Global Academic Journal of Medical Sciences

Available online at www.gajrc.com
DOI: 10.36348/gajms.2022.v04i06.017

OPEN ACCESS

ISSN: 2706-9036 (P)
ISSN: 2707-2533 (O)

Original Research Article

Patterns of Presentation and Prognostic Indicators in Pediatric Retinoblastoma

Dr. A.K.M. Mamunur Rahman[1*], Dr. Kripadhan Chakroborty[2], Prof. Dr. A. H. M. Enayet Hussain[3], Dr. Dewan Fazle Ghani[4], Dr. Rafia Islam Jui[5]

[1]Associate Professor, Department of Ophthalmology, Jahurul Islam Medical College, Kishoreganj, Bangladesh
[2]Associate Professor, Department of Ophthalmology, Kumuduni Women's Medical College, Mirzapur, Tangail, Bangladesh
[3]Professor and Head, Department of Pediatric Ophthalmology and Strabismus, National Institute of Ophthalmology & Hospital, Dhaka, Bangladesh
[4]Junior Consultant, Department of Ophthalmology, Ispahani Islamia Eye Institute and Hospital, Dhaka, Bangladesh
[5]Student, Department of Ophthalmology, Bangladesh Sheikh Mujib Medical University, Dhaka, Bangladesh

***Corresponding Author**
Dr. A.K.M. Mamunur Rahman
Associate Professor, Department of Ophthalmology, Jahurul Islam Medical College, Kishoreganj, Bangladesh

Article History
Received: 22.11.2022
Accepted: 27.12.2022
Published: 30.12.2022

Abstract: ***Background:*** Retinoblastoma remains the most common intraocular malignancy of childhood, and despite being a potentially curable disease, delayed presentation and advanced stage at diagnosis continue to contribute to poor outcomes in low- and middle-income settings. The purpose of this study was to evaluate the clinical presentation patterns and identify prognostic indicators in children diagnosed with retinoblastoma. ***Methods:*** This hospital-based descriptive study at the Department of Ophthalmology, National Institute of Ophthalmology and Hospital, Dhaka (April 2011–March 2013) included 46 children with retinoblastoma. Demographic and clinical data, presenting features, lag time, and laterality were recorded. Tumors were staged per eye using IIRC (A–E) and categorized as early (A–C) or advanced (D–E). Management included enucleation or eye-preserving approaches, and data were analyzed using descriptive and comparative statistics to identify factors associated with advanced disease and enucleation. ***Results:*** Among 46 children with retinoblastoma, most were 1–3 years old (56.5%), male (56.5%), and had unilateral disease (71.7%). Leukocoria was the most common presentation (69.6%), followed by leukocoria with proptosis (15.2%). Over half presented within 3 months of symptoms, while 21.7% had >6 months' delay. Advanced tumors (IIRC D/E, 58.6% of eyes) were strongly associated with enucleation (92.3% vs. 17.6%, $p < 0.001$) and proptosis (26.9% vs. 0%, $p = 0.013$). ***Conclusion:*** Early detection of retinoblastoma is crucial, as advanced-stage tumors, delayed presentation, and proptosis significantly increase the risk of enucleation in affected children.

Keywords: Retinoblastoma, Pediatric, Prognostic Indicators.

INTRODUCTION

Retinoblastoma (RB) is an uncommon pediatric tumor that originates from the retina and constitutes approximately 3% of all childhood cancers. It is the most frequent intraocular malignancy in children and typically presents in early life, with nearly two-thirds of cases diagnosed before 2 years of age and about 95% identified before 5 years [1]. Birth-cohort–based analyses indicate that the global incidence of retinoblastoma ranges from 1 in 15,000 to 1 in 20,000 live births, with an estimated 8,000 new cases diagnosed annually worldwide [2–5]. Retinoblastoma remains the leading primary ocular malignancy of childhood [6], with an overall incidence of approximately 11 cases per million children under five years of age [7,8], accounting for

nearly 3%–4% of all malignant tumors in children aged 0–14 years [9,10].

Leukocoria is the most common presenting feature of retinoblastoma, followed by strabismus, while less frequent signs include atrophia and proptosis [11]. In most cases, the initial abnormality is detected by parents. Despite being a potentially curable disease, the global survival rate remains around 50%, largely due to limited diagnostic and therapeutic resources and suboptimal healthcare infrastructure in low-income settings [12,13]. These constraints frequently lead to delayed diagnosis, increased rates of extraocular extension, and higher risks of metastatic disease. In developing regions, up to 90% of children present with extraocular involvement as a consequence of late recognition. Contributing factors include older age at diagnosis [14], prolonged symptom duration prior to treatment initiation, and inadequate awareness among caregivers and primary healthcare providers, resulting in delayed referral to specialized tertiary centers [15,16].

Accurate staging is critical for assessing disease severity and guiding therapeutic decision-making in retinoblastoma. The International Intraocular Retinoblastoma Classification (IIRBC) allows more precise assessment and follow-up of intraocular tumor size and location, offering improved risk stratification compared with the Reese–Ellsworth classification, particularly in the chemotherapy era [12]. Prognosis is favorable when retinoblastoma is detected early, disease extent is appropriately assessed, and timely treatment is instituted [17]. Thus, treatment outcomes are closely linked to clinical presentation, promptness of diagnosis, and the degree of tumor progression at detection.

Management of retinoblastoma requires a coordinated multidisciplinary approach involving ophthalmologists, pediatric oncologists, pediatric radiation oncologists, pathologists, nurses, and social workers. The primary objective of treatment is patient survival, followed by preservation of the globe and visual function. Therapeutic strategies include surgery, chemotherapy, and radiotherapy, selected according to disease stage and severity. In high-income countries, advances in early detection and comprehensive care have resulted in excellent survival outcomes, with increasing emphasis on globe and vision salvage [18]. Conversely, in low- and middle-income countries, mortality remains unacceptably high due to delayed presentation and restricted access to specialized care [19].

Despite progress in diagnostic and therapeutic strategies, retinoblastoma continues to pose major challenges in resource-limited settings, where delayed presentation and advanced disease at diagnosis are common. Variations in clinical presentation, symptom duration prior to diagnosis, and tumor stage at presentation significantly influence treatment decisions, eye salvage rates, and survival outcomes. Identifying factors associated with advanced disease and enucleation is therefore crucial, particularly in low-resource environments where early intervention may substantially improve prognosis. However, data describing patterns of presentation and prognostic indicators of pediatric retinoblastoma from tertiary care centers in developing regions remain limited. The purpose of the study is to evaluate the clinical presentation patterns and identify prognostic indicators in children diagnosed with retinoblastoma.

OBJECTIVE

- To evaluate the clinical presentation patterns and identify prognostic indicators in children diagnosed with retinoblastoma.

METHODOLOGY & MATERIALS

This hospital-based descriptive study was conducted at the Department of Ophthalmology, National Institute of Ophthalmology and Hospital, Dhaka, Bangladesh, from April 2011 to March 2013. A total of 46 children diagnosed with retinoblastoma, including patients referred from other hospitals, were enrolled based on specific inclusion and exclusion criteria. Data were collected to evaluate demographic characteristics, clinical presentation patterns, tumor staging, and prognostic indicators in pediatric retinoblastoma.

Inclusion Criteria:

- Children clinically diagnosed with retinoblastoma.
- Patients presenting to the National Institute of Ophthalmology and Hospital, Dhaka.
- Referred cases from other hospitals within the study period (April 2011 – March 2013).

Exclusion Criteria:

- Patients with ocular conditions other than retinoblastoma.
- Patients with incomplete clinical records.

Data Collection

Demographic and clinical data, including age at diagnosis, sex, and laterality, were recorded for all patients. A detailed history of presenting features such as leukocoria, proptosis, pseudohypopyon, hyphema, and other ocular manifestations was obtained. The duration of symptoms prior to

diagnosis (lag time) was documented and categorized for analysis.

Ophthalmic Evaluation and Tumor Staging

All patients underwent comprehensive ophthalmic evaluation, including anterior and posterior segment examination. Tumors were staged on a per-eye basis using the International Intraocular Retinoblastoma Classification (IIRC, Groups A–E), and eyes were further categorized as early-stage disease (Groups A–C) or advanced disease (Groups D–E).

Management

Treatment strategies, including enucleation and eye-preserving approaches, were determined according to tumor stage and clinical severity.

Data Analysis

Factors associated with advanced disease at presentation and predictors of enucleation, including age, lag time, laterality, and presence of proptosis, were analyzed. Data were entered into Microsoft Excel, with descriptive statistics used to summarize demographic characteristics, presenting features, lag time, tumor stage, and treatment outcomes. Comparative analyses were performed to evaluate associations, with p-values reported where applicable.

RESULTS

Table 1: Demographic Characteristics of the Study Population (n = 46)

Variable		Frequency	Percentage (%)
Age at diagnosis	<1 year	8	17.4
	1–3 years	26	56.5
	3–5 years	7	15.2
	>5 years	5	10.9
Sex	Male	26	56.5
	Female	20	43.5
Laterality	Unilateral	33	71.7
	Bilateral	13	28.3

Table 1 summarizes the demographic profile and laterality of children diagnosed with retinoblastoma. Of the 46 patients, 56.5% (n = 26) were male and 43.5% (n = 20) were female. The majority were diagnosed between 1–3 years of age (56.5%, n = 26), followed by infants younger than 1 year (17.4%, n = 8). Unilateral disease was observed in 71.7% (n = 33) of cases, while bilateral involvement was present in 28.3% (n = 13).

Table 2: Presenting Clinical Features of Retinoblastoma at Diagnosis (n = 46)

Presenting Feature	Frequency	Percentage (%)
Leukocoria	32	69.6
Leukocoria with proptosis	7	15.2
Pseudohypopyon	5	10.9
Hyphema / others	2	4.3

Table 2 outlines the initial clinical manifestations at presentation. Leukocoria was the most common presenting feature, seen in 69.6% (n = 32) of patients. Leukocoria associated with proptosis was noted in 15.2% (n = 7), while pseudohypopyon accounted for 10.9% (n = 5) of presentations. Hyphema or other atypical features were observed in 4.3% (n = 2) of cases.

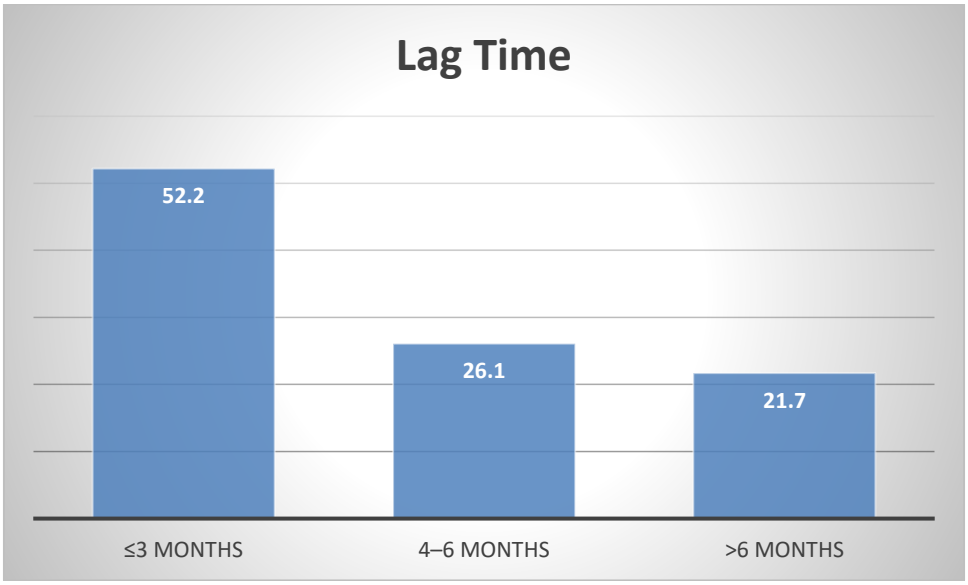

Figure 1: Duration of Symptoms Prior to Diagnosis (Lag Time) (n = 46)

Figure 1 presents the interval between symptom onset and diagnosis. More than half of the patients (52.2%, n = 24) presented within 3 months of symptom onset. A lag time of 4–6 months was observed in 26.1% (n = 12), while delayed presentation exceeding 6 months occurred in 21.7% (n = 10) of children.

Table 3: Tumor Classification According to the International Intraocular Retinoblastoma Classification (IIRC)

IIRC Group	Number of Eyes	Percentage (%)
A	4	6.5
B	10	16.3
C	12	19.6
D	20	32.6
E	16	26.0
Advanced disease (Groups D + E)	**36**	**58.6**

Table 3 shows tumor staging based on the IIRC system analyzed on a per-eye basis. Early-stage disease (Groups A–C) accounted for 42.4% of eyes, while advanced disease (Groups D and E) constituted 58.6% (n = 36). Group D tumors were most frequent (32.6%, n = 20), followed by Group E tumors (26.0%, n = 16).

Table 4: Factors Associated with Advanced Retinoblastoma at Presentation

Factor	Advanced Disease (IIRC D/E) (n = 27)	Early Disease (IIRC A–C) (n = 19)	p-value
Lag time >6 months	8 (29.6%)	2 (10.5%)	0.160
Proptosis at presentation	6 (22.2%)	1 (5.3%)	0.200
Age >3 years	10 (37.0%)	2 (10.5%)	0.070
Unilateral disease	22 (81.5%)	11 (57.9%)	0.090

Table 4 compares selected clinical and demographic factors between patients presenting with advanced disease (IIRC Groups D/E, n = 27) and those with early-stage disease (Groups A–C, n = 19). Advanced disease was more frequently observed among patients with symptom duration greater than 6 months (29.6% vs 10.5%), proptosis at presentation (22.2% vs 5.3%), age greater than 3 years (37.0% vs 10.5%), and unilateral disease (81.5% vs 57.9%), although none of these associations reached statistical significance.

Table 5: Factors Associated with Enucleation in Retinoblastoma

Factor	Eyes Enucleated (n = 26)	Eyes Preserved (n = 17*)	p-value
IIRC Group D/E	24 (92.3%)	3 (17.6%)	<0.001
Lag time >6 months	9 (34.6%)	1 (5.9%)	0.061
Presentation with proptosis	7 (26.9%)	0 (0.0%)	0.013
Age >3 years	10 (38.5%)	2 (11.8%)	0.067

Table 5 analyzes factors associated with enucleation on a per-eye basis. Eyes classified as IIRC Group D or E were significantly more likely to undergo enucleation compared with eyes in earlier stages (92.3% vs 17.6%, $p < 0.001$). Presentation with proptosis was also significantly associated with enucleation (26.9% vs 0%, $p = 0.013$). Longer symptom duration and age greater than 3 years were more common among enucleated eyes, though these associations did not reach statistical significance.

DISCUSSION

Retinoblastoma is the most common intraocular malignancy of childhood and remains a major cause of ocular morbidity and mortality when diagnosis and treatment are delayed. Clinical presentation patterns, symptom duration prior to diagnosis, and tumor stage at presentation are key determinants of treatment strategy, eye salvage, and survival outcomes. The findings of this study demonstrate that a substantial proportion of children presented with advanced-stage disease (IIRC Groups D–E), with leukocoria being the predominant presenting feature and proptosis and advanced staging significantly associated with enucleation. These results highlight the critical role of early recognition and timely referral in reducing advanced disease at presentation and improving eye preservation outcomes in resource-limited settings.

The demographic characteristics of our study highlight the early onset and typical laterality patterns of pediatric retinoblastoma. Among the 46 patients, the majority (73.9%) were diagnosed at or before 3 years of age, and 89.1% before 5 years, underscoring the predominance of early childhood presentation. Most cases occurred in the 1–3-year age group (56.5%), followed by infants younger than 1 year (17.4%). These findings are consistent with Saiju *et al*.[20], who reported that 83% of patients were 3 years or younger, and with Wong *et al*.[21], who observed that approximately 95% of cases are diagnosed before age 5. A slight male predominance (56.5%) was noted, although retinoblastoma generally shows no significant sex predilection. Unilateral disease was more common (71.7%) than bilateral involvement (28.3%), aligning with previous reports reflecting the higher prevalence of sporadic, non-hereditary retinoblastoma.

Clinical presentation patterns in our cohort mirror established literature, with leukocoria being the most frequent presenting feature (69.6%). This aligns with findings by Bukhari *et al*.[22] (56.5%) and Abramson *et al*.[23] (56.2%), confirming leukocoria as the hallmark sign of retinoblastoma. A subset presented with leukocoria accompanied by proptosis (15.2%), indicative of more advanced disease, consistent with Bukhari *et al*.[22], who reported proptosis in 24.2% of cases. Less common presentations, such as pseudohypopyon (10.9%) and hyphema or atypical signs (4.3%), were observed in a minority of patients, reflecting the rarity of inflammatory or masquerade presentations.

The duration of symptoms prior to diagnosis revealed a notable diagnostic lag. Over half of the patients (52.2%) presented within 3 months of symptom onset, whereas 26.1% and 21.7% presented after 4–6 months and >6 months, respectively. This pattern mirrors Wirix *et al*.[24], who reported a mean time to diagnosis of 3.2 months (range 2 months–1 year), emphasizing that delayed presentation is associated with more advanced disease and poorer outcomes.

Tumor staging demonstrated a predominance of advanced intraocular retinoblastoma, with 58.6% of eyes classified as IIRC Groups D and E. Group D tumors were most frequent (32.6%), followed by Group E (26.0%), whereas early-stage disease (Groups A–C) represented a smaller proportion. Jamalia *et al*.[25] similarly reported advanced disease as the most common stage at presentation, particularly Group E (62.4%). Although our cohort had a relatively higher proportion of Group D tumors, both studies highlight that advanced disease remains a frequent presentation, reinforcing the impact of delayed diagnosis and referral.

Several factors were more common among patients with advanced disease (IIRC D/E). Symptom duration exceeding 6 months occurred in 29.6% of advanced cases versus 10.5% in early-stage disease. Proptosis was observed in 22.2% versus 5.3%, age >3 years in 37.0% versus 10.5%, and unilateral disease in 81.5% versus 57.9%. These trends are consistent

with Rodrigues *et al*.[26], who demonstrated that longer lag time correlates with more advanced or metastatic retinoblastoma, emphasizing that delayed presentation, older age, and clinical signs like proptosis or unilateral disease are important indicators of disease severity.

Advanced intraocular disease was strongly associated with enucleation. Eyes classified as IIRC Groups D/E were significantly more likely to undergo enucleation (92.3% vs. 17.6%, $p < 0.001$). Prolonged lag time (>6 months) and proptosis were also more frequent among enucleated eyes, while age >3 years showed a similar trend. These results align with Mallipatna *et al*.[27], who reported that unilateral eyes with advanced tumors, particularly Group E, required primary enucleation and were associated with adverse histopathological features. Balaguer *et al*.[28] similarly demonstrated that longer intervals to enucleation were linked to more invasive histopathology, such as choroidal and ciliary body invasion. Collectively, these findings underscore that advanced tumor stage, delayed presentation, and overt clinical signs are critical predictors of eye loss, highlighting the importance of early detection and timely intervention to optimize globe salvage in pediatric retinoblastoma.

Limitations of the study

The study had several limitations:

- Hospital-based descriptive study at a single tertiary care center, limiting generalizability.
- Relatively small sample size.
- Advanced genetic testing and newer imaging or treatment modalities were not routinely available.
- Long-term visual and survival outcomes could not be fully assessed due to loss to follow-up in some patients.

CONCLUSION

In conclusion, pediatric retinoblastoma remains a significant intraocular malignancy in children, typically presenting in early childhood. In our study, the majority of patients were diagnosed between 1–3 years of age, with a slight male predominance and unilateral disease being more common. Leukocoria was the most frequent presenting feature, while delayed diagnosis beyond six months was observed in a notable subset of patients. Advanced tumors were predominant at presentation, and factors such as prolonged symptom duration, proptosis, older age, and unilateral involvement were more frequently associated with advanced disease. Eyes with advanced-stage tumors were significantly more likely to undergo enucleation, and proptosis emerged as a significant predictor of eye loss. These findings highlight the critical need for early detection and timely intervention to improve outcomes and optimize eye preservation in children with retinoblastoma.

REFERENCES

1. Stiller CA, Parkin DM. Geographic and ethnic variations in the incidence of childhood cancer. British medical bulletin. 1996 Oct 1;52(4):682-703.
2. Freedman JE, Goldberg LE. Incidence of retinoblastoma in the Bantu of South Africa. The British Journal of Ophthalmology. 1976 Sep;60(9):655.
3. Suckling RD, Fitzgerald PH, Stewart J, Wells E. The incidence and epidemiology of retinoblastoma in New Zealand: a 30-year survey. British Journal of Cancer. 1982 Nov;46(5):729-36.
4. Seregard S, Lundell G, Svedberg H, Kivelä T. Incidence of retinoblastoma from 1958 to 1998 in Northern Europe: advantages of birth cohort analysis. Ophthalmology. 2004 Jun 1;111(6):1228-32.
5. KOCK E, NAESER P. Retinoblastoma in Sweden 1958–1971: a clinical and histopathological study. Acta ophthalmologica. 1979 Jun;57(3):344-50.
6. Knudson Jr AG. Mutation and cancer: statistical study of retinoblastoma. Proceedings of the National Academy of Sciences. 1971 Apr;68(4):820-3.
7. Islam F, Zafar SN, Siddiqui SN, Khan A. Clinical course of retinoblastoma. J Coll Physicians Surg Pak. 2013 Aug 1;23(8):566-9.
8. Balmer A, Zografos L, Munier F. Diagnosis and current management of retinoblastoma. Oncogene. 2006 Aug;25(38):5341-9.
9. Parkin DM, Kramarova E, Draper GJ, Masuyer E, Michaelis J, Neglia J, Qureshi S, Stiller CA, editors. International incidence of childhood cancer, Volume II. 1998.
10. Terracini B, Young JL, Parkin DM, Stiller CA, Draper GJ, Bieber CA, International Agency for Research on Cancer. International Incidence Of Childhood Cancer. InInternational Incidence Of Childhood Cancer 1988 (pp. 398-p).
11. El Zomor H, Nour R, Alieldin A, Taha H, Montasr MM, Moussa E, El Nadi E, Ezzat S, Alfaar AS. Clinical presentation of intraocular retinoblastoma; 5-year hospital-based registry in Egypt. Journal of the Egyptian National Cancer Institute. 2015 Dec 1;27(4):195-203.
12. Shields JA, Shields CL, Meadows AT. Chemoreduction in the management of retinoblastoma. American journal of ophthalmology. 2005 Sep 1;140(3):505-6.
13. Chantada G, Fandiño A, Manzitti J, Urrutia L, Schvartzman E. Late diagnosis of retinoblastoma

in a developing country. Archives of disease in childhood. 1999 Feb 1;80(2):171-4.
14. Mutale N. *Modes of presentation, management and short term outcome of retinoblastoma at the University Teaching Hospital (UTH), Lusaka* (Doctoral dissertation, The University of Zambia).
15. Nyawira G, Kahaki K, Kariuki-Wanyoike M. Survival among retinoblastoma patients at the Kenyatta National Hospital, Kenya. J Ophthalmol East Cent S Afr. 2013;17:15–19.
16. Kao LY, Su WW, Lin YW. Retinoblastoma in Taiwan: survival and clinical characteristics 1978–2000. Japanese journal of ophthalmology. 2002 Sep 1;46(5):577-80.
17. Rodriguez-Galindo C, Wilson MW, Chantada G, Fu L, Qaddoumi I, Antoneli C, Leal-Leal C, Sharma T, Barnoya M, Epelman S, Pizzarello L. Retinoblastoma: one world, one vision. Pediatrics. 2008 Sep 1;122(3):e763-70.
18. MacCarthy A, Draper GJ, Steliarova-Foucher E, Kingston JE. Retinoblastoma incidence and survival in European children (1978–1997). Report from the Automated Childhood Cancer Information System project. European Journal of Cancer. 2006 Sep 1;42(13):2092-102.
19. Bowman RJ, Mafwiri M, Luthert P, Luande J, Wood M. Outcome of retinoblastoma in east Africa. Pediatric blood & cancer. 2008 Jan;50(1):160-2.
20. Saiju R, Moore G, Shrestha U, Shrestha MK, Ruit S. Retinoblastoma: geographic distribution and presentation at a tertiary eye care centre in Kathmandu, Nepal. Nepalese Journal of Ophthalmology. 2013 Sep 23;5(2):169-76.
21. Wong JR, Tucker MA, Kleinerman RA, Devesa SS. Retinoblastoma incidence patterns in the US Surveillance, Epidemiology, and End Results program. JAMA ophthalmology. 2014 Apr 1;132(4):478-83.
22. Bukhari S, Aziz-ur-Rehman IA, Qidwai U. Presentation pattern of retinoblastoma. Pakistan Journal of Ophthalmology. 2011 Sep 30;27(3).
23. Abramson DH, Frank CM, Susman M, Whalen MP, Dunkel IJ, Boyd NW 3rd. Presenting signs of retinoblastoma. J Pediatr. 1998 Mar;132(3 Pt 1):505-8.
24. Wirix M, Parys-Vanginderdeuren R, Casteels I, Uyttebrouck A. Delayed diagnosis of retinoblastoma. Bull Soc Belge Ophtalmol. 2000;(278):37-41.
25. Jamalia R, Sunder R, Alagaratnam J, Goh PP. Retinoblastoma registry report-Hospital kuala lumpur experience. Med J Malaysia. 2010 Jun 1;65(Suppl A):128-30.
26. Rodrigues KE, Latorre MD, Camargo BD. Atraso diagnóstico do retinoblastoma. Jornal de Pediatria. 2004;80:511-6.
27. Mallipatna AC, Sutherland JE, Gallie BL, Chan H, Héon E. Management and outcome of unilateral retinoblastoma. J AAPOS. 2009 Dec;13(6):546-50.
28. Balaguer J, Wilson MW, Billups CA, Mancini J, Haik BG, Qaddoumi I, Khoury JD, Rodriguez-Galindo C. Predictive factors of invasion in eyes with retinoblastoma enucleated after eye salvage treatments. Pediatr Blood Cancer. 2009 Mar;52(3):351-6.