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# Clinical and histopathological study of retinoblastoma in bukavu from 01 january 2014 to 31th december 2020

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## Abstract

***Introduction:*** *The aim of this study was to determine the histopathological and clinical characteristics of retinoblastoma in patients followed in Bukavu, Democratic Republic of Congo.*

***Methods:*** *It is a cross-sectional and analytical study that included 125 consecutives, exhaustively included subjects followed for retinoblastoma at CELPA ophthalmology clinic from January 2014 up to December 2020. Clinical and histopathological data were analyzed with Epi Info and SPSS 16.0 software.*

***Results:*** *A total of 7200 children aged 1-5 years old were consulted, including 125 cases of retinoblastoma, representing a frequency of 1.7%. The mean annual incidence was 13.8. The age group under 24 months predominated (54.4%), with a mean age of 24.6 months. The majority of patients had no family history of retinoblastoma (79.2%). Ocular protrusion and ocular pain were the most frequent complaints on admission (51.2%). The extraorbital form was found in 59.2% of patients. The average time period between the first symptoms and the consultation was 6 months, and the time period between the first consultation and the beginning of management was 14 days. 112 patients (89.6%) had received enucleation combined with chemotherapy. The survival rate observed after 3 years of follow-up was 40.8%. There was a signifcative association between evolution of the retiboblastoma and the delay between consultation and the management, clinical form and management, and the treatment mode both in bivariate and multivariate analysis ($p<0.05$, CI=95%). Extraorbital retinoblastoma (61.6%), endophytic (74.4%), with classic cytology showing Flexner-Wintersteiner rosettes (96.3%), numerous mitoses (98.4), necrosis and calcification (92%) dominated. Images of infiltration of the internal structures of the eye were observed (18.4%).*

***Conclusion:*** *Retinoblastoma, a highly malignant tumor of children, remains a real public health problem in Bukavu. Advanced and severe histological forms were the most frequent. Early diagnosis and treatment are essential to improve the prognosis. A survival rate of 40.8% obtained in our limited conditions is a beginning of success which could be improved with the involvement of all the disciplines concerned.*

**Keywords:** Retinoblastoma, Histopathology, Clinical, Survival, Bukavu.

## Introduction

Retinoblastoma is a genetically determined tumor of childhood that develops at the expense of retinal cones. It is the most common and deadly intraocular malignancy of infancy and childhood; with an incidence of 1/15,000 to 20,000 live births. The two most common telltale symptoms of retinoblastoma are leukocoria primarily, and strabismus [1-5].

Over 60% of retinoblastomas are unilateral and mostly sporadic, with a mean age at diagnosis of 2 years. Bilateral retinoblastoma is seen in 35-40% of cases, with a mean age at diagnosis of 1 year [6-8]. In Canada, the mean age at diagnosis is 27 months for unilateral retinoblastoma; 18 and 15 months for bilateral retinoblastoma [9]. In Kenya, the mean age at diagnosis is 36 months for unilateral retinoblastoma and 25 months for bilateral retinoblastoma [10].

A person with a constitutional mutation in the RB1 gene (hereditary retinoblastoma) has a high risk of developing retinoblastoma and other cancers [11-14]. From a genetic point of view, familial sporadic hereditary and non-hereditary retinoblastoma can be considered as major forms of retinoblastoma. In developing countries, non-hereditary retinoblastoma accounts for a larger proportion, while taking into account the complexity of imprinting and mosaic advances [11-14].

In developed countries, the survival of children with retinoblastoma has increased from 30 to 95% in a century due to early diagnosis and adequate treatment. In developing countries, where most affected children live, the mortality rate is around 90% due to late diagnosis and difficult management [15]. Sub-Saharan Africa is particularly characterized by a high rate of extraorbital forms of retinoblastoma, which, associated with delayed diagnosis and treatment, constitute factors of poor prognosis [15-19, 20-24]. The greatest burden of retinoblastoma disease is in large populations with high birth rates, such as Asia [18-21] and Africa [22-24,26]. Regions with the highest prevalence have the highest mortality; 40% to 70% of children with retinoblastoma in Asia and Africa die [20,23,26,29], compared with 3% to 5% in Europe, Canada and the United States [16,25,31].

The overt extraorbital form of retinoblastoma, including distant metastatic spread, is more common in low-income countries, accounting for up to 50% of new retinoblastoma cases. In contrast, in most middle-income countries, metastatic disease is present in >10% of cases at diagnosis [32-34]. Treatment with neoadjuvant chemotherapy followed by secondary enucleation and adjuvant therapy is the current approach in most retinoblastoma management centers [35-37]. Several combination therapies are used [35,38-44].

The aim of this study was to determine the histopathological and clinical characteristics of retinoblastoma in Bukavu, Democratic Republic of Congo.

## Materials and Methods

The study took place at CELPA ophthalmology clinic in Bukavu, in South-Kivu province of the Democratic Republic of Congo. CELPA Ophthalmology Clinic, is a referral center for ophthalmology in South-Kivu province, that receives and treats children with retinoblastoma, in addition to the common eye diseases. The study included 125 consecutive children, aged 0 to 5 years, who were diagnosed with retinoblastoma and received treatment. The study was conducted over a 7-year period from 2014 to 2021. All children included in the study had a complete and actionable medical record for the study and had been followed from admission until at least 3 years after discharge, at least for survivors.

Parents or guardians, if applicable, were interviewed to collect necessary information about the family history of retinoblastoma. A mobile phone was given to each parent to allow the clinic to monitor the child's overall clinical course, the occurrence of metastases, and compliance with treatment from a distance.

The parameters studied included epidemiological parameters (frequency and prevalence); sociodemographic parameters (age in months, sex, and urban or rural origin); clinical parameters (reason for consultation : ocular protrusion and pain, deviation of the gaze and neck, whitish spot in the eye), family history of retinoblastoma (direct relative or first-degree relative), time period from onset of disease to consultation (in months), time period from the first consultation to the beginning of treatment (in days), treatment applied (chemotherapy only or enucleation combined with chemotherapy), evolution of the treated retinoblastoma after a 3-year follow-up (metastasis-free survival or death).

Enucleation specimens, suspected of retinoblastoma, were received in the laboratory, preferably fresh, and oriented with sutures. Each specimen was subjected to macroscopic examination. The optic nerve segment was examined and measured. Fixation was performed with 10% formalin solution. For fixation of the intraorbital compartment elements, 1 ml of intraocular fluid was withdrawn with a syringe and replaced with an equivalent volume of 10% formalin solution. The fixation time was 24 to 48 hours maximum. The first fragment removed was a slice of terminal optic nerve section that was embedded in its entirety in a cassette. Then, a sagittal posterior-anterior section of the eyeball was taken. The tumor was endophytic when it consisted of one or more independent or coalescing protruding tumors.

It was exophytic when it developed posteriorly with invasion of the optic nerve, and it was diffuse when it invaded in both directions, with the absence of a classical retinal mass. The macroscopic aspects of the tumor were described (yellowish or pinkish white, smooth and homogeneous, granular, calcification). Retinal detachment was sought. Any enucleation specimen was included in its entirety. Samples of 2 mm thick biopsy sections were taken and placed in embedding cassettes. These sections were dehydrated in a series of alcohol baths, cleared with xylol, impregnated in kerosene heated to 57°C, and embedded in kerosene blocks. Microtome sections of the 3 to 5 µm thick ribbons were then cut into segments. These ribbon segments were then mounted on slides previously coated with albumin.

After drying in the oven, the preparations were subjected to basic staining with hemalin-eosin. All histological sections were subjected to double reading under an Olympus light microscope by two experienced pathologists. The positive microscopic diagnosis of retinoblastoma was based on the presence of a classic microscopic image showing small round undifferentiated cells with cytonuclear atypia and expressing numerous mitoses, foci of necrosis and calcification. The presence of rosettes in the form of Flexner-Wintersteiner and Homer-Wright bodies allowed tospecify the degree of differentiation. We used the IRC classification according to Murphree, to categorize the patients.

The management of retinoblastoma was based on the protocol of the Groupe Franco-Africain d'Oncologie Pédiatrique (GFAOP).

Children with retinoblastoma were managed and included in the study after a written or verbal informed consent from the biologicalparents, taking into account the usual recommendations, local possibilities, and the recommendations of the Groupe Franco-Africain d'Oncologie Pédiatrique (GFAOP) table 1-3.

The present study had received the approval of the Ethics Committee of the Official University of Bukavu. Data entry and analysis were performed on Epi Info and SPSS 16.0 software

## Results

**Table 1: Epidemiological data.**

| **Frequency of ocular pathologies in children from 2014-2022 n=7200** | | | |
|---|---|---|---|
| Ocular Pathologies | n | % | |
| Ocular tumors | 206 | 2,9 | |
| Retinoblastoma | 125 | 1,7 | |
| Other | 6869 | 95,4 | |
| **Incidence of Retinoblastoma n=125, Mean=18** | | | |
| 2014 | 19 | 15,2 | Incidence= 13,8 |
| 2015 | 16 | 12,8 | |
| 2016 | 17 | 13,6 | |
| 2017 | 16 | 12,8 | |
| 2018 | 18 | 14,4 | |
| 2019 | 20 | 16 | |
| 2020 | 19 | 15,2 | |
| **Sociodemographics of Retinoblastoma patients n=125** | | | |
| Age range in months n % | n | % | Average age: 24,6 |
| 0-12 | 68 | 54,4 | |
| 13-24 | 42 | 33,6 | |
| 25-59 | 15 | 12 | |
| **Sex n=125** | | | |
| Female | 65 | 52 | Sex-ratio F/M:1.1 |
| Male | 60 | 48 | |
| **Patient's origin n=125** | | | |
| Bukavu | 34 | 27,2 | |
| Out of town | 91 | 72,8 | |

**Table 2: Clinical data.**

| **Reasons for consultation n=125** | | | |
|---|---|---|---|
| **Reason** | **n** | **%** | |
| Eyeball protrusion and eye pain | 64 | 51,2 | |
| Deviation of gaze and neck | 26 | 20,8 | |
| White spot in the eye | 35 | 28 | |
| **Family history of retinoblastoma n=125** | | | |
| **History** | **n** | **%** | |
| Present | 26 | 20,8 | |
| Absent | 99 | 79,2 | |
| **Time period between consultation and the onset disease n=125** | | | |

| | | | |
|---|---|---|---|
| **Time period in months** | **n** | **%** | Mean time period: 6 months |
| 1-3 months | 34 | 27,2 | |
| 4-6 months | 74 | 59,2 | |
| > months | 17 | 13,6 | |
| **Physical examination findings n = 125** | | | |
| **Laterality of involvement** | **n** | **%** | |
| Unilateral | 84 | 76,2 | |
| Bilateral | 41 | 32,8 | |
| **Physical signs** | **n** | **%** | |
| Exophthalmos | 64 | 51,2 | |
| Leukocoria and strabismus | 48 | 38,4 | |
| Buphthalmia | 13 | 10,4 | |
| **Average time period between consultation and the initiation of management: 14 days** | | | |
| **Treatment initiated n= 125** | | | |
| **Traitment** | **n** | **%** | |
| Enucleation and chemotherapy | 112 | 89,6 | |
| Chemotherapy | 13 | 10,4 | |
| **Outcome after 3 years of follow-up n=125** | | | |
| **Outcome** | **n** | **%** | |
| Good (metastasis-free survival) | 51 | 40,8 | |
| Poor (death) | 74 | 59,2 | |
| **Causes of poor outcome n =74** | | | |
| **Causes** | **n** | **%** | |
| Poor adherence to treatment | 28 | 37,8 | |
| Delayed consultation, metastasis | 41 | 55,4 | |
| Refusal of treatment | 5 | 6,8 | |
| Histopathological parameters n=38 | | | |
| **Internal macroscopic examination (section slice) n=38** | | | |
| | **n** | **%** | |
| Endophytic tumor | 31 | 81,6 | |
| Exophytic tumor | 6 | 15,8 | |
| Diffuse tumor | 1 | 2,6 | |
| Yellowish white appearance | 35 | 93 | |
| Granular appearance | 31 | 81,6 | |
| Presence of calcifications | 30 | 78,9 | |
| **Microscopic examination n=38** | | | |
| Flexner-Wintersteiner rosettes | 27 | 73 | |
| Homer-Wright rosettes | 8 | 21,6 | |
| Florets | 2 | 5,4 | |
| Necrosis focus | 33 | 86,8 | |
| Focal points of calcification | 32 | 84,2 | |
| Marked mitotic activity | 33 | 88,6 | |
| Infiltration of internal structures | 4 | 10,5 | |
| **ABC classification (Murpphree)** | | | |

| | | | |
|---|---|---|---|
| Favorable group (A, B) | 1 | 2,6 | |
| Unfavorable group (C, D) | 3 | 7,9 | |
| Without functional recovery (E) | 34 | 89,5 | |

**Table 3: Time period of the onset disease consultation, consultation-management, clinical form, management and outcome of retinobastoma (bivariate and multivariate analysis).**

| | Outcome | | OR (CI=95%) | p-V | Chi2 | ORA | p-v |
|---|---|---|---|---|---|---|---|
| | Good | Poor | | | | | |
| **Disease onset and consultation** | | | | | | | |
| > 6 months | 1 | 17 | 0,067(0,008-0,52) | 0,0005 | 9,17 | 0,23 (0,03-1,4) | 0,1201 |
| < 6months | 50 | 57 | | | | | |
| **Time period between consultation and management** | | | | | | | |
| ≥ 1month | 3 | 72 | 0,001(0,0003-0,01) | 0,00000 | 101,35 | 1,6 (0,16-2,4) | 0,0000 |
| ≤ 1month | 48 | 2 | | | | | |
| **Form of disease** | | | | | | | |
| Extra-ocular | 3 | 72 | 0,001(0,0003-0,01) | 0,00000 | 101,35 | 1,6 (0,16-2,4) | 0,0000 |
| Intra-ocular | 48 | 2 | | | | | |
| **Management** | | | | | | | |
| Chemotherapy and enucleation | 49 | 61 | 5,22(1,12-24,24) | 0,01 | 4,11 | 5,25 (4,13-38,21) | 0,0478 |
| Chemotherapy | 2 | 13 | | | | | |

There was an association between the majority of the explanatory factors and the evolution of Rb ($p<0.05$). Indeed, the delay between the consultation and the management, the clinical form and the management of the Rb influenced its evolution. A significant positive association was observed (OR>1 and 1 excluded by the lower limit). On the other hand, by relating the time between the onset of the disease and the consultation to the evolution, a negative association emerged. Hence, to assess the association noted at first degree, using a bivariate analysis and eliminate the confounding factor; we had carried out a multivariate analysis (OR added); crossing all the explanatory variables and the evolution of the Rb. It emerged that all the explanatory factors influenced the evolution of Rb (according to the pV and CI=95%); except the time between the onset of the disease and the consultation.

## Discussion

### Epidemiological Parameters

***Frequency and incidence:*** In our study out of 7200 patients seen in consultation in 2014-2020, 125 patients had retinoblastoma, a frequency of 1.7%. The average incidence was 13.8%.

Numerous studies, including those conducted in Nigeria [8,16], in 2008 and from 2000 to 2007 mention, respectively that retinoblastoma represents 25.6% of all orbito-ocular neoplasms in Enugu region and occupies the first place of malignant neoplasms of children under 5 years old in Zaria region.

The Alliance of African and Mediterranean Leagues against Cancer [46], which includes 4 countries of the Maghreb, 21 countries of sub-Saharan Africa and 3 countries of the Indian Ocean, shows that in sub-Saharan Africa, 5 malignant tumors account for 70% of childhood cancers, including retinoblastoma. A study on the distribution of childhood cancers in Africa, which processed data from 1985 to 2011 [45], presents retinoblastoma as the most frequent childhood tumor, accounting for 20.1% of all malignant tumors of the African child.

In addition, in sub-Saharan Africa and in some developed countries, the overall incidence reported by several authors is 5,000 to 9,000 new cases per year. This corresponds to 1 in 15,000 to 20,000 live births [1-5]. In developed countries, the mean age at diagnosis is less than 2 years for unilateral cases (about 60 percent of cases) and less than 1 year for bilateral cases [6-10,45,48,49,50,51,52,53,55]. Our results reflect the burden of retinoblastoma in pediatric oncologic pathology in Bukavu as might be observed in any similar low-income setting. These appear to be lower than those reported by other studies, most likely due to sampling bias.

***Age:*** In our series, 54.4% of the patients were younger than 24 months and the mean age of the patients was 24.6 months.

Our results were consistent with those of the literature, which gives overall mean ages at diagnosis of 25 months for unilateral forms and 15 months for bilateral forms of retinoblastoma [6-10,54,55]. In all cases, it is evident that retinoblastoma presents as a tumor of early childhood.

***Sex:*** Our results showed a predominance of female patients (52% vs 48%). The sex ratio was 1.1. The literature does not mention the influence of gender on the occurrence, evolution or prognosis of retinoblastoma. Studies conducted in Nigeria [7], Brazil [49], and the DRC [2] have shown a predominance of male retinoblastoma.

In the USA, based on available data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute, authors have calculated the incidence of Rb in the United States from 1974 to 1985 without finding a difference between the sexes [53]. For the present study, we did not find an explanation for the predominance of the female sex.

## Origin of Patients

In our study, the majority of patients came from the outskirts of the city of Bukavu with a frequency of 72.8%. Most studies do not align the origin of patients among the study parameters.

Indian studies that investigated the role of infectious agents in the pathogenesis of retinoblastoma mention the interaction between the tumor suppressor Rb and oncoproteins of oncogenic DNA viruses such as human papillomavirus (HPV) [58], as well as the presence of oncogenic human papillomaviruses (HPV) in 69.7% of retinoblastoma specimens that had been analyzed; with 5. 3% for HPV16, 41% for HPV 18 and 48.2% for HPV 16 and 18 [59]. The oncogenicity of HPV serotypes 16 and 18 is known in some types of cancers.

In addition, a study in Mexico has shown the risk of confusion between toxocariasis and retinoblastoma. This is, in fact, a parasitic nematode of dogs and cats, whose larvae from hatching eggs released in the human intestinal lumen can migrate into several other tissues, including the eyes and indicate enucleation [60].

In the present study, this observation could be explained by the fact that CELPA ophthalmological center is the only ophthalmological referral facility in South Kivu province. It is likely that retinoblastoma patients living in the city were transferred to foreign countries for treatment. The analysis of the origin of the question raised by this study as to the role that the environment would play in the pathogenesis of retinoblastoma in Bukavu.

## Clinical Data

***Reason for Consultation:*** Eyeball protrusion and eye pain were the most frequent reasons for consultation in our series and were found in 51.2% of patients.

For high-income settings, the literature generally presents leukocoria first and strabismus the second, as the early signs detectable by parents and that may lead to an ophthalmologic consultation [1-5,49,51].

The discrepancy between our results and those presented in the literature in general would be related to ignorance and insufficient information of parents who should, as elsewhere, notice leukocoria early. Exophthalmos, being more impressive, would have alerted the parents much more quickly.

***Family History of Retinoblastoma:*** In our series, 79.2% of patients did not mention a family history of retinoblastoma during the interview. Numerous studies indicate that in 60% of cases, retinoblastoma is unilateral and not hereditary and that it is the most frequent form in low-income countries [11,29,45,52].

Our results are in agreement with those of the literature. Indeed, insufficient information about retinoblastoma and the absence of a well-maintained medical documentation could, in part, explain this result. Hence, the rationale for a genetic investigation and an early screening program for retinoblastoma suggested by the study

***Physical Examination Findings:*** In our study, the most frequent physical signs were, in order of frequency: exophthalmos (51.2%), leukocoria (38.4%) and buphthalmos (10.4%).

The literature almost unanimously presents leukocoria and strabismus as the major clinical signs indicative of retinoblastoma [1-5,49,51].

Overall, the predominance of exophthalmos in our study (61.6%) may be correlated with the high frequency of extraorbital forms of retinoblastoma characteristic of low-income settings.

***Laterality of the Disease:*** The present study showed that unilateral forms were found in 67.2% of patients. These results are in agreement with those of the literature, which almost unanimously report an average frequency of 60% for unilateral retinoblastoma said not to be hereditary and 40% for bilateral retinoblastoma said to be hereditary [1-8]. Our results are in agreement with those of the literature.

Clinical form of Retinoblastoma: In our series, extraorbital retinoblastoma was the most common clinical form, and was found in 77% of patients. The literature presents extraorbital retinoblastoma as the most common clinical form in low-income settings, due to late diagnosis and management [1, 32-34,49,56].

When relating the clinical form to the evolution of retinoblastoma, there was a statistical dependence between the extraorbital form and mortality ($X^2$=109,11 and p=0). This form was associated with high mortality. The extraorbital form would also account for a large proportion of all deaths.

## Average Time Period between Consultation and the Onset Disease

Our results showed that the average time period between consultation and the onset of the disease was 4 to 6 months. This long time period is characteristic of low-income environments as mentioned by many authors. It justifies, among other things, the high frequency of advanced forms of retinoblastoma in ophthalmologic consultations [1,32-34,49,56].

Statistically, there was a dependency of the time period between the beginning of the retinoblastoma and the consultation on the one hand and its evolution on the other hand ($X^2$=11,67 and p<0.0006). Thus, it was found that a late consultation was associated with a poor evolution of the tumor.

### Average Time Period from Consultation to Initiation of Management

In our series, the average time period from consultation to initiation of management was 14 days. The literature shows that in low-income settings, the time period between the onset of the first symptom of retinoblastoma and consultation is generally prolonged. It also demonstrates the negative influence of this long time period on the outcome of retinoblastoma [1-4,29,51,52,56]. Statistically, there was a dependent relationship between the time period taken for consultation and the beginning of the retinoblastoma intake on the one hand and the evolution of the retinoblastoma on the other hand ($X^2$ =109,11 and p=0). Thus, it was found that the later the time between consultation and treatment, the worse the outcome of the retinoblastoma.

### Treatment Undertaken

In our series, 89.6% of patients had undergone enucleation combined with chemotherapy and 10.4% had undergone only the enucleation. The literature shows that this treatment regimen is applied to advanced retinoblastomas in several treatment centers [1-4,15,35-37,61].

This regimen conformed to the GFAOP protocol and reflected that the retinoblastomas that were managed at CELPA ophthalmologic center in Bukavu were advanced forms.

By relating the type of treatment to the evolution of the retinoblastoma, it appears that statistically, there is a relationship of dependence between the form of retinoblastoma and its evolution ($X^2$=8,203, p=0,0041). Both forms (extra and intraorbital) were associated with high mortality. In all cases, these were the advanced forms of retinoblastoma, which are always associated with high mortality.

### Evolution of Treated Retinoblastoma after 3 years of Follow-up

Analysis of the data obtained at 3-year follow-up showed that 59.2% of patients died and 40.8% survived without developing metastasis. Overall, the survival rate is low in the low and middle-income settings [1-4,52].As in all low-income settings, in Bukavu this is explained by the existence of certain limiting factors such as late diagnosis and management, as well as insufficient diagnostic and therapeutic means. The correction of these factors, most of which are modifiable, could improve the prognosis and the survival rate.

Considering the bivariate analyses integrating the time period between the beginning of the disease and the consultation, the consultation and the management, the clinical form and the treatment in relation to the outcome, with p<1, we can evoke the existence of confounding factors. Thus, by using logistic regression, a positive association only between management and outcome emerges, which could mean that only management would directly influence outcome (df=1,p=1). The other factors would indirectly influence the evolution or would be considered as confounding factors.

### Causes of Poor Outcome

Among the 74 patients who died, 28 (37.8%) were noncompliant with treatment, 41 (55.4%) had delayed visits and had metastatic forms of retinoblastoma on admission, and 5 (6.7%) had refused treatment. These are explanatory factors for the high mortality of retinoblastoma in low-income settings described in the literature [1-4,15].

In Bukavu, as in other low-income settings, not only poverty, insufficient education, dissemination of erroneous information, and a certain social understanding of the disease, but also the interference of phytotherapy and other traditional therapies would be at the basis of the above results.

### Histopathological Data

In our series, only 38 patients (30.4%) had histopathologic examination. The literature presents poverty as an obstacle to the correct management of retinoblastoma [1-4,22-24,52], thus evoking the diagnosis and treatment of the disease. This is a limitation in the management of retinoblastoma in Bukavu.

Macroscopically, the majority of patients presented an endophytic form (81.6%). Yellowish-white (93%), granular (81.6%) and calcification (78.9%) aspects dominated. The ABC classification used gave the group of patients with no hope of functional recovery (group E) as dominant (89.5%). Microscopically, Flexner-Wintersteiner rosettes (73%), Homer Wright rosettes (21.6%), necrosis (86.8%), calcification (84.2%) and mitoses (88.6%) were noted. Infiltration of the internal structures of the eye was observed in 10.5% of patients.

The macroscopic and microscopic features presented by the study are described as characteristic and differentiating elements of retinoblastoma by the literature [47].

### Conclusion

The present study, had collated 125 patients with retinoblastoma, followed at CELPA clinic in Bukavu (DRC) over a period of 7 years from 2014 to 2020 with an average of 18 patients per year. The frequency of retinoblastoma was estimated at 1.7% and the incidence at 13.8%. The average age at diagnosis was <24 months, with a predominance of unilateral (67.2%) and extraorbital (77%) forms. The most frequent reason for consultation was ocular protrusion and pain (51.2%), family history of retinoblastoma was rare (20.8%). The group of untreatable patients with no hope of functional recovery (group E) was dominant (89.5%). The most common treatment was chemotherapy combined with enucleation (89.6%). The overall survival rate after a 3-year follow-up was 40.8% and the main cause of poor outcome was delayed consultation and the presence of metastases at admission (55.4%). Only 30.4% of patients had histological confirmation. The retinoblastomas were differentiated and in advanced stages. Delayed diagnosis and treatment seemed to influence the prognosis.

There was an association between the majority of the explanatory factors and the evolution of Rb (p<0.05). Indeed, the delay between

the consultation and the management, the clinical form and the management of the Rb influenced its evolution. A significant positive association was observed (OR>1 and 1 excluded by the lower limit). On the other hand, by relating the time between the onset of the disease and the consultation to the evolution, a negative association emerged. Hence, to assess the association noted at first degree, using a bivariate analysis and eliminate the confounding factor; we had carried out a multivariate analysis (OR added); crossing all the explanatory variables and the evolution of the Rb. It emerged that all the explanatory factors influenced the evolution of Rb (according to the pV and CI=95%); except the time between the onset of the disease and the consultation.

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