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Research Article

IMMUNOHISTOCHEMICAL EVALUATION OF E-CADHERIN AND VIMENTIN EXPRESSION AS PREDICTORS OF EPITHELIAL–MESENCHYMAL TRANSITION IN ORAL POTENTIALLY MALIGNANT DISORDERS

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Abstract

Background

Oral cancer continues to be a significant global health issue, especially in developing nations like India, where it represents a considerable share of cancer-related morbidity and mortality. Oral potentially malignant disorders (OPMDs) are lesions that could become oral squamous cell carcinoma (OSCC). The epithelial-mesenchymal transition (EMT) is an important biological process that helps tumors grow. It is marked by the loss of epithelial markers like E-cadherin and the gain of mesenchymal markers like Vimentin.

Aim

To analyze the expression levels of E-cadherin and Vimentin in oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC), and to determine their prognostic significance in malignant transformation.

Materials and Methods

A cross-sectional study was performed in a hospital setting on histopathologically validated cases of OPMDs and OSCC. An immunohistochemical analysis was conducted to evaluate the expression of E-cadherin and Vimentin. We used SPSS software to do the statistical analysis, and we set the significance level at $p < 0.05$.

Outcomes

From mild dysplasia to OSCC, E-cadherin expression went down and Vimentin expression went up in a steady way. There was a statistically significant link between marker expression and histopathological grading ($p < 0.05$).

Conclusion

E-cadherin and Vimentin are dependable biomarkers of epithelial-mesenchymal transition (EMT) and can be utilized to anticipate malignant transformation in oral premalignant lesions.

Keywords: E-cadherin, Vimentin, EMT, OPMDs, OSCC, Immunohistochemistry

Introduction

Oral cancer is a prevalent malignancy globally and constitutes a significant public health issue, especially in low- and middle-income nations [1]. India plays a big role in the world's health problems because many people their smoke, drink alcohol, and chew betel quid [2]. Even though treatments have gotten better, the overall survival rate for oral squamous cell carcinoma (OSCC) is still low. This is mostly because the disease is often diagnosed too late and comes back too often [3].

Oral potentially malignant disorders (OPMDs), such as leukoplakia, erythroplakia, oral submucous fibrosis, and oral lichen planus, are the main causes of oral cancer [4]. These lesions show different levels of cancer risk based on clinical and histopathological features [5]. Immunohistochemical grading of E-cadherin

and Vimentin expression was performed according to the scoring criteria defined in the present study, based on staining intensity and proportion of positively stained cells. Oral carcinogenesis entails a sequence of genetic and molecular modifications that result in the disruption of normal cellular homeostasis [6]. Histopathological grading of epithelial dysplasia is frequently employed to evaluate malignant potential; however, it is constrained by interobserver variability and insufficient predictive accuracy [7]. Consequently, there is a necessity for dependable molecular markers capable of detecting high-risk lesions at an early stage.

Epithelial–mesenchymal transition (EMT) is a critical mechanism in tumor progression, invasion, and metastasis [8]. During epithelial-mesenchymal transition (EMT), epithelial cells lose their polarity and the ability to stick to each other, and they gain mesenchymal traits like more mobility and invasiveness [9]. E-cadherin is a transmembrane glycoprotein that needs calcium to work. It is very important for keeping epithelial cells together and the tissue healthy [10]. When E-cadherin is not expressed, cells stick to each other less and tumors become more invasive [11]. Vimentin, a mesenchymal intermediate filament protein, is elevated during epithelial-mesenchymal transition (EMT) and correlates with aggressive tumor behavior [12].

The inverse correlation between E-cadherin and Vimentin expression is regarded as a characteristic feature of epithelial-mesenchymal transition (EMT) [13]. Assessing these markers in premalignant lesions can yield significant insights into early molecular alterations and assist in forecasting malignant transformation.

Scoring System

Aims and Objectives

Aims

To assess the predictive significance of E-cadherin and Vimentin as indicators of epithelial–mesenchymal transition in oral premalignant lesions.

Objectives

1. To evaluate E-cadherin expression in OPMDs and OSCC [10]
2. To evaluate Vimentin expression in OPMDs and OSCC [12]
3. To relate the levels of marker expression to the histopathological grading [7].
4. To assess their function in forecasting malignant transformation [13]

Materials and Methods

Design of the Study

A cross-sectional study conducted at the Department of Pathology, CIMS Bilaspur. The people in the study

Patients exhibiting clinically suspicious oral lesions.

Criteria for Inclusion

• OPMDs that have been confirmed by histopathology
• Cases of OSCC

Criteria for Exclusion

• Biopsy samples that aren't big enough
• Cases that have already been treated

Sample Processing

Ten percent formalin was used to fix biopsy samples, which were then embedded in paraffin and cut into 4–5 µm thick sections. We used haematoxylin and eosin staining to make a histopathological diagnosis [14].

Immunohistochemistry

Monoclonal antibodies were used to do IHC staining against:

• E-cadherin
• Vimentin

Table 1: Immunohistochemical Grading of E-cadherin

Grade	Interpretation
1+	Weak membranous staining (<25% cells)
2+	Mild staining (25–50% cells)
3+	Moderate staining (50–75% cells)
4+	Strong staining (>75% cells)

Table 2: Immunohistochemical Grading of Vimentin

Grade	Interpretation
1+	Weak cytoplasmic staining (<25% cells)
2+	Mild staining (25–50% cells)
3+	Moderate staining (50–75% cells)
4+	Strong staining (>75% cells)

Statistical Analysis

The association between E-cadherin and Vimentin expression with histopathological grading was analysed using the Chi-square test. A statistically significant association was observed ($p < 0.05$), indicating that both markers show significant correlation with disease progression. [18].

4. Results

Table 3: Age Distribution

Age Group	Number	Percentage
<30 years	6	12%
31–50 years	22	44%
>50 years	22	44%

Table 4: Gender Distribution

Gender	Number	Percentage
Male	36	72%
Female	14	28%

Table 5: Diagnostic Categories

Diagnosis	Number	Percentage
Mild Dysplasia	10	20%
Moderate Dysplasia	15	30%
Severe Dysplasia	10	20%
OSCC	15	30%

Table 6: E-Cadherin Expression

Lesion Type	1+	2+	3+	4+
Mild Dysplasia	0	2	5	3
Moderate Dysplasia	2	6	5	2
Severe Dysplasia	3	4	2	1

OSCC	6	5	3	1

Table 7: Vimentin Expression

Lesion Type	**1+**	**2+**	**3+**	**4+**
Mild Dysplasia	7	2	1	0
Moderate Dysplasia	6	5	3	1
Severe Dysplasia	2	3	4	1
OSCC	1	3	5	6

Table 8: Association of Marker Expression with Lesion Severity

Marker	**Test Used**	**p-value**	**Significance**
E-cadherin	Chi-square	0.001	Significant
Vimentin	Chi-square	0.002	Significant

Figures

Figure 1: Age distribution bar chart

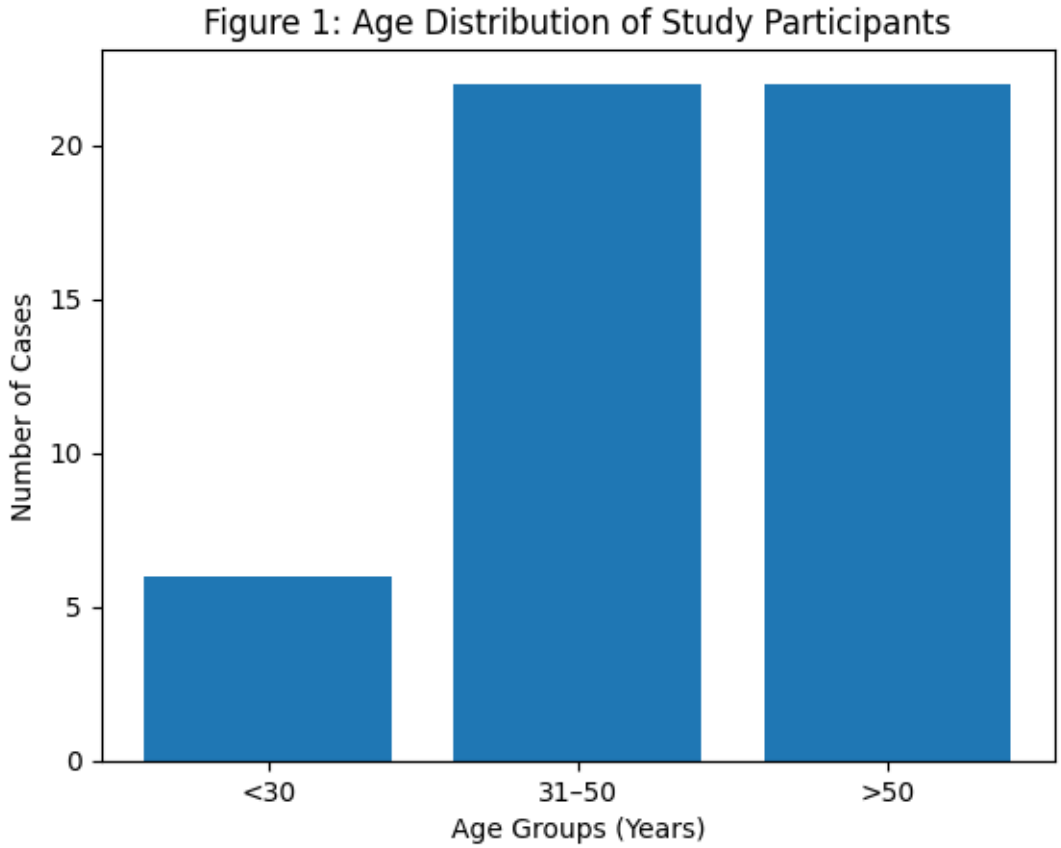


Figure 2: E-cadherin decreasing trend

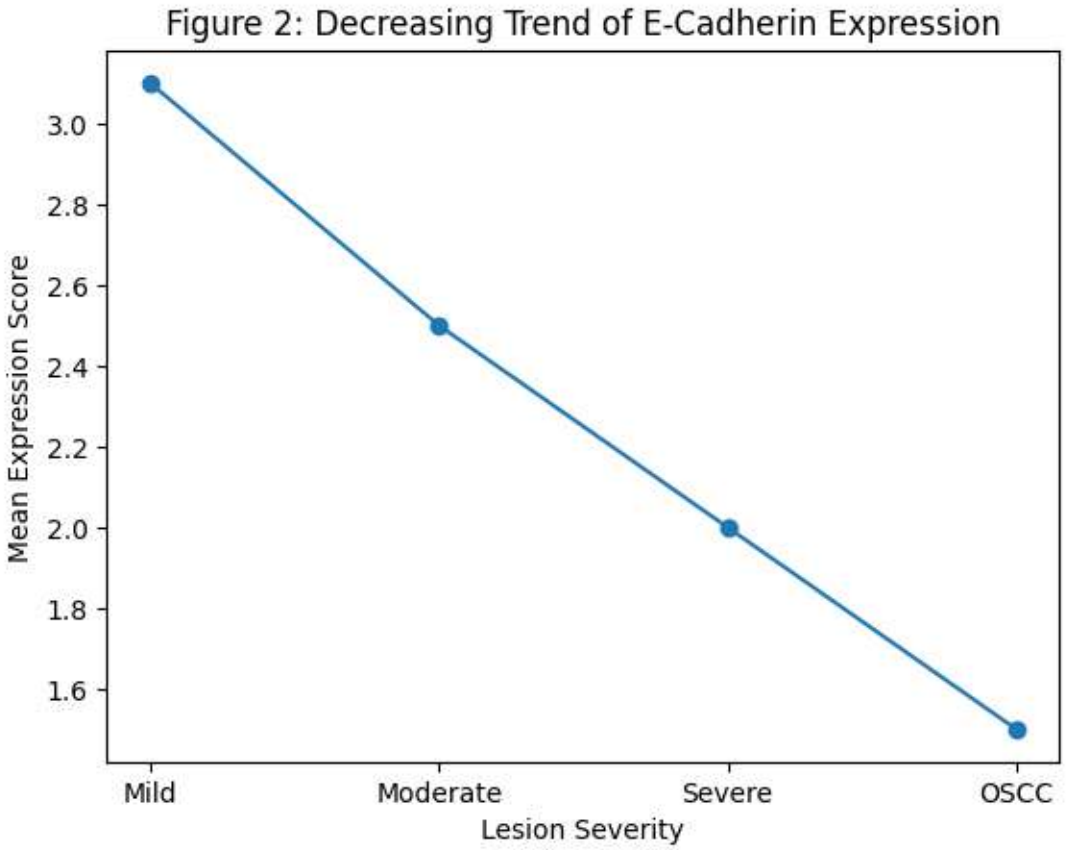


Figure 3: Vimentin increasing trend

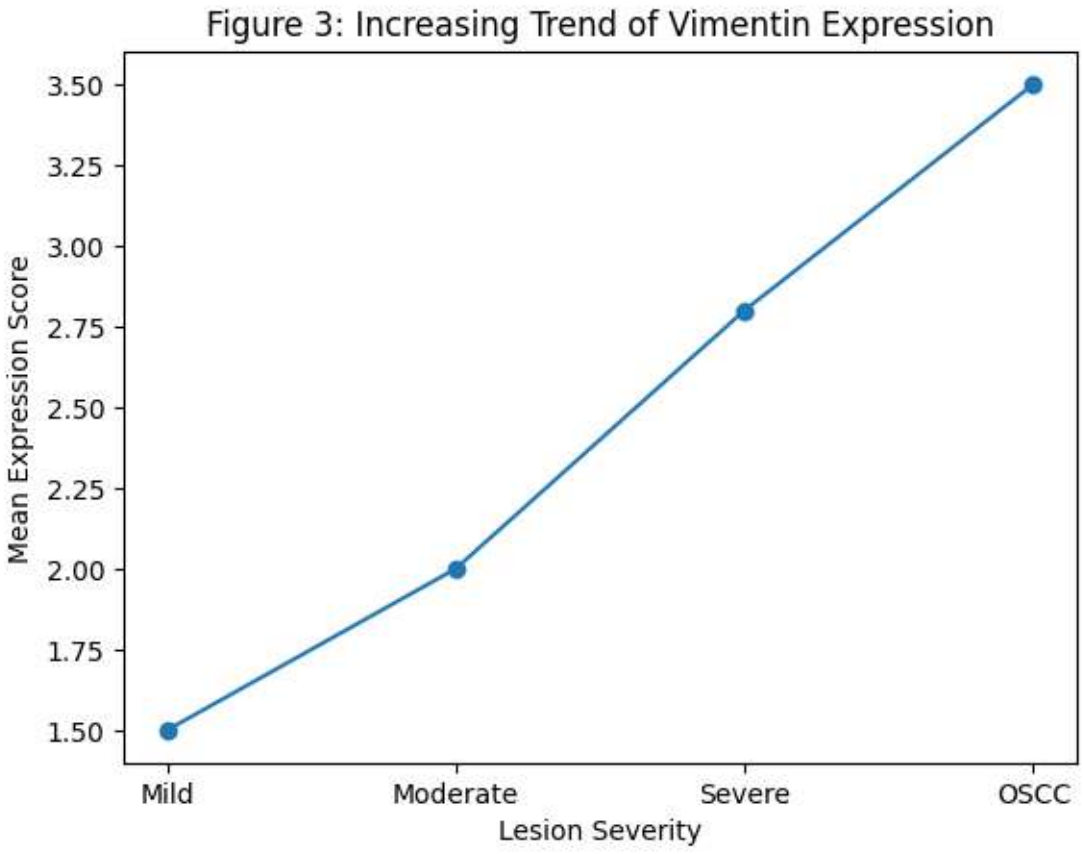
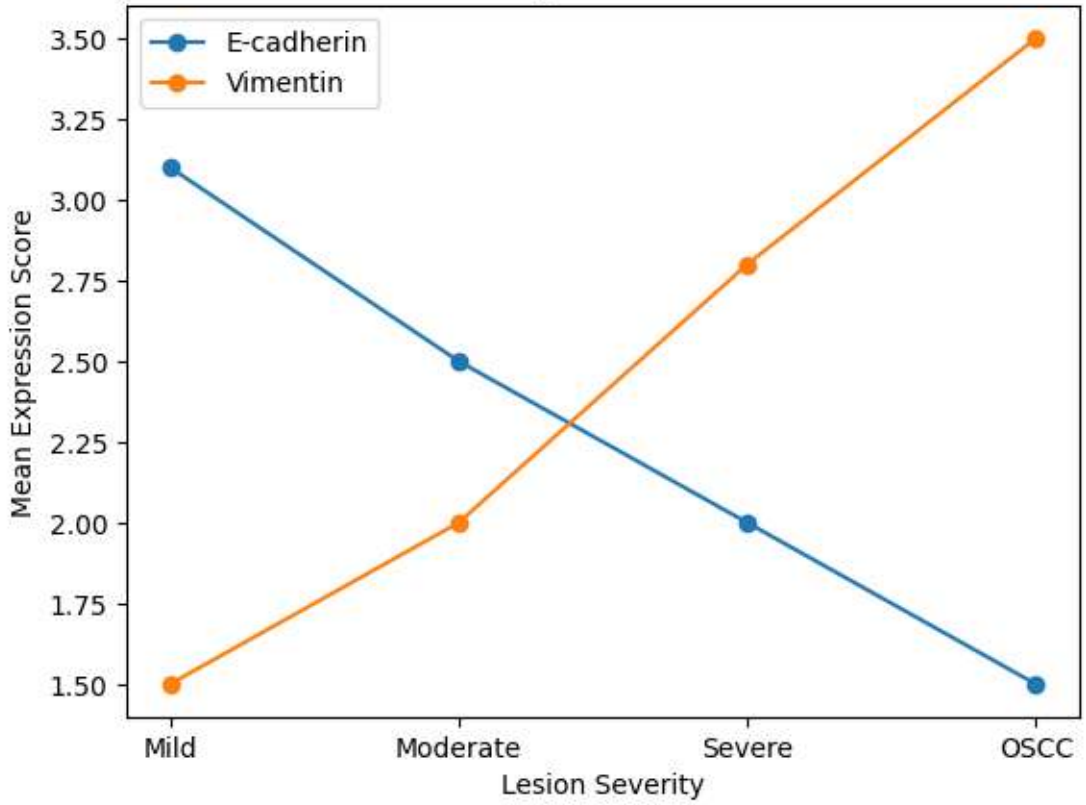


Figure 4: Inverse Relationship Between E-Cadherin and Vimentin



Discussion

The current study illustrates a notable inverse correlation between E-cadherin and Vimentin expression across various oral lesions, thereby endorsing the involvement of epithelial–mesenchymal transition (EMT) in the initial stages of oral carcinogenesis.

The demographic results of this study align with global epidemiological patterns, indicating a greater prevalence among males and older age cohorts [1,2]. This indicates heightened exposure to carcinogenic behaviours, including tobacco use and alcohol consumption [3].

Histopathological grading, despite its widespread application, exhibits constraints in forecasting malignant transformation [7]. The current study demonstrated that molecular modifications in epithelial-mesenchymal transition (EMT) markers transpire even in the initial stages of dysplasia, suggesting that biochemical changes precede morphological alterations.

The expression of E-cadherin was observed to diminish progressively with the escalating severity of dysplasia and carcinoma. This finding aligns with prior studies that emphasise its function as a tumour suppressor protein [10,11]. When E-cadherin is lost, cells can't stick together as well, and tumours become more invasive.

On the other hand, vimentin expression went up as the disease got worse, which showed that the cells were taking on mesenchymal traits [12]. This is linked to higher motility, invasiveness, and resistance to apoptosis.

The inverse correlation among these markers validates EMT activation and corroborates prior literature [13]. Several signalling pathways, such as TGF-β and Wnt pathways, control EMT. These pathways help tumours grow [8].

In the present study, statistical analysis revealed a significant association between marker expression and histopathological grading. The Chi-square test demonstrated that the decrease in E-cadherin expression and the corresponding increase in Vimentin expression with increasing severity of dysplasia were statistically significant ($p < 0.05$). This finding strongly

supports the role of epithelial–mesenchymal transition (EMT) as an early event in oral• carcinogenesis and highlights the prognostic• value of these biomarkers in identifying high-• risk lesions.

The identification of EMT markers in premalignant lesions indicates that EMT initiates early in carcinogenesis. This shows how important molecular markers are for finding lesions that are at high risk.

Conclusion

The results of this study offer compelling evidence that epithelial–mesenchymal transition (EMT) is crucial in the initial phases of oral carcinogenesis. The gradual decline of E-cadherin expression, alongside the simultaneous rise in Vimentin expression across various oral lesions, ranging from mild dysplasia to invasive carcinoma, indicates a definitive molecular transition towards a mesenchymal phenotype.

E-cadherin, a crucial component for maintaining epithelial integrity, exhibited a significant reduction in advanced stages of dysplasia and oral squamous cell carcinoma (OSCC), signifying diminished cell adhesion and heightened invasive capability [10,11]. On the other hand, Vimentin expression went up a lot, which means that the tumour was more aggressive and had a higher chance of spreading [12].

The inverse relationship between these markers emphasizes their dependability as indicators of epithelial-mesenchymal transition (EMT) and underscores their effectiveness in forecasting malignant transformation [13]. Significantly, these alterations were noted even in early premalignant lesions, indicating that epithelial-mesenchymal transition (EMT) commences before evident histological transformation. From a clinical perspective, the evaluation of E-cadherin and Vimentin expression can function as a significant complement to histopathological analysis. These markers can help sort patients by risk, which makes it easier to find high-risk lesions early and decide on the best course of treatment. Additionally, targeting EMT pathways may provide novel therapeutic approaches to inhibit tumour progression and metastasis.

Limitations

Small sample size

Single-centre study

Lack of longitudinal follow-up

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