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ORIGINAL ARTICLES

Patterns of Retinoblastoma in Zimbabwe: 2000-2009

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Abstract

Objective: To document the pattern of retinoblastoma in children in Zimbabwe for the period 2000-2009.
Design : Retrospective study.
Methods : Analysis of data from the Zimbabwe National Cancer registry and records of patients admitted to the Paediatric Oncology unit. Data collected from cancer registry were basis of diagnosis, age and gender. Data from the patients medical records included clinical presentation, time to diagnosis and treatment.
Settings : The Zimbabwe National Cancer Registry and Paediatric Oncology Unit at Parirenyatwa Tertiary Hospital.
Results: 196 patients with retinoblastoma were registered at the cancer registry over the study period. The diagnosis was confirmed histologically on 89% of the cases and in 7% the diagnosis was based on clinical grounds. The age ranged from less than one month to 7 years with median age of 24 months. Males were 111 (56%) with male:female ratio of 1.3:1. Forty three patients (84%) had unilateral and 8 (16%) bilateral disease. Medical records were retrieved from only 54 /196 cases (27.5%). The commonest clinical presentation was proptosis 35/54 (65%). Leucocoria was present in 14/54 (26%). Time interval between first symptoms and diagnosis ranged from less than one month to 24 months with mean duration of 7.7 months (SD=6.9). Enucleation was performed on 33/ 54 (61%), exenteration on 20/54 (37%) chemotherapy was given to 34/54 (63%) and only 6/54 (11%) received radiotherapy.
Conclusion: Retinoblastoma is the third commonest registered malignancy of childhood in Zimbabwe, characaterised by late presentation and poor access to therapy.

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Introduction

Retinoblastoma is the most common intraocular malignant tumour of childhood but it remains a rare disease.[1] It occurs more commonly in less affluent regions of the world compared to richer regions. The incidence of retinoblastoma within age group 0-4 years varies from country to country. Africa generally has a higher incidence especially in the sub Saharan Africa region ranging from 10.6 to 42.5cases per million. This is in contrast to developed countries where in the USA, the incidence is 11.8 and in Europe it ranges from 6-12. Bulgaria has the lowest incidence of 3.4 cases per million.[2,3] In Zimbabwe the incidence of retinoblastoma is estimated at 23.3 per million ranking 3rd highest in the world after Uganda and Mali.[4]

The mode of presentation varies between countries with leucocoria being the commonest presentation in developed countries[5] and proptosis being common in developing countries.[6,7] Late presentation is a feature in many developing countries accounting for the poor outcome.[6-10] The trend in management for early

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presentation is for conservative local treatment with preservation of vision.[13] However in developing countries where majority present late with advanced disease, enucleation remains a common form of treatment.[8,14,15]

Over 95% of children with retinoblastoma in the United States and other medically developed nations survive their malignancy due largely to early detection when the tumour is contained in the eye.[13] In developing nations, the survival is much less with late presentation, poor treatment compliance and limited treatment options being the major causes for these poor results.[16]

The purpose of this study is to document the pattern of presentation of children in Zimbabwe diagnosed with retinoblastoma over a 10 year period from 2000-2009. The findings will help in recommendations for improving the management of this condition.

Methods

This was a retrospective analysis of data on children diagnosed with retinoblastoma over a 10 year period from 2000-2009. Formal approval for the study was obtained from the Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Committee. The main source of data for the study was collected from the Zimbabwe National Cancer Registry. The Cancer Registry follows Standard procedures which ensure that only incident cases are recorded and that multiple notifications of the same cancer have been detected. The Registry methods have been described in previous publications.[17,18] The other source of data was from case notes of patients who were admitted to the Paediatric Oncology Unit (POU) who were mainly referrals from Sekuru Kaguvi Eye Unit.

The POU is placed at the Parirenyatwa Teaching Hospital and provides cancer treatment for children up to 12 years of age. It has a maximum capacity of 15 cots/beds and occupies a section of a general paediatric medical ward.

Children seen at Sekuru Kaguvi Eye Unit with diagnosis of Retinoblastoma are referred to POU for chemotherapy.

The information collected from the case notes of patients admitted to POU were the clinical presentation, time to diagnosis and treatment.

Statistical methods.

Data was entered into EPIINFO soft ware for analysis. Statistical methods used were those for descriptive studies. Median with Q1 and Q3 was calculated for age. Mean, SD, and 95% confidence interval (CI) were calculated for the time to diagnosis. P value of <0.05 was taken as statistically significant.

Results

A total of 196 cases of retinoblastoma were registered in the Zimbabwe National Cancer Registry from January 2000 to December 2009. All these children were below 15 years of age. During the same period of time a total of 1766 cases of childhood malignancies below 15 years of age were registered in the cancer registry, with retinoblastoma accounting for 13 % of all malignancies in children registered in Zimbabwe.

The diagnosis of retinoblastoma was confirmed on histology in 89% of the cases and in 7% the diagnosis was based on clinical grounds. In 4% of the cases there was no record on how the diagnosis was made.

Of the 196 registered retinoblastoma cases, medical records could be retrieved for only 54 cases (27.5%).

Age at presentation.

The ages of the children ranged from less than one month to 7 years of age with a median age of 24 months (Q1 = 20 months and Q3= 36 months). Ninety five percent of the children were 5 years of age or below and 58% were 2 years or below.

Gender.

There were 111 males and 85 females giving a male: female ratio of 1.3:1. There was no statistically significant age difference between the gender groups ($p=0.489$).

Clinical presentation.

Data on clinical presentation was available on 51 patients. Of these, the majority of patients, 43 (84%) had unilateral disease and 8 (16.0%) had bilateral disease. The median age of children with unilateral disease was 36 months (Q1=24, Q3=48) and bilateral 23.5 months (Q1=17.5 and Q3=30.5). There was no difference in gender distribution between the two groups.

The commonest clinical presentation in our experience was proptosis35/54 (65%) and leucocoria 14/54 (26%). There were no cases of strabismus.

Time to diagnosis.

The time interval between first symptoms and diagnosis ranged between less than one month to 24 months with mean duration of symptoms of 7 .7 months (SD=6.9).

Treatment.

The majority of patients 33/54 (61%) had enucleation and 20 /54 (37%) had exenteration. Chemo therapy was given to 34/54 (63%) of the cases. At the time of the study, the chemotherapy regimen used was Vincristine, Doxorubicin and cyclophosphamide for 6-8 courses. Only 6/54 patients (11%) received radiotherapy.

Discussion

Of the total of 1766 malignancies registered in children under 15 years during the period of the study, retinoblastoma accounted for 13% and ranked third most common malignancy after Wilm's tumour 17 %

and Kaposi Sarcoma 15.7%. The relatively high frequency of retinoblastoma seen in our series is similar to reports from researchers in developing countries with Tanzania 12.9%, Malawi 11.3% and Nigeria 8%.[9,20,21] This high frequency of retinoblastoma is in contrast to developed countries where retinoblastoma represents only 3% of all malignant tumours in children.[22]

The diagnosis of retinoblastoma was confirmed on histology in 89% of the cases and in only 7% was the diagnosis made on clinical grounds. The rate of histological confirmation in our series was very high compared to reports from East Africa where only 35% of the diagnosis was based on histology and the rest on clinical grounds.[19] In Nigeria, histology was performed in only 3 cases out of a series of 13 children seen over a 10 year period.[14]

Age at presentation.

Almost all patients in our study (96%) were aged 5 years and below with a median age of 24 months which although lower than that reported in other developing countries[6-8,15] is still higher than 19 months reported in developed countries such as the UK.[23] The late presentation of retinoblastoma commonly reported in low income countries is often attributed to poor awareness of presenting signs of retinoblastoma, low parental education and limited access to health care services.[22]

Gender.

Although various studies reveal no significant differences between males and females[15,24,25] in our series although not significant, there was a slight predilection to males with M:F ratio of 1.3:1 which is similar to 1.4:1 reported in Uganda.[4] In Mali[7] which has the highest incidence of Retinoblastoma in the world,[4] the male:female ratio was 2:1. The gender distribution is in marked contrast to that reported in Native Alaska[26] where retinoblastoma is much higher in girls than in boys with male: female ratio of 1:3.

Of the 196 cases registered only 54 patients (27.5%) were able to access chemotherapy at the Tertiary Hospital. The majority of our patients with Retinoblastoma do not have access to chemotherapy and therefore remain untreated with fatal outcome. This poor access to treatment of retinoblastoma is common in developing countries.[16] In East Africa researchers reported only 18% of their patients with retinoblastoma having access to treatment.[19]

Clinical presentation.

The incidence of bilateral retinoblastoma in our patients is16%. This compares well with findings from other African series[7,14] whereas the incidence of bilateral disease is much higher in Western countries.[24,27] The median age at presentation of bilateral disease in our patients is 23.5 months much younger compared to 36 months in our patients with unilateral disease (84%). The younger age of bilateral disease at presentation compared to unilateral disease is widely reported in other countries in Africa,[6,7,14] Asia[10,12] and in Western countries[5,28] although the mean ages of presentation is lower in both unilateral and bilateral diseases in Western countries. In Japan, over the years there has been a decrease in mean ages at presentation in both unilateral and bilateral disease and that was attributed to increased parental knowledge and advances in diagnostic modalities.[29]

In our study, the majority of our patients 35/54 (65%) presented with propotosis whilst 14/54 (26%) presented with leucocoria. Proptosis is a common presentation of retinoblastoma in developing countries and is due to late presentation and diagnosis. In a study in Mali,[7] among 55 patients with retinoblastoma, 54% presented with exophthalmous followed by leucocoria 38.2%. Similarly in Nepal,[10] 40.42 % presented with proptosis followed by leucokoria in 29.78 % of cases. This is in contrast to that reported in developed countries such as Great Britain[28] where leucocoria was the commonest presentation in 50% followed by squint 25%. The differences in presentation is not only confined to developed and developing countries but even within the same country but in different regions there are also differences in presentation. Owoeye *et al*[15] from Ilorin, West Central part of Nigeria found proptosis to be the commonest presentation accounting for 84.6% of the cases compared to another region in the South of Nigeria[14] where only 15.4% of patients presented with extra ocular retinoblastoma and the majority 61.5% presented with leucocoria.

Time to diagnosis.

The mean time to diagnosis (duration of symptoms reported by parents prior to diagnosis) in our study was 7 months which is much longer than 8 weeks reported by researchers in the UK.[23] In developing countries in Africa[8,14] and Asia[10, 12] the mean time to diagnosis is longer than in developed countries.[24,25,30] Researches from Brazil[31] and Argentina[22] have noted that children with a longer period of time to diagnosis of disease were more likely to have more clinically advanced disease. In Mali[7] the delay in presentation was attributed to factors such as patients moving from one traditional healer to another, and to lack of knowledge among social health workers and doctors about the early signs of the disease. Our experience concerning delays in health seeking behavior is pretty much similar to that above.

Treatment.

The approach to treatment of Retinoblastoma in our centre includes, enucleation, exenteration and systemic chemotherapy. Eye conserving treatment is not usually offered because our patients present late with advanced disease. In many developing countries where a multimodal approach is not available, enucleation is the most common treatment option.[8,10,14,15]

In our series, enucleation was performed on 33/54 (61%) of the patients while 20/54 (37%) had

exenteration. The rate of enucleation among our patients is slightly below the trend of 65-75% reported by researchers in the USA[32] but higher than the rates reported in Mali and Nigeria[7,14] where the relatively lower rates of enucleation were attributed to lack of radiotherapy, cultural factors and financial constraints by the families unable to meet the cost of enucleation.

Most of our patients 34/54 (63%) were treated aggressively with chemotherapy using Vincristine, Cyclophosphamide and Doxorubicin. The use of chemotherapy among our patients was much higher than reported from Nigeria[15] where only 3 (15%) had chemotherapy and in Tanzania[10] where only 6% received chemotherapy.

In their series of 33 patients with orbital retinoblastoma Doz F *et al*[33] reported improved outcome in their patients who received intensive chemotherapy even where there was associated extra CNS metastases.

Radiotherapy was not easily available to our patients as only 6/54 (11%) had radiotherapy. It is difficult to assess the impact lack of radiotherapy has on the outcome of our patients. Researchers in Ibadan in Nigeria reported improvement in the treatment outcome and prognosis of children with retinoblastoma who had radiotherapy.[34] In Brazil[35] combination of chemotherapy and radiotherapy is the mainstay in the treatment of patients with advanced retinoblastoma.

We do acknowledge a limitation of this study. The small numbers of case notes of patients admitted that were analysed in comparison to the total numbers of cases registered makes it impossible to make inferences for the whole population from this series.

Conclusion

Retinoblastoma is the third commonest registered malignancy of childhood in Zimbabwe, characaterised by late presentation and poor access to therapy. Awareness campaigns on signs and symptoms of retinoblastoma and its good response to chemotherapeutic agents may assist in early disease detection and resource mobilization.

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