Turkish Archives of Pediatrics

ORIGINAL ARTICLE
DOI: 10.5152/TurkArchPediatr.2025.24203

Retinoblastoma in Albania: A 25-Year Retrospective Analysis

Enkeleda Duka[1], Eduart Hashorva[2], Mirzana Kapllanaj[1], Mirela Xhafa[1], Anila Godo[1], Alketa Tandili[3], Eneda Rustemi[3], Elizana Petrela[4], Mattan Arazi[5], Ido Didi Fabian[5,6], Anila Babameto[7], Mirela Tabaku[7], Lila Shundi[8], Donjeta Bali[1]

[1]Pediatric Hemato Oncology Service, UHC Mother Teresa, Tirana, Albania
[2]University Obstetrics Gynecology Hospital "Queen Geraldina," Tirana, Albania
[3]Ophthalmology Department, UHC Mother Teresa, Tirana, Albania
[4]Public Health Department, University of Medicine, Tirana, Albania
[5]Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Tel-Aviv University, Tel-Aviv, Israel
[6]International Centre for Eye Health, London School of Hygiene and Tropical Medicine, London, UK
[7]Clinical Genetic Service, UHC Mother Teresa, Tirana, Albania
[8]Public Health Institute, Tirana, Albania

What is already known on this topic?

- *Retinoblastoma is a very well-studied disease and with a very good prognosis if diagnosed and treated at an early stage, with a survival rate of nearly 100% in developed countries, but still very challenging in treatment and with high morbidity and mortality rate in countries in development.*

What does this study add?

- *This study provides the first reported case series of RB in Albania, showing an incidence of 1 in 24,000 births, lower than in other European countries.*
- *The study aimed to report the diagnosis, treatment and outcome of RB in Albania from the only referral center in the country.*
- *This retrospective study highlights delayed diagnosis, advanced stages of disease at presentation, and high mutilation burden, emphasizing the need for improved early screening and treatment options in Albania.*

Corresponding author:
Enkeleda Duka
✉ dukaenkeleda@gmail.com
Received: September 15, 2024
Revision Requested: October 12, 2024
Last Revision Received: December 10, 2024
Accepted: December 18, 2024
Publication Date: March 3, 2025

ABSTRACT

Background: Retinoblastoma (RB), the most common intraocular cancer worldwide, has been extensively investigated. To the best of our knowledge, however, no reports exist on RB in Albania. We aimed to present the first case series of RB in Albania, including presentation, treatment, and outcome of patients.

Materials and Methods: This was a retrospective case series of patients diagnosed with RB from 1998 to 2023 at a single country Mother Teresa University Hospital Center in Albania. Epidemiologic and clinical data were extracted from follow-up clinical charts.

Results: During the 25-year study period, 22 patients were diagnosed with RB, of whom 59% were females. The average age at diagnosis was 21.8 months (SD—18.8 months). In 13 (59%) cases, the disease was diagnosed within the first year of life, and less than 5% were diagnosed after the age of 5 years. Overall, 18% of patients had family history of RB, and 41% had bilateral RB. The time from the first symptom to diagnosis was less than a month in 32% of cases, while 77% of patients were diagnosed within 4 months. The main presenting symptom was leukocoria in 6 (27%) cases, strabismus in 3 (14%) cases, and combination of both in 3 (14%) cases. Treatment was mainly a combination of enucleation and systemic chemotherapy in 15 (71%) cases. Only 13 (59%) patients continued treatment within Albania, with the rest being treated abroad.

Conclusion: We present the first cohort of children with RB from Albania, a country with limited diagnostic and treatment resources. The advanced disease states of these children underscore the importance of implementing national pediatric screening programs.

Keywords: Retinoblastoma Albania, ocular oncology, pediatric oncology

INTRODUCTION

With a global incidence of 8000 cases a year, retinoblastoma (RB) is the most common intraocular cancer in children; a majority of cases are diagnosed before the age of 5 years old.[1,2,3] The prognosis of RB is potentially favorable if diagnosed and treated at an early stage. In high-income countries, the survival rate has been reported to be nearly 100%.[4] Untreated, however, the malignancy is fatal, with high mortality rates observed in many low- and middle-income countries. Overall, geographic and socioeconomic inequities drive global discrepancies in RB care, leading to delays in diagnosis, non-standardized pathways, and unequal access to treatment.[5,4,]

Cite this article as: Duka E, Hashorva E, Kapllanaj M, et al. Retinoblastoma in Albania: A 25-year retrospective analysis. *Turk Arch Pediatr.* 2025;60(2):159-163.

Albania is an upper-middle-income European country in the Balkans, with a population of less than 3 million and a crude birth rate of less than 10 births per 1000 people.[6] Moreover, the healthcare system operates under a centralized model, with the state playing a dominant role in providing services and comprehensive care.[7] Geographic and socioeconomic disparities across Albania have created significant gaps in healthcare access for children, particularly those in rural areas and low-income communities.[8] Moreover, compared to its neighboring countries in Europe, Albania faces significant challenges in managing cancer due to limited resources and healthcare access.[9]

All cases of RB in Albania are referred to "Mother Theresa" University Hospital Center in Tirana. While some children are managed locally, others are referred abroad for treatment. However, to the best of our knowledge, apart from participating in the Global Retinoblastoma Studies, which was limited to new cases in a single year, there has never been a comprehensive report on RB in Albania describing diagnosis, management, and outcomes.[4]

This report aims to provide an overview of RB cases managed at Albania's single referral center.

Materials and Methods

This retrospective case series included consecutive children diagnosed with RB from January 1, 1998, to February 28, 2023, at the Pediatric Onco-Hematology center of Mother Theresa University Hospital Center in Albania. Children with a newly confirmed RB diagnosis, verified by both a pediatric ophthalmologist and oncologist, were included, while cases lacking diagnostic confirmation were excluded.

Clinical diagnosis consisted of a thorough ophthalmic examination under anesthesia, magnetic resonance imaging (MRI) of the brain and orbits when available, and histopathological analysis following enucleation. In recent years, ocular ultrasonography and ocular computed tomography (CT) scans have been used, though rarely, as these devices are typically available only in private clinics.

Clinical data collected included age at presentation, sex, geographic location, family history of RB, presenting symptoms, disease severity, treatment modalities (e.g., enucleation, systemic chemotherapy), and available outcomes (e.g., death, metastasis). Tumor staging was reported according to the classifications documented in medical chart reviews, reflecting the staging practices used throughout the study period.

This study adhered to the tenets of the Declaration of Helsinki and received approval from the country Ethics Committee at the Ministry of Health in Albania on September 9, 2024 with approval number 66/51.

Statistical Analysis

Statistical analysis was performed using Microsoft Office Excel (Microsoft Corporation, Redmond, WA, USA). Calculations included indicators such as means and SDs, conducted in Statistical Package for the Social Science (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). The calculated incidence was derived by dividing the total number of cases by the length of the study period in years. The expected incidence was estimated using Albania's average annual birth rate of 28 000 live births and applying the globally reported RB incidence of 1 in 14 000-17 000.[4,10]

RESULTS

The cohort included 22 children with an average age of 21.8 ± 18.8 months at diagnosis, corresponding to an incidence of 1 case per 32 000 live births over the 25-year period; this translates to approximately 0.87 cases per year. However, the estimated incidence of RB in Albania is approximately 1.65-2 cases per year.[10]

Of these children, 9 (41%) were males and 4 (18%) had a positive family history of RB. The initial symptoms appeared within the first year of life in 13 (59%) patients, and the time from the first symptom to diagnosis was around 4 months. The symptoms, in decreasing order of frequency, were leukocoria, strabismus, pain, proptosis, and vision loss. Most of the cases came from cities in the central region of the country, where most of the population is concentrated (Table 1).

Disease severity varied, and data on clinical and pathological classification were limited. In this cohort, at least 8 children (36%) were found to have distant metastasis, classified as stage

Table 1. Summary of Demographic and Clinical Data on All Children with Retinoblastoma Who Presented to Mother Theresa University Hospital Center in Albania from January 1, 1998, to February 28, 2023

Category	n (%)
Sex	
Female	13 (59)
Male	9 (41)
Region	
Tirane	6 (28)
Fier	5 (24)
Berat	3 (14)
Durres	3 (14)
Others	5 (24)
Age at first symptom	
0-12 months	13 (59)
13-24 months	3 (14)
Over 24 months	6 (27)
Family history	
No	15 (68)
Yes	4 (18)
N/A	3 (14)
First symptom	
Leukocoria	6 (27)
Strabismus	3 (14)
Leukocoria+Strabismus	3 (14)
Pain+edema	5 (22)
Vision loss	2 (9)
Pain+vision loss	1 (4.5)
Otomastoiditis (Dex)	1 (4.5)
N/A	1 (4.5)

Table 2. Available Staging Information of All Children with Retinoblastoma Who Presented at Mother Theresa University Hospital Center in Albania

Clinical Information	n (%)
Classification	
Stage IV (distant metastasis)	8 (36)
pT3	1 (4.5)
pT1	2 (9)
N/A	11 (50)
Total	22 (100)
Localization	
Bilateral	9 (41)
Dexter	8 (36)
Sinister	4 (18)
N/A	1 (5)
Total	22 (100)
Optic nerve affected	
Yes	10 (45)
No	5 (23)
N/A	7 (32)
Total	22 (100)

IV of the International Retinoblastoma Staging System (IRSS), with 6 cases spreading to the central nervous system; though the exact timing of this event (at initial diagnosis or during follow-up) could not be determined.[11] Bilateral RB was present in 9 children (41%), and optic disc involvement was observed in 10 children (45%) (Table 2).

Treatment modalities included a combination of enucleation and systemic chemotherapy in 15 (71%) children (Table 3). The rest of the children underwent enucleation only, chemotherapy treatment only, or a combination of both with external beam radiation. Of all the children, 20 (91%) had 1 or both of their eyes enucleated. During the 25 years, 13 children (59%) were treated within the country, and 9 (41%) traveled abroad for treatment after the initial diagnosis. The overall survival could not be estimated due to a lack of information on patients treated outside the country (Table 3).

Table 3. Treatment Modalities Used for Children with Retinoblastoma Who Presented to Mother Theresa University Hospital Center in Albania

Treatment and Outcome	n (%)
Type of treatment	
Surgery+chemotherapy	15 (71)
Surgery	2 (9)
Chemotherapy	1 (5)
Surgery+chemotherapy+radiation	2 (10)
N/A	1 (5)
Country of treatment	
Albania	13 (59)
Out of country	9 (41)
Enucleation	
Yes	20 (91)
No	1 (4.5)
N/A	1 (4.5)
Metastasis	
Central nervous system	6 (27)
Stage IV	2 (9)
No	13 (59)
N/A	1 (5)

DISCUSSION

We present the first report on the burden of RB in Albania over a 25-year study period. The observed incidence in Albania is less compared to other European countries, which has been approximated to be 1 in 13 844 live births.[12] Albania was expected to have approximately 41.5-50.3 cases for its birth rate during the study time period.[1,10,3] However, only 22 cases were observed, suggesting an underreporting effect. Moreover, this may be due to many patients leaving the country at the first suspicion of diagnosis to continue treatment and follow-up overseas, primarily in Italy, Türkiye, and Switzerland, which are known to have higher standards of care. For this reason, they are not reported in Albania, reducing the reported incidence rates in our country.

With the geographic distribution of cases matching the population density, and more than half originating from central Albania, this report supports centralizing RB services in the country. This, coupled with targeted efforts to establish screening programs and referral pathways, would help bridge potential diagnostic gaps and ensure equitable access to early diagnosis and specialized treatment for children in remote areas of Albania.

Age at diagnosis was under 1 year of age in 59% of cases, but the median age at diagnosis of this cohort was 21.8 months. Less than 5% of cases were over 5 years old, comparable with world data, and the oldest diagnosed patient was 6 years old.[1,2] Regarding inheritance pattern, 18% of our patients had a known family history of a brother or a sister previously diagnosed with RB. However, genetic testing was not performed and therefore we could not confirm germline mutations. Moreover, with 41% of bilateral RB reported in our study group, these findings suggest that heritable forms of the disease are prevalent in Albania, highlighting the need to expand genetic services in the country.[1,13]

Clinical presentation paralleled other studies worldwide, with leukocoria as the main presenting sign, found in 40% of our cases at the first visit or as the primary complaint, followed by strabismus, found in 27% of our sample. Other less frequent presenting symptoms in our cohort included eye pain, vision loss, eye swelling, eye redness, and heterochromia.[14,15] No cases of RB in our cohort were detected early through screening, which could have reduced the extent of extraocular involvement. Moreover, establishing a robust referral system for RB, improving access to specialized care, and integrating pediatric and ophthalmology services could help address the issue of late presentation in these children.

Tumor staging at presentation could not be assessed due to inconsistencies in clinical recording between different clinics and 10 patients missing any staging information in their reco rds.[15,16,17] Out of the 12 cases with complete follow-up data, 8 children experienced extraocular involvement or relapsed

with metastasis. This ratio is very high compared to developed countries, where metastatic disease in RB is low.[18,19] In the 2017 Retinoblastoma Global Study, which included a cohort of 4064 patients from 149 countries, the presentation at stage cT4 with extraocular spread ranged from 0.8% in higher-income countries to 42% in lower-income countries, highlighting significant disparities in early diagnosis and access to care.[4] In our study, the optic nerve was affected in 10 of our cases (45%).[20] Therefore, these findings underscore the paramount significance of establishing a unified pediatric cancer registry with standardized data collection, independent of the ophthalmology treating center. Additionally, it is crucial to develop an integrated healthcare system characterized by strong collaboration among all specialties.[21]

In our cohort, nearly all patients underwent enucleation of 1 eye, with 13% requiring enucleation of both eyes. Enucleation is a common life-saving procedure for RB worldwide, with a prevalence of 65% reported in the Global Retinoblastoma Study Group. However, bilateral enucleation occurs in only 3% of cases globally, significantly contributing to the burden of disability.[4,13] Local treatment modalities such as cryotherapy, brachytherapy, laser therapy, intra-arterial chemotherapy, and intravitreal chemotherapy—commonly used for low-risk tumors or refractory and recurrent seeding—have not yet been introduced in Albania.[2,16,17] Implementing local treatment modalities will be a significant advancement in preserving both the globe and vision.

This study presents several limitations. Since approximately 59% of patients were treated in Albania, and the rest overseas, complete follow-up information was difficult to acquire, thereby providing accurate reported outcome measures, including metastasis and mortality rates. Overall, our underreported cohort, advanced patient stage, limited treatment options, and incomplete follow-up data underscore the urgent need for measures to improve outcomes to levels comparable to developed countries.

CONCLUSION

Retinoblastoma, even though a rare disease, carries a high mortality burden if diagnosed late, especially in low-income countries with limited diagnostic and treatment resources. During the last 25 years, Albania had a high percentage of patients with advanced and metastatic disease. This warrants comprehensive screening programs across the country to facilitate earlier diagnosis, an integrated healthcare system, and introduction of new treatment modalities for a better outcome in these children.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Country Ethics Committee at the Ministry of Health in Albania (approval no.: 66/51, date: September 9, 2024).

Informed Consent: Verbal informed consent was obtained from the patients' parents who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.D., D.B.; Design – D.B., E.H.; Supervision – A.G., M.Xh.; Resources – M.K., E.R.; Materials – M.T, L.S.H.; Data Collection and/or Processing – E.H., A.T; Analysis and/or Interpretation – E.H., E.P.; Literature Search – D.B., A.B.; Writing – E.D., D.B.; Critical Review – M.A., I.D.F.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: This study received no funding.

REFERENCES

1. Fabian ID, Sagoo MS. Understanding retinoblastoma: epidemiology and genetics. *Community Eye Health*. 2018;31(101):7.
2. Lohmann DR, Gallie BL. Retinoblastoma. 2000 Jul 18 [Updated 2023 September 21]. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. *GeneReviews® [Internet]*. University of Seattle (WA): Washington, Seattle; 1993-2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1452/.
3. 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;111(6):1228-1232. [CrossRef]
4. Global Retinoblastoma Study Group. The Global Retinoblastoma Outcome Study: a prospective, cluster-based analysis of 4064 patients from 149 countries. *Lancet Glob Health*. 2022;10(8):e1128-e1140. [CrossRef]
5. Arazi M, Baum A, Casavilca-Zambrano S, et al. Treatment outcomes and definition inconsistencies in high-risk unilateral retinoblastoma. *Am J Ophthalmol*. 2024;268:399-408. [CrossRef]
6. INSTAT: Albania in figures 2022. Available at: https://www.instat.gov.al/en/children-and-youth-official-statistics/population/crude-birth-rate-per-1-000-number/.
7. World Health Organization. (n.d.). Albania health system information. Geneva: World Health Organization; Available at: https://eurohealthobservatory.who.int/countries/albania#:~:text=In%202022%2C%20Albania%20had%2043,located%20in%20Tirana%2C%20the%20capital.
8. Mone I, Vasil S, Alia A, Xinxo S, Muça K, Burazeri G. Socio-demographic correlates of barriers to access healthcare services among children in post-communist Albania. *Sustainability*. 2023;15(11):8455. [CrossRef]
9. Mati K, Pozzo C, Cekani E, et al. Gynecological malignancies in Albania: the challenges of cancer care in a low resource country. *Clin Exp Obstet Gynecol*. 2023;50(7):139. [CrossRef]
10. INSTAT. Population of Albania Jan. 2023. Available at: //efaidnbmnnnibpcajpcglclefindmkaj/https://www.instat.gov.al/media/11654/population-of-albania-on-1-january-2023.pdf.
11. Fabian ID, Reddy A, Sagoo MS. Classification and staging of retinoblastoma. *Community Eye Health*. 2018;31(101):11-13.
12. Stacey AW, Bowman R, Foster A, et al. Incidence of retinoblastoma has increased: results from 40 European countries. *Ophthalmology*. 2021;128(9):1369-1371. [CrossRef]
13. Stacey AW, Clarke B, Moraitis C, et al. The incidence of binocular visual impairment and blindness in children with bilateral retinoblastoma. *Ocul Oncol Pathol*. 2019;5(1):1-7. [CrossRef]
14. Abramson DH, Beaverson K, Sangani P, et al. Screening for retinoblastoma: presenting signs as prognosticators of patient and ocular survival. *Pediatrics*. 2003;112(6 Pt 1):1248-1255. [CrossRef]
15. Butros LJ, Abramson DH, Dunkel IJ. Delayed diagnosis of retinoblastoma: analysis of degree, cause, and potential consequences. *Pediatrics*. 2002;109(3):E45. [CrossRef]

16. Lin P, O'Brien JM. Frontiers in the management of retinoblastoma. *Am J Ophthalmol*. 2009;148(2):192-198. [CrossRef]
17. National Institutes of Health – National Cancer Institute. Available at: https://www.cancer.gov/types/retinoblastoma/hp/retinoblastoma-treatment-pdq#_813_toc.
18. Finger PT, Harbour JW, Karcioglu ZA. Risk factors for metastasis in retinoblastoma. *Surv Ophthalmol*. 2002;47(1):1-16. [CrossRef]
19. Mohney BG, Robertson DM. Ancillary testing for metastasis in patients with newly diagnosed retinoblastoma. *Am J Ophthalmol*. 1994;118(6):707-711. [CrossRef]
20. Shields CL, Shields JA, Baez K, Cater JR, De Potter P. Optic nerve invasion of retinoblastoma. Metastatic potential and clinical risk factors. *Cancer*. 1994;73(3):692-698. [CrossRef]
21. McIntyre A, Chandrakanth ARE. Cancer on the global stage: incidence and cancer-related mortality in Albania. The ASCO post. 2016. Available at: https://ascopost.com/issues/november-25-2016/cancer-on-the-global-stage-incidence-and-cancer-related-mortality-in-albania/.