



EXPLORING THE PREVALENCE AND CLINICOPATHOLOGICAL LANDSCAPE OF ORAL NON-HODGKIN LYMPHOMA: A COMPREHENSIVE SINGLE-CENTER RETROSPECTIVE ANALYSIS

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ABSTRACT

Objective: Our retrospective study aimed to determine the prevalence of Non-Hodgkin's lymphoma (NHL) in the oral cavity of patients referred to our medical facility.

Materials and Methods: This research is a retrospective single-centre 10-year study comprising 50 cases conducted at Saraswati Dhanwantari Dental College and Hospital, Postgraduate Research Institute, Parbhani, India, between September 2013 and September 2023

Results: Over 10 years, 50 patients (29 male and 21 female) were diagnosed with primary NHL of the oral cavity. The most common oral cavity site is buccal mucosa (twelve patients). 90% of patients presented with swelling. Among the different types of lymphomas observed during the study, diffuse large B-cell lymphoma was the most common subtype, accounting for 40% of all cases, followed by Plasmablastic lymphoma (36%) Immunohistochemistry showed B-cell type CD20+ in 48% of patients, CD38+, CD 138+, Kappa +, MUM1+ in 36%, while T-cell type CD3+ was observed in only 16%. Regarding treatment, 40% of the patients underwent chemotherapy.

Conclusion: During the span of nearly two decades, our observations have shown a noticeable rise in oral Non-Hodgkin's Lymphoma (NHL) cases. In the case of oral non-Hodgkin's lymphoma (NHL), conducting a comprehensive evaluation is of utmost importance to prevent incorrect or late diagnosis.

Keywords: Oral Cancer, Non-Hodgkin Lymphoma, Extranodal site, Diffuse large B cell lymphoma, Plasmablastic lymphoma.

INTRODUCTION

Lymphoma is the second most common malignant lesion in the head and neck, following only squamous cell carcinoma [1]. Lymphoma can be classified into two distinct types - Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL).

Hodgkin's lymphoma typically presents as a nodal disease, with a particular preference for neck and mediastinal nodes. Non-Hodgkin's lymphoma, on the other hand, can occur up to 40% of the time at an extranodal site, with 2-3% of these cases arising primarily in the oral cavity and jaws [2-4]. Oral lymphoma presents in two forms, either as a localised primary extranodal disease in the oral cavity or jaws or as part of a disseminated disease that affects regional lymph nodes [5].

Diagnosing the underlying cause requires considering several factors, including gram stain, fungal stain, culture, and histopathologic examination of biopsy specimens and immunohistochemistry studies [6,7]. The incidence



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of NHL affecting the oral cavity is infrequent. The oral cavity constitutes only 2% of all extranodal lymphomas. Non-Hodgkin lymphoma (NHL) is a malignancy that arises predominantly from B lymphocytes, with only a minority of cases originating from T lymphocytes or natural killer cells [8,9]. NHL typically presents with diverse extranodal manifestations, and intraoral NHL explicitly affects the oral cavity's soft tissues, including the palatal mucosa, gingiva, tongue, cheek, floor of the mouth, and lips [10-14]. Non-Hodgkin lymphoma (NHL) is a cancer without fully understood cause [15]. NHL, or non-Hodgkin's Lymphoma, is a type of cancer and risk factors can be attributed to multiple environmental factors that include exposure to certain chemicals and radiation, as well as viral infections like Epstein-Barr virus, human immunodeficiency virus (HIV), hepatitis B and C virus (HBV and HCV), and autoimmune disorders such as rheumatoid arthritis, Sjogren's syndrome and systemic lupus erythematosus. These are potential risk factors for developing non-Hodgkin's lymphoma (NHL) [16,17]. Our retrospective study sought to establish the prevalence of Non-Hodgkin's lymphoma (NHL) in the oral cavity among patients referred to our medical facility between September 2013 and September 2023.

MATERIALS AND METHOD

This research is a retrospective single-centre 10-year study comprising 50 cases conducted at Saraswati Dhanwantari Dental College and Hospital, Postgraduate Research Institute, Parbhani, India, between September 2013 and September 2023. The study aimed to investigate oral lymphoma in patients with oral masses and a primary diagnosis. The study consisted of a meticulous analysis of patient case records to extract data on age, gender, symptoms, mass location within the oral cavity, immunohistochemistry report, EBV, and retroviral positivity status.

RESULTS:

Over 10 years, 50 patients (29 male and 21 female) were diagnosed with primary NHL of the oral cavity. The oral cavity sites involved were as follows: Tongue (eight patients), Buccal mucosa (twelve patients), Palate (seven patients), Gingiva (two patients), Cheek (four patients), Maxilla (eleven patients), Mandible (six patients). Most patients presented with swelling or mass gradually increasing in size (90%), while 50% had ulcerations. Among the different types of lymphomas observed during the study, diffuse large B-cell lymphoma was the most common subtype, accounting for 40% of all cases as depicted in Fig 1. Plasmablastic lymphoma was the second most

common subtype, constituting 36% of cases as depicted in Fig 2.

Other less common subtypes included Anaplastic large cell lymphoma (8%) as depicted in Fig 3, Burkitt lymphoma (2%), follicular lymphoma (2%), small lymphocytic lymphoma (4%), and Angioimmunoblastic T cell lymphoma (8%) as depicted in Fig 4.

All patients were diagnosed with NHL based on histopathological analysis, which revealed nuclear pleomorphism and altered N: C ratio in all cases. Immunohistochemistry showed B-cell type CD20+ in 48% of patients, CD38, CD 138+, Kappa +, MUM1+ in 36%, while T-cell type CD3+ was observed in only 16%. Regarding treatment, 40% of the patients underwent chemotherapy, 20% received combined chemotherapy and radiotherapy, and the remaining 40% of the patient data regarding treatment was unavailable. The serological analysis revealed that 9 HIV+ patients (18%) and 5 EBV+ patients (10%) had positive results. Out of the 30 patients, only 25 survived while 05 died, and the five-year survival data is available for this limited group. Please refer to the accompanying table 1 for more information.

DISCUSSION

The most common method for identifying non-Hodgkin lymphomas (NHLs) is to perform a biopsy on an enlarged lymph node or mass [18,19]. Extranodal non-Hodgkin lymphoma occurs most frequently in the gastrointestinal tract, but the head and neck are the second most commonly affected areas [20,21]. Malignant lymphomas tend to affect extranodal sites, with Waldeyer's tonsillar ring and cervical lymph nodes being the most common locations [22]. Other frequently affected areas include the nose, paranasal sinuses, orbits, and salivary glands. Although squamous cell carcinoma accounts for approximately 90% of all malignancies, primary lymphomas of the oral cavity, which make up only 3% of all lymphomas in the general population, are becoming more prevalent [23,24]. Studies on NHL distribution have observed a slight male predominance, with a male-to-female ratio of 1.36:1, as per literature [25-27]. Patients with oral NHLs commonly report swelling or pain as their initial symptom. In a cross-sectional study that included a sizable population, Iguchi et al. reported that lymphomas accounted for 14% of all malignancies observed in the head and neck area. Among these, non-Hodgkin lymphoma (NHL) represented 97% of the cases, with a notable proportion of extranodal manifestations. The intraoral localisation of NHLs can affect hard and soft tissues, such as the tongue, gingiva, buccal mucosa, cheek, floor of the mouth, lips, palate, and bones [28,29]. Non-Hodgkin's lymphomas (NHLs)

situated in the intraoral region can affect various hard and soft tissues such as the tongue, gingiva, buccal mucosa, cheek, floor of the mouth, lips, palate, and bones. A retrospective study observed that soft tissues were more commonly affected than hard tissues, with the buccal mucosa being the most frequently affected area, followed by uncommon locations such as the tongue, gingiva, and cheek. A study conducted by Tseng et al. [30] observed 607 cases of oral lymphoma and concluded that the gingiva was the most common area affected. However, other regions such as the palate, maxilla, mandible, tongue, buccal mucosa, lip, and floor of the mouth were also frequently affected. Oral NHL is rare, but its diagnosis is often delayed due to non-specific clinical signs such as pain, discomfort, local swelling, ulcers, gingival oedema, and tooth mobility [31]. These signs can also be related to other oral diseases, such as endodontic infection, periodontitis, osteomyelitis, autoimmune diseases, and other malignant lesions [32,33]. The delay in diagnosis often results in incorrect treatment plans. NHL affects 4% to 10% of HIV patients; its cause is still unknown. However, recent studies suggest a possible link between NHL and immunodeficiency conditions. HIV-related patients have a higher incidence of oral NHL due to systemic complications.

Out of the patients in Non-Hodgkin's Lymphoma group, it was discovered that six patients had Epstein-Barr Virus while five others had Human Immunodeficiency Virus. The remaining patients had varying causes of immunosuppression. The diagnosis of Non-Hodgkin's Lymphoma is determined by examining histologic specimens and is primarily linked to B-cell lineage. The most common histopathological subtypes observed were diffuse large B-cell lymphoma and plasmablastic lymphoma. The use of chemotherapy alone or in combination with radiotherapy had a beneficial outcome, as evidenced by the 5-year overall survival rate of 60% reported in the study [34].

CONCLUSION

During the span of nearly two decades, our observations have shown a noticeable rise in oral Non-Hodgkin's Lymphoma (NHL) cases despite the rarity of such cases in the oral cavity. In the case of oral non-Hodgkin's lymphoma (NHL), conducting a comprehensive evaluation is of utmost importance to prevent incorrect or late diagnosis. The disease can manifest with non-specific symptoms such as tooth mobility, bleeding, and mucosal ulcerations. The literature suggests that the B-cell form of oral NHL is more prevalent and may cause swelling accompanied by pain and discomfort. Further research is needed to determine the characteristics and prevalence of NHL in the oral cavity.

Abbreviations

EBV: Epstein Barr virus
HIV: Human Immunodeficiency virus
NHL: Non-Hodgkin's Lymphoma
HL: Hodgkin's Lymphoma

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Ethics Approval and Consent to Participate: The study was approved by the Ethics Committee of Saraswati Dhanwantari Dental College and Hospital, Post Graduate Research Institute, Parbhani, Maharashtra, India.

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Consent for Publication: Not applicable.

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Legends

Figure 1: Diffuse large B cell lymphoma: A. Histopathology shows lymphoma cells arranged in sheets, possessing large nuclei and distinct nucleoli. B. Immunostaining for CD 20 is positive on the cell membrane of lymphoma cells.

Figure 2: Plasmablastic lymphoma: A. The histopathological analysis reveals large lymphoma

cells exhibiting amphophilic cytoplasm and prominent nucleoli.

B. Immunostaining for CD 138 is positive on the cell membrane of lymphoma cells.

C. Immunostaining for MUM1 is positive on the nucleus of lymphoma cells.

Figure 3: Anaplastic large cell lymphoma: Histopathology shows small cells with irregularly folded nuclei admixed with occasional large blastic cells.

Figure 4: Angioimmunoblastic T cell lymphoma: A. The histopathological analysis reveals the presence of prominent venules along with a mixture of lymphoid cells, including clear cells, eosinophils, and plasma cells in the background.

B. Immunostaining shows, atypical cells are stained by CD3.

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Table 1: Analyzing variables in oral NHL cases

Features	cases	Percentage
<u>Gender</u>		
Male	29	58%
Female	21	42%
<u>Age</u>		
0-10	0	0
11-20	0	0
21-30	03	06%
31-40	12	24%
41-50	16	32%
51-60	17	34%
61-70	01	02%
71-80	01	02%
<u>Site</u>		
Tongue	08	16%
Buccal Mucosa	12	24%
Palate	07	14%
Gingiva	02	04%
Cheek	04	08%
Maxilla	11	22%
Mandible	06	12%
<u>Signs and symptoms</u>		
Swelling	45	90%
Ulceration	25	50%

Pain	32	64%
Paresthesia	08	16%
Difficulties in swallowing	37	74%
Tooth mobility	05	10%
Mucosal bleeding	06	12%
<u>Microscopic features</u>		
Nuclear pleomorphism	50	100%
Altered N: C ratio	50	100%
Mitosis	31	62%
Perivascular invasion	18	36%
<u>Histopathological diagnosis</u>		
Diffuse large B-cell lymphoma	20	40%
Plasmablastic lymphoma	18	36%
Burkitt lymphoma	01	02%
Follicular lymphoma	01	02%
Anaplastic large cell lymphoma	04	08%
Small lymphocytic lymphoma	02	04%
Angioimmunoblastic T cell lymphoma	04	08%
<u>Immunohistochemistry CD3/CD20</u>		
Bcell type CD20+, CD38+, CD 138+, Kappa +, MUM1+	24	48%
Tcell type CD3+	18	36%
	08	16%
<u>Serological test</u>		
Ebstein Barr virus	05	10%
HIV(Human Immunodeficiency virus)	09	18%
<u>Treatment</u>		
Chemotherapy	20	40%
Chemotherapy+ Radiotherapy	10	20%
Not available	20	40%
<u>Outcome</u>		
Alive	25	50%
Died	05	10%
Not available	20	40%

Figure 1

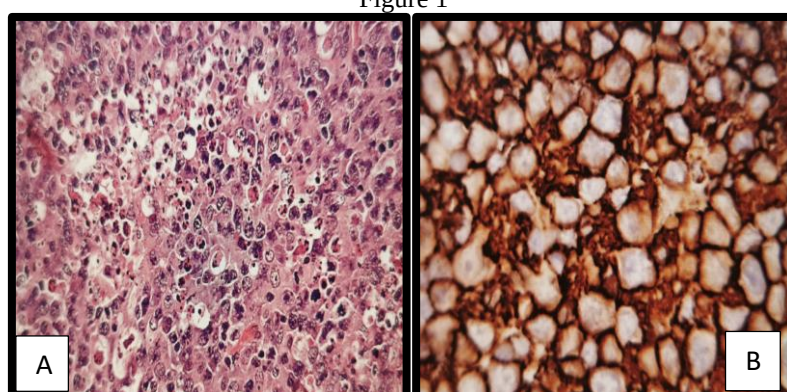


Figure 2

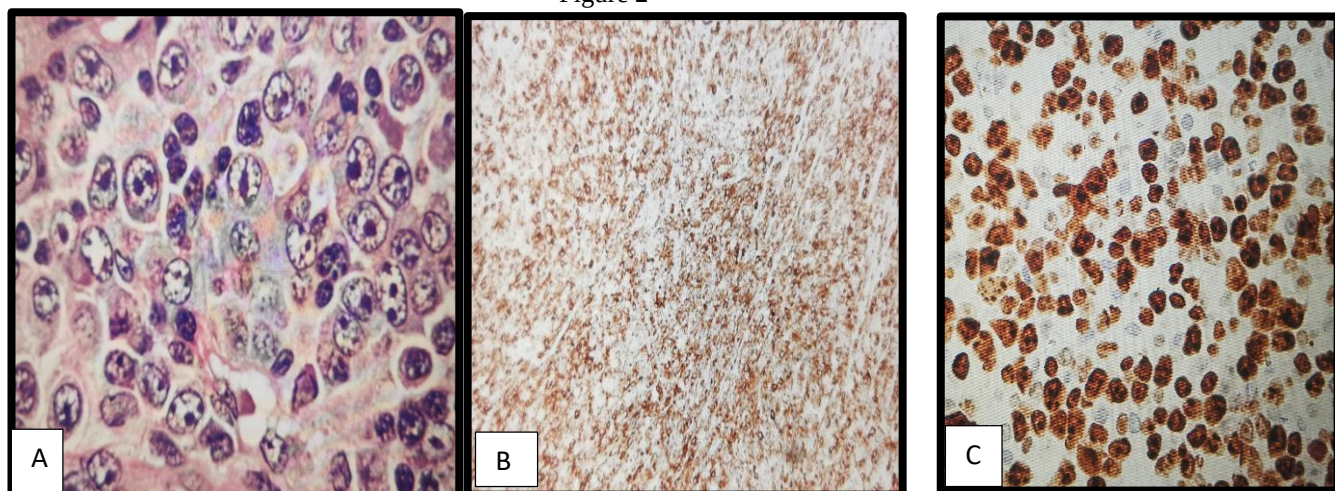


Figure 3

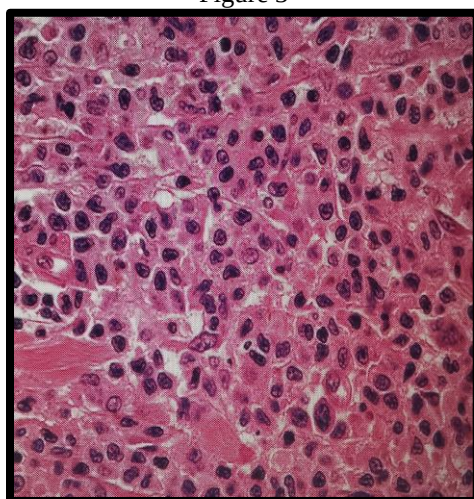


Figure 4

