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Evaluation of platelet indices in oral squamous cell carcinoma

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Abstract

Context: Platelet indices are markers of inflammation which are being studied in various cancers; however, data for oral cancers are limited. **Aims:** We aimed to study the platelet indices such as platelet count, mean platelet volume (MPV), plateletcrit, and platelet distribution width (PDW) in oral squamous cell carcinoma (SCC) patients and to compare them with healthy controls. **Settings and Design:** Retrospective cross-sectional study. **Subjects and Methods:** The study included 107 patients with oral SCC and 68 controls who did not meet exclusion criteria. Platelet indices were estimated and compared with controls. The results were statistically evaluated. **Statistical Analysis Used:** Student's *t*-test (two-tailed, independent) was used for statistical analysis. The relationship between measured characteristics of continuous data was determined using Pearson's correlation coefficient. $P<0.05$ was considered statistically significant. **Results:** Platelet count was slightly increased in cases though not statistically significant ($P > 0.05$). MPV was significantly increased in cases than controls ($P < 0.05$). Plateletcrit and PDW were similar in both cases and controls. **Conclusions:** Further studies are needed to assess the utility of platelet indices in oral SCC.

Keywords: *Oral, platelet indices, squamous cell carcinoma*

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Introduction

Oral cancers are a major health problem in India and account for about 30% of all types of cancers. Around 90%–95% of oral cancers are squamous cell carcinomas (SCCs) which are known for early metastasis and high rates of locoregional recurrence.[1]

The interaction between tumor cells and platelets has been known for a long time. Platelet activation and thromboembolic events are known to frequently occur in cancer. Recent experimental and clinical data suggest that activation of platelets is a hallmark in the natural course of cancer, by promoting neoangiogenesis, degradation of the extracellular matrix, release of adhesion molecules, and growth factors, all of which are essential components for further tumor growth and metastatic spread.[2]

New hematology analyzers have enabled the evaluation of platelet indices such as mean platelet volume (MPV), plateletcrit, and platelet distribution width (PDW) that can be used clinically in addition to platelet count. MPV denotes the average size of platelets in bloodstream and reflects production rate and stimulation though the changes in platelet size are not observed microscopically. Larger platelets are more metabolically and enzymatically active than smaller platelets. PDW is calculated as the coefficient of variation in MPV and is an indicator of variation in platelet size, which can be a sign of active platelet release.

Platelet indices have been investigated and found to be altered in several clinical settings such as myocardial infarction, diabetes mellitus, and in preeclampsia states, thus indicating the activation of platelets in such conditions. The high reproducibility, low cost, and high applicability of these parameters make it suitable in terms of usability. In recent years, the number of studies suggesting that platelet and their indices can be used as inflammatory markers in cancer cases is increasing.

Platelet indices have been evaluated in lung cancer, head and neck cancer, and gastric and colon cancer and have shown an increase in platelet count and MPV.[3],[4],[5],[6] The role of platelet inhibitors in counteracting the effect of platelets and thus having a protective effect in cancer is also being studied.[7] The use of drugs with antiplatelet activity such as aspirin has been found to be associated with better prognosis and survival in head and neck cancers.[7] In this study, we aimed to determine the platelet indices such as platelet count, MPV, plaletetcrit, and PDW in oral

SCC patients and to compare it with age- and sex-matched controls.

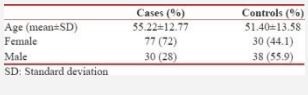
Subjects and Methods

The study included 107 cases of oral SCC diagnosed by biopsy and/or histopathological examination during July 2013 to December 2014. Preoperative blood parameters from these patients were retrieved, and platelet count, MPV, plateletcrit, and PDW were analyzed. Complete blood count from random age- and sex-matched controls was taken. Blood was collected in ethylenediaminetetraacetic acid (EDTA) vacutainers and samples were analyzed in Beckman Coulter Ac.T5 Diff autoanalyzer (Beckmann Coulter, USA). Platelet count, MPV, plateletcrit, and PDW from 68 controls were studied. Patients with hematologic disorders, cardiac disorders, autoimmune diseases, inflammatory or infective diseases, patients with other site cancers, hepatic and renal diseases, and taking drugs which affect the coagulation cascade were excluded from the study.

Within the cases and control, a statistical analysis of all parameters including age and gender was carried out. Categorical data were analyzed using Chi-square test/Fisher's exact test. The values of platelet count, MPV, plateletcrit, and PDW were evaluated for normal distribution using Kolmogorov–Smirnov test. Data are shown as mean ± standard deviation (SD) where applicable. Data were statistically analyzed using Statistical Package for the Social Sciences version 15.0 (SPSS 15.0, Strata 10.1, Med Calc9.0.1, Systat 12.0, and R environment version 2.11.1). Student's *t*-test (two-tailed, independent) was used for statistical analysis. The relationship between the measured characteristics of a continuous type was determined using Pearson's correlation coefficient. $P < 0.05$ was considered statistically significant.

Results

A total of 175 cases were included in the study with 107 cases of oral SCC and 68 controls. The age and sex characteristics of patient and controls are shown in [Table 1]. The platelet count in oral SCC cases was slightly increased when compared to controls (336.82 ± 100.66 and 314.25 ± 44.47). However, the difference was not statistically significant ($P > 0.05$). The MPV was increased in oral SCC cases (7.89 ± 0.92) than controls (7.61 ± 0.26) and was statistically significant. PDW was slightly higher in oral SCC (12.35 ± 2.97) than controls (11.67 ± 1.42) though the difference was not statistically significant. Plateletcrit was similar in both cases and controls (0.26 ± 0.07 and 0.25 ± 0.04). Comparison of platelet indices in cases and controls is shown in [Table 2].



	Cases (%)	Controls (%)
Age (mean±SD)	55.22±12.77	51.40±13.58
Female	77 (72)	30 (44.1)
Male	30 (28)	38 (55.9)

SD: Standard deviation

Table 1: Age and sex characteristics of patients and controls

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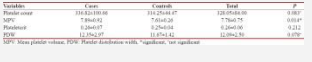

Table 2: Comparison of platelet indices in patients and controls

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There was a positive correlation between plateletcrit and platelet count (r = 0.897) and between PDW and MPV (r = 0.955) in cases of oral SCC, whereas there was a negative correlation between PDW and platelet count (r = −0.377) in cases of oral SCC. The comparison of other parameters did not show the existence of any correlation between plateletcrit and PDW.

Discussion

The relation between platelets and cancer progression suggests a possible role that extends beyond their hemostatic function. Platelets secrete cytokines and growth factors such as transforming growth factor-β, vascular endothelial growth factor (VEGF), matrix metalloproteinase-2, platelet factor-4, and platelet-derived growth factor which in turn induce hallmarks of cancer progression such as epithelial–mesenchymal transition, angiogenesis, cell migration, and/or proliferation and also facilitate the retention of tumor emboli in microcirculation.[8] Platelets also stimulate the release of pro-inflammatory cytokines (interleukin 1, 3, and 6) by cancer cells.[9] Thus, platelets are essential and have a multifunctional role in cancer development.

In the present study, platelet indices were evaluated in patients with oral SCC and compared with healthy controls. Platelet count was found to be slightly increased, whereas MPV was significantly increased in patients with oral SCC than controls. Although there are several studies suggesting that platelets increase in various organ cancers, there also some studies suggesting no change in platelet count in colon cancer, breast carcinoma, and gastric cancer.[6],[10],[11] This variation in platelet count in different cancers may be due to the underlying host inflammatory response. Although genetic factors are known to be the basic mechanism underlying cancer development, host inflammatory response may also play a role in carcinogenesis. A systemic inflammatory response which is identified by pro-inflammatory cytokines and acute phase reactants is seen with local tumor-associated inflammation. These pro-inflammatory cytokines lead to proliferation of megakaryocytes and platelets. Platelets in turn synthesize and release VEGF that is involved in tumor angiogenesis and further tumor inflammation.

Studies have shown that the values of MPV are also different in different types of cancer. Increased MPV has been observed in studies of head and neck cancer, gastric cancer, colon cancer, and epithelial ovarian cancer.[4],[5],[6],[12] However, Oncel *et al*. found lower MPV values in lung carcinoma when compared to controls.[3] No studies as such have shown the evaluation of MPV in oral SCC cases. Variability of MPV values in cancer may be due to different study methods used and effects of EDTA on the results.[13] Furthermore, since one of the factors is the time of analysis, the value of MPV may vary since this variable is not taken in retrospective studies. The recommended optimal measuring time of MPV is within 120 min after venipuncture.[14] Platelets exhibit a time-dependent swelling when blood samples are anticoagulated with EDTA, while this swelling does not occur in the presence of citrate. With impedance counting, the MPV increases over time as platelets swell in EDTA, with an increase

of 7.9% within 30 min having been reported and an overall increase of 13.4% over 24 h although the majority of this increase occurs within the first 6 h.

PDW is the SD of the logarithmic transformation of platelets. The increase of PDW shows that abnormal large and small platelets are in circulation. PDW is a more useful parameter compared to MPV in differentiating thrombocytopenia due to increased destruction from decreased production. Few studies have shown the evaluation of PDW and plateletcrit in cancer. In the present study, PDW was similar in both cases and controls. However, Oncel *et al*. and Karagoz *et al*. found an increase in PDW in lung carcinoma patients.[3],[15] In normal individuals, PDW is linearly related to MPV.[16] In the present study, there was a positive correlation between PDW and MPV in cases of oral cancer. However, other studies of cancer patients have shown that MPV and PDW are not found to be parallel with each other.[10],[17]

Plateletcrit is a measure of platelet mass and is calculated using platelet count and MPV. Plateletcrit in the present study was similar in both cases and controls. While Ozaksit *et al*. observed no difference in plateletcrit in ovarian cancer and controls, Ma *et al*. have determined that higher plateletcrit values are seen in epithelial ovarian cancer when compared to controls.[18],[19] Oncel *et al*. found lower plateletcrit values in lung carcinoma patients.[3] More studies of evaluation of plateletcrit in cancer are needed.

Limitations of the present study were that only cases with histological type of SCC in oral cavity were included in the study. There were only two cases of adenocarcinoma during the period which were excluded from the study. The platelet indices in our study were also not evaluated according to stage, grade, and metastasis status, due to loss of biopsy cases to follow-up. Literature reveals varied results of platelet indices when they are evaluated according to stage, histological type, and metastasis status in various types of cancer. While platelet count in breast cancer patients was decreased in metastasis, there was no change in MPV and PDW.[10] Oncel *et al*. observed an increase in platelet count in cases of lung cancer with metastasis though there was no difference observed in other platelet indices in relation to tumor stage, histological type, and metastasis status.[3] Karagoz *et al*. observed that platelet indices in lung cancer did not change depending on tumor stage and histological types.[15] Li *et al*. observed that there was no difference in MPV with metastasis and without metastasis in cases diagnosed with colon cancer.[6]

Platelets are thus involved in the pathogenesis of inflammation in cancer, in addition to their role in coagulation system. Our study revealed that MPV was increased in oral SCC cases. Further ongoing research in a larger population is needed in determining the utility of platelet indices in diagnosis, determination of recurrence, and follow-up treatment of oral cancer.

Conclusions

Platelet indices can be used as new markers of inflammation in cancer. These indices can be studied easily in the new hematology analyzers. MPV was significantly increased in oral cancer cases suggesting that platelet activation plays an important role in cancer development. Utility of platelet indices in diagnosis of oral cancer, determination of recurrence and in follow-up

treatment, needs to be evaluated by further studies conducted on a larger population.

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Conflicts of interest

There are no conflicts of interest.

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