Journal of Institute of Medicine Nepal
Institute of Medicine, Kathmandu, Nepal

OPEN ACCESS

Original Article

JIOM Nepal. 2024 Dec;46(3):44-48.

Clinical Presentation and Staging of Retinoblastoma Patients

Jyoti Baba Shrestha

Author(s) affiliation

Department of Ophthalmology, Maharajgunj Medical Campus, BP Koirala Lions Center for Ophthalmic Studies, Institute of Medicine, Kathmandu, Nepal

Corresponding author

Jyoti Baba Shrestha, MBBS, MD
jyotibaba@gmail.com

ABSTRACT

Introduction

Retinoblastoma is the most common curable primary intraocular malignancies of childhood. It has high incidence of ocular morbidity and even mortality if the condition is not diagnosed in time and treated appropriately. The prognosis of disease depends on various modes of presentation, grouping and staging of retinoblastoma. The burden of disease in children is of great importance because early detection and management will have a lifelong impact on other domains of development.

Methods

This was a hospital-based cross-sectional study conducted at B.P. Koirala Lions Centre for Ophthalmic Studies. Children diagnosed with retinoblastoma were enrolled by purposive sampling method. After obtaining informed written consent, data was taken in semi-structured proforma. Data was analysed in the SPSS version 21.0.

Results

A total 17 cases of retinoblastoma were analysed. Majority of the cases were male, belonging to low-class family, and from rural areas. Sixty four percent of cases had leukocoria, followed by proptosis and red eye. One eye was affected in 71% and both eyes in 29% of cases. Province 2 accounted for the highest patient numbers (35%). Group D and Group E lesions were seen in 37% and 50% of cases respectively whereas stage 1 disease was seen in 86%. More than 80% of intraocular tumors were in advanced Group D and Group E category.

Conclusion

Leukocoria was the most common clinical presentation. More than 80% of tumours were in advanced Group D and Group E category. The study highlights delayed presentation which is a significant challenge in achieving better outcomes.

Keywords
Clinical presentation; grouping; retinoblastoma; staging

DOI
10.59779/jiomnepal.1310

Submitted
Oct 27, 2024

Accepted
Dec 2, 2024

INTRODUCTION

Retinoblastoma is the curable primary intraocular malignancies of childhood.[1] It has high incidence of ocular morbidity and even mortality if the condition is not diagnosed in time and treated appropriately. It is a rare tumor, occurring in only about 1 in 18, 000 live births.[1] Both the genders are equally affected. It is bilateral in 20-35% of cases. [2] The average age of disease presentation is 18 months. However unilateral cases are diagnosed at around 24 months and bilateral cases before 12 months of age.[2] The mean age of presentation of children from high-income countries is 20 months, whereas children from low-income countries present at age of 35 months.

The assessment of RB is based on grouping and staging of disease. By grouping and staging researchers can estimate prognosis, which includes possibility of treatment success, potential for recovery and the risk of complications. The new international classification of intraocular Retinoblastoma (ICRB) is used to guide treatment options in terms of whether the affected eye can be saved and vision be preserved.[3] The new international staging system which incorporates five stages.[3] In most developed countries, majority of RB patients are diagnosed at an early stages, which leads to the overall survival of 90-98%.[4] In contrast, advanced retinoblastomas are associated with a very poor outcome which developing countries like ours frequently encounter.[5]

There are very few reports published on clinical presentation and staging of retinoblastoma in Nepal. The study helps to predict the likely course of the disease and also support in individualizing the management.

METHODS

The study was done at BP Koirala Lions Centre for Ophthalmic Studies, Kathmandu. It was a hospital based quantitative, prospective, and observational study, duration being of 12 months from October 2023 to September 2024. All children diagnosed with retinoblastoma were included in the study. Data collection was initiated after obtaining ethical approval from the Ethical Review Board of Tribhuvan University (ERB-TU).

An informed written consent was obtained from each participant's parents/legal guardian before their enrollment into the study. Detail demographic information was collected. Examination of eyes was done under general anaesthesia. Each case was classified on the basis of International classification of retinoblastoma (ICRB) and International staging system.[3] Data was entered and analysed in the SPSS version 21.0.

RESULTS

A total of 17 retinoblastoma cases were received during one year period from age group 2 months to 4 years. The youngest child seen was 2 months of age and the oldest one was 4 years. The median age group was 20 months (range 2 months- 48 months ± 12.69 std deviation). The majority of our participants were male comprising of 65% (11) and females 35% (6). Of the 17 cases, 12 (71%) had unilateral involvement. The right eye was affected in 2 and left eye in 10 participants. The remaining 5 (29%) cases had bilateral retinoblastoma. Among the study participants, 3 were Janjati, 4 were Madhesi, 2 were Chhetri, 3 were Brahmin, 1 was Dalit, 1 was Muslim and 3 were Newar. Most of our cases were from Madhesh Province (35%), followed by Bagmati Province (29%), Gandaki Province (18%), Koshi Province (12%), Karnali Province (6%) and there were no patients from Lumbini and Sudur Paschim Provinces (0%). Two participants belonged to middle-class family whereas all 15 belonged to low classes socioeconomic status. None of the participants had family history of RB and non

Table 1. Demographic features of retinoblastoma cases

Characteristics	Number (%)
Gender	
Males	11 (65%)
Females	6 (35%)
Laterality	
Unilateral	12 (71%)
Bilateral	5 (29%)
Family history of RB	0
Socioeconomic status	
Middle class	2 (11%)
Lower class	15 (88%)
Ethnicity	
Upper caste group	5 (29%)
Relatively advantaged janjati	3 (18%)
Dalits	1 (6%)
Disadvantaged non-Dalit Terai caste group	4 (24%)
Disadvantaged Janjatis	3 (18%)
Religious minority Muslims and Churaute	1 (6%)
Geographical distribution	
Koshi	2 (12%)
Madhesh	6 (35%)
Bagmati	5 (29%)
Gandaki	3 (18%)
Lumbini	-
Karnali	1 (6%)
Sudur pashchim	-

Table 2. Distribution of clinical presentation at the time of presentation

Clinical presentation	Number (%)		Total Number (%)
	Unilateral	Bilateral	
Leukocoria	9 (75%)	5 (50%)	14 (64%)
Proptosis	1 (8%)	3 (30%)	4 (18%)
Red eye	2 (17%)	-	2 (9%)
Squint	-	-	-
Phthisis bulbi	-	-	-
Asymptomatic	-	2 (20%)	2 (9%)
Total	12 (100%)	10 (100%)	22 (100%)

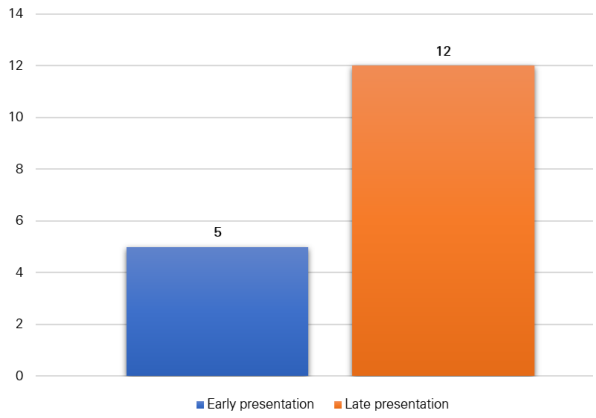

Figure 1. Bar diagram showing lag time of participants

Table 3. Distribution of eyes as per ICRB group

Group	Laterality			Total Number (%)
	Right eye	Left eye	Bilateral eyes	
A (small tumour)	-	-	1 (5%)	1 (5%)
B (large tumour)	-	-	2 (8%)	2 (8%)
C (local seeds)	-	-	-	-
D (diffuse seeds)	5 (23%)	-	3 (14%)	8 (37%)
E (extensive RB)	2 (9%)	5 (23%)	4 (18%)	11 (50%)
Total	7 (32%)	5 (23%)	10 (45%)	22 (100%)

Table 4. Distribution of eyes as per ICRB staging

Stage	Number (%)		Total Number (%)
	One eye	Both eyes	
0 (intraocular disease)	-	3 (14%)	3 (14%)
I (tumour completely resected)	12 (54%)	7 (32%)	19 (86%)
II (microscopic tumours after enucleation)	-	-	-
III (regional extension)	-	-	-
IV (metastatic disease)	-	-	-
Total	12 (54%)	10 (46%)	22 (100%)

revealed parental marriage consanguinity. The demographic distribution is shown in Table1.

This study showed, leukocoria, the most common clinical presentation, which was seen in 75% of cases in unilateral retinoblastoma 50% in bilateral retinoblastoma. It was followed by extraocular involvement. The clinical features of RB at presentation is shown in Table 2.

Each case of retinoblastoma was grouped according to International Classification of RB (ICRB) following meticulous examination under anaesthesia. The majority of cases were found in advanced group D (7, 37%) and group E (10, 50 %) which have worse prognosis. However bilateral RB cases presented in Group A (1%) and Group B (8%) in one of 2 eyes had relatively good prognosis in relation to preservation of eyes. The distribution of cases as per ICRB groups in unilateral and bilateral RB is shown in Table 3.

The mean lag time which is delayed presentation of more than one month from onset of symptom ranged from 14 days to 120 days (mean 42.2 days). Seventy percent of RB cases had delayed presentation of more than 30 days, which may limit treatment options and potentially leading to poorer outcome Figure 1. The reason behind this was, the parents were unsure about the symptoms they are experiencing; they were ignorant about seeking medical attention, and their financial constraints making them difficult to afford healthcare services.

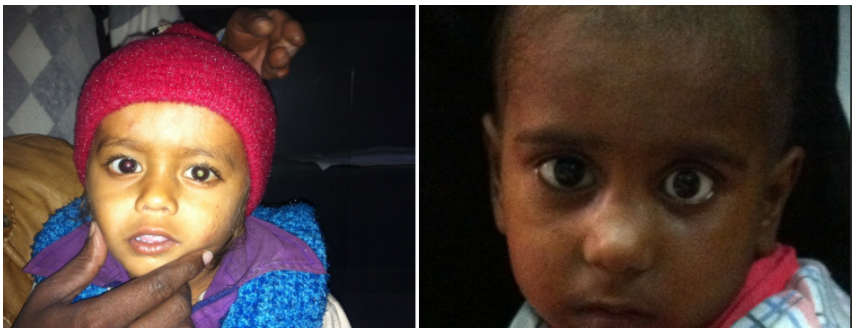

Figure 2. (a) Leukocoria LE (b) Left prosthetic eye after enucleation

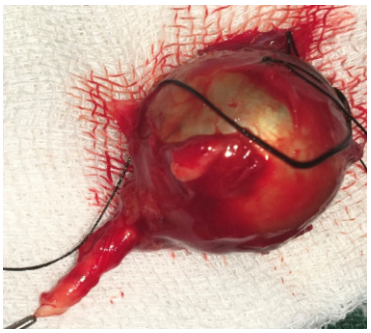

Figure 3. Enucleated eye ball with optic nerve stump

The clinical presentation, post-surgical outcome of a representative case has been shown in Figure 2. An enucleated specimen of eye ball with optic nerve stump is shown in Figure 3.

DISCUSSION

In this study the mean age of patients at presentation was 20 ± 12.69 months (range 2 months- 48 months), which is similar with other studies.[6-8] The mean age at presentation was 33.5± 20.31 months (range, 1.5–73 months) in one of the recent studies done in Nepal in 2019.[19] Delayed presentation of RB in our set up can be influenced by a variety of factors, which could be patient related, health care system related and societal factors.

Male predominance over female found in this study is consistent with other researches done in other parts of world including previous reports from Nepal.[9-11] Some other studies have shown no significant gender differences in the occurrence of RB. Other similar studies have found equal distribution of RB in the male and female population.[12,13] However, RB occurring more frequently in females compared to males have been reported.[14,15]

Many RB cases had unilateral involvement 12 (71%) and only 5 (29%) cases had bilateral involvement which was similar to previous studies done in Nepal and world- wide.[5,6,10,11,14,16]

The current study revealed, approximately one-third of cases were from the upper caste 5 (29%), which means Chhetri and Brahmin have the highest represntation. It was followed by Disadvantaged non- Dalit Terai caste group 4(24%). In 18% (n=3) of cases, Janjatis and Advantaged Janjatis were affected with RB. Disadvantaged groups like Dalits and Muslim each occupied 6% (n=1) of total cases.

Interestingly, none of our cases had family history of RB and history of consanguineous marriage. Similar reports have been published from Nepal reporting, consanguinity is not typically considered a major risk factor for RB among Nepalese children.[11,16] Some studies have shown genetic predisposition plays a role in increasing the likelihood of developing RB due to inherited genetic variation.[16-18]

Leukocoria was the most common clinical presentation which is similar to the studies done in other developing countries.[6,10,11,14,16,19] Tumors were intraocular in 65% and extraocular in 25% cases. This is similar to a study done by Chawla B et al, where intraocular tumours were 72% and extraocular tumours were 27%.[20]

Every patient included in the study was diagnosed with advance stage of disease, that is Group D and Group E retinoblastomas resulting in poor outcomes.

The cases were monitored until the histopathological report was obtained, typically 2-3 weeks, as both disease staging and subsequent treatment depend on it. Fortunately none of the cases required additional treatments (systemic chemotherapy, radiotherapy).

Enucleation for RB is typically performed in advanced stages of the disease. Naturally the treatment outcome in such cases is unfavorable regarding both globe salvage and vision restoration

The mean lag time was 42.2 days (range 14 days to 120 days) in the present study. This is comparable to the mean lag time of 49 days (range 7 to 560 days) as reported by Goddard et al.[21] However delayed presentation up to 75 days (range of 3 to 365 days) and even longer mean lag time up to 1,000 days were reported by earlier studies done in Nepal.[5,16] We did not find any RB cases with intracranial spread and or distant metastasis at presentation in this study. It could be due to fewer numbers of patients in this study.

More than 2/3 cases were seeking medical attention 30 days after the onset of symptoms. The reason for this delay was lack of awareness about the disease, 30% of parents were mistaken for less serious conditions leading to delays in seeking specialist care and 20% due to financial burden.

CONCLUSION

Leukocoria was the most common presenting feature, with Group D & Group E and Stage 1 being most frequently observed. This underscores delayed presentation and the significant challenges associated with treatment.

FINANCIAL SUPPORT

The author(s) did not receive any financial support for the research and/or publication of this article.

CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Bishop JO, Madsen EC. Retinoblastoma. Review of current status. Surv Ophthalmol 1975; 19:342-66
2. Shields JA, Shields CL. Intraocular tumours- A text and atlas. Philadelphia PA, USA, WB Saunders company, 1992
3. Shields CL, shields JA. Basic understanding of current classification and management of retinoblastoma. Curr opin Ophthalmol 2006; 17: 228-34. https://doi.org/10.1097/01.icu.0000193079.55240.18
4. Donaldson SS, Egbert PR, Newsham I et al. Retinoblastoma. In: Pizzo PA, Poplack DG, eds. Principles and practice of pediatric oncology, 4th edn. Philadelphia: Lippincott- Raven, 2002; 825–846
5. Badhu B, Sah SP, Thakur SKD et al. Clinical presentation of retinoblastoma in eastern Nepal. Clin Exp Ophthalmol. 2005; 33(4):386-9 https://doi.org/10.1111/j.1442-9071.2005.01010.x
6. Zhao J, Li S, Shi J et al. Clinical presentation and group classification of newly diagnosed intraocular retinoblastoma in China. Br J Ophthalmol 2011; 95(10):1372–1375 https://doi.org/10.1136/bjo.2010.191130
7. Naseripour M, Nazari H, Bakhtiari P et al. Retinoblastoma in Iran: outcomes in terms of patients' survival and globe survival. Br J Ophthalmol 2009;93 (01):28–32 https://doi.org/10.1136/bjo.2008.139410
8. Chung SE, Sa HS, Koo HHet al. Clinical manifestations and treatment of retinoblastoma in Korea. Br J Ophthalmol 2008;92(09):1180–1184 https://doi.org/10.1136/bjo.2008.140046
9. Kaliki S, Patel A, Iram S et al. Retinoblastoma in India: clinical presentation and outcome in 1,457 patients (2,074 eyes). Retina 2019;39(02):379–391 https://doi.org/10.1097/IAE.0000000000001962
10. Kazadi Lukusa A, Aloni MN, Kadima-Tshimanga B et al. Retinoblastoma in the democratic republic of Congo: 20-year review from a tertiary hospital in Kinshasa. J Cancer Epidemiol 2012; 920468 https://doi.org/10.1155/2012/920468
11. Shrestha JB, Shrestha GB, Joshi SN. Retinoblastoma at a tertiary level eye centre, Nepal. J IOM 2018; 40: 42-46 https://doi.org/10.59779/jiomnepal.823
12. MacCarthy A, Birch JM, Draper GJ et al. Retinoblastoma in Great Britain 1963-2002. Br J Ophthalmol 2009;93(01):33–37 https://doi.org/10.1136/bjo.2008.139618
13. Chen YH, Lin HY, Hsu WM et al. Retinoblastoma in Taiwan: incidence and survival characteristics from1979 to 2003. Eye (Lond) 2010;24(02):318–322(Lond Engl) https://doi.org/10.1038/eye.2009.80
14. Pedram M, Alghasi A, Salari F, et al. Retinoblastoma in southwest Iran. Iran J Blood Cancer 2015;7(03):143–148
15. Azar D, Donaldson C, Kalapesi F, Cumming R. Retinoblastoma in New SouthWales 1975 to 2001. J Pediatr Hematol Oncol 2006;28 (10):642–646 https://doi.org/10.1097/01.mph.0000212983.51867.46
16. Saiju R, Moore G, Shrestha U et al. Retinoblastoma:geographic distribution and presentation at a tertiary eye care centre in Kathmandu, Nepal. Nepal J Ophthalmol 2013;5(02):169–176 https://doi.org/10.3126/nepjoph.v5i2.8708
17. Sah KP, Saiju R, Roy P et al. Retinoblastoma: ten years experience at Kanti Children's Hospital. J Nepal Med Assoc 2013; 52(192):576–579 https://doi.org/10.31729/jnma.2429
18. Harini R, Ata-ur-Rasheed M, Shanmugam MP et al. Genetic profile of 81 retinoblastoma patients from a referral hospital in southern India. Indian J Ophthalmol 2001;49(01):37–42
19. Chuluunbat T, Jamiyanjav B, Munkhuu B et al. Retinoblastoma in Mongolia: clinical characteristics and survival from1987 to 2014. Taiwan J Ophthalmol 2016;6(02):79–84 https://doi.org/10.1016/j.tjo.2016.04.004
20. Chawla B, Hasan F, Azad R, et al. Clinical presentation and survival of retinoblastoma in Indian children. British Journal of Ophthalmology 2016;100: 172-178. https://doi.org/10.1136/bjophthalmol-2015-306672
21. Goddard AG, Kingston JE, Hungerford JL. Delay in diagnosis of retinoblastoma: risk factors and treatment outcome. Br J Ophthalmol 1999; 83(12):1320–1323 https://doi.org/10.1136/bjo.83.12.1320