

Histopathological Pattern of Nasopharyngeal Malignancy in Lagos University Teaching Hospital (LUTH) Lagos Nigeria

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Abstract: It has been noticed that Nasopharyngeal cancer (NPC) is now found to be increasing in incidence in Nigeria. The objectives of this study are to determine the prevalence, histologic types, age and sex distribution of nasopharyngeal cancer in our centre.

A retrospective review of histologically-diagnosed cases of nasopharyngeal cancer at Anatomic and Molecular Pathology Department of Lagos University Teaching Hospital between January 2003 and December 2012, was carried out

A total of seventy five (75) histologically-confirmed cases of NPC were seen during the study period, which constituted 1.1% of the total cancer recorded at the centre. The male to female ratio was 1.7:1 while the age ranged from 3 to 75 years with the overall mean age of 44.1 years. The peak age of incidence was 40 - 49 and 50 – 59 years for males and females respectively.

The commonest presenting complaint was cervical lymphadenopathy (36.2%), then nasal blockage (22.3%) and epistaxis (16.0%) while the least common presentation was cranial nerve palsy (1.1%). Other symptoms seen were hearing impairment 6.4%, proptosis 5.3%, nasal discharge 4.3%, visual impairment 4.3%, ear pain 2.1% and weight loss 2.1%.

Nasopharyngeal carcinoma accounted for 82.6% of the total cases of the NPC seen. Undifferentiated nasopharyngeal carcinoma (WHO type III) constituted the commonest (49.3%) histologic type while differentiated non-keratinizing squamous cell carcinoma (WHO type II) and keratinizing squamous cell carcinoma (WHO type I) accounted for 24% and 9.3% respectively. Other types seen were non-Hodgkin lymphoma 13.3%, well differentiated adenocarcinoma 2.7% and low grade mucoepidermoid carcinoma 1.3%.

Conclusion: This study has shown that nasopharyngeal malignancy is not uncommon in our centre. Undifferentiated carcinoma was the commonest nasopharyngeal malignancy reported from this study. The cancer occurred more frequently in males than in females with the peak age of incidence at 5th decade of life.

Keywords – Lagos University Teaching Hospital (LUTH), Lagos Nigeria, Nasopharyngeal cancer, nasopharynx, undifferentiated nasopharyngeal carcinoma.,



1. INTRODUCTION

Nasopharyngeal cancer is fairly rare in most parts of the world [1]. Worldwide, there were an estimated 84,400 incident cases of nasopharyngeal malignancy and 51,600 deaths in 2008, representing about 0.7% of the global cancer burden [2]. The disease may be considered one of the rarer cancers globally, ranking as the 24th most frequently diagnosed cancer worldwide and 22nd within the developing world [2]. It accounts for less than 1% of malignancies in North America, Western Europe and Japan, with incidence rate of 1 to 1.5 cases per 100,000 populations per year [2]. This cancer is, however, more common in certain parts of Asia, particularly in South east China and North Africa [2].

In Southern China, particularly Hong Kong and Guangzhou (formerly known as Canton, and the capital of the province of Guangdong), there is a higher incidence, with documented rate of 10 to 150 cases per 100,000 population per year [2]. It is also more common among Inuit of Alaska, Canada and Greenland with the incidence rate of 15 to 20 cases per 100,000 population per year, similar rates were recorded among some immigrant groups in the United States, such as recent Chinese and Southeast Asian (non-Chinese like Hmong, Karen, Akha) ethnic immigrants [3], [4]. Descendants of Chinese who immigrated to Western countries have lower nasopharyngeal cancer incidence rates than do Chinese in Asia, but their rates remain higher than those of White populations in Western countries [2], [3], [5].

The malignancy has an intermediate incidence rate of 5 to 9 cases per 100,000 population per year in inhabitants of northern China, the Mediterranean basin (southern Italy, Greece and Turkey), North Africa and South east Asia (Thailand, Vietnam, Indonesia, Malaysia and Singapore), and in persons of southern Chinese heritage who were born in the West (Australia, Hawaii and California) [1], [2].

Thus, the geographic pattern of incidence of nasopharyngeal malignancy suggests an interaction between genetic and environmental factors [3], [4], [5].

The earlier surveys of cancer in the African continent suggested that nasopharyngeal malignancy was a rare disease as shown by the following studies; Gelfand [6] found no evidence of the disease in 334 cancer biopsies in Southern Rhodesia, now Zimbabwe. Shapiro et al [7] in a comparative survey of the European and Bantu population in the Transvaal, South Africa noted that this tumour was rare in the Bantu. Edington [8] in Gold Coast, now Ghana, reported only 14 cases in 1000 biopsies and 4395 autopsies. Davies [9] in a survey of malignant diseases in Uganda found no nasopharyngeal cancer (NPC) in a series of 531 cases recorded in Kampala cancer registry.

In follow up studies, Hou-Jensen and Martin [10] showed that the disease was occasionally seen in Uganda. Clifford and Linsell [11], [12] at two different periods reported that NPC is not rare in Kenya

accounting for 10% and 2-3% respectively of the total cancer seen in the study periods.

According to Globocan 2008 series of International Agency for Research on Cancer (IARC), the incidence rates of nasopharyngeal cancer were low in the West, East and Central Africa with age standardised incidence rates (ASR) per 100,000 in male being 1.6, 1.3, and 1.0 respectively and in female 0.6 in all the regions[2]. The incidence rates are higher in Southern Africa, (ASR per 100,000 is 4.5 in male and 1.6 in female) and Northern Africa, particularly in Tunisia, Algeria, and Sudan (ASR per 100,000 are 2.7 in male and 1.0 in female)[2].

One of the earliest references to nasopharyngeal cancer in Nigeria was the work of Elmes and Baldwin [13] in 1947 who reported a case of nasopharyngeal cancer (1 case in 1,000 tumours), constituting 0.001% of all malignancies seen, and noted that it was rare. The work of Martinson et al [10], [14] in Ibadan in 1968 and 1984 showed that cancer of the nasopharynx was not uncommon as previously reported and constituted 1.4% and 1.6% of malignancies seen in the studies respectively.

Reports on the overall pattern of head and neck cancers from different regions of Nigeria cited nasopharynx as the commonest site, except in Ilorin where the nasopharynx was reported to be the third commonest site of head and neck cancer [15], [16], [17], [18].

In a report from Ibadan, South Western Nigeria, of the cases seen in a period extending from 1981 to 2000, a steady increase in the incidence of nasopharyngeal cancer over the last two decades was demonstrated. It constituted 2% of all cancers reported from Ibadan Cancer Registry, with M: F of 2.3:1 and mean age of 41.1 years (age range 10 to 81 years) [19]. The females had a mean age of 36.1 years (age range 11 to 80 years) and males 43.2 years (age range 10 to 81 years). The peak age group of incidence for the females was 20-29 and 50-59 for the males [19].

In a report from Maiduguri, North Eastern Nigeria, 1991-2005, nasopharyngeal cancers constituted 35.1% of all malignancies of ear, nose and throat during the study period. The M: F was 2.1:1, the mean age was 39(+/- 16.5) years and a peak age group was in the 40-49 years [20]. Similar findings were reported from Sokoto, North Western Nigeria [21].

Nasopharyngeal carcinoma accounted for approximately 2% of the total reported cancer from Ilorin cancer registry during a retrospective study period between January 1st 1999 and December 31st, 2008 [18], which is not too different from 1.7% earlier reported in Plateau, also in the North-Central region of Nigeria [22]. The M: F was 2:1, the mean age of 48.7 years at presentation is slightly higher than figures from earlier reports from different parts of Nigeria where the mean age ranges from 41.1 to 44.4 years [18], [22], [23].

In a retrospective study of pattern of Head and Neck cancers in LUTH over a 10 year period (1988-1998) by Nwawolo et al [24], nasopharyngeal cancer was the commonest (16.8%). However, no data is available on previous study to assess the histopathological pattern of nasopharyngeal cancer in LUTH.

It is important to note that recent epidemiological studies show that, the incidence of nasopharyngeal malignancy in Hong Kong has decreased steadily by 30% since 1980 [25]. Similar downward trend in incidence have been observed in several populations of both native and foreign Chinese (Chinese in United State of America) over the last 2 decades [5], [26], while it has been increasing in incidence in part of Africa, and Nigeria where it was earlier thought to be rare [3,11,15]. Changing environmental risk factors and improvements in diagnosis and treatment were speculated to be the major factors contributing to these trends [3], [5], [25], [26].

2. MATERIALS AND METHODS

The materials for this study consisted of paraffin embedded tissue blocks, hospital request forms; patients case notes and duplicate copies of histopathology reports of cases of histologically-diagnosed nasopharyngeal cancer at Anatomic and Molecular Pathology Department of Lagos University Teaching Hospital (LUTH) between January 2003 and December 2012.

The cancer was reclassified into epithelial and non-epithelial malignancy. Under the epithelial malignancy, is the nasopharyngeal carcinoma which is reclassified in accordance with World Health Organisation (WHO) classification.

3. RESULTS

A total of seven thousands four hundred and eleven (7411) cancer cases were seen during the study period. Seventy five (75) of these were histologically confirmed nasopharyngeal cancer, these constituted approximately 1.1% of the total cancer seen. The annual incidence, sex and age distribution are shown in Figures 1 and 2.

Fig.1 shows the total annual incidence of nasopharyngeal malignancy, which rose sharply from six cases in 2006 to thirteen cases in 2008. Similar incidence of thirteen cases was recorded in 2009 and then there was a sharp decrease in 2010 and 2011 to 6 and 4 cases respectively. However, this incidence rose sharply again to eleven cases in 2012.

These patterns of annual incidence were seen in both sexes (male and female) but were more pronounced in the male gender, however there is no significant association between this yearly distribution and the sex, ($p = 0.412$)

There were 47 males (63%) and 28 females (37%) with a male to female ratio of 1.7:1. The age ranged from 3 to 75 years with an overall mean age of 44.1years. The

females had a mean age of 44.5 years (age range 14 – 70years) while the mean age for males was 41.7 years (age range 3 – 75years).

The peak age of incidence was 40 -49 years age group (26.7%) closely followed by 50 – 59 years age group (21.3%), (Fig.2).

The commonest symptom at presentation was cervical lymphadenopathy thirty (34) patients (36.2%), (bilateral cervical lymphadenopathy were seen in four (4) of these patients), followed by nasal blockage (22.3%) and epistaxis (16.0%) while the least common presentation was cranial nerve palsy (1.1%). Other symptoms seen were hearing impairment 6.4%, proptosis 5.3%, nasal discharge 4.3%, visual impairment 4.3%, ear pain 2.1% and weight loss 2.1% as shown in Fig.3

The undifferentiated carcinoma (type III WHO classification) was the commonest histological type,

constituting 37 (49.3%) cases (Table 1). This comprised of Schmincke's type 18 (48.6%) cases, Regaud's type 14 (37.8%) cases and the remaining 5 (13.5%) cases having overlapping features of the two aforementioned entities. These three variants of undifferentiated carcinoma were seen more frequently in males than females (Table 2). The differentiated, non-keratinizing squamous cell carcinoma (type II WHO classification) was 18 (24%) cases, while keratinizing squamous cell carcinoma (type I WHO classification) was 7 (9.3%) cases. All the other histologic types seen were, non-Hodgkin lymphoma constituting 10 (13.3%) cases and were all B-cell lymphoma, well differentiated adenocarcinoma 2 (2.7%) cases and low grade mucoepidermoid carcinoma 1 (1.3%) case constituted the remaining types (Table 1).

4. TABLES AND FIGURES

Table 1: shows sex distribution of different histologic types of nasopharyngeal cancer

	UNDIFFERENTIATED CARCINOMA		NKSCC		KSCC		NHL		ADENOCAR CINOMA		MC		Total	
	FREQ.	%	FREQ.	%	FREQ.	%	FREQ.	%	FREQ.	%	FREQ.	%	FREQ.	%
Male	23	62.2	9	50	5	71.4	8	80	1	50	1	100	47	62.7
Female	14	37.8	9	50	2	28.6	2	20	1	50	0	0	28	37.3
Total	37	100	18	100	7	100	10	100	2	100	1	100	75	100
Total %		49.3		24		9.3		13.3		2.7		1.3		100

KEYS

NKSCC- non-keratinizing squamous cell carcinoma

KSCC- keratinizing squamous cell carcinoma

NHL- non-Hodgkin lymphoma

MC- mucoepidermoid carcinoma

FREQ- frequency

% - percentage

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Table 2: shows sex distribution of subtypes of WHO type III nasopharyngeal carcinoma

Subtype	Frequency		Total	Percentage
	Male	Female		
Schmincke	11	7	18	48.6
Regaud	9	5	14	37.8
Mixed	3	2	5	13.6
Total	23	14	37	100
Percentage	62.2	37.8	---	---

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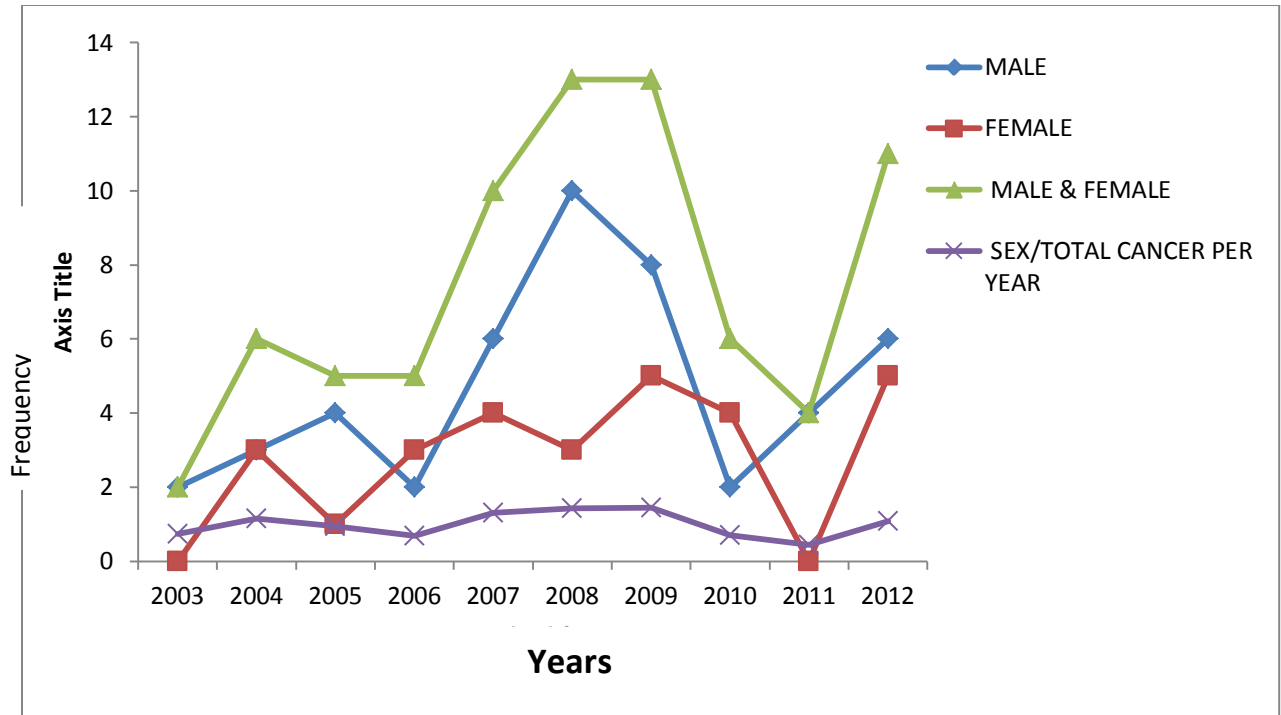


Figure 1:- Graph showing yearly distribution by sex of patients with nasopharyngeal cancer

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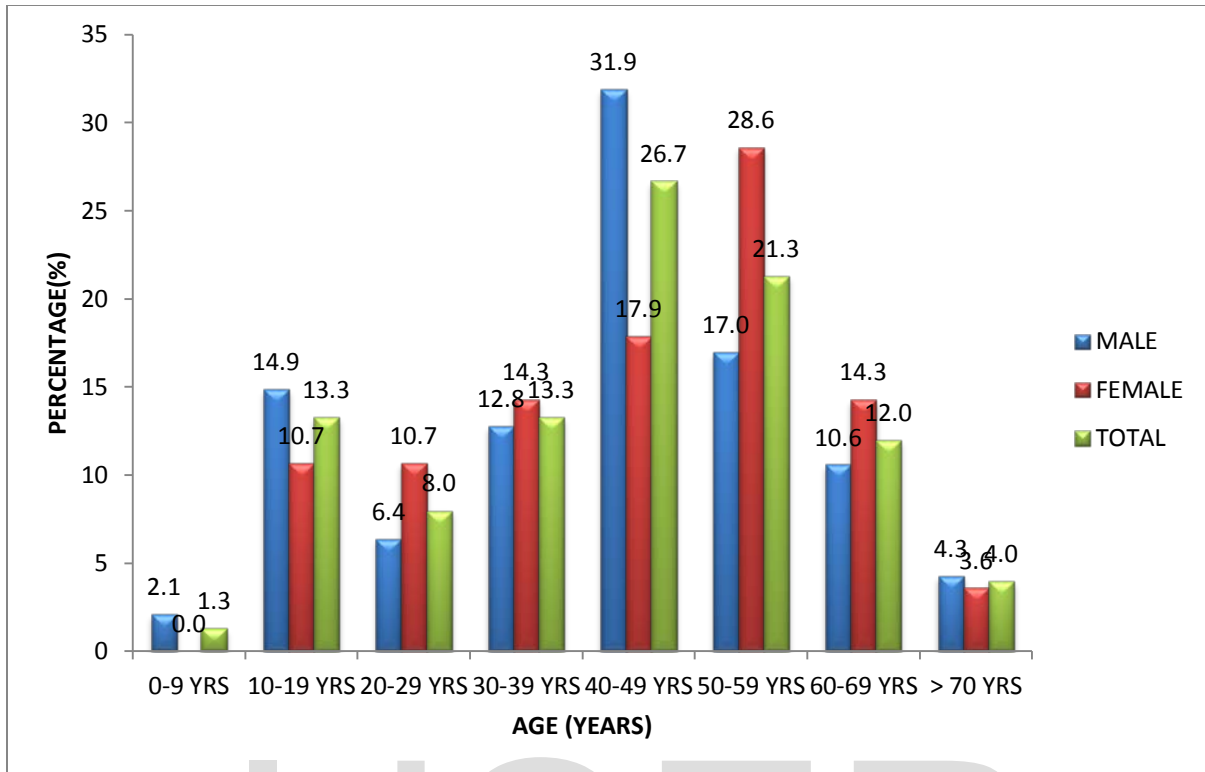


Figure 2- Bar chart comparing age and sex distribution of nasopharyngeal cancer

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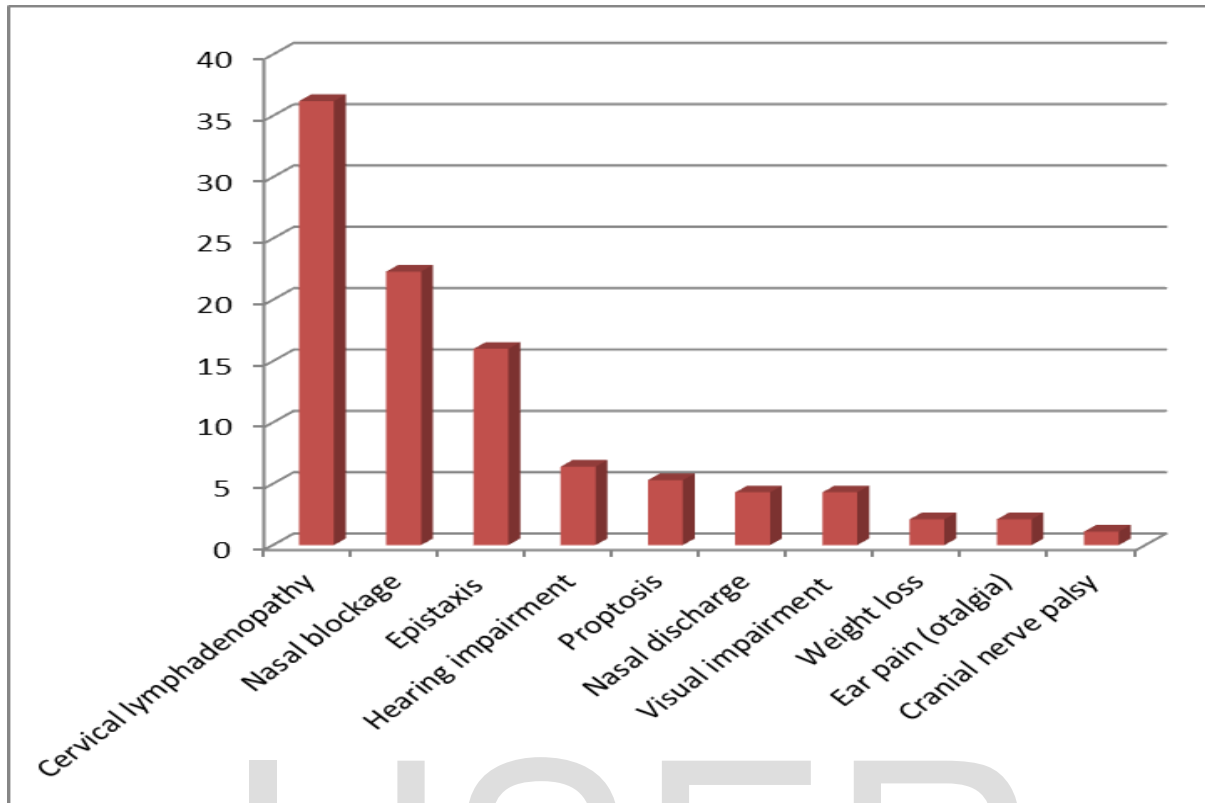


Figure 3: - Bar chart showing common clinical presentation by patients with nasopharyngeal cancer

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4. DISCUSSION

Nasopharyngeal cancer (NPC) has been reported as the commonest head and neck cancer in Nigeria [24], however, it is an uncommon cancer worldwide except for the areas of endemicity earlier mentioned [2]. It accounts for approximately 1.1% of the total cancer seen in this study. This figure is however slightly lower than the reports from Ibadan in the same south western area of Nigeria and other parts of the country where earlier studies have been done [18], [19], [20], [21], [22], but the previous study done in LUTH only considered NPC as a component of head and neck cancer and it accounted for 16.8% of the head and neck cancer [24]. Similarly, earlier surveys of cancer in the African continent suggested that NPC was rare among malignant tumours as documented by Gelfand [6] in Zimbabwe, Shapiro et al [7] among Bantu in South Africa, Edington [8] in Ghana and Davies [9] in Uganda, but follow up studies from different parts of Africa and different regions of Nigeria as well as in this study show that the disease is not as rare as earlier reported [10], [11], [12], [19].

The disease tends to occur more in males than in females in this study, in a ratio of 1.7:1 which is consistent with what has been reported in the literature [13], [14], [15], [16], [17], [18], [23]. The mean age in this study is 44.1 years which compares favourably with the study in Ibadan that falls within the same South

Western Nigeria where the mean age was 41.1 years [19]. It is also similar to findings from studies in Jos [22], [23], but, it is slightly lower than the report from Ilorin and slightly higher when compared with the report from Sokoto [18], [21]. However, the mean age of incidence is a decade lower than seen in patients from Northern America, Western Europe and China [1]. The reason for this is unknown; however, it may not be unconnected with the life expectancy in Nigeria which is lower compared to these countries [27]. The peak age of incidence is in the fifth decade showing that majority of the patients (26.7%) presented at the height of their productivity between 40 – 49 years with likely far reaching implications for socioeconomic output. However, it is noted that the single peak age of incidence in this study is similar to the second peak in the previous studies from other parts of the country with bimodal age distribution where the first peak occurred at second or third decade of life [16], [18], [19]. The peak age of incidence in this study is about a decade lower when compared to patients from endemic region such as South East Asia which also shows bimodal age distribution [28]. The least age at presentation in this study is 3 years which is in contrast to what was seen in some parts of Nigeria and Southern China [18], [19], [22], [29]. Report from Uganda, Kenya, Sudan, and Tunisia (intermediate risk region) showed that NPC were frequently seen at younger age group (0-19 year), but the reason for this was not known [29].

The obscure location of this cancer coupled with its vague, non-specific symptoms makes it difficult to diagnose, thus most patients present at the advanced stage of the disease. The most common form of presentation in this study was cervical lymphadenopathy (36.2%), which unfortunately indicates advanced disease (stage III or IV). Other common symptoms seen were nasal blockage (22.3%), epistaxis (16.0%), hearing impairment (6.4%) and nasal discharge (4.3%), these forms of clinical presentations are similar to reports in patients from different parts of Nigeria as well as in both the endemic and non-endemic areas of the world [18], [19], [21], [30].

Other important but less common symptomatology seen in this study includes neuro –ophthalmic manifestations such as proptosis (5.3%), visual impairment (4.3%) and cranial nerve palsy (1.1%), which sometimes may be the sole presentation and as such misleading with resultant delay in treatment. These symptoms also signify advanced disease with poor prognosis [31]. Nasopharyngeal cancer can also present early, but the symptoms are vague and non-specific, these include nasal congestion, nasal discharge, recurrent ear infection, and otalgia (ear pain) as reported in this study, other parts of Nigeria and in endemic regions [18], [20], [21], [32]. Thus, screening patients with these symptoms as it is done in areas endemic for NPC, even though Nigeria is not an endemic area, will aid in its

early detection and diagnosis and thus, curative medical intervention.

Most lesions in this study were WHO type III undifferentiated carcinoma (49.3%) which is similar to findings in other centers across the country as well as in the endemic regions of the world, even though Nigeria is not a high-incidence country [18], [19], [20], [21], [22], [32]. The undifferentiated carcinoma (type III) is also the predominant histological type seen in children and adolescent in this study which is consistent with the finding of the previous studies in Ibadan and Sokoto [19], [21], but no children or adolescent was found in the studies at Ilorin and Jos [18], [23]. The undifferentiated carcinoma comprised of Schmincke type (24.0%), Regaud type (18.7%), with the remaining 6.7% (mixed type) having overlapping features of these two entities.

Other histological variants in the study include differentiated non-keratinizing squamous cell carcinoma (24%), non-Hodgkin lymphoma (13.3%), keratinizing squamous cell carcinoma (9.3%), adenocarcinoma (2.7%), and mucoepidermoid carcinoma (1.3%). These variants are also seen in the studies from other parts of the country, Kenya, Britain, Denmark and China [19], [23], [33], [34], [35]. This confirms the reports that various tissues found in the nasopharynx can give rise to malignancy [36], [37].

The three patients who were above 70 years in this study have WHO type I keratinizing squamous cell carcinoma (KSCC) which is consistent with what has been reported in the literature that the KSCC variant occur more in the elderly [38], [39].

Nasopharyngeal carcinoma is not as rare as earlier reported in this environment. The obscure location of this cancer coupled with its vague, non-specific symptoms make patients to present late with metastasis making it impossible for curative medical interventions. Screening patients with early symptoms of NPC as it is done in countries endemic for the disease, will aid in its early detection, diagnosis and curative medical intervention.

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REFERENCES

- [1] Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB. Cancer incidence in five continents. *International Agency for Research on Cancer*. 7. 1997, 334–337.
- [2] Ahmedin J, Freddie B, Melissa MC, Ferlay J, Elizabeth W, David F. Global cancer statistics. *A cancer journal for clinician*. 61. 2011, 74-108.
- [3] Buell P. The effect of migration on the risk of nasopharyngeal cancer among Chinese. *Cancer Res*. 34. 1974, 1189–91.
- [4] Marks JE, Phillips JL, Menck HR. The National Cancer Data Base report on the relationship of race and national origin to the histology of nasopharyngeal carcinoma. *Cancer*. 83. 1998, 582–588.
- [5] King H, Haenszel W. Cancer mortality among foreign- and native-born Chinese in the United States. *J Chronic Dis*. 26. 1973, 623-46
- [6] Gelfand M. Malignancy in Africa. *S Afr Med J*. 23. 1949, 1010-1016.
- [7] Shapiro MP, Keen P, Cohen L, Moor NG. Malignant disease in the Transvaal. *S Afr Med J*. 29. 1955, 95-101.
- [8] Edington GE. Cancer mortality patterns in Ghana: a 10-year review of autopsies and hospital mortality. *Brit J Cancer*. 10. 1956, 594-599.
- [9] Davies JN. The pattern of African cancer in Uganda. *East Afr Med J*. 38. 1961, 486–491.
- [10] Martinson FD. Cancer of the Nasopharynx in Nigeria. *J Laryngol Otol*. 82. 1968, 1119-1126.

- [11] Clifford P. Malignant disease of the nose, paranasal sinuses and post-nasal space in East Africa. *J Laryngol Otol.* 75. 1961, 707-733.
- [12] Linsell CA. Nasopharyngeal Cancer in Kenya: Pathology. *Br J Cancer.* 18. 1964, 49-57.
- [13] Elmes GGT, Baldwin RGT. Malignant disease in Nigeria: An analysis of a thousand tumours. *Ann Trop Med Parasit.* 41. 1947, 321-328.
- [14] Martinson FD, Aghadiuno PU. Nasopharyngeal cancer in Nigeria. *IARC Sci Publ.* 63. 1984, 501-511
- [15] Okeowo PA, Ajayi DOS. Nasopharyngeal Cancer in Nigeria. In Ibadan tropical Medicine series. *University of Ibadan Press.* 1978, 117-122.
- [16] Ketiku KK, Igbinoba F, Okeowo PA. Nasopharyngeal cancer in Nigeria – A revisit. *Niger Postgrad Med J.* 5. 1998, 7-12.
- [17] Ologe FE, Adeniji KA, Segun-Busari S. Clinicopathological study of head and neck cancer in Ilorin, Nigeria. *Tropical Doct.* 35. 2005, 2-4.
- [18] Alabi BS, Badmos KB, Afolabi OA, Buhari MO, Segun-Busari S. Clinico-pathological pattern of nasopharyngeal carcinoma in Ilorin, Nigeria. *Nig J clinical pract.* 13. 2010, 445-448.
- [19] Nwaorgu OG, Ogunbiyi JO. Nasopharyngeal cancer at the University College Hospital Ibadan Cancer registry: an update. *West Afr J Med.* 23. 2004, 135-8
- [20] Garandawa HI, Ahmad BM, Nggada HA. Nasopharyngeal cancer in North- Eastern Nigeria: clinical trends. *Niger J Clin Pract.* 12.2009,379-82.
- [21] Iseh KR, Abdullahi A, Malami SA. Clinical and histological characteristics of nasopharyngeal cancer in Sokoto, North Western Nigeria. *West Afr J Med.* 28.2009, 151-155.
- [22] Obafunwa JO, Bhatia PL. Nasopharyngeal carcinoma in Plateau State, Nigeria: a pathological study. *Eur J Surg Oncol.* 17.1991, 335-7
- [23] Lilly-Tariah da OB, Somefun AO. Malignant tumours of the Nasopharynx at Jos University Teaching Hospital, Nigeria. *Niger Postgrad Med J.* 10.2003, 99-102.
- [24] Nwawolo CC, Ajekigbe AT, Oyeneyin JO, Nwankwo KC, Okeowo PA. Pattern of head and neck cancers among Nigerians in Lagos. *West Afr J Med.* 20.2001, 111-116.
- [25] Lee AW, Foo W, Mang O. Changing epidemiology of nasopharyngeal carcinoma in Hong Kong over a 20-year period (1980-99): an encouraging reduction in both incidence and mortality. *Int J Cancer.* 103. 2003, 680-5.
- [26] Li-Min S, Meire E, Christopher IL, Vaughan TL, Weiss NS. Trends in the incidence rates of nasopharyngeal carcinoma among Chinese living in Los Angeles and the san Francisco metropolitan, 1992-2002. *Am J Epidemiol.* 162.2005, 1174-1178.
- [27] Paul O. WHO Report: Nigeria, Angola, Others' life expectancy stagnant. 18 May 2014
- [28] Chang ET, Adam HO. The enigmatic epidemiology of nasopharyngeal carcinoma. *Cancer Epidemiol Biomarkers Prev.* 15.2006,1765-1766.

- [29] Ellouz R, Cammoun M, Attia RB, Bahi J. Nasopharyngeal carcinoma in children and adolescents in Tunisia: clinical aspects and the paraneoplastic syndrome. *IARC Sci Publ.* 20.1978, 115–129.
- [30] Voke EE, Liebowitz DN, Weichelsbaum RR. Nasopharyngeal carcinoma. *Lancet.* 350.1997, 1087-1103.
- [31] Ogunleye AO, Nwaorgu OG, Adaramola SF. Ophthlmo-neurologic manifestation of nasopharyngeal carcinoma. *West Afr J Med.* 18.1999, 106-9
- [32] Zong YS, Zhang RF, He SY, Qiu H. Histopathologic types and incidence of malignant nasopharyngeal tumors in Zhongshan County. *Chin Med J (Engl).* 1983, 511-516
- [33] Godtfredsen E. Histopathology of malignant nasopharyngeal tumors. *Acta path microbiol. Scand Suppl.* 55.1944, 319-325
- [34] Clifford P, Beecher JL. Nasopharyngeal Cancer in Kenya; Clinical and Environmental Aspects. *Br J Cancer.* 18.1964, 25–43.
- [35] Lambert V. Malignant disease of post-nasal space. *J Laryngol Otol.* 74. 1960, 1-21.
- [36] Juan R. Rosai and Ackerman's Surgical Pathology; Nasal cavity, paranasal sinuses and nasopharynx, 10th Ed., Mosby-Year Book, Inc., St. Louis, Missouri 63146, 2010; Vol 1: 291 – 299
- [37] Vinay K, Abul KA, Nelson F, Jon CA. Robins and Cotran Pathologic Basis of Disease. 8th Ed., Saunders, Elsevier Inc., Philadelphia, 2010; 750 -751
- [38] Heng DM, Wee J, Fong KW, Lian LG, Sethi VK, Chua ET et al. Prognostic factors in 677 patients in Singapore with nondisseminated nasopharyngeal carcinoma. *Cancer.* 86.1999, 1912-1920.
- [39] Nicholls JM, Nasopharyngeal carcinoma: classification and histologic appearances. *Adv Anat Pathol.* 4. 1997, 71-84