Original Article

Clinical Staging of Retinoblastoma at Presentation: A Frequency Analysis

Farhat Khan[1], Aziz-ur-Rehman[2], Baby Nisha[3], Kunza Zahid[4]
[1-4]Jinnah Postgraduate Medical Center, Karachi

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ABSTRACT

Purpose: To determine the frequency of different clinical stages of retinoblastoma at the time of initial presentation.

Study Design: Retrospective study.

Place and Duration of Study: Jinnah Postgraduate Medical Center, Karachi from June 2024 to February 2025.

Methods: Records of patients with confirmed diagnosis of retinoblastoma were reviewed. There were 85 patients who qualified the inclusion criteria. Data included staging of retinoblastoma at presentation using Intraocular Retinoblastoma Classification (IIRC), age at presentation, gender, laterality (unilateral or bilateral) and comprehensive ocular examination details. For patients with bilateral disease, each eye was staged individually, resulting in a total of 114 eyes for analysis. Demographic details such were also retrieved.

Results: Among 85 retinoblastoma patients (114 eyes), the most common stage at presentation was Group D (42.1%) followed by Group E (32.4%). None of the patients had Group A retinoblastoma. Groups B and C were frequent in bilateral cases (32.8%). Mean age at presentation was 2.6±1.4 years, and52.9% were male. Bilateral cases demonstrated a shorter symptom duration (6.7 vs. 9.1 weeks, p = 0.02) and a higher frequency of positive family history (24.1% vs. 3.6%, p = 0.004). No significant association was observed between gender and disease stage.

Conclusion: Most of the retinoblastoma patients presented in advanced stages (Group D and E), indicating delayed diagnosis and referral. These findings highlight the need for increased awareness, early screening, and improved access to specialized ocular oncology services.

Keywords: Retinoblastoma, Malignancy, Pakistan, Oncology, Neoplasm.

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Correspondence: Farhat Khan
Jinnah Postgraduate Medical Center, Karachi
Email: zoonizaqi@gmail.com

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INTRODUCTION

Retinoblastoma is the most common primary intraocular malignancy of childhood, accounting for approximately 3% of all pediatric cancersand11% of cancers diagnosed in the first year of life.[1] It arises from biallelic inactivation of the RB1 tumor suppressor gene located on chromosome 13q14. The disease can present unilaterally or bilaterally and may occur sporadically or as part of a heritable syndrome.[2,3] Early diagnosis and timely intervention are crucial for improving survival, preserving vision, and reducing treatment-related morbidity. Globally, the incidence of retinoblastoma is estimated at 1 in 15,000 to 20,000 live births, with approximately8,000 new cases diagnosed annually.[4] Although the prognosis for retinoblastoma in developed countries is excellent with survival rates exceeding 95%,outcomes in developing and low-resource settings remain suboptimal.[5] In these countries, children present late, with extraocular extension or advanced intraocular disease, due to lack of awareness, poor health infrastructure, and limited access to pediatric ocular oncology services.[6]

The clinical classification of intraocular

retinoblastoma is primarily guided by the International Intraocular Retinoblastoma Classification (IIRC), which categorizes disease severity from Group A (small, localized tumors)to Group E (extensive intraocular disease with poor prognosis).[7]This classification is critical in guiding treatment decisions: early-stage disease (Groups A–C) is generally amenable to globe-conserving therapies such as systemic or intra-arterial chemotherapy combined with focal laser or cryotherapy, while advanced stages (Groups D and E) often necessitate enucleation or intensive multimodal treatment. Thus, the stage at presentation directly influences the child's chance of eye salvage and visual rehabilitation.[8] Multiple studies from high-income countries, where routine pediatric eye screenings and timely referrals are standard, have reported a greater proportion of retinoblastoma cases being diagnosed in earlier stages, allowing for better visual outcomes and reduced reliance on enucleation.[9] In contrast, reports from countries such as India, Pakistan, Nigeria, and other parts of Africa and Asia often show a majority of patients presenting in Groups D or E, reflecting significant delays in diagnosis.[10,11] This study was conducted to highlight the stage distribution of retinoblastoma at presentation, aiming to identify diagnostic delays and inform strategies for earlier detection and improved outcomes.

METHODS

This retrospective chart review was conducted at Jinnah Postgraduate Medical Center, Karachi from June 2024 to February 2025. The study was approved by the Institutional review board/Ethical review board **(F.2-81/2024-GENL/249/JPMC)**. There were 85 patients diagnosed with retinoblastoma and staged according to IIRC. Patients with extraocular or metastatic retinoblastoma and with incomplete medical records were excluded. The data was collected for age, gender, complete ocular examination, staging of the disease at the time of first presentation and laterality of disease (each eye was staged individually in bilateral cases). There were 114 eyes which qualified the inclusion criteria.

The data were entered and analyzed using SPSS version 26. Quantitative variables such as age were expressed as mean ± standard deviation, while categorical variables such as gender, laterality, and retinoblastoma staging were presented as frequencies and percentages. Due to the descriptive nature of the study, inferential statistics were not applied, and emphasis was placed on summarizing the stage frequencies at initial diagnosis.

RESULTS

Mean age at presentation was 2.6±1.4 years. The gender distribution showed 52.9% males and 47.1% females, with no significant difference between unilateral and bilateral groups (p = 0.87). The duration of symptoms before presentation was significantly longer in unilateral patients (9.1 weeks) compared to bilateral (6.7 weeks, p = 0.02), indicating delayed recognition in unilateral cases. Table 1 shows stratification of data with laterality.

Most patients presented with Group D (42.1%)and Group E (32.4%). Only10.5%were in Group B and15.0%in Group C. There was no case in Group A. Further details regarding stage distribution with respect to laterality and gender are shown in Table 2 and Table 3, respectively.

Table 1: *Comparison of cases by Laterality.*

Characteristic	Total (n=85)	Unilateral (n=56)	Bilateral (n=29)	p-value
Age at Presentation (years)	2.6 ± 1.4	2.8 ± 1.3	2.4 ± 1.5	0.21
Gender (Male)	45 (52.9%)	30 (53.6%)	15 (51.7%)	0.87
Gender (Female)	40 (47.1%)	26 (46.4%)	14 (48.3%)	0.87
Mean Duration of Symptoms (weeks)	8.2 ± 3.6	9.1 ± 3.8	6.7 ± 2.9	0.02
Family History of Retinoblastoma	9 (10.6%)	2 (3.6%)	7 (24.1%)	0.004

Table 2: *Stage Distribution with respect to laterality.*

IIRC Stage	Total Eyes (n=114)	Unilateral (n=56 eyes)	Bilateral (n=58 eyes)
Group A	0 (0.0%)	0	0
Group B	12 (10.5%)	4 (7.1%)	8 (13.8%)
Group C	17 (15.0%)	6 (10.7%)	11 (19.0%)
Group D	48 (42.1%)	27 (48.2%)	21 (36.2%)
Group E	37 (32.4%)	19 (33.9%)	18 (31.0%)

Table 3: *Stage Distribution with respect to Gender (n = 114 eyes).*

IIRC Stage	Male Eyes (n=62)	Female Eyes (n=52)	Stage B/C in Males	Stage B/C in Female	Stage D/E in Males	Stage D/E in Female
Group A	0 (0.0%)	0 (0.0%)	0	0	0	0
Group B	6 (9.7%)	6 (11.5%)	6	6	0	0
Group C	9 (14.5%)	8 (15.4%)	9	8	0	0
Group D	27 (43.5%)	21 (40.4%)	0	0	27	21
Group E	20 (32.3%)	17 (32.7%)	0	0	20	17

Table 4: *Distribution of Retinoblastoma Stages (Groups B–E) by Gender and Laterality at Presentation.*

Stage of Retinoblastoma	Males with Unilateral disease (n=30)	Females with Unilateral disease (n=26)	Males with Bilateral disease (n=15)	Females with Bilateral disease (n=14)	p-value
Group B or C	6 (20.0%)	4 (15.4%)	8 (53.3%)	7 (50.0%)	-
Group D or E	24 (80.0%)	22 (84.6%)	7 (46.7%)	7 (50.0%)	0.03

Table 5: *Stage Distribution by Age Group.*

Age Group	Most Common Stage(number of patients)	Number of cases with Group B and C disease (%)
<1 year	Group D (12)	1 (8.3%)
1–3 years	Group D (39)	11 (28.2%)
3–5 years	Group E (23)	6 (26.1%)
>5 years	Group E (11)	1 (9.1%)

Table 4 shows that patients with unilateral disease presented in late stages of retinoblastoma (80% and 84.6% for males and females, respectively.

Among children under 1 year (n=12), Group D was most common; only 1 child (8.3%) presented in early stages. In children aged 3–5 years (n=23),Group E dominated, with 26.1% early-stage presentation. The trend was advanced stage with increasing age (Table 5).

DISCUSSION

This study analyzed the clinical staging of retinoblastoma at the time of presentation using the International Intraocular Retinoblastoma Classification (IIRC) system, with a specific focus on age, gender, laterality, family history, and duration of symptoms. Among the 85 patients (114 affected eyes), most of the eyes had advanced intraocular disease, Group D in 42.1%and Group E in 32.4% eyes. Only 25.5%of eyes were diagnosed with early stages (Group B or C). The mean age at presentation was 2.6 years, with slightly younger age in bilateral cases (2.4 years)compared to unilateral (2.8 years). Although the age difference was not statistically significant, bilateral cases had a significantly shorter symptom duration (6.7 weeks) compared to unilateral cases (9.1 weeks, p = 0.02), and a much higher rate of positive family history (24.1% vs. 3.6%, p = 0.004). These findings suggest that bilateral disease, often hereditary in origin, is more likely to be recognized earlier, possibly due to family awareness or prior counseling.

Factors contributing to delayed presentation include lack of public awareness, misdiagnosis by non-specialists, traditional healing practices, and geographical and financial barriers to accessing specialized care.[12] Limited integration of eye screening in routine pediatric or neonatal health checkups contributes to missed early detection opportunities.[13] Understanding the distribution of clinical stages at presentation not only reflects the effectiveness of the current healthcare system in identifying ocular malignancies but also provides a baseline to assess the impact of future awareness campaigns and screening programs. A shift toward earlier presentation trends can help reduce the number of children who undergo enucleation or require high-dose chemotherapy.[14] In Pakistan, published data on the stage distribution of retinoblastoma at diagnosis remain limited, particularly in the context of nationwide trends.

Similar patterns have been observed in international studies where bilateral cases were diagnosed earlier due to family screening protocols.[15,16] Although both unilateral and bilateral cases predominantly presented in Group D and E,

bilateral eyes had a slightly higher proportion of early stage (32.8%) than unilateral eyes (17.8%). This highlights the role of genetic vigilance and the impact of bilateral presentation in prompting earlier clinical evaluation. These results are consistent with other studies which found no gender-based disparities in retinoblastoma stage at diagnosis, indicating that socio-cultural gender biases did not significantly impact time to diagnosis in this population.[17,18]

Children under 3 years of age had a slightly higher proportion of early-stage diagnoses compared to older children. This is also consistent with previous research suggesting that delayed diagnosis and lack of symptom recognition in older children often results in presentation at more advanced stages.[19,20] However, even in younger age groups, advanced stages remained predominant, indicating systemic barriers to early recognition. In our study, children with Group B or C disease presented at a mean age of2.3–2.4 years, while those with Group D and E presented later, at 2.7–2.9 years, respectively. This gradual age-stage shift further supports the hypothesis that diagnostic delays play a role in disease progression, and that even short time differences can result in significant advancement of intraocular retinoblastoma. Overall, these findings mirror patterns reported in several developing countries, where lack of awareness, limited access to specialized care, and absence of routine pediatric eye screening contribute to delayed diagnosis and advanced-stage presentation.[21]

The strength of this study lies in providing valuable local epidemiological data on stage distribution of retinoblastoma at presentation using standardized clinical staging. However, its single-center design, relatively small sample size, and lack of socioeconomic or outcome data limit generalizability and comprehensive interpretation. Future multicenter studies with larger cohorts, incorporating socioeconomic determinants and long-term outcomes, are recommended to better understand factors influencing stage at presentation and to guide strategies for earlier detection and improved management of retinoblastoma.

CONCLUSION

Majority of children with retinoblastoma present with advanced stages of retinoblastoma. Unilateral disease was more common, but bilateral cases showed slightly earlier-stage detection and were more frequently associated with a positive family history. These findings reflect diagnostic delays and emphasize the urgent need for improved public awareness, routine pediatric eye screening, and timely referral systems to facilitate earlier detection and increase opportunities for globe salvage and vision preservation.

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Patient's Consent: Researchers followed the guide lines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(F.2-81/2024-GENL/249/JPMC)**.

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Authors Designation and Contribution

Farhat Khan; Postgraduate Trainee: *Concepts, Data Acquisition, Data Analysis, Manuscript Preparation.*

Aziz-ur-Rehman; Consultant Vitreoretinal Surgeon: *Design, Manuscript Review.*

Baby Nisha; Postgraduate Trainee: *Statistical Analysis.*

Kunza Zahid; Postgraduate Trainee: *Statistical Analysis, Manuscript Editing.*