Original Research Article

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Expression of vimentin in endometrial carcinoma: Association with histological subtypes, tumor grade, and T stage

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Abstract

Introduction: Endometrial carcinoma (EC) is one of the most common gynecological malignancies, with varying histopathological subtypes and biological behaviors. Accurate classification and grading are essential for prognosis and treatment planning. Immunohistochemical (IHC) markers, such as vimentin, have gained attention for their potential role in differentiating tumor types and predicting tumor aggressiveness. This study aims to evaluate the expression of vimentin in different histological types, grades, and stages of EC and to explore its diagnostic and prognostic relevance.

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

Results: Among the 46 patients, the mean age was 56.9 years, with most (39.1%) in the 51–60 age group. Endometrioid carcinoma was the predominant histopathological type (76.1%), followed by serous (21.7%) and carcinosarcoma (2.2%). Grade 3 tumors were the most common (45.7%). High vimentin expression was observed in 69.6% of cases, with a significant association noted between high vimentin expression and endometrioid type ($P < 0.001$) as well as lower tumor grade ($P = 0.009$). No significant association was found between vimentin expression and pathological T stage ($P = 0.099$).

Conclusion: The association of vimentin with histopathological type and grade of EC was found statistically significant ($P < 0.05$). However, the association between vimentin and the stage of EC was not statistically significant ($P > 0.05$). Routine use of vimentin expression in EC may provide prognostic information to predict disease outcomes.

Keywords: Endometrial carcinoma, histological subtypes, tumor grade, vimentin expression

Introduction

Endometrial cancer is the sixth most commonly occurring cancer in women and the fifteenth among all cancer type. In 2020, there were about 417,000 new cases of endometrial cancer.[1] In Southeast Asia, endometrial carcinoma (EC) is the third

most frequent gynecologic cancer and the fourth most common cancer in women. Over the past few decades, the prevalence of EC has increased in developing nations.[2] According to GLOBOCAN (2020), the estimated new cases in Bangladesh for EC were 1049, whereas deaths were 376. In 2020, the incidence, mortality, and 5-year prevalence rate of EC were 0.18, 0.07, and 3.15, respectively, in Bangladesh.[3] EC is a type of adenocarcinoma that arises from the endometrium and is most frequent throughout the reproductive and menopausal years. Most of the patients are between the ages of 50 and 59.[4] Bokhman's model has been used to classify EC into two subtypes based on clinicopathological and molecular criteria. Type I includes grade 1 and grade 2 cancers with strong estrogen and progesterone receptor expression, while type II tumors are linked to endometrial atrophy.[5] Stage, grade of differentiation, histological subtypes, and myometrial and lymphovascular invasion are all prognostic markers of EC.[6-8] The surgical approach, extent of surgery, and adjuvant therapy depend on the microscopic examination assessing the histological type and grade of cancer and the depth of myometrial invasion.[9,10] Vimentin, a cytoplasmic intermediate filament protein, has been recently identified to be a prognostic biomarker in some cancers.[11] Furthermore, vimentin is crucial for the epithelial-mesenchymal transition, though its functional contribution to that process remains unclear.[12,13] Previous studies showed that vimentin immunoreactivity was common in normal proliferative endometrium, and its persistence in EC might indicate a less malignant phenotype.[14] For example, Papadopoulos *et al*. demonstrated that expression of vimentin decreased as a lesion progressed to malignancy,[14] and a recent research work by Nesina *et al*.[15] also found that aggressiveness of tumors is associated with reduced expression of vimentin in EC. Zhang *et al*. showed that vimentin negativity is more common in type 2 than that in type 1 and vimentin-negative patients had poorer overall survival compared with vimentin-positive patients. However, there are only a few studies thus far focusing on the relationship between vimentin expression and EC prognosis currently, and its underlying molecular mechanism in EC is unclear.[11] The present study evaluated the immunohistochemical (IHC) expression of vimentin in EC and assessed its association with histological types, grades, and stages among Bangladeshi patients.

Methods

This cross-sectional observational study was conducted in the Department of Pathology, Sir Salimullah Medical College, Dhaka. IHC of Vimentin was done at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from March 2022 to February 2024. Histopathologically diagnosed EC 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. IHC was done in the Pathology Department, BSMMU. Sections have been examined under ×40 magnification. Distinct granular cytoplasmic staining was taken as positive. Five independent areas of each slide were examined under a microscope and an 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), immunoscore ranged from 0 to 9; where 0 was negative expression and low expression ranged from 1 to 3, and high expression of vimentin was 4–9.[16] A case record form has been developed to collect data from the patients. The statistical analysis was carried out by using the Statistical Package for the Social Sciences 26 for Windows. Descriptive statistics (frequencies, percentages) were used to summarize the patient's demographic characteristics and presented in tables, figures, charts and diagrams. The frequencies of different entities were expressed as percentages. The Fisher's Exact test was used to analyze the association between different categorical variables.

A $P < 0.05$ was considered statistically significant. Ethical clearance has been taken from the Ethical Review Committee, at Sir Salimullah Medical College. Informed written consent was taken from all patients.

Results

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 1].

Among the 42 patients, 9 (21.4%) had irregular vaginal bleeding, while 33 (78.6%) had postmenopausal bleeding [Figure 1].

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 2].

Out of the 46 cases, 13 (28.3%) had grade 1, 12 (26.1%) had grade 2, and 21 (45.7) had grade 3 carcinoma [Table 3].

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

Age group (in years)	Frequency (*n*)	Percentage
31–40	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	

SD: Standard deviation

Table 2: 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

According to the pathological T stage, 28 (60.9%) cases were in stage pT1, 8 (17.4%) were in stage pT2, and 10 (21.7%) patients were in stage pT3 [Figure 2].

IHC 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 4].

Among the endometrioid type carcinomas, 31 (88.6%) had high vimentin expression, while among the serous type carcinomas, 1 (10.0%) had high vimentin expression. Moreover, 8 (80.0%) serous carcinomas had negative expression. Endometrioid-type carcinomas had significantly high vimentin expression, while serous carcinomas had negative vimentin expression ($P < 0.001$) [Table 5].

Among the grade 1 carcinomas, all 13 (100.0%)

Table 3: Distribution of cases (endometrioid, Serous, and carcinosarcoma) by grade (*n*=46)

Grade	Frequency (*n*)	Percentage
1	13	28.3
2	12	26.1
3	21	45.7

Table 4: Distribution of study cases by vimentin expression (*n*=46)

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

Table 5: Association of histopathological type with vimentin expression (*n*=46)

Histopathological type	Negative expression (%)	Low expression (%)	High expression (%)	*P*-value
Endometrioid	1 (2.9)	3 (8.6)	31 (88.6)	
Serous	8 (80.0)	1 (10.0)	1 (10.0)	<0.001*
Carcinosarcoma	0 (0.0)	1 (100.0)	0 (0.0)	

*Fisher's Exact test

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

There was no significant association between pathological T stage and vimentin expression ($P = 0.099$) [Table 7].

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 and 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.[11,15,17] In the present study, 21.4% had irregular vaginal bleeding, while 78.6% had postmenopausal bleeding. This finding follows Zhang *et al*.,[11] where it was found that 62.7% of patients had postmenopausal bleeding. This indicates that postmenopausal women are susceptible to EC. 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*.,[11] where it was found that 90.6% were endometrioid type and 9.4% were serous type EC. Morice *et al*.[18] stated that the most prevalent histological form is endometrioid carcinoma, which is frequently identified when the pathology is still

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

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

*Fisher's exact test

Table 7: Association of pathological T stage with vimentin expression (n=46)

Stage	Negative expression (%)	Low expression (%)	High expression (%)	*P*-value
1	4 (14.3)	2 (7.1)	22 (78.6)	
2	4 (50.0)	1 (12.5)	3 (37.5)	0.099*
3	1 (10.0)	2 (20.0)	7 (70.0)	

*Fisher's exact test

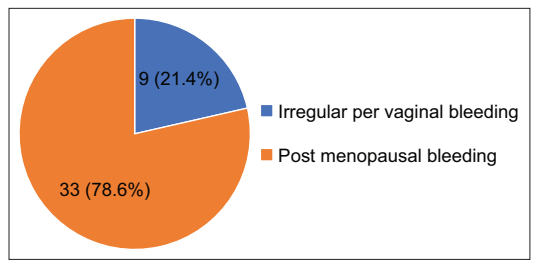

Figure 1: Distribution of patients by symptoms

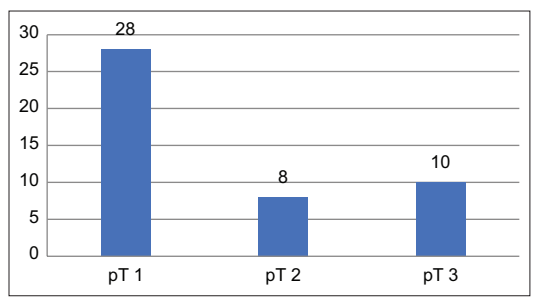

Figure 2: Distribution of study cases according to pathological T stage (n=46)

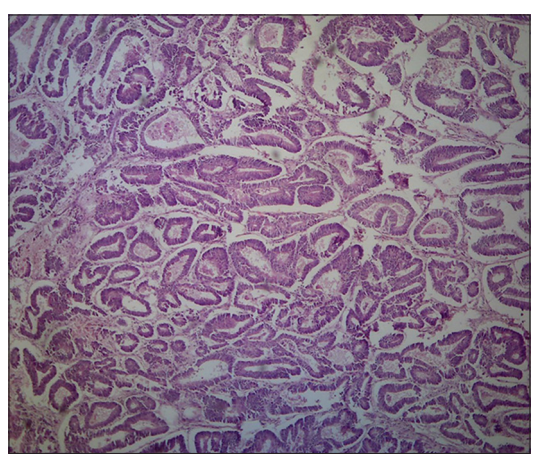

Figure 3: Photomicrograph showing grade 1 endometrioid carcinoma (Case No.- 45, Hematoxylin and Eosin, ×40)

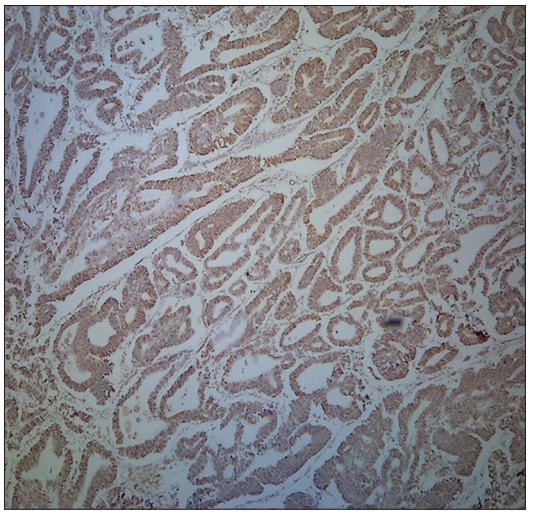

Figure 4: Photomicrograph showing grade 1 endometrial carcinoma with high vimentin expression (Case No- 45, IHC, ×40)

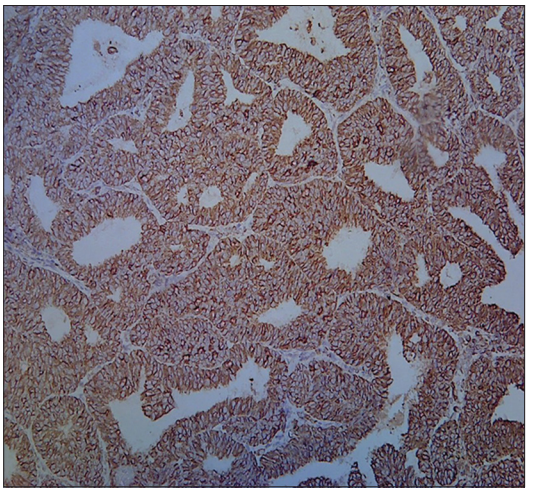

Figure 6: Photomicrograph showing grade 2 endometroid carcinoma with high vimentin expression (Case No- 05, IHC, ×40)

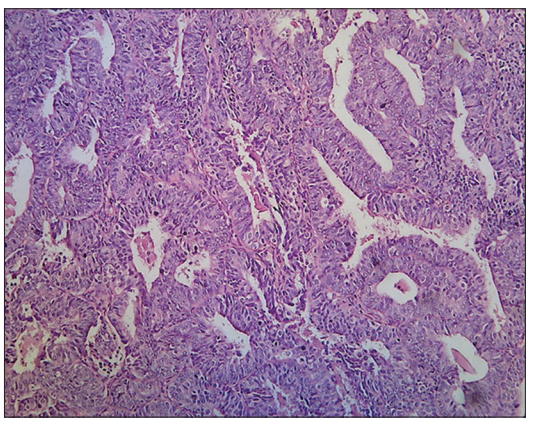

Figure 5: Photomicrograph showing grade 2 endometrioid carcinoma (case No.- 05, Hematoxylin and Eosin, ×40)

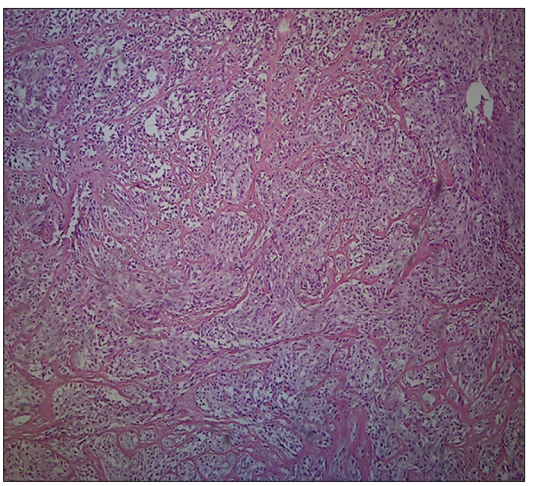

Figure 7: Photomicrograph showing grade 3 endometrioid carcinoma (Case No- 10, Hematoxylin and Eosin, ×10)

restricted to the uterus, which shows concordance with this study. In the present study, out of the 46 cases of EC, 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 findings of Nesina *et al*.,[15] where grade 1, grade 2, and grade 3 carcinoma were 7.2%, 41.8%, and 50.9%, respectively. Zhang *et al*. (2022) 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%. This study shows that 60.9% of cases were in stage pT1, 17.4% were in stage pT2, and 21.7% were in stage pT3. Zhang *et al*.[11] did staging according to the Federation of Gynecology and Obstetrics (FIGO) stage, where stage I was 73.3%, stage II was 7.33%, stage III was 15.24% and stage IV was 4.10%. Desouki *et al*.[19] also found that 72.0% of patients had FIGO

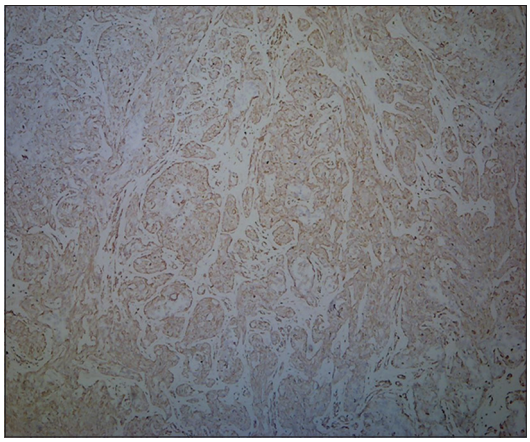

Figure 8: Endometroid carcinoma with high vimentin expression (Case No- 10, IHC, ×10)

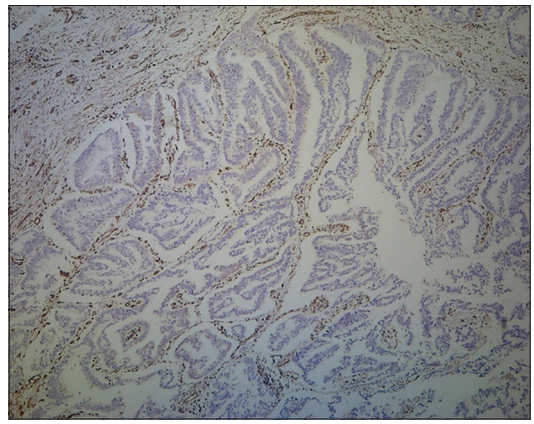

Figure 10: Photomicrograph showing serous endometrial carcinoma with low vimentin expression (Case No- 24, IHC, ×40)

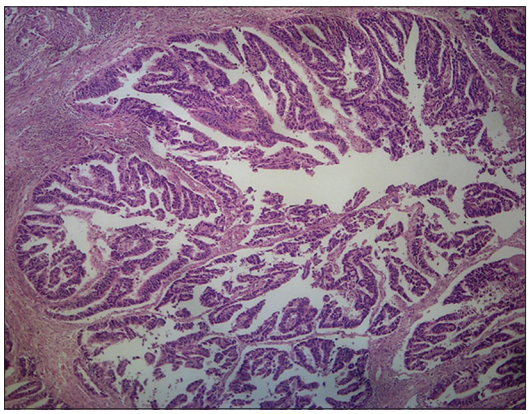

Figure 9: Photomicrograph showing serous carcinoma (Case No- 24, Hematoxylin and Eosin, ×40)

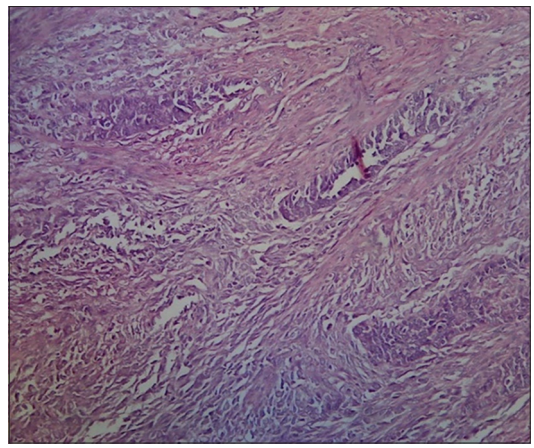

Figure 11: Photomicrograph showing carsinosarcoma (Case No- 04, Hematoxylin and Eosin, ×40)

stage I carcinoma, while a few were in FIGO stage II and III. It indicates that most of the cases were in the early stages, which may be due to the early clinical presentation and low-grade morphology of the tumor. 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*.,[17] while Desouki *et al*.[19] also found 82.0% of cases with EC s had positive vimentin expression. In the study of Zhang *et al*.,[11] high vimentin expression was seen in 81.23% of cases and low in 18.77% of cases. In the present study, among the ECs, 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*.[11] study, which showed high vimentin expression in endometrioid type carcinoma (95.58%) and less in serous type (5.42%) of EC. The present study shows statistical

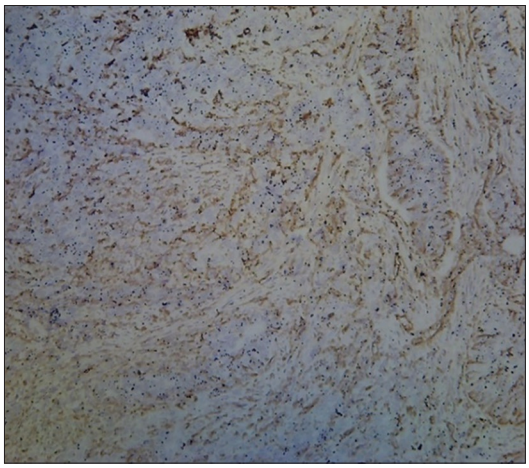

Figure 12: Photomicrograph showing carcinosarcoma with low vimentin expression (Case No- 04, ×40)

significance with the grade of EC ($P < 0.009$). 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*.,[11] 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. Grade is one of the prognostic factors applied in clinical decisions regarding treatment. The present study shows no significant association between pathological T stage and vimentin expression ($P = 0.099$). Reid-Nicholson *et al*.[17] also found no significant association between the FIGO stage and vimentin expression ($P = 0.49$). This may be due to the small sample size, heterogenicity of the population, and differences in vimentin detecting methods. During the evaluation of the association between vimentin with histological type, grade, and stage in this study, a statistically significant ($P < 0.05$) association was found between vimentin and histopathological type and grade. Vimentin expression was high in the endometrioid type and low in the serous type and carcinosarcoma. The immunoreactivity of vimentin was also associated with the histological grade, which showed high expression in grade 1.

Limitations of the study

The study was conducted in a single hospital with a small sample size. Hence, the results may not represent the whole community. Moreover, complete staging of all patients could not be done due to a lack of lymph node sampling and a lack of information about distant metastasis.

Conclusion

The association of the vimentin with histopathological type and grade of EC was found statistically significant ($P < 0.05$). However, the association between vimentin and with stage of EC was not statistically significant ($P > 0.05$). Routine use of vimentin expression in EC may provide prognostic information to predict disease outcomes.

Recommendation

- Routine use of vimentin in EC specimens with routine Hematoxylin and Eosin stain may help clinicians and patients regarding surgical management and advanced treatment, such as adjuvant chemotherapy or radiotherapy.
- Long-term follow-up of the patients to correlate the expression of this molecular marker with the progression and recurrence of the disease and survival of the patients is needed to understand the prognostic role of the biomarker.

Funding

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Conflict of Interest

None declared.

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