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The Pattern of Orofacial Lymphoma and Their Histopathologic Subtypes Among Children in a Tertiary Hospital in Southern Nigeria

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Abstract

Background: Lymphomas are heterogeneous group of malignant tumours of the hematopoietic system and are characterized by the aberrant proliferation of mature lymphoid cells or their precursor. Lymphoma of the orofacial region constitute one of the commonest malignancies in childhood.

Objective: To determine the frequency and pattern of lymphomas and the different histopathological subtypes in the orofacial region in Nigerian children.

Method: A retrospective study of all histopathologically diagnosed lymphomas of the orofacial region in children of 16years and below seen within a 15-year period, (2008 to 2022). Data were retrieved from the archives of the Department of Oral and Maxillofacial Pathology and Medicine, University of Benin Teaching Hospital, Benin City, for statistical analysis.

Results: Overall, a total of 105 neoplastic lesions were seen in children within the study period. Lymphoma constituted 32.4% (n = 34) and were the most frequent of all the neoplasms. Of the Lymphomas, there were 25 (73.5%) males and 9 (26.5%) females with a male to female ratio of 2.8:1. The histopathologic types of lymphoma were non-Hodgkin's lymphoma (NHL). The subtypes were the Burkitt's lymphoma type (22; 64.7%), the diffused NHL lymphoma (11; 32.4%) and the follicular lymphoma (1; 2.9%).

Conclusion: Orofacial lymphoma among children in Southern Nigeria were mostly seen in males with the mandible been the commonest site. All the cases of orofacial lymphoma were NHL with Burkitt lymphoma as the commonest subtype.

Keywords: *Burkitt's lymphoma, Hodgkin's lymphoma, Malignancy, Orofacial lymphoma, Histopathological subtypes.*

Introduction

Lymphomas are heterogeneous group of malignant tumours of the haematopoietic system and are characterized by the aberrant proliferation of mature lymphoid cells or their precursor.¹ It is the third most common malignancy worldwide

representing 3% of all malignant tumours² and the third most common malignant lesions of the orofacial region.³ Studies done in different parts of Nigeria showed lymphomas constitute the most common group of childhood malignancies

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and also the commonest orofacial malignancies in paediatric patients.^{4,5}

The aetiology of lymphomas has not been fully elucidated but some risk factors have been highlighted; viral infections have been listed as the major cause within Africa than the rest of the world.⁶ Over thirty (30) subtypes of lymphomas have been identified and several classifications have been developed over the years for lymphomas. The currently used classification (2016) is that of the World Health Organization (WHO) and is based on the principles of the Revised European-American Classification of Lymphoid Neoplasm (REAL) from 1994. This scheme classified lymphomas into two broad types: Hodgkins (HL) and Non-Hodgkin's (NHL). The NHL is further subtyped based on cells of origin as: B-cells (Burkitt's lymphoma), T-cells and natural killer cell (lymphoblastic lymphoma, anaplastic large cell lymphoma).⁷ HLs frequently involve lymph nodes of the neck and mediastinum, whereas extranodal sites account for only 5% (for example in the tonsils), while NHLs of the orofacial region frequently affect extranodal sites such as major salivary glands, paranasal sinuses, mandible, maxilla and Waldeyer's ring, all affecting 11–33% of patients.⁸

Lack of specific clinical characteristics of lymphoma is always a challenge in determining diagnosis without histopathological examination.⁹ Due to the increase in the incidence of malignancies in recent years, lymphomas have become one of the most common malignancies, particularly in young children, as shown in the studies done in western and northern parts of Nigeria,^{4,10} hence this study aimed to determine the frequency and pattern of lymphoma in the orofacial region and the different subtypes among Nigerian children.

Methods

This is a retrospective study of all histopathologically diagnosed lymphomas of the orofacial region in patients of age 16 years and below over 15-years, (from January 2008 to December 2022). The histopathologic reports were retrieved from the archives of the Department of Oral and Maxillofacial Pathology and Medicine, University of Benin Teaching Hospital, Benin City, Nigeria. The age ranged from 0-16 years and they were grouped into age groups: 0 – 4 years, 5 – 8 years, 9 – 12 years and 13 – 16 years. Data such as age, gender, site and histopathologic type and subtypes were entered into IBM SPSS 21 for a descriptive analysis.

Results

A total of 105 orofacial neoplastic lesions were seen in children within the study period among which malignant lesions accounted for 46.7% (n = 49). The malignant lesions included lesions such as lymphoma, squamous cell carcinomas, adenocarcinomas, malignant fibrous histiocytoma and rhabdomyosarcoma while the benign lesions included lesions such as benign odontogenic tumours, central giant cell granuloma, haemangioma, lymphangiomas, and lipomas. Lymphoma constituted 32.4% (n = 34) of all the neoplastic lesions and 69.4% of all the malignant lesions. It was followed by epithelial malignancies (14.3%; n = 7).

There were 25 males (73.5%) and 9 (26.5%) females with a male to female ratio of 2.8:1. The mean age was 7.92±3.28 years. The cases were more frequent in the 5 to 8 years age group (n = 19; 55.9%) (Table I). The mandible (n = 13; 38.2%) was the most affected site (Table II). The histopathologic type of lymphoma recorded was the non-Hodgkin's lymphoma (Table III). The subtypes seen were the Diffuse NHL lymphoma (n = 11; 32.4%) [Figures 1 and 2], the Burkitt's lymphoma type (n = 22, 64.7%) [Figure 3] and the follicular lymphoma in 1 case (2.9%).

Table I. Age distribution of the histopathologically diagnosed orofacial childhood lymphoma cases

Age (years)	Frequency (%)
0 – 4	7 (20.6)
5 – 8	19 (55.9)
9 – 12	7 (20.6)
13 – 16	1 (2.9)
Total	34 (100)

Table II Site distribution of the histopathologically diagnosed orofacial childhood lymphoma cases

Site	Frequency (%)
Cheek	1 (2.9)
Face	5 (14.7)
Gingival	1 (2.9)
Mandible	13 (38.2)
Multiple sites	6 (17.6)
Maxilla	7 (20.6)
Palate	1 (2.9)
Total	34 (100)

Table III: The histological types of the orofacial childhood lymphomas

Histopathologic Subtypes	Frequency (%)
Burkitt's lymphoma	22 (64.7)
Diffuse B cell NHL lymphoma	11 (32.4)
Follicular lymphoma	1 (2.9)
Total	34 (100)

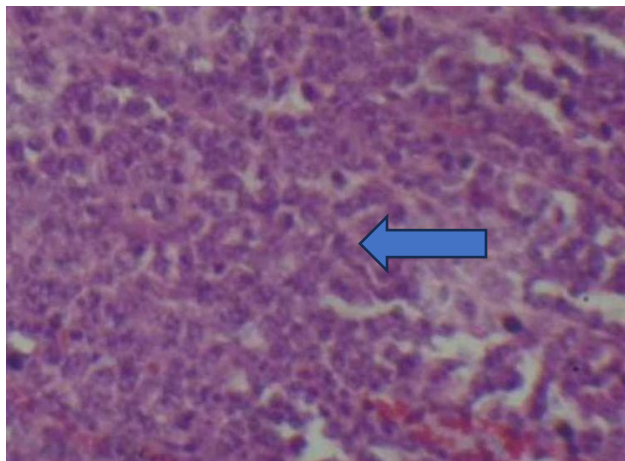


Figure 1: Diffuse Non-Hodgkins Lymphoma. Photomicrograph showing sheets of atypical lymphocytic cells within a loose fibrous connective tissue stroma (H&E x100).

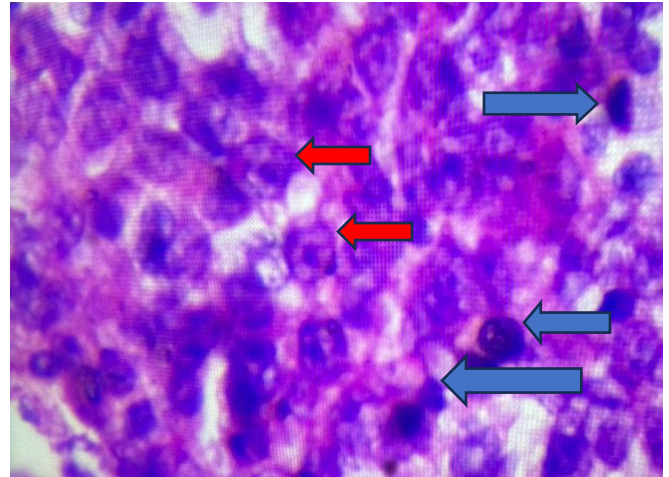


Figure 2: Diffuse Non-Hodgkins Lymphoma, A high power photomicrograph showing sheets of atypical lymphocytes characterized by pleomorphism, vesicular nuclei, prominent nucleoli (red arrow) and mitotic figures (blue arrow) within a loose stroma. (H&E x400)

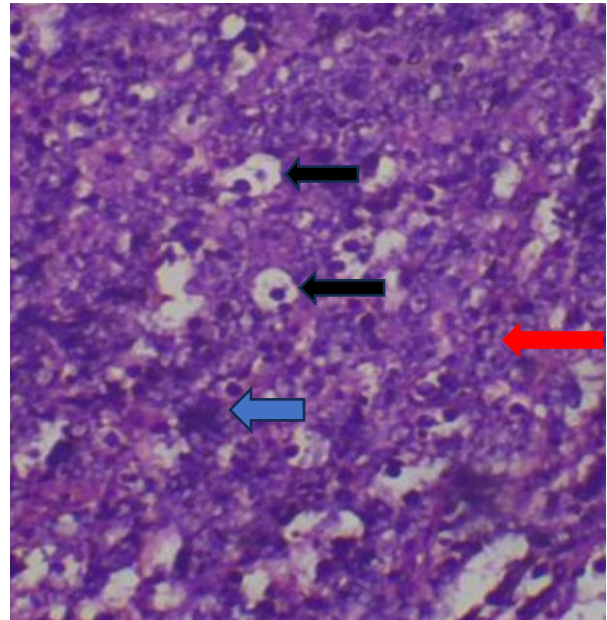


Figure 3: Burkitt's lymphoma. Photomicrograph showing sheets of atypical lymphocytes (red arrow) with tangible body macrophages (black arrow) giving a starry sky appearance. There are mitotic figures and abnormal mitosis (blue arrow) within the tumour cells (H&E x100).

Discussion

Orofacial lymphomas were observed as the most common orofacial malignancy among children in this present study. This is in consonant with studies done by Akinyele *et al.*⁴ and Arboleda *et al.*¹¹ On the other hand, this is contrary to the study by Okoturo *et al.*¹² which showed that epithelial malignancies were the commonest orofacial malignancies in children. This study showed male predilection of orofacial lymphomas among children and this have been observed in previous similar studies in children^{4,5,11} and the general population.^{2,12} Orofacial lymphomas occurred more frequently in children less than ten years of age in the present study and in the study by Akinyele *et al.*⁴ observed the highest occurrence in the 6-10years age group.⁴ The study by Okoturo *et al.*⁵ observed the highest incidence in the 10-14 years age group. Hodgkin's lymphomas (HL) rarely occur in children less than 5 years.¹² Although no case of HL was seen in this study, studies have reported that orofacial HL rarely occur in children,^{5, 12} especially in children aged less than 5 years.⁴

Clinical manifestations of orofacial lymphomas are not specific and the manifestations depend on the site, histological type and stage of the tumour at diagnosis.³ Localization of orofacial lymphomas have been described differently depending on the frequency observed by different authors. Zucca *et al.* stated that two-thirds of lymphomas in the orofacial region manifest as localized tumorous lesions or as part of generalized lymphadenopathy while the remaining third of cases are extranodal lymphomas, sometimes even originating from organs without lymphoid tissue.¹³ The study by Kararzyna *et al.* suggested that more than two-thirds of orofacial lymphoma involved extranodal sites and less than a third involved the cervical lymph nodes.¹⁴ Also, a systematic review by Silva *et al.* on oral manifestations of lymphomas revealed higher extranodal sites with the highest

frequency of occurrence in the tonsils, closely followed by the salivary glands; the maxilla, is the most affected bone of the orofacial region.¹⁵ Nevertheless, in the present study, orofacial lymphomas were mostly extranodal, with the higher incidence of occurrence in the mandibles.

Extranodal sites include both organs that housed lymphoid tissue (such as parotid, tonsils, base of the tongue) and those that housed no lymphoid tissue (such as paranasal sinuses, submandibular gland, nose, gingival, cheek). The histological types in relation to sites vary in the literature. Studies have shown that HL are mostly nodal,⁹ in more than 90% of cases with only 1-4% involving extranodal sites of the orofacial region,² while NHL is more frequent in extranodal sites with greater than 90% as reported by Storch *et al.*² On the other hand, the study by Kamiński observed NHL more frequently in the nodes than in extranodal sites.⁹ All the cases observed in this study were NHL and they were mainly extranodal.

For the histological subtype, Burkitt's lymphoma, which is a B-cell NHL was observed in the present study, as the commonest orofacial lymphoma among children. The B-cell type NHL had previously been reported as the commonest type of orofacial lymphomas.¹⁴ Some studies also observed diffused B-cell NHL have highest frequency of orofacial lymphomas generally^{15,16} but in young children, orofacial Burkitt lymphoma dominate.^{4,5,11} A systematic review of studies within Nigeria have shown that the jaw in orofacial region is the commonest site for Burkitt lymphoma followed by the abdomen.¹⁷ The jaws were also recorded the commonest sites in the present study.

Okoh *et al.* in a study of non-odontogenic orofacial tumours described Burkitt's lymphoma as a rapidly growing swelling in young patients characterized by expansile radiolucent jaw mass

and dental anarchy.¹⁸ Three variants of Burkitt lymphoma have been described sixty years ago by Denis Burkitt based on geographical location.¹⁹ The endemic variant has been associated with Epstein Barr virus and *Plasmodium falciparum* infection in malaria endemic regions like Nigeria and most of sub-Saharan Africa.²⁰ Though, Burkitt lymphoma is still the most common childhood malignancy in our region, a systematic review by Brown has shown a recent decline in its frequency which may be attributed to improved socioeconomic status and better malaria control.¹⁷

Conclusion

This study showed that orofacial lymphomas in children in our environment affected mostly male children and especially, those aged less than 10 years. The mandible was the most commonly involved site. NHL was the type seen and Burkitt lymphoma was the most common type of the NHL. This high frequency of lymphomas among childhood neoplastic diseases of the orofacial region shows the need for early biopsy of suspicious rapidly growing lesion for prompt diagnosis and early treatment.

Authors' Contributions: EJI, ODS and OPU conceived the study and curated the data. EJI and ODS analysed and interpreted the data. EJI, ODS and OOF did literature review and drafted the manuscript. All the authors revised the draft for sound intellectual content and approved the final version.

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