
# ADDIS ABABA UNIVERSITY

## COLLEGE OF HEALTH SCIENCES

## SCHOOL OF GRADUATE STUDIES

## DEPARTMENT OF RADIOLOGY

### CT AND MRI IMAGING PATTERN AND STAGING OF RETINO BLSATOMAS EVALUATED IN TIKUR ANBESSA TERTIARY REFERRAL HOSPITAL, ADDIS ABABA, ETHIOPIA

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## Approval sheet

I, the undersigned declare that I have submitted my original work on a title imaging pattern and staging of retino blsatoma at TASH pediatrics oncology unit from January 2018 to January 2021.

**Summited by:**

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|---|---|---|
| Name of student | Signature | Date |

This thesis work has been submitted for examination with my approval as an advisor.

**Approved by:**

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|---|---|---|
| 1. Name of Major Advisor | Signature | Date |
| 2. Name of Co-Advisor | Signature | Date |
| 3. | | |

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**ABBREVIATIONS**

AAU- Addis Ababa University

CT- Computed tomography

IIRC – International intraocular Retinoblastoma Classification

AJCC – American Joint Committee of cancer

TNM – Tumor Nodes Metastasis

MDCT- Multidetector computed tomography

MRI- Magnetic resonance imaging

TASH –Tikur Anbessa specialized Hospital

## Abstract

**Background**: Retinoblastoma is a rare eye malignant neoplasm which arises from the retina and represents the most common intraocular malignancy during infancy and childhood, the study will aim to assess the cross sectional imaging pattern and stage of retinoblastoma in children evaluated at Tikur Anbessa specialized hospital

**Methods:** Hospital based retrospective cross sectional study was conducted at Tikur Anbessa Specialized hospital in a period of 3 years from January 2018to January 2021. The study population will be all patients with retinoblastoma having both cross sectional imaging and pathology result during data collection period. The exclusion criterion includes patients with orbital tumors having incomplete investigations and incomplete recorded medical data

**Data collection and analysis**: Data was collected from the registry in the pediatric oncology unit, using structured questionnaires. The data was checked for clarity and completeness. SPSS (statistical package for the social sciences) version 25 software was used to make analysis and results displayed using tables and graphs.

**Result:** There were a total of 83 patients included in the study, 42 (50.6%) are male and 41(49.4%) were female. The age of the patients ranged from 1- 12 year of age with a mean age of 3.4± 2 years The most common clinical symptom at presentation was swelling around the eye with 42(50.6%) patients followed by leucocorea 37(44.6%), eye discharge 3(3.6%), loss of vision 1(1.2%). And the mean Duration of Symptom was around 5 ± 4 month And 6(7.1%) of the patients were staged I, 12(14.2%) stage II, 14 (16.6%) stage IIIB, 33(39.2%) is stage IVA and 18(21.4%) stage IVB.

**Conclusion:** From the study we can conclude that most of the patients presented with advanced stage of the disease .Therefore their needs to be a creation of awareness about the disease among the community through various information spreading methods like Television, Radio programs, Social media platforms and community gatherings so that children can come to medical institution at earlier stages where they can have a better prognosis

## INTRODUCTION

Retinoblastoma is a rare eye malignant neoplasm which arises from the retina and represents the most common intraocular malignancy during infancy and childhood with most of the cases occurring before the age of 2 years of age.(1)

Retinoblastoma is the most common primary intraocular malignancy in children affecting 1 in 15,000- 20,000 live births. Which corresponds to about 9000 new cases every year (2)

Retinoblastoma occurs following the mutations of the RB1gene which was the first described tumor suppresser gene. The loss of one RB1 allele predisposes an individual to cancer; loss of the other allele from a developing retinal cell initiates development of retinoblastoma tumors. Although RB1 loss means that a susceptible retinal cell can become malignant, it only produces retinoma, the benign precursor of retinoblastoma What causes a benign retinoma to become a malignant retinoblastoma could be accumulation of genomic instability, or an as-yet unidentified event.(3,4)

Currently there are no identified regions and populations with predisposition to retinoblastoma. The greatest disease burden is usually seen in regions with large populations which have a higher level of birth rates such reasons such as Africa and Asia. Additionally, the regions with the greatest prevalence of retinoblastoma also have the highest mortality with over 40-70 % of children with retinoblastoma in Africa and Asia dying from the disease while only 3-5% children with the disease die in Europe, Canada and USA.(5)

The most common clinical presenting feature of retinoblastoma is a white pupillary reflex called leukocoria usually first recognized by parents. Strabismus and decreased vision are also common. Patients with advanced disease can present with changes in the colour of the iris, enlargement of the globe and cornea and in most advanced cases exophthalmos. And early diagnosis and treatment is pivotal in patients with retinoblastoma because it has been shown thata delay of more than 6 months from the first clinical sign to diagnosis is associated with 70% mortality recorded in developing countries.(2,6)

Classification of the extent of the disease is fundamental for the assessment of the prognosis, the predication of the outcome and to determine in how to best treat the patients. And over the years several staging schemes were used in retinoblastoma. The first classifications were by Rees and

Elisworth classification in 1980, which was followed by the international intraocular retinoblastoma classification (IIRC) which was adopted back in 2003. Currently its recommended to use the IIRC classification for assessment of intraocular disease at diagnosis in each eye and to use the TNM classification system by the American Joint Committee on cancer to assess the whole patient by extent of the extra ocular disease as well.(7)

Cross-sectional imaging plays a valuable role in characterization of these lesions and in evaluation of disease extent, supplementing clinical ophthalmologic examination and providing additional information to reach to the final diagnosis.

Determination of tumor staging can also be performed in orbital pathologies using cross sectional imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). Advancement in cross sectional imaging techniques also allows an integration of CT and MRI images into radiation planning systems(8)

The management of retinoblastoma is complex and is best accomplished by using a multidisciplinary approach which includes pediatric oncologists, ophthalmologists, pediatric nurses, radiologists, pathologists as well as social workers. And it's been shown using an electronic medical record system designed to specifically capture data relevant to retinoblastoma could help to manage the complexity of care and improve communications and promote adherence to care guidelines and research.(7)

Retinoblastoma is currently the most common orbital malignancy in children and the morbidity and mortality associated with retinoblastoma directly correlates with the stage of the disease at presentation with children who present early having a survival rate of more than 95% while children who present late having a much worse prognosis with mortalities reaching up to 70%. (9) The stage of the disease can usually correlate with the presenting symptom of the child and studied conducted in Addis Ababa, Ethiopia show that the most common presenting symptom was exophthalmos which is due to the late presentation of patients which would inadvertently signify a poor outcome for the children.(10)

Imaging plays an important role in the evaluation of patients with Retinoblastoma and in resource limited countries like Ethiopia, proper utilization of imaging modalities like CT and MRI is of utmost importance. And currently there are no studies which have shown the imagining pattern of retinoblastoma in patients in our setup

This study aims to address the imaging patterns of Retinoblastoma in patients seen at black lion hospital, pediatric oncology unit which is the largest referral hospital and service provider in the country for oncologic cases.

Currently many studies conducted in the western countries have shown that there is an increment in the incidence of retinoblastoma over the past years(11). But currently there are few literatures which have studied the patterns of retinoblastoma in sub-Saharan Africa.

And currently there are no studies which have shown the imagining pattern of retinoblastoma in patients in our setup and this study aims to address the incidence and imaging pattern of Retinoblastoma in our setup.

## METHODS AND MATERIALS

### STUDY AREA AND PERIOD

The study was conducted at the pediatric oncology clinic of TASH which is located in Amestegna, Addis Ababa, Ethiopia. This unit of TASH was established in January 2008 E,C with primary goal of providing both inpatient and outpatient oncologic services for adult and pediatric patients .An average of 50 patients per day pay a visit .The institution has permanent staff of 24 health workers excluding supporting staff, residents and senior pediatric and adult oncologists who are available daily. It is equipped with the necessary lab investigation and for imaging requirement patients are send to TASH. There is a vision to make it an independent well equipped independent institution in the near future providing all oncologic treatments including chemotherapy and state of the art radiotherapy services .TASH is located in the capital city of Ethiopia, Addis Ababa is the largest referral hospital nationwide and also teaching hospital. The study will be conducted on patients evaluated who have been diagnosed with retinoblastoma during the study period

### STUDY DESIGN

Retrospective Hospital based cross sectional study was employed patients data was collected from September 6 2021 up to September 12 2021 by the principal investigator

## SOURCE POPULATION

The source population was all pediatric oncology patients that were evaluated during the study period

## STUDY POPULATION

The study population were all patients with retinoblastoma who had both cross sectional imaging and pathology result being evaluated at pediatric oncology unit at black lion hospital.

## INCLUSION AND EXCLUSION CRITERIA

### INCLUSION CRITERIA

All patients with Retinoblastoma having cross sectional imaging and pathology results during the study period and having all the required information for the study.

### EXCLUSION CRITERIA

- Patients with incomplete data including imaging and pathology reports

## DATA COLLECTION INSTRUMENTS, TECHNIQUES AND DATA COLLECTOR

First patients will be recruited into the study when they have both cross sectional imaging and histopathology results.

Data was collected by the principal investigator using a structured questionnaire. Patient's chart will be identified from the registry at the pediatric oncology unit. And using the questionnaire, Demographic data of participant patients such as age, gender and presenting symptoms will be collected and additional CT , MRI and histopathology reports will be obtained from the patient data.

Data collection will be conducted after receiving ethical clearance from the TASH radiology department ethical review committee and pediatric department oncology unit

### Operational Definition

- **Leukocorea:** is an abnormal white reflection from the retina of the eye

- **Ecchymosis:** A small bruise caused by blood leaking from broken blood vessels into the tissues of the skin or mucous membranes

## DATA QUALITY CONTROL

Using the pretest to evaluate the clarity of the questionnaire, the findings and observations obtained will be used to modify the questionnaire and the data collection process accordingly.

## DATA ANALYSIS AND INTERPRETATION

The data will be checked for clarity and completeness. Data will be analyzed by using SPSS version 25 computer software. Then summarization and comparison of data will be done.

## ETHICAL CONSIDERATIONS

In order to respect patient's right, and the regulation of the hospital where the study will be conducted, ethical considerations will be taken into account. Written formal letter will be obtained from radiology department Research and publication committee prior to commencing the data collection process.

# Results

## Socio demographic parameters

- There were a total of 83 patients included in the study, 42 (50.6%) are male and 41(49.4%) were female. The age of the patients ranged from 1- 12 year of age with a mean age of 3.4± 2 years.(Table 1) Most of the patients came from the region of oromiya with 36 (43.4%), Amhara 16(19.3%) and SSNP 14(16.9%) of the patients. (Figure 1)

### Clinical findings

- The most common clinical symptom at presentation was swelling around the eye with 42(50.6%) patients followed by leucocorea 37(44.6%), eye discharge 3(3.6%), loss of vision 1(1.2%). And the mean Duration of Symptom was around 5 ± 4 months. And In 37(44.6%) of the patients in the Left Eye was involved and in 28(33.7%) of patients the right eye was involved and in 18(21.7%) of the patients both Eyes were involved. And based on the clinical staging at presentation using the IRCR staging 63(75.9%) of the patients were grouped as Group E, 19 (22.9%) were grouped as Group D and 1(1.2%) patient was grouped as group C (Table 2)

### Imaging Findings

- 82 (98.8%) patients had cross sectional imaging done with 27(32.5%) of the patients evaluated using a Head CT scan and 57(68.7%) of them having a Brain MRI, with 1() patient having both CT and MRI images done. Extraocular extension was noted in 43(51.8%) of the patients, which was limited to the intraconal space in 20(46.5%) patients while the rest 23(53.5%) patients had extra conal extension. Calcification was seen in 78(93.9%) of the cases while necrosis was noted in only 11(13.25%). All cases showed enhancement on the post contrast images on both CT and MRI. With 3(3.6%) cases showing homogenous enhancement while the rest 80(96.4%) of the cases showing heterogeneous enhancement. (Table 3)

### Staging and Treatment

- The patients were staged using the international Retinoblastoma staging system based using either a CT or MRI. And 6(7.1%) of the patients were staged I, 12(14.2%) stage II, 14 (16.6%) stage IIIA, 33(39.2%) is stage IVA and 18(21.4%) stage IVB. (Table 4)

- Majority of the patient 54(65.9%) were treated using chemotherapy and surgery, and 24(29.3%) were only treated with Chemotherapy, 2 (2.4%) patient was treated with surgery alone and 1(1.2%) patient was treated using laser ablation. (Table 5)

Table 1: Age and Sex distribution of patients with Retinoblastoma seen at Black Lion Hospital pediatric Oncology Department

| Variables | Categories | Number | Percentage |
|---|---|---|---|
| Sex | Male | 42 | 50.6% |
| | Female | 41 | 49.4% |
| Age Range | ≤ 1 year | 10 | 12 % |
| | 1 - 2 year | 22 | 26.5 % |
| | 2 - 3 year | 16 | 19.3% |
| | 3 - 4 year | 14 | 16.9 % |
| | 4 – 5 year | 14 | 16.9% |
| | 5 – 6 year | 1 | 1.2% |
| | ≥ 6 years | 6 | 7.2 % |

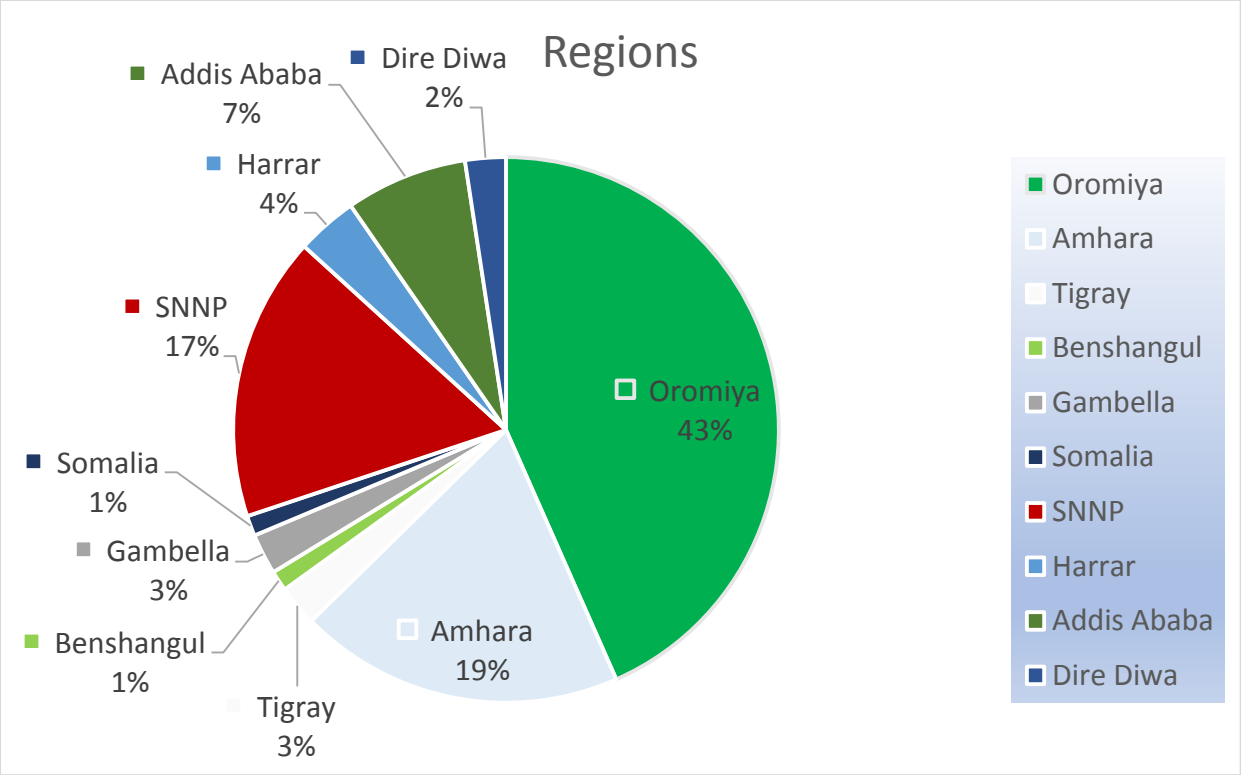


Fig 1: Distribution by region of Retinoblastoma patients seen at Black Lion Hospital pediatric oncology department

**Table 2: Clinical presentation of Retinoblastoma patients seen at Black Lion Hospital pediatric oncology department**

| Variables | Categories | Number | percentage |
|---|---|---|---|
| Clinical Presentation | Eye swelling | 42 | 50.6 % |
| | Leucocorea | 37 | 44.6 % |
| | Loss of Vision | 1 | 1.2 % |
| | Eye Discharge | 3 | 3.6 % |
| Involved Eye | Right Eye | 28 | 33.7 % |
| | Left Eye | 37 | 44.6 % |
| | Both Eyes | 18 | 21.7 % |
| Clinical Staging | Group A | 0 | 0% |
| | Group B | 0 | 0% |
| | Group C | 1 | 1.2% |
| | Group D | 19 | 22.9% |
| | Group E | 63 | 75.9% |

Table 3: imaging patterns of Retinoblastoma patients seen at Black Lion Hospital pediatric oncology department

| Variables | Findings | CT scan (n= 27 ) | MRI (n= 57) | Total |
|---|---|---|---|---|
| Location | Intraocular | 12 | 29 | 41 |
| | Extra ocular | 15 | 28 | 43 |
| Extra ocular location | Intraconal | 10 | 10 | 20 |
| | Extraconal | 5 | 18 | 23 |
| Lesion margin | Well defined | 14 | 35 | 49 |
| | Ill defined | 13 | 22 | 35 |
| Optic nerve invasion | Yes | 19 | 47 | 66 |
| | No | 8 | 10 | 18 |
| Intra cranial extension | Yes | 7 | 17 | 24 |
| | No | 20 | 42 | 62 |
| Necrosis | Yes | 4 | | |
| | No | 23 | | |
| Calcification | Yes | 23 | | |
| | No | 4 | | |
| Hemorrhage | yes | 7 | 10 | |
| | No | 20 | 47 | |
| Enhancement | Present | 27 | 57 | 84 |
| | Absent | 0 | 0 | 0 |
| Pattern of Enhancement | Homogenous | 1 | 2 | 3 |
| | Heterogeneous | 26 | 55 | 81 |
| T1 signal | Hypo intense | - | 49 | - |
| | Hyper intense | - | 1 | - |
| | Iso intense | - | 7 | - |
| T2 signal | Hypo intense | - | 38 | - |
| | Hyper intense | - | 8 | - |
| | Isointense | - | 12 | - |

Table 4: Staging of Retinoblastoma patients seen at Black Lion Hospital pediatric oncology department using the International Retinoblastoma staging System.

| Stages | CT scan(n = 27) | MRI(n = 57) | Total (84) |
|---|---|---|---|
| Stage I | 3 (11.1%) | 3(5.1%) | 6 (7.1%) |
| Stage II | 5 (18.5%) | 7(11.9%) | 12 (14.2%) |
| Stage IIIA | 12 (44.4%) | 2 (3.4%) | 14 (16.6%) |
| Stage IIIB | 0 (0% ) | 0 (0% ) | 0 (0%) |
| Stage IVA | 1 (1.2%) | 32 (54.2%) | 33 (39.2%) |
| Stage IVB | 6 (7.2%) | 12 (14.5%) | 18 (21.4%) |

**Table 5: Treatment given to Retinoblastoma patients seen at Black Lion Hospital pediatric oncology department**

| Treatment Given | Frequency | Percentage (%) |
|---|---|---|
| Surgery and Chemotherapy | 54 | 65.6 % |
| Surgery and Radiation | 1 | 1.4 % |
| Surgery Alone | 2 | 2.4 % |
| Chemotherapy Alone | 24 | 29.3 % |
| Laser Ablation Therapy | 1 | 1.2 % |

## Discussion

In the current study there was an equal gender distribution among the patient with a male to female ratio of 1.02: 1. This was similar to other studies done across the globe which had shown a lack of proof for any sex predilection in retinoblastoma. Although some studies conducted in Asia particularly in India have shown that there was a higher incidence of Retinoblastoma in males it's likely that the differences arose due to gender discrimination in the access to health care in these centuries rather than a true biological differences between the two sexes. (12)

During the current study the mean age of the child at diagnosis was around 39 month in our study which was significantly delayed compared to studies done in other developed countries like in North America and Europe where the Mean age of diagnosis was at 12 and 9 month of age respectively.(13,14) But it was comparable to other studies conducted in other studies in other African countries as well as Ethiopia. (10,15)This delay in diagnosis can be secondary to late recognition of the symptoms by the parents and the doctors and has significant implications on child's prognosis since studies done in developing countries have shown that the presence of a delay in the diagnosis and the initiation of Treatment by 6 month can increased the mortality of the children by a degree of around 70 %.(7)

The most common presentation sign of Retinoblastoma in the study was the swelling of the eyes with nearly half of the children having signs of Proptosis at the time of Presentation indicating the Advanced Disease at the time of presentation this was contrary to the clinical presentation seen in other studies conducted in north America where leukocoria is the most common presenting symptom. (16) But similar to other studies conducted in cote d'ivoire and Democratic republic of the Congo (9)

Imaging plays an important role in the Diagnosis of the Retinoblastoma and differentiate them from other simulating lesions and in addition can help delineate the extent of the Disease and Studies such as CT and MRI both provide Valuable help in the Evaluation of Retinoblastoma patients.in the current study 99.8% of the patient's had a cross sectional imaging with 27(32.5%) of the patients evaluated using a Head CT scan and 57(68.7%) of them having a Brain MRI. MRI has the advantage of better soft tissue contrast and spatial resolution and the lack of any associated Ionizing radiation which makes it ideal for the follow up of patients with already diagnosed (17) However MR imaging is not considered as specific as CT in detecting intraocular

calcification and usually requires additionally sequences such as susceptibility sequences and in phase imaging to confidently diagnose Calcifications which are a common findings in retinoblastoma patient's. (18)

The International Retinoblastoma Staging system was developed in 2006 and it sub classifies the disease from stage 0 to stage IV. With stage 0 reserved for purely intra ocular disease and stage IV given to Retinoblastoma patients with Metastasis.(19) In the Current study near Most of the patient's had an advanced Disease at the presentation with nearly 60.5% of the Cases having a Stage IV diagnosis at presentation. This finding was in line with other similar studies done in sub Saharan Africa and the possible reason for such advanced Extra ocular disease at diagnosis are due to delayed presentation and delayed initiation of treatment. (9) This should be combated by Educating the population on the early signs of Retinoblastoma as well as having instituting programs of ocular examination in neonates by testing for the red retinal reflex which has shown benefits in early detection of Retinoblastoma in multiple studies. (20)

The Treatment of Retinoblastoma mainly depends on the stage of the Disease with the mainstay Standard therapeutic option for the treatment of Retinoblastoma include surgical options of Enucleation alone or in combination of chemotherapy and External beam Radiation. But additionally laser photo ablation and brachytherapy can also be used to treat patients with retinoblastoma. And in the current study surgery with chemotherapy was the main stay of treatment for 65.6% of the patients while 24% of the patients were treated with only chemotherapy. This practice was similar to other studies conducted in the country. (10),Availability of the standard therapeutic options is also important factor in choosing treatment strategy

## Conclusion

From the study we can conclude that most of the patients presented with advanced stage of the disease with proptosis being the most common presenting symptom and most children being stage IV at Diagnosis. Therefore their needs to be a creation of awareness about the disease among the community so that children can come to medical institution at earlier stages where they can have a better prognosis.

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