RESEARCH ARTICLE

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Clinical Presentation and Survival of Children with Retinoblastoma Treated at the National Eye Centre in Indonesia

Anne Susanty[1]*, Primawita Oktarima[2], Friska Mardianty[3], Kanyawati Maliani[4], Angga Kartiwa[5], Adji Kusumadjati[6], Widia Noviyanti[7], Pujani Utami[8], Nindi Dwi Leoni[9], Dika Maulana[10], Karen Fischhuber[11], Petra Ketteler[12]

Abstract

Background: Retinoblastoma is a malignant ocular tumor in children. Patient characteristics differ between low- and middle-income countries and high-income countries. This study analyzes the clinical presentation and survival rates of patients with retinoblastoma at the National Eye Center (NEC) in Indonesia, a middle-income country. **Methods:** Clinical data of all children diagnosed with retinoblastoma at NEC between 2012 and 2021 were retrospectively analyzed. **Results:** In 10 years, 395 patients with retinoblastoma were diagnosed and treated at NEC. The number of diagnoses increased from 2012 to 2019, but declined during the COVID-19 pandemic. Most patients were diagnosed under 5 years of age. The most common sign was leukocoria (77.5%), followed by proptosis (14.0%). Proptosis was even more common in children from remote areas of Indonesia (20.0%). At NEC, 73.4% had unilateral and 26.6% bilateral retinoblastoma. Patients with bilateral retinoblastoma were statistically noticeably younger at diagnosis than unilateral retinoblastoma (unilateral: 27 months; bilateral 21 months; $p<0.001$). In patients diagnosed between 2017 and 2021, overt extraocular retinoblastoma (IRSS III and IV) was detected in 16.1% while only 5.4% of patients presented with IRSS 0/I at diagnosis. The 3-year overall survival rate for patients diagnosed between 2017 and 2021 was 53.5% (95%-CI: [43.1%, 66.4%]). **Conclusion:** In Indonesia extraocular disease at diagnosis is common contributing to low survival rates. To address this, early detection programs, standardized referral pathways, and treatment guidelines have been implemented. These efforts aim to improve survival outcomes and bring them closer in line with those of other middle-income countries.

Keywords: eye cancer- middle income country- relapse chemotherapy- death- metastasis.

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Introduction

Retinoblastoma is the most common malignant tumor of the eye in childhood. It originates from the developing retina and is characterized by biallelic pathogenic variants of the RB1 gene, a tumor suppressor gene. Retinoblastoma can present as unilateral or bilateral disease. Bilateral and familial retinoblastoma are typically caused by constitutional RB1 pathogenic variants (heritable retinoblastoma). Most but not all children with unilateral retinoblastoma have non-heritable retinoblastoma caused by two somatic RB1 mutations in a retinal progenitor cell. While there is no known racial predisposition, a slight gender bias exists, with a higher incidence in male infants [1].

In high-income countries (HICs), retinoblastoma is considered highly curable, with >95% disease-free survival rate. However, if left untreated, retinoblastoma can spread to the lymph nodes, bones, bone marrow, and the central nervous system (CNS), leading to a poor prognosis. Overall survival rates correlate with national income levels. While more than 80% of retinoblastoma cases worldwide occur in low- and middle-income countries (LMICs), with the highest proportion in Asia

*[1]Division of Pediatric, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [2]Division of Pediatric Ophthalmology and Strabismus, National Eye Center, Cicendo Eye Hospital, Faculty of Medicine Universitas Padjajaran, Bandung, Indonesia. [3]Division of Pathology, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [4]Division of Radiology, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [5]Division of Reconstructive Oculoplasty and Oncology, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [6]Radiotherapy Oncology, Hasan Sadikin General Hospital, Bandung, Indonesia. [7]Nurse Oncology, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [8]Division of Pharmacy, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [9]Psychology, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [10]Child Conselour, National Eye Center, Cicendo Eye Hospital, Bandung, Indonesia. [11]Institute of Biostatistics and Clinical Research, University of Muenster, Muenster, Germany. [12]Department of Pediatric Hematology and Oncology, University Hospital Essen, Essen, Germany. *For Correspondence: annesusanty05@gmail.com*

(53%), followed by Africa (29%), the 5-year overall survival in low-income countries (LICs) has been reported as low as 40% [2, 3]. Family history of retinoblastoma and screening of family members from birth are relatively rare in LICs [2], possibly due to low survival rates and early mortality before childbearing years in patients with heritable retinoblastoma. Delays in diagnosis and treatment contribute to poor outcomes in LMICs. The mean age of diagnosis of retinoblastoma also varies by income level, between 14.1 months in HICs and 30.5 months in LICs [2, 3]. In HICs, the most common first signs of retinoblastoma are leukocoria, followed by strabismus. In contrast, in LICs, retinoblastoma often presents with proptosis, red eye, and orbital cellulitis, indicating more advanced stages of retinoblastoma [2]. For this reason, Early detection and timely access to multidisciplinary treatment are key factors in improving survival rates [3].

Worldwide, the primary goal in retinoblastoma treatment is to ensure patient survival, followed by eye preservation, vision preservation, and minimizing side effects [4]. For intraocular retinoblastoma, treatment options include enucleation of the affected eye or, in less advanced cases, eye-preserving therapies. Enucleation is often the standard of care in LMICs to ensure survival. Eye-preserving therapies are applied mostly in bilateral retinoblastoma or when enucleation is refused. Standard eye-preserving methods include laser coagulation, cryotherapy, brachytherapy, systemic chemotherapy, and, historically, external beam radiotherapy. In recent decades, intra-arterial and intravitreal chemotherapy have emerged as advanced eye-preserving approaches in retinoblastoma centers, but these are not always available at retinoblastoma centers in LMICs [5]. Treatment of extraocular or metastatic retinoblastoma requires intensive multimodal therapy. And even in HICs, survival rates remain low for these advanced cases [6].

Indonesia is a middle-income country covering an area of 7.81 million km2, spread across 17,000 islands, with a population of 270 million, of which 26% are children and adolescents. Cicendo Eye Hospital is located in Bandung on Java Island, the most populous and developed island in Indonesia. Founded in 2009, Cicendo Eye Hospital became the first National Eye Center (NEC) in Indonesia and has achieved international accreditation. The retinoblastoma center at NEC was established in 2015. Challenges in treating retinoblastoma in Indonesia include, among others, late diagnosis, often at advanced stages and often due to misdiagnoses, long travel distances from remote islands with high financial burden for families, alternative treatment from traditional healers, and treatment abandonment [7]. These factors that are common in LMICs contribute to reduced survival rates compared to HICs. In 2014, the Government of Indonesia launched the national health insurance program (JKN) to provide universal health coverage for all citizens [8]. JKN facilitates access to specialized care for all Indonesian children with cancer diagnoses at referral centers across Indonesia, such as NEC for retinoblastoma. However, many of the above-mentioned challenges for families with children with childhood cancer remain.

In this study, we evaluate the clinical presentation of retinoblastoma at diagnosis in a referral center within a middle-income country, aiming to identify barriers to patient care and analyse the effect of recent advancements in its management.

Materials and Methods

We retrospectively reviewed the clinical data of all 395 children diagnosed with retinoblastoma between 2012 and 2021 at the NEC. The inclusion criteria for the study were diagnosis of retinoblastoma at NEC between 2012 and 2021, age under 18 years, and informed consent obtained from the parents for participation in the study. Written informed consent for research was obtained from all participants or their guardians. Families that did not consult rountinely to the hospital in 2022 were contacted regarding the follow-up information. If families could not be reached, data were censored at the date of the last appointment at NEC. When parents reported that their child had deceased, the date of death was recorded. If the parents did not disclose the date of death, the patients' follow-up time was censored at the date of their last appointment at NEC, which was recorded as the last date with status "alive" (16 patients reported deceased by parents with no available date of death). The primary endpoint was overall survival, which was estimated using the Kaplan–Meier method. Continuous variables were summarized descriptively using the median and standard deviation, and group differences were assessed using the Mann–Whitney U test. Categorical variables were reported as absolute and relative frequencies, with between-group differences evaluated using Fisher's exact test.

Results

Epidemiology

Between 2012 and 2021, 395 children were diagnosed with retinoblastoma at the NEC and included in this study (an average of 40 new cases per year). The number of diagnoses increased from 15 patients in 2012 to 49 patients in 2019, but declined to 40 patients per year during the COVID-19 pandemic in 2020 and 2021 (Figure 1). Slightly more male patients (203, 51.4%) than female patients (192, 48.6%) were diagnosed, resulting in a male-to-female ratio of 1.00:0.95. In the cohort, 290 patients (73.4%) presented with unilateral retinoblastoma, while 105 patients (26.6%) had bilateral retinoblastoma. Over the study period, the percentage of children with bilateral retinoblastoma per year increased (17.6% in 2012/2013 vs 32.5% in 2020/2021, $p = 0.118$). The median age at diagnosis was statistically noticably higher for unilateral disease at 27 months (range 1–113 months) compared to 21 months (range 2–61 months) for bilateral disease ($p<0.001$). Children with retinoblastoma referred to NEC were from Bandung (n = 78, 19.7%), other areas of Java Island (n = 272, 68.9%), or from other parts of Indonesia (n = 45, 11.4%) (Table 1).

First sign and lag time

Leukocoria was the most common presenting sign,

Table 1. Patient Characteristic Depending on Residential Area

Characteristics	Total	Residential area		
		Bandung city and district in absolute numbers (%)	Java Island other than Bandung (%)"	Indonesia outside Java Island (%)
Number of patients	395	78	272	45
Gender				
Male	203	43 (55.1)	143 (52.6)	17 (37.8)
Female	192	35 (44.9)	129 (47.4)	28 (62.2)
Age at diagnosis				
Median in years	2.08	2.00	2.17	2.00
Range in years	0.08-9.42	0.17-9.42	0.08-8.17	0.17-6.67
Age at diagnosis in groups				
0-11 month	71	20 (28.2)	43 (60.6)	8 (11.2)
12-23 month	98	18 (18.4)	68 (69.4)	12 (12.2)
24-35 month	126	22 (17.5)	90 (71.4)	14 (11.1)
36-47 month	53	9 (17)	38 (72)	6 (11)
48-60 month	19	1 (5.3)	16 (84.2)	2 (10.5)
>60 months	28	8 (28.6)	17 (60.7)	3 (10.7)
First Presentation				
Leukocoria	306	56 (71.8)	214 (78.7)	36 (80.0)
Proptosis	55	12 (15.4)	34 (12.5)	9 (20.0)
Strabismus	10	3 (3.8)	7 (2.6)	0 (0.0)
Infection	13	4 (5.1)	9 (3.3)	0 (0.0)
Other	10	3 (3.8)	7 (2.6)	0 (0.0)
Not recorded	1	0 (0.0)	1 (0.4)	0 (0.0)
Laterality				
Unilateral	290	58 (74.4)	199 (73.2)	33 (73.3)
Bilateral	105	20 (25.6)	73 (26.8)	12 (26.7)
Lag Time in months[1]				
0-6 month	245	52 (66.7)	163 (59.9)	30 (66.7)
7-12 month	43	7 (9.0)	33 (12.1)	3 (6.7)
>12 month	89	17 (21.8)	60 (22.1)	12 (26.7)
Other	18	2 (2.6)	16 (5.9)	0 (0.0)

[1], lag time was defined as time from first signs to diagnosis of retinoblastoma

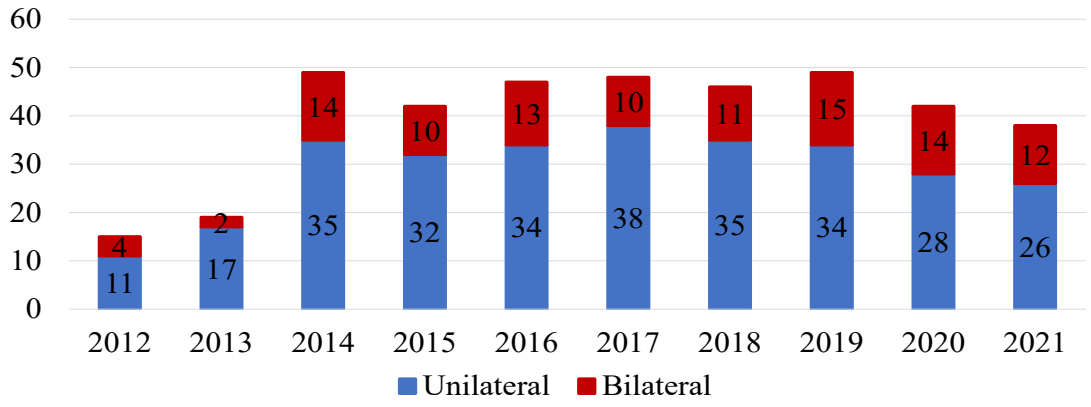

Figure 1. Number of Patients Diagnosed with Retinoblastoma at NEC. Percentage of bilateral retinoblastoma increased over the study period from 2012-2021.

observed in 306 patients (77.5%), followed by proptosis in 55 patients (14.0%) (Table 1). Proptosis is typically a sign of advanced retinoblastoma, and children from more remote areas of Indonesia (outside Java Island) presented with proptosis in 20.0% of cases, compared to 13.0% on Java Island, including Bandung. Other signs of

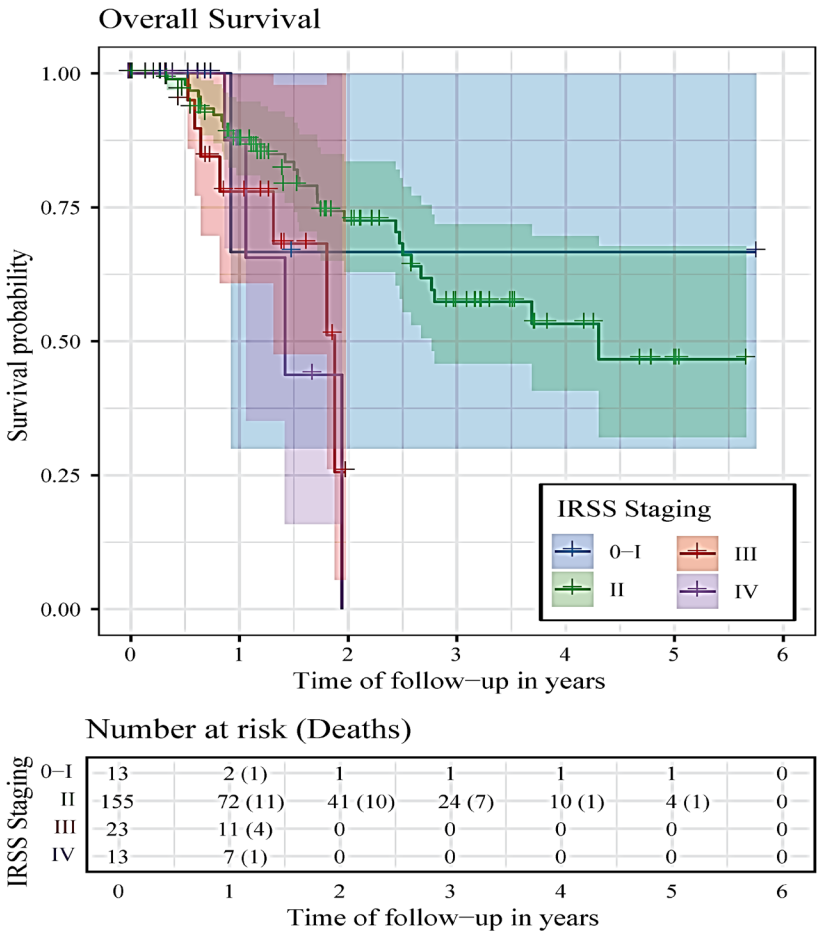

Figure 2. Overall Survival Probability and Its 95%-Confidence Interval for Each Timepoint Estimated by Kaplan-Meier Approximation Split by the IRSS Staging of the Retinoblastoma

retinoblastoma noticed by families included strabismus in 10 children (2.5%), eye infections in 13 patients (3.3%), and other reasons in 10 patients (2.5%). Information on presenting signs was missing for 1 child (0.2%) (Table 1).

Lag time was defined as the period from the onset of the first symptoms to the diagnosis of retinoblastoma. Most children (245, 62.0%) were diagnosed within a lag time of 0–6 months. For 43 children (10.9%), the lag time was 7–12 months, while 89 children (22.5%) had a lag time of more than 12 months. Information on lag time was not available for 18 patients (4.6%). The lag time did not show significant changes over the 10 years of the study period (Table 1).

Established guidelines for initial diagnostics and treatment

All 395 children in the study were diagnosed with retinoblastoma and treated according to established retinoblastoma guidelines. For accurate diagnosis, all patients underwent EUA along with photodocumentation using a RetCam, ultrasound, and MRI. At our center, the diagnostic process for retinoblastoma was gradually expanded between 2012 and 2021. During this period, 395 patients were assessed and documented through EUA. Retrospective data from RetCam imaging during EUA were available for 192 patients (48.6%). The RetCam examinations confirmed the diagnosis of retinoblastoma in 187 patients (47.3%). In 5 patients (1.3%), the RetCam images were not considered characteristicof retinoblastoma, but histopathological examination confirmed the diagnosis.

Ultrasound of the eye at the time of retinoblastoma diagnosis was used to assess the posterior segment of the eyeball. Over the study period, 81.0% of patients (320 out of 395) underwent ultrasound. Ultrasound confirmed the diagnosis of retinoblastoma in 305 of the 320 patients (95.3%). Ultrasound was not diagnostic of retinoblastoma in the remaining 15 patients, but the diagnosis was subsequently confirmed through histopathological examination following enucleation. Cross-sectional imaging, either a CT scan or MRI, was performed in 343 of 395 patients (86.8%). Imaging results confirmed the diagnosis of retinoblastoma in 341 of 343 patients (99.4%), while in 2 patients (0.5%), the imaging findings were not characteristic of retinoblastoma.

Cytological evaluation of bone marrow aspiration (BMA) and cerebrospinal fluid (CSF) was introduced on 8 October 2020, to detect systemic metastasis of retinoblastoma. BMA was performed in 27 of 55 patients (49.1%). Malignant cells were found in 11 of these 27 BMA samples (40.7%). Lumbar puncture to collect CSF was performed in 28 of 55 patients (50.9%), and malignant cells were detected in 2 of the 28 samples (7.1%) at diagnosis.

IRSS and IIRC Staging of retinoblastoma at diagnosis

All 395 patients were staged according to the International Intraocular Retinoblastoma Classification (IIRC). Among the 290 patients with unilateral retinoblastoma, 18 (6.2%) were classified as Group D, 249 (85.9%) as Group E, and 23 (7.9%) had missing classification data. Among the 105 patients with bilateral retinoblastoma, the more advanced eye was classified as Group D in 9 patients (8.6%), Group E in 89 patients (84.8 %), and 7 patients (6.7%) had missing information.

Clinical staging for extraocular disease extension with the International Retinoblastoma Staging System (IRSS, stages 0–IV) was performed since 2017 (223 patients), lumbar puncture and BMA since 2020. Of the 161 patients with unilateral retinoblastoma diagnosed between 2017 and 2021, 11 (6.8%) presented at first diagnosis with IRSS I, 107 (66.5%) with IRSS II, 21 (13.0%) with IRSS III, and 9 (5.6%) with IRSS IV. Information was missing for 13 patients (8.1%). Among the 62 patients with bilateral retinoblastoma, 1 patient (1,6%) presented with IRSS 0, 1 patient (1.6%) with IRSS I, 48 patients (77.4%) with IRSS II, 2 patients (3.2%) with IRSS III, and 4 patients (6.5%) with IRSS IV. Information was missing for 6 patients (9.7%).

Treatment of Retinoblastoma

The standard treatment for unilateral retinoblastoma at NEC was enucleation of the affected eye if classified as intraocular Group D with massive vitreous seeding or Group E. For bilateral retinoblastoma, the standard approach was enucleation of the more affected eye using the same grouping criteria, combined with eye-preserving treatment for the less affected eye, which included systemic chemotherapy in combination with photocoagulation and cryotherapy. Data on treatment were available for 249 of 395 patients (63.0%). Most children received enucleation of at least one eye (243 of 249 patients, 97.6%), 3 patients (1.2%) did not require enucleation, and 3 patients (1.2%) refused enucleation despite medical recommendation.

Overall survival

Follow-up data on survival were collected for patients diagnosed between 2017 and 2021 (223 patients). The cause of death in the 65 patients who died was not formally assessed, but in nearly all patients, metastatic retinoblastoma was the most likely cause based on the timing of death and previous clinical course. IRSS Staging was available for 204 of the 223 patients with survival data. The 1-year and 3-year overall survival (OS) rates correlated with the IRSS stage. The 1-year OS rate was 66.7% (95%-CI: [30.0%, 100.0%]) for children with IRSS 0/I, 87.6% (95%-CI: [80.9%, 94.7%]) with IRSS II, 77.9% (95%-CI: [60.8%, 99.9%]) with IRSS III, and 87.5% (95%-CI: [67.3%, 100.0%]) with IRSS IV. The 3-year OS rates was 66.7% (95%-CI: [30.0%, 100.0%]) with IRSS 0/I, 57.4% (95%-CI: [45.8%, 71.8%]) with IRSS II, and 25.6% (95%-CI: [5.5%, 100.0%]) with IRSS III (Figure 2). Treatment was abandoned in 19 of 223 patients (8.5%) and we have no data on their outcome.

Discussion

Clinical presentation and outcomes of patients diagnosed with retinoblastoma at a tertiary care center in Indonesia showed late diagnosis and lower overall survival rates compared to other middle-income countries. The retinoblastoma center at the National Eye Center was established in 2015. Since then, retinoblastoma care has been standardized, diagnostic and therapeutic tools have been continuously extended. The number of patients diagnosed and treated for retinoblastoma at the center increased from 15 in 2012 to 49 in 2019, with a slight decline during the COVID-19 pandemic in 2020 and 2021. Significantly affected the detection and treatment of retinoblastoma. Many patients experienced difficulties accessing healthcare services, resulting in delayed presentation. Consequently, in 2022 and 2023, there was an increase in the number of patients presenting with advanced-stage disease, accounting for 21 of 45 patients in 2022 and 31 of 64 patients in 2023. Consistent with findings from other studies, a slight predominance of male patients was observed in our cohort [9, 10].

Children with unilateral and bilateral retinoblastoma, from both Java Island and other regions of Indonesia, were diagnosed at a median age of 27 and 21 months, respectively. This is in line with data from other retinoblastoma centers in Indonesia and other low and middle-income countries, which reported an average age of presentation of 24.05 ± 10.74 months (range 6 to 50 months) [1, 2]. However, the age of diagnosis in Indonesia is higher than in HICs, with an average age of diagnosis of range 12 to 18 months [2]. Age of diagnosis reflects both the age at onset of retinoblastoma and the subsequent diagnostic delay (lag time). We defined lag time as the interval between the first recognized signs of retinoblastoma and the time of diagnosis. However, it is possible that the initial signs of retinoblastoma were noticed late by parents or caregivers, despite an earlier onset of disease. This delay in recognition could result in an artificially shortened lag time. The majority of patients in our study (n=245, 62.0%) had a lag time of 0–6 months, while 22.5% experienced a lag time exceeding 1 year. This is in line with studies from other LMIC in Central Asia, which reported a lag time of maximal 15 months and a correlation of distance from home to retinoblastoma treatment center [11] or from India involving 692 patients, a mean lag time of 150 days (median 69 days; range 0–1128 days) [12]. We did not detect significant differences in lag times observed between children from Java or other regions of Indonesia. The factors contributing to delays in diagnosing retinoblastoma in LMICs are multifactorial and include the level of parental education, socioeconomic status, and the availability and accessibility of health facilities [2]. We aim to assess these factors in detail in a prospective study. The majority of patients did not return to continue treatment because of financial constraints, which consequently contributed to delays in diagnosis. Delayed presentation to primary healthcare providers at the onset of symptoms also occurred due to limited parental awareness of the early clinical signs.

Similar to the first signs in HIC, leukocoria was the

most common sign at diagnosis in our study, observed in 306 patients (77.5%) [3, 9]. Alarming proptosis, a sign of very advanced disease, was the second most common sign in our center (55 patients [14%]). In LMICs, proptosis has been described as a common finding, with rates as high as 24.4% [13]. Most patients diagnosed with retinoblastoma at NEC were from Bandung (19.7%) or other parts of Java Island (68.9%), while only 11.4% are referred from more remote areas of Indonesia. Proptosis was slightly more common in children from outside Java (20.0% vs 13.0%), but we did not observe statistically noticeable differences in presentation between patients from Java and those traveling longer distances from remote areas of Indonesia. It is important to note that this study only includes patients treated at the NEC, and many patients with retinoblastoma from remote areas of Indonesia may never be referred to the NEC.

In our cohort, most patients presented with unilateral retinoblastoma (73.4%), while 26.6% had bilateral retinoblastoma. This distribution is consistent with other cohorts in LMICs, where the percentage of bilateral retinoblastoma typically ranges from 27.0% to 35.0% [9, 12-14]. In contrast, studies from HICs report a higher percentage of bilateral disease, generally around 40.0% of cases [15]. Over the 10-year study period, we observed a trend toward an increasing percentage of bilateral retinoblastoma cases. Several factors may contribute to the lower percentage of bilateral retinoblastoma in LMICs, including under-detection of tumors in both eyes, lower survival rates among patients with heritable forms of disease, and the reduced likelihood of familial transmission due to early mortality. In the past, many patients with bilateral retinoblastoma did not survive into adulthood to have children, thereby limiting the number of familial cases identified.

Most internationally recommended diagnostic procedures have been implemented at NEC over the study period. All children underwent an EUA as part of the standard protocol for detecting retinoblastoma. The EUA is important because, without indirect ophthalmoscopy, initial lesions might be missed [3]. In our study, 81.0% of patients underwent ultrasound examination. This emphasizes that ultrasonography is a valuable tool for examining children with eye diseases in a tertiary care setting [16]. Cross-sectional imaging was performed in 86.8% of patients diagnosed with retinoblastoma at diagnosis at NEC. However, many children received a CT as a routine MRI at diagnosis, aiming to spare radiation for young children with potential tumor predisposition syndrome, which is not easily accessible. Pathology results were retrospectively available for 234 of 395 patients (59.2%), 3 patients (0.8%) did not require enucleation, 3 patients (0.8%) refused enucleation despite medical recommendation, and in 154 patients, pathology results were not recorded (39.0%). As part of the advancing care of children with retinoblastoma, documentation of crucial details in the clinical notes has now been improved.

BMA for bone marrow evaluation and lumbar puncture for CSF analysis as part of systemic metastasis screening have been implemented during the study period. Detection of metastatic disease was common, with bone marrow involvement in 40.7% and malignant cells in the CSF in 7.1% of the examined patients. The rate of systemic metastasis in our cohort was high compared to studies from other MICs, with 10.9% of children with retinoblastoma presenting with distant metastases, including bone marrow metastases [9]. In total, 16.1% of patients presented at diagnosis with overt extraocular disease (stage III or IV). This percentage may even underestimate the rate of metastatic disease, as investigations of BMA and CSF have only been introduced toward the end of the study period.

In line with the advanced staging at diagnosis, 1-year and 3-year OS rates for our cohort of 204 of 223 patients diagnosed between 2017 and 2021 were low with 85.6% (95%-CI: [79.7%, 92.0%]) and 53.5% (95%-CI: [43.1%, 66.4%]), respectively. The median survival time was 1.88 years. Results from other tertiary care referral hospitals in Indonesia confirm the low survival rates, with a five-year event-free survival (EFS) rate for retinoblastoma patients of 20%. In this study, the five-year EFS estimate was significantly higher in younger children (42%) compared to older children (6%) ($P = 0.045$), pointing towards late diagnosis as one factor for low survival rates [1]. Compared to reported 3-year OS rates of 91.2% (95%-CI: [89.5%, 93.0%]) for children from upper-middle-income countries and 80.3% (95%-CI: [78.3%, 82.3%]) for children from lower-middle-income countries in the global retinoblastoma study [10], survival rates in these two Indonesian centers are significantly lower than expected. When analyzed per IRSS stage, the 1-year OS rates of 66.7% for IRSS I and 87.6% for IRSS II, respectively, were in line with results from other studies. This emphasizes that the advanced stage of disease at diagnosis due to delayed diagnosis contributes to low OS rates in Indonesia. Even in HICs, OS of metastatic disease remains reduced despite the use of multimodal therapy including high-dose chemotherapy and autologous stem cell transplant [6]. These high-dose chemotherapy protocols are associated with high mortality and morbidity and are not adequate for the LMICs settings, emphasizing again the importance of early diagnosis to improve survival rates. Reducing the number of advanced retinoblastoma cases in Indonesia is essential for improving survival outcomes [2].

Patients who abandoned treatment (8.5%), the majority did not return to the hospital, primarily due to financial constraints. Regular follow-up visits were often not feasible because many families did not have national health insurance. Even among those who were covered, transportation costs remained a significant barrier. This challenge was evident not only for families living nearby but was even more pronounced for those residing in distant areas, where both travel distance and cost further limited access to care. Outcome data were not available, as the patients did not return to the hospital following their initial visit. Delays in diagnosis could be reduced by establishing standardized referral pathways and setting up screening programs. Delay in diagnosis could be mitigated by establishing a screening program, and survival rates could be improved by creating specialized referral centers

with multidisciplinary medical teams and implementing treatment guidelines.

Of all patients with retinoblastomas worldwide, 11% reside in HICs, 69% in MICs, and 20% in LICs [2, 14, 17]. Despite the higher prevalence of retinoblastoma in middle- and low-income countries, the majority of treatment centers are located in high- and middle-income countries, leading to significant disparities in healthcare access. Consistent with income levels as a surrogate measure of living standards, retinoblastoma in Indonesia is associated with lower survival rates (53.5%) compared to HICs, where survival rates exceed 95%. Comprehensive national data for Indonesia are scarce, but crucial for healthcare policy and planning at both national and international levels. Many LMICs lack central childhood cancer registries and do not report data on retinoblastoma presentation and survival. However, this information is crucial for health care policy and planning at both national and international levels, particularly in efforts to reduce the number of advanced retinoblastoma cases in these countries [2].

As a limitation, this study was retrospective, the medical records were sometimes incomplete and we were unable to obtain follow-up data for some patients. Additionally, genetic studies were not included in this study due to their unavailability in Indonesia. These results may be influenced by referral bias, as patients from remote or underserved areas likely faced difficulties accessing healthcare. Consequently, such patients may be underrepresented, which could lead to an underestimation of disease burden and limit the generalizability of our findings.

In conclusion, the proportion of extraocular retinoblastoma at the study center was high and correspondingly, the 1 and 3-year OS rates were low. These findings highlight the urgent need for a national screening program to facilitate earlier detection of retinoblastoma and improve survival outcomes, aligning them in line with those of other middle-income countries. National and international collaboration will be critical to advancing early detection strategies and ensuring timely access to effective treatment for children with retinoblastoma in Indonesia.

Author Contribution Statement

Conceptualization: A.S., P.K. Methodology: P.K. Investigation: A.S. Manuscript preparation and revision: A.S., K.F., P.K. Contributing discussions about data and findings: A.S., K.F., P.K. Clinical care: A.S., P.O., F.M., K.M., A.Ka., A.Ku., W.N., P.U., N.D.L., D.M. Administration: P.K. Funding acquisition: A.S., P.K. All authors have read and agreed to the submitted version of the manuscript.

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Ethical Issue

The study was approved by the ethics committee of the NEC Cicendo Eye Hospital (approval number: DP.04.03/D.XXIV.16/19422/2024).

Data Availability Statement

The data that support the findings of this study are openly available in Zenodo at https://doi.org/10.5281/zenodo.16975214, reference number 16975214.

Conflict of Interest statement

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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