

Epidemiology of Endometrial Carcinoma Among Women with Postmenopausal Bleeding

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Abstract

Background: Postmenopausal bleeding (PMB) warrants prompt evaluation because it may indicate endometrial carcinoma and may also reflect premalignant endometrial disease. International estimates vary by geography and referral setting, while Albanian evidence is limited and has yielded markedly different hospital-based estimates.

Objective: To estimate the frequency of histologically confirmed endometrial carcinoma among women presenting with PMB, describe the histopathological spectrum, explore clinical and ultrasound characteristics associated with carcinoma, and reassess earlier Albanian hospital estimates using prospective consecutive ascertainment.

Methods: This prospective hospital-based observational cohort included all eligible consecutive women presenting with PMB at Queen Geraldine Obstetric–Gynecologic Hospital, Tirana, Albania, from January 2024 through December 2025. Clinical and transvaginal ultrasound variables were recorded before histopathological classification. The final cohort comprised 221 women with complete outcome data. Carcinoma frequency and histopathological proportions were reported with 95% confidence intervals (CIs). Exploratory between-group comparisons used Welch’s t test, Mann–Whitney U test, or Fisher’s exact test as appropriate.

Results: Endometrial carcinoma was diagnosed

in 24/221 women (10.9%; 95% CI 7.4–15.6). Atypical hyperplasia/endometrial intraepithelial neoplasia (EIN) occurred in 22.2% (95% CI 17.2–28.1) and hyperplasia without atypia in 28.5% (95% CI 23.0–34.8). Women with carcinoma were older, had more years since menopause, higher BMI, lower parity, longer bleeding duration, greater endometrial thickness, lower Doppler resistance and pulsatility indices, and higher vascularisation scores (all $p \leq 0.020$). Heterogeneous endometrium (OR 11.98, 95% CI 3.92–36.59), an intrauterine mass (OR 7.85, 95% CI 3.14–19.64), and high vascularisation (OR 23.97, 95% CI 7.70–74.60) were strongly associated with carcinoma.

Conclusions: Approximately one in nine women evaluated for PMB in this tertiary cohort had endometrial carcinoma, a frequency substantially lower than a previous 2018 Albanian hospital estimate and broadly consistent with international pooled evidence. The high burden of atypical hyperplasia/EIN indicates that PMB pathways must address both invasive malignancy and clinically important precursor lesions.

Keywords: Postmenopausal bleeding; Endometrial carcinoma; Endometrial intraepithelial neoplasia; Endometrial hyperplasia; Histopathology; Albania

INTRODUCTION

Postmenopausal bleeding (PMB) is a cardinal presenting symptom of endometrial carcinoma and requires structured evaluation. In a systematic review and meta-analysis of 129 studies, the pooled risk of endometrial cancer among women with PMB was approximately 9%, but estimates varied substantially by clinical setting and geography: about 5% in North America, 7% in Northern Europe, and 13% in Western Europe (1). This variation is clinically important because the observed diagnostic yield of a PMB pathway depends not only on disease occurrence but also on referral selection, background risk factors, and diagnostic practice. Endometrial cancer incidence has increased in several populations, in parallel with population ageing and the burden of obesity and metabolic disease (2).

Albanian evidence is sparse and heterogeneous. A retrospective series from Queen Geraldine Hospital published in 2016 included 102 women with PMB; 12% of histopathological diagnoses were malignant, and endometrial carcinoma accounted for 54.5% of the malignant diagnoses (3). A second retrospective study from the same tertiary hospital reviewed 200 women with PMB during 2018 and reported endometrial carcinoma in 33%. The authors explicitly attributed this high proportion to referral of more difficult cases to the tertiary center and recommended a large prospective study to reassess the percentage of endometrial cancer in Albania and investigate additional associated factors (4). These

discrepant local findings provide a clear rationale for contemporary, standardized ascertainment.

Current guidance and evidence emphasize comprehensive evaluation of PMB. In 2026, the American College of Obstetricians and Gynecologists updated its guidance to recommend combined transvaginal ultrasonography (TVUS) and endometrial tissue sampling as part of the initial evaluation for most patients with PMB, while allowing limited exceptions after individualized assessment (5). A 2025 systematic review and meta-analysis of 35 studies including 6,302 symptomatic postmenopausal patients found that an endometrial thickness threshold of ≤ 4 mm retained high sensitivity for excluding endometrial cancer, but was not perfectly sensitive, underscoring the need to interpret TVUS within the complete clinical context (6). PMB pathways must also identify premalignant disease: atypical endometrial hyperplasia/endometrial intraepithelial neoplasia (EIN/AEH) is a recognized precursor lesion for which concurrent carcinoma must be considered when management is planned (7). Contemporary European guidance from ESGO–ESTRO–ESP and ESMO likewise emphasizes histopathological confirmation, accurate classification, and risk-adapted management of endometrial carcinoma and its precursor lesions (8,9).

The primary objective of this study was to estimate the frequency of histologically confirmed endometrial carcinoma among women

presenting with PMB at Queen Geraldine Obstetric–Gynecologic Hospital from January 2024 through December 2025. Secondary objectives were to describe the complete histopathological spectrum, explore associations between carcinoma and prespecified clinical and ultrasound characteristics, and reassess earlier Albanian hospital-based estimates using prospective consecutive ascertainment.

MATERIALS AND METHODS

Study design and setting

This was a prospective, hospital-based observational cohort conducted at Queen Geraldine Obstetric–Gynecologic Hospital, Tirana, Albania, over 24 months, from January 2024 through December 2025. A prospective approach was used to permit consecutive enrolment at first presentation, standardized case definition, predefined collection of clinical and ultrasound variables, and recording of imaging findings before histopathological classification. These features reduce problems of incomplete or inconsistently recorded variables that can affect retrospective chart reviews; however, prospective enrolment does not eliminate referral or selection effects inherent to a tertiary hospital setting.

The 24-month study period constituted the operational sampling frame. No formal a priori sample-size calculation was performed because the study included all eligible consecutive presentations during this fixed period. The final analytic cohort comprised 221 women with complete diagnostic outcome classification.

Participants

PMB was defined as uterine bleeding occurring after at least 12 months of amenorrhoea in a woman not receiving cyclic hormone therapy. Eligible participants were postmenopausal women presenting with PMB who were evaluated at the study center and underwent definitive histopathological classification from endometrial sampling and/or a surgical specimen. Exclusion criteria were premenopausal bleeding, bleeding clearly attributable to a non-uterine source without uterine evaluation, absence of definitive histopathology, or incomplete outcome classification. Women were enrolled consecutively at their first presentation.

Clinical and imaging assessment

Standardized clinical assessment included age, years since menopause, body mass index (BMI), parity, hypertension, diabetes mellitus, tamoxifen exposure, hormone replacement therapy (HRT), and bleeding duration. All participants underwent pelvic examination and TVUS before histopathological classification. Endometrial thickness (ET) was measured in the midsagittal plane as the maximal double-layer thickness. Ultrasound findings were recorded in predefined fields, including endometrial heterogeneity, suspected endometrial polyp, intracavitary fluid, and intrauterine mass. Doppler assessment included resistance index (RI), pulsatility index (PI), and a four-grade vascularisation score; complete values were available for the primary cohort.

Reference standard

Histopathology served as the reference standard. Endometrial tissue was obtained by office endometrial biopsy, hysteroscopy-directed biopsy, operative curettage, and/or hysterectomy as clinically indicated. Final diagnoses were classified into mutually exclusive categories: endometrial atrophy, endometrial polyp, hyperplasia without atypia, atypical endometrial hyperplasia/EIN, other benign pathology, or endometrial carcinoma. Carcinoma subtype and grade were recorded when available.

Outcomes and variables

The primary epidemiological outcome was the proportion of women with histologically confirmed endometrial carcinoma among all 221 participants with complete outcome classification. Secondary descriptive outcomes were the frequencies of the mutually exclusive histopathological diagnoses. Exploratory association analyses compared women with and without carcinoma across clinical variables (age, years since menopause, BMI, parity, bleeding duration) and ultrasound/Doppler variables (ET, RI, PI, vascularisation, endometrial heterogeneity, and intrauterine mass).

Statistical analysis

Analyses were performed using IBM SPSS Statistics, version 28.0 (IBM Corp., Armonk, NY, USA). Distributional normality of continuous variables was assessed using the Shapiro–Wilk test. Approximately normally distributed variables are summarized as mean $\pm$ standard deviation (SD), and non-normally

distributed variables as median and interquartile range (IQR). Categorical variables are reported as n (%). The proportions of carcinoma and each histopathological diagnosis were calculated with Wilson 95% CIs.

Because a secondary objective was to explore characteristics associated with carcinoma, women with and without carcinoma were compared using Welch's t test for approximately normally distributed continuous variables, the Mann–Whitney U test for non-normal variables, and Fisher's exact test for selected categorical variables. Unadjusted odds ratios (ORs) with 95% CIs were calculated for categorical associations. All tests were two-sided and $p < 0.05$ was considered statistically significant. These association analyses were exploratory; no adjustment for multiple comparisons was applied and they should not be interpreted as causal or as a validated prediction model.

Ethical considerations

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, University of Medicine, Tirana, Albania, on 11 December 2023 (Protocol No. 287/1), before prospective recruitment. Written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the Declaration of Helsinki.

RESULTS

Participant characteristics

All 221 women in the analytic cohort had complete histopathological outcome

classification. Continuous baseline characteristics are presented separately from categorical characteristics to avoid mixing incompatible summary columns. Mean age was 63.2 ± 6.2 years, while median time since menopause was 13.0 years (IQR 8.0–17.0). Mean BMI was 29.5 ± 4.8 kg/m². Median ET was 6.3 mm (IQR 3.4–9.0), and mean RI and PI were 0.61 ± 0.10 and 1.56 ± 0.37 , respectively. (Table 1) Obesity was present in 98 women (44.3%), hypertension in 88 (39.8%), and diabetes in 46 (20.8%). Endometrial heterogeneity was recorded in 35.3%, an intrauterine mass in 25.3%, intracavitary fluid in 15.4%, and a suspected endometrial polyp in 13.1%. (Table 2)

Histopathological outcomes

Endometrial carcinoma was confirmed in 24 women, corresponding to 10.9% of the cohort (95% CI 7.4–15.6). Hyperplasia accounted for 112/221 diagnoses (50.7%): 63 women had hyperplasia without atypia and 49 had atypical hyperplasia/EIN. The mutually exclusive histopathological distribution and Wilson 95% CIs are shown in Table 3.

Table 1. Continuous clinical and ultrasound characteristics (N=221)

Characteristic	Summary
Age, years	63.2 ± 6.2
Years since menopause	13.0 (8.0–17.0)
BMI, kg/m ²	29.5 ± 4.8
Bleeding duration, days	5.0 (3.0–7.0)
Endometrial thickness, mm	6.3 (3.4–9.0)
Doppler resistance index	0.61 ± 0.10
Doppler pulsatility index	1.56 ± 0.37
Vascularisation score	2.0 (1.0–2.0)

Data are mean $\pm$ SD or median (IQR), according to distribution. BMI, body mass index; IQR, interquartile range; SD, standard deviation.

Table 2. Categorical clinical and ultrasound characteristics (N=221)

Characteristic	n	%
Obesity (BMI ≥ 30 kg/m ²)	98	44.3
Hypertension	88	39.8
Diabetes mellitus	46	20.8
Tamoxifen exposure	16	7.2
Hormone replacement therapy	29	13.1
Heterogeneous endometrium	78	35.3
Suspected endometrial polyp	29	13.1
Intracavitary fluid	34	15.4
Intrauterine mass	56	25.3
Parity = 0	33	14.9
Parity = 1	67	30.3
Parity = 2	60	27.1
Parity ≥ 3	61	27.6

BMI, body mass index.

Table 3. Histopathological diagnoses and 95% confidence intervals (N=221)

Histopathological diagnosis	n	%	95% CI
Hyperplasia without atypia	63	28.5	23.0–34.8
Atypical hyperplasia/EIN	49	22.2	17.2–28.1
Other benign pathology	36	16.3	12.0–21.7
Endometrial atrophy	30	13.6	9.7–18.7
Endometrial carcinoma	24	10.9	7.4–15.6
Endometrial polyp	19	8.6	5.6–13.0

Categories are mutually exclusive and sum to N=221. CI, confidence interval; EIN, endometrial intraepithelial neoplasia. Wilson 95% confidence intervals are shown.

Characteristics associated with endometrial carcinoma

Women with carcinoma differed from those without carcinoma across several clinical and ultrasound measures (Table 4). The carcinoma group was older and further from menopause, had higher BMI, lower parity, and longer bleeding duration. The largest imaging differences were greater ET, lower RI and PI, and higher vascularisation. Because these analyses are

unadjusted and exploratory, they describe associations within this cohort rather than independent causal effects.

Selected categorical ultrasound findings were also strongly associated with carcinoma (Table 5). Heterogeneous endometrium occurred in 83.3% of carcinoma cases versus 29.4% of non-carcinoma cases; an intrauterine mass occurred in 66.7% versus 20.3%; and high vascularisation (score 3–4) occurred in 83.3% versus 17.3%.

Table 4. Quantitative characteristics according to endometrial carcinoma status

Characteristic	No carcinoma (n=197)	Carcinoma (n=24)	p value
Age, years	62.49 ± 5.80	68.62 ± 6.65	<0.001
Years since menopause	12.00 (8.00–17.00)	18.00 (14.75–23.00)	<0.001
BMI, kg/m ²	29.06 ± 4.52	33.51 ± 4.91	<0.001
Parity	2.00 (1.00–3.00)	1.00 (0.00–2.00)	0.012
Bleeding duration, days	5.00 (3.00–7.00)	6.50 (4.00–8.00)	0.020
Endometrial thickness, mm	5.50 (3.30–8.20)	13.75 (10.47–16.05)	<0.001
Resistance index	0.63 ± 0.09	0.47 ± 0.08	<0.001
Pulsatility index	1.60 ± 0.36	1.22 ± 0.32	<0.001
Vascularisation score	2.00 (1.00–2.00)	3.00 (3.00–4.00)	<0.001

Values are mean ± SD or median (IQR). Welch's t test or Mann–Whitney U test was used as appropriate. BMI, body mass index.

Table 5. Selected categorical ultrasound findings associated with endometrial carcinoma

Finding	No carcinoma n (%)	Carcinoma n (%)	Unadjusted OR (95% CI)	p value
Heterogeneous endometrium	58 (29.4)	20 (83.3)	11.98 (3.92–36.59)	<0.001
Intrauterine mass	40 (20.3)	16 (66.7)	7.85 (3.14–19.64)	<0.001
High vascularisation (score 3–4)	34 (17.3)	20 (83.3)	23.97 (7.70–74.60)	<0.001

Fisher's exact test was used. CI, confidence interval; OR, odds ratio. Percentages are within carcinoma-status groups.

DISCUSSION

Principal findings and comparison with international evidence

In this prospective hospital-based cohort, endometrial carcinoma was diagnosed in 10.9% of women presenting with PMB (95% CI 7.4–15.6). This estimate is close to the pooled 9% risk reported by Clarke et al. and lies within the range reported across major geographic strata (1). The finding therefore provides a contemporary local benchmark while reinforcing that the diagnostic yield of PMB evaluation is setting-dependent. The high frequency of hyperplasia—particularly atypical hyperplasia/EIN in 22.2%—also demonstrates that a PMB service is not solely a cancer-detection pathway; it identifies a substantial group with clinically important precursor disease.

Comparison with previous Albanian studies

The present estimate is substantially lower than the 33% endometrial carcinoma proportion reported from the same tertiary hospital in the 2018 retrospective series by Dema (4). That earlier report explicitly noted that benign cases were often managed outside the tertiary centre while more difficult cases were referred, and it recommended prospective verification of the Albanian percentage. The current study directly responds to that methodological concern by using consecutive prospective enrolment across a defined 24-month period and standardized ascertainment before histopathological classification. Nevertheless, the difference between 10.9% and 33% cannot be attributed to

study design alone. Changes in referral practice, calendar period, case definitions, diagnostic pathways, and the denominator of women reaching histopathological verification may all contribute.

The earlier Cakoni and Manoku series also illustrates heterogeneity in local case mix: 12% of histopathological diagnoses among 102 women with PMB were malignant, and only 54.5% of those malignant diagnoses were endometrial carcinoma (3). Taken together, the three Albanian reports should not be treated as directly interchangeable prevalence estimates. Rather, they indicate that hospital-based frequencies are sensitive to referral structure and ascertainment. A multicentre prospective study including primary, secondary, and tertiary care would be required to estimate a national PMB-associated carcinoma frequency with greater external validity.

Associated clinical and ultrasound characteristics

The exploratory association analyses showed a coherent risk profile. Women with carcinoma were older, had been postmenopausal longer, had higher BMI, lower parity, and longer bleeding duration. Ultrasound differences were more pronounced: carcinoma was associated with greater ET, lower RI and PI, and higher vascularisation. Heterogeneous endometrium, an intrauterine mass, and high vascularisation also showed large unadjusted ORs. The association with higher BMI is biologically plausible and consistent with the established metabolic risk

profile of endometrial cancer; a recent meta-analysis reported approximately a two-fold higher incidence of endometrial cancer among women with metabolic syndrome (10). However, the present analysis was not designed to establish independent etiologic effects or a prediction rule; the associations are unadjusted, multiple comparisons were performed, and only 24 carcinoma events were available.

Contemporary PMB evaluation is moving toward more comprehensive initial assessment. The 2026 ACOG update recommends combined TVUS and endometrial tissue sampling for most patients with PMB rather than relying on a thin endometrial measurement alone (5). The most recent quantitative synthesis supports the continuing value of a ≤ 4 -mm ET threshold as a sensitive rule-out component, while also showing that no ET threshold is perfectly sensitive (6). Earlier meta-analytic evidence similarly demonstrated the sensitivity–specificity trade-off of ET-based triage (11). In addition, a 2024 diagnostic study among Black patients in the United States found that a clinically relevant proportion of endometrial cancers occurred below commonly used ET thresholds; although that population is not directly generalizable to Albania, the study illustrates why ET should not be interpreted in isolation in symptomatic patients (12). Our findings are compatible with this more integrated approach: ultrasound features differed strongly by outcome group, but histopathology remained necessary for definitive classification, particularly because precursor

lesions were common. Direct hysteroscopic biopsy may improve sample adequacy and reduce diagnostic failure for focal pathology compared with blind sampling in selected settings (13).

Atypical hyperplasia/EIN and future research

Atypical hyperplasia/EIN was identified in 49 women (22.2%; 95% CI 17.2–28.1), a clinically important finding because EIN/AEH is a precursor to endometrial carcinoma and management must consider the possibility of concurrent malignancy (7). The updated 2025 ESGO–ESTRO–ESP guideline and the ESMO Clinical Practice Guideline similarly emphasize accurate histopathological classification and risk-adapted management (8,9). A logical next step is longitudinal follow-up of this 49-woman subgroup to document definitive surgical pathology where available, management strategy, regression or persistence, progression to carcinoma, recurrence, time to treatment, and patient outcomes. Such follow-up would determine whether the high precursor-lesion burden observed here translates into a correspondingly high downstream treatment and cancer burden. This follow-up priority is supported by pooled evidence showing a substantial risk of both concurrent and subsequent endometrial carcinoma in women with endometrial hyperplasia, particularly atypical hyperplasia (14), and by contemporary cohort data demonstrating clinically important rates of carcinoma at hysterectomy after a preoperative diagnosis of EIN (15).

Strengths

Strengths include prospective consecutive enrolment over an explicitly defined 24-month period, standardized collection of clinical and ultrasound variables before histopathological classification, complete primary outcome ascertainment, and presentation of carcinoma and histopathological frequencies with 95% CIs. The study also extends the original descriptive objective by reporting real, prespecified clinical and imaging variables according to carcinoma status, thereby providing a more informative epidemiological profile without converting the analysis into an overfitted prediction exercise.

Limitations

Several limitations should be considered. First, this was a single-centre tertiary-hospital study and therefore represents a time-limited hospital sample rather than a probability sample of Albanian women with PMB; referral and selection effects may influence the observed case mix. Second, the number of carcinoma events was modest ($n=24$), resulting in limited precision for some estimates and precluding extensive multivariable etiologic modelling. Third, association analyses were exploratory, unadjusted, and not corrected for multiple comparisons. Fourth, histopathological tissue was obtained by different clinically indicated procedures, which may differ in their ability to characterize focal pathology. Finally, the study did not include longitudinal outcomes for women with atypical hyperplasia/EIN, so progression, concurrent carcinoma at definitive surgery, and

treatment outcomes cannot be estimated from the present analysis.

CONCLUSIONS

Among 221 consecutive women evaluated for PMB at a tertiary hospital in Tirana from January 2024 through December 2025, endometrial carcinoma was diagnosed in 10.9% (95% CI 7.4–15.6). This contemporary estimate is substantially lower than a previous 2018 retrospective estimate from the same hospital and is broadly consistent with international pooled evidence, although referral differences prevent direct equivalence. Atypical hyperplasia/EIN was frequent, affecting 22.2% of the cohort. Clinical and ultrasound characteristics differed significantly by carcinoma status, but these associations are exploratory and do not replace histopathological diagnosis. Multicentre prospective validation and longitudinal follow-up of the atypical hyperplasia/EIN subgroup are warranted.

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