

Association of Vimentin Expression with Tumor Grade in Endometrial Carcinoma: A Cross-Sectional Study

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ABSTRACT

Introduction: Endometrial carcinoma is one of the most common gynecological malignancies, with tumor grade serving as a critical determinant of prognosis and treatment planning. In recent years, immunohistochemical markers such as vimentin have gained attention for their potential role in tumor characterization. Vimentin, a mesenchymal marker, is often associated with epithelial-mesenchymal transition and may reflect tumor differentiation status. This study investigates the association between vimentin expression and tumor grade in endometrial carcinoma to evaluate its diagnostic and prognostic relevance.

Methods: This cross-sectional observational study was conducted in the Department of Pathology, Sir Salimullah Medical College, Dhaka. Immunohistochemistry of Vimentin was done at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from March 2022 to February 2024. Histopathologically diagnosed 46 endometrial carcinoma cases were included in this study. The statistical analysis was carried out by using the SPSS 26 for Windows.

Result: In this study of 46 endometrial carcinoma cases, 28.3% were grade 1, 26.1% were grade 2, and 45.7% were grade 3. High vimentin expression was observed in 69.5% of cases, low expression in 10.9%, and negative expression in 19.6%. A significant association was found between tumor grade and vimentin expression ($p=0.009$), with high expression most common in grade 1 tumors and decreased expression observed in higher-grade carcinomas.

Conclusion: This study highlights a significant association between vimentin expression and tumor grade in endometrial carcinoma. High vimentin expression was more frequently observed in lower-grade tumors, whereas reduced or absent expression was more common in higher-grade cases. These findings suggest that vimentin may serve as a useful immunohistochemical marker for assessing tumor differentiation and could aid in prognostication of endometrial carcinoma.

Keywords: Vimentin Expression, Tumor Grade, Endometrial Carcinoma, Immunohistochemistry

Introduction

Endometrial carcinoma (EC) is the most common gynecologic malignancy in developed countries and ranks second in developing countries, with an increasing global incidence due to rising obesity, aging populations, and metabolic syndromes [1]. It primarily affects postmenopausal women, with most

cases diagnosed in early stages owing to the early presentation of abnormal uterine bleeding. Despite early detection, a subset of patients presents with aggressive histological subtypes and poor prognostic outcomes [2]. Endometrial carcinoma is broadly classified into two clinicopathological types: Type I (estrogen-dependent, endometrioid histology, favorable prognosis) and Type II (non-estrogen-dependent, non-endometrioid, including serous and clear cell carcinomas, with poorer prognosis) [3]. Tumor grade, which refers to the degree of glandular

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differentiation, plays a pivotal role in treatment planning and prognosis assessment [4]. The molecular landscape of endometrial carcinoma is complex and heterogeneous. Recent advances in molecular classification by The Cancer Genome Atlas (TCGA) have identified four molecular subtypes—POLE-ultramutated, microsatellite instability-hypermutated, copy-number low, and copy-number high—with prognostic implications [5]. However, molecular profiling is not routinely available in all settings, especially in low-resource countries. Hence, immunohistochemical markers are increasingly being explored to complement histological evaluation and provide surrogate indicators for prognosis.

Vimentin, a type III intermediate filament protein, is a key component of the cytoskeleton of mesenchymal cells. It plays a crucial role in maintaining cell integrity, migration, adhesion, and signal transduction [6]. While vimentin is normally expressed in mesenchymal tissues, its aberrant expression in epithelial tumors signifies epithelial-mesenchymal transition (EMT)—a critical process in cancer invasion and metastasis [7]. In endometrial carcinoma, the role of vimentin has been increasingly investigated as a potential biomarker for tumor differentiation, invasiveness, and progression. Several studies have reported an association between vimentin expression and well-differentiated endometrioid carcinomas, whereas non-endometrioid and poorly differentiated tumors often exhibit decreased or absent vimentin expression [8,9]. This paradoxical pattern suggests that vimentin expression in EC may have context-dependent implications, and its interpretation must be nuanced. Furthermore, the pattern of vimentin expression may vary with tumor grade. Lower-grade endometrioid carcinomas tend to retain vimentin expression, whereas higher-grade tumors, especially non-endometrioid types, often lose this expression [10]. In this context, understanding the association between vimentin expression and histological grade can improve diagnostic accuracy and prognostication [11]. This study aims to explore the association of vimentin expression with tumor grade in endometrial carcinoma.

Methods

This cross-sectional observational study was conducted in the Department of Pathology, Sir Salimullah Medical College, Dhaka. Immunohistochemistry of Vimentin was done at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from March 2022 to February 2024. Histopathologically diagnosed endometrial carcinoma cases were included in this study. Samples were collected from adult female patients who underwent total abdominal hysterectomy. 46 cases were included in the present study. After receiving fresh hysterectomy samples, the gross examination was done as per standard procedure. Immunohistochemistry was done in the Pathology Department, BSMMU. A case record form has been developed to collect data from the patients. Sections have been examined under 40x magnifications. Distinct granular cytoplasmic staining was taken as positive. Five independent areas of each slide were examined under a microscope & Immunoscore was calculated for vimentin-stained slides according to the formula. To evaluate vimentin protein expression from IHC, the semi-quantitative staining index (SI) scoring method was used. SI was calculated by multiplying a staining intensity score (loss = 0, weak = 1, moderate = 2, strong

= 3) with the percent area of positive stained tumor tissue (<10% = 1, 10–50% = 2, >50% = 3), immunscore ranged from 0 to 9; where 0 was negative expression and low expression ranged from 1 to 3, and high expression of vimentin was 4 to 9 [12]. The statistical analysis was carried out by using the SPSS 26 for Windows. Descriptive statistics (frequencies, percentages) were used to summarize the patient's demographic characteristics and presented in tables, figures, charts & diagrams. The frequencies of different entities were expressed as percentages. The Fisher Exact test was used to analyze the association between different categorical variables. A p-value less than 0.05 was considered statistically significant. Ethical clearance has been taken from the Ethical Review Committee (ERC), at Sir Salimullah Medical College. Informed written consent was taken from all patients.

Results

Table 1: Distribution of patients by age (n=46)

Age group (in years)	Frequency (n)	Percentage (%)
31 to 40	5	10.9
41-50	5	10.9
51-60	18	39.1
61-70	14	30.4
71-80	4	8.7
Total	46	100.0
Mean (±SD)	56.9 (±9.3)	
Range(min-max)	35.0-72.0	

Out of the 46 patients, 18 (39.1%) were in the 51-60 years age group while 14 (30.4%) were in the 61-70 years age group. The mean age of the patients was 56.9 years which ranged from 35.0 to 72.0 years (table 4.1). [Table 1]

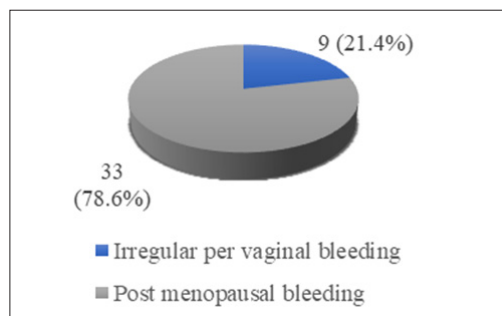


Figure 1: Distribution of patients by symptoms

Among the 42 patients, 9 (21.4%) had irregular vaginal bleeding while 33 (78.6%) had postmenopausal bleeding.

Table 2: Distribution of patients by co-morbidity (n=42)

Comorbidity	Frequency (n)	Percentage (%)
Diabetes mellitus	7	16.7
Hypertension	7	16.7
Both diabetes mellitus and hypertension	25	59.5
None	3	7.1

Table 3: Distribution of study cases by histopathological type (n=46)

Histopathological type	Frequency (n)	Percentage (%)
Endometrioid	35	76.1
Serous	10	21.7
Carcinosarcoma	1	2.2

The majority of 35 (76.1%) cases had endometrioid carcinoma. Ten (21.7%) had serous-type carcinomas and one patient (2.2%) had Carcinosarcoma. [Table 3]

Table 4: Distribution of cases (Endometrioid, Serous, and Carcinosarcoma) by grade (n=46)

Expression	Frequency (n)	Percentage (%)
Negative/loss of expression	9	19.6
Low expression	5	10.9
High expression	32	69.5

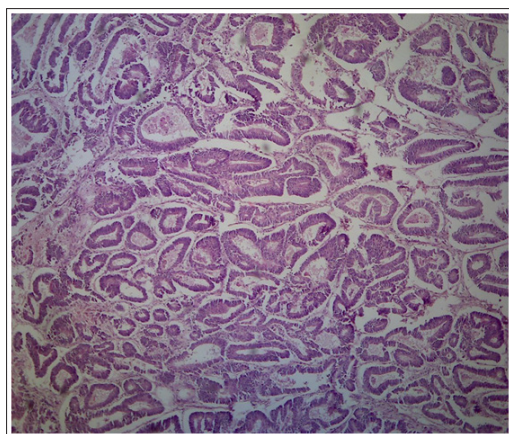
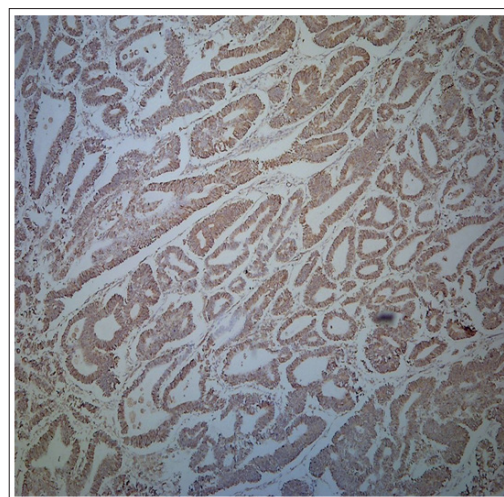
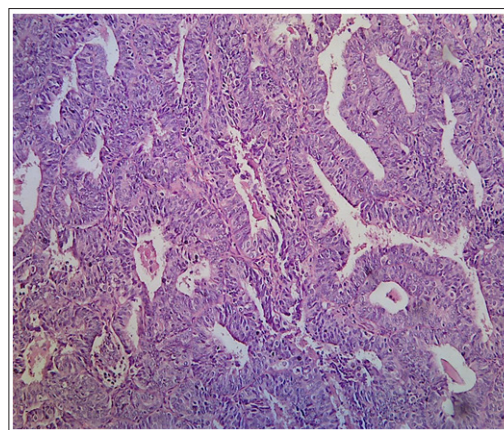
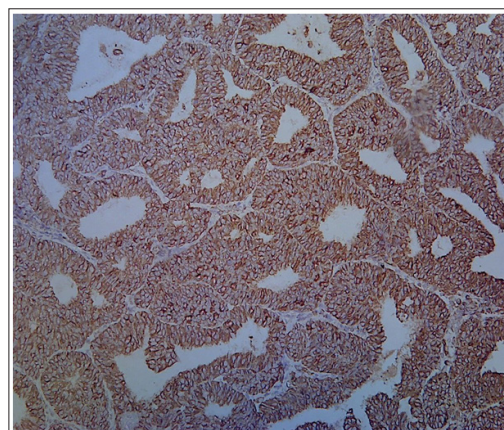
Immunohistochemical expression of vimentin was assessed in all cases. Nine (19.6) cases were negative, low expression was observed in 5 (10.9%) patients while 32 (69.6%) cases had high vimentin expression. [Table 5]

Table 6: Association of grade with vimentin expression (n=46)

Grade	Negative expression	Low expression	High expression	p-value
Grade 1	0 (0.0%)	0 (0.0%)	13 (100.0%)	0.009*
Grade 2	1 (8.3%)	2 (16.7%)	9 (75.0%)	
Grade 3	8 (38.1%)	3 (14.3%)	10 (47.6%)	

*Fisher Exact test

Among the grade 1 carcinomas, all 13 (100.0%) cases had high vimentin expression while among the grade 2 carcinomas, 9 (75.0%) cases had high vimentin expression and among the grade 3 carcinomas, 10 (47.6%) cases had high vimentin expression. Grade 1 carcinomas had significantly higher vimentin expression compared to grade 2 and 3 carcinomas ($p=0.009$). [Table 6]

**Figure 2:** photomicrograph showing Grade 1 Endometrioid carcinoma (case no-45, H&E, 20X)**Figure 3:** photomicrograph showing Grade 1 Endometrial carcinoma with high Vimentin expression (case no-45, H&E, 20X)**Figure 4:** photomicrograph showing Grade 2 Endometrioid carcinoma (case no-05, H&E, 40X)**Figure 5:** Photomicrograph showing grade 2 Endometrioid carcinoma with high Vimentin expression (case no-05, H&E, 40X)

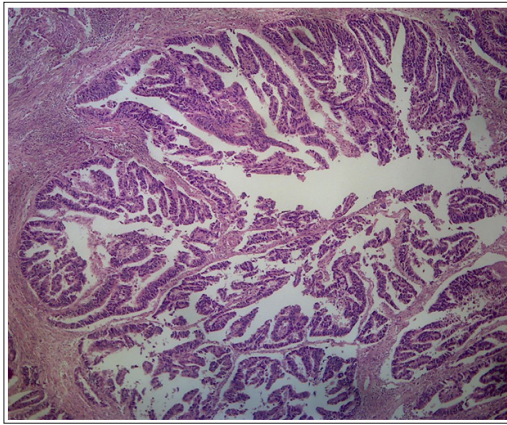


Figure 6: Photomicrograph showing serous carcinoma (Grade 3/ high grade) (case no-24, H&E, 20X)

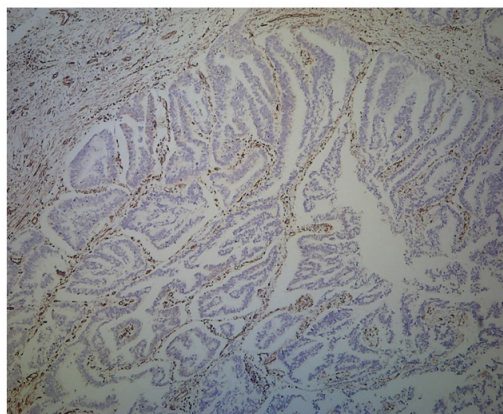


Figure 7: photomicrograph showing serous Endometrial carcinoma (grade 3/ high grade) with low Vimentin expression (case no-24, H&E, 20X)

Discussion

In this study, the mean age of the study population was 56.9 (± 9.3) years which ranged from 35.0 to 72.0 years & a large number of the patients 39.1% belonged to the age group of 51-60 years. Similar findings were found in other studies where the mean age of patients was found near about 58 years [13,14]. Though endometrial carcinomas are prevalent in the seventh decade of life, a lower age range was observed in this study [15]. Irregular uterine bleeding is the presenting sign in 90% of cases of endometrial carcinoma and postmenopausal bleeding (PMB) accounts for ~90% of patients with EC [2,16]. In the present study, 21.4% had irregular vaginal bleeding while 78.6% had postmenopausal bleeding. This finding follows Zhang et al. where it was found that 62.7% of patients had postmenopausal bleeding [17]. This indicates postmenopausal women are susceptible to endometrial carcinoma. In this study, 76.1% of cases were endometrioid type EC while 21.7% were serous type and 2.2% were carcinosarcoma. It is similar to the finding of Zhang et al. where it was found that 90.6% were endometrioid type and 9.4% were serous type endometrial carcinoma [18]. Morice et al. stated that the most prevalent histological form is endometrioid carcinoma, which is frequently identified when the pathology is still restricted to the uterus, which shows concordance with this study [19]. In the present study, out of the 46 cases of endometrial carcinoma including endometrioid, serous, and carcinosarcoma, 28.3% cases were grade 1, 26.1% were grade 2 and 45.7% were grade 3. It is slightly different

from the finding of Nesina et al. where grade 1, grade 2 and grade 3 carcinoma were 7.2%, 41.8%, and 50.9% respectively [15]. Zhang et al. also showed a dissimilar result. It was seen that grade 1 carcinoma comprised 31%, grade 2 carcinoma 47.5%, and grade 3 carcinoma comprised 11.4% [17]. Out of 46 cases of the present study, 19.6% of cases were vimentin negative, low vimentin expression was observed in 10.9% of cases while 69.5% of cases had high vimentin expression. Higher vimentin expression was observed in other studies also. Vimentin was found positive in 97% of endometrial adenocarcinomas in the study of McCluggage et al. [20]. The reported positive expression of vimentin was 86.5% in the study of Reid-Nicholson et al., while Desouki et al. also found 82.0% of cases with endometrial carcinomas had positive vimentin expression [14,21]. In the study of Zhang et al. high vimentin expression was seen in 81.23% of cases and low in 18.77% of cases [18]. In the current study, among the Endometrial carcinomas, vimentin expression was highest in Endometrioid type 31 (88.6%) followed by serous type 1 (10.0%) and carcinosarcoma 0 (0.0%), which was statically significant ($p < 0.001$). It is in accordance with the results of Zhang et al. study, which showed high vimentin expression in endometrioid type carcinoma (95.58%) and less in serous type (5.42%) of endometrial carcinoma [18]. The present study shows statistical significance with the grade of endometrial carcinoma (p -value < 0.009). High vimentin expression was found in 100.0% of cases of grade 1, 75% of cases of grade 2, and 47 % of cases of grade 3. It is similar to the result of Zhang et al. where high vimentin expression was seen in 88.7% of grade 1 carcinoma, compared to 85.18% of grade 2 and 71.8% of grade 3 carcinoma [18]. Grade is one of the prognostic factors applied in clinical decisions regarding treatment.

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion

This study highlights a significant association between vimentin expression and tumor grade in endometrial carcinoma. High vimentin expression was more frequently observed in lower-grade tumors, whereas reduced or absent expression was more common in higher-grade cases. These findings suggest that vimentin may serve as a useful immunohistochemical marker for assessing tumor differentiation and could aid in prognostication of endometrial carcinoma.

Recommendation

Based on the findings, it is recommended that vimentin expression be routinely assessed through immunohistochemistry in endometrial carcinoma cases, particularly to support tumor grading and differentiation. Incorporating vimentin as a supplementary marker may enhance diagnostic accuracy and assist clinicians in identifying patients with more favorable tumor biology and predicting prognostic significance.

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Conflict of interest

None declared

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