RESEARCH PAPER

Moesin Expression in Oral Squamous Cell Carcinomas: Insights into Its Biomarker Potential

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ABSTRACT

Background: Membrane organizing extension spike protein (Moesin) belongs to the ERM (Ezrin, Radixin and Moesin) family proteins. It acts as cross linker between transmembrane proteins and actin filaments of the cytoskeleton, playing a key role in the control of cell growth, cell survival, cell morphology, cell adhesion, cell migration, etc., through various signal transduction pathways under normal physiological conditions. Immunohistochemical (IHC) studies revealed its upregulation in multiple human cancers including Oral Squamous Cell Carcinoma (OSCC).

Objectives: This IHC study aimed to assess the expression patterns of Moesin in the tissues of OSCC & epithelium of normal oral mucosa and to observe its potential role in the diagnosis of OSCC.

Materials and Methods: An analytical cross-sectional invitro study was conducted using 45 tissue specimens (N=45), divided into two groups, Group A (30 OSCC cases) and Group B (15 Normal healthy oral mucosa as controls). Serial sections were stained with hematoxylin & eosin (H&E) for histopathological confirmation of cases and controls, followed by IHC staining for the Moesin protein. Two blinded observers evaluated the sections using a trinocular research microscope for subcellular staining & its expression patterns. The results were tabulated in Microsoft excel and statistically analyzed.

Results: Moesin expression was strongly membranous in the basal & parabasal layers of normal oral mucosa and found to be significantly upregulated in all grades of OSCC with combined & strong cytoplasmic expressions. Variable expression patterns with strong immunopositivity were evident across all the histopathological grades of OSCC. Immunopositivity score was slightly higher in the moderately differentiated OSCC compared to the other variants of OSCC.

Conclusion: This study demonstrated higher cytoplasmic localization of Moesin, correlating with loss of cellular cohesion, epithelial mesenchymal transition (EMT) and metastatic potential of malignant cells. Henceforth, Moesin in conjunction with routine histopathological examination, may help in early detection of aggressive behaviour, invasive potential and nodal metastasis risk of OSCC.

Keywords: Moesin, Oral Squamous Cell Carcinomas, Nodal metastasis, ERM proteins

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1. INTRODUCTION

Oral Squamous Cell Carcinoma (OSCC) is the most common malignancy which ranked 16th among all malignancies worldwide. [1] Despite the marked advancements in diagnosis and treatment of OSCC, the prognosis still remains poor, with overall 5-year survival

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rate being as low as 50%–60%. [2] The most common traditional method used to determine the rate of malignant transformation and prognosis is histopathological grading of OSCC (well-differentiated, moderately differentiated and poorly differentiated types). However, this is considered to be subjective and meager, leading to inaccurate results and poor prognosis. The epigenetic and molecular changes that can occur within a cell during the carcinogenetic process can be detected by an in-detail study of cell moiety using new emerging biomarkers. Therefore, the development of molecular markers for diagnosis, therapy and prognosis as an adjuvant diagnostic aid for OSCC is essential. [3]

Biomarkers, being the products of malignant cells used to assess the rate of malignant transformation, can serve as targets for intervention of therapy and can, therefore, prove to be more promising prognostic factors in understanding the molecular pathogenesis of OSCC [4]. Few specific and nonspecific markers were introduced in the past, but their day-to-day applications, on a clinical basis, are still lacking. This can be one of the contributing factors for lack of early detection and poor prognosis. Hence, there is a need for introducing new emerging biomarkers as an interventional therapy for effectively addressing OSCC at an early stage, thus preventing it from further proceeding to the advanced stage. [5,6] One such biomarker currently under research is membrane-organizing extension spike protein (MOESIN).

Moesin is a crucial cytoskeletal protein, a 577-amino acid polypeptide with a molecular mass of 75 kDa, belonging to the FERM domain (4.1 protein, Ezrin, Radixin and Moesin), that links the plasma membrane to the actin cytoskeleton [7], ensuring structural stability, cell motility, and shape predominantly related to Lymphocytes [8], Microglial cells in CNS [9], T cell responses to suppress autoimmune diseases. [10] Mutations, genetic loss, or abnormal activation of Moesin are heavily linked to disease states such as Immunodeficiencies disorder. Patients suffer from recurrent bacterial and viral infections, low naïve T-cell counts, and autoimmune manifestations. [11] Oncology and metastasis by aberrant overexpression and activation of Moesin drive epithelial-mesenchymal transition (EMT) was shown in few studies. [12] It is widely used as an unfavorable prognostic marker for cancer progression, correlating with tumor invasion and metastasis in cancers like breast, head and neck, and oral squamous cell carcinomas. [12,13,14] Further, pathogenic forms of Tau protein promote over-stabilization of actin, relying on the pathological upregulation of Moesin to induce cell-cycle activation and neuronal death leading to neurodegeneration (Alzheimer's Disease). [15] Moesin (MSN) is an emerging therapeutic target, primarily investigated for its role in oncology, immunology, and neurology as it is found to act as a linker between the cell membrane and actin cytoskeleton, it drives cancer cell motility, immune suppression, and neuroinflammation.

The aim of the present study was to elucidate the clinical significance of expression patterns of Moesin in patients with oral squamous cell carcinoma (OSCC).

2. MATERIALS & METHODOLOGY

This is an analytical cross-sectional invitro study conducted at Government Dental College and Hospital in the Department of Oral Pathology. Institutional ethical committee approval was taken with protocol no.15/D001/IEC/GDC&H/2023-24dated.08/04/2024.

Materials utilized for this study were formalin-fixed tissue specimens of OSCC and Normal oral mucosa, processing solutions, Leica semiautomatic microtome, the primary antibody - Moesin Rabbit Monoclonal IgG antibody (ABclonal, A4915) with a dilution of 1:200. The secondary antibody-HRP Goat Anti-Rabbit IgG (H+L) (ABclonal, AS014) at 1:1000 dilution, Hematoxylin and Eosin (H&E) stains, Magnus Trinocular research microscope (Mx2li LEDFS11) with 5 MP camera attachment (Magcam DC-5), glass slides, coverslips, beakers, staining jars, forceps, gloves, tissue processing equipment (slide warming table & hot air oven). The study was carried out in the following steps,

- Sample collection and Preparation
- Tissue sectioning and Staining with Hematoxylin & Eosin, and Moesin IHC marker
- Evaluation of H&E-stained sections and Moesin IHC stained sections
- Statistical Analysis

2.1 Sample Collection and Preparation

A total of 45 tissue samples were used in this study. Sample size was calculated using G* power 3.1.9.7 software. Sample selection was based on inclusion criteria of histopathologically diagnosed cases of OSCC (graded according to WHO criteria) and normal oral mucosa preferably from the extraction sites of impacted mandibular third molars and crown lengthening procedures in healthy individuals. Exclusion criteria include any diseased oral mucosa and unwilling patients.

Thirty formalin-fixed tissue specimens of diagnosed OSCC cases were obtained from the archives of the Department of Oral Pathology and 15 Normal oral mucosal tissues were collected from the department of Oral surgery from willing patients with prior informed consent. Tissue blocks were prepared after routine tissue processing of normal oral mucosal specimens. The study samples (N=45) were grouped into 2 groups as follows,

Group A: Tissue specimens of OSCC cases- 30 no.

Group B: Tissue specimens of normal oral mucosa-15 no.

2.2. Tissue Sectioning and staining tissue sections with H&E and Moesin IHC marker

Each tissue specimen was sectioned into two equal halves and two serial sections of 4µm thickness were taken. First Section was stained with H&E for confirmatory histopathological diagnosis. Second Section was stained Immunohistochemically for Moesin protein primary

antibody: Moesin Rabbit Monoclonal IgG antibody (ABclonal, A4915)

2.3 Evaluation of H&E stained sections and Moesin IHC stained sections

The H&E-stained sections were independently evaluated by two blinded observers using a Trinocular research microscope with camera attachment under 4x, 10x, and 40x magnifications for confirmatory histopathological diagnosis of OSCC. The parameters like expression patterns of Moesin and immunopositivity score were evaluated through semiquantitative methods. Two blinded investigators independently evaluated the results of immunohistochemical staining without prior knowledge of clinicopathologic data. The interobserver agreement of the two pathologists was high (α=0.977 and α=0.965). The intraobserver agreement of the scoring also showed high concordance (α=0.935). Conflicting results were resolved using a multiheaded microscope. Representative histological sections from each case were evaluated for Moesin expression. For each section, five random high-power fields were selected and analyzed. Expression patterns were classified as membranous pattern - membranous expression more dominant than cytoplasmic expression; mixed pattern - membranous expression approximately equal to cytoplasmic expression; and cytoplasmic pattern - membranous expression weaker than cytoplasmic expression. [16] A semi-quantitative immunopositivity scoring was employed to assess final scores in the samples. Quantitative analysis was performed using Image J Analysis software. The final score of immunopositivity was calculated as the sum of staining intensity and the percentage of positively stained cells, as described by Faustino et al., 2008.[17] The percentage of positive cells was scored on a scale of 0 to 4, representing 0 for no positive cells, 1 for 25% positive cells, 2 for 25–50% positive cells, 3 for 51–75% positive cells, and 4 for more than 75% positive cells respectively. Staining intensities of Moesin were graded on a scale of 0 to 4, representing 0 for no staining, 1 for weak, 2 for moderate, 3 for strong and 4 for very strong intensities respectively. The final immunopositivity score was obtained by adding both the percentage of positive cells score and the intensity score. Based on the final score, Moesin expression was categorized as weak immunopositivity (scores 1–5) and strong immunopositivity (scores 6-8).

2.4 Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS version 26.0 (IBM Corp., USA). Descriptive statistics were expressed as mean ± standard deviation (SD), standard error (SE), and 95% confidence intervals (CI) for continuous variables, while categorical data were presented as frequencies and percentages. The association between categorical variables across different grades of OSCC and comparison of mean intensity scores & immunopositivity scores were assessed using the Chi-square (χ^2) test. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 45 samples (Group A & B) were evaluated for Moesin staining and the observations were as follows.

Table 1 showed expression patterns of Moesin in various epithelial layers of normal oral mucosa. All cells in basal and parabasal layers (100%) and few cells in spinous layers (12.26%) demonstrated membranous expression of Moesin. Whereas rest of the suprabasal cells exhibited no expression for Moesin. Combined membrano-cytoplasmic, cytoplasmic or nuclear expressions were absent [Figure1a,b]. The statistical analysis demonstrated a statistically significant association between epithelial layers and Moesin expression patterns ($p < 0.05$).

Table 2 showed expression patterns of Moesin in histopathological grades of OSCC. All cells in OSCCs exhibited expression for Moesin. Well differentiated OSCC predominantly exhibited combined expression (38.66%), followed by membranous expression (32.18%) and cytoplasmic expression (29.96%). Moderately differentiated OSCC demonstrated a marked reduction in membranous expression (7.7%) with a substantial increase in cytoplasmic expression (59.56%). Poorly differentiated OSCC showed predominant cytoplasmic expression (88.18%) with minimal combined and negligible membranous expression patterns. No nuclear expression was observed in any of the OSCC groups. The statistical analysis demonstrated a highly significant association between Moesin expression patterns and histopathological grades of OSCC ($p < 0.05$).

Table 3 showed comparison of expression patterns of Moesin in well differentiated OSCC with normal mucosa [Figure 2a,b]. Normal mucosal epithelium showed predominantly membranous expression (56.13%) with no combined or cytoplasmic expression. Whereas, well differentiated OSCC demonstrated increased combined (38.66%) and cytoplasmic expression, with decreased membranous expression. The statistical analysis demonstrated significant difference ($p < 0.0001$) between Moesin expression patterns in well differentiated OSCC and normal mucosal epithelium.

Table 4 showed comparison of expression patterns of Moesin in moderately differentiated OSCC with normal mucosa [Figure 3a,b]. Moderately differentiated OSCC showed marked cytoplasmic expression (59.56%) compared to normal oral mucosa where only membranous expression was seen. The statistical analysis demonstrated a significant difference ($p < 0.0001$) between Moesin expression patterns in moderately differentiated OSCC and normal mucosa.

Table 5 showed comparison of expression patterns of Moesin in poorly differentiated OSCC with normal mucosal epithelium [Figure 4a,b]. Poorly differentiated OSCCs showed high cytoplasmic expression (88.18%) compared to only membranous expression in normal mucosal epithelium. The statistical analysis demonstrated a significant difference ($p < 0.0001$) between Moesin expression patterns in moderately differentiated OSCC

and normal oral mucosa.

Table 6 showed comparison of expression patterns of Moesin in histopathological grades of OSCC with normal oral mucosal epithelium [Figure 5]. Normal oral mucosal epithelium showed only membranous expression (56.13%) with complete absence of combined & cytoplasmic expression. In contrast, malignant cells in well differentiated OSCC predominantly exhibited combined expression (38.66%), whereas moderately differentiated OSCC predominantly demonstrated cytoplasmic expression (59.56%). Poorly differentiated OSCC exhibited the highest cytoplasmic expression (88.18%) with almost complete reduction in membranous staining. The statistical analysis demonstrated a statistically highly significant association between expression patterns and progression from normal mucosa to OSCC ($p < 0.05$).

Tables

Table 1: Expression patterns of Moesin in the epithelium of N ormal oral mucosa

Layers	Membranou s (M) (%)	Combined (M+C) (%)	Cytoplasm (C) (%)	C+N (%)	Nuclear (%)	No Expression (%)
Basal and Parabasal layers	100(%)	0	0	0	0	0
Supra basal layers	12.26%	0	0	0	0	87.73
Total	56.13	0	0	0	0	43.87
Chi-square value = 154.854, df = 10, p-value = 0.000**(Highly significant)						

Inference-These findings suggested that Moesin expression in normal oral mucosal epithelium is primarily localized to the basal proliferative layers and plays an important role in maintaining epithelial structural integrity and cell adhesion.

Table 2: Expression patterns of Moesin among histopathological grades of OSCC

Grades of OSCC	M (%)	M+C (%)	C (%)	C+N (%)	N (%)	No Expression (%)
Well differentiated	32.18	38.66	29.96	0	0	0
Moderately differentiated	7.7	32.74	59.56	0	0	0
Poorly differentiated	0.92	10.9	88.18	0	0	0
Chi-square value = 83.833, df = 10, p-value = 0.000**(Highly significant)						

Inference-These findings indicated that translocation of Moesin from the cell membrane to the cytoplasm increases with loss of tumor differentiation and may reflect enhanced tumor invasiveness, cytoskeletal reorganization, and metastatic potential.

Table 3: Comparison of expression patterns of Moesin in well differentiated OSCC with the normal oral mucosal epithelium.

GROUPS	M (%)	M + C (%)	C (%)
Normal oral mucosal epithelium	56.13	0.0	0.0
Well differentiated OSCC	32.18	38.66	29.96
Chi-Square value = 28.51, p<0.0001			

Inference –These findings indicate early alteration of Moesin distribution during malignant transformation, with slight reduction in membranous expression and significant rise in combined and cytoplasmic expressions.

Table 4: Comparison of expression patterns of Moesin in moderately differentiated OSCC with the normal oral mucosal epithelium

GROUPS	M (%)	M + C (%)	C (%)
Normal oral mucosal epithelium	56.13	0.0	0.0
Moderately differentiated OSCC	7.7	32.74	59.56
Chi-Square value = 41.26, p<0.0001			

Inference –This finding indicates a marked shift of membranous expression to cytoplasmic expression in moderately differentiated OSCC, associated with increased dedifferentiation of tumor.

Table 5: Comparison of expression patterns of Moesin in poorly differentiated OSCC with the normal mucosal epithelium

GROUPS	M (%)	M + C (%)	C (%)
Normal Oral mucosal Epithelum	56.13	0.0	0.0
Poorly differentiated OSCC	0.92	10.9	88.18
Chi-Square value = 48.93, p<0.0001			

Inference –This suggests profound alteration in Moesin expression and extreme cytoplasmic expression, localization, with near complete loss of membrane correlating with EMT, aggressive behavior and metastasis.

Table 6: Comparison of expression patterns of Moesin in all grades of OSCC with the normal mucosal epithelium

Group	M (%)	M+C (%)	C (%)
Normal oral mucosal epithelum	56.13	0	0
Well differentiated OSCC	32.18	38.66	29.96
Moderately differentiated OSCC	7.7	32.74	59.56
Poorly differentiated OSCC	0.92	10.9	88.18
Chi-square value = 246.785, df = 6, p-value = 0.000**(Highly significant)			

Inference-These findings suggest that cytoplasmic translocation of Moesin may represent an important event during malignant transformation and tumor progression in oral squamous cell carcinoma.

Figures

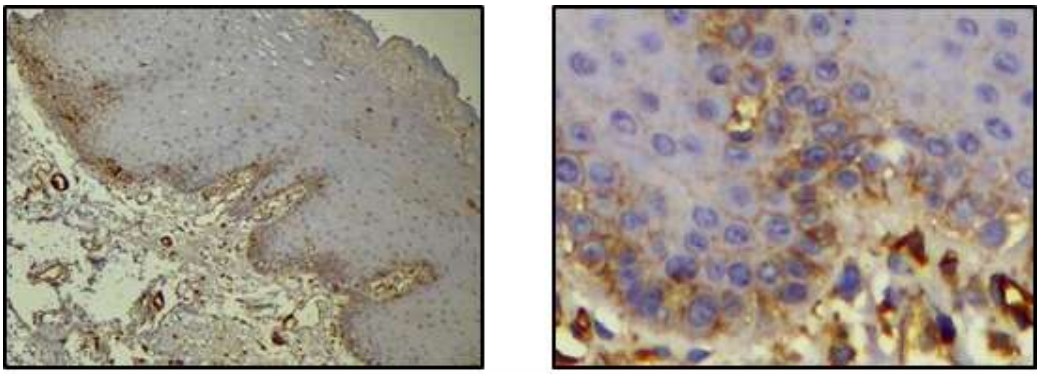

Figure 1a,b - IHC Staining of epithelium of normal oral mucosa with Moesin

a. Expression of Moesin restricted to cells of basal, parabasal and few suprabasal layers (10X magnification)

b. Cells showing predominant membranous expression with weak staining intensity (40X magnification)

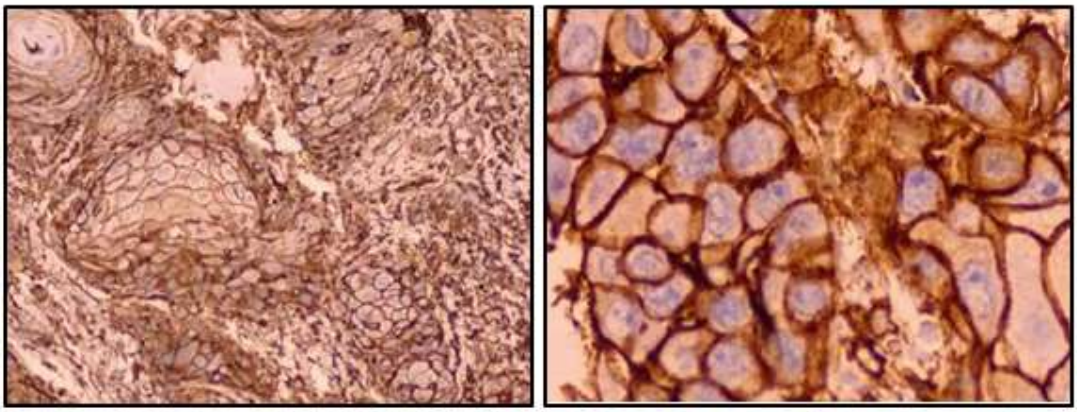

Figure 2 a,b - IHC staining of Well Differentiated Squamous Cell Carcinoma with Moesin

a. Malignant cells showing predominant membranous expression of Moesin in keratin pearl areas (10X magnification)

b. Staining intensity was moderate (40X magnification)

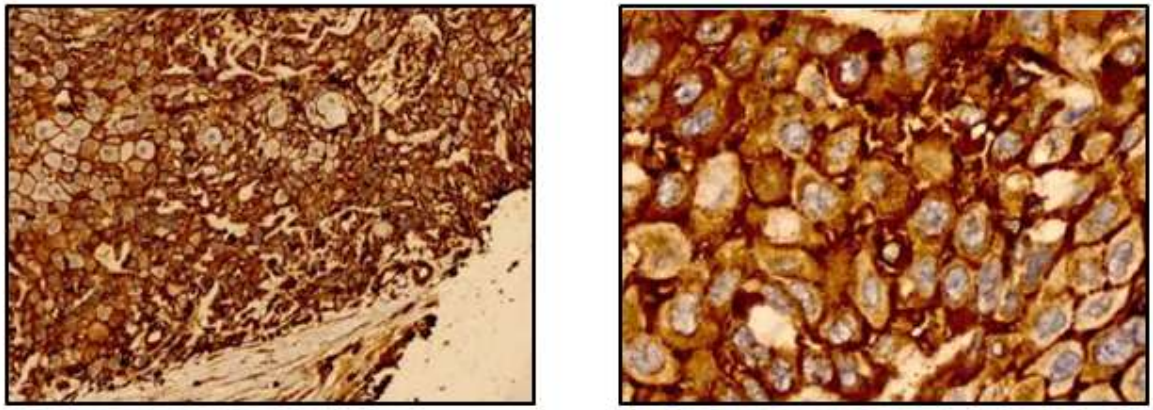

Figure 3 a,b - IHC Staining of Moderately Differentiated Squamous Cell Carcinoma with Moesin

a. Malignant cells showing predominant combined expression of Moesin (10X magnification)

b. Staining intensity was very strong (40X magnification)

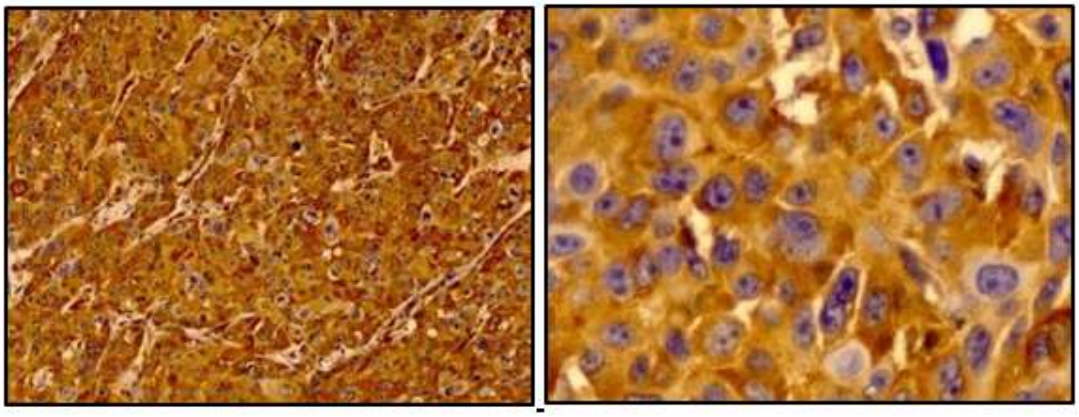

Figure 4 a,b - Moesin IHC Staining of Poorly Differentiated Squamous Cell Carcinoma

a. Malignant cells showing predominant cytoplasmic expression of Moesin (10X magnification)

b. Staining intensity was strong (40X magnification)

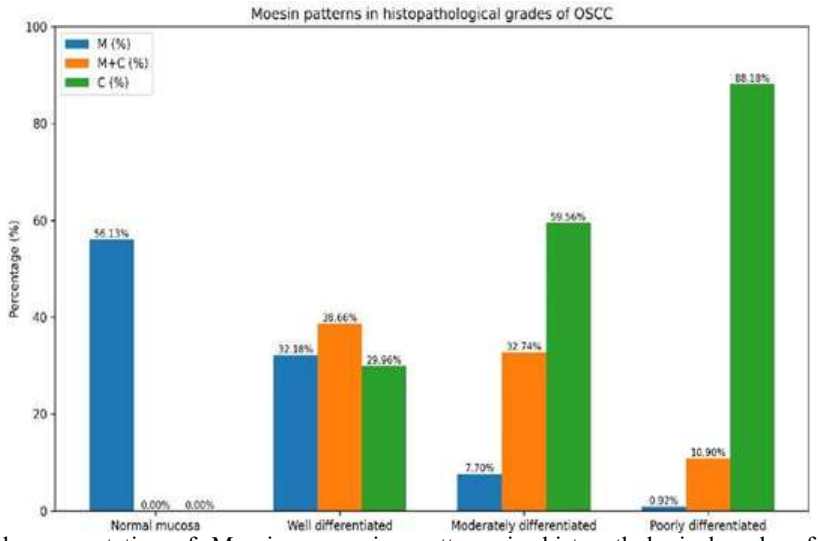

Figure 5: Graphical representation of Moesin expression patterns in histopathological grades of OSCC with normal mucosal epithelium

DISCUSSION

The study observed statistically significant distinct variations of Moesin expression patterns in the epithelium of normal oral mucosa between the basal and parabasal layers and the suprabasal layers (Table 1,Figure 1a,b). The basal and parabasal layers demonstrated complete membranous expression of Moesin, indicating normal localization of Moesin in the proliferative compartment of the oral epithelium. No cytoplasmic, nuclear, or combined staining patterns were observed in these layers. In contrast, the suprabasal layers demonstrated minimal membranous expression with absence of cytoplasmic and nuclear expression, while the majority of the cells showed no expression. These findings suggested that Moesin localization in basal & parabasal proliferative layers of normal oral mucosal epithelium, associate with important role of Moesin in maintaining epithelial structural integrity, cell adhesion, actin cytoskeleton remodelling and cell migration to suprabasal layers. Whereas, the absence of Moesin expression in suprabasal layers may suggest shifting from actin based cortical network to keratin intermediate filament network, with decreased Moesin requirement as epithelial cells migrate upward. This study results coincide with that of the studies conducted by Kobayashi H et al., 2003 [18] and Belbin TJ et al., 2005 [19] who concluded predominant membranous expression of Moesin restricted to the basal and parabasal layers of normal oral mucosa, with no expression in suprabasal layers.

The study results showed a statistically highly significant association between Moesin expression patterns and histopathological grades of OSCC ($p < 0.05$) (Table 2). Majority of the invading malignant epithelial cells in Well differentiated OSCC exhibited combined membranous & cytoplasmic expression. Moderately differentiated OSCC demonstrated a marked reduction in membranous expression with a substantial increase in cytoplasmic expression. Poorly differentiated OSCC showed predominant cytoplasmic expression with minimal combined expression and negligible membranous expression. No nuclear expression was observed in any of the OSCC groups. This study results coincided with the studies done by Kobayashi H et al., 2003 [18], Schelcht NF et al., 2012 [13], Jubair KK et al., 2016 [20], Assao A et al., 2018 [21] and in contrast to studies done by Kobayashi H et al., 2004 [16] and Bommanavar S et al., 2023 [14] where there was slight reduction in cytoplasmic expression of Moesin in higher grades of OSCCs. These findings indicated that translocation of Moesin from the cell membrane to the cytoplasm increases with loss of tumor differentiation and may reflect enhanced tumor invasiveness, cytoskeletal reorganization, and metastatic potential demonstrated progressive alterations in cellular localization with worsening tumor differentiation. The observed increase in strong & very strong staining intensities with decreasing cellular differentiation and intense Moesin expression in higher-grade OSCCs suggested that Moesin overexpression is associated with aggressive tumor behavior and may serve as a useful prognostic biomarker for assessing disease progression and metastatic potential in oral squamous cell carcinoma. This study results were consistent with Assao A et al., 2018 [21] and Barros FBA et al., 2018 [22], showing weak staining expression in more differentiated cells and keratin pearl areas. Their findings concluded that increased Moesin expression is associated with tumor progression, increased cellular motility, and aggressive biological behavior in oral squamous cell carcinoma.

The study noticed a statistically highly significant association between expression patterns and progression of Moesin from normal mucosal epithelium to well differentiated OSCC ($p < 0.05$) (Table 3). Slight reduction in membranous expression with concomitant increase in combined and cytoplasmic expressions suggested early

stages of Moesin translocation from membrane to cytoplasm in well differentiated OSCC [Figure 2a,b] compared with that of normal mucosa where membranous expression in basal layers and no expression in superficial layers observed. This study results coincide with the studies done by Kobayashi H et al., 2003 [18], Schelcht NF et al., 2012 [13], Jubair KK et al., 2016 [20], Assao A et al., 2018 [21] who concluded that Moesin expression demonstrates reduction in membranous expression and slight increase in combined and cytoplasmic expressions in the initial stages of OSCCs.

The study showed a statistically highly significant association between expression patterns of Moesin in normal mucosal epithelium to moderately differentiated OSCC ($p < 0.05$) (Table 4). These findings suggested a marked shift of Moesin from membrane to cytoplasm in moderately differentiated OSCC [Figure 3a,b] ccompared with that of normal oral mucosal epithelium. The drastic reduction in membranous expression together with the predominance of cytoplasmic staining suggested a more aggressive biological phenotype compared to normal oral mucosal epithelium. These observations supported the concept that cytoplasmic translocation of Moesin is associated with increasing histological dedifferentiation and may contribute to enhanced cellular motility, invasion, and metastatic potential. This study results coincide with the studies done by Kobayashi H et al., 2003 [18], Schelcht NF et al., 2012 [13], Jubair KK et al., 2016 [20], Assao A et al., 2018 [21] who concluded that stages of OSCC in between lower and higher grades show drastic decrease in membranous expression and increased cytoplasmic expression of Moesin.

There was a statistically highly significant association between expression patterns of Moesin in normal mucosal epithelium to poorly differentiated OSCC ($p< 0.05$) in this study (Table 5). The findings demonstrate that poorly differentiated OSCC is characterized by an almost complete loss of membranous Moesin expression and a striking predominance of cytoplasmic localization[Figure 4a,b] . The predominance of cytoplasmic Moesin expression in poorly differentiated OSCC likely reflects enhanced activation of signalling pathways involved in epithelial–mesenchymal transition (EMT), tumour cell motility, invasion, and metastatic dissemination. This study results were in accordance with the studies done by Kobayashi H et al., 2003 [18], Schelcht NF et al., 2012 [13], Jubair KK et al., 2016 [20], Assao A et al., 2018 [21] who concluded predominant cytoplasmic expression in higher grades of OSCC, with almost negligible membranous expression.

The results observed a statistically highly significant association between expression patterns and progression from normal mucosal epithelium to OSCC ($p < 0.05$) (Table 6) (Figure 5). Normal oral mucosal epithelium predominantly exhibited membranous expression with complete absence of cytoplasmic expression, indicating normal localization of Moesin within healthy epithelial cells. In contrast, OSCC groups demonstrated progressive reduction in membranous expression and increasing cytoplasmic localization with worsening tumor differentiation. Well differentiated OSCC showed mixed membranous and cytoplasmic expression, whereas moderately differentiated and poorly differentiated OSCC predominantly demonstrated cytoplasmic expression. Poorly differentiated OSCC exhibited the highest cytoplasmic expression with almost complete loss of membranous staining. This study results were consistent with Kobayashi H et al., 2003 [18], Kobayashi H et al., 2004 [16], Belbin TJ et al., 2005 [19], Schelcht NF et al., 2012 [13], Jubair KK et al., 2016 [20], Assao A et al., 2018 [21], and Bommanavar S et al., 2023 [14]. These findings suggested that cytoplasmic translocation of Moesin may represent an important event during malignant transformation and tumor progression in oral squamous cell carcinoma.

LIMITATIONS

- Smaller sample size
- Minimal availability of monoclonal primary antibody of Moesin IHC biomarker in India
- Higher cost of the Moesin biomarker, comparing with other routinely used biomarkers
- Decreased staining intensity when the marker was subjected to multiple freeze-thaw cycles

CONCLUSION

The study results concluded that the shift of Moesin localization from membrane to predominant cytoplasmic expression with increasing grades of OSCCs, and moesin could play a vital role in malignant transformation through loss of cellular adhesion, epithelial mesenchymal transition, aggressive invasion, nodal metastasis and poor prognosis. A thorough knowledge and extensive research on Moesin with large sample sizes is necessary in the future, to confirm the potential role of Moesin as a standard prognostic biomarker and therapeutic usage in OSCCs.

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Conflicts of Interest -None

Ethical Clearence-IEC No.15/D001/IEC/GDC&H/2023-24 dated 08.04.2024

REFERENCES

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2024). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.who.int/today.
2. Sathiasekar AC, Mathew DG, Jaish Lal MS, Arul Prakash AA, Goma Kumar KU. Oral Field

Cancerization and Its Clinical Implications in the Management in Potentially Malignant Disorders. J Pharm Bioallied Sci. 2017 Nov;9(Suppl 1): S23-S25. doi: 10.4103/jpbs.JPBS_109_17. PMID: 29284929; PMCID: PMC5731019.

3. Suri S, Boora GS, Kaur R, Chauhan A, Ghoshal S, Pal A. Recent advances in minimally invasive biomarkers of OSCC: from generalized to personalized approach. Front Oral Health. 2024 Aug 2;5:1426507. doi: 10.3389/froh.2024.1426507. PMID: 39157206; PMCID: PMC11327221.

4. Ravindran S, Ranganathan S, R K, J N, A S, Kannan SK, Prasad K D, Marri J, K R. The role of molecular biomarkers in the diagnosis, prognosis, and treatment stratification of oral squamous cell carcinoma: A comprehensive review. J Liq Biopsy. 2025 Jan 4;7:100285. doi: 10.1016/j.jlb.2025.100285. PMID: 40027232; PMCID: PMC11863969.

5. Brockmeyer P. Prognostic biomarkers in oral squamous cell carcinoma: current evidence and future directions. Front Oncol. 2025 Dec 5;15:1692294. doi: 10.3389/fonc.2025.1692294. PMID: 41426322; PMCID: PMC12714599.

6. Liu L, Zhong X, Zhong Y, Li L. Recent advances in biomarker detection of oral squamous cell carcinoma. Front Oncol. 2025 Jun 19;15:1597086. doi: 10.3389/fonc.2025.1597086. PMID: 40612351; PMCID: PMC12222140.

7. Bommanavar S, Kanetkar SR, Datkhile KD, More AL. Membrane-organizing extension spike protein and its role as an emerging biomarker in oral squamous cell carcinoma. J Oral Maxillofac Pathol. 2022 Jan-Mar;26(1):82-86. doi: 10.4103/jomfp.jomfp_182_21. Epub 2022 Mar 31. PMID: 35571321; PMCID: PMC9106235.

8. Hirata T, Nomachi A, Tohya K, Miyasaka M, Tsukita S, Watanabe T, Narumiya S. Moesin-deficient mice reveal a non-redundant role for moesin in lymphocyte homeostasis. Int Immunol. 2012 Nov;24(11):705-17. doi: 10.1093/intimm/dxs077. Epub 2012 Aug 8. PMID: 22875842.

9. Okazaki T, Saito D, Inden M, Kawaguchi K, Wakimoto S, Nakahari T, Asano S. Moesin is involved in microglial activation accompanying morphological changes and reorganization of the actin cytoskeleton. J Physiol Sci. 2020 Oct 31;70(1):52. doi: 10.1186/s12576-020-00779-6. PMID: 33129281; PMCID: PMC10717892.

10. Shaffer MH, Dupree RS, Zhu P, Saotome I, Schmidt RF, McClatchey AI, Freedman BD, Burkhardt JK. Ezrin and moesin function together to promote T cell activation. J Immunol. 2009 Jan 15;182(2):1021-32. doi: 10.4049/jimmunol.182.2.1021. PMID: 19124745; PMCID: PMC3491660.

11. Liu Q, Zhang A, Bai Y, Yang X, Liu X, Yang L, Ying Y, Luo X, Fang F, Liu C. The Immunodeficiency Profile of Lymphocytes in the Patient with Moesin Gene Mutation During Different Infection. J Clin Immunol. 2025 Aug 11;45(1):122. doi: 10.1007/s10875-025-01899-7. PMID: 40788322; PMCID: PMC12339625.

12. Wang CC, Liau JY, Lu YS, Chen JW, Yao YT, Lien HC. Differential expression of moesin in breast cancers and its implication in epithelial-mesenchymal transition. Histopathology. 2012 Jul;61(1):78-87. doi: 10.1111/j.1365-2559.2012.04204.x. Epub 2012 Mar 22. PMID: 22439598.

13. Schlecht NF, Brandwein-Gensler M, Smith RV, Kawachi N, Broughel D, Lin J, Keller CE, Reynolds PA, Gunn-Moore FJ, Harris T, Childs G, Belbin TJ, Prystowsky MB. Cytoplasmic ezrin and moesin correlate with poor survival in head and neck squamous cell carcinoma. Head Neck Pathol. 2012 Jun;6(2):232- 43. doi: 10.1007/s12105-011-0328-1. Epub 2012 Jan 7. PMID: 22228071; PMCID: PMC3370015.

14. Bommanavar S, Kanetkar SR, Datkhile KD. Comparative Study of Immunohistochemical Expression of Moesin and FLOT 1 in OSCC and Their Correlation with Histopathological Prognostic Factors. J Contemp Dent Pract. 2023 Mar 1;24(3):195-201. doi: 10.5005/jp-journals-10024-3483. PMID: 37272132.

15. Beckmann A, Ramirez P, Gamez M, Gonzalez E, De Mange J, Bieniek KF, Ray WJ, Frost B. Moesin is an effector of tau-induced actin overstabilization, cell cycle activation, and neurotoxicity in Alzheimer's disease. iScience. 2023 Feb 8;26(3):106152. doi: 10.1016/j.isci.2023.106152. PMID: 36879821; PMCID: PMC9984563.

16. Kobayashi, H., Sagara, J., Kurita, H., Morifuji, M., Ohishi, M., Kurashina, K. and Taniguchi, S. (2004). Clinical significance of cellular distribution of moesin in patients with oral squamous cell carcinoma. Clin. Cancer Res. 10, 572-580.

17. Faustino SE, Oliveira DT, Nonogaki S, Landman G, Carvalho AL, Kowalski LP. Expression of vascular endothelial growth factor-C does not predict occult lymph-node metastasis in early oral squamous cell carcinoma. Int J Oral Maxillofac Surg. 2008 Apr;37(4):372-8. doi: 10.1016/j.ijom.2007.11.021. Epub 2008 Mar 4. PMID: 18295452.

18. Kobayashi H, Sagara J, Masumoto J, Kurita H, Kurashina K, Taniguchi S. Shifts in cellular localization of moesin in normal oral epithelium, oral epithelial dysplasia, verrucous carcinoma and oral squamous cell carcinoma. J Oral Pathol Med. 2003 Jul;32(6):344-9. doi: 10.1034/j.1600-0714.2003.00111.x. PMID: 12787041.

19. Belbin TJ, Singh B, Smith RV, Socci ND, Wreesmann VB, Sanchez-Carbayo M, Masterson J, Patel S, Cordon-Cardo C, Prystowsky MB, Childs G. Molecular profiling of tumor progression in head and neck cancer. Arch Otolaryngol Head Neck Surg. 2005 Jan;131(1):10-8. doi: 10.1001/archotol.131.1.10. PMID: 15655179.

20. Jubair KK, Younis WH, Abdulla BH. A Comparative Study of Immunohistochemical Expression of Moesin, Cytokeratin 14 andMMP7 in Oral Squamous Cell Carcinoma and Oral Verrucous Carcinoma. J Bagh Coll Dent [Internet]. 2016 Jun. 15 [cited 2025 Nov. 13];28(2):52-7. 27.

21. Assao A, Yoshino PM, Medeiros MCM, Carvalho AL, Soares FA, Kowalski LP, Oliveira DT. Moesin Involvement in Oral Carcinogenesis of the Lower Lip. Anticancer Res. 2018 May;38(5):2755-2760. doi: 10.21873/anticanres.12518. PMID: 29715096.

22. Barros FBA, Assao A, Garcia NG, Nonogaki S, Carvalho AL, Soares FA, Kowalski LP, and Oliveira DT: Moesin expression by tumor cells is an unfavorable prognostic biomarker for oral cancer. BMC cancer 18: 53, 2018. 2