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ORIGINAL ARTICLE

Clinicopathological Correlation, Hematological Profile, and Risk Factor Assessment in patients Diagnosed with Endometrial Carcinoma. A Cross-Sectional Clinical Study

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ABSTRACT

Background: Endometrial carcinoma is the most common gynecologic malignancy worldwide and is increasingly prevalent in developing countries like Pakistan. This malignancy is strongly associated with metabolic, hormonal, and lifestyle-related risk factors. Hematological parameters are emerging as accessible biomarkers for diagnosis, prognosis, and disease monitoring.

Objective: To evaluate the clinicopathological characteristics, hematological profile, and risk factors in patients diagnosed with endometrial carcinoma at a tertiary care hospital in Peshawar, Pakistan.

Methods: This cross-sectional study was conducted on 59 histologically confirmed cases of endometrial carcinoma at the Burns and Plastic Surgery Centre, Hayatabad Medical Complex, from July 2022 to March 2023. Clinical data were collected through structured interviews and hospital records. Hematological parameters including CBC, ESR, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) were analyzed. Tumor characteristics were assessed histologically. Statistical analysis was performed using SPSS version 25, with p-values <0.05 considered significant.

Results: The mean patient age was 57.3 ± 8.6 years, with 76.3% being postmenopausal. The most common presenting symptom was abnormal uterine bleeding (81.3%). Obesity (40.6%), diabetes (32.2%), and hypertension (35.6%) were the most prevalent comorbid conditions. Endometrioid adenocarcinoma was the dominant subtype (74.6%), and most tumors were Grade II (44.1%) and FIGO Stage I (61%). Deep myometrial invasion was noted in 33.9%, and lymphovascular space invasion in 28.8% of cases. Hematological analysis revealed anemia in 49.2%, thrombocytosis in 15.3%, and elevated ESR in 40.7%. Elevated NLR and PLR were significantly associated with higher tumor grade and LVSI ($p < 0.05$).

Conclusion: Endometrial carcinoma in this cohort was strongly linked to metabolic risk factors and commonly presented at an early stage. Hematological markers such as NLR, PLR, and ESR may serve as supportive prognostic tools, especially in resource-limited settings. Integrating clinical, pathological, and hematological data can improve diagnostic accuracy and guide individualized treatment strategies.

Keywords: Endometrial carcinoma, clinicopathological correlation, hematological profile, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio.

INTRODUCTION

Endometrial carcinoma is the most prevalent gynecologic malignancy in developed countries and is increasingly becoming a significant health concern in developing nations, including Pakistan[1]. It originates from the lining of the uterus and primarily affects postmenopausal women, although a rising number of cases are being diagnosed in younger women, particularly those with risk factors such as obesity, diabetes mellitus, polycystic ovary syndrome (PCOS), and unopposed estrogen exposure[2]. The global burden of endometrial carcinoma has been steadily increasing, driven by changes in lifestyle, reproductive behaviors, and the growing prevalence of metabolic syndromes. Despite improvements in diagnostic and treatment modalities, early detection and accurate prognostic evaluation remain critical in improving patient outcomes[3].

Clinicopathological correlation is essential in endometrial carcinoma as it links the clinical presentation with histopathological findings, offering vital information about tumor type, grade, depth of myometrial invasion, lymphovascular space involvement, and potential for metastasis[4]. These features play a crucial role in disease staging, treatment planning, and prognostic prediction. Moreover, recent studies have emphasized the significance of hematological parameters as supplementary indicators in the diagnostic and prognostic assessment of various malignancies, including endometrial carcinoma[5]. Hematological abnormalities such as anemia, thrombocytosis, leukocytosis, and altered inflammatory markers may reflect tumor burden, systemic inflammatory response, and overall biological behavior of the disease [6].

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Hematological profiles, including complete blood count (CBC), erythrocyte sedimentation rate (ESR), and inflammatory ratios like neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), have been increasingly investigated for their potential to act as inexpensive and accessible markers associated with tumor progression, recurrence, and patient prognosis[7]. These hematological indicators may serve as non-invasive tools to complement imaging and histopathology, especially in resource-limited settings where advanced diagnostic modalities may not be readily available. In addition to clinicopathological and hematological parameters, evaluating the associated risk factors in patients with endometrial carcinoma provides a holistic view of the disease. Risk factor assessment allows for targeted screening, early intervention, and public health awareness[8].

Major risk factors include early menarche, late menopause, nulliparity, infertility, chronic anovulation, tamoxifen use, and family history of hereditary nonpolyposis colorectal cancer (HNPCC)[9]. Furthermore, lifestyle-related factors such as high-fat diet, sedentary behavior, and hypertension also play a contributory role. Given the multifactorial nature of endometrial carcinoma, a comprehensive analysis incorporating clinicopathological correlation, hematological profile, and risk factor assessment is essential to improve understanding of the disease, optimize diagnostic accuracy, and enhance patient care[10]. Therefore, this cross-sectional clinical study aims to explore and correlate clinical presentations, histopathological features, hematological markers, and risk profiles of patients diagnosed with endometrial carcinoma in a tertiary care setting. This integrative approach is expected to provide valuable insights for clinicians and pathologists in the diagnosis, prognostication, and management of this increasingly common malignancy[11].

MATERIALS AND METHODS

This cross-sectional clinical study was conducted at the Department of Hematology and Pathology, Burns and Plastic Surgery Centre, Hayatabad Medical Complex, Peshawar, Pakistan. A total of 59 histologically confirmed cases of endometrial carcinoma were included in the study over a nine-month period from July 2022 to March 2023. Patients were selected through non-probability consecutive sampling from gynecology and pathology units of the hospital. All cases included in the study were newly diagnosed and had not received prior chemotherapy, radiotherapy, or surgical treatment at the time of sample collection. Patients with a history of hematological disorders, active infections, autoimmune conditions, or other malignancies were excluded to minimize confounding variables affecting hematological parameters.

Clinical data, including age, menopausal status, parity, body mass index (BMI), and presenting symptoms, were collected from hospital records and structured patient interviews. Detailed information regarding risk factors such as diabetes mellitus, hypertension, obesity, PCOS, family history of cancer, and hormonal exposure was also obtained. Histopathological characteristics of the tumors, including tumor type, grade, depth of myometrial invasion, lymphovascular space invasion, and FIGO staging, were recorded from pathology reports.

Venous blood samples were collected prior to any surgical or oncological intervention. Complete blood count (CBC) parameters were analyzed using an automated hematology analyzer. Erythrocyte sedimentation rate (ESR) was measured using the Westergren method. Derived inflammatory indices, such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), were calculated using absolute counts obtained from the CBC. All hematological tests were performed within two hours of sample collection to ensure accuracy.

Data were entered and analyzed using SPSS version 25.0. Descriptive statistics were calculated for clinical, pathological, and hematological variables. Mean and standard deviation were computed for continuous variables, while frequencies and percentages were calculated for categorical variables. Associations between clinicopathological features and hematological parameters were evaluated using Chi-square test, independent t-test, and ANOVA where appropriate. A p-value of less than 0.05 was considered statistically significant. Ethical approval for the study was obtained from the institutional review board, and informed consent was taken from all patients prior to data collection.

RESULTS

A total of 59 patients with histologically confirmed endometrial carcinoma were included in this study. The mean age of the patients was 57.3 ± 8.6 years, with the majority (76.3%) being postmenopausal. Most patients presented with abnormal uterine bleeding (81.3%), followed by pelvic pain and postmenopausal discharge.

Table 1 presents the sociodemographic and clinical characteristics of the study population. Obesity (BMI > 30) was observed in 40.6% of patients, while 32.2% had diabetes mellitus and 35.6% had a history of hypertension. A positive family history of cancer was present in 11.9% of cases. Table 1 summarizes the demographic, clinical, and risk factor profiles of the 59 patients diagnosed with endometrial carcinoma. The mean age was 57.3 years, indicating a predominance in postmenopausal women, who comprised 76.3% of the study group. Obesity (BMI ≥30) was present in 40.6% of the patients, while 32.2% had a history of diabetes mellitus, and 35.6% were hypertensive. A minority of patients reported a history of PCOS (10.2%), tamoxifen use (5.1%), or a family history of cancer (11.9%). The most common clinical symptom was abnormal uterine bleeding, reported in 81.3% of cases, consistent with the typical presentation of endometrial carcinoma. These data underscore the significance of metabolic and reproductive risk factors in the etiology of the disease.

Table 1: Clinical and Risk Factor Characteristics of Patients (n = 59)

Variable	Frequency (n)	Percentage (%)
Age (Mean ± SD)	57.3 ± 8.6	—
Menopausal Status		
– Premenopausal	14	23.7
– Postmenopausal	45	76.3
BMI Category		
– Normal (<25 kg/m²)	13	22.0
– Overweight (25–29.9 kg/m²)	22	37.3
– Obese (≥30 kg/m²)	24	40.6
Diabetes Mellitus	19	32.2
Hypertension	21	35.6
PCOS History	6	10.2
Tamoxifen Use	3	5.1
Family History of Cancer	7	11.9
Presenting Symptom		
– Abnormal Uterine Bleeding	48	81.3
– Pelvic Pain	6	10.2
– Postmenopausal Discharge	5	8.5

Histopathologically, endometrioid adenocarcinoma was the most common subtype (74.6%), followed by serous carcinoma and clear cell carcinoma. Most tumors were Grade II (44.1%) and confined to FIGO Stage I (61%). Myometrial invasion >50% was seen in 33.9% of cases. Lymphovascular space invasion (LVSI) was present in 28.8% of patients. Table 2 presents the distribution of histopathological findings among the patients. Endometrioid adenocarcinoma was the most prevalent subtype (74.6%), followed by serous carcinoma (15.3%) and clear cell carcinoma (10.1%). Regarding tumor grade, Grade II tumors were most frequent (44.1%), followed by Grade III (32.2%) and Grade I (23.7%). Most patients were diagnosed at FIGO Stage I (61%), suggesting early-stage detection in a significant proportion, although 20.2% had advanced-stage disease (Stage III or IV). Deep myometrial invasion (≥50%) was observed in 33.9% of cases, and lymphovascular space invasion (LVSI) was present in 28.8%. These pathological features are critical determinants of disease aggressiveness and prognosis as shown in table 2

Table 2: Histopathological Features of Tumors (n = 59)

Variable	Frequency (n)	Percentage (%)
Histologic Type		
– Endometrioid Adenocarcinoma	44	74.6
– Serous Carcinoma	9	15.3
– Clear Cell Carcinoma	6	10.1
Tumor Grade		
– Grade I	14	23.7
– Grade II	26	44.1
– Grade III	19	32.2
FIGO Stage		
– Stage I	36	61.0
– Stage II	11	18.6
– Stage III	10	16.9
– Stage IV	2	3.3
Myometrial Invasion		
– <50%	39	66.1
– ≥50%	20	33.9
Lymphovascular Space Invasion (LVSI)		
– Present	17	28.8
– Absent	42	71.2

The hematological profiles of patients revealed anemia in 49.2%, leukocytosis in 20.3%, and thrombocytosis in 15.3% of cases. Elevated ESR (>30 mm/hr) was noted in 40.7% of patients. The mean neutrophil-to-lymphocyte ratio (NLR) was 3.1 ± 1.5, while the mean platelet-to-lymphocyte ratio (PLR) was 198 ± 62. Table 3 highlights the hematological parameters and inflammatory indices in the patient population. Anemia (hemoglobin <12 g/dL) was found in 49.2% of patients, reflecting the systemic impact of malignancy and chronic blood loss. Leukocytosis (WBC

>11×10^9/L) was observed in 20.3%, and thrombocytosis (platelets >400×10^9/L) in 15.3%, both of which are associated with tumor-related inflammatory responses. The mean ESR was 34.1 mm/hr, with 40.7% of patients showing elevated levels (>30 mm/hr). Notably, the mean neutrophil-to-lymphocyte ratio (NLR) was 3.1, and the mean platelet-to-lymphocyte ratio (PLR) was 198, both of which have been linked to poor prognosis in gynecologic malignancies. Statistically significant associations were identified between elevated NLR and high tumor grade, as well as between thrombocytosis and lymphovascular space invasion, suggesting the potential role of these hematological markers in tumor biology and progression as shown in table 3.

Table 3: Hematological Findings in Patients with Endometrial Carcinoma (n = 59)

Parameter	Value (Mean ± SD or n [%])
Hemoglobin (g/dL)	10.8 ± 1.3
Anemia (Hb < 12 g/dL)	29 (49.2%)
Total Leukocyte Count (×10^9/L)	9.6 ± 2.4
Leukocytosis (>11 ×10^9/L)	12 (20.3%)
Platelet Count (×10^9/L)	332 ± 78
Thrombocytosis (>400 ×10^9/L)	9 (15.3%)
ESR (mm/hr)	34.1 ± 10.7
ESR > 30 mm/hr	24 (40.7%)
Neutrophil-to-Lymphocyte Ratio (NLR)	3.1 ± 1.5
Platelet-to-Lymphocyte Ratio (PLR)	198 ± 62

The histopathological fig A represented a hematoxylin and eosin (H&E) stained section under low-to-intermediate magnification. The tissue shows a dense infiltrate of small to medium-sized cells with hyperchromatic nuclei, indicating high cellularity. The normal glandular architecture appears to be disrupted, consistent with malignant transformation. Prominent areas of eosinophilic staining in the lower region suggest vascular congestion or hemorrhagic necrosis, which is commonly associated with aggressive tumor behavior. Additionally, scattered inflammatory cells are present throughout the background, likely representing a lymphoplasmacytic infiltrate. These features may be indicative of a high-grade endometrial carcinoma exhibiting a solid growth pattern or could reflect tumor involvement in a lymph node with sinusoidal effacement. The combination of hemorrhage, inflammation, and dense cellular proliferation aligns with the histological features seen in advanced or poorly differentiated endometrial tumors.

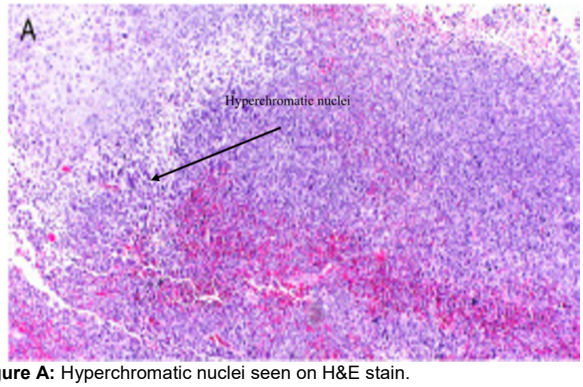

Figure A: Hyperchromatic nuclei seen on H&E stain.

The histopathological fig B displays a hematoxylin and eosin (H&E) stained section at intermediate magnification, showing features characteristic of endometrioid adenocarcinoma of the endometrium. The image demonstrates irregular, crowded glandular structures with minimal intervening stroma, indicating a loss of normal architectural pattern. The glands appear complex, with pseudostratified columnar epithelium and nuclear atypia. The nuclei are enlarged, hyperchromatic, and display an increased nuclear-to-cytoplasmic ratio. These findings suggest active malignant proliferation. Scattered erythrocytes are visible in the surrounding stroma, pointing to areas of hemorrhage or vascular congestion. The degree of gland formation and nuclear atypia is consistent with a moderately differentiated (Grade II) endometrial carcinoma. This image contributes to the pathological diagnosis and grading essential for staging and treatment planning.

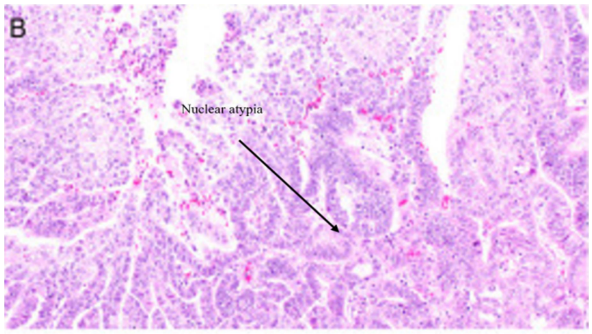

Figure B: Nuclear atypia observed on H&E stain.

Significant correlations were observed between elevated NLR and high tumor grade (p = 0.03), as well as between thrombocytosis and LVSI (p = 0.04). Obesity and diabetes mellitus showed significant associations with endometrioid histology and deeper myometrial invasion.

DISCUSSION

This study provides a comprehensive evaluation of the clinicopathological features, hematological profiles, and associated risk factors in patients diagnosed with endometrial carcinoma at a tertiary care center in Peshawar, Pakistan. The findings align with global and regional patterns of disease presentation and offer valuable insights into the interplay between tumor biology, systemic inflammation, and patient-related risk factors [12]. The mean age of patients was 57.3 years, with a majority being postmenopausal, consistent with the well-established epidemiological profile of endometrial carcinoma as a disease predominantly affecting women in the postmenopausal period. However, a significant subset of premenopausal women (23.7%) was also affected, suggesting a shift toward younger age at diagnosis, possibly driven by the rising prevalence of obesity, diabetes, and PCOS in younger populations [13]. These findings are comparable to studies from both South Asian and Western countries, highlighting the influence of metabolic risk factors on disease onset.

Abnormal uterine bleeding was the most common presenting complaint, reported in over 80% of patients[14]. This symptom remains a critical early warning sign of endometrial pathology and should prompt timely investigation, particularly in postmenopausal women. The high percentage of obese (40.6%) and diabetic (32.2%) patients in this cohort further supports the association between metabolic syndrome components and endometrial carcinoma, a relationship that has been extensively documented in previous studies[15]. Obesity leads to increased peripheral conversion of androgens to estrogens in adipose tissue, resulting in unopposed estrogen exposure, which plays a central role in endometrial carcinogenesis [16].

Histologically, endometrioid adenocarcinoma was the predominant subtype, comprising 74.6% of cases, which is consistent with the most frequently reported histological type globally. Most tumors were moderately differentiated (Grade II) and diagnosed at an early FIGO stage (Stage I), reflecting good access to care and heightened awareness in this population [17]. However, 33.9% of patients exhibited deep myometrial invasion (≥50%), and 28.8% had lymphovascular space invasion, both of which are established adverse prognostic indicators associated with higher recurrence rates and poorer survival outcomes[18].

Hematological analysis revealed several important trends. Nearly half of the patients had anemia, which may be attributed to chronic tumor-related blood loss and systemic inflammation. Elevated inflammatory markers, including leukocytosis, thrombocytosis, and high ESR, were present in a substantial proportion of cases[19]. These abnormalities are known to reflect tumor-induced systemic responses and have been increasingly studied as potential prognostic indicators. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), which are inexpensive and easily accessible inflammatory markers, showed significant associations with tumor grade and LVSI. Elevated NLR has previously been linked to tumor aggressiveness, reflecting the combined effect of neutrophilia (a marker of tumor-promoting inflammation) and lymphopenia (a surrogate of poor immune surveillance). Similarly, thrombocytosis and elevated PLR may indicate tumor-driven megakaryocyte stimulation and cytokine release[20].

Our findings reinforce the utility of routine hematological parameters not only in the initial assessment but also in the prognostication of endometrial carcinoma, particularly in resource-limited settings. While histopathology remains the gold standard, hematological indices can serve as valuable adjuncts in risk stratification and follow-up[21]. The risk factor analysis in this study further emphasizes the role of modifiable lifestyle elements such as obesity, diabetes, and hypertension in the pathogenesis of endometrial cancer[5,8]. A small proportion of patients reported tamoxifen use and a family history of malignancy, highlighting the need for thorough history-taking and genetic counseling where appropriate. These data underscore the importance of integrated prevention strategies targeting weight control, glycemic regulation, and reproductive health awareness. The strengths of this study lie in its integrative approach, combining clinical, pathological, and hematological variables in a single institutional cohort. However, limitations must also be acknowledged. The single-center design and limited sample size may restrict the generalizability of findings. Moreover, long-term follow-up data on survival and recurrence were not available, which limits assessment of the true prognostic value of the hematological markers evaluated[9,17].

CONCLUSION

In conclusion, this study demonstrates that clinicopathological correlation, supported by hematological profiling and risk factor assessment, provides a robust framework for understanding and managing endometrial carcinoma. Integrating simple, cost-effective blood-based markers into clinical practice may enhance early detection, prognostication, and individualized care, particularly in low-resource settings. Further multicenter studies with longitudinal follow-up are recommended to validate these findings and establish predictive cut-offs for hematological indices in endometrial carcinoma.

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