SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Dhatrak *et al*., 2024
DOI: 10.21276/SSR-IIJLS.2024.10.4.16

Research Article

open access

Incidence of Lymphovascular Emboli, Perineural Invasion and Lymph Node Spread with Relation to Tumour Grading in Oral Cancer Specimen in Konkan Region

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Received: 20 Apr 2024/ Revised: 15 May 2024/ Accepted: 15 Jun 2024

ABSTRACT

Background: To study the Incidence of lymphovascular emboli (LVE), perineural invasion (PNI) and lymph node status with relation to tumour grading in oral cancer (Hemimandibulectomy) specimens in the Konkan region.

Methods: A record-based observational cross-sectional study was conducted at a tertiary care hospital from January 2021 to June 2023 period. A total of 96 cases of hemimandibulectomy specimens were studied. The tissue was processed using paraffin wax processing, consisting of Tissue Processing, embedding, Section Cutting and H And E Staining.

Results: Oral cancer was more common in male (69%) patients as compared to female (31%). Age groups of 50-60 years were highly affected compared to other age groups. Males and females were found to be equally affected by lymph node metastasis. Maximum cases 68.80% were found to be of well-differentiated OSCC followed by well to moderately differentiated 18.80% then moderately differentiated 6.30% and poorly differentiated 3.10%. Total lymph node-positive cases were 44 (45.8%), and maximum cases were from the age group of 40 - 60 yrs. A total of 45 (46.8%) cases show lymphovascular emboli and 44 (45.8%) cases show perineural invasion.

Conclusion: LVE and PNI on routine H&E slides, become mainstay and important sensitive markers for metastasis and overall prognosis of the patient irrespective of tumour grade.

Key-words: Lymphovascular Emboli (LVE), Perineural Invasion (PNI), Oral Squamous Cell Carcinoma (OSCC), Oral Cancer (OC), Lymph node metastasis (LNM)

INTRODUCTION

Oral cavity cancer ranks among the most common malignancies worldwide. In the world, approximately 2,63,000 new cases of oral cancer are detected and 127,000 people die from the disease annually. In India, around 30% of cancers are oral squamous cell carcinoma (OSCC) and it accounts for almost 40% of deaths among all cancer.[1-3]

The most common sites of OSCC are the gingiva buccal sulcus of the mandible, followed by the tongue and floor of the mouth.[4] The most common cause is chewing tobacco (smokeless tobacco) and pan masala. It can be chewed or kept in the oral cavity, such as the gingiva buccal sulcus (GBS), leading to continuous exposure and constant irritation, eventually resulting in submucosal fibrosis over time.[5] The treatment and Prognosis are primarily determined by the tumour stage and lymph node status. Early-stage cancer and no metastasis (T1/2 N0 M0) tumors are associated with a favorable outcome. However, the prognosis for patients with early-stage

How to cite this article
Dhatrak S, Fegade L, Nesargi A, Borkar A. Incidence of Lymphovascular Emboli, Perineural Invasion and Lymph Node Spread with Relation to Tumour Grading in Oral Cancer Specimen in Konkan Region. SSR Inst Int J Life Sci., 2024; 10(4): 5900-5906.

Access this article online
https://iijls.com/

DOI: 10.21276/SSR-IIJLS.2024.10.4.16

OSCC is heterogeneous.[6,7] Among different clinical and histological parameters nodal metastasis is a well-known histological risk factor such as lymphovascular emboli (LVE) and perineural invasion (PNI). However, evaluating LVE and PNI is challenging, especially in small biopsies. A higher risk of LN metastasis and poor disease-free survival is associated with an invasive pattern of infiltration.[2,8] Lymph node metastases occur in about 40% of oral cancer patients, predominantly affecting males over 60 years old with an incidence of 75%. Unlike many other types of cancer, oral cancer characteristically metastasizes to the regional lymph nodes through the draining lymphatics in the early stages. Moreover, the hematogenous spread of cancer may originate from tissues outside the head and neck region. Lymph node involvement is considered the first indication of spread and a strong prognostic factor. Currently, patients with lymph node metastasis achieve a 5-year survival rate of only 25%-40%, whereas patients without metastasis typically achieve approximately 90% survival. In recent years, the incidence of metastasis has been observed to increase, possibly due to the development of new and highly sensitive detection methods like immunohistochemistry and molecular analysis.[9,10] This study was conducted to investigate the incidence of lymphovascular emboli, perineural invasion, and lymph node status about tumor grading in oral cancer (Hemimandibulectomy) specimens in the Konkan region.

MATERIALS AND METHODS

Study setting- A tertiary care hospital.

Study design- Observational cross-sectional study.

Study period- Record of specimens in the Histopathology department from January 2021 to June 2023.

Methodology- The study was carried out in compliance with protocol in the department of histopathology and tumour differentiation data was retrieved from the histopathology registry for 3 years. After staining slide was observed under a microscope. The tissue was processed using paraffin wax processing, which consists of the following steps-

- ✓ Tissue Processing
- ✓ Embedding, Section Cutting
- ✓ H And E Staining

Inclusion Criteria- Hemimandibulectomy specimen with oral cancer cases with regional lymph nodes including all ages, both male and female.

A total of 96 patients were included in this study. All demographic and clinical characteristics were recorded from the case record forms of patients maintained in an electronic database. Data on DOI, tumor characteristics, clinical N-classification, LVI, and PNI were reviewed.

Exclusion Criteria- Biopsy specimen of buccal mucosa, hemimandibulectomy specimen with no tumour.

Statistical Analysis- Patient characteristics were compared between the two LN groups (lymph node-positive and lymph node-negative). All data was compiled in Microsoft Excel and represented as frequency and percentage.

Ethical Approval- The study was approved by the Institutional Ethical Committee (BKLWRMC/LEC/104/2022 dated 29/08/2023).

Fig. 1: Hemimandebulectomy specimen for growth involving alveolus and buccal mucosa

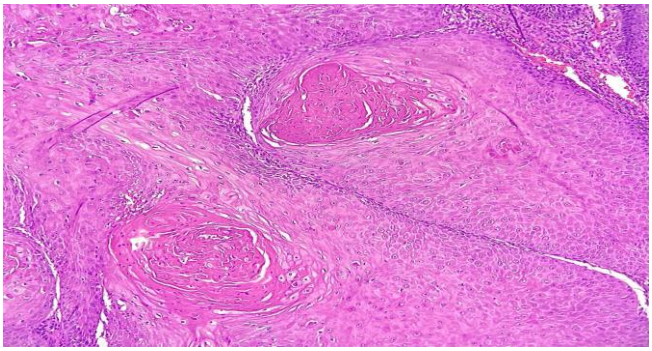

Fig. 2: Well-differentiated squamous cell carcinoma-showing epithelium shows marked keratinization and minimal nuclear pleomorphism with multiple keratin pearls (4X,40X, H&E stain)

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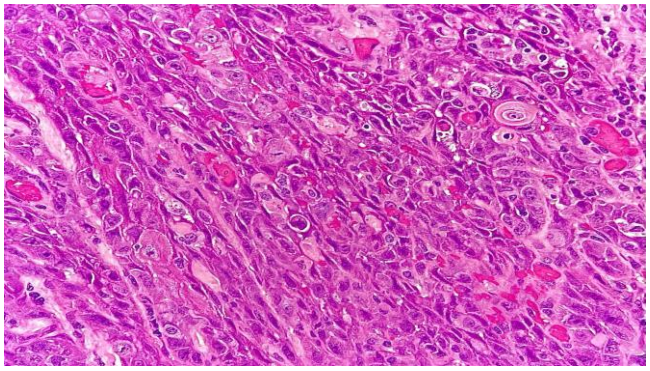

Fig. 3: Moderately differentiated squamous cell carcinoma: showing more obvious pleomorphism, but the squamous nature of the tumor remains apparent. (4X, 40X, H&E stain)

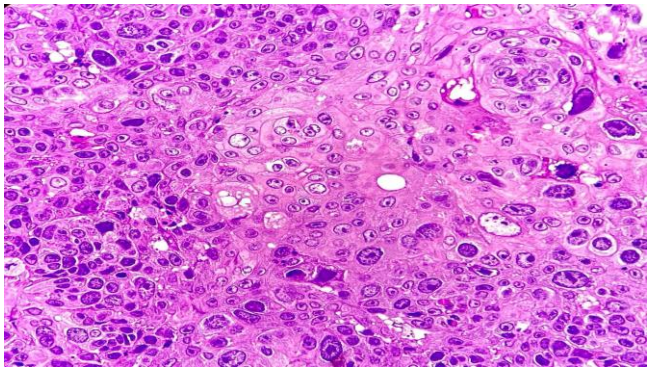

Fig. 4: Poorly differentiated squamous cell carcinoma: tumor cells arranged in sheets showing marked pleomorphism, hyperchromasia without keranization. (40X, H&E stain)

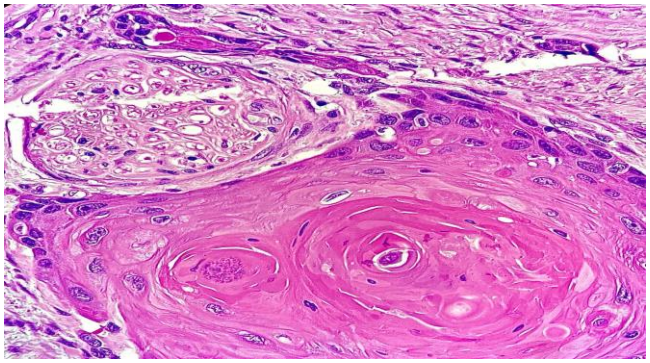

Fig. 5: Perineural invasion by malignant squamous cells (40X, H&E stain)

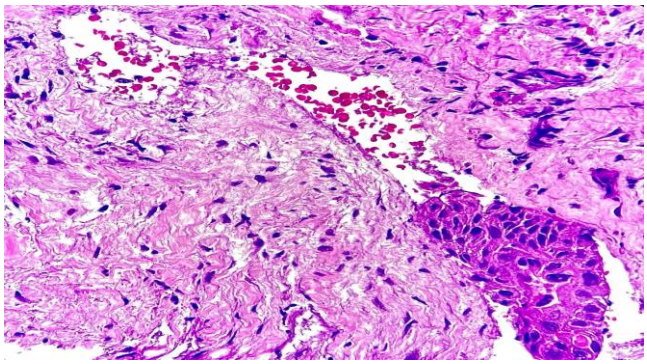

Fig. 6: Lymphovascular emboli as the presence of neoplastic structures inside the lumen of a vessel (40X, H&E stain)

RESULTS

The study was conducted on 96 samples of mandibulectomy. Fig. 7 shows the largest number of patients in the present study were seen in the age group of 50-60 years with male predominance. Out of 96 cases, 49.0% LVE was present, 51.0% LVE was absent, 46.90% PNI was present, 53.10% PNI was absent, 36.5% LVE & PNI Present, 32.4% LVE & PNI Absent. This shows that in the present study, maximum Cases (53.10 %) show PNI absent.

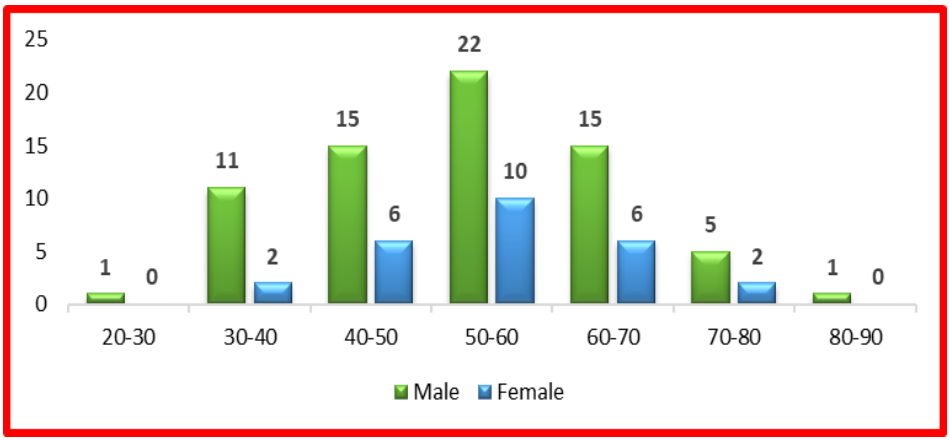

Fig. 7: Distribution of cases according to age and gender (Number)

Fig. 8 shows a total number of cases 96 out of which 68.80% cases were well differentiated SCC, 18.80% were well to moderately differentiated SCC, 6.30% cases were moderately differentiated SCC, 3.10% were poorly differentiated SCC, 2.10% were superficial micro invasive and 1% was micro-invasive. This shows that maximum cases were well-differentiated.

DOI: 10.21276/SSR-IIJLS.2024.10.4.16

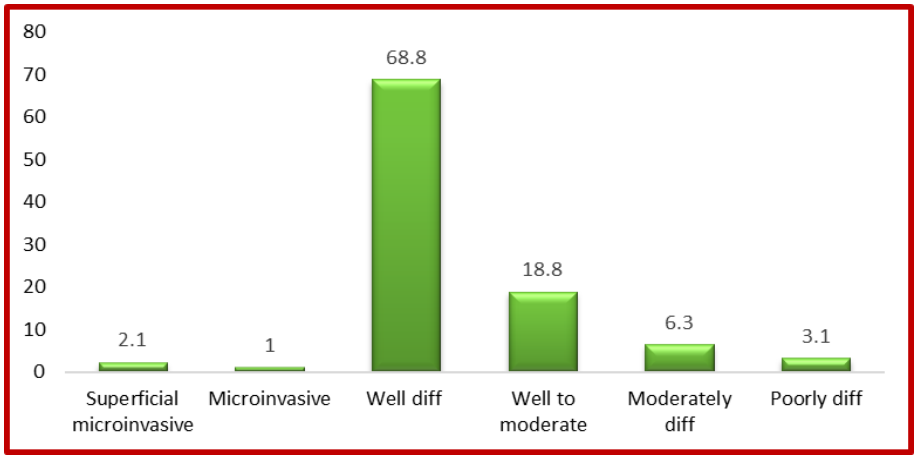

Fig. 8: Grading Wise Distribution of specimens (%)

Fig. 9 shows that in the present study, well-differentiated tumour cases were 66, out of these in 31 cases LVE was present and in 30 cases PNI was present. Well to moderately differentiated tumour cases were 18, out of these in 11 cases LVE was present and in 11 cases PNI was present. Moderately differentiated tumour cases were 02 and in a single case LVE and PNI were present. Poorly differentiated tumour cases were 03, out of these in 02 cases LVE was present and in 02 cases PNI was present. A single microinvasive tumour case shows no presence of LVE and PNI. Superficial microinvasive tumour cases were 02 and none showed LVE and PNI presence.

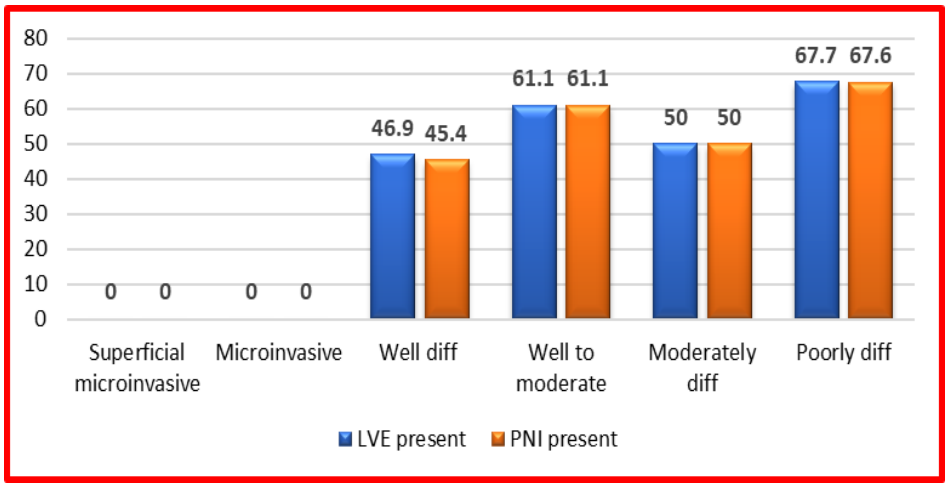

Fig. 9: Distribution of LVE & PNI (%)

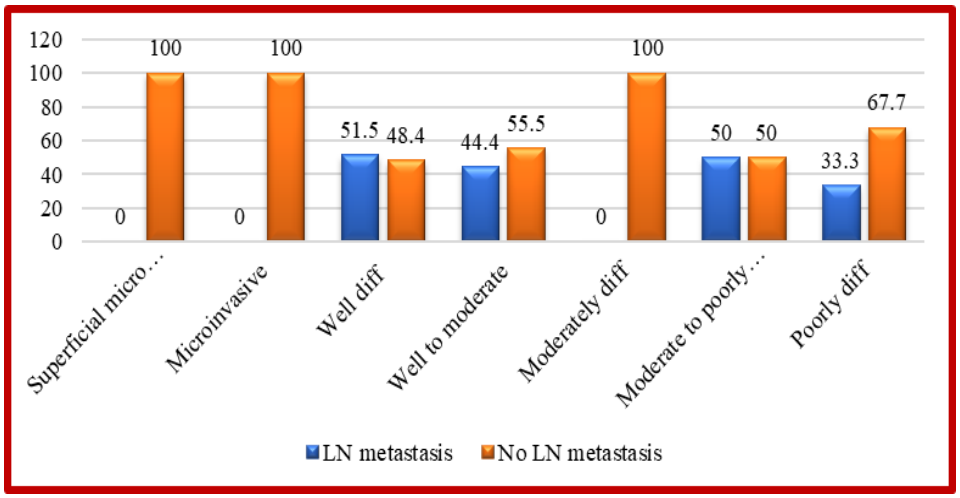

Fig. 10: Distribution of lymph node metastasis (%)

DOI: 10.21276/SSR-IIJLS.2024.10.4.16

Fig. 10 shows that in the present study well-differentiated tumour cases were 66, out of these 34 (51.5%) cases show lymph node metastasis and 32 (48.4%) cases show no lymph node metastasis. Well to moderately differentiated tumour cases were 18, out of these 08 (44.4%) cases show lymph node metastasis and 10 (55.5%) cases show no lymph node metastasis. Moderately differentiated tumour cases were 02 and both cases were free of lymph node metastasis. Moderately to poorly differentiated tumour cases were 04, out of these 02 (50%) cases showed lymph node metastasis and 02 (50%) cases were without lymph node metastasis. Poorly differentiated tumour cases were 03, out of these 01(33.3%) cases show lymph node metastasis and 02 (67.6%) without lymph node metastasis. Single microinvasive tumour case is without lymph node metastasis.

DISCUSSION

Squamous cell carcinomas of the oral cavity are one of the most common causes of morbidity in developing countries like India with more prevalence among males.[11] Our study found that there were 69% male patients and 31% female patients. A similar study was conducted by Sekhar *et al.* out of 90 patients 75.55% of male patients and 24.44% of female patients [12] while Pandey *et al.* study, out of 25 patients 68% of male patients and 32% of female patients [13]. In Saini *et al.* Study, out of 127 patients 77% of male patients and 23% of female patients [14] and Bhattacharjee *et al.* study out of 83 patients 57.5% of male patients and 46.33% of female patients [15].

In our study, the largest number of patients (34%) were in the age group of 50-60 years followed by 60-70 years and 40-50 years (22%) Singh *et al.* [16] also found the maximum number of cases (25%) in 50–60-year age group followed by 40–50-year age group (24%). Alshami *et al.* [17] found significantly higher cases above 40 years of age compared to less than 40 years. We also found 64% of cases above 40 years.

Our study's most common site of oral cancer was buccal mucosa and gingivo buccal sulcus. In Western countries most common site is the tongue and floor of mouth but in India the buccal mucosa and gingivo buccal sulcus are common site due to habit of keeping tobacco and other tobacco products there.[18] Singh *et al.* also found most common site was also buccal mucosa and gingivo buccal sulcus. [16]

In the present study, Lymphovascular emboli (LVE) was present in 49% and Perineural invasion (PNI) was present in 46.9% of cases. Sekhar *et al.* [12] found LVE in 57.77% and PNI in 31.33% of cases. As compared to Beumer *et al.* study LVE was present in 20% and PNI was present in 63% of cases [19] while Chatterjee *et al.* study LVE was present in 10.31% and PNI Present in 18.25% of cases [20]. In present studies, tumour with well-differentiated cases were 68.75%, moderately differentiated were 2% and poorly differentiated cases were 3.12%. As compared to Beumer *et al.* study well differentiation cases were 50%, moderately were 40% and poorly differentiated cases were 10% [19]. As compared to Chatterjee *et al* study well differentiation cases were 7.94%, moderately were 29.37% and poorly differentiated cases were 0.79% [20]. Compared to Al-Rawi *et al.* study well differentiation cases were 70.73 %, moderately were 12.92% and poorly differentiated cases were 9.22% [21].

CONCLUSIONS

Oral cancer was more common in male (69%) patients as compared to female (31%). Age groups of 50 - 60 years were highly affected compared to other age groups. Maximum cases 68.80% were found to be of well-differentiated OSCC followed by well to moderately differentiated 18.80% then moderately differentiated 6.30% and poorly differentiated 3.10%. Total lymph node-positive cases were 44 (45.8%), and maximum cases were from the age group of 40 - 60 yrs. A total of 45 (46.8%) cases shows lymphovascular emboli and 44 (45.8%) cases show perineural invasion. After this study, we propose that the meticulous hunt for LVE and PNI on routine H&E slides becomes the mainstay and important sensitive marker for metastasis and overall prognosis of the patients. The classification of patients with OSCC based on the TNM staging system combined with LVE and PNI may be more comprehensive and accurate. Further studies with larger sample sizes are warranted to confirm our findings, preferably with prospective designs.

CONTRIBUTION OF AUTHORS

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Research design- Lokesh Fegade, Avinash Borkar

DOI: 10.21276/SSR-IIJLS.2024.10.4.16

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Data analysis and Interpretation- Avinash Borkar, Swapnali Dhatrak, Lokesh Fegade
Literature search- Swapnali Dhatrak, Lokesh Fegade, Aditya Nesargi
Writing article- Avinash Borkar, Lokesh Fegade, Swapnali Dhatrak
Critical review- Avinash Borkar, Lokesh Fegade
Article editing- Avinash Borkar, Lokesh Fegade, Swapnali Dhatrak
Final approval- Swapnali Dhatrak, Lokesh Fegade, Aditya Nesargi, Avinash Borkar

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