

# UPTAKE OF SURGERY IN THE MANAGEMENT OF RETINOBLASTOMA IN BENIN CITY

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## ABSTRACT

**Aim:** The aim of this study is to determine the level of acceptance of surgical treatment and the reasons for delay in or non-acceptance of surgery in the management of retinoblastoma.

**Methods:** This is a retrospective study of patients seen in the eye clinic of University of Benin Teaching Hospital, Benin City between June 2003 and December 2015. Information was retrieved from the case notes using a protocol which included age at presentation, sex, clinical presentation, duration of disease, time from presentation to surgery, acceptance of enucleation by parents and other treatment modalities offered.

**Results:** A total of sixty-three eyes of 46 patients were analyzed in the period under review. There were 27 males and 19 females giving a male to female ratio of 1.4:1. Leucocoria was the most common clinical feature seen in 29 eyes (46.0%) followed by proptosis in 16 eyes (25.4%). Twenty six patients (56.5%) accepted enucleation while 16 patients (34.8%) did not accept enucleation. Surgery was not performed in four (8.7%) patients as they were offered systemic chemotherapy. Reasons for non-acceptance included parent's refusal to have the eyes of their children removed for cosmetic reasons and cultural beliefs and parent's denial that their child had cancer. Surgery was delayed in 15 out of 26 patients who accepted enucleation (57.7%) with the time from presentation to surgery ranging from 2 weeks after presentation to 24 months. Reasons for delay in surgery included financial constraint, defaulting after commencing chemotherapy, anaemia, initial refusal by parents, initial chemoreduction, parents absconding with their children only to return after the disease became more advanced and parent/caregiver going to consult traditional herbalist.

**Conclusion:** There are challenges managing retinoblastoma surgically. These problems can be resolved through proper counseling of parents/caregivers on the fatality of this malignancy and the need for early surgical intervention where indicated.

**Keywords:** acceptance, enucleation, surgery, retinoblastoma, delay

## INTRODUCTION

Retinoblastoma is the commonest primary intraocular childhood malignancy accounting for

1: 15,000-20,000 live births in the United States of America.<sup>1</sup> In developing countries of Africa and Asia, it was found to occur in 1 in 18,000 live births with a range of 1 in 10,000 to 20,000 live births.<sup>2-3</sup> The management of retinoblastoma includes surgery, chemotherapy, external beam radiation, laser photocoagulation, transpupillary thermotherapy, cryotherapy and brachytherapy.<sup>4</sup> Enucleation and exenteration are techniques used in the surgical management of retinoblastoma. In the developed world, management of retinoblastoma has gradually changed from

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enucleation and external beam radiation to more conservative techniques aimed at preserving the globe and vision when patients present early.<sup>5</sup> However in developing countries, because of the problem of late presentation and late diagnosis, surgery is still an option in the management of retinoblastoma.<sup>6,7</sup> Indications for surgery in retinoblastoma include advanced disease with no hope for useful vision in the affected eye or if there is a concern of invasion of the tumour into the optic nerve, choroid or orbit.<sup>6</sup> Eyes with secondary glaucoma, pars plana seeding or anterior chamber invasion are best managed with enucleation.<sup>6</sup>

In developing countries, techniques used in the surgical management of retinoblastoma include enucleation, exenteration and modified exenteration.<sup>4,8</sup> Previous studies have shown high levels of acceptance of surgery as a treatment modality ranging from 84 to 100%.<sup>4,8</sup> However, the study by Bekibele *et al* reported a lower level of acceptance of surgery of 57.7% (15 out of 26 patients).<sup>9</sup> In Port Harcourt<sup>7</sup>, there was also poor acceptance as 7 patients out of 13 patients (53.8%) with stage D and E retinoblastoma (International Classification of Intraocular Retinoblastoma)<sup>10</sup> accepted enucleation as a treatment modality.

The aim of this study is to determine the level of acceptance of surgical treatment, the time period from presentation to surgery and reasons for delay in or non-acceptance of surgery in retinoblastoma patients in order to proffer solutions on how to improve acceptance and early uptake of surgery when patients present with intraocular disease.

### MATERIALS AND METHODS

This is a retrospective study of patients who presented with retinoblastoma at the eye clinic of the University of Benin Teaching Hospital, Benin City between June 2003 and December 2015. The patients were identified from the outpatient records as well as the theatre and admission

registers. Patients whose case records were either incomplete or unavailable were excluded from the study. Information was retrieved using a protocol which included age at presentation, sex, clinical presentation, duration of disease, stage of disease, time from presentation to surgery, acceptance of enucleation by parents and treatment offered. Management protocol in our centre included 1) Dilated funduscopy under general anaesthesia with binocular indirect ophthalmoscope 2) Diagnosis of retinoblastoma based on findings on B mode ocular ultrasound and examination under anaesthesia and 3) confirmation by histology. The 2006 International Classification for Intraocular Retinoblastoma<sup>10</sup> based on tumor size, location and associated seeding was used to classify the disease in this study. The classification was as follows: Group A-retinoblastoma up to 3mm in size, Group B-retinoblastoma more than 3mm in size, macular location and mild subretinal fluid, Group C-retinoblastoma with localized seeds, Group D-retinoblastoma with diffuse seeds and Group E-massive retinoblastoma necessitating enucleation. Extraocular retinoblastoma was defined as tumour extending beyond the globe evident by the presence of a fungating mass or when there is involvement of the extraocular tissues resulting in marked proptosis. Metastatic retinoblastoma was diagnosed when there was evidence of metastasis such as scalp swellings, involvement of the brain, liver and bone marrow. The treatment options offered in our centre includes systemic chemotherapy, external beam radiation and enucleation for advanced retinoblastoma as well as cryotherapy for small tumours located anterior to the equator. Acceptance of surgery was defined as the parent or caregiver agreeing to have enucleation performed on the patient the first time surgery is offered once the diagnosis of retinoblastoma had been made and the need for enucleation is communicated to the parent or caregiver. Data collated was analyzed using Graphpad Instat version 2.05a. Frequency distribution tables were generated for all data collected. The ranges and means were determined. At the adopted

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confidence level of 95%, a p value of 0.05(5%) or less was regarded as significant.

### RESULTS

A total of 46 patients were analyzed out of the sixty two patients managed in the period under review. There were 27 males and 19 females giving a male to female ratio of 1.4:1. The age and sex distribution is shown in Table 1. The minimum age at presentation was 3 months and the maximum age was 9 years (mean age  $2.4 \pm 1.73$  years). There was unilateral involvement in 29 patients (63.0%) with involvement of the left eye in 12 patients and right eye in 17 patients. Both eyes were involved in 17 patients (37.0%).

Table 1: Age and sex distribution

Age (months)	Male (%)	Female (%)	Total	Percentage%
3-24	18(39.1%)	7(15.2%)	25	54.3%
25-36	5(10.9%)	9(19.5%)	14	30.4%
37-48	1(2.2%)	1(2.2%)	2	4.4%
49-60	1(2.2%)	1(2.2%)	2	4.4%
61-108	2(4.3%)	1(2.2%)	3	6.5%
Total	27(58.7%)	19(41.3%)	46	100

The clinical presentation is shown in Table 2. Leucocoria was the most common clinical feature seen in 29 eyes (46.0%) followed by proptosis in 16 eyes (25.4%). Extraocular retinoblastoma (proptosis and fungating mass) accounted for 38.1% (n=24 eyes). Seven patients (15.2%) presented within one month of the onset of symptoms. Thirty one patients (67.4%) presented between 2 and 12 months, 6 patients (13.0%) between 12 and 24 months and 2 patients (4.4%) after 24 months. Thirty-five (55.6%) out of 63 eyes were staged with the International

Classification for Intraocular Retinoblastoma as follows: 12 eyes (19.0%) were Group B, 2 eyes (3.2%) were Group C, 2 eyes (3.2%) were group D and 19 eyes (30.2%) were Group E. Of the remaining 28 eyes (44.4%), twenty-four eyes (38.1%) had extraocular and four eyes (6.3%) had metastatic retinoblastoma.

The parents of twenty six patients (56.5%) accepted enucleation while the parents of 16 patients (34.8%) did not accept enucleation as part of the management of their children. Surgery was not performed in the remaining four (8.7%) patients as they were offered only systemic chemotherapy. Reasons for non-acceptance included parent's refusal to have the eyes of their children removed for cosmetic reasons and cultural beliefs (5 patients) and parent's denial that their child had cancer (1 patient). The parents of 10 patients took their children away when the diagnosis was explained to them.

Surgery was delayed in 15 out of the twenty-six patients who accepted surgery (57.7%) with the time from presentation to surgery ranging from 2 weeks after presentation to 24 months. Eleven patients (42.3%) had their surgery within the first week of presenting at the facility. Reasons for delay in surgery included financial constraint (3 patients), defaulting after commencing chemotherapy (3 patients), anaemia in the children who needed to be transfused before they could be fit for surgery (3 patients), initial refusal by parents who later agreed (2 patients), initial chemoreduction (2 patients), parents initially absconding with their children only to return after the disease became more advanced (1 patient) and parent/ caregiver going to consult traditional herbalist (1 patient).

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**Table 2: Clinical presentation of patients with retinoblastoma**

Presenting feature	Number of eyes (n=63)	Percentage (%)
Leucocoria	29	46.0
Proptosis	16	25.4
Fungating mass	8	12.7
Uveitis	3	4.8
Strabismus	3	4.8
Metastasis	2	3.1
Orbital cellulitis	1	1.6
Bupthalmous	1	1.6
	63	100

Enucleation was carried out in 56.5% of cases (n=26). Twenty patients had enucleation followed by chemotherapy, 3 had initial chemoreduction followed by enucleation, 2 had enucleation only and one had a combination of enucleation, brachytherapy and chemotherapy. No exenteration was done.

### DISCUSSION

The management of retinoblastoma, though a rare intraocular tumour, presents challenges in the developing African nations. The male-to-female ratio in this study was 1.4: 1 which has a slightly higher male preponderance compared to other hospital studies in various parts of Nigeria where a ratio 0.8-1.1:1 has been found.<sup>12,13</sup> However, in the Kano study,<sup>4</sup> more females were affected with the male-to- female ratio of 1:1.8 while in the previous study carried out in Benin,<sup>14</sup> the males were still more affected with a ratio of 4:1.

In this study, the average age at presentation of the children was high at 29 months (2.4 years). This finding compares to previous studies in developing countries where the mean age ranged between 29- 36.3 months.<sup>12,13,15</sup> This is in contrast

with what obtains in the developed countries where the mean age at presentation is less than 24 months.<sup>16</sup> The reasons for late presentation was attributed by an author to lack of awareness of the disease, delayed referral prompted by consultation with traditional medical practitioners, poor affordability, and poor access to available medical facilities.<sup>12</sup> In this study, reasons given included consultation with traditional healers and delayed presentation at the health facility following referral by health personnel the patient initially presented to. Delayed presentation in this study was attributed to financial constraints, initial denial that their child had cancer and ignorance of the parents about the fatality of the disease.

Leucocoria was the most common clinical presentation accounting for 46.0% of the patients. This is in agreement with the study by Akang *et al*<sup>13</sup> where leucocoria was the most common clinical manifestation. Proptosis was the second most common presentation in 25.4% of patients. Proptosis together with other signs such as secondary glaucoma, fungating mass and hyphema are known signs of advanced disease or high risk of metastasis.<sup>13</sup> In this study, the presence of proptosis, fungating mass and metastatic retinoblastoma may be attributed to delay in the presentation of patients for diagnosis and treatment as well as defaulting from treatment with chemotherapy. Erwenne *et al*<sup>17</sup> concluded in their study of 158 consecutive cases of retinoblastoma that extra-ocular disease was strongly dependent on the age at diagnosis and lateness of referral.

Enucleation is a frequently used and an important method for managing retinoblastoma.<sup>6</sup> In this study, enucleation was the most common method of treatment. Majority of the patients (56.5%) had enucleation because the tumour had filled the eye and there was no hope of retaining useful vision. Studies<sup>8,12</sup> conducted in other hospitals have shown enucleation to be the most common mode of treatment for patients with retinoblastoma often combined with chemotherapy. There was no case of exenteration

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as seen in the study by Ajaiyeoba *et al*<sup>8</sup> where 7 patients had exenteration while 37 patients had enucleation. In Kano,<sup>4</sup> modified exenteration was done in 31 patients (74%) as compared to enucleation in 11 patients (26%). Modified exenteration was done because the patients presented late. This technique involves the removal of all the orbital contents excluding orbital periosteum. Adjuvant chemotherapy was used in the twenty four patients who had had enucleation in this study. In addition to these, eight patients had commenced on chemotherapy to reduce the tumour mass before enucleation.

Acceptance of surgery (56.5%) was not as high as what obtained in the Kano study (100%). In the study by Bekibele *et al*<sup>9</sup> and Adio *et al*<sup>7</sup>, acceptance rate was 57.7% (15 out of 26 patients) and 53.8% (7 out of 13 patients) respectively which compares with what was obtained in this study. Ajaiyeoba *et al*<sup>8</sup> in Ibadan reported a high acceptance of surgery (100%). However when compared to the more recent study by Bekibele *et al*,<sup>9</sup> the acceptance rate in Bekibele's study was lower. Reasons proffered for this lower rate included fear of enucleation, the cultural stigma/cosmetic defect associated with eye removal as well as failure to realize the severity of the situation at the time.<sup>9,10</sup> However, in this study, reasons for non-acceptance of surgery included parent's refusal to have the child's eye removed, parent's denial that their child had cancer and parents leaving with the child when the diagnosis was explained to them. This showed the poor knowledge that the parents had about the fatality of the disease. These were similar to the reasons proffered in the study by Adio *et al*<sup>7</sup> in Port Harcourt and Bukhari *et al*<sup>18</sup> in Pakistan.

Uptake of surgery within 1 week of presenting (42.3%) was good compared to previous studies<sup>7,9</sup> though more effort would need to be made to reduce delay in surgery uptake. It was observed that even among patients who accepted surgery, there was a delay between the time the patient presented and the time the surgery was performed. This could affect the patient outcome even when surgery is eventually done. In this

study, reasons for delay in surgery included financial constraints regarding investigations and medications, defaulting after commencing chemotherapy, anaemia in the child requiring transfusion before surgery, initial refusal by parents who later agreed, initial chemo reduction, parents/ caregivers absconding with their children only to return after the disease became more advanced or after consulting traditional herbalist. Abdu<sup>4</sup> in Kano identified factors which contributed to late onset of treatment even for patients who presented with early disease. These included socioeconomic factors such as poverty and cultural beliefs. In the Ibadan study<sup>9</sup>, reasons for late uptake of surgery included refusal of early surgery by parents and late diagnosis. Late diagnosis was due to ignorance, late presentation, missed diagnosis and previous treatment in a private hospital. These patients tend to come with advanced disease. Once there is advanced disease, metastasis could occur as early as 9 months after enucleation in about a tenth of patients.<sup>10</sup>

In Conclusion, there are challenges managing retinoblastoma surgically. These challenges include financial constraint, defaulting treatment, anaemia, initial refusal by parents, parents initially absconding with their children only to return after the disease has become more advanced and parent/ caregiver going to consult traditional herbalist prior to presentation. These problems can be resolved through proper counselling and health education of parents/ caregivers on the fatality of this malignancy and the need for early surgical intervention where indicated. There would also be a need to devise ways of encouraging caregivers through creating associations where they can meet and interact with other caregivers and the managing team in order to increase acceptance rate and surgery uptake.

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