PATTERN OF PRESENTATION OF ORBITO-OCULAR TUMORS IN UNIVERSITY COLLEGE HOSPITAL (UCH), IBADAN

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DEDICATION

This dissertation is dedicated to Almighty God, the loving memory of my father, my affectionate mother and supportive family.

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ABSTRACT

Background: Orbito-ocular tumors are stereotypic, monotonous new growth of the tissues in the orbito-ocular region, made up of the orbit, eyeball and extra-orbital anatomic areas. Orbito-ocular tumors are reported to be more common in tropical Africa than in other parts of the world. Orbito-ocular tumors are of great public health importance and the challenges facing the patients include cosmetic deficits, visual loss, and threat to life. There is relative paucity of information on the prevalence of the different types of orbito-ocular tumors and treatment outcome in Nigerian patients. This study thus aims to determine the pattern of presentation of patients with histologically confirmed orbito-ocular tumors seen at University College Hospital (UCH), Ibadan, between January 1990 and December 2009.

Methods: This was a retrospective case series with descriptive and analytical components. Patients presenting for the first time to the Eye Clinic of UCH, Ibadan, with histological diagnosis of orbit-ocular tumors were identified from the register at the Pathology Department, and their case records were retrieved. Information on age, sex, clinical history, type of tumor, clinical and histological diagnoses, adjuvant therapy, treatment status, recurrence and duration of follow-up was collected and analysed with the use of SPSS 16. Analysis was considered to show significant association when the p value was less than 0.05.

Results: A total of 205 patients were analysed giving a proportional morbidity of 0.4%. The median age of patients with orbito-ocular tumors was 7.0 years (range 4 months to 81 years) with a male to female ratio of 1.1:1. About 56% of the patients were children. Retinoblastoma accounted for 46.8% and ocular surface squamous neoplasia 21% of the

tumors. About 72% of the patients had lost vision from the tumor, while almost half of the patients presented with proptosis. More than half (51.4%) of the patients who did not complete their treatment schedule had had recurrence at one year of diagnosis, and patients with retinoblastoma who did not complete their treatment were about 52 times more likely to have recurrence ($p = 0.001$). More than half (53%) of the patients did not keep their follow-up appointments. There was a strong correlation (87%) between clinical and histological diagnoses of patients with orbito-ocular tumors.

Conclusion: Orbito-ocular tumors still remain uncommon in our health institution. There appears to be a reduction in the number of cases seen compared to previous studies. Retinoblastoma was the commonest type of tumor in the orbito-ocular region, while melanomas are rare. There is urgent need for public enlightenment through the electronic media in both English and local languages on the signs of orbito-ocular tumors especially retinoblastoma, and encourage early presentation for treatment to increase the overall patient survival.

Key words: Nigeria, Ocular, Orbit, Orbito-ocular, Tumor.

Word count: 448

CHAPTER ONE

INTRODUCTION

1.0 Background

The orbit is a bony cavity which houses the organ of sight, the eyeball and other structures. The orbito-ocular region is made up of the bony orbit, the eyelids and other peri-ocular structures. The bony orbit is pyramidal in shape with an average volume of 30cc in adults of which the eyeball contributes 7.5cc. It has four walls made up of seven bones- frontal, sphenoid, lacrimal, maxilla, ethmoid, zygomatic and palatine (Dutton and Waldrop, 1994). The orbits are surrounded by air-filled cavities, the paranasal sinuses from which lesions including tumors readily spread into the orbits (Shields and Shields, 1999).

Virtually all types of tissues in the body are seen in the orbito-ocular region, therefore, a diversity of lesions that can arise in this region (Gunalp and Gunduz, 1994). Orbito-ocular disorders can be developmental, inflammatory, traumatic, vascular, neoplastic, or associated with general or metabolic diseases (Kennedy, 1984). Tumors or neoplasia are stereotypic, monotonous new growth of a particular tissue phenotype, and can be broadly classified as primary, secondary or metastatic (Shields and Shields, 1999). They represent a varied group of lesions found in the orbito-ocular region and can be generally described as orbital, intra-ocular, conjunctival or eyelid tumors (Onwasigwe, 2002).

Primary orbito-ocular tumors originate directly from the eyeball, orbital or adnexal tissues. Secondary tumors are those that spread from the adjacent structures, most importantly, the paranasal sinuses and intracranial cavity, while spread of tumor from

distant organs like the breast and prostate are referred to as metastasis (Gunalp and Gunduz, 1994). Tumors spreading to the orbit can give rise to distinctive signs and symptoms that point to the origin of the tumor. Metastatic prostatic carcinoma for example can present clinically as idiopathic orbital inflammation while metastatic neuroblastoma, a highly vascular tumor, may produce a characteristic periocular ecchymosis.(Shields et al., 2001).

Orbito-ocular tumors can also be described as either benign or malignant. By definition, benign tumors do not penetrate or invade adjacent tissue borders, nor do they spread or metastasize to distant sites. They remain as localized overgrowths in the area in which they arise. Usually, benign tumors are more differentiated than malignant ones, that is, they more closely resemble their tissue of origin.

By contrast, however, malignant tumors, or cancers, have the added property of invading contiguous tissues and metastasizing to distant sites, where subpopulations of malignant cells take up residence, grow anew, and again invade (Rootman, 1988). However, there is a possibility of benign tumors transforming into malignant ones. An example is pleomorphic adenoma of the lacrimal gland becoming malignant (adenocarcinoma) following incomplete excision.

In general, neoplasms are irreversible, and their growth is, for the most part, autonomous. Neoplasms are derived from cells that normally maintain a proliferative capacity. Thus, mature neurons and cardiac myocytes, for example, do not give rise to tumors (Giordano et al., 2008).

A tumor may express varying degrees of differentiation, from relatively mature structures that mimic normal tissues to a collection of cells so primitive that the cell of origin cannot

be identified. The stimulus responsible for the uncontrolled proliferation may not be identifiable; in fact, it is not known for most human neoplasms. Neoplasia arises from mutations in genes that regulate cell growth, apoptosis, or DNA repair (Knudson, 2002).

1.1 Statement of the Problem

Orbito-ocular tumors are of great public health importance. The challenges that patients encounter include cosmetic deficits, visual loss, and in some instances, threat to life (Kennedy, 1984). Orbito-ocular tumors can increase in size to become unsightly with disturbing foul odour.

Visual loss resulting from the tumor has severe implications for all aspects of development especially in children (Gilbert and Forster, 2001). If not managed promptly, malignant tumors can spread from the orbito-ocular region to other parts of the body, eventually leading to loss of life. A good understanding of tumors that spread to the orbit can help in their diagnosis and management, and thereby reduce their associated morbidity and mortality.

Making accurate diagnosis of orbito-ocular tumors can be a major challenge, and, usually, a multidisciplinary approach is required into diagnosis and management of the patients, with input from the ophthalmologist, oculoplastic surgeon, internist, otorhinolaryngologist, neurosurgeon, plastic surgeon, pediatric and radiation oncologist (Kennedy, 1984).

Reported occurrence of orbito-ocular tumors vary widely from rare (Johansen et al., 2000; Margo and Mulla, 1998) to fairly common (Mohammed et al., 2006). These tumors are more common in tropical Africa than in other parts of the world (Templeton, 1971).

The great variation in the reported incidence of orbito-ocular tumors, in different studies depends on the source of data reviewed. This could be from the Pathology Department, Clinical Ophthalmology Service, Neurosurgical Department, or from different geographic areas (Demirci et al., 2002).

1.2 Study Justification

Majority of the studies on orbito-ocular space-occupying lesions are from the developed countries (Gunalp and Gunduz, 1994; Kennedy, 1984; Shields et al., 1984; Seregard and Sahlin, 1999). The reported frequency of occurrence of these tumors varies in different studies even in these countries. While Templeton, (1967) described orbital tumors as occurring relatively more commonly, identifying 312 cases over 7 years. Johansen and associates, (2000) described orbital lesions as rare with of 965 cases identified over 24 years.

However, orbito-ocular tumors are more common in the tropical African region than in other parts of the world (Templeton, 1967). Reports from earlier studies show that they account for a far greater percentage of all malignancies in Mozambique (Pirates, 1958) and Nigeria (Elmes and Baldwin, 1947) compared to tumors in developed countries. There is paucity of information on the prevalence and pattern of presentation of orbito-ocular tumors in Nigerian patients. Since the earliest reports of malignant diseases in the country (Elmes and Baldwin, 1947; Mulligan, 1970), there had been only a few reports of orbito-ocular tumors in the country (Samaila, 2009; Ajaoyeoba et al., 1992; Ekwerekwu et al., 1997), hence, this study is imperative to describe new trends in the occurrence of the disease. Most of these patients present to, or are eventually referred to a tertiary

health care facility, thus, there is need to review the records from a tertiary health care facility.

Late presentation at health facilities has been identified as a major challenge in the management of ophthalmic patients in developing countries (Fasina and Ubah, 2009). Unfortunately, this has grave consequences for patients with orbito-ocular tumors, where timely intervention can make a great difference in morbidity and mortality. Also, importantly, a good knowledge of the different types of tumors occurring locally, including an understanding of their pattern of presentation will help in educating the populace against late presentation.

. Histopathological evaluation is the most accurate method of diagnosing lesions and in the absence of a biopsy, it may be difficult to document the nature of a lesion precisely (Gunalp and Gunduz, 1994). Thus, it is imperative to evaluate the prevalence and pattern of presentation of all biopsied/surgically removed and histologically confirmed orbital tumors as this will allow for better management and more favourable outcome in this group of patients.

1.3 Definition of Terms

1. Tumor or neoplasia: abnormal proliferation of any tissue; new growth
2. Orbito-ocular tumor: any tumor involving the eyeball, orbital or periocular tissues.
3. Benign tumors: tumors without propensity to metastasis
4. Malignant tumors: tumors which can metastasis
5. Metastasis: ability of a tumors to spread beyond its tissue of origin

6. Proptosis: anterior protrusion of the eyeball.

7. Leucocoria: white pupillary reflex

8. Recurrence: appearance of signs and symptoms of a tumor after initial resolution

1.3 Aim and Objectives

General objective:

To determine the pattern of presentation of patients with histologically confirmed orbito-ocular tumors seen at University College Hospital (UCH), Ibadan, between January 1990 and December 2009.

Specific objectives:

(1) To determine the proportion of morbidity due to orbito-ocular tumors among biopsied lesions seen at the Pathology Department, UCH, Ibadan.

(2) To determine the types of orbito-ocular tumors seen in the hospital

(3) To describe the presentation and clinical features of orbito-ocular tumors

(4) To assess the outcome of management of patients with orbito-ocular tumors

(5) To identify the factors affecting the outcome of management of the patents.

CHAPTER TWO

LITERATURE REVIEW

2.0 Anatomy of orbito-ocular region

The orbit is a pyramidal or cone-shaped space comprised of seven bones (frontal, greater and lesser wings of the sphenoid, zygoma, maxilla, lacrimal, palatine, and ethmoid). The medial wall is composed of the frontal process of the maxilla, the lacrimal bone, the lamina papyracea of the ethmoid, and a portion of the lesser wing of the sphenoid. The ethmoid bone forms the thinnest portion of the wall permitting easy spread of ethmoid sinus lesions including tumors into the orbit. The inferior wall, or orbital floor is composed mainly of the orbital plate of the maxilla, the zygomatic bone anterolaterally, and the orbital plate of the palatine bone posteriorly. Its inferior relation is the maxillary sinus, an air filled cavity lined by mucosa, and a frequent source of spread of tumor into the orbit. The lateral wall is composed of the frontal process of the zygoma and the greater wing of the sphenoid lateral to the optic foramen. while, the superior orbital wall, or orbital roof, is comprised of the orbital plate of the frontal bone with a small contribution, posteriorly, from the lesser wing of the sphenoid (Dutton and Waldrop, 1994).

The major structures within and around the orbit, from which tumors may arise, are the eyeball, optic nerve and its surrounding meninges, extra-ocular muscles, lacrimal gland, blood vessels, nerves, connective tissues and the eyelids. The tissues of the eyeball from which tumors can arise include the conjunctiva, retina and uveal tract (Shields and Shields, 1999).

2.1 Prevalence of orbito-ocular tumors

Orbito-ocular tumors are uncommon disorders, with variations in observed prevalence in different populations depending on the race and age group studied, and the source of data reviewed (Johansen et al., 2000; Margo and Mulla, 1998). Prevalence figures differ depending on whether the sources of data are from the pathology referral centers (Shileds et al., 1984; Ochicha and Ima-Obong, 1999), clinical ophthalmology services (Hoshino and Ichikawa, 1980), radiology departments (Kennedy, 1984), pediatric centers (Onwasigwe, 2002), neurosurgical (MacCarty and Brown, 1964), or otorhinolaryngological units. For example, cases derived from neurosurgical practice would include more tumors of neural origin such as meningiomas and optic pathway gliomas (MacCarty and Brown, 1964), while reports from an otorhinolaryngology practice would include more secondary lesions such as paranasal sinus neoplasms and mucocele.

Reports from general ophthalmic practice are expected to have a greater incidence of common, non-tumor lesions like thyroid-related orbitopathy and inflammatory pseudotumor (Kennedy, 1984). Reports that included only histologically confirmed lesions show bias towards cases who had undergone surgical resection because of visual threat or suspicion of malignancy, and fewer lesions like inflammatory pseudotumor, capillary hemangioma and optic nerve tumors, which are less likely to have undergone surgical procedures (Porterfiled, 1962).

Reports including childhood cases often yield greater incidence of such lesions like dermoid cyst and capillary hemangioma (Bullock et al., 1989; Munirulhaq, 1989), compared to those in older patients which have higher incidence of orbital metastases and

lymphomas (Demirci et al., 2002). As a result of these factors, it is often difficult to attain an accurate perspective of the true incidence of orbito-ocular tumors (Shields et al., 2004).

Johansen et al (Johansen et al., 2000) in a 24-year review, reported 965 orbital lesions. Although they studied histologically confirmed lesions, they included tumors as well as other inflammatory and non-specific lesions. Margo and Mulla, (1998) in a 13-year review reported 314 cases. This study however included only primary malignant orbital tumors. Verma et al, (1999) who studied both primary and secondary orbital tumors, found 176 cases over 21 years, while about 950 cases were indentified over 25 years by Demirci et al., (2002) of which 200 occurred in those aged 60 years and above. Shinder et al., (2010) in a survey of orbital tumors in a comprehensive cancer centre in the United States found a total of 268 tumors over a 10 year period. The data however included histologically confirmed cases as well as lesions diagnosed based on clinical and radiological findings.

Reports from other African countries, Mozambique (Templeton, 1967) and Kampala (Pirates, 1958), showed a frequency of 3.2% and 3.3% respectively.

Olurin and Williams, (1972) in one of the earliest studies in Nigeria, reported 191 histologically-proven cases of orbito-ocular tumors. These constitute 2.2% of all tumors recorded in the cancer registry over a 9 year interval. Mohammed et al., (2006) in Zaria, found 124 malignant tumors over 10 years representing 5% of all malignant tumors seen within that period. Ekwerekwu et al., (1997) reported 94 cases among the adults studied, which accounted for 0.4% of all histologically diagnosed tumors over 11 years.

Abdu and Mohammed, (2006) identified 57 cases of orbito-ocular tumors in children over a 5 year period, but an earlier study by Abiose et al., (1985) found that childhood orbito-ocular malignancy represented about 60% of all childhood cancers.

2.2 Classification of Orbito-Ocular Tumors

Orbito-ocular tumors, like other tumors, can broadly be classified as primary, secondary or metastatic. Primary tumors originate directly from tissues of the eyeball, orbit or adnexa, while secondary tumors spread to the orbito-ocular region from adjacent structures most commonly the paranasal sinuses and intracranial tissues. Metastatic tumors to the orbit on the other hand, originate from distant tissues including the breast, prostate, and lungs (Shields et al., 1984).

Orbito-ocular tumors can also be classified as ocular, arising from the eyeball; orbital, arising from the orbital tissues; and extra-orbital arising from the adnexal tissues (Shields et al., 1984). Shields et al., (2004) classified orbital tumors into major sub-groups as cystic, vasculogenic, peripheral nerve, optic nerve and meningeal, fibrocystic, osseous and fibro-osseous, cartilaginous, lipocytic and myxoid, myogenic, lacrimal gland, primary melanocytic, metastatic, lymphoid and leukemia, secondary, histiocytic, thyroid related orbitopathy, other inflammatory, and miscellaneous.

They can also be classified as benign or malignant. Benign orbito-ocular tumors, in general, are well differentiated, closely resemble normal cells and it may be impossible to recognize them as a tumor by microscopic examination of individual cells, however, massing them into a nodule discloses the neoplastic nature of the lesion (Giordano et al., 2008). Malignant neoplasms, in contrast, range from well differentiated to

undifferentiated. Those composed of undifferentiated cells are termed anaplastic. The level of differentiation of a tumor relates to the maturity of the proliferating cells (Giordano et al., 2008).

2.3 Grading of orbito-ocular tumors

Grading of a tumor is based on the degree of differentiation of the tumor cells and the number of mitoses within the tumor. They are thus classified as grades I to IV with increasing anaplasia. The criteria for the individual grades vary with each tumor, but they attempt to judge the extent to which the tumor cells resemble or fail to resemble their normal counterparts. There is no direct perfect correlation between the histologic appearance and clinical behavior of a tumor, hence, in common practice, neoplasia are characterized in descriptive terms like a well differentiated retinoblastoma or highly undifferentiated carcinoma (Kumar et al., 2005).

2.4 Aetiology of orbito-ocular tumor

Neoplasms are derived from cells that normally maintain a proliferative capacity. The stimulus responsible for the uncontrolled proliferation may not be identifiable; and, in fact, it is not known for most human neoplasms. Tumors arise from mutations in genes that regulate cell growth, apoptosis, or DNA repair, and because this is a disorder of cell growth and behavior, the ultimate cause is defined at the cellular and sub-cellular levels (Boon and Van Den Eynde, 2003).

Studying the pattern of presentation of tumors in populations can contribute substantially to the knowledge about the origins of tumors, thus, major insights into the cause of

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Studying the pattern of presentation of tumors in populations can contribute substantially to the knowledge about the origins of tumors, thus, major insights into the cause of

tumors can be obtained by epidemiologic studies that relate particular environmental, hereditary, and cultural influences to the occurrence of neoplasms (Wilson et al, 1996). Also, studies of certain diseases associated with an increased risk of developing tumors can provide insights into tumor pathogenesis (Giordano et al., 2008). Besides the dominantly inherited precancerous conditions, some conditions are inherited in an autosomal recessive pattern. They are a group of cancer-predisposing conditions, characterized by defects in DNA repair and resultant DNA instability. Tumors may also occur at higher frequencies in certain families without a clearly defined pattern of transmission. The clinical features of these familial tumors include early age at onset, tumors arising in two or more close relatives of the index case, and sometimes, multiple or bilateral tumors. It is generally difficult to sort out the hereditary and acquired etiologic basis of a tumor because they often interact closely, and, the only certain way of avoiding the risk of tumor is not to be born; for to live is to incur this risk (Knudson, 2002). Chronic inflammatory reactions have also been implicated in tumor pathogenesis. The precise mechanisms linking inflammation and cancer development have not been established (Coussens and Werb, 2002), but may be through the production of cytokines, which stimulate the growth of transformed cells.

Radiation carcinogenesis- Radiant energy, whether in the form of the UV rays of sunlight or as ionizing electromagnetic (x-rays, γ-□rays) and particulate (α-□particles, β-particles, protons, neutrons) radiations, can transform virtually all cell types in vitro, and induce neoplasms in vivo in both humans and experimental animals. UV light has been clearly implicated in the causation of skin cancers, and ionizing radiation exposure from medical or occupational exposure and industrial accidents have produced a variety of malignant

neoplasia (Cleaver and Crowley, 2002). There is ample evidence from epidemiologic studies (Perera, 1997) that UV rays derived from the sun induce an increased incidence of squamous cell carcinoma, basal cell carcinoma, and possibly malignant melanoma of the skin. This risk depends on the type of UV rays, the intensity of exposure, and the quantity of light-absorbing melanin in the skin. UVB is believed to be responsible for the induction of cutaneous cancers (Kraemer et al., 1994).

2.5 Diagnosis of orbito-ocular tumors

The first approach in the correct diagnosis in a patient with an orbito-ocular tumor is centered on a thorough ophthalmic evaluation. A good history and thorough physical examination are essential to the development of a diagnosis (Rootman, 1988). The most important clinical manifestation of these tumors is proptosis, and often, is the chief complaint. Other complaints include leucocoria, changes in visual acuity, diplopia, eyelid mass, and/or pain.

Defining the extent and localization of orbital tumors are most dependent on imaging techniques. Ultrasonography is a relatively inexpensive and safe method of evaluating the orbit (Shamma et al., 1980). However, its use has been largely supplanted by computed tomography and magnetic resonance imaging (Roden et al., 1988). Computed tomography scanning is currently the best available technique for detection and localization of the extent of orbital lesions as it provides more information regarding bony landmarks, and is therefore, indispensable in surgical planning (Bilaniuk, 1999).

The clinician and the pathologist have important roles to play in facilitating the correct diagnosis of orbito-ocular tumors (Grove, 1979). Adequate clinical data are invaluable

for optimal pathologic diagnosis; moreover, the laboratory evaluation of the biopsied lesion can be only as accurate as the specimen made available to the pathologist for examination. This must be adequate, representative, and properly preserved. The sampling approaches used in histological examination of biopsied tissues include excision or incision biopsy, fine-needle aspiration, and cytologic smears.

2.6 Treatment options for orbito-ocular tumors

Enucleation, the surgical removal of the eye, leaving the eye muscles and the contents of the eye socket intact is used to treat intra-ocular tumors. It is performed when there is no other way to remove the tumor completely from the eye. Exenteration is the removal of the eyeball and all the tissues in the socket, and is performed for orbital tumors with loss of visual potential. Unfortunately, loss of vision in these procedures is permanent because an eye cannot be transplanted (Honavar, 2009).

However, some orbital and eyelid tumors can be completely excised with minimal disruption of vision depending on their size, location and delineation.

Chemotherapy, the treatment of malignant tumors by means of drugs that selectively destroys cancerous cells, can be used as adjuvant to surgery to destroy microscopic tumor cells. There are many chemotherapeutic drugs available, each type having potential side effects such as skin problems, nausea, vomiting, and infections (Boubacar et al., 2010).

Cryotherapy is the use of low temperatures to treat diseases. The goal of cryotherapy is to freeze the malignant tissues in order to stimulate inflammation and scarring in them and is usually recommended for conjunctival or eyelid tumors (Singh et al., 2007).

Radiation therapy uses high-energy radiation from x-rays and other sources to kill cancer cells and shrink tumors. Radiation that comes from a machine outside the body is called external-beam radiation therapy as opposed to radiation that is administered by placing a radiation plaque over or very near the tumor (internal radiation therapy or brachytherapy). External beam radiation therapy may be used to treat some choroidal metastasis, eyelid tumors, retinoblastoma post enucleation or exenteration, lymphomas and orbital tumors. Radiation plaque therapy is the most commonly used "eye-sparing" treatment for choroidal melanoma or intra-ocular retinoblastoma (Singh et al., 2007).

2.7 Complications of orbito-ocular tumors

The clinical significance of tumors ultimately lies in their effects on patients. Although malignant tumors are more threatening than benign tumors, any tumor, including benign ones, may cause morbidity and mortality. Indeed, both malignant and benign tumors may cause problems because of their location and impingement on adjacent vital structures, functional activity such as hormone synthesis, bleeding and infections when the tumor ulcerates, and, symptoms that result from rupture or infarction. The location of the tumor is crucial in its clinical manifestation. A small carvenous hemangioma, though, benign and possibly nonfunctional, can compress the optic nerve, if located at the orbital apex, and thus lead to severe visual impairment, while squamous cell carcinoma of the eyelids typically presents as a fungating, foul-smelling, ulcerative mass with severe cosmetic embarrassment (Johansen et al., 2000).

CHAPTER 3

METHODOLOGY

3.0 Study design

This is a retrospective case review with descriptive and analytical components. The descriptive component of the study includes the prevalence, types, presentation and outcome management of orbito-ocular tumors, while the analytical component includes the determination of the factors associated with survival of patients with tumor, and the outcome of management.

3.1 Study location

The study was conducted using data generated at the Eye clinic and Pathology Department of the University College Hospital, Ibadan, Oyo State. The University College Hospital was established in 1957 and is the first tertiary health institution in Nigeria. It is a major referral centre for other hospitals not only in south-western Nigeria, but from all parts of the country. The Eye clinic of the hospital provides general ophthalmic medical services as well as sub-specialist eye care to patients from all over south western Nigeria through daily clinic sessions. The sub-specialist units of the clinic include the orbit, oculopasty and ocular oncology unit, pediatric ophthalmology, cornea and anterior segment, glaucoma, retina and vitreous, neuro-ophthalmology and community ophthalmology units. The orbit, oculopasty and ocular oncology unit is one of such few centers in the country and receives referral from all over the nation.

The Eye clinic has seven consulting rooms, three refractions rooms, two nurses' stations, medical records' section, and visual field investigation and laser therapy rooms. There are

eleven consultant ophthalmologists, twenty resident doctors, three optometrists, twenty ophthalmic nurses, seven medical records officers, six public health nurses and variable number of medical assistants working in the Eye clinic.

Patients are usually referred to be seen in the Eye clinic. The sources of referral include the General Out-patient Department and other clinics in the hospital, other government and private hospitals in the state and other parts of the country. The orbit, oculoplasty and ocular oncology clinic runs two days in a week. Newly presenting patients are seen by the consultant ophthalmologist. Patients returning for follow-up visits are usually managed by the resident doctors under the supervision of the consultant. Patients requiring surgery are admitted a day prior to surgery, or present on the day of surgery, depending on the procedure. All patients with suspected tumor undergo incision or excision biopsy of the lesion and the specimen will be sent for histological confirmation in the Pathology Department of the hospital. Members of staff of the Pathology Department include seven consultant pathologists, eight resident doctors, ten laboratory scientists and some medical assistants.

3.2 Study Population

The study population comprised all patients with histologically confirmed orbito-ocular tumor presenting for the first time to the Eye clinic during the study period (1990-2009).

3.3 Inclusion Criteria

All patients with complete clinical and histopathological data were included in the study.

3.4 Exclusion Criteria

Patients with missing records or incomplete variables were excluded from the study.

3.5 Sample Size Determination

There was no patient selection done in this study due to the uncommon presentation of the tumors. Hence all patients that met the inclusion criteria were recruited and included.

3.6 Data Collection

Data of patients with histologically confirmed orbito-ocular tumors during the study period was generated from the register at the Pathology Department. Also, patients' records were retrieved from the Medical Records unit of the Eye clinic. Information was retrieved from the records of each patient with the use of a proforma. The data retrieved included age at presentation, sex, clinical history, type of tumor (primary, secondary or metastatic), visual acuity, site of tumor, clinical diagnosis, surgical procedure, histological diagnosis, adjuvant therapy (if completed or not), tumor recurrence (clinical re-appearance of tumor after initial resolution or surgical excision) and time to recurrence, (if present), and duration of follow-up. Clinical information retrieved included ocular symptoms, duration of symptoms (interval between onset of first symptom and presentation to health facility), family history of tumor, treatment received before presenting, size of tumor, degree of proptosis, presence of lymph node enlargement, evidence of metastasis (primary tumors) and other vital medical history.

3.7 Data Management and Analysis

Data collected with the proforma was painstakingly entered into a database on a personal computer by the investigator, and statistical analysis was performed with the aid of Statistical Package for Social Sciences version 16 software (SPSS Inc, Chicago IL., USA).

Data entered were cleaned and analyzed by generating summary indices for the variables. Categorical variables were presented as frequencies (tables, charts), while quantitative variables were presented as measures of central tendency (mean, median) as well as measures of dispersion (standard deviation). Binary logistic regression was carried out to determine if age at onset of_symptoms and treatment status can predict the recurrence of retinoblastoma. A survival curve was plotted to estimate the median time of tumor recurrence in patients with retinoblastoma and other tumors.

3.8 Ethical Consideration

Ethical approval was sought and obtained from the University of Ibadan/University College Hospital Institutional Review Board. All information retrieved and data collected were treated with utmost confidentiality. Data was stored in the investigator's personal computer and password protected.

3.9 Limitations

1. The retrospective nature of the study limited the completeness of the information available for retrieval in the case notes. Such details about patients' demographics like state/town of origin and parents' occupation could not be analysed due to inaccurate recording.

2. Some patients (10) could not be included in the analysis as their case records were missing.

CHAPTER FOUR

RESULTS

A total of two hundred and fifteen biopsied and histologically confirmed orbito-ocular tumors were examined out of a total of 49,685 biopsied specimens in the Pathology Department during the study period. Ten cases were excluded from the final analysis on account of incomplete information.

4.0 Demographic characteristics of patients with orbito-ocular tumors

The age and sex distribution are shown in Figure 4.1. The median age of the patients with orbito-ocular tumors was 7.0 years, (range 4 months to 81 years). There were 109 males (53.2%) and 96 females (46.8%). The male to female ratio was 1.1:1.

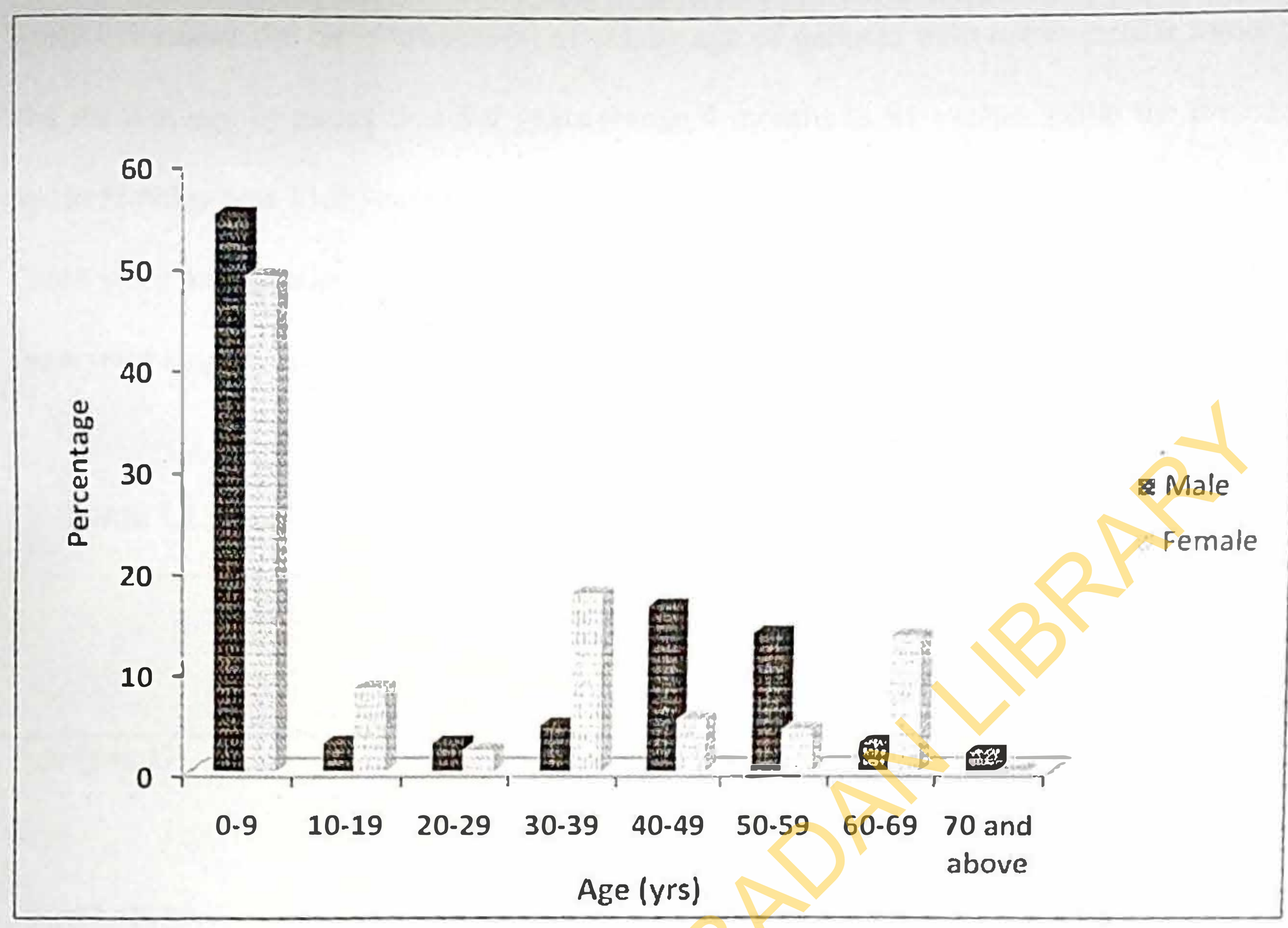

Figure 4.1: Age and Gender distribution of patients with orbito-ocular tumors

Table 4.1 shows the cross tabulation of sex by age of patients with orbito-ocular tumors. The median age in males was 6.0 years (range 4 months to 81 years), while the median age in females was 11.0 years (range 1.0 - 69.0 years).

There were more children with orbito-ocular tumors than adults, and in both age groups, there were slightly more males than females.

Table 4.1: Sex by Age distribution of patients with orbito-ocular tumors

	Gender		
	Males (%)	Females (%)	Total (%)
Age (years)			
0-15	61(53.5)	53(46.5)	114(100.0)
16 and above	48(52.7)	43(47.3)	91(100.0)
Total	109	96	205

4.1 Clinical history of patients with orbito-ocular tumor

Table 4.2 shows the eye affectation in patients with orbito-ocular tumors. The right side was affected by the tumor in 103 (50.2%) patients, the left side in 82 (40%), while 20 (9.8%) patients had bilateral involvement. Eighteen of the 20 patients (90%) with bilateral involvement were histologically confirmed retinoblastoma cases and the remaining two (10%) had ocular surface squamous neoplasia.

Table 4.2 Eye affectation in patients with orbito-ocular tumors

	Laterality			
Tumor type	Right eye (%)	Left eye (%)	Both eyes (%)	Total (%)
Retinoblastoma	42(43.7)	36(37.5)	18(18.8)	96(100.0)
Rhabdomyosarcoma	5(35.7)	9(64.3)	0(0.0)	14(100.0)
Ocular surface squamous neoplasia	23(53.5)	18(41.9)	2(4.6)	43(100.0)
Squamous cell carcinoma eyelids	7(53.8)	6(46.2)	0(0.0)	13(100.0)
Non-Hodgkin lymphoma	4(50.0)	4(50.0)	0(0.0)	8(100.0)
Others	22(71.0)	9(29.0)	0(0.0)	31(100.0)
Total	103	82	20	205

The frequencies of symptoms are presented in Table 4.3. A total of 146 (71.2%) of the patients had lost vision at the time of presentation while 95 (46.3%) presented with proptosis. Ninety-one patients (44.4%), who were histologically confirmed retinoblastoma cases, presented with leucocoria and 81 patients (39.5%) presented with palpable swellings. Other presenting symptoms included pain, ulcerating mass, bleeding, redness, jaw swelling, and squint.

Table 4.3 Distribution of symptoms among patients with orbito-ocular tumors

*Clinical history	Number of patients	Percent
Loss of vision	146	71.2
Proptosis	95	46.3
Leucocoria	91	44.4
Mass/swelling	81	39.5
Pain	47	22.9
Ulcer/fungating mass	34	16.6
Bleeding	22	10.7
Redness	21	10.2
Jaw swelling	8	3.9
Squint	7	3.4
Hyphema	3	1,5
Epistaxis	5	2.4
Rupture globe	2	1.0

* More than 1 option possible

The median duration of symptoms before presentation was 10.0 months with a range of 1.0 - 156 months.

Positive family history of tumor was obtained in only six (2.9%) patients, two of whom had squamous cell carcinoma of the eyelid, and were albinos (oculo-cuteneous), while another two had ocular surface squamous neoplasia of the conjunctiva.

4.2 Types of orbito-ocular tumors

The type and tissue affectation of orbito-ocular tumors are presented in Table 4.4. One hundred and eighty-nine (92.2%) patients were diagnosed with primary tumors while 16 (7.8%) had secondary tumors. There were no metastatic tumors. Ninety-six patients (46.8%) had intraocular tumors, 20 patients (9.8%) had tumors involving the eyelids, while the orbits were affected in the remaining 89 patients (43.4%).

Table 4.4 Type and tissue affectation in orbito-ocular tumors

Tumor	Frequency	Percent
Primary	189	92.2
Secondary	16	7.8
Total	205	100.0

Tissue affectation of tumor	Frequency	Percent
Intra-ocular	96	46.8
Orbit	89	43.4
Eyelids	20	9.8
Total	205	100.0

The clinical and histological diagnoses of the patients are presented in Table 4.5. In terms of specific diagnoses, 100 patients (48.8%) were clinically diagnosed as having retinoblastoma, 96 (96.0%) of whom were confirmed histologically. All 43 patients with ocular surface squamous neoplasia were confirmed histologically. Out of the 14 patients with histological confirmation of rhabdomyosarcoma, only five had prior clinical suspicion of the tumor.

Table 4.5 Clinical and histological diagnoses of patients with orbito-ocular tumors

	Clinical diagnosis		Histological diagnosis	
	Number of patients	Percent	Number of patients	Percent
Retinoblastoma	100	48.7	96	46.8
Ocular surface squamous neoplasia	43	21	43	21
Squamous cell carcinoma	14	6.8	13	6.4
Rhabdomysarcoma	5	2.4	14	6.8
Pleomorphic adenoma	8	3.9	1	0.5
Meibomian gland carcinoma	2	1.0	2	1.0
Optic nerve glioma	5	2.4	1	0.5
Sino-nasal-orbital tumor	8	3.9	5	2.4
Maxillary carcinoma	3	1.5	8	3.9
Hemangioma	1	0.5	5	2.4
Non-Hodgkin lymphoma	4	2.0	3	1.5
Basal cell carcinoma	1	0.5	5	2.4
Astrocytoma	1	0.5	3	1.5
Pseudotumor	4	2.0	0	0.0
Others	6	2.9	6	2.9
Total	205	100.0	205	100.0

Others: fibrous dysplasia and nevus (2 cases each), ossifying fibroma and systemic lymphoma (1 case each).

Table 4.6 shows the distribution of misclassification of orbito-ocular tumors among the patients based on their clinical diagnosis. There was a low proportion of misclassification among patients with retinoblastoma and squamous cell carcinomas and high proportion among patients with pleomorphic adenoma, optic nerve glioma, hemangioma and basal cell carcinoma.

Table 4.6 Misclassification of orbito-ocular tumors among patients

Diagnosis	Clinical (number)	Histological (number)	Mis-classified (number)	Mis-classified (%)
Retinoblastoma	100	96	4	4.0
Ocular surface squamous neoplasia	43	43	0	0.0
Squamous cell carcinoma	14	13	1	7.1
Rhabdomysarcoma	5	14	9	64.3
Pleomorphic adenoma	8	1	7	87.5
Meibomian gland carcinoma	2	2	0	0.0
Optic nerve glioma	5	1	4	80.0
Sino-nasal-orbital tumor	8	5	3	37.5
Maxillary carcinoma	3	8	5	62.5
Hemangioma	1	5	4	80.0
Non-Hodgkin lymphoma	4	3	1	25.0
Basal cell carcinoma	1	5	4	80.0
Astrocytoma	1	3	2	66.7

4.3 Survival status of patients with orbito-ocular tumors

Table 4.7 shows the survival status of patients with orbito-ocular tumors. There was high level of recurrence among childhood malignant tumors (retinoblastoma and rhabdomyosarcoma), while a lower proportion of adults with tumors had recurrences. However, there were a large proportion of patients whose status could not be determined as they either defaulted before completing their adjuvant treatment or were lost to follow-up.

Table 4.7 Survival status of patients with orbito-ocular tumors

Histological diagnosis	Survived (frequency)		Dead (frequency)	Status not known	Total (frequency)
	With recurrence	No recurrence			
Retinoblastoma	36	26	4	30	96
OSSN	11	20	0	12	43
SCC	8	0	0	5	13
Rhabdomyosarcoma	9	4	1	0	14
Maxillary carcinoma	0	2	0	6	8
Others	6	21	0	4	31
Total	70	73	5	57	205

OSSN= ocular surface squamous carcinoma, Others= pleomorphic adenoma, meibomian gland carcinoma, optic nerve carcinoma, sino-nasal-orbital tumor, hemangioma, non-Hodgkin lymphoma, basal cell carcinoma, astrocytoma.

4.4 Factors affecting recurrence at one year in patients with orbito-ocular tumors

Chi square analysis was carried out to determine the factors that are associated with recurrence in the patients. There was no statistically significant association in the duration of symptoms and recurrence (chi square 0.476, df = 4, p = 0.490). However, there were more recurrences among patients who did not complete their treatment (chi square 96.713, df = 1, p = 0.001). Table 4.8

Table 4.8 Factors affecting recurrence at one year in patients with orbito-ocular tumors

Duration of Symptoms at first presentation	No recurrence	Recurrence	Total
< 1 year	41(48.2)	44(51.8)	85(100.0)
> 1 year	34(54.0)	29(46.0)	63(100.0)
Total	**75(50.7)**	**73(49.3)**	**148(100.0)**
$X^2 = 0.476$, df = 4, p = 0.490			
Adjuvant treatment			
Complete	61(95.3)	3(4.7)	64(100.0)
Incomplete	52(48.6)	55(51.4)	107(100.0)
Total	**113(66.1)**	**58(33.9)**	**171(100.0)**
$X^2 = 96.713$, df = 1, p = 0.001			

Table 4.9 shows the chi square analysis to determine the factors that are associated with recurrence in the patients with retinoblastoma. There was no statistically significant association in age of onset of tumor and recurrence (chi square = 0.571, df = 2, p = 0.751 . However, those who completed their treatment were statistically at a higher risk of having recurrence when compared with those who did not (chi square = 48.644, df = 1, p = 0.001).

Table 4.9 Factors affecting recurrence at one year in patients with retinoblastoma

	Recurrence	Non-recurrence	Total
Age at onset			
0-1 year	3(75.0)	1(25.0)	4(100.0)
>1-years	20(58.8)	14(41.2)	34(100.0)
>2 years	107(64.1)	60(35.9)	167(100.0)
Total	130(63.4)	75(36.6)	205(100.0)
$X^2 = 0.571$, df = 2, p = 0.751			
Adjuvant treatment			
Complete	68(94.4)	4(5.6)	72(100.0)
Incomplete	49(43.8)	63(56.3)	112(100.0)
Total	117(63.6)	67(36.4)	184(100.0)

$X^2 = 48.644$, df = 1, p = 0.001).

4.5 Logistic regression predicting recurrence at one year in patients with retinoblastoma

Table 4.10 shows prediction of recurrence in patients with retinoblastoma using binomial logistic regression analysis. In those with retinoblastoma (n= 96), patients who developed the tumor in their second year of life were twice as likely to have recurrence compared with those who had tumors in the first year of life, (OR 2.10, 95% CI = 0.197-22.33, p = 0.538). Persons who developed the tumor after their second year were one and half times more likely to have recurrence, (OR 1.47, 95% CI = 0.150-14.491, p = 0.74). These were however, not statistically significant. Patients who did not complete their treatment were 52 times more likely to have recurrence (OR 52.0, 95% CI = 6.67-405.66, p = 0.001.

Table 4.10 Logistic regression predicting the recurrence in patients with retinoblastoma

Variable	OR(95% CI)	P-value
Age at onset of symptoms		
0-1 years	1.00	
>1-2 years	2.10(0.197- 22.330)	0.538
>2 years	1.47(0.150 -14.491)	0.740
Adjuvant treatment		
Complete	1.00	
Incomplete	52.00(6.67 – 405.66)	0.001

4.6 Recurrence in patients with orbito-ocular tumors

Using the survival analysis to estimate recurrence in the patients, 36 of the 96 children (37.5%) with retinoblastoma had tumor recurrence over the 40-month period after diagnosis. The median time to recurrence was 8 months (95% CI = 1.6-14.4 months), Figure 4.2. The median time to recurrence for the remaining 109 patients was 11 months (95% CI = 14.0-57.9 months), Figures 4.3.

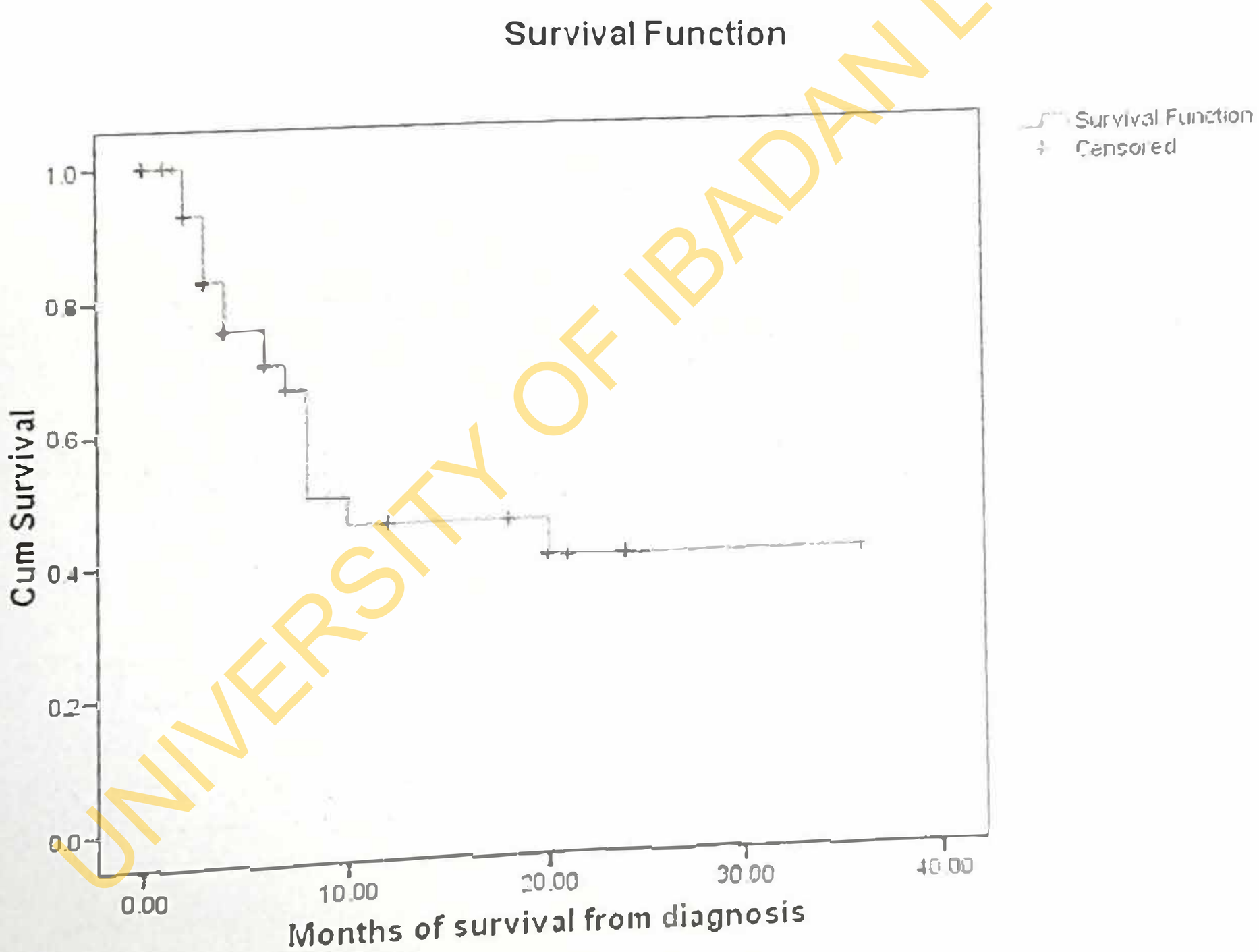

Figure 4.2: Survival curve for patients with retinoblastoma

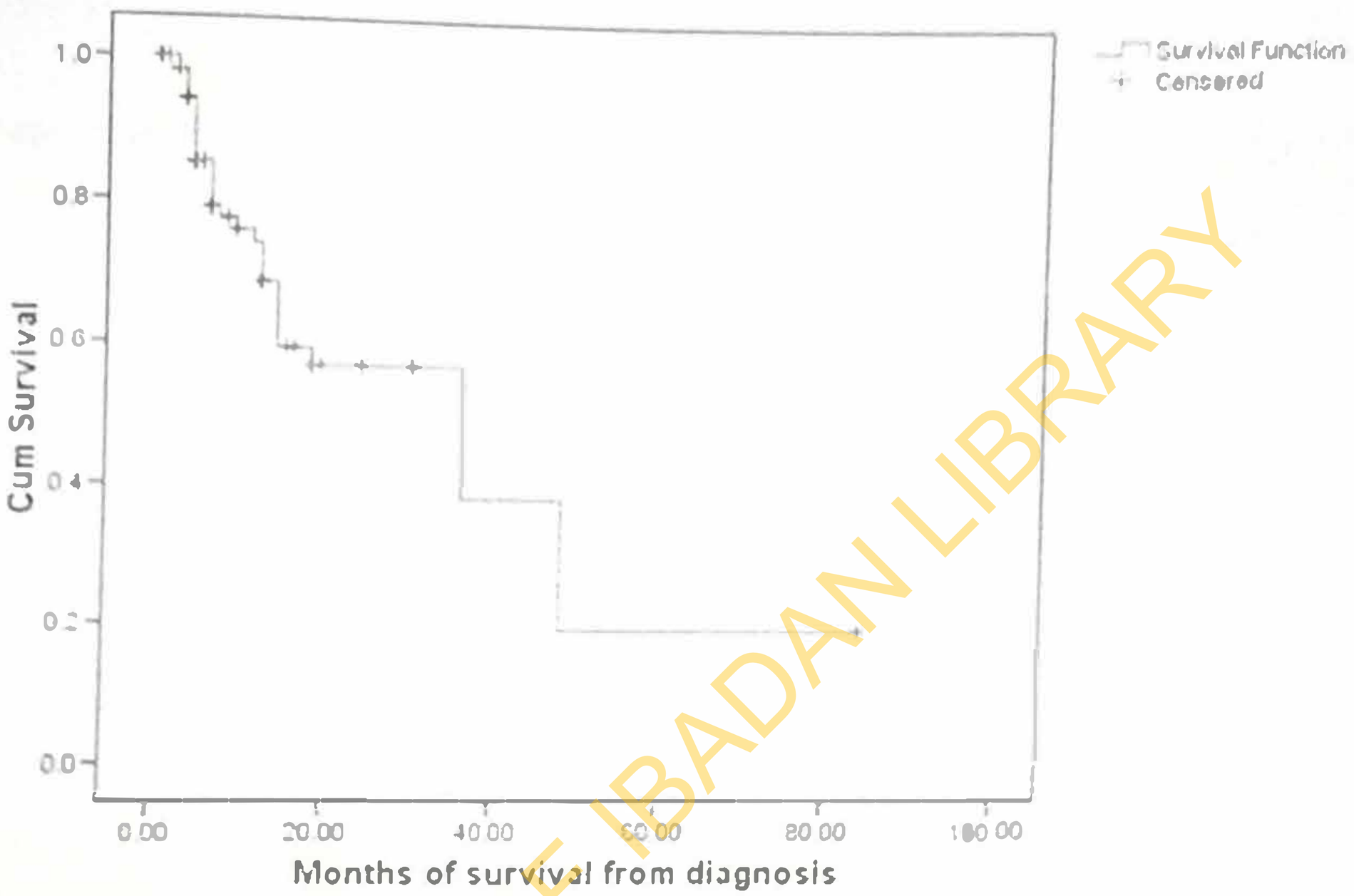

Figure 4.3: Survival curve for patients with other tumors

CHAPTER FIVE

DISCUSSION

5.0 Proportional morbidity of orbito-ocular tumors

The proportional morbidity percent of orbito-ocular tumors among all biopsied tumors in this study was found to be 0.4% (205 out of 49,685 lesions) over the 20-year period. This is lower than 2.2% (191 cases) reported by Olurin and Williams (1972) over a nine year period and 252 cases seen by Ajaiyeoba et al., (1992) over 11 years in the same institution. This disparity may be because the earlier studies included patients with inflammatory and other non-tumor cases that had enucleation, while this study reviewed only confirmed tumor cases. Also, there are now more expertise and more teaching hospitals in the country, which are able to manage these cases, thereby reducing the number of patients that would have otherwise been referred to our center for treatment. It may also indicate a true reduction in the number of patients with tumors that needed to undergo tissue biopsy and histological confirmation, as improvement in imaging techniques has increased over the years. Also, the management of some tumors like rhabdomyosarcoma had changed from surgical to the use of chemotherapeutic agents, hence such patients present to the pediatric oncologists.

It is difficult to compare our results with those from other centers in Nigeria (Ekwerekwu et al., 1997; Abdu and Mohammed, 2006; Mohammed et al., 2006; Abiose et al., 1985; Onwasigwe, 2002) because of disparity in the source of data used and type of lesions studied.

5.1 Types of orbito-ocular tumors

As observed by other researchers, retinoblastoma was the major tumor diagnosed in our series. Similar findings had been reported in previous reviews involving all age groups (Ajaiyeoba et al., 1992; Mohammed et al., 2006; Abiose et al., 1985; Olurin and Williams, 1972; Ochicha and Ima-Obong, 1999), and those amongst children (Onwasigwe, 2002; Abdu and Mohammed, 2006). This is also similar to the findings by Johnson et al.,(1990), who reviewed pediatric orbital tumors in Saudi Arabia, and found secondary invasion of the orbit by retinoblastoma accounting for a third of the cases. However, reports on orbital tumors from developed countries (Shinder et al., 2010; Shields et al., 2004; Johansen et al., 2000; Liaricos and Gekas, 1984) did not reflect a high prevalence of secondary invasion of the orbit by retinoblastoma. This may be because of the late presentation to the health facility and subsequent delayed treatment of patients in developing countries (Fasina and Ubah, 2008).

Ocular surface squamous neoplasia, a range of tumors involving the epithelial lining of the ocular surface ranked second in occurrence (21%). A similar trend had been reported in previous studies in the African region (Ajaiyeoba et al., 1992; Mohammed et al., 2006; Templeton, 1967) and other tropical areas (Verma et al., 1999). This is however at variance with an earlier study in the region (Olurin and Wiliams, 1972), which reported Burkitt's lymphoma as second to retinoblastoma, and with reports from the western countries which reported more cases of lymphomas (Margo and Mulla, 1998; Johansen et al., 2000; Shields et al., 2004). The higher proportion of Burkitt's lymphoma reported by Olurin and Williams (1972) may be because at that time, the diagnosis of Burkitt's lymphoma was based on histopathologic examination. Presently, diagnosis can be made

clinically and treatment instituted. The relatively higher proportion of squamous neoplasia in the tropical countries may be as a result of intense exposure to the sun which had been implicated its etiology (Shields and Shields, 2004).

Rhabdomyosarcoma is the commonest primary malignant tumor of the orbit in children and this accounted for 6.8% of the cases in our series. This had also been documented in previous studies (Liaricos and Gekas, 1983; Abdu and Mohammed, 1986; Gunalp and Gunduz, 1994; Margo and Mulla, 1998; Johansen et al., 2000). Another plausible reason for the high proportion of the tumor diagnosed in the present series is the fact that the health facility is one of the few specialist centers in the country with facilities for radiotherapy treatment for cancer. Radiotherapy is now a major treatment modality for rhabdomyosarcoma (Kumar et al., 2005).

The commonest lid tumor was squamous cell carcinoma (6.3%). This is similar to earlier reports within and outside the country (Akpe et al., 2009; Mohammed et al., 2006; Ekwerekwu et al., 1997; Ajaiyeoba et al., 1992; Demirci et al., 2002; Olurin and Williams, 1972; Templeton, 1967). Studies among Caucasians however, reported higher prevalence of basal cell carcinoma (Shinder et al., 2010; Gunalp and Gunduz, 1994; Reifler and Hornblass, 1986). The lower prevalence of basal cell carcinoma had been adduced to the heavy dark skin pigmentation of Negroes. Meibomian gland carcinoma is not a common tumor of the eyelids, and we had only two cases (1%). Previous reports had also reported few cases (Shields et al., 2004; Demirci et al., 2002; Verma et al. 1999; Gunalp and Gunduz, 1994) or none (Shinder et al.,2010; Mohammed et al., 2006; Ekwerekwu et al., 1997; Ajaiyeoba et al., 1992).

Worthy of note is the fact that no case of melanoma, and only four cases (2%) of lymphomas (primary orbital or systemic) were recorded during this period confirming previous reports that it is a rare type of malignancy in Africans (Akpe et al., 2009; Bekibele and Oluwanisola, 2003; Ajaiyeoba et al., 1992).

The paranasal sinuses were a common source of secondary spread of tumors to the orbito-ocular region because of their contiguous location with the orbit. Thirteen cases of sino-nasal tumors (6.3%) were present in the review (5 cases of sinonasal tumors and 8 of maxillary carcinoma). This has been previously documented (Shinder et al., 2010; Shields et al., 2002; Demirci et al., 2002; Gunalp and Gunduz, 1994).

Other uncommon tumors- fibrous dysplasia (2), ossifying fibroma (1), both of bone origin, nevus (2), and systemic lymphoma (1), constitute about 3% of the cases in our series. These are slowly growing tumors, diagnosis could be made by imaging, clinically, or by laboratory tests and rarely do such patients undergo surgical biopsy, thus contributing to the few numbers recorded over the study period.

5.2 Clinical history of patients with orbito-ocular tumor

About 56% of the tumors reviewed affected children. This is not surprising as retinoblastoma is the commonest primary intra-ocular tumor in children with peak age at 18 months. This also agrees with other reports (Mohammed et al., 2006; Olurin and Williams, 1972; Amusa et al., 2004(61); Otoh et al., 2004). Low prevalence of childhood involvement was reported in studies of orbital lesions excluding ocular and adnexa tumors (Johansen et al., 2000; Shinder et al., 2010).

Bilaterality is not common in orbito-ocular tumors. Of the different tumors found in this region, retinoblastoma is noted to present with bilateral lesions due to its genetic

predisposition. However, even this is uncommon (Abiose et al., 1984; Abdu and Mohammed, 2006; Ahmadi et al., 2008; Olurin and Williams, 1972). Very rarely, ocular surface squamous neoplasia may present with bilateral lesions, probably due to the environmental factors implicated in its etiology (Ogun et al., 2009; Olurin and Williams, 1972; Ahmadi et al., 2008). About 19% of our patients with retinoblastoma had bilateral disease while 5% of those with ocular surface squamous neoplasia had bilateral lesions. There were no bilateral cases in the other tumors.

Over 70% of our patients had lost vision at the time of presentation. This is not surprising as the average duration of symptoms before presentation was 10 months (as high as 156 months). Late presentation and delayed treatment had been reported to be very common among ophthalmic patients in south west Nigeria (Fasina and Ubah, 2008), thus, patients do not present until the disease has progressed and is affecting vision. Unfortunately, this has serious consequence for patients with tumors. Delayed treatment may lead to spread of the tumor to secondary sites, and thereby reducing the chances or period of patient survival.

Almost half of the patients presented with proptosis. This is not surprising, as a space-occupying lesion in the bony orbit, would result in a forward protrusion of the eyeball (Shields et al., 2001; (6) Abdu and Mohammed, 2006; Owoeye, et al., 2005). Demirci et al. (2002) however, reported that majority of their patients presented with palpable masses followed by proptosis. This is probably due to early presentation at health facilities by patients in the developed countries.

Leucocoria is the most common presentation in patients with retinoblastoma (Kanski, 1999; Akang et al., 2000; Sang and Albert, 1982; Abrahamson et al., 2003) and about 95% of our patients with retinoblastoma presented with this.

5.3 Factors affecting recurrence status of patients with orbito-ocular tumors

It is customary to assess prognosis of patients with tumors by estimating their survival rates. In developed countries, where regular follow-up of patients is possible, 5-year survival rates of most tumors had been estimated. This refers to the percentage of patients who live at least 5 years after being diagnosed of the tumor. Many socio-cultural factors make this difficult in developing countries. Patients are often lost to follow-up, and do not complete their treatment regimen. High cost of treatment, poverty, and lack of health insurance schemes have also contributed to this. About half of the patients were lost to follow-up, unfortunately, making it difficult to determine prognosis and survival time.

Hence, we assessed recurrence status (as an indirect measure of survival) and the factors contributing to recurrence. Long duration of symptoms before presentation, with consequent delay in diagnosis and treatment had been associated with a greater risk of metastasis of retinoblastoma (Haik et al., 1985; Finger et al., 2002). However, in this study, there was no statistically significant difference in the duration of symptoms and tumor recurrence. This may be due to the small data set as there was only data on 148 patients. There were however, more recurrences among patients who did not complete their treatment when compared with those who completed. This is quite worrisome as over half of the patients with data of treatment status could not complete their treatment schedule. Reasons given were distance to the managing health facility, financial

constraints, and advanced/progressive disease. This could possibly contribute to a higher mortality among patients with malignant tumors in our area.

Also, children with retinoblastoma, who did not complete their treatment schedule, were 52 times at higher risk of having recurrence after 1 year of diagnosis. Tumor recurrence and metastasis are more difficult to treat than the primary tumor and are associated with reduced patient survival (Boubacar et al., 2010). In the United States, the 5-year survival for patients with retinoblastoma improved over a 30 year period from 92.3% to 96.5% (Broaddus et al., 2009). Early detection and treatment play a key role in the improved patient survival and the goal of retinoblastoma management now is early detection to maximize the visual outcome and the quality of life of the affected child (Honavar, 2009). However, late presentation, delayed, and incomplete treatment still remain high in our patients resulting in poor outcome.

5.4 Misdiagnoses of patients with orbito-ocular tumors

The distribution of the level of misclassification between clinical assessment and histopathology revealed a low proportion of misdiagnoses in patients with retinoblastoma, ocular surface squamous neoplasia and squamous cell carcinoma. There was however, a high proportion of misclassification in the other tumors. This could have been due to the small number of these tumors, thus, suggesting their relative uncommon presentation among tumors in this region. The low level of misclassification among the more common tumors, thus, suggests a fairly accurate clinical diagnosis when compared with the confirmatory histological diagnosis.

CONCLUSION

Orbito-ocular tumors still remain uncommon in our health institution. There appears to be a reduction in the number of cases seen compared to previous studies. Retinoblastoma was the commonest type of tumor in the orbito-ocular region, while melanomas are rare. Leucocoria is the commonest presenting complaint in patients with retinoblastoma. Late presentation to the health facility is still high among the patients with a large proportion having lost their vision before presenting. A large proportion of patients did not complete their treatment regimen, resulting in short median time to tumor recurrence and possible poor survival. Also, the follow-up rate was suboptimal with more than half defaulting from follow-up visits. There is a low level of misdiagnoses between clinical assessment and histology in the patients, suggesting a fairly accurate clinical assessment of patients with orbito-ocular tumors. This can reduce the cost of pre-operative diagnostic investigations in the patients.

RECOMMENDATIONS

1. There is need for public enlightenment possibly through the electronic media in both English and local languages on the signs of orbito-ocular tumors especially retinoblastoma, and encourage early presentation for treatment to increase the overall patient survival.

2. The capacity of secondary health facilities should be improved, and health personnel trained on early recognition, diagnosis and referral of patients with orbito-ocular tumors.

3. The National Health Insurance Scheme should enhanced as a way to reduce the cost of treatment of patients with tumors as this may likely ensure that they complete their treatment schedule.

4. Counselors experienced in the care of tumor patients need to be employed in tertiary health facilities involved in the care of patients with tumor to stress the need for regular follow-up to patients and their care-givers.

5. More centers for cancer management need to be created in the different geo-political zones in the country, thereby reducing the number of patients that would hitherto have been lost to follow-up due to long distance from our hospital.

6. Continuous training of specialists to improve their clinical acumen in the recognition and diagnosis of orbito-ocular tumors should be done.

7. Further research on the orbito-ocular tumors in our locality, especially their genetics, is necessary to better understand the causes, risk factors, and treatment outcome of these tumors in our population.

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APPENDIX

Proforma for data collection on patients with orbito-ocular tumors

Hospital Number .....

Patient initials .....

A. Demographic variables

1. Age .....
2. Sex .....
3. State of origin .....
4. Occupation .....
5. Residence (a) Rural (b) Urban

B. Clinical history

6. Main presenting complaint(s) 1. Proptosis 2. Mass 3. Poor vision 4.Leucocoria 5. Pain
7. Other complaints .....
8. Duration of symptoms ..... (Days/weeks/months/ years)
9. Ocular history
   a. (i) Ocular surgery 1. Yes 2. No (ii) If yes, what type? .....
   b. Ocular trauma 1. Yes 2. No
   c. Other significant history .....
10. Medical history
    a. Hypertension 1. Yes 2. No
    b. Diabetes 1. Yes 2. No
    c. Swelling in other parts 1. Yes 2. No
    d. ENT symptoms 1. Yes 2. No
    e. Other significant history .....
11. (a) Family history of tumor 1. Yes 2. No
    (b) If yes, what is the tissue affected .....

C. Examination findings

12. Visual acuity RE ..... LE .....

13. Tissue affected .....

14. Laterality 1. Right 2.Left 3. Both eyes

15. Degree of proptosis .....

16. Anterior segment pathology 1. Yes 2. No

If yes specify .....

17. Posterior segment pathology 1. Yes 2. No

If yes specify .....

D. Tumor examination

18. Palpable 1. Yes 2. No

19. If yes, dimensions .....

.....

E. Diagnosis and management

18. Clinical Diagnosis .....

19. Type of tumor 1. Primary 2. Secondary 3. Metastatic

20. Primary tumor site (if 2° or metastatic) .....

21. Investigation/diagnosis 1. USS 2. CT 3. MRI

4. Other (specify).....

22. Surgical treatment/findings

1. Incision biopsy
2. Excision biopsy
3. FNAC
4. Enucleation
5. Exenteration

23. Histologic diagnosis .....

24. Duration of follow-up .....

25. Status at last follow-up .....