

# Increasing Response to the Call for Complete and Updated Data on Retinoblastoma in the Philippines

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In 2022, the need for updated and complete data on retinoblastoma as an initial measure to create an effective national response was underscored here in the Philippine Journal of Ophthalmology (PJO).<sup>1</sup> Three courses of actions were outlined to address the need. While the first one, a 25-year cohort study in the Philippine General Hospital, is in the process of manuscript writing, the second one has wrapped up. A multicenter, clinico-epidemiologic study, called the Philippine Retinoblastoma Initiative Multi-Eye center Study (PRIMES), ran from August 2021 to August 2023. It was conducted by 29 ophthalmologists from 11 hospitals located all over the Philippines namely: Philippine General Hospital in Manila City, Southern Philippines Medical Center in Davao City, East Avenue Medical Center in Quezon City, Baguio General Hospital and Medical Center in Baguio City, Manila Doctors Hospital in Manila City, Northern Mindanao Medical Center in Cagayan de Oro City, Rizal Medical Center in Pasig City, Cebu Velez General Hospital in Cebu City, Legazpi Eye Center in Legazpi City, Cagayan Valley Medical Center in Tuguegarao City, and the Jose B. Lingad Memorial Regional Hospital in San Fernando City, Pampanga.

There were 636 patients (821 eyes) with retinoblastoma included in the study from all the 17 administrative regions of the country. The major study finding was that geography significantly affected access to eye care and clinical outcomes of retinoblastoma patients. Only 30% of the retinoblastoma patients lived in the same region as the hospital they were seen in. Furthermore, retinoblastoma patients from the Visayas travelled significantly longer distances to be seen in the eye care facility compared to patients from Luzon and Mindanao. The distance between the patient's hometown and the treating hospital was found to be significantly correlated to the delay in consult. In addition, the disease stages of patients from Visayas were significantly worse compared to those of patients from Luzon and Mindanao. Lastly, the clinical outcomes of patients from the Visayas were also significantly different compared to those of patients from Luzon.

In order to run a longitudinal comparison between 2 time periods, the timeline in the original study protocol of 2015 to 2020 was extended to 2010 to 2020. Between 2010 to 2015 and 2016 to 2020, there was no improvement in the delay at first consult. Enucleation was the most common

treatment mode and surgery performed in both time periods. Compared to 2010-2015, there was a decrease in the number of patients who did not need systemic chemotherapy and an increase in the number of patients who completed systemic chemotherapy from 2016 to 2020. There was also improvement in clinical outcomes over time. However, the overall proportion of alive patients was low at 39% compared to other countries such as India, China and Pakistan.<sup>2-4</sup>

The third course of action, the creation of a national retinoblastoma registry, remains elusive. Logistics presents a significant challenge. However, recent efforts are promising. As a consequence of the PRIMES study, a few of the participating institutions that did not have existing retinoblastoma database started one, using their study database as starting point. Clinicians from 1 hospital even opted to move forward with their own institutional retinoblastoma study and will apply for an ethics approval for a prospective research proposal. Another participant, the Southern Philippines Medical Center (SPMC) which is a tertiary and Department of Health-retained hospital in Mindanao, published its data on 157 retinoblastoma patients seen from 2011-2020.<sup>5</sup> Noteworthy, SPMC also had the second most retinoblastoma patients in the PRIMES study. Malabanan-Cabebe *et al.* were the first to present comprehensive data on retinoblastoma patients from the Zamboanga Peninsula, Northern Mindanao, Davao Region, SOCCSKSARGEN, Caraga, and the Bangsamoro Autonomous Region of the Muslim Mindanao.<sup>5</sup> They were also first to publish data on secondary enucleation and on patients with trilateral retinoblastoma in the country. Although the proportion of their patients with advanced intraocular disease was lower, the proportion of their patients with extraocular disease was higher compared to those from the Philippine General Hospital.<sup>6</sup> Similar to data from Northern Luzon, their survival rate was low while the rate of lost to follow-up was high.<sup>7</sup>

Another participant of the PRIMES study, So *et al.*, published their data on 118 patients seen from 2000-2020 at the East Avenue Medical Center (EAMC) in this journal issue. EAMC had the third most retinoblastoma patients in the PRIMES study. Pertinent in their results is the high survival rate at 72% in 5-years compared to the data from Northern Luzon and Southern Philippines.<sup>3-5,7</sup> This can be attributed to the shorter delay at first consult of 4

months in their study which they attributed to difference in their patients' socioeconomic status and access to health care.<sup>5,7,8</sup>

In this journal issue, Worak *et al.* also shared their results on the capacity to treat retinoblastoma of most hospitals in the country, in terms of (1) human resources, (2) technology to diagnose and treat, and (3) education & network. Based on the presence of the three capacities, a three-tier classification was created with tier 3 hospitals being more equipped at managing retinoblastoma cases in terms of human resources and technology. Forty-one (41) out of the 70 hospital respondents were classified as tier 3. The study also identified 17 and 11 institutions that offer intravitreal chemotherapy and intra-arterial chemotherapy, respectively. However, 54% of the tier 3 hospitals are located in the National Capital Region (NCR) highlighting the concentration of capable institutions in the metropolis. Worak *et al.* also identified 8 tier 1 and 2 hospitals outside the NCR that can potentially be improved to accommodate retinoblastoma patients in their regions.

Mercado *et al.* published their results on the use of intravitreal melphalan and topotecan to address vitreous seeding in retinoblastoma patients seen in the Philippine General Hospital, the institution with the most patients in the PRIMES study. It is the first and only published literature on the use of intravitreal chemotherapy in the country, and was found effective in two patients with International Intraocular Retinoblastoma Classification Group C.<sup>9</sup>

In 2021, a super-selective intra-arterial chemotherapy delivery was attempted to the left eye diagnosed with International Classification of Retinoblastoma Group D that was unresponsive to intravenous chemotherapy of a then 22-month-old girl with bilateral retinoblastoma at the Philippine General Hospital (DL Sacdalan, JS Catibog, GJV Mercado, personal communications, January 20, 2023). In 2022, Dr. Andrei P. Martin presented the first successfully delivered super-selective intra-arterial chemotherapy in the country carried out by his team at the St. Luke's Medical Center. This was shortly followed by another successfully delivered super-selective intra-arterial chemotherapy at the Philippine Children's Medical Center.

It is also reassuring that more institutions already maintain a retinoblastoma database. Torno *et al.* published their data on 31 patients seen from 2011

to 2020 at the Jose R. Reyes Memorial Medical Center.<sup>10</sup> Pertinent in their findings is that 52% of their cohort were from outside NCR, with 2 patients from the Visayas. Similar to the data from Northern Luzon, their survival rate was also low.<sup>7</sup>

The journey to achieve an ideal and standardized management system for retinoblastoma patients all over the Philippines remains long and arduous. The proportion of patients with advanced intraocular and extraocular disease remains high. Long treatment delays are due to accessibility and affordability of eye care. Most capable institutions are also concentrated in the metropolis. Survival rates remain low compared to other developing countries.

Among other initiatives to improve the retinoblastoma situation in the Philippines, the dream of having a National Retinoblastoma Registry remains. The increasing number of published data from all over the country is an encouraging development. Newer routes of chemotherapy drug delivery are now locally available, both in private and government hospitals. To keep the momentum going, we are planning to continue into a prospective, multicenter study that will invite more hospitals, especially in the Visayas and Mindanao, to participate. There are already new institutions that expressed their intention to join. This new study aims to come up with a more representative data that can be utilized by the DOH, and other stakeholders involved in the care of patients with retinoblastoma to address future disease burden. This data can also be vital in the creation of a better referral and treatment system that is more responsive to the needs of our fellow Filipinos with retinoblastoma and those caring for them. The data can also help with the improvement in the provisions of existing policies such as the National Integrated Cancer Control Act as well as monitoring the effects of their implementation.<sup>11,12</sup>

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