carry a favorable prognosis, while Type II tumors, which arise independently of stimulation of estrogen, comprise serous, clear cell, and carcinosarcoma histologies, and are related with more aggressive behavior and adverse outcomes.[9] The endometrioid carcinoma is constantly reported as the predominant subtype globally, accounting for around 70 to 80% of cases in most large series, however the proportion of non-endometrioid and other rare histological alternatives, including squamous cell carcinoma (SCC), clear cell carcinoma, and malignant mixed Müllerian tumor, fluctuates considerably across diverse populations and the healthcare settings.[10] Recently, the incorporation of molecular classification, based on POLE mutation status, mismatch repair deficiency, abnormality of p53, and no specific molecular profile, has been progressively integrated alongside traditional histology to refine the stratification of prognosis and guide planning for individualized treatment.[11]

According to the regional data from South Asia, including Pakistan have revealed a broadly similar predominance of the endometrioid histology, commonly ranging from 78% to 88% of the patients, though distinguished variation exists in the reported frequency of rarer subtypes like as SCC and carcinosarcoma between different institutions and the populations.[11,12] Regardless of this rising body of regional literature, comprehensive, updated data labeling the recent histopathological spectrum of EC particularly among women presenting with PMB remain limited in many local regions, and existing studies vary substantially in sample size, diagnostic methods and distribution reported subtype. Determining an accurate, contemporary picture of this histopathological spectrum is important not only for the proper diagnostic and management protocols but also for recognizing any population-specific patterns that may vary from international norms. Therefore this study was conducted to assess the spectrum of histopathological findings of EC specimens taken from women with postmenopausal bleeding.

Methodology

A cross-sectional study was conducted at the Department of Pathology and Microbiology, Liaquat University of Medical and Health Sciences (LUMHS), Hyderabad/Jamshoro, over a period of six months (March 2023 to August 2023) after obtaining ethical approval from the Ethical Review Committee of LUMHS (Ref. No. LUMHS/REC-206). The sample size of 138 patients was calculated using the standard sample size formula, assuming a prevalence of postmenopausal bleeding of 10%, a 95% confidence level, and a 5% margin of error. Non-probability purposive sampling was employed.

All endometrial biopsy specimens obtained from women aged over 45 years presenting with postmenopausal bleeding and diagnosed with endometrial carcinoma were included in the study. Scanty, poorly fixed or autolyzed specimens, specimens from patients who had already received hormonal therapy or chemotherapy, and specimens diagnosed as benign lesions were excluded.

The biopsy specimens were identified, grossly examined, fixed in 10% neutral buffered formalin, processed using an automated tissue processor, embedded in paraffin wax, sectioned into 2–5 µm thick slices using a microtome, and stained with hematoxylin and eosin (H&E) according to standard laboratory protocols. The stained slides were examined microscopically under different magnifications to establish the diagnosis based on Rosai and Ackerman's criteria, including histological grading and staging where applicable. Histopathological findings

were defined as abnormal microscopic tissue changes and were categorized according to the different histological types of endometrial carcinoma.

All relevant data were entered and analyzed using SPSS version 22. Continuous variables, such as age, were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. After stratification, the chi-square test was applied to assess associations, and a p-value of <0.05 was considered statistically significant.

Results

A total of 138 patients with endometrial carcinoma were included in the study. The patients ranged in age from 45 to 80 years, with a mean age of 56.32 ± 8.55 years. Most patients (71.0%) were from urban areas, while 29.0% resided in rural areas. Histopathological examination showed that endometrioid carcinoma was the most common subtype, accounting for 85.5% of cases, followed by serous carcinoma (6.5%) and moderately differentiated squamous cell carcinoma (SCC) (4.3%). Clear cell carcinoma and endometrial stromal sarcoma each accounted for 1.4% of cases, whereas malignant mixed Müllerian tumor was the least frequent histopathological subtype (0.7%) (Table I).

Table I: Histopathological evaluation of women with PMB. (n=138)

Histopathological evaluation	N	%
Serous carcinoma	09	6.5
Clear cell carcinoma	02	1.4
Endometrioid carcinoma	118	85.5
Moderately differentiated squamous cell carcinoma	06	4.3
Malignant mixed Müllerian tumor	01	0.7
Endometrial stromal sarcoma	02	1.4
Total	138	100.0

Post-stratification analysis demonstrated that endometrioid carcinoma remained the predominant histological subtype across all age groups, with the highest frequencies observed among patients aged 51–60 years (33.3%) and 45–50 years (31.9%). No statistically significant association was found between histological subtype and age group (p = 0.946) (Table II).

Similarly, endometrioid carcinoma was the most common histological subtype among both urban (63.0%) and rural (22.5%) residents. Overall, most patients were from urban areas (71.0%). There was no statistically significant association between histological subtype and residential status (p = 0.946) (Table III).

Table III: Histological diagnosis according to residential status. (n=138)

Histological diagnosis	AGE GROUPS			p-value
	Urban	Rural	**Total**	
Serous carcinoma	6	3	9	0.946
	4.3%	2.2%	6.5%	
Clear cell carcinoma	1	1	2	
	0.7%	0.7%	1.4%	
Endometrioid carcinoma	87	31	118	
	63.0%	22.5%	85.5%	
Moderately differentiated SCC	3	3	6	
	2.2%	2.2%	4.3%	
Malignant mixed Müllerian tumor	1	0	1	
	0.7%	0.0%	0.7%	
Endometrial stromal sarcoma	0	2	2	
	0.0%	1.4%	1.4%	
Total	98	40	138	
	71.0%	29.0%	100.0%	

Discussion

The mean age of women presenting with postmenopausal bleeding (PMB) in the present study was 56.32 ± 8.55 years, which is consistent with previous studies. Talwar et al.[13] reported a comparable

Table II: Histological diagnosis according to age groups. (n=138)

Histological diagnosis	AGE GROUPS				p-value
	45-50 yrs	**51-60 yrs**	**61-70 yrs**	**71-80 yrs**	
Serous carcinoma	5	3	1	0	0.946
	3.6%	2.2%	0.7%	0.0%	
Clear cell carcinoma	1	0	1	0	
	0.7%	0.0%	0.7%	0.0%	
Endometrioid carcinoma	44	46	23	5	
	31.9%	33.3%	16.7%	3.6%	
Moderately differentiated SCC	2	3	1	0	
	1.4%	2.2%	0.7%	0.0%	
Malignant mixed Müllerian tumor	0	1	0	0	
	0.0%	0.7%	0.0%	0.0%	
Endometrial stromal sarcoma	1	0	1	0	
	0.7%	0.0%	0.7%	0.0%	
Total	53	53	27	5	
	38.4%	38.4%	19.6%	3.6%	

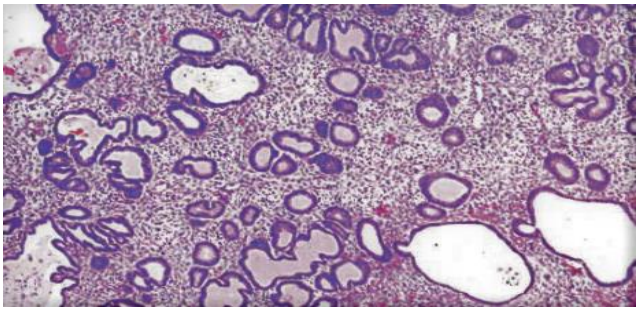


Fig: 1: Endometrial Polyp

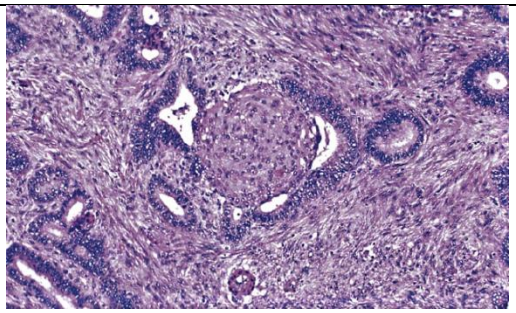


Fig: 2. Adenomyomatous Poly

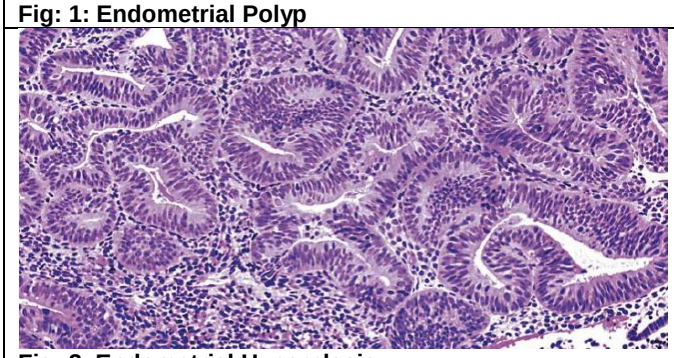


Fig: 3. Endometrial Hyperplasia

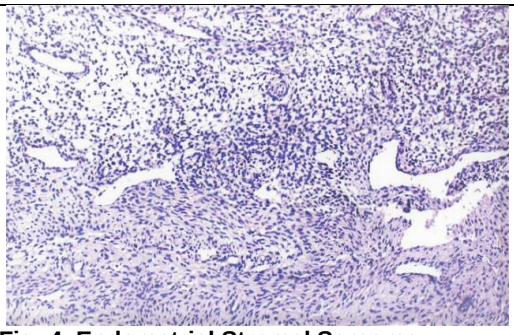
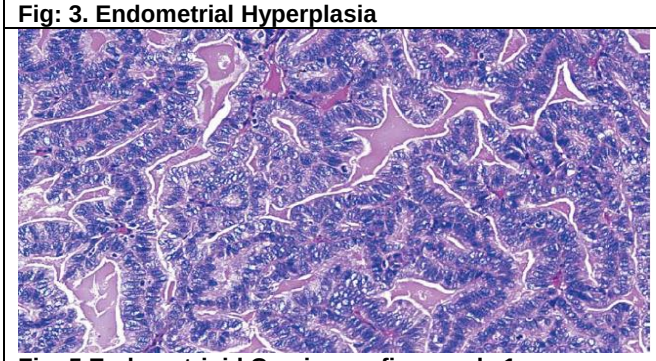


Fig: 4. Endometrial Stromal Sarcoma



Fig; 5.Endometrioid Carcinoma figo grade 1

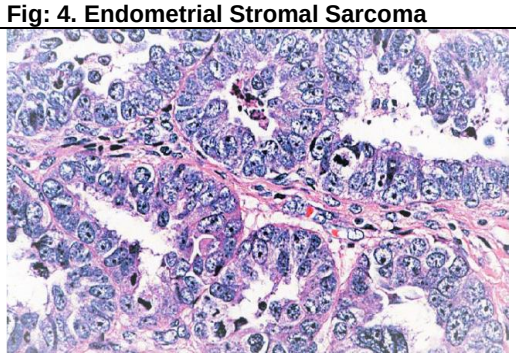


Fig: 6: Endometroid Carcinoma figo grade 3

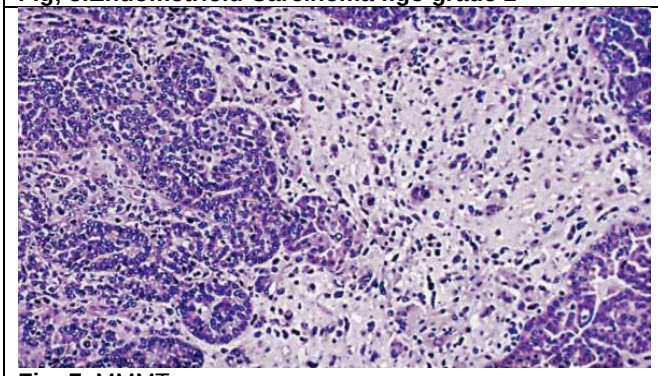


Fig: 7. MMMT

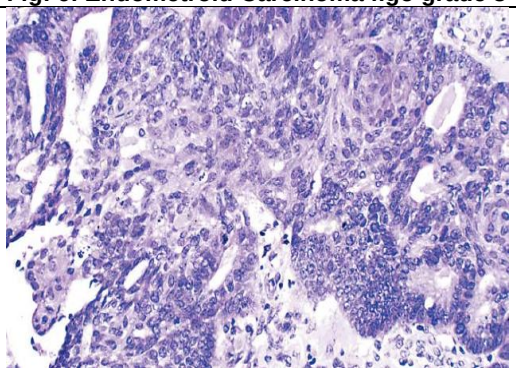


Fig: 8. Moderately differentiated SCC

age range of 45–80 years, with a mean age of 54.97 ± 5.86 years. In their study, 49.16% of women presented with PMB within three years of menopause, and parity of three was the most common (30.83%). Similarly, Anita et al.[15] reported a mean age of 56.26 years, with the highest incidence of malignancy observed among women aged 55–70 years. Devi et al.[14] documented a slightly younger menopausal population, reporting a mean menopausal age of 48.64 years with patients ranging from 45 to 70 years. The similarity in the mean age across these studies suggests that PMB predominantly affects women in the sixth decade of life. Minor variations may be attributed to differences in study populations, geographical settings, demographic characteristics, inclusion criteria, and sociocultural factors influencing healthcare-seeking behavior.

In the present study, endometrioid carcinoma was the predominant histopathological subtype, accounting for 85.5% of all cases. This was followed by serous carcinoma (6.5%) and moderately differentiated

squamous cell carcinoma (SCC) (4.3%), while clear cell carcinoma and endometrial stromal sarcoma each constituted 1.4% of cases. Malignant mixed Müllerian tumor was the least frequent subtype, representing only 0.7% of cases. These findings are consistent with both national and international literature, where endometrioid carcinoma remains the most common histological subtype of endometrial carcinoma.

A study from Lahore by Tanvir et al.[16] reported a similar distribution, with endometrioid adenocarcinoma accounting for approximately 80% of cases, followed by serous carcinoma (11%), clear cell carcinoma (4%), and SCC (4%). Likewise, Samoon et al.[17] reported endometrioid carcinoma in 81.56% of patients, further supporting the predominance of this subtype in the Pakistani population.

Comparable findings have also been reported from neighboring countries. Pradhan et al.[10], in a tertiary care study from Eastern India, observed endometrioid carcinoma in 78.6% of cases, followed by serous carcinoma (10.1%), mucinous carcinoma (4.8%), clear cell carcinoma (4.2%), and carcinosarcoma (2.4%). Although the distribution followed the same overall pattern, the proportion of endometrioid carcinoma was slightly lower than that observed in the present study. Similarly, Latha et al.[18] reported endometrioid adenocarcinoma in 85.72% of patients, a proportion almost identical to that observed in our cohort. Masih et al.[19] also demonstrated a high prevalence of endometrioid carcinoma (88.4%), with most tumors being moderately differentiated (FIGO Grade 2), highlighting that tumor grade, in addition to histological subtype, has important prognostic implications.

Prem et al.[20] from Kerala also reported endometrioid carcinoma as the predominant subtype (80%), although carcinosarcoma (8%), serous carcinoma (6.3%), and clear cell carcinoma (3.6%) were relatively more frequent than in the present study, whereas SCC was exceedingly rare (0.2%). Similarly, Olatunde et al.[21] from Nigeria reported endometrioid adenocarcinoma in approximately 80% of cases and identified serous carcinoma as the most common Type II tumor (20%), representing a substantially higher proportion than the 6.5% observed in our study. These differences may reflect variations in demographic characteristics, obesity, reproductive factors, menopausal age, genetic predisposition, environmental exposures, referral patterns, and sample selection across different populations.

Post-stratification analysis demonstrated that endometrioid carcinoma remained the predominant histological subtype across all age groups, with the highest frequencies observed among women aged 51–60 years (33.3%) and 45–50 years (31.9%). However, no statistically significant association was found between histological subtype and age group ($p = 0.946$). Similar observations have been reported by Prem et al.[20] and Tanvir et al.[16]

Overall, the findings of the present study reinforce the established predominance of endometrioid carcinoma among women with endometrial carcinoma in Pakistan. The relatively higher proportion of endometrioid carcinoma and the presence of SCC comparable to other local studies suggest that regional biological, environmental, and healthcare-related factors may influence the histopathological spectrum of endometrial carcinoma. Nevertheless, these findings should be interpreted cautiously, as they are based on a single-center study. Larger multicenter studies involving diverse populations are warranted to validate these observations and better characterize the histopathological profile of endometrial carcinoma in the region.

Conclusion

Study revealed the endometrioid carcinoma as dominant histopathological subtype among women with PMB, closely reflecting the regional and international literature pattern. Overall findings emphasize the importance of thorough histopathological evaluation of PMB, though also highlighting the importance of further larger, multi-centre studies specifically at local level to better understand and validate these local findings in the histopathological spectrum of endometrial carcinoma.

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