Assessing for potential correlation between platelet count and varying grades of oral squamous cell carcinoma

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Abstract

Introduction: The histopathological grade of oral squamous cell carcinoma (OSCC) is considered as a vital indicator for predicting the prognosis including the potential for local and distant metastasis. Similar to the histopathological grading, tumor-related angiogenesis is also an essential indicator of metastasis as it provides a pathway for the passage of tumor cells to distant sites. Studies have shown platelets to promote angiogenesis, which, in turn, could increase the risk of metastasis. Based on the above premise, the present study investigates the association between platelet count and the various grades of OSCC. The hypothesis of the study is that platelet counts increase with increasing grades of tumor, thus could be a potential prognostic marker for OSCC.

Aim: The study aims to assess any potential correlation between platelet count and varying grades of OSCC.

Materials and Methods: Clinical data and hematological data were retrieved from 140 histopathologically diagnosed cases of OSCC. Data were tabulated and statistically analyzed to correlate its association with tumor differentiation.

Results: Comparisons were made based on gender, tumor differentiation, and platelet counts. The correlation of platelet count with different grades of OSCC was statistically insignificant.

Conclusion: The lack of correlation between platelet count and OSCC grade could be due to the uneven distribution of the cases, especially due to the underrepresentation of poorly differentiated OSCC. Thus, further large-scale multicenter prospective studies with equal distribution of OSCC grades are needed to determine the interrelationship between platelets and tumor grade.

Keywords
Grading, Metastasis, Oral squamous cell carcinoma, Platelets, Prognosis

Introduction

Oral squamous cell carcinoma (OSCC) is one of the most common cancers worldwide with tobacco, alcohol consumption, constituting the prime etiologic agents.¹ Despite remarkable advancement in therapeutics, metastasis remains to be the Ultimate Foe for the survival of cancer patients.² The most common predisposing factor for metastasis is tumor-associated angiogenesis. These newly developed blood vessels around the tumor provide a pathway for the transport of cancer cells to distant sites.³ Studies have shown platelets to promote angiogenesis. The substances stored in platelet granules are responsible for mediating angiogenesis.³ Thus, an increase in the number of platelets could potentially increase the risk of metastasis. Based on this premise, an increased platelet count could well be a potential indicator of poor prognosis.⁴ In addition to platelets, the grade of OSCC is considered to be a prime prognostic indicator with several studies depicting a direct correlation between grade and tumor progression.⁵ Thus, the present study aims to investigate the potential correlation between the platelet count and the varying grades of OSCC. The hypothesis is that the platelet count would increase with the OSCC grade, thus could serve as a potential prognostic indicator.

Materials and Methods

Clinical and hematological data of histopathologically diagnosed cases of OSCC of the past 7 years were retrieved from the
hospital records of Sinhgad Dental College and Hospital and Smt. Kashibai Navale Medical College and Hospital. The data were presented in the tabular form with respect to the grades of a tumor and were statistically analyzed to correlate its association with tumor differentiation.

**Inclusion criteria**
Primary OSCC was included in the study.

**Exclusion criteria**
Cases with insufficient clinical and hematological data were excluded from the study.

**Sample size**
Sample consisted of 140 histopathologically diagnosed cases of OSCC. The cases were categorized based on tumor differentiation into well differentiated, moderately differentiated, and poorly differentiated tumors. Clinical details including age, gender, and hematological details including platelet count were retrieved.

**Results**
A total of 140 OSCC were studied. Of the 140 cases, 89 were male and 51 were female. Male:female ratio was 1.75. Refer to Table 1 for distribution of cases according to gender.

The platelet counts were divided into low, normal, and high (normal - 1.5 to 4 lakhs/cu.mm, low was taken <1.5 lakhs/cu.mm, and high was taken >4 lakhs/cu.mm). Refer to Table 2 for distribution of cases according to platelet count.

We segregated the tumors according to differentiation into well, moderate, and poorly differentiated squamous cell carcinoma. 109 (77.86%) cases were well differentiated, 26 (18.57%) cases were moderately differentiated, and 5 (3.57%) cases were poorly differentiated. Refer to Table 3 for distribution of cases according to OSCC grading.

Considering the gender, among males - of 89 cases, 68 were of well differentiated, 17 were moderately differentiated, and 4 of poorly differentiated OSCC. Among females, of 51 cases, 41 were well differentiated, 9 were moderately differentiated, and 1 was poorly differentiated. Refer to Table 4 for distribution of males and females according to OSCC grading.

When the platelet level was compared between males and females on the grounds of low, normal, and high platelet count, 85 cases showed normal and 4 cases showed high platelets in males, whereas in females, only 39 cases showed normal platelet count and 8 cases showed high platelet count. Low platelet count was observed in 4 cases of females while none of the males showed low platelet count. Refer to Table 5 for distribution of males and females according to platelet count.

**Table 1: Gender distribution**
| Gender | Frequency (%) | Valid percent | Cumulative percent |
|--------|---------------|---------------|--------------------|
| Male   | 89 (63.6)     | 63.6          | 63.6               |
| Female | 51 (36.4)     | 36.4          | 100.0              |
| Total  | 140 (100.0)   | 100.0         |                    |

**Table 2: Distribution of platelet count among the cases**
| Platelet Count | Frequency (%) | Valid percent | Cumulative percent |
|----------------|---------------|---------------|--------------------|
| Low            | 4 (2.9)       | 2.9           | 2.9                |
| Normal         | 124 (88.6)    | 88.6          | 91.4               |
| High           | 12 (8.6)      | 8.6           | 100.0              |
| Total          | 140 (100.0)   | 100.0         |                    |

**Table 3: Distribution of OSCC grades among the cases**
| OSCC grading | Frequency (%) | Valid percent | Cumulative percent |
|--------------|---------------|---------------|--------------------|
| Valid        |               |               |                    |
| Well         | 109 (77.9)    | 77.9          | 77.9               |
| Moderate     | 26 (18.6)     | 18.6          | 96.4               |
| Poor         | 5 (3.6)       | 3.6           | 100.0              |
| Total        | 140 (100.0)   | 100.0         |                    |

OSCC: Oral squamous cell carcinoma

**Table 4: Gender-wise distribution of the OSCC grades**
| Gender | Well | Moderate | Poor | Total |
|--------|------|----------|------|-------|
| Male   | 68   | 17       | 4    | 89    |
| Female | 41   | 9        | 1    | 51    |
| Total  | 109  | 26       | 5    | 140   |

OSCC: Oral squamous cell carcinoma

**Table 5: Gender-wise distribution of the platelet counts**
| Gender | Low | Normal | High | Total |
|--------|-----|--------|------|-------|
| Male   | 0   | 85     | 4    | 89    |
| Female | 4   | 39     | 8    | 51    |
| Total  | 4   | 124    | 12   | 140   |

**Table 6: Statistical correlation between platelet count and OSCC grades**
| Correlation Tests | Value | df | Asymp. Sig. (two-sided) |
|-------------------|-------|----|-------------------------|
| Pearson Chi-square| 1.066 | 4  | 0.900                   |
| Likelihood ratio  | 1.600 | 4  | 0.809                   |
| Linear-by-linear association | 0.001 | 1  | 0.978                   |
| n of valid cases  | 140   |    |                          |

OSCC: Oral squamous cell carcinoma
However, this difference in platelet count between the genders was statistically insignificant ($P = 0.001$). The present study did not find any significant correlation between platelet count and the different grades of OSCC. Refer to Chart 1 and table 6 for OSCC grade-wise distribution of platelet counts.

**Discussion**

The relation between circulating platelets and carcinoma progression suggests that platelets have a more important role beyond just the hemostatic function.$^{[9]}$ Platelets act as mediators of angiogenesis, wound healing, and immune modulation. They secrete cytokines and growth factors such as transforming growth factor-beta, matrix metalloproteinase-2, platelet factor 4, and platelet-derived growth factor.$^{[10-13]}$ All of these induce cancer progression including epithelial, mesenchymal transition, angiogenesis, cell migration, and proliferation.$^{[14]}$

Production of interleukin-6 (IL-6) in some malignancies like in ovarian carcinoma has been proved to result in increased thrombocytosis. It was proposed that the production of IL-6 by ovarian cancer cells stimulates liver producing thrombopoietin, further stimulating megakaryocyte progenitors in bone marrow.$^{[14]}$

Platelets may contribute to cancer progression by:

a. Stabilizing tumor cell arrest in the vasculature  
b. Stimulating tumor cell proliferation  
c. Promoting tumor cell extravasation by potentiating tumor cell-induced endothelial cell retraction  
d. Enhancing tumor cell interaction with the extracellular matrix.$^{[15]}$

Several studies reported a decrease in platelet count during aging and also the presence of higher platelet count in women than in men.$^{[16]}$ The present study did not show any significant results associating the platelet number with the gender or age. The reason could be due to the unequal number of division of cases among male and female.

![Bar Chart](image)

**Chart 1:** Oral squamous cell carcinoma grade-wise distribution of platelet counts

Higher platelet count has been proved to be an adverse prognostic factor in several types of cancers including gynecologic, breast, lung, and genitourinary.$^{[14-18]}$ Different studies have shown a positive correlation between the platelet count and various grades of OSCC, wherein well-differentiated OSCC showed normal or low platelet count and poorly differentiated carcinoma showed high platelet count.$^{[16]}$ However, the present study did not find any significant correlation between platelet count and OSCC grades.

**Conclusion**

The unequal distribution of cases among different OSCC grades was a major limitation in the study. It could have been the reason for the lack of correlation between the platelet count and the OSCC grades. Further, large-scale prospective studies based on multiple centers with equally distributed OSCC grades can aid in accurately determining the association between platelet count and OSCC grading.

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