

JIMMA UNIVERSITY
FACULTY OF MEDICINE
DEPARTMENT OF PATHOLOGY



HISTOPATHOLOGICAL PATTERNS OF OPHTHALMIC LESIONS AND ASSOCIATED FACTORS IN JIMMA UNIVERSITY MEDICAL CENTER, JIMMA, SOUTH WEST ETHIOPIA: A 5 YEAR RETROSPECTIVE CROSS SECTIONAL STUDY, 2021

BY HABIB EBRAHIM (MD)

ADVISORS:

ABDO KEDIR (MD, ASSISTANT PROFESSOR OF PATHOLOGY)

LELISA SENA (MPH, Ph.D.)

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Jimma University
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Histopathological patterns of ophthalmic lesions and associated factors in Jimma University Medical Center, Jimma, Southwest Ethiopia: A 5 year retrospective cross sectional study.

By Habib Ebrahim (MD)

ADVISORS:

ABDO KEDIR (MD, ASSISTANT PROFESSOR OF PATHOLOGY)

LELISA SENA (MPH, Ph.D.)

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Jimma, Ethiopia

ABSTRACT

Background: Among the few special sensory organs of our body, the eye shows to be a distinctive and special sensory organ displaying several histologic characters. Ophthalmic lesions comprise a wide range of disorders ranging from benign, precancerous to malignant lesions.

Objective: The main objective of the study was to determine the histopathological patterns of ophthalmic lesions and associated factors in Jimma University Medical Center, Jimma, South west Ethiopia, 2021.

Methods: an institution based retrospective cross sectional study was conducted based on a review of all medical records of 209 patients who were histopathologically diagnosed with ophthalmic lesions over a period from September 2016 to August 2020. Data were entered and cleaned Using an excel spreadsheet and analyzed in SPSS version 26. Finally, data were presented using tables, figures, and narrative form.

Results: 209 cases of ophthalmic lesions were reviewed, of these 118 (56.5%) were malignant and 58 (27.8%) were benign lesions. Conjunctiva was the most common site of ophthalmic lesions 128 (61.2%). Squamous cell carcinoma is the leading ophthalmic malignancy 58 (49.1%). There was a bimodal distribution of age, in the first decade due to retinoblastoma and the fourth decade due to Squamous cell carcinoma. Age (AOR: 0.125 (CI: 0.029-0.542), Site of lesion (AOR: 22.054, CI: 2.548- 190.875) were significantly associated with malignant diagnosis. Sex (AOR: 0.451(CI: 0.242-0.841) has significant association with OSSN diagnosis. Solar elsatosis was seen 32 (36.3%) throughout the spectrum of OSSN. Most SCC 53 (96.3%) and retinoblastomas 18 (78.2%) were well-differentiated.

Conclusion and recommendation: The commonest ophthalmic lesions were malignant neoplasms. Age and site of ophthalmic lesions were statistically significant for malignant ophthalmic diagnosis. Request forms should be complete as Clinico-pathological correlation is very important for reaching a histopathological diagnosis. The pathological reporting should also be standardized to include basic information about the nature of lesions.

Keywords: histopathology, squamous cell carcinoma, ophthalmic lesions

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ABBREVIATIONS AND ACRONYMS

AOR	Adjusted Odds Ratio
BCC	Basal Cell Carcinoma
CI	Confidence Interval
CIN	Conjunctival Intraepithelial Neoplasia
COR	Crude Odds Ratio
COVID-19	Coronavirus Disease 2019
EBV	Epstein–Barr Virus
EPI-info	Epidemiological Information
FBS	Foreign Body Sensation
FNAC	Fine Needle Aspiration Cytology
HIV	Human Immunodeficiency Virus
HSV	Herpes Simplex Virus
IRB	Institutional Review Board
JU	Jimma University
JUMC	Jimma University Medical Centre
KSHV	Kaposi Sarcoma Herpes Virus
NHL	Non-Hodgkin Lymphoma
NOS	Not Otherwise Specified
MSRBCT	Malignant Small Round Blue Cell Tumor
OSSN	Ocular Surface Squamous Neoplasia
SCC	Squamous Cell Carcinoma
SD	Standard Deviation
SPSS	Statistical Package For The Social Science
WHO	World Health Organization

1. INTRODUCTION

1.1 BACKGROUND

Ophthalmic pathology is a subspecialty of pathology which studies the diagnosis and patterns of eye diseases. Ophthalmic lesions comprise a wide range of disorders ranging from benign to precancerous and malignant lesions. The diagnosis of these lesions is based on the clinical as well as histopathological features (1). Among the few special sensory organs of our body, the eye shows to be a distinctive and special sensory organ displaying diverse histologic characters (2). The variety of neoplasms of the eye and ocular adnexa has been well recognized; their great heterogeneity is attributable to the fact that the eye and its adnexa are embryologically derived from all of the three fetal germ cell layers: the ectoderm, mesoderm, and endoderm. To add to this intrinsic variety, malignant tumors from neighboring anatomic sites such as the nasal cavity and Paranasal sinuses, and bordering skin of the forehead and eyelids may also infiltrate the orbital space (3).

Ethiopia has one of the highest blindness prevalence rates globally, with 1.2 million blind people and an estimated 5 million people suffering from visual impairment. Over 80% of blindness and visual impairment in the country is preventable (4). Low vision and blindness are recognized as one of the major public health problems worldwide, especially in less affluent countries where 90% of the blind lives (5). Especially childhood blindness has a grave impact on development, education, and future occupational opportunities for the affected child (6). Several studies all over the globe have identified orbito-ocular neoplasms as one of the most common indications for surgical eye removal resulting in monocular blindness, being second only to ocular trauma or third behind both trauma and infections in this regard (3, 7).

Tumors of the eye and ocular adnexa are some of the least frequent locations of malignancies in the human body. Yet, these tumors are also some of the more serious eye conditions and are the most challenging cases seen by ophthalmologists and, leading probably to loss of vision and death (7) most orbital lesions are benign, with hemangiomas and dermoids being the most common. This was followed by pleomorphic adenoma of the lacrimal gland while

the commonest orbital malignancies include rhabdomyosarcoma and lymphoma in pediatric and adults respectively. The most common malignant tumor in children is Retinoblastoma while in adults uveal melanoma is the most common intraocular malignancy. Basal cell carcinoma and squamous cell carcinoma are the most common eyelid tumors (7). Malignant orbital tumors are commonly treated by orbital exenteration (1). Enucleation refers to the removal of the eye alone, sparing the conjunctiva and eyelids, while, evisceration denotes the evacuation of intraocular contents and replacement with space occupying material to maintain motility of a cosmetically acceptable prosthesis (1). Ophthalmic histology techniques differ from those of other normal tissue in fixation, processing and sectioning (1, 8).

Many studies have been done on the non-neoplastic conditions of eye diseases however, there is a scarcity of studies done in the neoplastic aspect of ophthalmic conditions although they can cause as much morbidity and blindness. (1, 3, 7, 9) The present study was aimed to focus on the comparative frequencies and distribution of age of various benign and malignant ophthalmic tumors and compare and contrast their geographical variation that can help to investigate the trend of these tumors in this part of the world and as well as the relationship of morphological and clinicopathological features of ophthalmic lesions, to help understand the prevalence and pattern of various ophthalmic lesions in the JUMC catchment area.

1.2 STATEMENT OF PROBLEM

Ocular tumors comprise a wide range of benign, precancerous to malignant tumors (1). Globally, Malignancies of the eye and adnexa account for 0.2–0.8% of all human malignancies (8). However, local data on cancer epidemiology in Ethiopia are scarce. Studies from the Cancer Incidence in Five Continents Collaboration (CI5) and the global burden of disease cancer collaboration have projected cancer incidence by cause for countries worldwide, and both studies used evidence from neighboring African countries to estimate cancer incidence in Ethiopia (9) but the true scale of the ophthalmic tumors is still unknown.

Several risk factors were assessed for ophthalmic tumors. Conjunctival cancer was seen to be strongly associated with HIV infection (10, 11), additionally, Solar elastosis was much more frequently found in OSSN (12) Risks for melanoma, familial history of uveal melanoma and pre-existing naevi have been postulated as predisposing factors. (13). The surgical technique of tumor management was also found to be a possible risk factor to tumor metastases and death (14). Concerning retinoblastoma, assessment of High-risk Pathological Risk Factor (HRF) was done and shows major invasion to the choroid, pre and post lamina optic nerve, and intra-trans sclera invasion (15).

Given their delicate location, early diagnosis and treatment are necessary (16). Ophthalmic tumors are a significant cause of debilitation and a major public health concern, however, only a few studies have been done specifically on ophthalmic tumors. Pathological profiles of orbito-ocular lesions when characterized according to demographic data, presentation of illness, and clinical findings provide information on the existence and prevalence of these diseases and may help guide diagnosis before biopsy or resection and for determination of treatment strategy. There is however a paucity of studies on the pattern and characteristics of these diseases in, southwest Ethiopia, thus limiting available information applicable to the area.

Specific tumor related studies are reported in the literature, a study of all the ocular malignancies is very limited, this study was undertaken to investigate the prevalence and clinicopathologic relations of ophthalmic lesions in Jimma University Medical Center catchment areas. Therefore, the present study aimed in addition to adding more context specific knowledge regarding ophthalmic tumors and also to further discuss histopathologic findings.

1.3 SIGNIFICANCE OF STUDY

This study seeks to review and provide data on demography (age and sex) and prevalence of common orbito-ocular lesions in the catchment area as well as describe their clinicopathological features, in comparison to other parts of the country and the world. The finding of this study can be an input for a nationwide description of histopathologic patterns of ophthalmic tumors. It will be useful to clinicians, patients, students, health care administrators, and service providers as a source of information. It can also be used as a baseline along with other researches as guiding information for health-related policymakers on these issues. Additionally, this research will be a baseline for other researches and clinical activities in JUMC as there is significant variation in ophthalmic lesions distribution in different geographic areas of the world.

2. LITERATURE REVIEW

2.1 CLASSIFICATIONS OF OPHTHALMIC LESION

Orbital lesions can be classified in many ways depending on the tissue of origins such as histological, histopathological, or embryonal, based on anatomical site it is grouped into orbital, eyeball, conjunctiva, lacrimal gland, and eyelids, and depending on the clinical course it is divided into either acute and chronic forms. One of the commonest and useful classifications is the site of origin which is further divided into primary, secondary & metastatic (17). Ophthalmic lesions show heterogeneous histologic characteristics which is due to its embryologic origin which is derived from all of the three fetal germ cell layers: the ectoderm, mesoderm, and endoderm (3).

2.2 PRESENTATION OF COMMON OPHTHALMIC TUMORS

There are geographical variations in the frequency of various tumors. However, Retinoblastoma should be kept on top of the list while making differentials in the pediatric age group (18). There is bimodal age distribution (19), The first peak is largely due to retinoblastoma whereas conjunctiva squamous cell carcinoma largely account for the second peak in especially black Africans (3). There is no significant difference in the sex distribution of patients with ocular surface squamous neoplasia (11). Concerning the site, Conjunctiva is the commonest site of presentation (2, 7), from orbital lesions, primary orbital lesions are the most common orbital lesions followed by secondary orbital lesions, hematopoietic reticuloendothelial, and metastatic lesions (18).

2.3 TREATMENT OPTIONS

Generally, ophthalmic tumors are treated by either surgical intervention or chemotherapy and radiation. Benign and malignant conjunctiva lesions are usually treated by wide excision. After resection, treatment with topical eye drops is followed (20). Intraocular tumors can be treated by Chemotherapy and/or Photocoagulation and cryopexy. The susceptibility of the tumors to chemotherapy and radiation decides the choice of treatment and the dosage. Management of intraocular tumors very often needs a multidisciplinary approach including an

ophthalmologist, oncologist, radiation physicist, and radiotherapist (21). Malignant orbital tumors are generally treated by orbital exenteration or enucleation (1).

2.4 RISK FACTORS FOR OPHTHALMIC TUMORS

Common oncogenic viruses HPV, KSHV, and EBV were identified in OSSN and pterygia tissues (22). Cancer of conjunctiva affects relatively young individuals of both sexes and is strongly associated with HIV infection, most likely to be mediated via immunosuppression (10, 11). The risk increases in those not using ART treatment (23). Solar elastosis is a risk factor for OSSN and is much more commonly found in cases with OSSN than in their matched controls (12). Risks for melanoma, familial history of uveal melanoma and pre-existing naevi have been postulated as predisposing factors. A large range of risk factors has also been investigated including, sex-related factors, social class, and socioeconomic factors, lightness of complexion and hair, eye color, sunlight exposure, smoking, viruses, chemicals, links with other cancers (13). Conjunctival malignant melanoma is a potentially deadly tumor and The surgical technique of tumor management was found to be a possible risk factor to tumor metastases and death (14).

The parents living residence, mothers who give food to pets earlier to pregnancy, experience to dangerous chemicals of a father before pregnancy were the risk factors of retinoblastoma (24). There is no family history relationship observed but High-risk Pathological Risk Factor was evaluated and comprises major invasion of the choroid, pre and post lamina optic nerve invasion, and intra-trans sclera invasion (15), and precise measurement of level of invasion is an important pathologic risk factor in that supporting the need for more intensive adjuvant chemotherapy is warranted (25).

A study done in Addis Ababa University, Ethiopia, Medical Faculty, Department of Ophthalmology shows from 299 ophthalmic lesions examined, 20% were from children. 50% of the lesions showed an epithelial origin, about 30% were found to be malignant neoplasms, 22.6% of the cases were benign and 16.4% had a potential for malignancy. SCC was the commonest conjunctival, eyelid and ocular neoplasms among adults and elderly people while only 6% of eyelid neoplasms BCC. In children, the commonest intraocular, and orbital neoplasm, was

retinoblastoma, found in 39%, followed by several benign lesions (24%). More than 50% of request forms were incomplete (26).

A study done in Menilik II tertiary eye Hospital, Addis Ababa, Ethiopia on presenting signs of retinoblastoma in children shows Among 41 patients observed during the study period, 24 (58.5%) were found to be males, The most common presentation of illness was proptosis 22(53.7%) and leukocoria seen in nine (22%) cases, ocular inflammation four (9.0 %), strabismus seen in three (7.3%), glaucoma was observed in one (2.4%), loss of vision one (2.4%)and hyphema occurred in (2.4%) but the study did not describe other tumors of the eye in children age groups. (27).

A study from Gondar, Ethiopia on ocular surface squamous neoplasia (OSSN) shows the mean age of the participants was 41.26 years (age range 18-75) and 72% of the cases were found to be males. HIV was positive in about 22% of the cases. Histopathological examination showed that OSSN in 96% of the participants. Among these 36% showed carcinoma in situ, followed by 36% of the cases had invasive squamous cell carcinoma, 18% had shown conjunctival/corneal intraepithelial neoplasia and 10% had presented with pterygium clinically and on histopathological diagnoses as well (28).

A study done in Nigeria after observing 66 cases of ophthalmic lesions, 54 cases were investigated, They found 30 cases of Ocular Surface Squamous Neoplasia along with a male-to-female ratio of 0.9:1. Squamous cell carcinoma (SCC) was the most frequent OSSN showed by 17 cases. The mean age of cases with SCC was 37.1 ± 7.6 years. (11). Another study from Nigeria observed sixty-seven eye tumors. 43 males and 18 females with a (male-to-female ratio = 2.4:1). Patients were found to have a mean of 13.4 ± 18.3 and a double peak in age distribution. The commonest presentation of illness was visual loss (90.2%), followed by leukocoria (59%), proptosis (55%), and lastly fungating mass (49.2%). The symptoms lasted for ≥ 6 months in 57.4% and showed unilaterality in 82.1%. (29).

A study done among pediatric age groups in Nigeria in 2020 shows A total of 104 tumors of the eye and ocular adnexa were diagnosed. The male to female ratio was 1.7:1 and malignant tumors greatly outnumbered benign tumors by a ratio of 5.5:1. The majority [76%] of the tumors that occurred in the retina with retinoblastoma are presenting all the tumors diagnosed in this location. Rhabdomyosarcoma was seen as the most common orbital tumor in the pediatric age group accounting for 53.8% of all neoplasms of the orbit (3).

In Benin City, Nigeria one study assessed a total number of 105 orbito-ocular lesions. Malignant tumors of the eye made up 33 (31.4%) of all ocular biopsies/samples and 1% of all malignancies. The range of ages was found to be between 1 and 80 years. Squamous cell carcinoma (n=12) and retinoblastoma (n=12) accounted for the majority (76%) of all the orbito-ocular malignancies. While 99.7% of retinoblastoma was observed in children of less than 9 years of age, 66.7% of SCC occurred in people between the age range 20 and 39 years. Squamous cell carcinoma affected both males and females equally (30).

In Nepal, ophthalmic neoplasms prevalence was observed to be 139 (55.37%), of which 74 (53.24%) showed benign diagnosis and 65 (46.76%) were malignant cases. Benign was most commonly observed in females of the second decade of life while malignancy was more frequent in males and seventh decade respectively. Conjunctiva and cornea in 52 (37.41%) was the most common location for those neoplastic lesions. Squamous cell carcinoma (46.16%) and conjunctival intraepithelial neoplasia (7.0%) were the most common malignant lesions among the specimens investigated (2).

Another study in Nepal showed the mean age of patients was found to be 30 years [range 1-78], with a male preponderance of 15(55.6%). Generally, patients presented with a duration of 18 months (2 months-8.5 years). The commonest presentation of illness was a proptosis of eyeball, 4(50%) primary site of a tumor was intraocular in 10 patients (35.7%) and total orbital exenteration was the commonest performed type of surgery in 16(57.1%) out of 27 patients. Exenteration was commonly done for retinoblastoma in the pediatric age group, while conjunctival SCC for adults (16).

In Pakistan, one study showed that 66% of the malignant neoplasms were primary, 25% secondary, 8% hematopoietic reticuloendothelial, and 1% were metastatic. Almost 50% of the cases were found to be children. Retinoblastoma was the most common tumor (43% overall and 87% among children). Squamous cell carcinoma was the second most common (15.6% overall and 31% among adults). These were followed by Adenoid cystic carcinoma of Lacrimal Gland (9%), Lymphoma/ Leukemia (8%), and (6.3%) Rhabdomyosarcoma (17).

In India, one study shows Squamous cell carcinoma was found to be the most common primary ocular malignancy. A bimodal distribution of age was observed in the age groups, during the first decade and fourth decade due to retinoblastoma and due to the other malignancies respectively. Squamous cell carcinoma was found to be the most common malignancy with 38.04%, followed by retinoblastoma 25% (8).

A study done in central India among 488 patients shows that bimodal distribution. Ophthalmic tumors were found to be the highest (44.8%) in the less than 20 years age group. Eyelid (33.6%) was the commonest involved site. In approximately 76% of cases, Clinical diagnosis was consistent with pathological diagnosis. The non-neoplastic were 61.1%. Retinoblastoma in 40.1%, sebaceous carcinoma (19.1%) and Squamous Cell Carcinoma (10.5%) were the commonest malignant neoplasms (19). Another study in India evaluated 62 cases, 53.22% were males, About 38 (61.29%) ophthalmic biopsies were found to be non-neoplastic and 24 (38.71%) were neoplastic. Among all malignancies, retinoblastoma was the commonest with 45.83% of cases evaluated (1).

A study in Pakistan showed, out of 1246 cases 54.57% (n = 680) were neoplastic and 45.42% (n = 566) were non neoplastic lesions. Among the neoplastic tumors 86.17% (n = 586) were found to be malignant and 13.82% (n = 94) were found benign. Primary orbital tumors were the commonest orbital tumors making up 963 (77.29%) followed by secondary orbital neoplasms accounting for 232 (18.62%) followed by hematopoietic reticuloendothelial making up 47 (3.77%) and metastatic lesions being 04 (0.32%) of the cases (18). A study in Taiwan, China on the incidence of eye cancers showed for cases less than 15 years of age, the most common eye malignancy was retinoblastoma (86.0%), followed by rhabdomyosarcoma (3.9%)

and lymphoma (2.8%). In cases with, 15 years of age and older, the commonest eye malignancy was found to be melanoma (28.6%), followed by SCC (21.0%) and lymphoma (20.8%) of the cases (31).

In the Philippines, a study showed that a total of 1,551 biopsies were included, of these, 254 were located in the conjunctiva (155 was benign, 99 malignant), 530 located in the eyelids (360 benign, 170 malignant), 394 were intraocular neoplasms (21 benign, 373 malignant), and 373 were from the orbit (231 benign, 142 malignant). Retinoblastoma was the commonest tumor of the eye and ocular adnexa in the case series, Squamous cell carcinoma was found to be the most frequent cancer of the conjunctiva, while basal cell carcinoma and sebaceous gland carcinoma were the most common eyelid malignancies observed (7).

A study done in the USA from 1643 consecutive patients showed that the tumor was categorized as melanocytic in 872 cases (53%) and nonmelanocytic in 771 cases (47%). The nonmelanocytic classification comprised congenital choristomatous, fibrous, neural, xanthomatous, lipomatous, lacrimal gland origin, lymphoid, metastatic and lastly secondary tumors. From the 872 cases with a diagnosis of melanocytic neoplasms, specific neoplasm with histopathological diagnoses were nevus in 454 cases (52%) followed by melanoma in 215 (25%) cases, and primary acquired melanosis was observed in 180 (21%). African-American demographics showed only 7% of epithelial tumors, <1% of melanomas, and 8% of lymphoid tumors (32).

In Ethiopia, currently, there is no updated data regarding the distribution and clinicopathological correlation study on ophthalmic tumors, and none that was done in southwest Ethiopia. There are no studies done to assess histopathological features other than a diagnosis of ophthalmic tumors in Ethiopia. This study will fill the gap regarding the scarcity of information and emphasize the clinical presentation of patients, sex, age, site, and pathologic findings of ophthalmic tumors in improving disease outcomes and can be used as a basis for future researchers on this topic and provide as a source of reference.

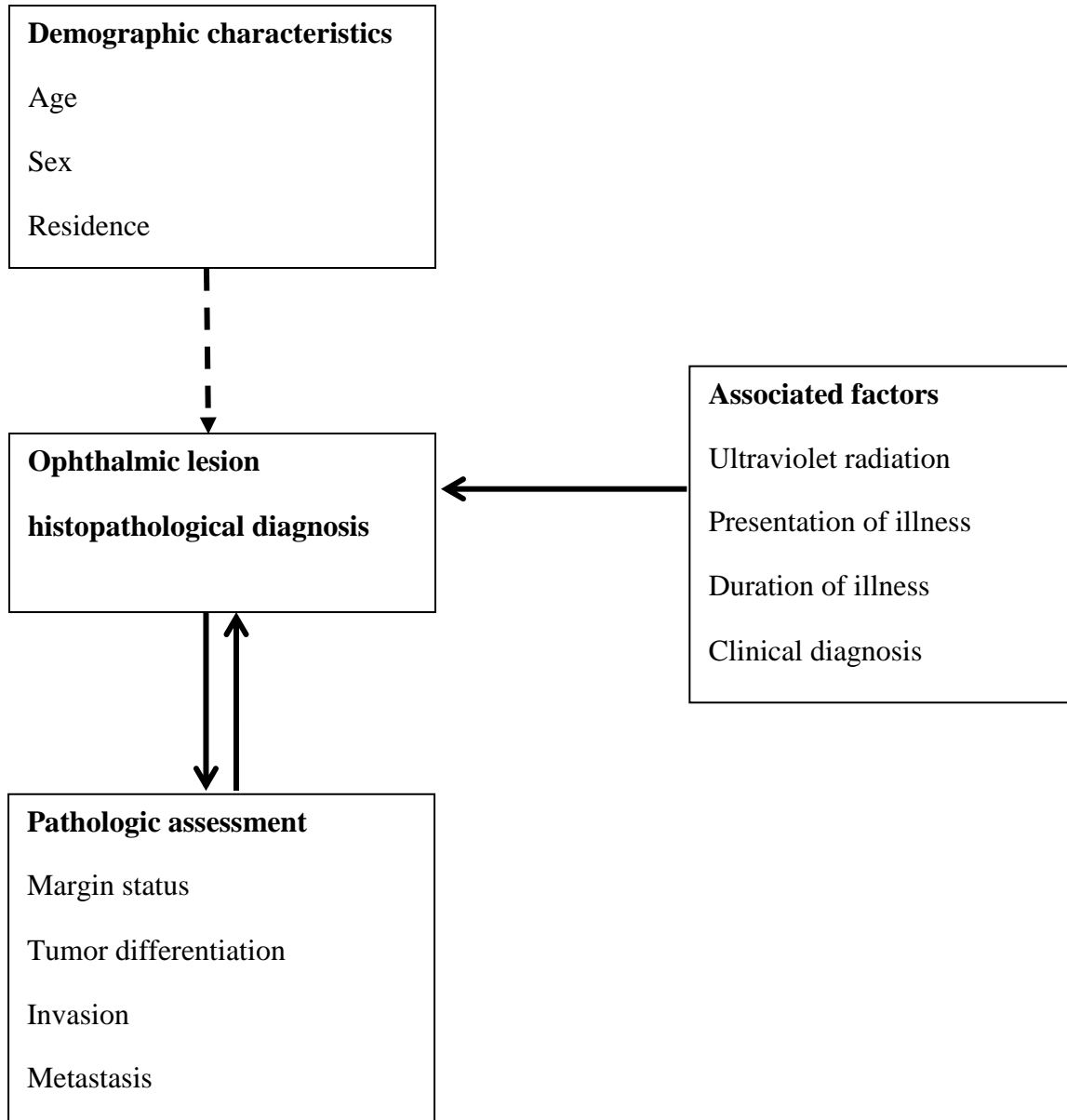


Figure 1 Conceptual framework showing factors affecting ophthalmic lesions in Jimma University Medical Center, Jimma, Southwest Ethiopia, 2021

3. OBJECTIVES

3.1. GENERAL OBJECTIVE

The main objective of the study was to determine the histopathological patterns of ophthalmic lesions and associated factors in Jimma University Medical Center, Jimma, Southwest Ethiopia, 2021

3.2. SPECIFIC OBJECTIVES

- To determine the prevalence of malignancy among patients with ophthalmic lesions in Jimma University Medical Center, Jimma, South west Ethiopia, 2021
- To assess factors associated with histopathological patterns of ophthalmic lesions in Jimma University Medical Center, Jimma, South west Ethiopia, 2021
- To investigate histopathological features in ophthalmic lesions in Jimma University Medical Center, Jimma, South west Ethiopia, 2021

4. METHODS

4.1. STUDY AREA AND PERIOD

The study was conducted in Jimma University Medical Center, located in Jimma, which is 352 km from the capital city Addis Ababa to the southwest part of Ethiopia. The study was based on a review of patient records covering the period from September 2016- August 2020. The JUMC has a catchment population of around 15 million populations and serves about 200,000 patients annually. The pathology department of JUMC has four pathology seniors, 12 residents, three histopathology technicians, and seven assistant technicians. Services given by the pathology department of JUMC include histopathology, FNAC and hematopathology. The pathology department receives about 2000 biopsies annually. The study was conducted from June to November 2021.

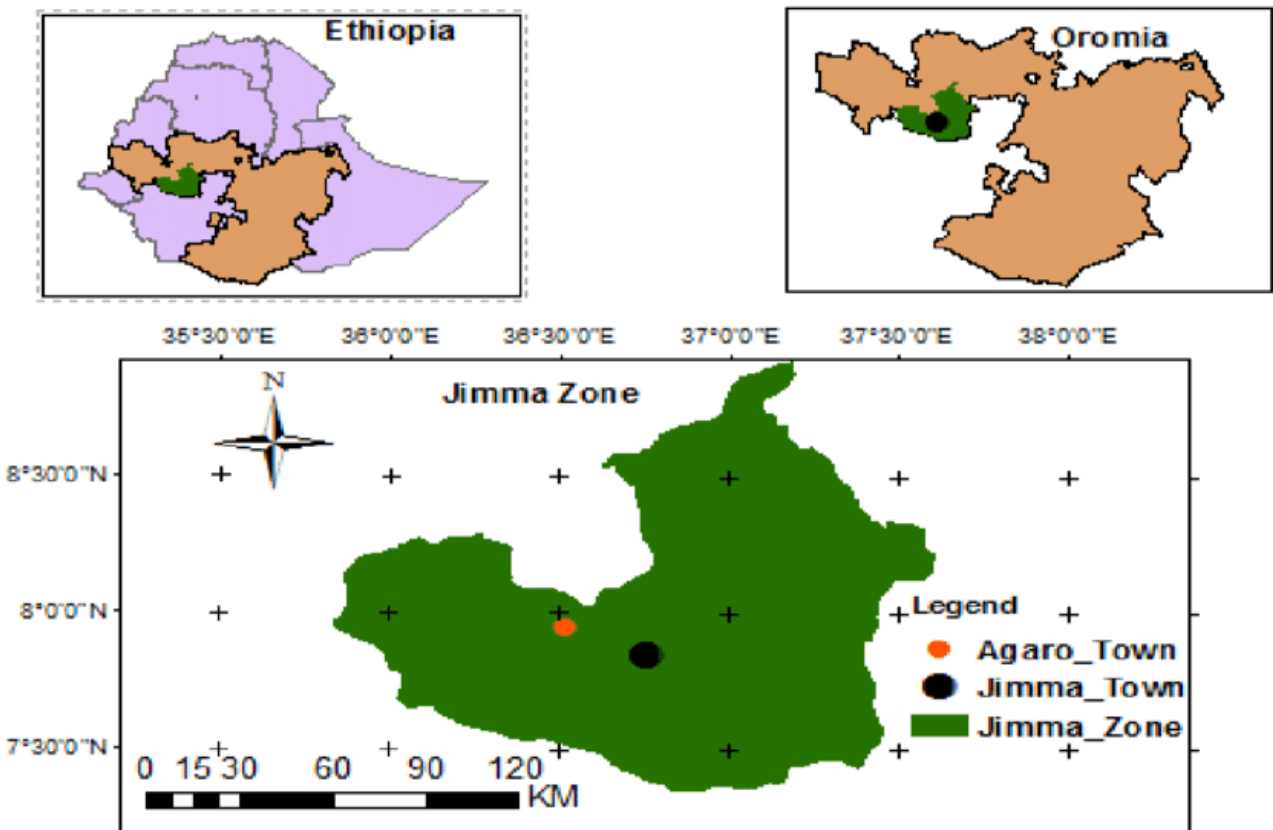


Figure 2 Map of the Jimma Zone, Oromia Region, Ethiopia

Source: Municipal administration of Jimma Zone, 2017

4.2. STUDY DESIGN

The study design of the research was a health institution based retrospective descriptive cross sectional study design which was based on a review of patient medical records of five years

4.3. POPULATION

4.3.1. SOURCE POPULATION

All patients with ophthalmic lesion visiting JUMC: from September 2016 to August 2020.

4.3.2. STUDY POPULATION

All patients with ophthalmic lesions for whom biopsy was done: from September 2016 to August 2020

4.4. INCLUSION AND EXCLUSION CRITERIA

4.4.1. INCLUSION CRITERIA

All biopsy report records on ophthalmic lesions were included in the study.

4.4.2. EXCLUSION CRITERIA

Records that missed at least two of the variables such as age, sex, site, or histological diagnosis

4.5. SAMPLING TECHNIQUE

All biopsy records with ophthalmic lesions on a biopsy request form from September 2016 to August 2020 were identified. 216 cases were identified. 209 Cases fulfilling the inclusion criteria and exclusion criteria were selected.

4.6. DATA COLLECTION PROCEDURES

Data was collected using structured checklists from the patient's biopsy records in the pathology department manually by technicians working in the department. Demographics of the patients, location of the lesion, and diagnosis were collected from the patient's biopsy records. One supervisor from junior pathology residents and three data collectors from cytopathology technicians were enrolled. Training was given to the data collectors and supervisor on the

objective of the study, data collection tools, and procedures. The principal investigator was supervising data collection daily.

4.7. STUDY VARIABLES

4.7.1. DEPENDENT VARIABLE:

The dependent variable of the study was the histopathological diagnosis.

4.7.2. INDEPENDENT VARIABLES:

The independent variables of the study were demographic characteristics (age, sex, and address), site, duration of illness, presentation of illness and histopathological features.

4.8 OPERATIONAL DEFINITION

Histological patterns and/or sub-patterns - are characteristic features of particular tumors or groups of tumors

Lesion - is any damage or abnormal change in the tissue of an organism.

OSSN - is a term for pre-cancerous and cancerous epithelial lesions of the conjunctiva and cornea. It includes the spectrum of Dysplasia, Carcinoma in-situ (CIS) and Invasive SCC

Precancerous lesion or potentially malignant - is a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart and has generalized state associated with a significantly increased risk of cancer.

Non-diagnostic or inconclusive - is one that for qualitative and/or quantitative reasons provides insufficient diagnostic material to provide an informative interpretation.

4.9 DATA PROCESSING AND ANALYSIS

Data were entered into an excel spreadsheet, it was then cleaned and exported to SPSS V.26 for analysis and descriptive statistics such as frequency, percentage and mean were used for analysis. Tabulation was done to measure the relationship between multiple variables and results was presented using narration, tables, and figures and analysis involving two categorical variables was done using bivariate and multivariate logistic regression models to measure the

degree of association between dependent and independent variables considering a statistical significance level of $p\text{-value} \leq 0.05$.

4.10 DATA QUALITY MANAGEMENT

Data were collected by trained histopathological technicians and for Completeness, accuracy, and clarity of collected data. They were checked carefully by the principal investigator and supervisor on daily basis.

4.11 ETHICAL CONSIDERATION

Before the study begins ethical clearance was obtained from the Ethical Review Committee of Health Institute of Jimma University. Before the conduct of the study, permission was also obtained from the pathology department. The name of patients was excluded from all information obtained from patients and confidentiality was ensured. COVID–19 prevention procedures were used while training data collectors and throughout the data collection process.

4.12 DISSEMINATION PLAN

The results of this study will be disseminated to Jimma University and other concerned bodies. Publication on an appropriate journal will also be done.

5 RESULTS

5.1 DEMOGRAPHIC CHARACTERISTICS OF STUDY CASES

The study included ophthalmic lesion biopsies from 209 patients over five years of data records. This accounted for 2.4 % of 8612 biopsies sent to Jimma University Medical Center over the study period. From 2016 a total of 31 (14.8%) cases were collected, from 2018 a total of 49 (23.4%) of cases, while 2019 accounted for the largest category with 65 (31.1%) of biopsy cases and from 2020 a total of 43 (20.6%) cases were collected (Fig. 3). All of the biopsy requests were sent from JUMC. Regarding age, it was categorized into 8 groups. The mean age was 32.3 ± 19.5 SD (years) and the age range was 2months – 80 years. The largest category of age was the third decade of life making up 49 (23.4%) of study subjects followed by the fourth decade with 40 (19.1%). The least age category was seen in those who were less than 1 year of age making up 2 (0.9%) of the cases observed. Apart from this, males constituted 132 (63.2%), with a male to female ratio of 1.7:1 (Table 1).

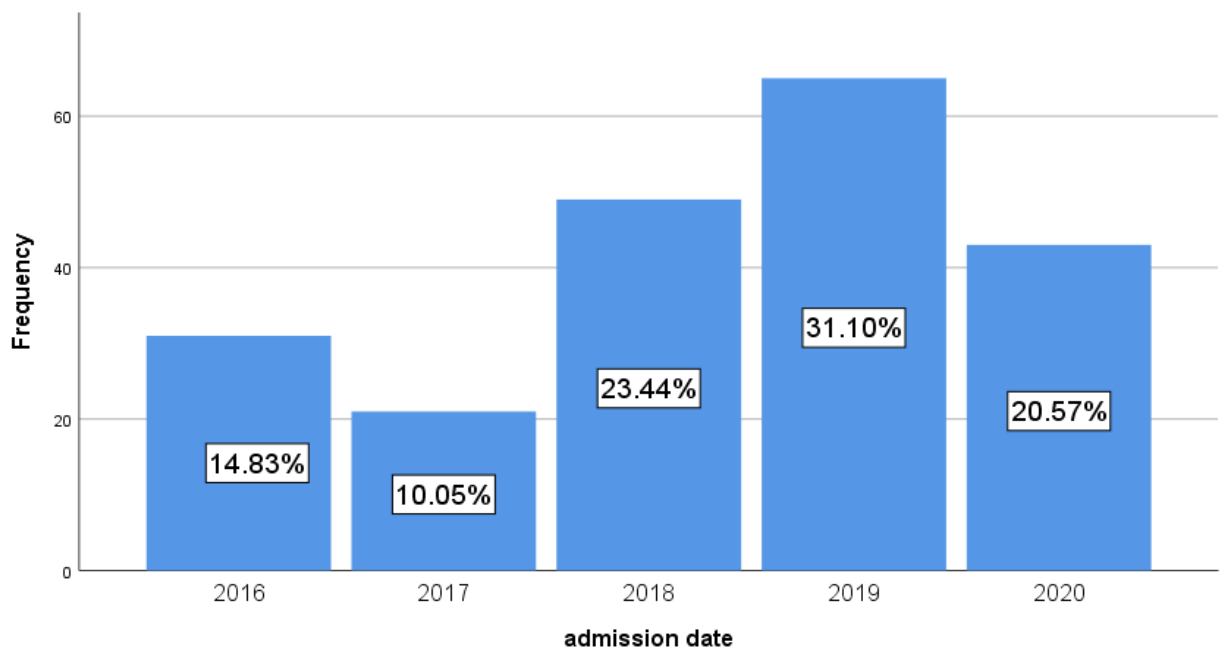


Figure 3 Number of biopsy cases of ophthalmic lesions in Jimma University Medical Center, Jimma Zone, South west Ethiopia 2021

According to the residence, Most of the cases reviewed were from outside Jimma city areas 173 (82.7%) and 36 (17.2%) were from Jimma city (Table 1). From those that came from Jimma city females account for 16 (44.4%) and concerning histopathological diagnosis, malignant neoplasms accounted for 17 (48.5%) cases, 15 (42.8%) benign neoplasms, 2 (5.7%) of cases were conjunctival intraepithelial neoplasia (CIN) and 1 (2.8%) of the cases was inflammatory lesions. In contrast, those that come from outside Jimma city areas females were accounting for 61 (35%) of the cases lesser in percentage when compared to females that come from Jimma city. Regarding diagnosis, malignant neoplasms accounted for 101 (59.4%) of cases, 25.2% benign lesions, 18 (10.5%) of cases were CIN and 7 (4.2%) cases were inflammatory lesions.

Table 1 Demographic characteristic of study cases, Jimma University Medical Center, Jimma Zone, Southwest Ethiopia, 2021

Variables		Frequency	Percentage (%)
Age (in years)	≤10	31	14.7
	11-20	30	14.3
	21-30	49	23.4
	31-40	40	19.1
	41-50	19	9.1
	51-60	23	11.0
	> 60	17	8.1
Sex	Male	132	63.2
	Female	77	36.8
Residence	Jimma city	36	17.2
	Outside Jimma city	173	82.8
Admission year	2016	31	14.8
	2017	21	10.0
	2018	49	23.4
	2019	65	31.1
	2020	43	20.6

5.2 CLINICAL FEATURES OF OPHTHALMIC LESIONS

Out of 209 cases, observed conjunctiva lesions were the most common cases with 128 (61.2%) followed by orbital lesions 28 (13.4), eye lid lesions 25 (12%) and intra-ocular lesions 24 (11.5%). The lowest number of cases observed were corneal lesions accounting for only 2 (1%) of cases. Regarding laterality, the right eye was affected in 103 (51.2 %) of cases and one patient had both eyes affected due to NHL accounting for 0.5% of the cases. Apart from this, more than half of patients presented with a duration of illness of 1month up to 6 months constituting 102 (51.2 %) of the cases. The lowest number of cases have a duration of greater than 1 year accounting for 30 (15%) of the cases (Table 2).

The most common presentation of illnesses was a growth of mass observed in 152 (72.7%) cases, followed by foreign body sensation in 24 (11.5%) cases, proptosis of the eyes which is bulging of the eyeball occurred in 17 (8.1%) cases and leukocoria in 8 (3.8%) cases. Redness of the eye was observed less commonly in 4 (1.9%) of the cases. The least frequent presentation of illnesses observed was pain and loss of vision each accounting for only 2 (1%) of cases (Table 2). Regarding clinical diagnosis, squamous cell carcinoma was the commonest diagnosis by clinicians accounting for 78 (37.3%) of the cases, followed by a diagnosis of retinoblastoma in 24 (11.5%) of cases.

When comparing the site of lesions with the presentation illness, most conjunctival lesions presented with growth of mass in 100 (78.1%) out of 128 conjunctival lesions followed by foreign body sensation in 22 (17.1%) of cases. Cases with intraocular lesions mostly presented with proptosis of the eyes making up 9 (37.5%) of the cases followed by leukocoria in 8 (33.3%). Orbital lesions mainly presented with mass in 21 (75%) of the cases and proptosis in 14.2% (4) of the cases. Regarding eyelid lesions, a growth of mass was the commonest presentation 24 (96%) followed by one case of foreign body sensation while lacrimal glands presented with growth of mass and proptosis in the 2 cases observed, and finally, corneal lesions presented with redness of the eye and growth of mass in the two cases observed.

Table 2 Clinical features of ophthalmic lesions in, Jimma University Medical Center, Jimma Zone, South west Ethiopia, 2021

Variable	Frequency	Percentage (%)	
Site of lesion	Conjunctiva	128	61.2
	Orbital	28	13.4
	Eye Lid	25	12.0
	Intra ocular	24	11.5
	Lacrimal Gland	2	1.0
	Cornea	2	1.0
Presentation of illness	Mass	152	72.7
	FBS	24	11.5
	Proptosis	17	8.1
	Leukocoria	8	3.8
	Redness	4	1.9
	Loss of vision	2	1.0
	Pain	2	1.0
	Right	103	51.2
Affected eye laterality	Left	97	48.2
	Bilateral	1	0.5
Duration of illness	≤ 1 Month	31	15.5
	1 Month - 6 Months	102	51.2
	6 Months - 1 Year	36	18
	> 1 year	30	15

5.3 HISTOPATHOLOGICAL DIAGNOSIS OF OPHTHALMIC LESIONS

Out of the total of 209 cases, in contrast, malignant neoplasms were more frequent than benign lesions accounting for 118 (56.5%) of the cases while benign lesions make up 58 (27.8%), CIN accounted for 20 (9.6%). Non-neoplastic lesions had the lowest group of cases observed accounting for 8 (3.8%) of the cases, and one case was diagnosed with borderline neoplasm. Four cases were diagnosed as inconclusive for diagnosis. Almost all of the ophthalmic lesions were primary lesions accounting for 199 (97%) whereas hematopoietic reticuloendothelial lesions accounted for 6 (3%) of the cases, in which all were diagnosed as Non-Hodgkin lymphoma. It was not mentioned whether this lymphoma arose primarily from ocular sites or as a systemic lymphoma. None of the specimens were found to be metastatic or secondary.

There were a total of 42 different histopathologic diagnoses made from the 209 ophthalmic lesion cases. The most common malignant diagnosis was squamous cell carcinoma 58 (49.1%) cases followed by retinoblastoma at 23 (19.4%) while conjunctival intraepithelial neoplasms making up to 20 (9.6%) of cases, and pterygium accounted for 14 (6.7%) of cases from all cases. The rest included mainly benign neoplasms, non-neoplastic disorders, and other malignant neoplasms (Table 3). Regarding, the anatomical site of lesions, from the conjunctiva which accounts for 61.2 % of all ophthalmic lesions, most of the lesions diagnosed at this location were malignant neoplasms. Squamous cell carcinoma is the most common neoplasm of conjunctiva accounting for 55 (42.9%) of the cases followed by conjunctival intraepithelial neoplasia at 20 (15.6%) of cases, pterygium made up 13 (10.1%) of the cases and carcinoma in situ (CIS) accounted for 9 (7%) of cases.

There were 85 (40.6%) cases with Ocular Surface Squamous Neoplasia (OSSN) diagnoses with males having more OSSN than females accounting for 64 (75.2%) with male to female ratio of 3:1. Squamous cell carcinoma was the most common lesion 55 (64.7%). The mean age of cases with SCC was 41.8 ± 17.7 SD (years) with a range of 18-75 years. Conjunctival intraepithelial neoplasia constituted 20 (23.5%) of the cases with males accounting for 17 (85%) out of the 20 cases. Mild dysplasia accounted for 4 (5%) cases, moderate dysplasia at 2 (2.5%) of cases, and severe dysplasia made up 14 (16.4%) of the cases. Carcinoma in situ

was found in 9 (10.5%) cases and mucoepidermoid carcinoma (MEC) was found in one case (0.4%). Squamous papilloma was diagnosed in two cases.

Solar elastosis was assessed in 88 (68.7%) cases with a histopathological diagnosis from conjunctiva lesions and it was present in 32 (36.3%) of the cases while 40 (31.8%) of the histopathological reports did not mention solar elastosis. From cases with a diagnosis of squamous cell carcinoma 9 (19.1%) of the cases had solar elastosis while in conjunctival intraepithelial neoplasia 6 (40%) were positive and from carcinoma in situ 2 (28.5%) of cases have solar elastosis. It was also seen in pterygium in 12 (85%) of cases and in pinguecula 3 (75%) of the observed cases.

On the contrary, concerning orbital lesions, more than half of the lesions 15 (53.5%) diagnosed at this anatomical site were benign. Benign soft tissue tumors were the commonest benign lesion diagnosed constituting 4 (26.6%) of cases followed by inflammatory lesions 2 (13.3%) of the cases, while NHL and rhabdomyosarcoma were malignant neoplasms and each accounted for 2 (15%) of the cases. Likewise, lacrimal gland tumors were also diagnosed as benign with pleomorphic adenoma occurring in both of the cases observed from the location. There were two corneal lesions diagnosed with pterygium and acute inflammation.

Regarding eyelid lesions, malignant neoplasms were more frequent than benign tumors with malignant neoplasms making up 14 (56%) of the cases while benign lesions accounted for 11 (44%) of the cases. From the malignant neoplasms, sebaceous carcinoma was the most common eyelid neoplasm accounting for 5 (35.7%) of cases followed by NHL at 3 (21.4%), and Squamous cell carcinoma and basal cell carcinoma each accounting for 2 (14.2%) of cases. From the benign eyelid lesions, chronic inflammation was also diagnosed lesion among 3 (27.2%) of cases followed by lymphangioma and benign soft tissue tumors each accounting for 2 (18.1%) of the cases.

Table 3 Malignant histopathological diagnoses of ophthalmic lesions, in Jimma University Medical Center, Jimma Zone, South west Ethiopia, 2021

Malignant lesions	Frequency	Percentage (%)
Squamous cell carcinoma	58	49.15
Retinoblastoma	23	19.49
Carcinoma in situ	9	7.62
NHL	6	5.08
Sebaceous carcinoma	6	5.08
Rhabdomyosarcoma	3	2.54
Melanoma	2	1.69
Basal cell carcinoma	2	1.69
Mucoepidermoid carcinoma	2	1.69
Adenoid cystic carcinoma	1	0.84
Sarcoma	1	0.84
MSRBCT	1	0.84
Angiosarcoma	1	0.84
Kaposi sarcoma	1	0.84
Mucinous carcinoma	1	0.84
Malignant adnexal carcinoma	1	0.84
Hemangioendothelioma	1	0.84

Childhood ophthalmic lesions (0 -15 years of age) accounted for about a fifth of the total cases making up 39 (18.6%) of cases. Malignant neoplasms were more common than benign lesions in this age category constituting about two-thirds 27 (69.2%) of the cases. Benign neoplasms accounted for 9 (23%) cases and inflammatory lesions made up 3 (7.6%) of cases. The commonest malignant tumors diagnosed were retinoblastoma 23 (58.9%) and rhabdomyosarcoma 3 (7.6%). The mean age of cases with retinoblastoma was 3.04 ± 1.5 SD (years) with an age range of 2 months to 7 years out of a total of 23 cases. Benign lesions including inflammatory lesions was observed in 4 (10%) of cases followed by benign vascular lesions and benign soft tissue lesions each making up 3 (7.6%) of the cases observed (Table 4).

Table 4 Distribution of Childhood ophthalmic lesions by anatomical site in, Jimma University Medical Center, Jimma Zone, Southwest Ethiopia, 2021

Anatomic site	Lesion	Frequency	Percentage (%)
Conjunctiva	Benign soft tissue	2	5.1
	Lymphangioma	1	2.5
	Rhabdomyosarcoma	1	2.5
	Pterygium	1	2.5
Intra ocular	Retinoblastoma	23	58.9
Orbit	Rhabdomyosarcoma	2	5.1
	Benign soft tissue	1	2.5
	lymphangioma	1	2.5
	Fibrous dysplasia	1	2.5
	hemangioendothelioma	1	2.5
Eyelid	Chronic inflammation	2	5.1
	lymphangioma	1	2.5
	Granulation tissue	1	2.5
Cornea	Acute inflammation	1	2.5

Likewise in adults, malignant neoplasms were more frequent than benign lesions accounting for 91 (54.8%) of the cases while benign neoplasms accounted for 49 (29.5%) of cases. The commonest malignant neoplasm seen in this age group was Squamous cell carcinoma making up 58 (34.9%) of the cases followed by sebaceous carcinoma and Non-Hodgkin lymphoma each accounting for 6 (3.6%) of cases. The commonest benign lesion was pterygium 13 (7.8%) followed by benign soft tissue tumors 8 (4.8%) and pinguecula and nevus each making up 4 (2.4%) of the observed cases.

The most common surgical approach used for ophthalmic biopsies was excisional biopsy for 166 (79.4%) of cases, with the most common indication being squamous cell carcinoma making up 56 (33.7%) of cases. Enucleation was done in 24 (11%) of cases while incisional biopsy was done for 16 (7%) of cases. Exentration was done for 4 (1.9%) cases (Fig. 4).

Unilateral surgery was done for almost all cases 208 (99.5%) while one case underwent bilateral eye surgery 1 (0.5%).

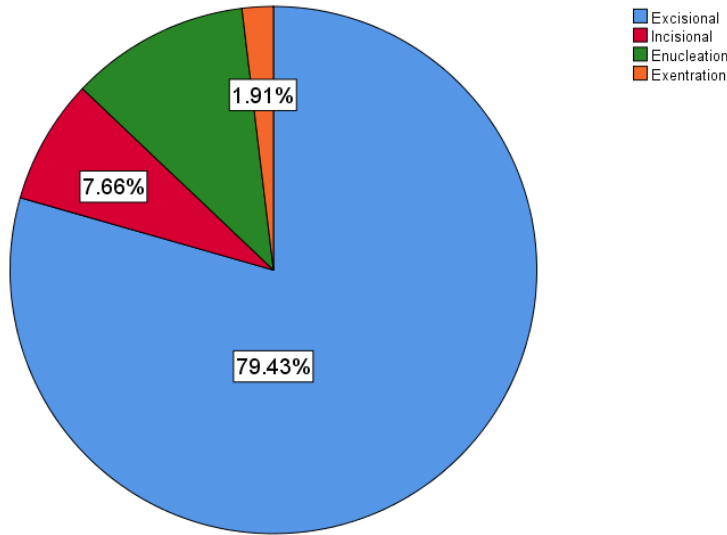


Figure 4 Types of surgery done for ophthalmic lesions in, Jimma University Medical Center, Jimma Zone, Southwest Ethiopia, 2021

Although some cases with malignancy diagnoses had missing data while observing the level of invasion of tumor margin which accounted for 24 (20%) cases, in 94 (80%) of the cases it was reported. The result showed that 11 (5.3%) cases had an invasion of tumor margin while for 83 (39.7%) cases there was none. Most of the invasion seen was in cases diagnosed with retinoblastoma in 10 (90.1%) cases. From the total o 23 retinoblastoma cases, invasion to optic nerve occurred in 6 (54.5%) cases the others were invasion to local tissue in 3 (27.2%) cases and both uveal tracts and optic nerve and only uveal tracts each accounting for 1 (9%) of the cases.

Regarding cases with a diagnosis of malignancy the level of differentiation was assessed and for Retinoblastoma well-differentiated malignancies accounted for 18 (78.2%) cases while poorly differentiated malignancy accounted for 5 (21.7 %) of cases. Squamous cell carcinoma showed well differentiation accounting for 53 (96.3%) of cases followed by moderate differentiation accounting for 2 (3.6 %) of the cases. Concerning Request forms sent by the

clinicians, they were filled adequately in 159 (76.1%) cases while it was incomplete in 50 (23.9%) of the cases. While comparing clinical diagnosis to the pathological diagnosis 42.1 % were the same, 81 (38.7%) were different and for 40 (19.1%) cases clinical diagnosis was not written in the request paper.

5.4 HISTOPATHOLOGICAL DIAGNOSIS OF OPHTHALMIC LESIONS AND ASSOCIATED FACTORS

The study identified that, there was a bimodal peak in malignant neoplasms during the first decade of life due to retinoblastoma and the fourth decade due to squamous cell carcinoma. Benign lesions were more commonly seen in the second decade of life. The study also found out that, the second decade of life had an 87% decrease in the odds of developing malignancy, and also the third decade of life has an 85% decrease in the odds of developing malignancy as shown by a p-value of 0.006, (AOR: 0.125 (CI: 0.029-0.542) and p-value of 0.007, (AOR: 0.145(CI: 0.036-0.589) respectively.

Additionally, in the current study, male sex is significantly associated with the diagnosis of Ocular Surface Squamous Neoplasia (OSSN). Males accounted for about three quarters of the cases with male to female ratio of 3:1. This was found to be statistically significant with females having a 55% decrease in the odds of being diagnosed by OSSN as shown by a p-value of 0.012 (AOR: 0.451(CI: 0.242-0.841). Although male sex is more frequently observed in the diagnosis of malignancy 61.8%, it falls short to show a statistically significant association with a malignant diagnosis with a p value of 0.34 (AOR: 1.345(CI: 0.743-2.532).

In addition, patients who presented with intra-ocular lesions were 22 times more likely to be diagnosed by a malignant diagnosis than other anatomical sites. Hence, the anatomical site of lesions in particular intraocular lesions have a statistically significant association to the diagnosis of malignancy with a p-value of 0.026 (AOR: 22.054, CI: 2.548- 190.875). Retinoblastoma is the most commonly diagnosed intraocular neoplasm and it is also the most commonly diagnosed childhood malignant neoplasm in the current study accounting for 22 (91.6%) of the cases followed by Melanoma and Staphyloma each accounting for only 1 (4.1%) of the cases.

The study also found out that, the surgical approach was statistically significant to the nature of the specimen. Enucleation of the eye in which retinoblastoma was the most common indication was done in 11% of all cases. Retinoblastoma is also the commonest childhood ophthalmic malignancy. Enucleation was associated with 10 times more likely to be done than an excisional biopsy for malignant neoplasms as shown by a p-value of 0.002 (AOR: 10.732 (CI: 2.443-47.141)).

Table 5 Factors affecting histopathological diagnoses of ophthalmic lesions among study cases, Jimma University Medical Center, Jimma Zone, Southwest Ethiopia, 2021

Variables	Categories	Malignancy		Odds ratio(95% CI)		P-values (Adjusted)
		Yes	No	Crude	Adjusted	
Age	≤10	27	4	1.4(CI:0.2-7.4)	1.4(CI:0.2-7.3)	0.676
	11-20	11	19	0.1(CI:0.03-0.5)	0.1(CI:0.02-0.5)	0.006*
	21-30	19	28	0.1(CI:0.03-0.6)	0.1(CI:0.03-0.5)	0.007*
	31-40	23	17	0.3(CI:0.07-1.2)	0.2(CI:0.07-1.2)	0.091
	41-50	10	8	0.2(CI:0.06-0.1.3)	0.2(CI:0.05-1.2)	0.097
	51-60	15	8	0.4(CI:0.09-1.9)	0.4(CI:0.09-1.9)	0.27
	>60	13	3	1	1	
Site of lesion	Conjunctiva	68	61	1.09(CI:0.4-2.5)	1.1(CI:0.4-2.7)	0.8
	Intra ocular	23	1	21(CI:2.4-182.3)	22(CI:2.5-190.8)	0.005*
	Orbital	14	13	0.9(CI:0.3-2.9)	1.1(CI:0.3-3.4)	0.863
	Eye Lid	13	12	1	1	
Type of surgery	Enucleation	22	2	10.7(CI:2.4-47.1)	10.7(CI:2.3-48)	0.002*
	Excisional	82	80	1	1	
Residence	Jimma city	17	18	0.6(CI:0.3-1.3)	0.6(0.3-1.3)	0.265
	Outside Jimma city	101	69	1	1	
Duration of illness	≤1 month	14	17	0.6(CI:0.2-1.3)	1.02(0.7-1.3)	0.265
	>1 month	96	68	1	1	

Note: *Significantly associated with Malignant diagnosis.

6 DISCUSSION

After reviewing a total of 209 cases, the study reveals that ophthalmic biopsies accounted for 2.5% of all the biopsies sent to Jimma University Medical Center, Jimma Zone, Southwest Ethiopia. In general, malignant neoplasms were more frequent than benign lesions, 56.5% of the cases were malignant neoplasms. This observation is consistent with previous studies in Ethiopia (26), Pakistan (18) and Nigeria (11) and, conversely, studies from India (1), the Philippines (7) and USA (32) showed that benign neoplasms were more frequent than malignant neoplasms. However, the Philippines study also showed that 94% of intraocular neoplasms were malignant. The study also expressed a bimodal age distribution within the first and fourth decades as also seen in other studies (3, 8).

Previous studies (1, 8, 17, 27). conducted in various settings reported that there was a marginal increase in ocular lesions among the male sex. The current study also showed there is an increased presentation of ocular lesions in males than females. The reason for this could be that males have an upper hand in socioeconomic and cultural status when compared to females (33). Therefore males can access health facilities more easily and tend to have better care. They also have the freedom to seek for their health needs; however, the females rely on their spouses for finances and also for approval to attend hospital and may be left at home without seeking treatment.

Furthermore, the study also showed that patients who were coming from outside Jimma city areas were more frequent than in the city of Jimma. Additionally, the number of female patients coming from outside Jimma city areas was lower when compared to those from the city of Jimma. This was also observed by a previous study on the causes of blindness and low vision in Ethiopia (5). This may be due to the large catchment area JUMC accommodates. Additionally, many patients are referred to JUMC from the peripheral health centers and hospitals due to a lack of appropriate setup for an ophthalmic clinic since that JUMC is the only Referral Hospital in southwest Ethiopia that has accommodations for surgical procedures for ophthalmic lesions. Additionally most patients outside the city have occupations outside an office setting and may increase their risk of exposure to physical hazards for instance sunlight exposure.

The current study also showed that age has a statistically significant association with malignant histopathological diagnosis. The study found a bimodal peak in age distribution in both males and females in the first decade of life due to retinoblastoma and the fourth decade of life due to squamous cell carcinoma. Benign lesions were more commonly seen in the second decade of life. The bimodal age distribution is consistent with various other study findings (2, 3, 7, 8, 31) showing comparable results. However, the study from Nepal (2) and the Philippines (7) showed that the second peak was observed to be in the fifth decade.

Regarding the presentation of illness a growth of mass was the commonest accounting for 72 % of all cases followed by foreign body sensation, proptosis, leukocoria, and redness of the eye and loss of vision. This finding is in alignment with a study from Zambia (34) and in contrary to the finding from Kano, Nigeria (29) showed that the commonest presentation was a visual loss, leukocoria, proptosis and mass and a study in Malaysia (35) showed that leukocoria was the commonest presentation followed by proptosis of eye and redness of eyes. This discrepancy from the current study stem from the later researches having a predominance of intraocular location with most of their study subjects having retinoblastoma diagnosis while in the former conjunctival lesion with SCC was the predominant finding. This can increase the finding of more clinical presentations with conjunctival features. The finding of leukocoria, proptosis and visual loss as the primary presentation of cases from retinoblastoma from the current study further supports the justification.

A previous study in Kano, Nigeria (29) discussed that the duration of symptoms before seeking medical care was mostly more than 6 months. This is in alignment with the current study that also showed similar findings with most patients presenting 1 month to 1 year. Delay in presentation to the hospital could be due to the absence of awareness, misapprehension of the illness, and economic difficulties. Furthermore, the sociocultural belief and probably lack of accessibility to tertiary eye hospitals could have attributed to the late presentation. Regarding the laterality, the current study showed that Orbito-ocular tumors involved the right eye than the left at 51.2 % and with only one case of bilateral illness, likewise, a study in Nepal (16) showed similar findings.

When compared by age, the commonest ophthalmic childhood malignancies were retinoblastoma and rhabdomyosarcoma in order of frequency. This goes along with various studies including a previous study from Ethiopia (11, 17, 26) having comparable findings. Retinoblastoma was also the commonest intraocular malignancy. Other intraocular malignancies were Melanoma and Staphyloma. In contrast in adults, the study found that Squamous cell carcinoma, sebaceous carcinoma and Non Hodgkin lymphoma as the most common malignant neoplasms. Pterygium and benign soft tissue tumors were the commonest benign neoplasms. This is in alignment with several other studies (2, 7, 8, 26) done in Ethiopia and abroad and discussed afterward.

In adults, biopsies sent from Conjunctiva showed that Squamous cell carcinoma was the commonest neoplasm with 42.9% prevalence. This finding was similar to various studies (2, 8, 16, 26, 29, 31). Alternatively, research done in Egypt (36) evaluated 192 conjunctival lesions and found that the commonest lesion was pyogenic granuloma followed by nevus. Although cases with OSSN were seen, there was no squamous cell carcinoma seen in the study and another study from the United States of America (32) showed melanotic tumors as the commonest conjunctival tumors. This discrepancy could be explained by the more relatively common incidence of melanoma in white individuals than squamous cell carcinoma in these demographics.

Considering other OSSN diagnoses following SCC, conjunctival intraepithelial neoplasms were the commonest followed by carcinoma in situ. This is in alignment with the previous study from Nepal (2) but as opposed to this, the study in northern Nigeria (11) showed carcinoma in situ was the commonest lesion following SCC. Although, there was no significant difference in the percentages of sex of patients with OSSN as shown by reports from sub-Saharan Africa and study of OSSN epidemiology study in Africa (37), The current study, showed that sex has a significant association with a diagnosis of Ocular Surface Squamous Neoplasia. It showed that females were less likely to have OSSN than males. This finding was consistent with most parts of the globe where there is a substantial difference between the two sexes (38-40). The predominance of males in these neoplasms can be explained by the more

outdoor work done by men than women, which increases Sun and UV exposure that has been linked to a higher risk of squamous cell carcinoma of the eye (8, 31).

In association with Ocular Surface Squamous Neoplasia, solar elastosis was assessed and was seen in about a fifth of SCC cases and half of the cases diagnosed with conjunctival intraepithelial neoplasia and almost all cases of pterygium and pinguecula. Conversely, there was an increased incidence of solar elastosis in other studies and more emphasized from the study of OSSN in Zambia (34) in which the presence of solar elastosis reached about 95% throughout the spectrum of OSSN. The current study falls short to show such a strong statistically significant association between solar elastosis and Ocular Surface Squamous Neoplasia. This could be due to the decrease in frequency in the current study due to the retrospective nature of the study which may lack in the reporting of such specific risk factors.

Out of the total orbital lesions observed benign neoplasms were more frequent than malignant neoplasms. Benign soft tissue tumors and inflammatory lesions were the most common. NHL and Rhabdomyosarcoma were the most common orbital malignancies observed. Similar results were also seen in the previous researches done in Ethiopia (26), Pakistan (17), and the Philippines (7). Furthermore, the study found eyelid malignant tumors were more frequent than benign lesions. The most common was sebaceous carcinoma followed by NHL and SCC. This finding is in alignment with various studies (7, 18, 26) Alternatively, from Minnesota (41) BCC was found to be the most common malignant eyelid neoplasm followed by melanoma and SCC. This can be due to a common incidence of BCC and melanoma in white and fair-skinned people. Similar to reports from other countries Pakistan(17) and Philippines (7) most Lacrimal gland tumors in this study were also found to be benign with the commonest being pleomorphic adenoma.

The most common surgical approach to ophthalmic tumors was excisional biopsy followed by enucleation and exenteration. On the contrary, a study from Nigeria (29) showed that the commonest approach to surgery was exenteration followed by enucleation and excisional biopsy. This finding was also consistent with studies From Malaysia and Australia (35, 42) which showed that the commonest surgical approach was enucleation. This could be explained

by due to the predominance of conjunctival lesions in the current study, while the latter studies had a predominance of cases with retinoblastoma which requires removal of the eye for definitive treatment while most conjunctival lesions are treated by wide local excision. The study also found out that, enucleation was associated with 10 times more likely to be done than an excisional biopsy for malignant neoplasms which was statistically significant.

While assessing the level of invasion of tumor margin, most cases with retinoblastoma had involvement of tumor margin with a frequency of 43% from the total cases. The invasion was mainly to the optic nerve in more than half of the cases followed by local soft tissue and uveal tracts. This is in alignment with various studies from several countries including India (1), Malaysia (35), USA (43), and Saudi Arabia (44). The level of differentiation of retinoblastoma in the current study was evaluated and showed that most were well-differentiated while about a fifth was poorly differentiated this is consistent with previous researches from the USA (43) and a study done in Saudi Arabia (44).

The study also assessed biopsy request forms sent by clinicians for completeness and found out that about a quarter was incompletely filled. This was also consistent with a finding from a study in Minilik II and Black lion hospitals in Ethiopia (26) which found about half of the forms were incomplete. The study also further emphasized that the request forms sent for pathologic assessment are vital to pathologists as clinicopathologic correlation is very important to reach a diagnosis. Regarding the time trend, the prevalence of ophthalmic lesions was relatively showing increment from 2016 to 2020. This relative increase in the prevalence of ophthalmic lesions was also observed by a study done in Taiwan (31) and the need for further study to confirm the statement was also underlined in the study. Whether the prevalence will show increment with years may necessitate more years of surveillance in the future.

In most cases in the current study, the clinical diagnosis did not correlate accurately with the histological diagnosis. There was a substantial number of discordance and some have no diagnosis written at all. Orbito-ocular tumors can be detected clinically with a high degree of accuracy. This could justify Neoadjuvant chemotherapy/chemo reduction in patients with advanced malignancy before surgery is implemented where indicated. an earlier study from

Nigeria (29) reported histological confirmation in 91% of patients and from the Philippines (7) showed about 68 % accuracy but likewise, to the current study, a previous study from Ethiopia (26) showed most of the clinical diagnosis was different from the histopathologic diagnosis. Histopathology still plays a vital role in the confirmation of orbital and ocular tumors. Nevertheless, with improved diagnostic skill and a high index of suspicion, chemo reduction and laser therapy of some ocular and orbital neoplasms could be given without expecting histopathological confirmation, particularly for patients under the care of an ocular oncology team.

7 LIMITATIONS OF STUDY

First, one limitation of this study was the lack of follow-up of the cases. Second, a systemic evaluation was not possible due to the retrospective nature of the study and retrieval of data from previous records. The study tried to get complete data from checking patients' charts when the request papers were incomplete. Finally, this is a hospital-based study, and as such, some of the findings may not necessarily reflect the occurrences in the population.

8 CONCLUSIONS

Ophthalmic tumors comprise a wide range of benign, potentially malignant to malignant tumors. This study revealed that malignant ophthalmic neoplasms are more common than benign lesions with a slightly more male preponderance. Squamous cell carcinoma was the leading primary malignancy of ophthalmic neoplasms while Retinoblastoma was the most common childhood ophthalmic malignancy. Second and third decade of life have a decreased incidence of malignant ophthalmic neoplasms. Most cases presented with a growth of mass followed by foreign body sensation. Conjunctival, eyelid and intraocular lesions were more associated with malignant neoplasms while most orbital and lacrimal gland tumors are observed to be benign. The study also revealed that Intra ocular location of tumor had an increased risk of malignant diagnosis. Solar elastosis was found throughout the spectrum of Ocular Surface Squamous Neoplasm. There was a significant difference in the sex distribution of patients with a diagnosis

of OSSSN with females having a decreased incidence. Excisional biopsy was the commonest surgical approach to ophthalmic lesions.

There is a wide geographical disparity in the occurrence of several ophthalmic lesions. This difference may be due to over-presentation or under-presentation of certain ophthalmic tumors related to specific age groups in different hospitals. Reporting of these differences in frequencies of various tumors of ophthalmic lesions can help a clinician in making an accurate clinical diagnosis and achieve a precise early management. However, by all counts and with proven results Retinoblastoma should be kept on top of the list while making differential diagnoses in the pediatrics age group and likewise, Squamous cell carcinoma should be considered in adults and elderly age groups.

9 RECOMMENDATIONS

It has been shown that ophthalmic lesions are an important cause of morbidity and loss of vision. In malignant cases, they can even pose threat to the life of individuals who are affected. Several previous studies showed early therapy is associated with better outcomes. Despite this, there still is a delay in the presentation and diagnoses of patients as shown by the current study. Thus, more attention should be given by private, governmental, non-governmental health sectors and administrators in raising awareness of ophthalmic lesions so patients can present early and also focus should be given to improving basic setups for ophthalmic tumor diagnosis and management.

Also, the study showed that there was a relative increase in the prevalence of ophthalmic lesions. Whether the prevalence will show increment with years to come may require further additional years of observation and evaluation in the future. This can be addressed better if a national registry is established by the federal ministry of health so that epidemiologic data may be obtained from the entire Ethiopian population and disease patterns observed through time. There is an established Addis Abeba city-based cancer registry but there is no population-based national cancer registry yet. Additionally, there was a marginal increase in ocular lesions among the male sex. The study also observed that females from outside Jimma city areas were less

likely to present to the hospital when compared to the ones from Jimma city. Further research should be done by future researchers to identify the causes and associated factors in these areas.

Regarding the request forms, they should be complete as several were found incomplete in this study. Clinicopathologic correlation is very important for reaching a histopathologic diagnosis. The pathological reporting should also be standardized to include basic information about the nature of lesions for instance level of differentiation and margin status as they affect the outcome of malignancies and the need for further treatments. So JUMC clinicians should fill request papers adequately and pathologists should include basic reporting formats. Clinicopathologic correlations involving staging, treatment, and outcomes are relevant topics for future investigations. So, future researchers should focus on these areas.

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Annex 1: DATA COLLECTION TOOL

HISTOPATHOLOGICAL PATTERNS OF OPHTHALMIC LESIONS AND ASSOCIATED FACTORS IN JIMMA UNIVERSITY MEDICAL CENTER, JIMMA, SOUTH WEST ETHIOPIA: A 5 YEAR RETROSPECTIVE CROSS SECTIONAL STUDY, 2021

Introduction Tumors of or around the eye are of enormous social importance since they constitute a serious threat to vision particularly in children where it presents enormous implications for their development. The loss of an eye is particularly devastating in the young and can result in diverse psychosocial reactions in the child,

Various studies all over the world have identified orbito-ocular tumors as one of the commonest indications for surgical eye removal leading to monocular blindness, being second only to ocular trauma or third behind both trauma and infections in this regard. The biopsy test is done for all lesions that are submitted to our department of pathology and all are hematoxylin and eosin stained biopsies.

Significance of the study: The purpose of this research is to describe the epidemiological and pathologic patterns in ophthalmic lesions by using age, sex, nature of the lesion, presentation of illness, and site. The research will be used as a source of information for future researchers

Part 1 Demographic Data

1. Age of the patient _____

2. Sex of the patient

A. Male

B. Female

3. Address of patient _____

4. Biopsy submitting Hospital

A. JUMC B. Other (specify) -----

PART 2 Clinical Presentations

5. Site of ophthalmic lesion

- A. intraocular B. conjunctiva C. orbital D. eyelid
 E. lacrimal glands F. Not Specified G. other (specify) -----

6. Presentation of illness

- A. foreign body sensation B. visual difficulty C. Proptosis D. swelling/mass
 E. leukocoria F. Other (specify) -----

7. Affected eye location

- A. Right B. Left C. Both D, Not specified

8. Presenting duration of eye morbidity -----

PART 3 Type of Diagnosis seen

9. Clinical diagnosis -----

10. Pathologic diagnosis -----

Part 4 Nature of Ophthalmic Lesion

11. Type of surgical Biopsy procedure

- A. Incisional Biopsy B. Excisional biopsy C. Enucleation D. Exenteration
 E. Others (specify) -----

12. Laterality of surgery

- A. Unilateral B. Bilateral C. Not specified

13. Please indicate what the Nature of the ophthalmic lesion is

Nature of lesion	1. Benign	
	2. Malignant	
	3. Inflammatory	
	4. Hematopoietic reticuloendothelial	
	5. Metastatic	
	6. Conjunctival intraepithelial neoplasia	
	7. others (specify)	

DECLARATION

I, the undersigned, declare that this research titled “HISTOPATHOLOGICAL PATTERNS OF OPHTHALMIC LESIONS AND ASSOCIATED FACTORS IN JIMMA UNIVERSITY MEDICAL CENTER, JIMMA, SOUTH WEST ETHIOPIA: A 5 YEAR RETROSPECTIVE CROSS SECTIONAL STUDY” is my work. I certify that the work is original and has been done by myself under the supervision of my research advisors. I further certify that the work has not been submitted to any other institution for any other degree/diploma/certificate in this institute or any other university in Ethiopia or abroad and there has been no significant financial support for this work that could have influenced its outcome. Furthermore, whenever materials from other sources are referenced, due credit is given in the text of the thesis, and details are given in the reference list.

Name_____

ID_____

Sign_____

APPROVAL OF ADVISOR

Name of the advisor:_____

Date._____

Signature _____