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# STUDY OF HISTOMORPHOLOGICAL PROGNOSTIC FACTORS IN ORAL SQUAMOUS CELL CARCINOMA AND COMPARISON OF GRADING SYSTEMS.

Pathology

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## ABSTRACT

Oral squamous cell carcinoma is one of the leading cause of mortality and morbidity in developing countries. Its aggressiveness depends on various parameters of tumour itself and regional lymph node metastasis as well. This was a retrospective study conducted in Krishna Institute Of Medical Sciences, Karad over a period of two years with aim to study histomorphological prognostic factors and compare most used grading system in squamous cell carcinoma. There were total 133 specimens including biopsies and resection specimens. Comparison between Border's classification and Anneroth's grading system was done. We found that despite the widespread use of Broder's classification, there is limited relationship with the grading and outcome of treatment and survival. Our study failed to observe any relationship between Broder's system and patient's prognosis. So multifactorial Anneroth's grading system can be taken as a valuable diagnostic tool, in predicting lymph node metastasis and patient outcome.

## KEYWORDS

Squamous cell carcinoma, Grading systems, Annethoth's grading system, Border's classification.

## INTRODUCTION

Oral cancer is the sixth most common cancer worldwide and represents third most common malignancy in developing countries[1]. Squamous cell carcinoma (SCC) is the most common malignancy accounting for about 95% of all oral malignant lesions[2]. The most affected sites are buccal mucosa, tongue, lips and floor of mouth. The major risk factors in oral SCC are use of tobacco or betel quid, smoking and alcohol. Also high risk Human Papillomavirus (HPV), and diet low in fresh fruits and vegetables has been recently implicated in etiopathogenesis of oral SCC[1,3]. The highest incidence and prevalence of oral SCC is found in Indian subcontinent[4]. Oral SCC has a great predisposition to produce metastasis in lymph nodes. In clinical practice, treatment plan and prognosis of oral SCC is mainly based on TNM staging system. But this staging system is not sufficient for optimal prognostication and must be supplemented by more reliable methods[5,6]. The aim of this study is to assess the demographics of oral SCC and study histomorphological factors in its prognosis.

## MATERIALS AND METHODS

The study included 133 patients who were diagnosed with oral malignancy with-in a period of 2 years from may 2014 to april 2016. All the biopsies and resection specimens were included. The data regarding age, sex, habits and relevant history was collected. In 30 resection specimens the tumor size and lymph node status was recorded. All the samples were fixed in 10% formalin, embedded in paraffin, and stained with Haematoxylin and Eosin stain. All the lesions were first categorized according to the morphology into Squamous cell carcinoma, basal cell carcinoma and verrucous carcinoma. Further, all biopsies of SCC were graded as: well, moderately and poorly differentiated tumors. The resection samples of oral SCC were classified according to Broder's grading and Anneroth's grading system (Table-1).

### Broder's classification (1920)

Tumors were graded on basis of degree of differentiation into

1. **Grade I :** Well differentiated tumors (75-100% of cell are differentiated)
2. **Grade II :** Moderately differentiated (50-75% cells are differentiated)
3. **Grade III :** Poorly differentiated (25-50% are differentiated)
4. **Grade IV :** Anaplastic tumor (0-25% cells are differentiated)

**Table 1 showing Anneroth's grading system**

| Anneroth's grading system: parameters 1-3 studied in tumor proper, parameters 4-6 in most invasive/nearest surgical margin | | | | | |
|---|---|---|---|---|---|
| No. | Morphologic pattern | Points | | | |
| | | 1 | 2 | 3 | 4 |
| 1. | Degree of keratinization | >50% cells | 20-50%cells | 5-20%cells | 0-5%cells |
| 2. | Nuclear pleomorphism | Little | Moderate | Abundant | Extreme |
| 3. | Number of mitosis | 0-1 | 2-3 | 4-5 | >5 |
| 4. | Pattern of invasion | Pushing, well delineated | Infiltrating, solid, cords, bands or strands | Small groups, cords or infiltrating cells | Wide spread cellular dissemination |
| 5. | Stage of invasion | Carcinoma-in-situ | Invasion up-to lamina propria | Invasion below lamina propria | Deep invasion up-to bone |
| 6. | Lymphocytic infilration | Marked | Moderate | Slight | None |

The sum of scores were grouped as follows:
1. Grade I : 6-12
2. Grade II : 13-18
3. Grade III : 19-24

## RESULTS

This study of 133 patients included 103 biopsies and 30 resection specimens.

Patients age ranged from 22-78 years, with maximum number of patients in sixth decade followed by seventh decade. Mean age was 57.5 years. Sixty five percent of patients were males and 35 percent were females.

According to microscopic types, 93.20% were squamous cell carcinoma, 5.40% were verrucous carcinoma, and 0.70% each were basal cell and undifferentiated carcinoma.

**Table 2 showing morphological distribution of cases in biopsy specimens**

| Diagnosis | Number of cases | Percentage |
|---|---|---|
| Carcinoma-in-situ | 2 | 1.9% |
| Verrucous carcinoma | 6 | 5.9% |
| Well-differentiated carcinoma | 41 | 39.9% |
| Moderately-differentiated carcinoma | 37 | 35.9% |
| Poorly-differentiated carcinoma | 16 | 15.5% |
| Undifferentiated carcinoma | 1 | 0.9% |

In resection specimens there were only 3 cases out of 30 cases which had lymph node metastasis. The diameter of tumors ranged from 1 to 7 cms with an average of 2.74 cms. According to clinical TNM staging regarding primary tumor size, all the 3 cases with nodal metastasis were T2 tumors. In non metastatic group 13 were T1 tumors, 9 were T2 tumors and 5 were T3 tumors. There was no relation of tumor size with lymph node metastasis.

**Table 3 showing distribution of resection specimens according to Broder's grading**

| Border's classification | Number of cases in metastatic group(%) | Number of non metastatic group(%) | Total number(%) |
|---|---|---|---|
| Well differentiated | 3(100%) | 16(59.2%) | 19(63.3%) |
| Moderately differentiated | 0 | 11(40.8%) | 11(36.7%) |
| Poorly differentiated | 0 | 0 | 0 |
| Anaplastic | 0 | 0 | 0 |
| Total | 3(100%) | 27(100%) | 30(100%) |

**Table 4 showing distribution of resection specimens according to Anneroth's multifactorial grading system**

| Anneroth's grading | Number of cases in metastatic group (%) | Number of cases in non metastatic group (%) | Total number(%) |
|---|---|---|---|
| Grade-I | 1(33.3%) | 26(96.3%) | 27(90%) |
| Grade-II | 2(66.7%) | 1(3.7%) | 3(10%) |
| Grade-III | 0 | 0 | 0 |
| Total | 3(100%) | 27(100%) | 30(100%) |

## DISCUSSION

In India Squamous cell carcinoma is not uncommon and oral cavity is one of the leading sites. Squamous cell carcinoma of the buccal mucosa, retromolar trigone and alveolus are together clubbed as gingivo-buccal complex and is rightly called as the "Indian Oral Cancer". It constitutes about 55-60% of all oral cancer in India.

Many investigators have studied clinical and histopathological features of the primary tumor, such as tumor size, degree of differentiation, NP, stromal response and pattern of invasion to determine the propensity for lymph node metastasis[7]

In our study 65% cases were males. Khandelkar et al[8] showed a prevalence of 61.25% in males, I. Yazdi et al[9] showed a prevalence of 60.4%. Majority of the cases in our study were in the age group of 51-60 years which corresponds to study done by Doshi N et al[10].

We found most common site as buccal mucosa followed by tongue and lower alveolus which was in concordance with a study done in western Up[11]. T1 tumors lacked metastases in our study which was in concordance with study done with Doshi N et al[8] and M Akhter et al[12], but some studies have shown poor prognosis on follow-up of T1 tumors[13]. Thus TNM system includes acceptable prognostic parameters but not sufficient for optimal prognostication and must be supplemented by other methods.

AC Broders' in 1920 initiated a quantitative grading system for the cancer of the lip. Broders' suggested that the grading of the tumors should be according to the differentiation of tumor cells. Despite the universal use of this system, or slight modifications of it, there has only been a limited relationship with the grading of cancer and the outcome of treatment and survival of the patients. Our study, and study done by Doshi et al[10] and Yazdi et al[9] failed to observe any relationship between Broder's system and node Metastasis.

But our study was not in concordance with study done by M Akhter et al[12]. Due to poor relationship between Broders' grading and patient survival, need for modified or new grading system was felt. It was recognized by many authors including Jakobsson, Moberger etc., that observing a number of factors in the biopsy along with cellular differentiation might give a better prognostic indicator for oral SCC.

Jacobson et al in 1973, was the pioneer in developing multifactorial grading system for oral cancer based on structure, differentiation, nuclear pleomorphism, mitosis, mode of invasion, vascular invasion and lymphoplasmacytic infiltration. After Jacobsson, many other researchers modified or developed new system based on the Jacobssons' grading system. One of them was Anneroth and Hansen's[14] (1984) system which was a modified and improved version of Jacobssons' grading system.

Anneroth grading system used the entire tumor cell population in a biopsy, to obtain a final grading of the tumor and hence this grading system is used more than other grading system for better evaluation of prognosis of the patient.

## CONCLUSION

Squamous cell carcinoma is one of the challenges for the treating surgeons. A significant percentage of patients with early stages of SCC have a poor prognosis despite better differentiation and small size of tumors hence Broder's grading and TNM staging provide very little information on prognosis. So multifactorial Anneroth's grading system can be taken as a valuable diagnostic factor and factor in predicting lymph node metastasis. As the most important prognostic factor for oral squamous cell carcinoma is regional lymph node metastasis status. Therefore the approach to the treatment and further management of oral squamous cell carcinoma should not only be restricted to tumor parameters but also to lymph node metastasis status.

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