Retinoblastoma Outcomes in a Tertiary Hospital in Northern Luzon, The Philippines: A 15-Year Experience

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Abstract

Objective  To describe the demographics, clinical profile, and outcomes of retinoblastoma patients seen in a tertiary hospital in northern Luzon.

Materials and Methods  This is a retrospective cross-sectional study of retinoblastoma patients at the departments of ophthalmology and pediatrics of a tertiary hospital in northern Luzon from 2005 to 2020.

Results  A total of 47 patients involving 53 eyes were included. Twenty nine (62%) are male and forty one (87%) had unilateral retinoblastoma. Mean age at consult was 24 ± 17 months, and mean interval from onset of symptoms to consult was 10 ± 11 months. Two (4%) had family history of retinoblastoma. Twenty-two (47%) patients had intraocular involvement. Leukocoria was the most common presenting symptoms at 62%. Overall survival was 53% with mean follow-up period of 24 ± 24 months. Difference in survival rates based on the extent of involvement was statistically significant (p < 0.001).

Conclusion  This is the first study that provided data on demographics, clinical profile, and outcomes of retinoblastoma patients in northern Luzon and the only study with data on clinical outcomes of retinoblastoma patients in The Philippines. Extraocular involvement is a significant factor in the low survival of retinoblastoma patients despite improvement in its management.
**Introduction**

Retinoblastoma is a malignancy of immature retinal cells of children and approximately 90 to 96% of cases are diagnosed before 5 years of age. It is initially diagnosed clinically, with leukocoria as the most common presenting sign which often presents unilaterally. Intraocular retinoblastoma is commonly classified using the International Intraocular Retinoblastoma Classification (IIRC) or the International Classification of Retinoblastoma (ICRB). ICRB better predicts prognosis of patients with intraocular retinoblastoma, who are likely to be cured without the need for enucleation or external-beam radiation treatment. However in low- to medium-income countries, including the Philippines, a significant portion of patients presents with extraocular disease. In Philippine General Hospital alone, 24% had extraocular involvement. In these cases, other classification systems are used such as the TNM system and the International Retinoblastoma Staging System (IRSS). Treatment options for retinoblastoma depend on its severity on presentation and laterality. An early intraocular disease can respond to globe salvage procedures. However, enucleation is indicated in advanced intraocular cases, while primary systemic chemotherapy is indicated for extraocular cases. Adjuvant systemic chemotherapy is indicated for enucleated eyes with high-risk features, including a positive optic nerve margin. Survival rate is significantly affected by the extent of involvement.

The estimated worldwide incidence of retinoblastoma is 1 in 16000 to 18000 births every year, although it varies from region to region, with India and Africa having higher incidence rates. It is also common among Filipinos with an incidence of 237/100,000 eye cases. However, the data from the Philippine General Hospital did not include data on clinical outcomes. Baguio General Hospital and Medical Center (BGHMC) is one of the government tertiary hospitals in northern Luzon and receives referral from other areas of northern Luzon. Its ophthalmology department manages referrals of childhood eye malignancies. There is no available data on demographics and clinical profile of retinoblastoma patients from northern Luzon and on clinical outcomes of retinoblastoma patients from The Philippines. It is significant to have these data for the BGHMC to better prepare its ophthalmology department in managing retinoblastoma patients in the future. Similarly, The Philippines is included in the list of six Asian countries where 43% of new retinoblastoma cases in 2023 will come from. It is vital to assess updated data on the demographics, clinical profile, and outcomes of retinoblastoma patients in northern Luzon to determine how BGHMC is faring compared with the other countries and to identify areas in retinoblastoma management which can be improved.

**Materials and Methods**

This is a retrospective cross-sectional study of retinoblastoma patients at BGHMC in northern Luzon from 2005 to 2020. Medical records of patients who consulted for leukocoria, intraocular tumor/mass, and strabismus in the departments of ophthalmology and pediatrics from 2005 to 2020 were reviewed. Patients diagnosed with retinoblastoma based on the clinical presenta-
Based on the IRSS, 22 have stage 1, 6 have stage 2, 9 have stage 3, and 6 have stage 4. Four patients were unclassified since they did not undergo cranial imaging and enucleation (Table 1). Patients with bilateral retinoblastoma were staged, based on their worse eye. IRSS staging was based on their clinical presentation and available imaging during initial consult and their clinical course at BGHMC.

### Outcomes

The mean follow-up period was 24 ± 24 months; 24 ± 24 for unilateral and 36 ± 36 for bilateral. Overall survival was 27/47 (57%) (Fig. 1). The survival rate of patients with unilateral retinoblastoma is 21/41 (51%), while 3/6 (50%) for those with bilateral retinoblastoma. There is no statistically significant difference in the survival rate between patients with unilateral retinoblastoma and with bilateral (p = 0.89).

There were also no significant differences in survival rates based on sex, age at consult (≤ 2 years vs. > 2), interval from onset of symptoms to consult (≤ 6 months vs. > 6), and period of consult (2005–2015 vs. 2016–2020). Difference in survival rate was only significant based on extent of involvement (100% for intraocular versus 0% for extraocular). However, there was no significant difference in the delay of consultation between patients with intraocular and extraocular disease (p = 0.36).

### Discussion

This study provided needed data on demographics and clinical profile of retinoblastoma patients from northern Luzon seen at BGHMC and on clinical outcomes in The Philippines. The presence of other government tertiary hospitals in northern Luzon can explain the smaller number of patients in our study compared with Noguerra et al152 in Philippine General Hospital, since those hospitals could have received the other patients.

In this study, 87% of patients had unilateral retinoblastoma, higher than those reported locally (65–70%), in Bangladesh (63%), in Indonesia (73%), in India (62%), and in Pakistan (62%). However, it is similar to China at 86%. The mean age at consult at 24 ± 17 months in this study is similar to a local study and within the range of those in India (21–30 months) but younger than those in China (26–30 months), Bangladesh (30 months), Indonesia (28 months) and Pakistan (≥ 36 months). The overall mean interval from onset of symptoms to consult of 10 ± 11 months in this study was longer than a local study (6–9 months), India (3–7 months) and China (2–6 months). It was initially assumed that distance was a factor since BGHMC receives patients from towns as far as 250 km. However, difference in mean delay of consultation between the area nearest BGHMC (region 1) to the farthest (other parts of CAR) was not statistically significant (p = 0.19). Leukocoria remained the most common presenting symptom similar to all the other studies.1,5,6,9,12–26

This is the first study in The Philippines with data on clinical outcomes. Enucleation is the most commonly performed procedure in this study at 74%, lower than China’s 86% but higher than India’s 40%. The low enucleation rate in India can be explained by the increasing use of chemotherapies and globe salvage procedures. The frequency of denial for any medical intervention is similar to that of India (9%) but higher than China (4%).  Exenteration was used as a surgical option in the tertiary hospital in northern Luzon similar to China and Pakistan. Only 30% of those advised to receive systemic chemotherapy completed their recommended cycles. Based on extent, 45% of our patients have extraocular involvement. This is higher than a local study (16%), Bangladesh (19%), Pakistan (18%), China (14.5%) and India (16%) but lower than Indonesia (53%).

Overall survival rate at BGHMC of 53% is lower than India (80%) and China (87%) but higher than Pakistan (23%). However, this low-survival rate at BGHMC does not reflect overall survival rate of Filipino retinoblastoma patients, since there are more advanced national referral centers in the country. There is no difference between the survival rates of patients with unilateral and bilateral retinoblastoma despite those with bilateral retinoblastoma having earlier mean age at consult and shorter delay of consult. There is also no significant difference between males and females. Extent

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**Table 1** Classification of retinoblastoma patients who consulted at BGHMC from 2005 to 2020 using the IRSS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Patient N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Patient treated conservatively</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>Eye enucleated, completely resected histologically</td>
<td>22 (47%)</td>
</tr>
<tr>
<td>2</td>
<td>Eye enucleated, microscopic residual tumor</td>
<td>6 (13%)</td>
</tr>
<tr>
<td>3</td>
<td>Regional extension</td>
<td>9 (19%)</td>
</tr>
<tr>
<td>4</td>
<td>Metastatic disease</td>
<td>6 (13%)</td>
</tr>
<tr>
<td>U</td>
<td>Unclassified</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>47</td>
</tr>
</tbody>
</table>

Abbreviations: BGHMC, Baguio General Hospital and Medical Center; IRSS, International Retinoblastoma Staging System.
of involvement (intraocular vs. extraocular) was the only factor that has significant effect in survival rates. All three findings were similar to that of Chawla et al.\textsuperscript{15}

However, there was no significant difference ($p = 0.98$) in the survival rate of patients who consulted after 6 months from onset of symptoms to those who consulted earlier. Similarly, the difference in delay of consult between those with intraocular and extraocular involvement in this study was not significant ($p = 0.41$). This is contrary to Chawla et al\textsuperscript{’} finding where those with delay of consult of more than 6 months had poorer prognosis that those who consulted within 3 months of onset of symptoms.\textsuperscript{15} This suggest that delay in diagnosis did not play a role in the survival of the retinoblastoma patients at BGHMC from 2005 to 2020.

Survival rates from 2005 to 2015 and 2016 to 2020 were compared to determine if changes introduced in retinoblastoma management in 2016, including improved surgical technique, inclusion of choroidal involvement in histopathology readings, changes in the chemotherapeutic treatment protocol, and information campaign through the local chapter of ophthalmologists were helpful in increasing survival rates. Despite having no statistically significant difference, a 12% increase in survival rate of retinoblastoma patients seen in the past 4 years is already a clinically significant increase.

**Author Contribution**

The authors equally contributed to the conceptualization, writing, and final approval of this manuscript.

**Ethical Approval**

This study was approved by the Baguio General Hospital and Medical Center Research Ethics Committee (REC-2020–29) and adhered to the Declaration of Helsinki.

**Note**

An earlier version of this paper was poster presented in the Asia Pacific Society of Pediatric Ophthalmology and Strabismus Inaugural Congress at Hong Kong, China, on October 2017.

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**Conflict of Interests**

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