ORIGINAL ARTICLE

OPEN ACCESS

CLINICAL PROFILE AND TREATMENT OUTCOMES OF RETINOBLASTOMA EXPERIENCE FROM A LOW-INCOME COUNTRY

Ayesha Latif[1],Hafiz Abdul Qaddus [2],Iqra Tariq[3],Benish Hira[4], Fozia Syed Rasool[5],Shakeel Ahmed[6]

[1,2,3,4,5,6-]Department of Pediatric Oncology-CMH, Rawalpindi

ABSTRACT

Background: Retinoblastoma (RB) is the most common intraocular malignancy in children representing 3% of all pediatric malignancies. Retinoblastoma affects very young children: two-thirds of the cases are diagnosed before 2 years of age and more than 90% before 5 years.

Objectives: To assess the demographic, clinical, and histopathological characteristics of pediatric retinoblastoma patients and to evaluate the association of age with disease presentation and tumor features.

Study Design and Setting : This retrospective descriptive study was conducted at the Paediatric Oncology Department of Combined Military Hospital (CMH), Rawalpindi, Pakistan, encompassing medical records from November 1, 2016, to February 29, 2024.

Material and Methods: This Study was conducted retrospectively at the Paediatric Oncology Department of Combined Military Hospital (CMH), Rawalpindi, Pakistan. IBM SPSS Statistics for Windows, version 25.0 (released 2017, IBM Corp., Armonk, NY) was used for statistical analysis. The descriptive analysis calculated frequencies and percentages for categorical variables, and the median (IQR) was for continuous variables. The chi-square test was used to associate age with RB characteristics in univariate analysis. P- values of <0.05 were considered significant.

Results: 96 patients admitted to the pediatric oncology department of CMH Rawalpindi were included in the study. The median age at presentation was 24 months. The most common presenting symptom was leukocoria in 67(69.8%), strabismus in 9 (9.4%), vision loss in 11 (11.5%), and proptosis in 9(9.4%). Extraocular disease was present in 24(25%). The grouping of Intraocular disease based on IIRC showed stage E as predominant with n=80(84%). Metastatic disease was present in 18(18.8%). Enucleation was done in 73(76.0%). With a median follow-up of 71 months, 19 patients died. Kaplan Meier's Survival showed an Overall survival of 83%.

Conclusion: Raising awareness and implementing screening for retinoblastoma are essential for diagnosing the disease at an intraocular stage, which can significantly improve survival rates in developing countries.

Keywords: malignancy, pediatric malignancies, Paediatric Oncology

How to cite this article: Latif A, Qaddus HA, Tariq I, Hira B, Rasool FS, Ahmed S. Clinical profile and treatment outcomes of retinoblastoma: Experience from a low-income country. **J Bacha Khan Med Coll**.2024;5(2):**157-165.**

Correspondence Author: Ayesha Latif
Fellow, Department of Pediatric Oncology-CMH, Rawalpindi
E-mail: ayeshalatif088@gmail.com
https://orcid.org/0009-0001-9309-4098

Received: 11th October, 2024
Revised: 12th November, 2024
Accepted: 13th December, 2024
Published: 1st January, 2025
DOI: https://doi.org/10.69830/jbkmc.v5i02.175

INTRODUCTION:

Retinoblastoma (RB) is the most common intraocular malignancy in children. It represents 3% of all pediatric malignancies [1]. It has a global incidence of 1:20,000 live births [2] National data regarding the incidence of RB in Pakistan is not available but the annual crude incidence of RB is 4/100000 in children under 5 years in Karachi, Pakistan [3]. In developed countries, the survival is more than 90% owing to diagnosis at an intraocular stage however in the Asian and African subcontinent where high tumor burden and advanced presentation are common the survival rates are poor [4,5]. Retinoblastoma affects very young children: two-thirds of the cases are diagnosed before 2 years of age and more than 90% before 5 years [6].Retinoblastoma can occur as a unilateral or bilateral tumor. The most common presenting symptoms of retinoblastoma are leukocoria followed by strabismus, decreased vision, anterior chamber inflammatory signs, spontaneous hyphema, and proptosis but the incidence of proptosis and metastasis as the leading presenting symptom is reported in developing countries [7,8,9]. The International Intraocular Retinoblastoma Classification (IIRC) was developed to stage intraocular disease and to describe the clinical response to chemotherapy. In this system, Retinoblastoma is staged from group A through E, with group A eyes having limited disease and better survival and group E disease having extensive disease and poor outcomes when managed with only chemotherapy [10]. Conservative modalities like systemic, intraocular, intra-arterial chemotherapy, radiotherapy as well and focal therapies including cryotherapy and brachytherapy are used as eye salvage approaches in case of tumors at early stages of presentation however enucleation remains the mainstay of treatment in advanced tumors [11]. External Beam Radiotherapy (EBRT) is considered an adjuvant therapy in large tumors, those with vitreous seeding and multifocal retinoblastoma [12].Although Retinoblastoma is a major health burden in developing countries, data regarding its clinical presentation and staging are scarce. The main objective of this study was to provide a comprehensive analysis of various modes of presentation in a resource-limited setting over seven years.

MATERIAL AND METHODS:

Study Design and Setting

This retrospective descriptive study was conducted at the Paediatric Oncology Department of Combined Military Hospital (CMH), Rawalpindi, Pakistan, encompassing medical records from November 1, 2016, to February 29, 2024.

Study Population

The study included newly diagnosed retinoblastoma patients aged one month to 15 years who had not received prior chemotherapy, confirmed via examination under anesthesia by a consultant ophthalmologist during the study period.

Ethical Approval Statement

Ethical approval was obtained from the Institutional Review Board of CMH Rawalpindi, Pakistan the Institutional Review Board **(IRB)under-Ref-no-CMH-730-04-015).**Informed consent was secured from parents/guardians. Patient data, including demographics, clinical history, and diagnostic evaluations, were collected. Diagnosis and staging were performed using MRI, EUA, and B-scan. Confidentiality and ethical research standards were strictly maintained. The initial workup included a full blood count and biochemical profile including hepatic and renal function tests. The diagnosis of retinoblastoma was made using MRI with contrast orbit and brain protocol under GA/sedation along with Examination under anesthesia (EUA) and B-scan that includes documentation of IIRC stage. Cerebrospinal fluid (CSF) examination and bilateral Bone Marrow aspirate and biopsy were done for patients with IIRC group E and extraocular RB. The patients were categorized into intraocular (IO) and extraocular (EO) disease and further staging of IO disease was done using IIRC. The patient was labeled as having EO disease if there was overt extra orbital disease on examination or MRI, trans scleral invasion, or lymph node involvement. Patients were treated according to the Children's Cancer and Leukaemia Group Retinoblastoma Working Group guidelines for managing children with intraocular retinoblastoma published in 2008. Unilateral Retinoblastoma with stage A was treated with focal therapy alone while groups B and C were treated with 6-9 cycles of JOE chemotherapy comprising of vincristine 1.5mg/m2, carboplatin 600mg/m2, and etoposide 300mg/m2.Group D and E disease were treated primarily with Enucleation and Adjuvant chemotherapy with JOE, unless enucleation was refused by the guardian in which a prior trial of Neoadjuvant chemotherapy with 2 cycles of JOE followed by reassessment was done. Stage E disease involves the involvement of the cut end of the optic nerve, and radiotherapy is also received. In the case of bilateral tumors, the treatment of each eye depends on the presenting stage in the individual eye. EO disease was treated with concomitant radiotherapy. Patients who relapsed or had the progressive disease were

subsequently treated with IVADo.IVADo regimen included ifosfamide 3g/m^2 on Days 1 and 2, vincristine 1.5 mg/m^2 on Day 1, actinomycin D 1.5mg/m^2 on Day 1, and doxorubicin on 30mg/m^2 on Days 1 and 2.

Inclusion Criteria:

All cases of newly diagnosed Retinoblastoma (Diagnosed on Examination Under Anesthesia by an ophthalmologist) from one month to 15 years of age enrolled between November 1, 2016, and February 29, 2024.

Previously not treated via chemotherapy (Focal or Systemic).

Exclusion Criteria:

- Patients with a diagnosis of retinoblastoma but subsequently lacking follow-up data.
- Patients who had already received chemotherapy at another center.
- Relapsed Retinoblastoma

STATISTICAL ANALYSIS

IBM SPSS Statistics for Windows, version 25.0 (released 2017, IBM Corp., Armonk, NY) was used for statistical analysis. The descriptive analysis calculated frequencies and percentages for categorical variables, and the median (IQR) was for continuous variables. In univariate analysis, the chi-square test was used to associate age with RB characteristics. P-values of <0.05 were considered significant

RESULTS:

During the period, of November 1, 2016, and February 29, 2024, 96 patients admitted to the pediatric oncology department of CMH Rawalpindi were included in the study. The median age at presentation was 24 months (IQR:1- 108). Data stratification was done in 3 age groups 53(55.2%) presented before 2 years,41(42.7%) in 25-60 months age group, and 2 (2.1%) above 60 months. Of these, 54 (56.3%) were males,42 (43.8%) were females,49 (51%) had unilateral disease and 47 (49%) had bilateral disease.

Table 1: Baseline Characteristics of Retinoblastoma

Characteristics		N (%)
Total no of patients		96(100)
Gender	Male	54(56.3)
	Female	42(43.8)
Age	1-24 months	53(55.2)
	60-180 months	41(42.7)
	60-180 months	2(2.1)
Laterality	Unilateral	49(51)
	Bilateral	51(49)
Symptom	Leukocoria	67(69.8)
	Strabismus	9(9.4)
	Vision loss	11(11.5)
	Proptosis	9(9.4)
Metastasis	Yes	18(18.8)
	No	78(81.2)
Relapse	Yes	5(5.2)
	No	91(94.7)

The most common presenting symptom was leukocoria in 67(69.8%), strabismus in 9 (9.4%), vision loss in 11 (11.5%), and proptosis in 9(9.4%). Extraocular disease was present in 24(25%). The grouping of Intraocular disease based on IIRC is presented in Figure 1 with stage E as predominant with n=80(84%). Metastatic disease was present in 18(18.8%). Regarding treatment,85(88.5%) received JOE chemotherapy while 11(11.5%) cases were given IVADo chemotherapy. Focal therapy mainly IAC chemo was given to 11(11.5%). Enucleation was done in 73(76.0%), and EBRT was given to 10(10.4%). Retinoblastoma relapsed in n=5(5.2%).When we performed stratification analysis and applied chi-square index with a value of 0.05, leukocoria was the predominant symptom in most patients n=67(69.7%) with a p-value of 0.02. In n=72(75%) disease was intraocular with a p-value of 0.001. The Association of RB with different age groups is summarized in Table2. The majority of patients with leukocoria presented with stage E n=58(60.4%) while all the patients with proptosis had stage E disease (Figure 2).

Figure 1:IIRC Grouping of Retinoblastoma

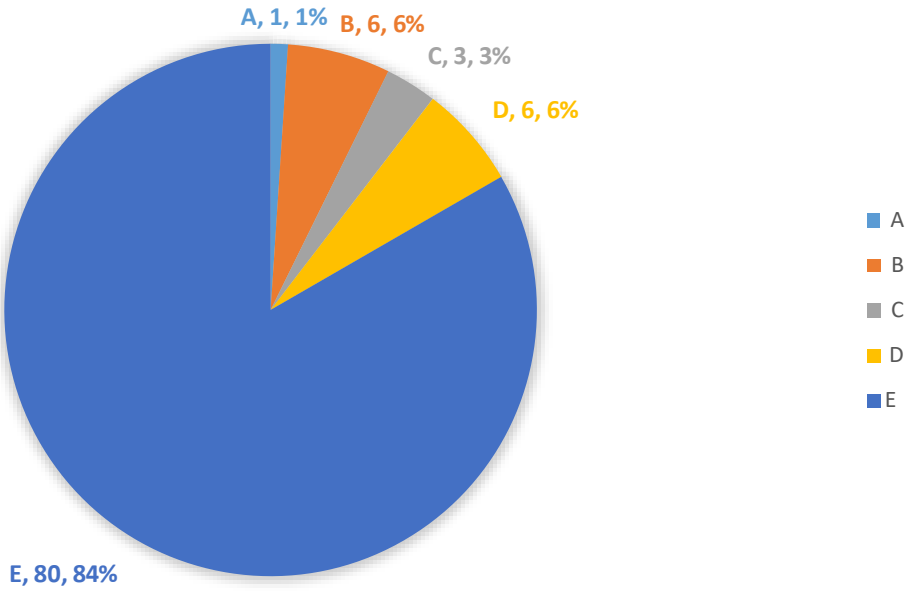
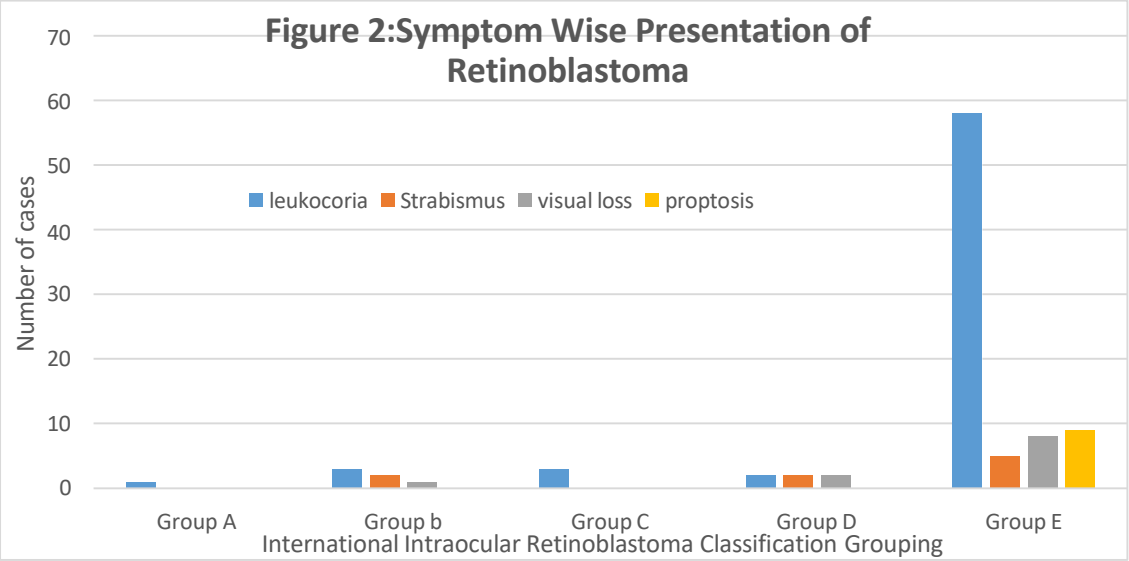


Table 2:Association of Retinoblastoma Characteristics with Age

Characteristic Of RB			Category			
			1-24 m	25-60 m	+61 m	
		n(%)	n (%)	n (%)	n (%)	p-value (Chi-Square <0.05)
Total Number of patients		96(100)	53(55.2)	41(42.7)	2(2.0)	
Laterality	Unilateral	49(51.0)	24(45.3)	23(56.1)	2(100)	0.219
	Bilateral	47(49.0)	29(54.7)	18(43.9)	0(0.0)	
Group	A	1(1.0)	1(1.9)	0(.0)	0(0.0)	0.873
	B	6(6.2)	5(9.4)	1(2.4)	0(0.0)	
	C	3(3.1)	1(1.9)	2(4.9)	0(0.0)	
	D	6(6.2)	3(5.7)	3(7.3)	0(0.0)	
	E	80(83.3)	43(81.1)	35(85.4)	2(100)	
Symptoms	Leukocoria	67(69.7)	37(69.8)	28(68.3)	2(100)	0.023

	Strabismus	9(9.3)	9(17.0)	0(0.0)	0(0.0)	
	Vision loss	11(11.4)	2(3.8)	9(22.0)	0(0.0)	
	Proptosis	9(9.3)	5(9.4)	4(9.8)	0(0.0)	
Metastasis	Yes	18(18.7)	6(11.3)	12(29.3)	0(0.0)	0.069
	No	78(81.2)	47(88.7)	29(70.7)	2(100)	
Extraocular	Yes	24(25.0)	6(11.3)	18(43.9)	0(0.0)	0.001
	No	72(75.0)	47(88.7)	23(56.1)	2(100)	
Enucleation	Yes	73(76.0)	36(67.9)	35(85.4)	2(100)	0.105
	No	23(23.9)	17(32.1)	6(14.6)	0(0.0)	



Treatment Outcomes:

When we compared the outcomes of different treatment modalities like systemic chemotherapy (p-value=0.143), Enucleation (p-value=0.784), Focal treatments like laser or intraarterial chemotherapy (p-value =0.165), and EBRT (p-value=0.001) as depicted in Table 3.

Table 3: Treatment Based Outcomes of Retinoblastoma

Treatment modality		Alive	Expired	P-value (Chi-square test)
		n (%)	n (%)	
Total Number of patients		77(80.2)	19(19.8)	
Chemo	JOE	70(90.9)	15(78.9)	0.143
	IVADO	7(9.1)	4(21.1)	
Enucleation	Yes	58(75.3)	15(78.9)	0.740
	No	19(24.7)	4(21.1)	
Focal	Yes	14(18.2)	1(5.3)	0.165
	No	63(81.8)	18(94.7)	
EBRT	Yes	4(5.2)	6(31.6)	0.001
	No	73(94.8)	13(68.4)	

With a median follow-up of 71 months, 19 patients died. Among these, 9 (47.3%) had metastatic disease, 5 (26.3%) experienced a relapse, 4 (21.0%) had refractory disease, and 1 (5.2%) patient died from Ifosfamide-induced neurotoxicity (Treatment-Related Mortality). The most common site of metastasis was CNS in 6(66.6%),2 in Bone marrow (22.2% and 1 (11.1%) had involvement of multiple sites. Kaplan Meier's Survival showed an Overall survival of 83% shown in Figure 3. The patient sex (p-value: 0.54), laterality (p-value: 0.48), and IIRC grouping (p-value: 0.27) were not statistically significant. However, extraocular disease (p-value: 0.045) and metastatic spread (p-value: 0.010) were identified as significant predictive factors as depicted in Figure 4.

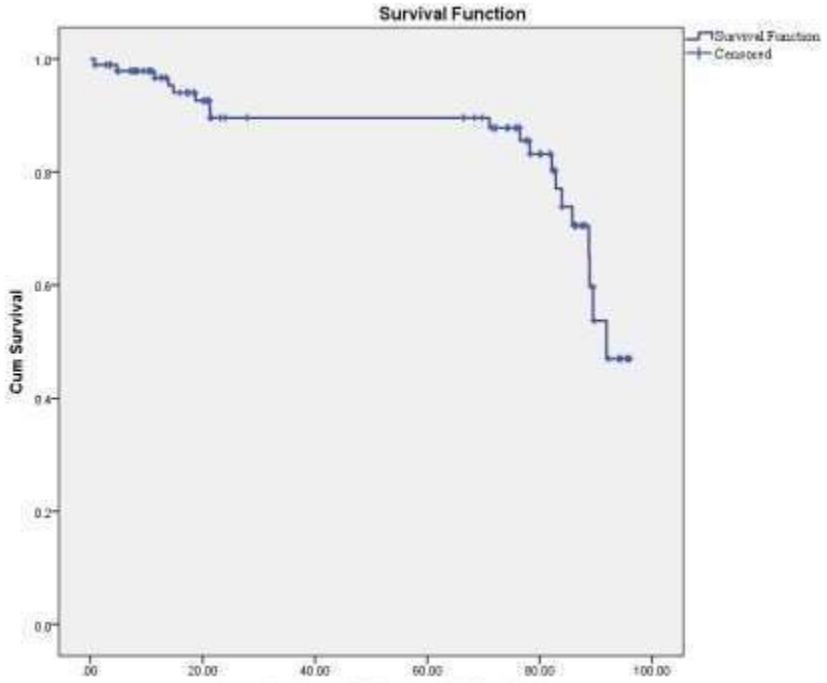


Figure 3:Overall Survival (Months)

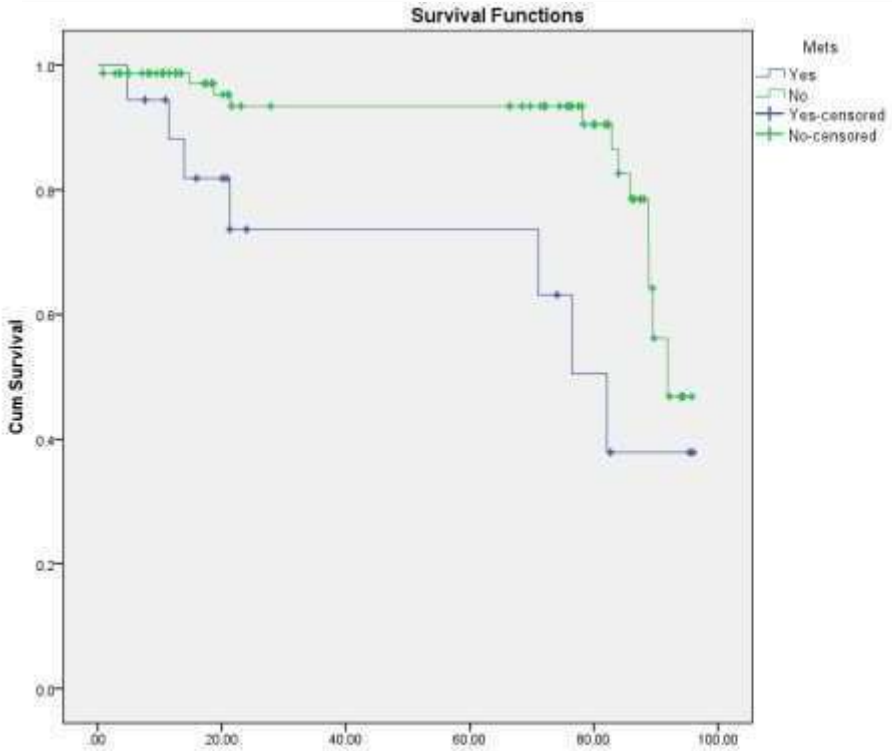


Figure 4:Association of Overall Survival and Metastasis

DISCUSSION:

Retinoblastoma is the most common intraocular malignancy in pediatrics. Although no definite racial or geographic variation has been noted, the greatest disease burden is noted in Asia and Africa owing to a large population with high birth rates [13]. Clinical presentation and treatment outcomes show a wide variation between developed and developing countries. When ocular salvage is a priority in developed countries, death from retinoblastoma is still a major concern in developing countries [14]. The Paediatric Oncology Department of Combined Military Hospital -Rawalpindi, Pakistan is one of the largest cancer care setups in our country with an annual turnover of 350 new cases. We conducted a prospective study to understand the presentation and outcomes of patients in Pakistan.The median age of presentation in our study was 24 months, which is similar to the age reported by Gao et al. in China [15]. Our study reported that 95% of Rb patients present before 5 years which is in congruence with previous literature [6]. Although Retinoblastoma does not have a sex predilection as proven by various studies [16], our study showed a slight male preponderance. This finding is attributed to the cultural and socioeconomic constraints on the health of a female child in our region [17]. Our findings of unilateral disease in more cases than bilateral disease is supported by the work of Limbu et al and others. Leukocoria was the main presenting symptom in our study, which was also supported by the research conducted in Karachi, Pakistan.[18]. Leukocoria was seen in 22.6% to 97.9% of patients with retinoblastoma at the time of presentation while strabismus was noted in 5.6% to 26% [19]. However, some studies from Pakistan have reported proptosis as the predominant presenting sign in contrast to our pattern of presentation [20]. The presence of extraocular disease in 25% of patients is also similar to that reported by another study conducted by Chantada et al., in which the differences in the presentation of RB between developed and developing countries were highlighted [21]. The presence of advanced Group E disease is consistent with a previous study from Ethiopia, where Group D and E diseases combined were found in 73% of patients [22]. This is different from data in developed countries, where most patients belong to groups B through D [23].Eye salvage depends on the stage of RB at diagnosis. Since most of our patients had advanced disease at the presentation Enucleating with or without neoadjuvant chemotherapy was given in 76% of cases. In a study by Kaliki et al., systemic chemotherapy was the most commonly used primary treatment modality in cases of advanced disease to salvage the eye [24]. The risk-benefit ratio of globe salvage versus enucleation should be carefully assessed, as eyes with such advanced tumors may harbor high-risk retinoblastoma, which can be fatal. The high percentage of enucleation in our patients highlights the necessity of implementing awareness programs at the primary healthcare level and within the general public for early disease identification. In the age of smartphones leukocoria as the presenting sign is easy to pick both by the parent and primary health care provider. The role of External Beam Radiotherapy as a treatment option has shrunk owing to the high risk of secondary malignancies with its use. In our study, only 10% of patients received EBRT, which is consistent with previous literature [25]. Focal therapies including intraarterial chemotherapy (IAC) are being increasingly used in the treatment of retinoblastoma. The high efficacy of intraarterial chemotherapy is attributed to the concentration of chemotherapeutics in ocular issues with IAC several times compared to systemic chemotherapy with a minimum adverse effect profile [26]. However, this was used in only 15% of our patients owing to advanced diseasepresentation and the limited availability of focal treatment options in our setup. Retinoblastoma is a treatable cancer, with an overall survival rate of about 97.8% in Europe, compared to 89.6% in India and 64.5% in Pakistan [27]. In our study, the survival rate was 83%, primarily because most patients presented with advanced disease. Zia et al. reported that extraocular disease and metastasis are associated with poor outcomes, which aligns with our findings [28].The main limitations in our country stem from the lack of focal therapies, palliative care facilities, and resource constraints, which result in poorer curative outcomes. The small size of the study population led to inconclusive results, highlighting the need for a multicenter collaborative trial. Such a trial would help identify additional risk factors associated with poor outcomes in developing countries and determine the necessary interventions to ensure early diagnosis.

.

CONCLUSION:

Raising awareness and implementing screening for retinoblastoma are essential for diagnosing the disease at an intraocular stage, which can significantly improve survival rates in developing countries. Furthermore, there is a need to include focal treatments to minimize the side effects of systemic chemotherapy when the disease is presented at an early stage.

ACKNOWLEDGMENTS:

The authors acknowledge pediatric oncology physicians, pharmacists, medical teams, nurses, and data managers at the Department of Pediatric Oncology, Combined Military Hospital, and Rawalpindi, Pakistan

Disclaimer: Nil

Conflict of Interest: Nil

Funding Disclosure: Nil

Authors Contribution

Concept & Design of Study: Ayesha Latif,Hafiz Abdul Qaddus ,

Drafting: Iqra Tariq,Benish Hira,

Data Analysis: Fozia Syed Rasool,Shakeel Ahmed

Critical Review: Fozia Syed Rasool5,Shakeel Ahmed6

Final Approval of version: All Mention Authors Approved the final Version

REFERENCES:

1. The Global Retinoblastoma Outcome Study: a prospective, cluster-based analysis of 4064 patients from 149 countries. The Lancet Global health. 2022;10(8):e1128-e40.

2. Arazi M, Baum A, Casavilca-Zambrano S, Alarcon-Leon S, Diaz-Coronado R, Ahmad A, et al. Treatment Outcomes and Definition Inconsistencies in High-Risk Unilateral Retinoblastoma. American journal of ophthalmology. 2024;268:399-408.

3. Buaboonnam J, Narkbunnam N, Vathana N, Takpradit C, Phuakpet K, Pongtanakul B, et al. Outcomes of pediatric retinoblastoma treated with ICEV regimen: A single-center study. Pediatric hematology and oncology. 2019;36(2):73-81.

4. Camp DA, Dalvin LA, Schwendeman R, Lim LS, Shields CL. Outcomes of neonatal retinoblastoma in pre-chemotherapy and chemotherapy eras. Indian journal of ophthalmology. 2019;67(12):1997-2004.

5. Fabian ID, Onadim Z, Karaa E, Duncan C, Chowdhury T, Scheimberg I, et al. The management of retinoblastoma. Oncogene. 2018;37(12):1551-60.

6. Ghose N, Agarwal P, Palkonda VAR, Kaliki S. RETINOBLASTOMA ASSOCIATED WITH TOTAL EXUDATIVE RETINAL DETACHMENT: Treatment and Outcomes. Retina (Philadelphia, Pa). 2023;43(5):808-14.

7. Gündüz AK, Mirzayev I, Temel E, Ünal E, Taçyıldız N, Dinçaslan H, et al. A 20-year audit of retinoblastoma treatment outcomes. Eye (London, England). 2020;34(10):1916-24.

8. Handayani K, Indraswari BW, Sitaresmi MN, Mulatsih S, Widjajanto PH, Kors WA, et al. Treatment Outcome of Children with Retinoblastoma in a Tertiary Care Referral Hospital in Indonesia. Asian Pacific journal of cancer prevention : APJCP. 2021;22(5):1613-21.

9. Janic A, Vincent A, Stinson J, Dimaras H. Values of Retinoblastoma Survivors and Parents Regarding Treatment Outcomes: A Qualitative Study. JCO oncology practice. 2022;18(6):e1000-e15.

10. Kheir WJ, Slim A, Hadi DE, Bechara E, Borghol R, Noun D, et al. Treatment outcomes in retinoblastoma and the effect of tumor topography. Pediatric blood & cancer. 2024;71(12):e31334.

11. Kim HM, Lee BJ, Kim JH, Yu YS. Outcomes of Cataract Surgery Following Treatment for Retinoblastoma. Korean journal of ophthalmology : KJO. 2017;31(1):52-7.

12. Kruger M, van Elsland SL, Afungchwi GM, Bardin R, Njodzeka B, Kouya F, et al. Outcome of retinoblastoma treatment protocol in Cameroon as per SIOP-PODC recommendation for a low-income setting. Pediatric blood & cancer. 2022;69(8):e29642.

13. Leclerc R, Olin J. An Overview of Retinoblastoma and Enucleation in Pediatric Patients. AORN journal. 2020;111(1):69-79.

14. Moin M, Malik TG, Siddiq L. Clinical Patterns And Outcomes Of Retinoblastoma In A Tertiary Care Centre Of A Developing Country. JPMA The Journal of the Pakistan Medical Association. 2023;73(9):1881-3.

15. Nag A, Khetan V. Retinoblastoma - A comprehensive review, update and recent advances. Indian journal of ophthalmology. 2024;72(6):778-88.

16. Negretti GS, Quhill H, Duncan C, Chowdhury T, Stoker I, Reddy MA, et al. Ruthenium plaque radiotherapy in the current era of retinoblastoma treatment. Ophthalmic genetics. 2022;43(6):756-61.

17. Payne JF, Hutchinson AK, Hubbard GB, 3rd, Lambert SR. Outcomes of cataract surgery following radiation treatment for retinoblastoma. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus. 2009;13(5):454-8.e3.

18. Raval V, Kaliki S. Cavitary retinoblastoma: A review of literature. Survey of ophthalmology. 2022;67(3):723-8.

19. Raval V, Singh A. Management of retinoblastoma: are we there yet? Canadian journal of ophthalmology Journal canadien d'ophtalmologie. 2024;59(6):376-9.

20. Reynolds MM, Sein J, Hayashi R, Lueder G. Treatment of small and medium retinoblastoma tumors with Iris diode laser. European journal of ophthalmology. 2021;31(6):3318-23.

21. Santapuram PR, Schremp EA, Friedman DL, Koyama T, Froehler MT, Daniels AB. Adverse Events, Treatment Burden, and Outcomes of Intravenous versus Intra-arterial Chemotherapy for Retinoblastoma. Ophthalmology Retina. 2021;5(3):309-12.

22. Sengupta S, Pan U, Khetan V. Adult onset retinoblastoma. Indian journal of ophthalmology. 2016;64(7):485-91.

23. Singh G, Daniels AB. Disparities in Retinoblastoma Presentation, Treatment, and Outcomes in Developed and Less-Developed Countries. Seminars in ophthalmology. 2016;31(4):310-6.

24. Singh S, Nishath T, Fabian ID, Li X, Othus M, Tzukikawa M, et al. Seasonal Variation in the Diagnosis of Retinoblastoma. Ophthalmic epidemiology. 2023;30(5):509-14.

25. Stacey AW, De Francesco S, Borri M, Hadjistilianou T. The Addition of Topotecan to Melphalan in the Treatment of Retinoblastoma with Intra-arterial Chemotherapy. Ophthalmology Retina. 2021;5(8):824-30.

26. Stathopoulos C, Sharkawi E, Stappler T, Munier FL. Goniosynechialysis for the treatment of angle-closure glaucoma in retinoblastoma. Clinical & experimental ophthalmology. 2023;51(7):739-42.

27. Tomar AS, Finger PT, Gallie B, Kivelä TT, Mallipatna A, Zhang C, et al. Global Retinoblastoma Treatment Outcomes: Association with National Income Level. Ophthalmology. 2021;128(5):740-53.

28. Warda O, Naeem Z, Roelofs KA, Sagoo MS, Reddy MA. Retinoblastoma and vision. Eye (London, England). 2023;37(5):797-808.