**Original Article**

**Presentation and Management of Orbito-Ocular Malignancies in a Tertiary Institution in Southwest Nigeria**



**Abstract**

**Purpose:** The aim of this study was to review the management of orbito-ocular malignancies in the Departments of Radiotherapy and Ophthalmology, Lagos University Teaching Hospital, between January 1997 and December 2011 in comparison to previous and recent studies globally. **Materials and Methods:** This was a retrospective study of orbito-ocular malignancies seen at the Departments of Radiotherapy and Ophthalmology, Lagos University Teaching Hospital from 1997 to 2011. Case files and treatment cards were retrieved through the Medical Records department and the information required was extracted with the aid of a data extraction form. **Results:** A total of 98 cases with histologically confirmed orbito-ocular malignancies seen during the 15-year study period were analysed. Retinoblastoma (51 [52.0%]) was the most common orbito-ocular malignancies seen in children, whereas squamous cell carcinoma of the conjunctiva (25 [25.5%]) was the most common in adults. Seventeen (17%) patients had a combination of radiotherapy, surgery, and chemotherapy. Thirty (33%) had enucleation, whereas 33 (36%) had exenteration. Thirty-six patients had chemotherapy, whereas 44 patients benefited from radiotherapy, and radical treatment was offered to 24 patients. Total radical treatment dose was 35–65 Gy in 20–35 fractions over 4–7 weeks. Most of the patients (84 [85.7%]) were lost to follow up. Five (5.1%) died from disease progression and four (4.1%) are still alive and on regular follow-up. **Conclusion:** This study showed that the use of multimodality treatment was implemented but did not improve survival because the majority of patients presented late. The need for a collaborative effort in early detection and prompt referral for treatment of cancer cases cannot be overemphasised.

**Keywords:** *Management, orbito-ocular malignancies, presentation*

**Introduction** The awareness and knowledge of OOM in developing countries such as Nigeria is low due to suboptimal awareness programs, poor health-seeking attitudes, and faith-healing beliefs. These had led to patients seeking alternative traditional treatment,

Orbito-ocular malignancies (OOM)

[1,2]

generally are rare tumours with

age-adjusted incidence rate of 0.8 per

100,000 per year in the United States.

[3]

Several studies on OOM suggest that

these malignancies are more common in thus increasing the number of patients children than adults.[4] These tumours are

presenting with advanced stage of the

disease.

limited to malignancies developing from

the eye, orbit or the lids. The eye consists of The challenges of management of patients various anatomic and functional elements with OOM are enormous. These include including the conjunctiva, cornea, uvea, late presentation with advanced disease, lens, vitreous, retina and optic nerve. All inappropriate or wrong diagnosis, delayed these structures can form malignancies with referral to the ophthalmologists, lack of pathologic processes. Secondary ocular expertise and facilities for early intervention, malignancies are rare but are more common poverty, fear of losing their vision and than primary malignancies of the eye.[5] challenges with preserving vision.[7] The There is an increase in the incidence of aim of the study was to review the pattern both primary and secondary malignancies of presentation, various histologic types, in both paediatric and adult tumours owing management and outcomes of OOM in to better diagnosis and increase awareness.[6] the Departments of Radiotherapy and Ophthalmology (Guinness Eye Centre),

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Lagos University Teaching Hospital (LUTH) in comparison with existing data globally. Furthermore, information gathered from the study could be useful in planning and allocating resources in the management of common oculo-orbital malignancies that were identified in the study.

This was a retrospective study of all patients with histologically confirmed malignancies listed in the Medical Records register and seen at the Departments of Radiotherapy and Ophthalmology of the LUTH from 1997 to 2011.

The study included all patients presenting or being referred for the treatment of OOM from other departments in LUTH or from State hospitals, private health institutions as well as those referred from other teaching hospitals and other referral centres all over Nigeria during the study period for surgery, chemotherapy, radiotherapy or other forms of treatment.

The inclusion criteria for patients enrolled for the study were histologically confirmed OOM, metastatic diseases with histologically-confirmed primary disease, adequate data in case notes including a detailed history, examination, investigation reports, complete documentation of treatment received by the patients, and adequate follow-up till the period of the end of the study or seen till demise or default from the clinic. Patients who did not fulfil the above-listed criteria were exempted from the study.



Case files were retrieved through the record department and the information required was extracted with the aid of a data extraction form. All possible information including patients’ age, sex, occupation, marital status, ethnic group, and histology were evaluated.

83 years with a mean of 22.94 years, standard deviation (SD) ± 24.64 years, and median age of 8.17 years. Majority (54 [55.1%]) of the patients were children less than 10 years of age [Tables 1 and 2]. Twenty-one and 13 patients were of ages 2 and 3 years, respectively. Ten patients were ≤ 1 year of age.

The right eye was affected in 46 (46.94%) individuals, whereas 42 (42.86%) had the left eye involved. Eight (8.16%) had bilateral involvement and in two (2.04%) cases, the site(s) affected was not mentioned [Figure 1].

Retinoblastoma was the most common OOM seen in 51 (52.0%) of the patients and other causes as shown in Table 3.

**Table 1: Age and sex distribution of orbito-ocular malignancies**

**Age range (years)** **Male** **Female** **Frequency** **%** 0–9 34 20 54 55.1 10–19 1 0 1 1.0 20–29 3 2 5 5.1 30–39 6 5 11 11.2 40–49 7 3 10 10.2 50–59 2 2 4 4.1 60–69 5 7 12 12.3 ≥70 0 1 1 1.0 Total 58 40 98 100

**Table 2: Sociodemographic characteristics of patients Marital** **Frequency** **%** **Ethnicity** **Frequency** **% status**

Married 36 36.7 Yoruba 51 52.0

The data were entered into a database and statistical analysis was performed using the IBM Statistical Package for the Social Sciences software, version 20 (IBM SPSS, IBM Corp., Armonk, New York). Data were expressed as frequency tables, charts, and cross-tabulations.

Ethical approval was obtained from the Health Research Ethics Committee (HREC) of the Lagos University Teaching Hospital, Idi-Araba, Lagos State, with protocol number ADM/DCST/HREC/1599 and approval dated from November 12, 2013 to November 12, 2014.

**Results**

There were one hundred and seven cases available for review. However, only 98 cases were eligible for the study. Of the 107 patients, nine were excluded; three of them had no histologic diagnosis, whereas six of them had insufficient data in their case notes. Patients were referred from all over Nigeria to the department of Radiotherapy and Ophthalmology in LUTH for treatment.

Single Widowed Separated Divorced

61 62.3 Igbo

1 1.0 Hausa 0 0 Others 0 0

25 25.6 2 2.0 20 20.4

Le Right Bilateral

Unknown

The study showed that 58 patients were males and 40

females (M:F = 1.5:1). The age range was 8 months to **Figure 1: Frequency of affected eye**

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The most common presenting complaints were proptosis seen in 47 (48%), leucokoria 20 (20.4%), lower eyelid swelling in 11 (11.2%), and red eye in 7 (7.1%) patients. Other symptoms included fungating eye mass seen in four (4.1%) patients, loss of vision in three (3.1%), conjunctiva swelling two (2.0%), cornea opacity one (1.0%), pain in the eye one (1.0%), and ptosis was seen in two (2.0%) patients.

A total of 17 (17.4%) patients had a combination of surgery, chemotherapy, and radiotherapy as a treatment modality. Another 24 (24.5%) had a combination of surgery and radiotherapy, 18 (18.5%) had a combination of surgery and chemotherapy, whereas 32 (32.7%) had surgery alone. Only one (1.1%) and three (3.1) patients received only chemotherapy and radiotherapy, respectively.

Three patients, who had a histologic diagnosis of their disease and were offered treatment, did not receive the treatment modalities recommended.

Surgical options include incisional biopsy 6 (7%), excision biopsy 22 (22.4%), whereas enucleation 30 (33%) and exenteration 33 (36%) were the surgical treatment modality. Seven (7.1%) patients had no surgery. The chemotherapy regimens used are shown in Table 4. Eighty-four (85.7%) of the patients, constituting the majority, were lost to follow up. Four (4.1%) patients had complete treatment response and are still attending the clinic on follow-up, whereas five (5.1%) had recurrence and received further treatment. Five (5.1%) died from disease progression within 2 years following treatment.



**Table 3: Orbito-ocular malignancies in the departments (1997–2011)**

**Orbito-ocular malignancy** **Frequency** **%** Retinoblastoma 51 52.0 Squamous cell carcinoma of the 25 25.5 conjunctiva

Melanoma 4 4.1 Rhabdomyosarcoma (unspecified) 3 3.1 Rhabdomyosarcoma (embryonal) 3 3.1 Non-Hodgkin’s lymphoma 3 3.1 Kaposi sarcoma 1 1.0

**Discussion**

OOM though rare are a common cause of morbidity and mortality. The rarity accounts for the low incidence seen over the period of study. Several Nigerian-based studies from Zaria, Benin, Ilorin, and Ibadan have reported incidence of 40.3%,[8] 22.8%,[9] 57.3%[10] and 51.5%[11] of OOM among OOT, respectively. These results are contrary to previous perception on the rarity of the disease in Africa.[12] Low number of cases seen during the early period of the study may be due to lack of radiotherapy machine or machine break down or facility shut down during strike action of health workers. Lack of awareness could also have been a contributing factor to the low number of cases. It was evident that several patients treated during this period had radiotherapy at nearby facilities and still came back to continue treatment at the clinic.

In this study, OOM occurred more in males than females in a ratio of 1.5:1; this is similar to findings on pattern of ocular tumours in Ibadan, Lagos, Ilorin, Kaduna and Ghana but at variance with a study done in Enugu where females outnumbered male subjects (M:F of 1:1.4).[5,10,13-15] The sociocultural similarity of the study areas in the Ibadan, Lagos, and Ilorin studies with our study area could be a possible explanation for the similar male-to-female ratios, whereas the variance with the Enugu Study could be as a result of the better health-seeking behaviour of the female patients in the part of the country.

The study identified the three most common OOM as retinoblastoma 52.0%, squamous cell carcinoma (SCC) of the conjunctiva 25.5% and melanoma 4.1%, which were similar to other findings from Nigeria[7,9,11,13,15] but different from findings in the Western World of retinoblastoma 53.6%, melanoma 19.2%, and 11.2% of SCC in Singapore,[16] whereas New York State reported 70.4% melanoma, 9.8% retinoblastoma, and 9.2% SCC.[17] The relative frequencies of these histologic types varied widely in order of occurrence but were also the most common OOM found in these areas. These can be attributed to their racial, genetic and environmental differences.

Sebaceous carcinoma 2 Basal cell carcinoma of upper eyelid 2 Metastasis 4

2.0 SCC of the conjunctiva was the most common in adults 2.0 and affected both sex equally similar to findings in Ilorin,[10] 4.1 Ibadan[11] and Lagos.[13] SCC is reported as the most common

**Table 4: Chemotherapy regimen**

Retinoblastoma

Non-Hodgkin’s lymphoma

Squamous cell carcinoma of conjunctiva Rhabdomyosarcoma

Metastasis Total

**VAC** **VACis** **VC** **CHOP** 13 10 –

– – 2 – 5 – – 4 – – 1 – – 18 5 10 2

**Capecitabine** **Total** – 23 – 2 1 6 – 4 – 1 1 36

VAC = vincristine, actinomycin-D and cyclophosphamide, VACis = vincristine, adriamycin, cisplatin, VC = vincristine, cyclophosphamide, CHOP = cyclophosphamide, doxorubicin, vincristine and prednisone

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conjunctival lesion in Nigeria and the most common ocular malignancy in adulthood..[10,11,13] Previous report from Ibadan has concluded that the carcinoma is common in the tropics and strongly associated with HIV/AIDS.[11] Five individuals (20%) with SCC of the conjunctiva had HIV in this study though the patients were not all screened. Uveal melanoma is rare in Africa as reported in this study and others.[11,12] This is in contrast to incidence in the United States of America and Europe where it accounts for the most common primary intraocular malignancy in adults.[1,2,5] Lymphoma were rare in this study, only two patients had non-Hodgkin’s lymphoma which is in contrast to studies reported by Chuka-Okosa *et al*.[15] and Ajaiyeoba *et al*.[18] in Eastern and Western Nigeria, respectively, which showed lymphomas as the most common orbital tumour including Burkitt’s Lymphoma.

The study showed a high frequency of OOM in children with retinoblastoma accounting for 50% of the study population. Anunobi *et al*.[13] and Umar *et al*.[19] in Nigeria also reported high frequencies of 85% and 44.5%, respectively. Studies done in Singapore and Pakistan also showed high frequencies of 53.6% and 43.7%, respectively.[16,20] This is contrary to a frequency of 9.8% recorded in a study carried out by Mahoney *et al*.[17] in New York. The differences in frequencies may suggest that environmental factors have a role to play in the aetiology of these malignancies. The age range was 8 months to 6 years with mean of 2.53 years, modal 2 years. The mean age of retinoblastoma in this study is similar to that of 2.42 years reported by Owoeye *et al*.[10] and 2.65 years by Bekibele and Oluwasola[11] in South West Nigeria. This is in variance with 18 months in Western Countries.[21] The variation in age incidence could be attributed to late presentation in developing countries, whereas environmental factors may be related to variations in geographic incidence of these malignancies.

The most common complaints were those of proptosis and leucokoria seen in 47 and 20 patients, respectively. Proptosis was also the most common presentation at Ilorin (84.6)% followed by leucokoria (61.5%).[12] Majority of the patients in developing countries present with proptosis a fact which validates the late presentation for treatment.[12] The delay in presentation is attributed to poverty and ignorance on the part of the patient, lack of adequate treatment facilities, lack of easy access to the few available treatment facilities and inadequate knowledge of some primary physicians with disease detection that negatively affects early referral.

Management of OOM has changed dramatically over recent decades and continues to evolve. It, now, includes a wide range of different techniques that can achieve good tumour control when used alone or in combination with other treatment modalities. Within the study period, the most common modality of treatment in LUTH was a combination of surgery, radiotherapy, and chemotherapy. In this study, 44 patients had radiotherapy, radical

treatment dose of 35 to 65Gy in 20 to 35 fractions over 4 weeks, using a Linear Accelerator for mostly adjuvant and neo-adjuvant treatment, whereas for palliation the doses varied from 18 to 30Gy in 10 fractions over 2 weeks of symptoms. External beam radiotherapy was avoided in children because of the risk of secondary malignancies and craniofacial asymmetry. However, because of late presentation, children above the age of 3 years received it frequently as adjuvant treatment following surgery or chemotherapy. High radiation doses could not be delivered because of acute side effects and complications following treatment because there was no facility for 3D conformal radiotherapy.

A review of exenterations by Ackuaku-Dogbe revealed that this is the surgical procedure most often performed in developing countries for neglected peri-orbital and ocular surface malignancies which may have resulted in fungating tumours which are no longer salvageable.[22]

Major prognostic factors in this study were stage at presentation and histological type. Inadequate staging of the disease is still a challenge as several patients were not staged. This is a significant prognostic index.

**Conclusion**

Poverty, irregular follow-ups, lack of treatment facility or frequent machine downtime/breakdown had all contributed to the poor outcome seen in most cases. Late presentation is still a dilemma in developing countries and the need for a collaborative effort, to create an enlightenment program to aid early presentation.

**Recommendation**

The study recommends improvement in patients’ information management to reduce significantly the challenge of incomplete data. Furthermore, joint interdisciplinary Oncology meetings should be a regular practice this will enable experts involved in the management of OOM to exchange knowledge on how to incorporate International guidelines for better treatment outcomes. Lastly, social workers, religious leaders and community leaders should be involved in patient care, to help reduce the rate at which patients are lost to follow up.

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**Conflicts of interest**

There are no conflicts of interest.

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