ORIGINAL ARTICLE

# Histopathological correlation of oral squamous cell carcinoma among younger and older patients

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## ABSTRACT

**Background:** Oral Squamous Cell Carcinoma (OSCC) is commonly noted in elder men, when occurring in younger individuals, its aggression and prognosis is questioned due to biased data in literature. Traditionally, various histopathological grading systems have been used for assessing aggression and prognosis of OSCC. However, multifactorial grading of Anneroth *et al*., is considered effective. **Materials and Methods:** In this retro-prospective study, files of 75 OSCC patients were retrieved from Oral Pathology Department; among this 50 patients were >40 years and 25 patients were ≤40 years of age. Archival formalin fixed paraffin embedded tissue blocks of these patients were used to prepare hematoxylin and eosin (H and E) stained sections for grading OSCC based on Broder's and Anneroth *et al*., criteria. Further, recurrence of OSCC among study subjects within 5 years of treatment was evaluated. Chi-square test was used to compare the disease in patients who were >40 years with ≤40 years. **Results:** Comparison according to Broder's classification didn't show any relevant variation. Three of the six parameters and overall grading according to Anneroth *et al*., criteria showed statistically higher grades of OSCC in the younger age-group; however, there was no significant difference in 5-year recurrence rate. **Interpretation and Conclusion:** Results of the study are suggestive of aggressive OSCC among young patients when compared to older. Conversely, this aggression didn't affect the recurrence in younger patients. Further studies on genetics, diet and demographics of patients below 40 years of age affected by OSCC will be of greater value.

***Key words:*** Anneroth *et al*. grading, multifactorial histopathological grading, oral squamous cell carcinoma, young patients

## INTRODUCTION

Oral cancer is one of the most familiar forms of cancers in the Indian subcontinent.[1,2] From the beginning of twentieth-century, frequency of oral cancer is known to be high in India.[3] Histopathologically, over 95% of oral cancers are squamous cell carcinomas.[1,4] Oral squamous cell carcinoma (OSCC) is more commonly noted in men usually above 40 years of age[5] and only about 0.4 to 3.9% of the patients are affected by OSCC earlier than 40 years.[6]

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Controversies exist in literature regarding aggression and prognosis of OSCC among young patients (below 40 years of age).[5] General view is that OSCC among young patients is more aggressive and has worse prognosis.[7-9] Few studies suggest that 5-year survival rate of patients below 40 years is better than that of patients above 40 years[10-12] and some other authors state that young patients have a similar clinical course and their survival rate is no different from other age-groups.[13-15]

Various histopathological grading systems of OSCC have been discussed in literature and Broder's grading has been popular since a long time.[16,17] Advances in diagnostic technology has led to introduction of multifactorial histopathological grading systems such as Anneroth *et al's* grading system, which is considered appropriate since it provides valuable diagnostic and predictive information of OSCC.[18,19] This study attempts to evaluate aggression of OSCC histopathologically by both Broder's and Anneroth *et al's.*, (1987) grading in patients above

forty and below forty years of age. Furthermore, an attempt is made to assess the prognosis of OSCC in younger patients by matching 5-year recurrence rate among patients >40 years with ≤40 years age-group.

## MATERIALS AND METHODS

Files of the patients reported with OSCC from 1997 to 2005 were retrieved from the records section of the Department of Oral Pathology of a Dental Institution in India. Only those patients whose archival formalin fixed paraffin embedded specimens were available for further processing were considered for this study. Patients who didn't take treatments, who had other systemic diseases and who were diagnosed with histopathological variants of OSCC were excluded from the study.

Final number of patients in the study was 75 of which 50 patients were >40 years of age were randomly selected to make group-I and 25 patients who were ≤40 years of age were similarly selected to make group-II. More patients in the elder group were used to increase the statistical power for comparison. Archival formalin fixed paraffin embedded tissue blocks of these patients were subjected to soft tissue microtomy for preparation of 5 μm thick tissue specimens. Subsequently they were stained by Hematoxylin and Eosin (H and E) and microscopic examination was carried out for the purpose of histopathological grading based on

- Broder's criteria to classify as well-differentiated squamous-cell carcinoma (WDSCC), moderately differentiated squamous-cell carcinoma (MDSCC) and poorly differentiated squamous-cell carcinoma (PDSCC)
- Anneroth *et al*., (1987) criteria which include six parameters assessing are as follows:
  - Tumor cell population: Degree of keratinization, nuclear polymorphism and mitotic figures [Figures 1-3]
  - Tumor-host relation: Pattern of invasion, depth of invasion and lympho-plasmacytic infiltration [Figures 4-6]. Each parameter was graded from 1-4 based on severity.[18] Further, individual patients were given an overall grade using the sum total grades of six parameters and classified into one of the following three grades; grade I: 6-12, grade II: 13-18 and grade III: 19-24.[19,20]

Recurrence of OSCC among study subjects within five years of treatment was also evaluated. Recurrent lesions are those,

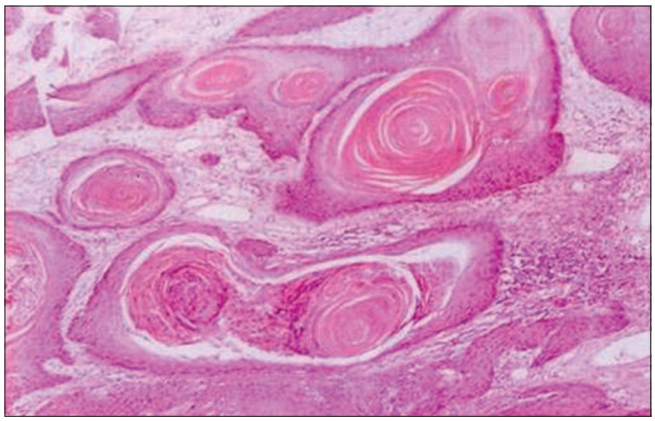

**Figure 1:** Photomicrograph showing grade 1 keratinization of OSCC according to Anneroth *et al*., criteria (H&E stain, ×50)

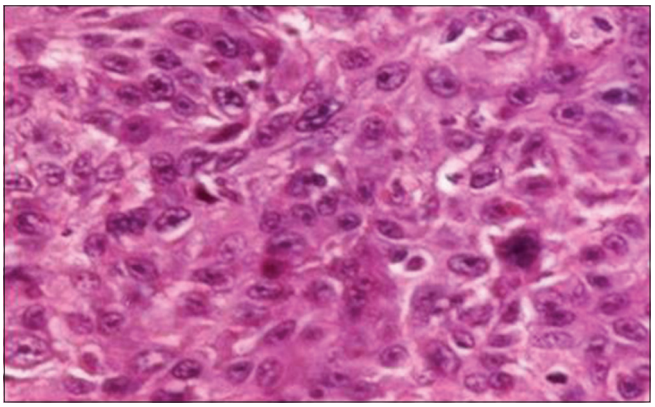

**Figure 2:** Photomicrograph showing grade 2 nuclear polymorphism of OSCC according to Anneroth *et al*., criteria (H&E stain, ×400)

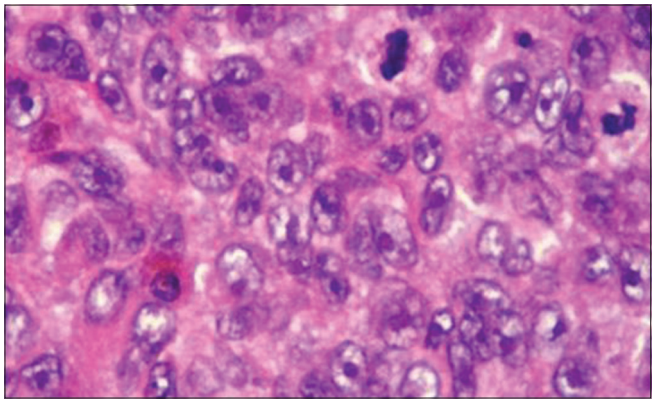

**Figure 3:** Photomicrograph showing grade 2 mitotic figures of OSCC according to Anneroth *et al*., criteria (H&E stain, ×1000)

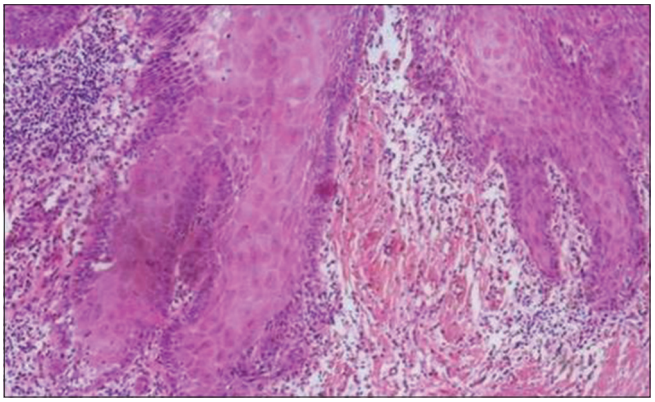

**Figure 4:** Photomicrograph showing grade 1 mode of invasion of OSCC according to Anneroth *et al*., criteria (H&E stain, ×100)

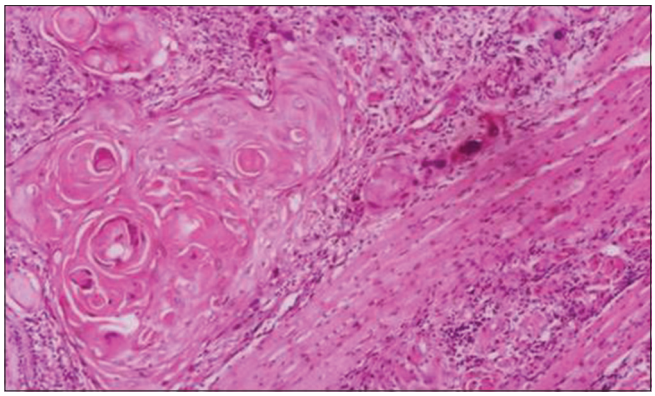

**Figure 5:** Photomicrograph showing grade 3 depths of invasion of OSCC according to Anneroth *et al*., criteria (H&E stain, ×100)

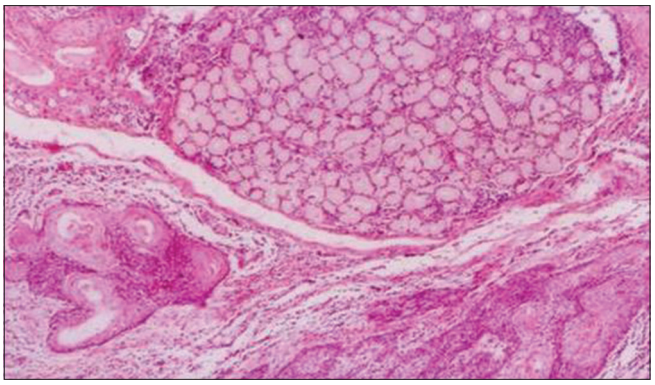

**Figure 6:** Photomicrograph showing grade 3 Lympho-plasmacytic Infiltrate of OSCC according to Anneroth *et al.,* criteria (H&E stain, ×50)

which showed local reappearance of OSCC or cervical lymph node metastasis or distant metastasis after treatment of the initial lesion. Comparison of all the parameters between group-I (>40 years) and group-II (≤40 years) was carried out statistically using Chi-square test.

## RESULTS

Distribution of study subjects according to Broder's classification is shown in Table 1; OSCC comparison between the younger and older group of patients didn't demonstrate any relevant difference. According to Anneroth *et al*.'s six histopathological parameters, three parameters showed significant difference between the age-groups. Consequently, overall grading also showed similar difference. All the parameters which exhibited variations were in higher grades among younger age group (Tables 2-4).

Total number of patients reported with recurrence in 5 years was 17 out of 75 irrespective of the age-groups. Comparison of 5 years recurrence rate between group-I and group-II didn't appear statistically significant [Table 5] 24% of patients showed recurrence in group-I as against 20% in group-II.

## DISCUSSION

While oral cancer accounts for only 2% of all malignancies in UK and USA,[21] it is one of the most common cancers in South East Asia,[2] and in India the incidence is as high as one third of all malignancies.[22,23] About 95% of oral cancers are squamous-cell carcinomas[1,4] and are commonly seen in elder adults (>40 years).[6] There is a long-standing debate over the aggression and prognosis of OSCC in young patients as compared to older patients and studies have suggested the need for additional research on this topic.[5]

Comparison of OSCC between younger and older age-groups in this study according to Broder's classification didn't show any significant difference. Most of the patients among young age groups were diagnosed with MDSCC (40%) followed by WDSCC (36%) and PDSCC (24%). Reports of similar studies such as Sasaki *et al*., in UK[5], Farnaz *et al*., in Iran,[24] and Iype *et al*., in India[25] suggest WDSCC as the most common type of OSCC followed by MDSCC and PDSCC. The difference between WDSCC and MDSCC cases in these studies and the present study is only nominal suggesting that the common histopathological type of OSCC is either WDSCC or MDSCC irrespective of age.

Broder's grading of OSCC is a time-honored pathologic tool,[26] but it is slowly expelled from the standard therapeutic planning strategies due to lack of consensus regarding its prognostic value.[27,28] Hence, grading of OSCC based only on Broder's criteria will be inconsistent and therefore needs to be reconfirmed with other acknowledged systems. There are various advanced grading systems of OSCC proclaiming to be better than Broder's but most of them are done at molecular level and are expensive[29,30] therefore difficult to adopt in low socioeconomic strata where the incidence of this disease is high.[19] However histopathologic grading that is sensitive and provides valuable diagnostic information that can effectively be applied in the pastoral areas of Indian subcontinent is suggested by Anneroth *et al*.[18]

In the present study three of the six parameters according to Anneroth *et al*., criteria showed statistically significant difference between the younger and older groups. Differences in nuclear polymorphism, mitosis index and depth of invasion were more obvious in higher grades among young patients when compared to old patients. A study by Sasaki *et al*., (2005)[5] used five of the six parameters of Anneroth *et al*., excluding nuclear polymorphism and found no significant difference between the age-groups.

Furthermore, when the overall grades of Anneroth *et al*., parameters were evaluated maximum number of patients in study irrespective of age-groups fell under grade 2 (54.66%) followed by grade 1 (40%) and grade 3 (5.33%). Similar trends were reported by Akhter *et al*.,[19] and Doshi *et al*.[20] Likewise, statistically significant difference in overall Anneroth

*et al*., parameters were also noted with higher grades of disease among the young patients. Studies describe that the histopathological parameters of Anneroth *et al*., are key indicators of tumor aggressiveness and prognostication since they reflect the relationship of the tumor with the host,[5,31] based on this our results are reminiscent of greater aggression of OSCC in younger patients when compared to the older.

Five-year recurrence rate irrespective of age in the study was lesser compared to other studies and the number of reported recurrences didn't show much variation between the groups. Pitman *et al*., (2000) have reported that 45% of their patients showed recurrence in 3 years period with older as well as younger age-groups showing equivalent distribution.[32] Similarly Pytinia *et al*., (2004) in their study on disease-free survival rates of patients <40 years and >40 years of age have not come across any difference.[33] Conversely, Lacy *et al*., (2000) have reported higher number of older patients with 5-years recurrence in their study (56% of older patients compare to 35% of younger patients).[34] These results are indicative of either similar or better survival rate for younger patients when compared to older.

**Table 1: Distribution of study subjects according to Broder's criteria**

| | Group-I | | Group-II | | Total |
|---|---|---|---|---|---|
| WDSCC | 16 | 32.00% | 9 | 36.00% | 25 |
| MDSCC | 21 | 42.00% | 10 | 40.00% | 31 |
| PDSCC | 13 | 26.00% | 6 | 24.00% | 19 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=0.6060, df=2, *P*=0.8949, NS | | | | | |

WDSCC: Well-differentiated squamous-cell carcinoma, MDSCC: Moderately differentiated squamous-cell carcinoma, PDSCC: Poorly differentiated squamous-cell carcinoma, NS: Not significant

**Table 2: Distribution of subjects according to Anneroth *et al*., criteria-tumor cell population**

| | Group-I | | Group-II | | Total |
|---|---|---|---|---|---|
| Degree of Keratinization | | | | | |
| Grade 1 | 17 | 34.00% | 4 | 16.00% | 21 |
| Grade 2 | 25 | 50.00% | 12 | 48.00% | 37 |
| Grade 3 | 6 | 12.00% | 5 | 20.00% | 11 |
| Grade 4 | 2 | 4.00% | 4 | 16.00% | 6 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=5.6690, df=3, *P*=0.1288, NS | | | | | |
| Nuclear polymorphism | | | | | |
| Grade 1 | 8 | 16.00% | 1 | 4.00% | 9 |
| Grade 2 | 32 | 64.00% | 14 | 56.00% | 46 |
| Grade 3 | 10 | 20.00% | 8 | 32.00% | 18 |
| Grade 4 | 0 | 0.00% | 2 | 8.00% | 2 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=7.9330, df=3, *P*=0.0474, S | | | | | |
| Mitosis | | | | | |
| Grade 1 | 32 | 64.00% | 8 | 32.00% | 40 |
| Grade 2 | 17 | 34.00% | 14 | 56.00% | 31 |
| Grade 3 | 1 | 2.00% | 3 | 12.00% | 4 |
| Grade 4 | 0 | 0.00% | 0 | 0.00% | 0 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=8.2770,df=3, *P*=0.0159, S | | | | | |

NS: Not significant, S: Significant

## CONCLUSION

Outcomes of the study are evocative of more aggressive OSCC in younger patients which didn't affect the recurrence rate

**Table 3: Distribution of subjects according to Anneroth *et al*., criteria tumor host relationship**

| | Group-I | | Group-II | | Total |
|---|---|---|---|---|---|
| Mode of invasion | | | | | |
| Grade 1 | 6 | 12.00% | 1 | 4.00% | 7 |
| Grade 2 | 14 | 28.00% | 10 | 40.00% | 24 |
| Grade 3 | 22 | 44.00% | 7 | 28.00% | 29 |
| Grade 4 | 8 | 16.00% | 7 | 28.00% | 15 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=4.1960,df=3, *P*=0.2410, NS | | | | | |
| Depth of invasion | | | | | |
| Grade 1 | 4 | 8.00% | 1 | 4.00% | 5 |
| Grade 2 | 24 | 48.00% | 3 | 12.00% | 27 |
| Grade 3 | 22 | 44.00% | 20 | 80.00% | 42 |
| Grade 4 | 0 | 0.00% | 1 | 4.00% | 1 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=12.2570, df=3, *P*=0.0065, S | | | | | |
| Lympho-plasmacytic infiltrate | | | | | |
| Grade 1 | 3 | 6.00% | 5 | 20.00% | 8 |
| Grade 2 | 27 | 54.00% | 10 | 40.00% | 37 |
| Grade 3 | 18 | 36.00% | 10 | 40.00% | 28 |
| Grade 4 | 2 | 4.00% | 0 | 0.00% | 2 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=4.7960, df=3. *P*=0.1873, NS | | | | | |

NS: Not significant, S: Significant

**Table 4: Distribution of study subjects according to overall grade from six parameters**

| | Group-I | | Group-II | | Total |
|---|---|---|---|---|---|
| Grade 1 | 26 | 52% | 4 | 16% | 30 |
| Grade 2 | 22 | 44% | 19 | 76% | 41 |
| Grade 3 | 2 | 4% | 2 | 8% | 4 |
| Total | 50 | 100% | 25 | 100% | 75 |
| Chi-square=9.02, df=2, *P*=0.011, S | | | | | |

S: Significant

**Table 5: Distribution of study subjects according to recurrence in five years**

| | Group-I | | Group-II | | Total |
|---|---|---|---|---|---|
| Uncontrolled | 12 | 24.00% | 5 | 20.00% | 17 |
| Controlled | 38 | 76.00% | 20 | 80.00% | 58 |
| Total | 50 | 100.00% | 25 | 100.00% | 75 |
| Chi-square=0.152, df=1, *P*=0.697, NS | | | | | |

NS: Not significant

when compared with older patients. The question that needs to be answered is the actual relationship of aggression and prognosis of OSCC among young individuals when compared with old individuals. Hence, further studies and research on genetics, diet, demographics and tumor host factors will be of a greater value to unveil the reason associated with oral squamous cell carcinoma affecting younger patients.

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