

COMPARISON OF ANNEROTH'S AND BRODER'S GRADING SYSTEMS IN ORAL SQUAMOUS CELL CARCINOMA – A STUDY AT TERTIARY CARE HOSPITAL IN HARYANA

Sakshi Aggarwal¹, Rajan Sachdeva¹, Sudipta Satpathi¹, Anandita Dalal¹, Yudhvir Singh², Rajeev Sen³

Received : 10/07/2023
Received in revised form : 07/08/2023
Accepted : 18/08/2023

Keywords:

Oral cavity, Oral squamous cell carcinoma, Broder's grading system, Anneroth's Grading system.

Corresponding Author:

Dr. Sakshi Aggarwal,

Email: sakshi.aggarwal94@gmail.com

DOI:10.47009/jamp.2023.5.4.352

Source of Support: Nil,

Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5(4); 1763-1767



¹Junior Resident, Department of Pathology, Faculty of Medicine and Health Sciences, SGT University, Gurugram, Haryana, India

²Assistant Professor, Department of Pathology, Faculty of Medicine and Health Sciences, SGT University, Gurugram, Haryana, India

³Professor & Head, Department of Pathology, Faculty of Medicine and Health Sciences, SGT University, Gurugram, Haryana, India

Abstract

Background: Oral cavity is becoming a pressing problem in the world. Oral squamous cell carcinoma (OSCC) is a commonly occurring head and neck cancer due to many etiological factors, but smoking and alcohol remain the most common risk factors. OSCC develops as a result of certain genetic and epigenetic variations in the squamous epithelium, which in turn leads to a series of consequences leading to the definitive stage of invasive squamous cell carcinoma. Broder's grading system for OSCC was based on degree of differentiation only; whereas Anneroth's multifactorial grading system was used for evaluation of prognosis and prediction of survival period for OSCC patients and includes many other parameters apart from differentiation. The objective is to Compare Anneroth's and Broder's grading systems in oral squamous cell carcinoma and to evaluate the Anneroth's grading as a standard in comparison to Broder's grading system over a period of last three years in SGT Hospital. **Materials and Methods:** This retrospective study was done on total 120 biopsies of head and neck region reported from May 2021 to June 2023 in SGT Hospital (Haryana) as squamous cell carcinoma. The data was collected from histopathology lab, Department of Pathology, SGT Hospital, Haryana. The previous reports were given according to Broder's system which is based on only differentiation of cells. All the cases were reexamined and reclassified according to Anneroth's system that gives detailed information about degree of keratinization, nuclear pleomorphism, number of mitosis/hpf, pattern of invasion, stage of invasion and lympho-plasmocytic infiltration. **Result:** In this study, the majority of the cases were males (76.6%) and were above 50 years of age (63.4%), according to Border's grading system out of 120 cases, 23.4% cases were grade I, 62.5% cases were grade II and 14.1% cases were grade III while according to Anneroth's grading system 13.4% were grade I, 45% were grade II, 40% were grade III and 1.6% were grade IV. **Conclusion:** Even though Broder's system is the most commonly used grading system in OSSC, the Anneroth's system of grading is more informative and gives better result regarding prognosis, action taking time and prediction of survival period than Broder's System.

INTRODUCTION

Oral cancer represents the third most common form of malignancy in the developing countries, whilst in the developed countries it is the eighth most common form of cancer.^[1] Oral squamous cell carcinoma (OSCC) is the most frequent malignancy in the mouth, accounting to 95% of all oral malignant lesions.^[2] The most affected sites are the

tongue, inferior lips and floor of the mouth. The typical demographic profile of oral SCC is one of a man in the fifth to eighth decades of life, who is a tobacco chewer and/or a smoker. In India, where tobacco chewing is used with betel nuts and reverse smoking (placing the lit end in the mouth) is practiced, there is a striking incidence of oral cancer.^[3] Less than 10.0% of cases arise in women.^[4]

Its high frequency in Central and South East Asian countries (India, Bangladesh, Sri Lanka, Thailand, Indonesia, Pakistan) has been well documented.^[5,6] Globally, the varied incidence rates of oral cancer (per 100,000 cases) are seen ranging from 2.0 (UK) to 9.4 (France); 4.4 in Colombia to 13.4 in Canada; 1.6 Japan to 13.5 India; and from 2.6 New Zealand to 7.5 in South Australia. Each year, about 5,75,000 new cases and 3,20,000 deaths occur world-wide. Oral cancer accounts for less than 3% off all cancer in United State, but is the sixth most common cancer in males and twelfth most common cancer in females. In some country, like India, it is the most common cancer.^[7]

Oral malignancy is complex and multi-factorial cancer. It is suspected that in India widespread malnutrition together with high-risk behaviour like betel chewing may contribute to the high incidence of OSCC. Areca nut chewing may cause oral leukoplakia and oral sub mucous fibrosis, both of which can be pre malignant in the oral cavity. Reactive oxygen species formed in human oral cavity causes oxidative DNA damage to tissue in oral cavity in liberation of carcinogenic chemical from tobacco.^[8,9]

The histological grading of tumors has been used as an important diagnostic tool to predict the clinical behavior of OSCC. The biological activity of oral SCC is evaluated and descriptively categorized as highly, moderately and poorly differentiated. Broder's has developed quantitative grading of oral cancer in 1920 but this system of SCC, based on the differentiation or maturation of the tumor cell is of a limited value as basis for choice of treatment as well as for prediction of the outcome of the disease.^[10,11] Anneroth's and Hansen developed another grading system for grading of OSCC's. According to this system, three parameters reflecting tumor cell features including keratinization, nuclear pleomorphism, and mitoses are evaluated in the whole thickness of the tumor. Tumor-host relationship is described in terms of Pattern of invasion, stage of invasion, and lymphoplasmacytic infiltration.^[12]

So, multifactorial malignancy grading system was developed to obtain a more precise morphologic evaluation of growth potential of squamous cell carcinoma in head and neck region. This malignancy grading system has been used during last few years in both its original form and modified version, especially for retrospective studies of squamous cell carcinoma. With this background, a study was undertaken to compare between Anneroth's & Broder's grading systems in oral squamous cell carcinoma.

MATERIALS AND METHODS

In this retrospective study 120 cases of oral squamous cell carcinoma were taken and were graded according to the two grading systems that is,

Broder's, and Anneroth reported from May 2021 to June 2023 in SGT Hospital (Haryana).

Inclusion Criteria

Those who were histopathologically proven to be the patient of oral squamous cell carcinoma and the tumors that originated from the tongue, floor of the mouth, cheek, gingiva, palate, or retro molar trigone, were included.

Exclusion Criteria

Other variants of OSCC, metastatic squamous cell carcinoma of oral cavity and surgical specimen after chemotherapy and radiotherapy were excluded.

Broder's (1920) classification:

Accordingly, tumors were graded on the basis of degree of differentiation and keratinization of tumor cells into;

Grade I: Well differentiated tumors – 75.0%-100.0% of cells are differentiated

Grade II: Moderately differentiated tumors – 50.0%-75.0% of cells are differentiated

Grade III: Poorly differentiated tumors – 25.0%-50.0% of cells are differentiated

Grade IV: Anaplastic tumor – 0.0%-25.0% of cells are differentiated

Anneroth's et al (1987) multifactorial grading system:

According to this system, three parameters reflecting tumor cell features including keratinization, nuclear pleomorphism, and mitoses were evaluated in the whole thickness of the tumor and each scored from 1-4. Pattern of invasion, stage of invasion, and lymphoplasmacytic infiltration representing tumor-host relationship were graded in the most invasive margins and scored from 1-4. Then the sums of scores were grouped as follows: Grade I - 6-12, Grade II 13-18, grade III- 19-24, and the results were compared in the metastasizing and non-metastasizing groups.

Statistical Analysis

The data was compiled in Microsoft Excel sheet and transferred to Statistical Package for the Social Sciences (SPSS) version 23.0. Both descriptive and inferential statistics have been applied. It was done by calculating number and percentage cases of different grades of OSCC according to both grading systems.

RESULTS

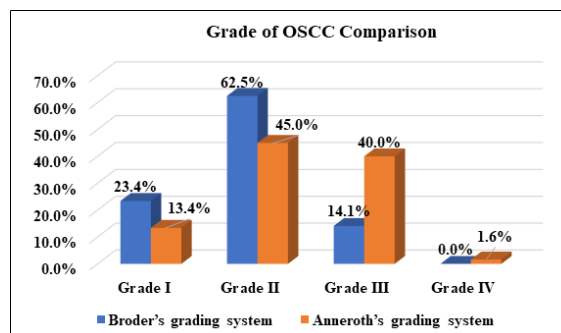


Figure 1: Comparison of results of Border and Anneroth's grading system

In this study of 120 studied cases majority were males (76.6%) and were above 50 years of age (63.4%). Grade II OSCC was in the majority of the cases (62.5%) followed by grade I (23.4%), grade III (14.0%) and there were no cases of grade IV

OSCC according to Border's grading system whereas according to Anneroth's grading system 45.0% cases were of grade II followed by 40.0% grade III, 13.4% grade I and 1.6% Grade IV.

Table 1: Malignancy grading system of oral squamous cell carcinoma according to Anneroth et al.^[14]

Histologic grading of malignancy of tumour cell population				
Morphologic parameter	Points			
	1	2	3	4
Degree of keratinization	Highly (>50% of the cells)	Moderate (20–50% of cells)	Minimal (5–20% of cells)	None (0–5% of cells)
Nuclear polymorphism	Little (>75% mature cells)	Moderately abundant (50–75% mature cells)	Abundant (25–50% mature cells)	Extreme (0–25% mature cells)
Number of mitotic cells/high-power field	0-1	2-3	4-5	>5
Histologic grading of malignancy of tumour-host relationship				
Pattern of invasion	Pushing, well-delineated infiltrating borders	Infiltrating, solid cords, bands and/or strands	Small groups or cords of infiltrating cells (n > 15)	Marked and wide-spread cellular dissociation in small groups of cells (n < 15) and/or in single cells
Stage of invasion (depth)	Carcinoma in situ and/or questionable invasion	Distinct invasion, but involving lamina propria only	Invasion below lamina propria adjacent to muscles, salivary gland tissues and periosteum	Extensive and deep invasion replacing most of the stromal tissue and infiltrating jawbone
Lympho-plasmocytic infiltration	Marked	Moderate	Slight	None

Table 2: Demographic details

Variables		No. of cases (n=120)	Percentage
Gender	Male	92	76.6
	Female	28	23.4
Age in years	≤50	44	36.6
	>50	76	63.4

Table 3: Distribution of the studied cases on the basis of Border's grading system

Grade of OSCC	No. of cases (n=120)	Percentage
Grade I	28	23.4
Grade II	75	62.5
Grade III	17	14.1
Grade IV	0	0.0

Table 4: Distribution of the studied cases on the basis of Anneroth's grading system

Grade of OSCC	No. of cases (n=120)	Percentage
Grade I	16	13.4
Grade II	54	45.0
Grade III	48	40.0
Grade IV	2	1.6

Table 5: Comparison of results of Border and Anneroth's grading system

Grade of OSCC	% of cases according to Broder's grading system	% of cases according to Anneroth's grading system
Grade I	23.4%	13.4%
Grade II	62.5%	45.0%
Grade III	14.1%	40.0%
Grade IV	0.0%	1.6%

DISCUSSION

In head and neck tumors, 90.0% of cases were OSCC whose unabatable growth and invasive potential increases the locoregional spread.^[15,16]Metastasis to lymph nodes signify the next stage in the progression of cancer. TNM staging is a prognostic factor to determine the extent of the diseases and to predict the outcome of cancer patients.^[17]However, rate of growth and

invasiveness depends not only on the clinical staging, but mostly on differences in the degree of differentiation of tumour cells which contributes to the heterogenous population.^[18,19]Histological prognostic factors are important in assessing the clinical and biological behaviour of the tumour. 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 (POI) to

determine the propensity for LNM.^[20] In 1920, Broder's quantitative grading system for cancer was initiated still it lacked a correlation with prognosis. To make the morphologic and histologic criteria to be more precise Anneroth and Hansen modified the histopathological grading system for application to OSCC.^[21]

In this study of 120 studied cases majority were males (76.6%) and were above 50 years of age (63.4%). Our findings were in accordance with the findings of Doshi NP et al,^[8] who reported that on 57 oral SCC's, males comprised of 73.7% of cases. Khandekar SP et al,^[3] in their study on 80 cases of oral cancer, showed a prevalence of cancer in 61.25% of males and Yazdi DMD et al,^[22] in their study on 48 cases of tongue SCC showed male prevalence of 60.4%. High proportion of cases among males may be due to high prevalence of tobacco consumption habits in them, coupled with smoking whereas in our society females less commonly indulge in tobacco smoking. Shrivastava S and Shakya R,^[1] reported that the mean age distribution was 53.2 with a range of 28 to 72 years. The mean age in males was 51.6 compared with 47.7 years in females similar to present study.

In our study Grade II OSCC was in the majority of the cases (62.5%) followed by grade I (23.4%), grade III (14.0%) and there were no cases of grade IV OSCC according to Border's grading system whereas according to Anneroth's grading system 45.0% cases were of grade II followed by 40.0% grade III, 13.4% grade I and 1.6% Grade IV. Our findings were consistent with the findings of Ghanghoria S et al,^[23] who reported that according to Border's grading system out of 600 cases 52.0% cases were grade I, 40.0% cases were grade II and 8.0% cases were grade III while according to Anneroth's grading system 37.0% were grade I, 55.0% were grade II, 7.0% were grade III and 1.0% were grade IV. A wide range of scoring (5 to 20+) along with six parameters enables Anneroth's classification to provide us a detailed analysis, graded the cases according to scoring of each parameter. Thus, it is more informative than Broder's grading system. Degree of keratinisation and nuclear pleomorphism has comparatively less value as compare to pattern of invasion and number of mitosis for evaluation.^[13]

In a study by Nadaf A et al according to Anneroth's system maximum cases comes under grade III while in Broder's system maximum cases are in grade I & II. Our study was also consistent with the findings of Doshi NP et al,^[8] they found most of the cases come under grade I according to Broders system & grade II as per Anneroth system. The findings of Akther M et al,^[25] were against our result as they didn't find significant differences in their cases between Broders & Anneroth grading systems.

A main difference between these two grading systems is that Broders grade considers features within the tumor only, whereas in Anneroth's new system show tumor cell features in addition to the

relationship between the tumor and underlying connective tissue. Anneroth's system is more reliable and gives more specific results.^[23] The clinical validity of this system was tested in a comprehensive study in a group of patients of squamous cell carcinoma in the floor of mouth. A statically significant correlation was found between mean total malignancy scores and clinical staging, frequency of recurrence, and death from first oral primary carcinoma.^[26]

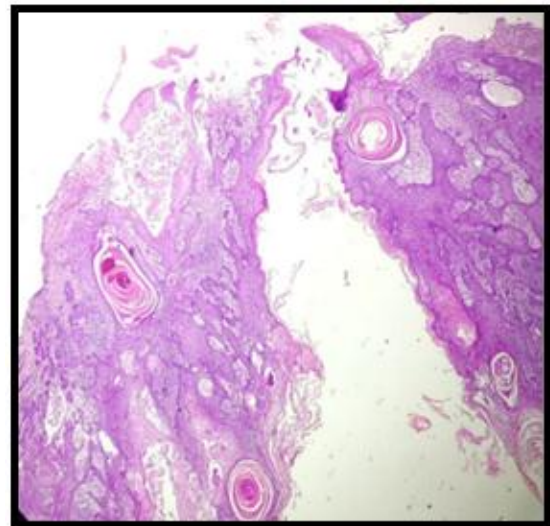


Figure 2: Well differentiated squamous cell carcinoma showing keratinization(H and E stain, 10X)

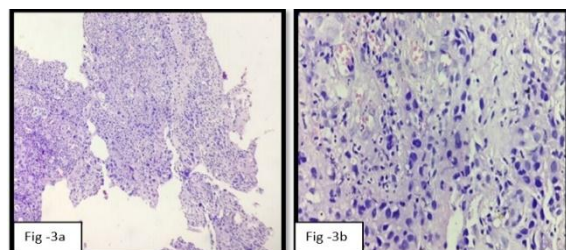


Figure 3: (a, b)-Moderately differentiated squamous cell carcinoma (H and E stain, 10X,40X)

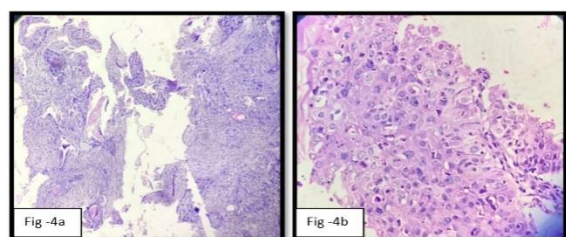


Figure 4: (a, b)-Poorly differentiated squamous cell carcinoma (H and E stain, 10X,40X)

Limitations of the study

- Relatively smaller sample size
- Biopsies are not necessarily representative of the whole tumor content, but the biopsy is the only tissue sample available for histological evaluation.

CONCLUSION

Anneroth's multifactorial grading system of OSSC included three parameters indicating histological feature of tumor and three parameters indicating tumor-host relationship. It can be taken as a valuable diagnostic tool and can be considered as a greater significance in reflecting the growth capacity and malignancy of the tumor and in predicting the outcome of the disease at an early stage and hence, it is more informative than Broder's grading system.

REFERENCES

1. Shrivastava S and Shakya R. Study on histological grading of oral squamous cell carcinoma and its co-relationship with regional lymph node metastasis. *International Journal of Scientific Research*. 2019;8(2):40-44
2. Dantas DD, Ramos CC, Costa AL, Souza LB, Pinto LP. Clinical-pathological parameters in squamous cell carcinoma of the tongue. *Braz Dent J*. 2003;14(1):22-5.
3. Khandelkar SP, Bagdey PS. Oral cancer and some epidemiological factors: A Hospital based study. *Indian Journal Of Community Medicine* 2006;31:3:157-162.
4. McClatchey KD, Zarbo RJ. The Jaws and Oral Cavity. *Sternberg's Diagnostic Surgical Pathology* 2004;2:884-915
5. Park K. Preventive and social medicine, 18th ed. India:Bhanot 2005;
6. Reinberg S. Cancer to suppress heart diseases as a world killer. *Oral cancer* 2008; 1: 24-8.
7. Sapp JP. *Maxillofacial Pathology*, 2nd ed. India:Mosby 2004;
8. Doshi NP, Shah SA, Patel KB, Jhabuawala MF. Histological Grading of Oral Cancer: A Comparison of Different Systems and Their Relation to Lymph Node Metastasis. *Natl J Community Med [Internet]*. 2011;2(01):136-42.
9. Fee WE, Schoepel SL, Rubenstein R et al. Squamous cell carcinoma of soft palate; arch otolaryngology 1979;105,717-718.
10. Chen CL, Chi CW, Liu TY. Hydroxyl radical formation and Oxidative DNA damage induced by areca quied in vivo. *J-Oral-Med* 1998; 27(9): 428-33.
11. Enwonwa- Co; Maks-VI. Bionutrition and oral cancer in human. *Crit-Rev- Oral- BioMed*, 1995; 6(1): 5-7
12. Akhter M, Hossain S, Rahman QB, Molla MR. A study on histological grading of oral squamous cell carcinoma and its co-relationship with regional metastasis. *J Oral Maxillofac Pathol*. 2011;15(2):168-76.
13. Anneroth G, Batsakis J, Luna M. Review of literature and recommended system of malignancy grading in oral squamous cell carcinoma. *Scand J Dent Res* 1984; 92:229-49.
14. Anneroth G, Batsakis J, Luna M. Review of the literature and a recommended system of malignancy grading in oral squamous cell carcinomas. *Scand J Dent Res*. 1987;95:229-49
15. Bhargava A, Saigal S, Chalishazar M. Histopathological grading systems in oral squamous cell carcinoma: A review. *J Int Oral Health*. 2010;2(4):01-00
16. Acharya S, Kumari N, Srivastava P, Arnold D, Nikhil K. Architectural changes in the regional lymph nodes of oral squamous cell carcinoma. *Journal of Oral and Maxillofacial Pathology*. 2019;23(2):305.
17. Gospodarowicz MK, Miller D, Groome PA, Greene FL, Logan PA, Sobin LH. The process for continuous improvement of the TNM classification. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2004;100(1):01-05.
18. Wittekind C, Compton CC, Greene FL, Sobin LH. TNM residual tumour classification revisited. *Cancer*. 2002;94(9):2511-17.
19. Rahima B, Shingaki S, Nagata M, Saito C. Prognostic significance of perineural invasion in oral and oropharyngeal carcinoma. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2004;97(4):423-31.
20. Shingaki S, Suzuki I, Nakajima T, Kawasaki T. Evaluation of histopathologic parameters in predicting cervical lymph node metastasis of oral and oropharyngeal carcinomas. *Oral Surg Oral Med Oral Pathol* 1988;66:683 8.
21. Bryne M, Koppang HS, Lilleng R, Stene T, Bang G, Dabelsteen E. New malignancy grading is a better prognostic indicator than Broders' grading in oral squamous cell carcinomas. *J Oral Pathol Med* 1989;18:432 7.
22. Yazdi DMD, M. Khalili DMD. Grading of Oral Cancer: Comparison of Different Systems with Respect to Lymph Node Metastasis in Tongue SCC.
23. Shikha Ghanghoria, Dr Sunil Jaiswal, Dr Priyanka Kiyawat, Prof. Dr Arvind Ghanghoria. Comparison of Anneroth's and Broder's grading systems in oral squamous cell carcinoma- A 5 year study. *JMSCR*. 2019;7(2):700-706
24. Afreen Nadaf, Rezhaz Abbas, Suheel Hamid Latoo. Comparison between Anneroth's & Broder's Grading Systems in Oral Squamous Cell Carcinoma in Relation to Histopathological Prognostic Factors. *AIMDR*. 2023;9(2):31-36
25. Akhter M, Hossain S, Rahman QB, Molla MR. A study on histological grading of oral squamous cell carcinoma and its co-relationship with regional metastasis. *J Oral Maxillofac Pathol*. 2011;15(2):168-76.
26. Suresh GM, Koppad R, Prakash BV, Sabitha KS, Dhara PS. Prognostic Indicators of Oral Squamous Cell Carcinoma. *Ann Maxillofac Surg*. 2019;9(2):364-370.