Original Article

Evaluation of Platelet Indices as Potential Hematological Biomarkers in Oral Squamous Cell Carcinoma: A Cross-Sectional Study

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Abstract

Background: Oral squamous cell carcinoma (OSCC) constitutes many oral malignancies and remains a major public health burden, particularly in India. Emerging evidence highlights the role of the tumor microenvironment in cancer progression, with platelets contributing significantly to tumor growth, angiogenesis, and metastasis. Platelet indices derived from routine hematological investigations have attracted attention as inexpensive, accessible biomarkers in malignancies. The aim is to evaluate alterations in platelet indices among patients with oral squamous cell carcinoma and to assess their potential utility as diagnostic and prognostic biomarkers. **Material and Methods:** A prospective cross-sectional study was conducted at a tertiary care hospital between January 2022 and April 2024. The study included 50 participants: 25 patients with histopathologically confirmed well-differentiated (Grade I) OSCC and 25 age- and sex-matched healthy controls. Platelet parameters—platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet large cell coefficient (P-LCC), and platelet large cell ratio (P-LCR)—were analyzed using automated hematology analyzers. Statistical comparison between groups was performed using independent t-tests, with $p < 0.05$ considered significant. **Results:** OSCC patients demonstrated a statistically significant reduction in platelet count compared to controls ($p < 0.001$). MPV was marginally elevated, while P-LCC and PCT showed a decreasing trend in OSCC cases; however, these differences were not statistically significant. No significant variation was observed in PDW and P-LCR between the groups. **Conclusion:** Platelet count appears to be a promising hematological biomarker in OSCC. Although other platelet indices showed suggestive trends, larger longitudinal studies are required to validate their diagnostic and prognostic relevance in oral squamous cell carcinoma.

Keywords: Oral Squamous Cell Carcinoma, Platelet Indices, Mean Platelet Volume, Hematological Biomarkers, Tumor Microenvironment.

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Introduction

Oral squamous cell carcinoma (OSCC) represents one of the most prevalent and clinically significant forms of malignancy within the head and neck region. Globally, oral cancers account for approximately 2–4 per 100,000 population annually, and they contribute substantially to cancer-related morbidity and mortality, particularly in developing regions where risk factors are prevalent. In India, OSCC ranks among the most common cancers, constituting about 10% of all cancer cases and demonstrating one of the highest age-standardized incidence rates worldwide. This elevated burden is driven predominantly by tobacco use (both smoked and smokeless forms), betel quid chewing, alcohol consumption, and poor oral hygiene, which collectively amplify carcinogenic exposure in the oral mucosa. Despite advancements in surgical techniques, radiotherapy, and systemic therapies, the 5-year survival rate for OSCC remains suboptimal due to late-stage presentation and high rates of recurrence and metastasis. Early detection and effective prognostic stratification are therefore critical to improving patient outcomes.[1,2]

The tumor microenvironment plays a central role in the initiation, progression, and dissemination of OSCC. Beyond the malignant epithelial cells, this complex milieu includes stromal fibroblasts, immune cells, cytokines, and circulating hematopoietic elements that interact dynamically with tumor cells. Among these, platelets have emerged as active participants in cancer biology. Once viewed solely as mediators of hemostasis, platelets are now recognized for their involvement in tumor growth, angiogenesis, immune modulation, and metastatic spread through direct and indirect interactions with cancer cells. Mechanistically, platelets secrete growth factors such as vascular endothelial growth factor and platelet-derived growth factor, which promote angiogenesis and tumor proliferation. Platelet–tumor interactions can also facilitate immune evasion and enhance tumor cell survival in circulation, thereby aiding metastatic colonization.[3,4]

Given their multifaceted contributions to cancer progression,

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platelets and platelet-related parameters have garnered interest as accessible biomarkers in oncology. Routine complete blood counts provide quantitative measures of platelet biology, including platelet count and indices such as mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet large cell ratio (P-LCR). These indices reflect platelet size, variability, and total circulating mass and have been investigated as surrogate markers of platelet activation and systemic inflammation in various malignancies. Elevated MPV and altered PDW, for example, have been associated with adverse clinicopathological features in cancers such as gastric, colorectal, and ovarian carcinomas, suggesting their potential value in cancer diagnosis and prognostication.[5–7]

Despite growing evidence for platelet indices in systemic malignancies, data on their utility in OSCC remain inconsistent. Some studies report significant alterations in platelet count and indices in OSCC patients compared to healthy controls, while others find limited or variable associations with tumor characteristics and outcomes. The prognostic implications of platelet indices in OSCC, independent of established clinical staging systems, are yet to be firmly established. The investigation of these easily obtainable, cost-effective hematological parameters, conducted both manually and with advanced hematological analyzers, is particularly relevant in resource-limited settings, where advanced molecular diagnostics may not be readily available. Therefore, this study aims to evaluate platelet count and platelet indices in patients with well-differentiated OSCC compared with healthy controls, to determine their potential role as diagnostic and prognostic biomarkers.[8–10]

Materials and Methods

Study Design and Setting: This prospective cross-sectional study was conducted in the Departments of Pathology at a tertiary care hospital over 28 months, from January 2022 to April 2024. The Institutional Ethical Committee approved it under IHEC number MMCRI/IEC/2023/015. The study was designed to evaluate alterations in platelet indices in patients with oral squamous cell carcinoma (OSCC) and to compare them with those of healthy individuals.

Study Population: A total of 50 participants were enrolled in the study and divided into two groups. The study group consisted of 25 patients with histopathologically confirmed well-differentiated (Grade I) oral squamous cell carcinoma. The control group included 25 apparently healthy, age- and sex-matched individuals with no history of malignancy or systemic illness. Participants' ages ranged from 40 to 65 years. All OSCC cases were newly diagnosed and evaluated before initiation of any form of treatment, including surgery, chemotherapy, or radiotherapy, to avoid treatment-related alterations in hematological parameters.

Inclusion and Exclusion Criteria

Patients diagnosed with well-differentiated (Grade I) OSCC were included in the study. Individuals with a history of hematological disorders, inflammatory or autoimmune diseases, chronic systemic illnesses, infections, or those on medications affecting platelet function were excluded. Pregnant individuals and patients with other malignancies were also excluded. Red blood cell and white blood cell parameters were intentionally excluded to focus specifically on platelet-related indices.

Sample Collection and Laboratory Analysis: Venous blood samples were collected from all participants with their informed consent as part of a routine follow-up protocol, under aseptic precautions, using ethylenediaminetetraacetic acid (EDTA)-anticoagulated tubes. The samples were analyzed using an automated hematology analyzer within the recommended time frame to avoid pre-analytical variations. The platelet parameters evaluated included platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet large cell coefficient (P-LCC), and platelet large cell ratio (P-LCR), with other hematological parameters requested. These indices reflect platelet size, distribution, total platelet mass, and proportion of large platelets.

Statistical Analysis: Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS). Descriptive statistics were used to summarize demographic variables and platelet parameters. Results were expressed as mean ± standard deviation. The independent Student's t-test was applied to compare platelet indices between OSCC patients and control subjects. A p-value of less than 0.05 was considered statistically significant.

Results

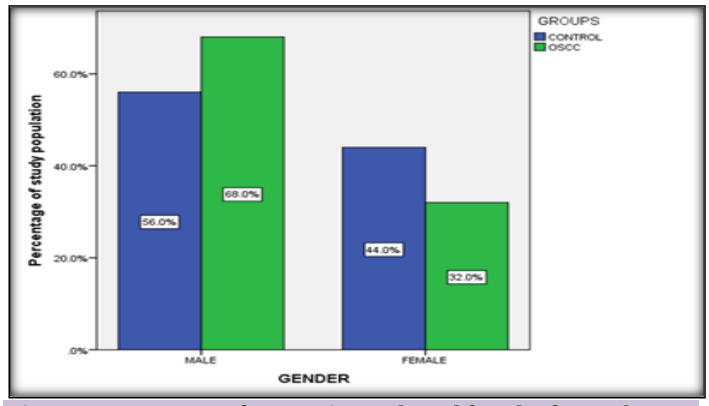

Figure 1: Percentage of presenting male and females for study.

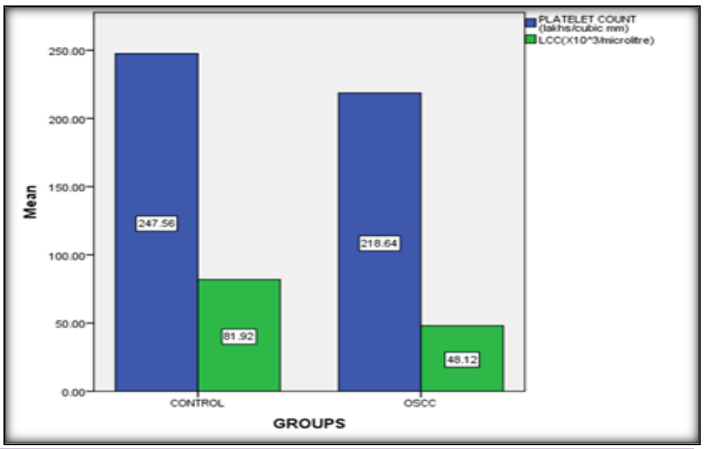

Figure 2: Platelet count and LCC comparison between control and OSCC subjects.

Table 1: Statistical analysis of platelet parameters among the groups

Group Statistics						
	Groups	**N**	**Mean**	**Std. Deviation**	**Compared to control, OSCC group has**	**P value (<0.05 is set as statistical significance)**
MPV (fl)	CONTROL	25	9.3480	.92562	Slightly high MPV	.081
	OSCC	25	9.7020	.67297		
PLATELET COUNT (lakhs/cubic mm)	CONTROL	25	247.5600	31.15563	Reduced platelet count	.000
	OSCC	25	218.6400	71.89163		
P-LCR (%)	CONTROL	25	24.1680	6.07225	Not much difference in PLCR	.218
	OSCC	25	23.6848	6.82702		
LCC(X10^3/microlitre)	CONTROL	25	81.9200	115.64382	Reduced LCC	.086
	OSCC	25	48.1200	9.88399		
PDW (%)	CONTROL	25	15.4120	2.94128	Not much difference in PDW	.116
	OSCC	25	14.8520	.34032		
PCT (%)	CONTROL	25	25.5720	11.98369	Slightly reduced PCT	.645
	OSCC	25	22.5424	7.35083		

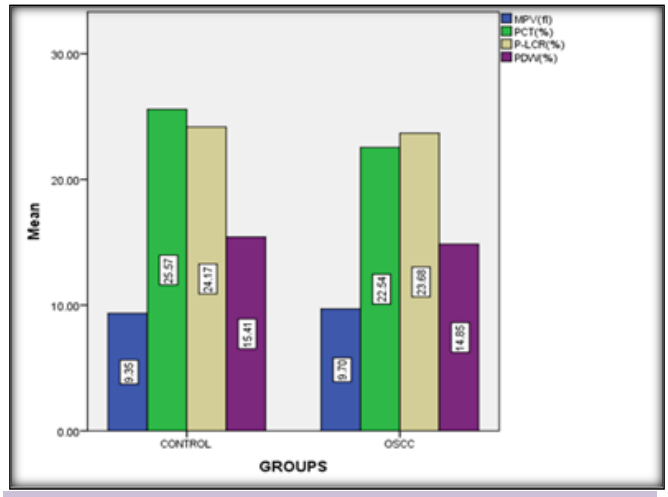

Figure 3: MPV, PCT, P-LCR and PDW comparison between control and OSCC subjects

Demographic Characteristics of the Study Population: The present study included 50 participants: 25 patients with well-differentiated (Grade I) oral squamous cell carcinoma (OSCC) and 25 healthy control subjects. Participants ranged in age from 40 to 65 years, with an overall mean age of 51.84 ± 7.26 years. Both the study and control groups were comparable with respect to age distribution, thereby minimizing age-related confounding effects on platelet parameters.

The gender distribution showed a male predominance, with 31 males (62%) and 19 females (38%) included in the study [Figure 1]. Among the OSCC group, males constituted a higher proportion compared to females, consistent with the known epidemiological pattern of oral cancer in the Indian population. The control group also demonstrated a similar gender distribution, ensuring adequate matching between the two groups. This demographic comparability enabled a reliable assessment of platelet indices without significant bias from age or sex.

Comparison of Platelet Parameters Between OSCC and Control Groups: The primary objective of the study was to evaluate and compare various platelet indices between patients with OSCC and healthy controls. The parameters analyzed included platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet large cell coefficient (P-LCC), and platelet large cell ratio (P-LCR). All values were expressed as mean ± standard deviation, and statistical significance was assessed using the independent Student's t-test.

Platelet Count: A statistically significant reduction in platelet count was observed in patients with OSCC compared to the control group. The mean platelet count in the OSCC group was 218.64 ± 71.89 lakhs/cubic mm, whereas the control group exhibited a higher mean platelet count of 247.56 ± 31.16 lakhs/cubic mm [Figure 2]. This difference was highly significant ($p < 0.001$). The marked reduction in platelet count among OSCC patients suggests altered platelet production or increased platelet consumption in the tumor microenvironment. This finding represents the most statistically significant hematological alteration observed in the present study and underscores the potential relevance of platelet count as a biomarker in oral squamous cell carcinoma.

Mean Platelet Volume (MPV): Mean platelet volume, an indicator of platelet size and activation status, was marginally higher in OSCC patients than in controls. The OSCC group demonstrated a mean MPV of 9.70 ± 0.67 fL, while the control group showed a mean MPV of 9.35 ± 0.93 fL [Figure 3]. Although the MPV values were higher in OSCC patients, the difference did not reach statistical significance ($p = 0.081$). Despite the lack of statistical significance, the observed trend toward increased MPV may indicate enhanced platelet activation in OSCC patients, warranting further investigation in larger studies.

Platelet Distribution Width (PDW): Platelet distribution width reflects platelet size variability and is an indirect marker of platelet activation and heterogeneity. In the present study, the mean PDW in the OSCC group was 14.85 ± 0.34%, compared to 15.41 ± 2.94% in the control group [Figure 3]. The difference between the two groups was not statistically significant (p-value = 0.116). The relatively comparable PDW values suggest that platelet size variability may not be markedly altered in well-differentiated OSCC or that changes, if present, are subtle and not detectable in a small cross-sectional cohort.

Platelet Large Cell Ratio (P-LCR): The platelet large cell ratio represents the percentage of circulating platelets with a volume greater than 12 fL and is associated with platelet reactivity. The mean P-LCR in the OSCC group was 23.68 ± 6.83%, whereas the control group showed a slightly higher mean value of 24.17 ± 6.07% [Figure 3]. This difference was not statistically

significant (p-value = 0.218). The absence of a significant difference in P-LCR indicates that the proportion of large platelets remains relatively stable in OSCC patients when compared to healthy individuals.

Platelet Large Cell Coefficient (P-LCC): The platelet large cell coefficient, which reflects the absolute number of large platelets, demonstrated a noticeable reduction in OSCC patients. The mean P-LCC value in the OSCC group was 48.12 ± 9.88 × 10^3/µL, compared to a substantially higher mean value of 81.92 ± 115.64 × 10^3/µL in the control group [Figure 2]. Although this reduction approached statistical significance, it did not meet the predefined threshold (p-value = 0.086). The reduced P-LCC in OSCC patients may suggest altered platelet morphology or consumption of larger, more reactive platelets in the tumor milieu.

Plateletcrit (PCT): Plateletcrit represents the total circulating platelet mass and is influenced by both platelet count and size. In the present study, the mean PCT in OSCC patients was 22.54 ± 7.35%, while the control group exhibited a higher mean PCT of 25.57 ± 11.98% [Figure 3]. This reduction in PCT among OSCC patients was not statistically significant (p-value = 0.645). The observed decrease in PCT likely reflects the lower platelet count observed in OSCC patients, although the difference was insufficient to reach statistical significance.

Overall, the comparative analysis of platelet indices [Table 1] revealed a significant reduction in platelet count among OSCC patients, which emerged as the most consistent and statistically robust finding in this study. Other platelet indices, including MPV, P-LCC, and PCT, showed trends toward alteration in OSCC patients but did not achieve statistical significance. PDW and P-LCR remained largely unchanged between the two groups. These findings suggest that while platelet count may serve as a potential hematological marker in OSCC, other platelet indices may require larger sample sizes and longitudinal evaluation to establish their diagnostic or prognostic value.

Discussion

In the present study, platelet count was significantly lower in OSCC patients than in healthy controls, suggesting altered platelet dynamics in malignancy. Platelets play a complex role in cancer biology by interacting with tumor cells, facilitating tumor growth, angiogenesis, and immune evasion. Prior research has highlighted alterations in platelet count and morphology in OSCC, suggesting that platelet parameters are influenced by tumor-associated inflammatory responses and systemic changes in hemostasis.[1,11] While thrombocytosis (elevated platelet count) has been associated with advanced disease and poor prognosis in several cancers, including some OSCC cohorts, platelet count alterations can vary depending on tumor stage, host factors, and inflammatory burden.[12,13] Our findings of reduced platelet count in well-differentiated oral squamous cell carcinoma may reflect increased platelet consumption within the tumor microenvironment through platelet–tumor interactions and microthrombus formation. This emphasizes its potential utility as a cost-effective marker that complements other clinicopathological parameters in OSCC.

MPV, a measure of the average size of circulating platelets, was marginally higher in OSCC patients, but this difference did not reach statistical significance in our cohort. MPV is considered a surrogate marker of platelet activation, with larger platelets being more reactive and metabolically active.[14,15] In cancer, activated platelets contribute to tumor progression through the release of growth factors and cytokines.[16] Several studies have demonstrated associations between elevated MPV and cancer presence or progression, suggesting that MPV may reflect systemic inflammation and tumor-platelet cross-talk. In OSCC, preoperative MPV has been proposed as a prognostic factor for overall survival, with some evidence indicating its relationship with advanced disease.[17] The lack of statistical significance in our study may be due to the sample size and the inclusion of only well-differentiated OSCC cases. Nevertheless, the observed trend aligns with broader oncologic literature suggesting MPV's potential value as a biomarker of platelet activation in cancer.

PDW reflects platelet size variability, an indirect measure of platelet production and activation heterogeneity. In this study, PDW did not differ significantly between OSCC patients and controls. Consistent with our findings, some prior investigations have shown limited alterations in PDW in early-stage or well-differentiated cancers, indicating that PDW may be less sensitive than other indices in reflecting subtle changes in platelet dynamics.[18] However, PDW has been reported to vary with tumor stage and lymph node involvement in other cancers, suggesting that its utility may be context-dependent(19). The absence of significant PDW changes in our cohort suggests that platelet size heterogeneity is relatively preserved in early or less aggressive OSCC, limiting its value as a standalone biomarker in such clinical settings.

P-LCR measures the proportion of large, reactive platelets in circulation. In our cohort, P-LCR values did not differ significantly between OSCC patients and controls. This may indicate that the proportion of larger platelets remains stable in well-differentiated OSCC, or that consumption and production of large platelets balance out. Previous studies have shown variable results for P-LCR in cancer, with some reports observing increased values in malignancy due to enhanced platelet activation.[20] The lack of a significant difference in P-LCR in our study suggests that this index may be of limited diagnostic utility in isolation but could still contribute to composite platelet-based indices or ratios used in systemic inflammation assessments.

P-LCC represents the absolute count of large platelets, which are often functionally active and involved in thromboinflammatory processes. Although reduced in OSCC patients in our study, the difference approached but did not reach statistical significance. Larger platelets contain more granules and express higher levels of pro-tumorigenic factors, and their altered numbers may reflect tumor-induced consumption or changes in megakaryocyte dynamics. While limited data exist specifically on P-LCC in OSCC, trends similar to ours have been reported, suggesting that the profile of larger platelets may change in cancer, while necessitating larger studies for confirmation.[1]

PCT, reflecting the total platelet biomass, was lower in OSCC patients, consistent with decreased platelet count in this cohort. Prior research on oral cancers has shown mixed results for PCT, with some studies reporting decreased values in malignancy that

reflect overall platelet depletion or activation states.[18] Since PCT integrates both platelet size and count, its reduction supports the notion of altered platelet homeostasis in OSCC. However, like other platelet indices, PCT's independent clinical utility may be limited without corroboration from larger datasets and longitudinal follow-up studies.

The present findings highlight that among routinely measured platelet indices, platelet count appears to be the most consistent and statistically significant hematological alteration in OSCC. While other indices showed trends suggestive of altered platelet activation and morphology, they did not reach statistical significance, highlighting the need for larger studies to validate these associations. Integration of platelet parameters with inflammatory ratios, such as the platelet-to-lymphocyte ratio (PLR), which has demonstrated prognostic relevance in OSCC and other cancers, may enhance the clinical utility of hematological biomarkers.[21] Ultimately, platelet indices derived from routine blood tests represent accessible, low-cost tools that could complement standard diagnostic and prognostic frameworks in OSCC, particularly in resource-limited settings.

Despite valuable insights, the present study has certain limitations that should be considered while interpreting the findings. The relatively small sample size may have limited the statistical power to detect significant differences in some platelet indices. Inclusion of only well-differentiated (Grade I) oral squamous cell carcinoma cases limits the generalizability of the results to other histological grades and advanced disease stages. The cross-sectional design precludes assessment of causal relationships and prognostic implications. Additionally, clinicopathological parameters, inflammatory markers, and platelet-based ratios were not correlated with platelet indices, which may have provided deeper insight into their clinical significance. Future multicentric, longitudinal studies addressing these limitations are warranted to validate and extend the present observations.

Conclusion

This study demonstrates that platelet indices reflect altered hematological dynamics in oral squamous cell carcinoma, highlighting the interaction between tumor biology and systemic inflammation. Among the parameters evaluated, platelet count showed a statistically significant reduction in patients with well-differentiated OSCC, suggesting increased platelet consumption within the tumor microenvironment and supporting its potential as a simple, cost-effective biomarker. Other indices, including mean platelet volume, platelet large cell coefficient, and plateletcrit, showed suggestive trends but lacked statistical significance. In contrast, platelet distribution width and platelet large cell ratio remained largely unchanged. These findings indicate that platelet count may be more relevant for diagnosis than other indices. Larger, longitudinal studies are required to validate these observations and establish the prognostic utility of platelet indices in OSCC.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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