

Addressing the Need for Complete and Updated Data on Retinoblastoma in the Philippines

Gary John V. Mercado, MD^{1,2}

Roland Joseph D. Tan, MD, MS, MIH^{1,2,3}

¹Department of Ophthalmology and Visual Sciences, Philippine General Hospital, Manila

²College of Medicine, University of the Philippines - Manila

³Department of Ophthalmology, Baguio General Hospital and Medical Center, Baguio

Correspondence: Roland Joseph D. Tan, MD, MS

Department of Ophthalmology and Visual Sciences, Philippine General Hospital

College of Medicine, University of the Philippines - Manila

Email address: rdtan@up.edu.ph

Disclaimer: The authors report no conflicts of interests.

Retinoblastoma has an estimated worldwide incidence of 1 in 16,000-18,000 births every year although it varies from region to region, with Asia having one of the highest incidence rates.^{1,2} The Philippines is listed as one of the six Asian countries that will be the source of 43% of the estimated world's retinoblastoma cases in 2023.³ Local incidence was reported at 237 per 100,000 new cases from 1997 to 2001.⁴ This data, together with those from Noguera *et al.*, were used by Usmanov and Kivela to estimate the retinoblastoma incidence in the Philippines at 142 (128-157) per live births in 2013 and is expected to increase to 152 (137-168) per live births in 2023.^{3,5}

Available data on Retinoblastoma in the Philippines

The data used by Usmanov and Kivela to estimate the Philippine retinoblastoma incidence were from the epidemiological studies of Espiritu *et al.* and Noguera *et al.*³⁻⁶ Both studies were done in the Philippine General Hospital (PGH), a national retinoblastoma referral center located in the

National Capital Region (NCR). The data do not reflect regional incidences since the majority of PGH's patients are from NCR and its immediate vicinity despite receiving patients from around the country.⁵ Similarly, PGH caters to patients who are mostly from socioeconomic classes D and E. The absence of data from other medical institutions which see retinoblastoma patients including private facilities and those that are located in the Southern Luzon, Visayas, and Mindanao poses a challenge in assessing the diagnostic and treatment capabilities of the country as a whole. This makes the identification of geographical areas which can benefit from expertise acquisition and technology development in properly managing retinoblastoma challenging. This also makes the creation of an effective referral network difficult. Although it is likely that there are many areas in the country that can benefit from assistance (e.g. funding for imaging procedures), both from the government and private institutions alike, in diagnosing retinoblastoma, an effective response depends on grounded and updated data on the capability of diagnosing retinoblastoma which the country does not have at the moment. Having data from other

institutions and regions can also identify populations or minority groups that are significantly affected by retinoblastoma and may benefit from directed screening programs.

The latest available data on retinoblastoma is from Baguio General Hospital Medical Center (BGHMC) covering years 2005 to 2020.⁶ Like any other diseases, changes in the patterns of clinical and treatment profiles for retinoblastoma occur and are only caught when a continuous supply of complete data is available. Knowledge on these changes can help policymakers in creating or revising existing management- and finance-related policies and programs to address retinoblastoma; and can update physicians in the diagnosis and management of diseases.^{7,8} Currently, a study on the clinical profile, treatment, and outcomes of retinoblastoma patients in the PGH is underway which can further provide data for policymakers to work on.

Noguera *et al.*, Espiritu *et al.*, and Tan and Ballesteros in their studies described clinical features of Filipino retinoblastoma patients in Luzon.^{4,5,6} Common and alarming in their results is the significant delay in consultation which is reflective of data from other low to medium income countries.⁹ This, in turn, delays diagnosis and management, which have been associated with a high proportion of extraocular disease and high mortality.¹⁰ Although Espiritu *et al.* found a decreasing trend in extraocular disease in PGH, the length of delay in consultation remained the same.⁴ Noguera *et al.* cited financial difficulties, misdiagnosis, and poor access to eye care as common causes.⁵ Tan and Dacuma identified other dimensions that affect pediatric eye care utilization in BGHMC such as unavailability of ophthalmologists in their hometown, steep costs of medical consultation including indirect and non-medical related expenses (e.g. transportation fare, food, and accommodation), and adequacy and acceptability of eye care.¹¹

A study on retinoblastoma in the Philippines included data on outcomes.¹² However, Cabrera *et al.* only included retinoblastoma patients with high-risk histopathological features in their analysis.¹² The study by Tan and Ballesteros retinoblastoma on treatment and outcomes was limited to experience in a single institution.⁶ Data on treatment and

outcomes are important in assessing the capability of the country as a whole to treat retinoblastoma and again, in identifying geographical areas in the country that would benefit from technology improvement and expertise acquisition, and in creating an effective referral network. Similarly, these data are important to assess the applicability of international retinoblastoma treatment protocols to Filipinos or the effectiveness and safety of local treatment protocols being used including the Metro Manila Retinoblastoma Treatment Protocol. There are already many advances in retinoblastoma treatment options globally. The Philippines is lagging behind in terms of the availability of options when compared to neighboring countries like Singapore and Thailand that some Filipinos even seek treatment in Singapore.¹³ However, recent attempts on performing intraarterial chemotherapy for retinoblastoma were reported in three institutions in the NCR, with 2 being successful. A case report on the successful use of intravitreal chemotherapy in a Filipino patient has also been published and another case series is on the way.¹⁵ Without data on treatment and outcomes, it is also difficult to identify treatment failures and to try new protocols to address them.¹⁵ Having data on treatment and outcomes can also invite research collaborations from international groups such as the American Joint Committee on Cancer Ophthalmic Oncology Task Force.¹⁶

The COVID-19 pandemic provided researchers globally extra time to conduct studies, COVID-19-related or otherwise, and publish them. The presence of a retinoblastoma registry significantly assisted retinoblastoma specialists in contributing to the global knowledge pool as proven by Kaliki *et al.* in India where the creation of a database in LV Prasad Eye Institute resulted to numerous vital papers on retinoblastoma diagnosis and management.^{9,16,17} This is not the case in the Philippines as there are no existing retinoblastoma registry in the country yet. For a country that ranks 11th globally, 6th in Asia, and 2nd in Southeast Asia in the incidence of retinoblastoma, a complete, updated, and more representative data are needed to better diagnose, manage the disease and reduce blindness and death.³

Addressing the need for updated and complete data on Retinoblastoma

In response, the authors planned three ways to address the need. Firstly, the Division of Ocular Oncology of the Department of Ophthalmology and Visual Sciences and the Division of the Pediatric Hematology-Oncology of the Department of Pediatrics of PGH consolidated data on retinoblastoma patients in the hospital seen from 1998 to the present which included data on treatment and outcomes. If the data will allow, the authors aim to determine changes in patterns on clinical features, treatment, and outcomes of retinoblastoma patients seen at the institution.

Secondly, a multi-center study determining the clinical features, treatment and outcomes of retinoblastoma patients from 2015 to 2020 is also underway. This involves different medical institutions, both public and private, in the different areas of Luzon, Visayas and Mindanao. We received overwhelming support from our colleagues around the country who are also dedicated in treating retinoblastoma. The study aims to provide updated data on retinoblastoma that is representative of the Philippines.

Finally, to make the supply of complete and updated on retinoblastoma sustainable, a national Retinoblastoma registry is being planned. A registry can serve as a foundation for the creation of a more effective referral network to address concerns on accessibility, affordability, and availability of ophthalmologists who treat retinoblastoma patients. A registry can also help in maintaining connections with relatives of retinoblastoma patients and assess through institutional review board (IRB) approved surveys on the causes of delays in consultation and treatment and find ways to address them. Similar surveys can be also be done to continuously assess factors that affect treatment acceptance and to assess the psychological, socioeconomic and other effects of retinoblastoma to the society as has been done by Domingo *et al.*¹⁸ Surveys can also be done to assess the overall quality of life of survivors similar to what was done in India.¹⁹

However, there are challenges. The success and sustainability of a disease registry rely heavily on data encoding. Many cancer registries which

relied on passive notifications have failed, from the National Cancer Registry in 1959 to the Department of Health (DOH) Rizal Cancer Registry in 1974.²⁰ Thus, active methods were employed afterward including retrospective review of death certificates. Other methods employed to promote data submission include incentives, monetary or otherwise. However, most did not last. The registry will also require infrastructure in the participating institutions and in the institution where it will be housed. It has to be maintained by a dedicated administrator and staff. Regular quality assessment should be carried out. Encryption and other measures should be observed to ensure the security of the database. Since data privacy has to be maintained, access to the database has to be controlled. All of these will require constant funding.

Articles on retinoblastoma from India, China, and other countries often used different classification and staging systems.^{21,22} As such, standardization of reporting has to be observed. This will require training for the data encoders to the ophthalmologists who will classify and stage the disease. However, proper staging may prove challenging to physicians who do not have access to necessary technology such as computed topography scan, magnetic resonance imaging, and ocular ultrasound, and the necessary expertise (i.e. ocular pathologists). Similarly, existing protocols may not be followed due to the unavailability of either technology (such as radiotherapy machines) or chemotherapeutic agents (e.g. vincristine, etoposide, carboplatin).

Nonetheless, there are opportunities too. Due to the intensified campaigns by the World Health Organization (WHO) and the DOH to address the growing global burden of non-communicable diseases including cancer, numerous registries have been created and more are on the way, even by the subspecialty societies of the Philippine Academy of Ophthalmology.²³ Organizations like the Cancer Registry and Research were also established to optimize cancer databases of hospitals and clinics mandated by the Republic Act No. 11215 or the "National Integrated Cancer Control Act".²⁴ Partnering with these organizations or learning from them can assist us to successfully launch a registry for retinoblastoma, the most common malignancy of the eye and ocular adnexae in the

Philippines.¹⁸ If achieved, this can be a great platform to build additional registries for other ophthalmic and orbital cancers which are similarly underreported and can push for the involvement of ophthalmologists in the expert panel of the National Cancer Control Committee.^{23,25} Considering that the ongoing COVID-19 pandemic, most hospitals and medical practitioners were forced to conduct telemedicine and, in turn, adapt to electronic medical records (EMR), this is the perfect time to integrate the registry to EMR. Data encoding does not need to be done separately for the registry with the proper provision in the maintenance of data privacy. There are also dedicated companies that can be hired for medical transcription. However, encoding options shall still be made widely available. Although, an online data encoding is highly preferred over the pen and paper process, paper submission shall still be included as an option since internet connectivity in the country is still not available everywhere and quality is unreliable. The process needs to be short and simple to increase acceptability among participating physicians as it can be perceived as additional work. Regular data quality assessment for completeness and accuracy is also needed to provide constructive feedback for those who are submitting data.

The authors considered partnering with organizations running cancer registry databases which already have existing infrastructures (including database software and encryption and Information Technology staff) and which have partnerships with other hospitals. However, after attending a workshop on establishing registries, the authors decided to start small and do a pilot retinoblastoma registry using the existing retinoblastoma databases of PGH. PGH is to establish partnerships with hospitals with the necessary infrastructures to diagnose and manage retinoblastoma and to run a database that can be deidentified and merged in a common registry for now. The COVID-19 pandemic has limited travel in the Philippines. This highlighted the significant role of local physicians in retinoblastoma management since patients who still travel to consult at tertiary institutions, especially in NCR, can no longer do so. The registry can help with the continuity of care as it can be used in the future as a platform for a better referral network and effective telemedicine. Follow-ups can be carried out by local physicians, a set-up that is ideal in the implementation of the Universal Health Care program.

REFERENCES

1. Kivelä T. The epidemiological challenge of the most frequent eye cancer: retinoblastoma, an issue of birth and death. *Br J Ophthalmol* 2009;93:1129–31.
2. Stiller C, Parkin D. Geographic and ethnic variations in the incidence of childhood cancer. *Br Med Bull* 1996;52:682-703.
3. Usmanov RH, Kivelä T. Predicted Trends in the Incidence of Retinoblastoma in the Asia-Pacific Region [published correction appears in *Asia Pac J Ophthalmol (Phila)* 2014; 3(6): 397]. *Asia Pac J Ophthalmol (Phila)* 2014;3(3):151-157.
4. Espiritu RB, de Jesus AA, Valera EG, Mercado GJ. Epidemiological pattern of retinoblastoma at the Philippine General Hospital. *Philipp J Ophthalmol* 2004;29:136-139.
5. Noguera SI, Mercado GJV, Santiago DE. Clinical Epidemiology of retinoblastoma at the Philippine General Hospital: 1998-2008. *Philipp J Ophthalmol* 2011;36(1):28-32.
6. Tan RJD, Ballesteros KFB. Retinoblastoma Outcomes in a Tertiary Hospital in Northern Luzon, The Philippines: A 15-Year Experience. *South Asian J Cancer* 2022;00(00)00-00.
7. Gogate P, Kalua K, Courtright P. Blindness in Childhood in Developing Countries: Time for a Reassessment? *PLoS* 2009; 6(12):e1000177.
8. Foster A, Yorston D. Corneal ulceration in Tanzanian children: relationship between measles and vitamin A deficiency. *Trans R Soc Trop Med Hyg* 1992;86:454–455.
9. Kaliki S, Ji X, Zou Y *et al.* Lag Time between Onset of First Symptom and Treatment of Retinoblastoma: An International Collaborative Study of 692 Patients from 10 Countries. *Cancers (Basel)* 2021;13(8):1956.
10. Chawla B, Singh R. Recent advances and challenges in the management of retinoblastoma. *Indian J Ophthalmol* 2017;65(2):133-139.
11. Tan RJD, Dacuma MGB. Factors affecting childhood blindness and visual impairment in Baguio General Hospital and Medical Center. *Philipp J Health Research Dev* 2021;25(3):54-63.
12. Cabrera PE, Mercado GJV, Domingo RED, Valenzuela R. Outcome of Retinoblastoma Patients with High-risk Histopathological Features in a Tertiary Hospital. *Philipp J Ophthalmol* 2013;38:43-49.
13. Jain M, Rojanaporn D, Chawla B, Sundar, *et al.* Retinoblastoma in Asia. *Eye* 2018;33(1): 87-96.
14. Redondo-Villanueva MJH, Mercado GJV. Intravitreal melphalan for persistent retinoblastoma vitreous seeds. *GMS Ophthalmol Cases* 2022;12:Doc03.
15. Honavar S, Manjandavida F, Reddy V. Orbital retinoblastoma: An update. *Indian J Ophthalmol* 2017;65(6):435.

16. Tomar AS, Finger PT, Gallie B, *et al.* A Multicenter, International Collaborative Study for American Joint Committee on Cancer Staging of Retinoblastoma: Part II: Treatment Success and Globe Salvage. *Ophthalmology* 2020;127(12):1733–1746.
17. Kaliki S, Patel A, Iram S, *et al.* Retinoblastoma in India. *Retina* 2019;39(2):379–391.
18. Domingo RE, Toledo MS, Mante BV. Psychosocial factors influencing parental decision to allow or refuse potentially lifesaving enucleation in children with retinoblastoma. *Asia Pac J Oncol Nurs* 2017;4:191-6
19. Seth R, Singh A, Guru V, *et al.* Long-term follow-up of retinoblastoma survivors: Experience from India. *South Asian J Cancer* 2017;6(4):176-179.
20. Esteban DB, Laudico AV, Uy NA, *et al.* Cancer Registration in the Philippines. *Asian Pacific J Cancer Prev* 2001; 2 IACR Supplement: 55-60.
21. Tan RJD. Clinical Features, Treatment, and Outcomes of Retinoblastoma in China. *Asian J Oncol* 2022. DOI:10.1055/s-0042-1744449.
22. Tan RJD, Umerez DC, Alindayu JIA, *et al.* Retinoblastoma in South Asia: A scoping review. *Asian Pac J Cancer Care* 2021; 6(4).493-500.
23. Department of Health. Philippine Cancer Control Program. n.d. : <https://doh.gov.ph/philippine-cancer-control-program> (Accessed September 12, 2021).
24. Department of Health. Implementing Rules for Cancer Act signed. 2019: <https://doh.gov.ph/press-release/implementing-rules-for-cancer-act-signed> (Accessed September 12, 2021).
25. The Global Cancer Observatory. Philippines. 2021: <https://gco.iarc.fr/today/data/factsheets/populations/608-philippines-fact-sheets.pdf> (Accessed September 12, 2021).