Original Article

Lag time for diagnosis and treatment in 1120 retinoblastoma children: Analysis from InPOG-RB-19-01

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Setting: Increased lag time for diagnosis and treatment is a key determinant of adverse retinoblastoma (RB) outcomes. Analysis from INPHOG-RB-19-01, a prospective, multicentric study of newly diagnosed RB with regard to lag time and its correlation with various variables, is presented. **Patient or Study Population:** All newly diagnosed RB patients treated at the participating centers during the study period were enrolled. **Observation Procedure:** Lag time was subdivided into parent-lag time (symptom onset to first consult) and system-lag time (including diagnosis lag time, defined as first consult to diagnosis, and treatment lag time, defined as diagnosis to treatment initiation.). Multivariate logistic regression analysis was used to assess factors predictive of increased lag time. **Main Outcome Measures:** In all, 1120 patients from 20 centers were enrolled over a 36-month period. Extraocular or metastatic disease was present in 25.2% of patients at diagnosis. The mean lag time from symptom onset to treatment initiation was 4.2 months (range 0.5–61.6 months). Parental, diagnosis, and treatment lag time contributed to 44%, 26%, and 31% of the total lag time, respectively. Increased lag time had significant correlation with the stage at presentation ($P < 0.05$), lower socio-economic status ($P = 0.006$), increased distance from treating center ($P = 0.001$), younger maternal age at pregnancy ($P < 0.05$), family history of cancer ($P = 0.031$), and first consultation with a non-specialist ($P = 0.001$), and showed a negative correlation with improved maternal education. Parental lag time is the major contributor to the cascading delay in RB diagnosis and treatment initiation. Efforts for earlier diagnosis, therefore, need to be directed towards community awareness and routine screening during contact with healthcare professionals, such as at immunization.

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Retinoblastoma (RB) is the most common intraocular malignant tumor in children. Worldwide, increased awareness and advances in management have facilitated early diagnosis and improved survival. Survival rates reported from high-income countries (HIC) range from 88% in the United Kingdom to 93% in the United States.[1,2] In India, Nepal, Africa, and South American countries, the prognosis is significantly inferior, with a higher proportion of these children presenting at an advanced stage. Orbital RB has been reported to be 18% in Mexico, 36% in Taiwan, and 40% in studies from Nepal, and ranges from 9%–45% in studies from India.[3-10] Ocular salvage and preservation of vision are essentially dependent on early diagnosis, and several studies have been conducted to identify the factors leading to delayed diagnosis at presentation.[11,12] Survival is dependent on the geographic location and the economic status of the country; the Global Retinoblastoma Outcome Study reiterated that children from low- and middle-income countries (LMICs) have significantly inferior (50%) 3-year survival compared to almost 100% survival in those from HICs.[13] Delay in diagnosis in RB has been associated with lower chances of globe salvage and higher mortality.[14,15] Studies from South America have noted prolonged time to diagnosis to be more associated with extraocular disease at presentation.[16,17] Reduced lag time to diagnosis has been associated with less advanced RB, as found in the Swiss

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study.[18] A large proportion of the delay in diagnosis has been attributed to delayed referral to specialists.[19]

The extent to which prolonged lag time is attributable to delayed presentation by the family (parental lag time) versus delay in the healthcare system (system lag time) is unclear. Whilst data from India and other LMICs is limited, there appears to be a significantly higher proportion of patients presenting in advanced stages. Prolonged time to diagnosis (TTD) and treatment is widely believed to be one of the key reasons for this. One of the aims of this study was to quantify the TTD, and in cases of prolonged TTD, evaluate whether this is attributable to delayed parental recognition or difficulties in access to specialist services in our system. To understand the concept of delayed diagnosis and treatment better, data from the INPOG-RB-19-01, a prospective, multicentric collaborative study aimed at assessing the epidemiological and clinical features of RB in India, and evaluating outcomes following a standardized treatment strategy, were analyzed with the objective of understanding the lag time and reasons for delay in diagnosis, leading to advanced presentation of RB in India.

Material and Methods

A prospective multicentric collaborative study was planned, and all the centers that treat RB in India were invited to participate in the study. Twenty centers consented to participate and enroll patients. This study was registered with the Indian Paediatric Oncology Group (InPOG-RB-19-01). Ethical clearance was obtained from all the centers, and the study adhered to the tenets of the Declaration of Helsinki. The desired patient-specific information was captured from the standard medical database of the hospital and did not involve any patient contact for additional information. Consent was obtained from parents or legal representatives at the time of registration at the hospital. All participating centers enrolled newly diagnosed children identified and treated at their center from August 2020 till September 2023. The demographic, clinical, treatment, and outcome data were collected for the enrolled patients. For the purpose of this study, the clinical and demographic data were analyzed. The lag time was subdivided into parent-lag time (symptom onset to first consultation with any healthcare provider) and system-lag time (first contact with a healthcare provider till treatment initiation). System-lag time included diagnosis lag time (first contact with healthcare provider till definitive diagnosis) and treatment lag time (time interval between diagnosis and treatment initiation). Epidemiological data inclusive of age, gender, geographical distribution of the patients according to the six zones of the country (North, East, West, South, Central, and North East), distance from specialized treatment center (defined as treatment centers with availability of a trained ocular oncologist and facilities for diagnosis and treatment of RB, including surgery and focal therapy), socio-economic and educational status of parents, and family history of RB were recorded.[20] Clinical details documented included grouping according to the International Classification of Intraocular Retinoblastoma (ICIR), staging according to the International Retinoblastoma Staging System (IRSS), and laterality.[21] The type (specialists, including ophthalmologists or pediatricians, and nonspecialists, including general physicians, alternative medicine practitioners, pharmacists, or nurses) and the number of healthcare professionals contacted were noted.

Statistical analyses were performed using Microsoft Excel Office Version 2016 and SPSS software. Quantitative data were expressed as mean ± SD, and qualitative data were expressed as percentages and proportions. Factors predictive of delayed time to diagnosis and treatment were assessed using univariate and multivariate logistic regression. A P value < 0.05 was considered significant.

Results

In all, 1120 (59% male and 41% female, mean age 2.5 years, median age 2.1 years) newly diagnosed RB children who met the eligibility criteria were enrolled for the study. The geographic location of the participating centers in this study is shown in Fig. 1. Mean age at presentation was 24 months. Age at presentation was <1 year in 24.2%, 1–5 years in 66.2%, and >5 years in 9.6%. The demographic details of the patients, presenting symptoms, and stage at diagnosis are provided in Table 1. Leukocoria was the commonest presenting symptom, occurring in 84.7%% patients. At presentation, 74.4% of patients had intraocular disease. Disease was extraocular at presentation in 285 patients (25.2%), with 2.1% having stage 2 disease, 15.1% having stage 3 disease, and 7.9% having stage 4 disease at presentation.

The majority of the participating centers were in the North Zone of the country (30%), and majority of patients belonged to the North Zone of the country (41.6% of enrolled patients). Data on zone-wise distribution of the study centers and the enrolled patients are shown in Table 2. Geographical distribution of all patients according to the stage at presentation is provided in Fig. 2a, and distribution of extraocular disease (stages 2, 3, and 4) is provided in Fig. 2b.

The mean lag time from symptom onset to treatment initiation was 4.2 months (range 0.5–61.6 months, SD 7.0). The details of individual lag time and proportion of each lag time out of the total delay is provided in Table 3. Mean parental lag time was 1.9 months (range 0.5–24 months, SD 3.4) and contributed to 44% of the mean total lag time. Parental lag time was less than 1 month in 78.3% (n = 877) of patients and more than 3 months in 13.1% (n = 147) of patients. The majority of intraocular RB patients had lag time <1 month at presentation (84.6%), and the majority of extraocular RB had lag time >6 months (45.9%) at presentation. There was a significant difference in the total lag time for intraocular (stage 0 and 1) and extraocular disease (stage 2, 3, and 4) at presentation, as shown in Table 4.

The first healthcare provider consulted was an ophthalmologist in 49.6% (n = 556) of patients and a pediatrician in 36.3% (n = 406) of patients. In the remaining 14.1% patients, the first healthcare provider contacted was a nonspecialist. Diagnosis was made at the first visit in 61.5%, 50.5%, and 12.7% of patients when the first healthcare practitioner consulted was an ophthalmologist, pediatrician, and nonspecialist, respectively This difference in the proportion of patients who were diagnosed by a specialist (ophthalmologist and pediatrician) versus nonspecialist was statistically significant (P < 0.001). The mean lag time for diagnosis was highest with nonspecialist, at 2.3 months (SD 4.5). The data on the healthcare provider contacted, proportion diagnosed at the first consultation, and mean lag time for diagnosis are provided in Table 5.

Figure 1: Geographic and state-wise distribution of the study centers (dark pink pointers) shown on the country map

On multivariate logistic regression analysis, factors predictive of increased parental lag time were maternal education level ($P = 0.002$), lower/lower middle socio economic status ($P = 0.006$), distance travelled for treatment ($P = 0.001$), family history of cancer ($P = 0.031$), maternal age at pregnancy <20 years ($P = 0.001$), and first consultation with a nonspecialist healthcare practitioner ($P = 0.001$). Factors predictive of increased diagnosis lag time were lower/lower middle socioeconomic status ($P = 0.002$) and first consultation with a nonspecialist ($P = 0.00$). For treatment lag time, bilateral disease ($P = 0.05$), presenting symptom other than leukocoria ($P = 0.04$), and first consultation with a

nonspecialist ($P = 0.005$) were significantly predictive of delay in treatment initiation. Table 6 provides the multivariate logistics regression data of the factors predictive of delay in diagnosis and treatment. There was no impact of age, gender, birth order, religion, place of delivery, or birth weight on diagnosis and treatment lag time.

Table 1: Demographic profile, presenting symptoms, and stage at diagnosis of 1120 retinoblastoma children

	Number	Percentage
Gender		
• Female	462	41.25
• Male	658	58.75
Religion		
• Hindu	810	72.32
• Muslim	277	24.73
• Christian	25	2.23
• Others	8	0.72
Distance travelled for treatment		
• 0–100 KM	216	19.29
• 100–500 KM	495	44.2
• >500 KM	409	36.52
Socio economic status of the family		
• Lower	8	0.71
• Lower/Upper lower	522	46.61
• Middle/Lower middle	287	25.62
• Middle/Upper middle	282	25.18
• Upper	21	1.88
Laterality at presentation		
• Unilateral	760	67.98
• Bilateral	358	32.02
Presenting symptom		
• Leucocoria	949	84.73
• Orbital Cellulitis	81	7.23
• Squint	36	3.21
• Decreased Vision	24	2.14
• Proptosis	16	1.43
• Asymptomatic	13	1.16
• Hyphema	1	0.09
Stage at presentation		
• Stage 0	562	50.1%
• Stage 1	273	24.29%
• Stage 2	25	2.14%
• Stage 3	170	15.09%
• Stage 4	90	7.95%

Discussion

Delayed diagnosis of RB has been associated with advanced stage of disease at presentation.[14,15] In India, the vast majority of patients presents at an advanced stage, leading to a worse prognosis. In the current study, 25.18% of patients had extraocular or metastatic RB at presentation, indicating a delay in diagnosis or treatment initiation. There is a lack of collaborative data from India highlighting the reasons and exact point of delay in the diagnosis of RB. Stage of presentation is also reported variably, with studies from North India reporting a 37% incidence of extraocular RB, whereas studies from South India have reported this incidence to be 9%.[6,22,23] Hence, there is a need for a collaborative pan-India study to have accurate and validated data for planning awareness and education initiatives and interventions aimed at improving RB outcome. The successful take-off of this collaborative study can serve as a major milestone in the direction of prospective collaborative RB research in India.

The correct diagnosis was established, and treatment initiated in the majority of patients in this study within 4.5 months of diagnosis. Lag time was maximum at the parental level, with 13.1% of families—or one fifth of the whole cohort—taking the first consultation 3 months after noticing the first symptom. Lack of awareness about the disease, especially in an otherwise asymptomatic young child who is unlikely to have visual complaints, can account for the delay at the parental level. Since early diagnosis and prompt treatment initiation are imperative for improving RB outcome, awareness initiatives need to be directed at the community level to ensure timely consultation by the family for early symptoms. Increased parental lag time was significantly associated with maternal education level (illiterate/primary education) and early maternal age at pregnancy. These factors again point toward the lack of awareness about the disease among parents and the community. Mothers, being the direct caregivers of the child in the majority of families, are in a privileged position to detect early symptoms of the disease and should be the primary targets in awareness initiatives. Awareness materials and initiatives should also be formulated keeping in mind the literacy level of the target audience.

Increased lag time also had a significant association with the socioeconomic status of families, with lower and lower/

Table 2: Distribution of the study participants and their stage at diagnosis among the different geographical zones of the country

Name of the country zone	Number of participating centres (percentage)	Number of enrolled patients (percentage)	Disease staging at presentation (Number/percentage)				
			Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
Central	1 (5)	10 (0.89)	10 (100)	0	0	0	0
East	4 (20)	191 (17)	73 (38.4)	50 (26.2)	9 (4.7)	36 (19)	23 (11.8)
North	6 (30)	466 (41.6)	115 (24.68)	197 (42.27)	6 (1.29)	99 (21.24)	49 (10.52)
North-East	1 (5)	46 (4.1)	15 (32.7)	13 (28.6)	2 (4.1)	6 (12.2)	10 (22.4)
South	5 (25)	340 (30.3)	265 (77.94)	65 (19.12)	3 (0.88)	5 (1.47)	2 (0.59)
West	3 (15)	67 (5.9)	35 (52.24)	12 (17.91)	1 (1.49)	14 (20.90)	5 (7.46)

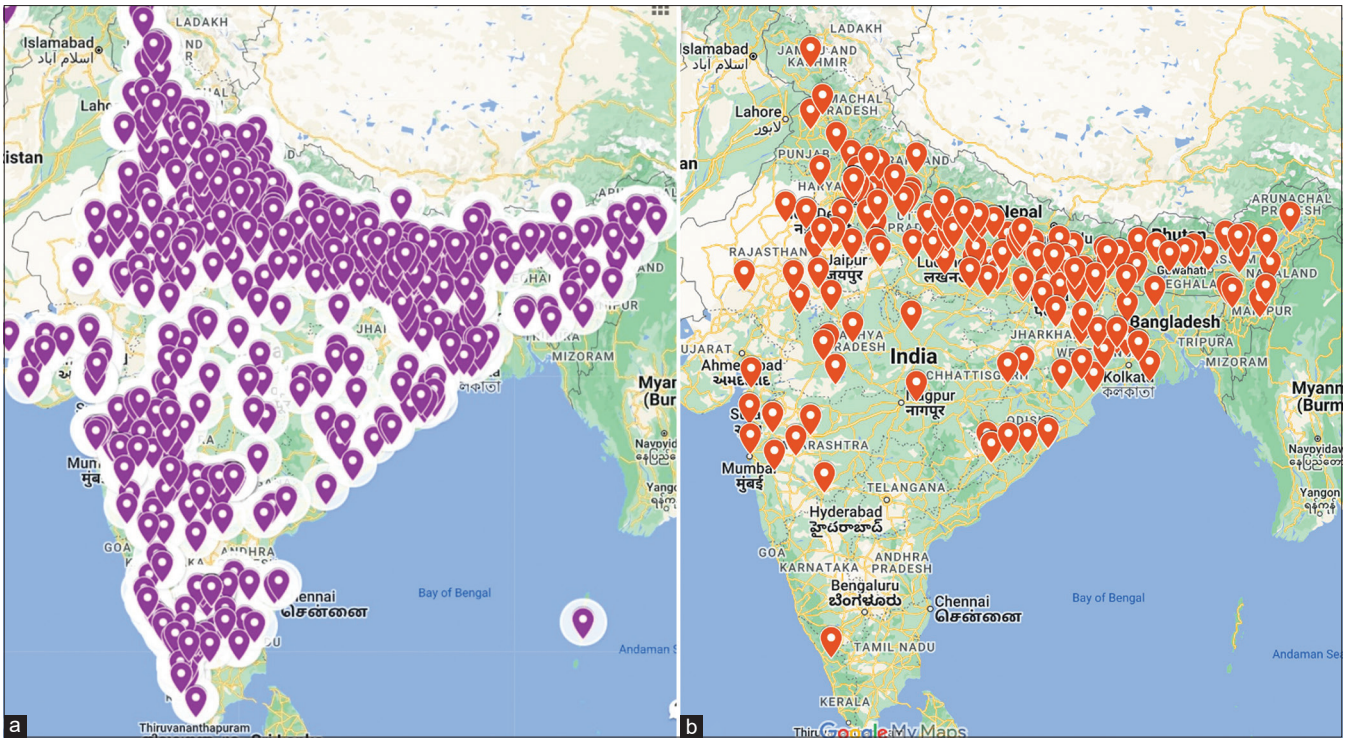

Figure 2: Geographic distribution of the study patients. (a) shows the geographic distribution of all study patients on a geographic map of the country (purple pointers). The distribution of stage 3 and stage 4 extraocular RB is shown in (b) (orange pointers)

Table 3: Lag time for first healthcare consult, diagnosis, and treatment for 1120 retinoblastoma children

Parameter	<1 month (%/number of patients)	1-3 months (%/number of patients)	3-6 months (%/number of patients)	> 6 months (%/number of patients)	Mean lag time (months)	SD	Min	Max	Proportion of total delay (contribution of each lag time in the total lag time)
Parental lag time	78.3 (877)	8.57 (96)	7.23 (81)	5.89 (66)	1.85	3.41	0.50	24	43.9%
Diagnosis lag time	82.95 (929)	7.5 (84)	3.93 (44)	5.62 (63)	1.09	3.19	0.00	23.5	25.8%
Treatment lag time	84 (924)	8.82 (97)	2.64 (29)	4.55 (50)	1.29	5.11	0.00	60.63	30.6%
Total lag time	32.41 (363)	35.09 (393)	12.86 (144)	19.64 (220)	4.21	7.04	0.50	61.6	

Table 4: Lag time in intraocular and extraocular RB at diagnosis

Total Lag time	Stage at presentation		*P*
	Intraocular RB (Number/ percentage)	Extraocular RB (Number/ percentage)	
<1 month	307 (84.60%)	56 (15.40%)	0.000
1–3 months	317 (80.70%)	76 (19.30%)	
3–6 months	95 (66.00%)	49 (34.00%)	
>6 months	119 (54.10%)	10 (45.90%)	

RB - Retinoblastoma

middle socio-economic groups having higher parental and diagnosis lag times. This finding is similar to the results from a study by Kaliki *et al.*[14], where lag time from first symptom to treatment initiation was significantly higher in low-income countries compared to high-income countries. Distance travelled for treatment is also associated with increased lag time for diagnosis and treatment. Thirty-six percent of patients in this study travelled a mean distance of over 500 km for treatment. RB management needs a multidisciplinary team, mostly oriented around an ophthalmic center for guiding treatment decisions. Most ophthalmic oncology centers in the country are concentrated in larger institutes and cities. Hence, most families must travel long distances either to get the diagnosis confirmed or to initiate appropriate treatment. Diagnosis and treatment of RB necessarily require examination under anesthesia. Dedicated pediatric anesthesia facilities are not readily available in many ophthalmic centers, necessitating travel of the family to a specialized center for the same. Interventions aimed at improving RB outcomes should therefore include initiatives to improve access to care through upgrading regional ophthalmic facilities to treat RB, providing pediatric anesthesia facilities, and training healthcare workers in RB detection and management.

The commonest presenting symptom in this study was leukocoria, seen in 84.7% of patients, higher than the 62.8% reported in the global RB study. Proptosis was observed in 1.4%, compared to 7.4% in global RB study. Seven point two

Table 5: Healthcare providers first consulted and the proportion of children diagnosed at first consultation

Healthcare Provider first consulted	No of patients seeking first consult	Diagnosis at first consultation Number (percentage)	No diagnosis at first consultation Number (percentage)	Diagnosis lag time in months (First presentation to Diagnosis) Mean±SD
Ophthalmologist	556 (49.6%)	341 (61.3%)	215 (38.7%)	1.03±3.18
Pediatrician	406 (36.3%)	205 (50.5%)	201 (49.5%)	0.70±2.35
Non-specialist	158 (14.1%)	20 (12.7%)	138 (87.3%)	2.34±4.52
Total	1120 (100%)	566 (50.5%)	554 (49.5%)	1.09±3.19
P		<0.001 (chi-sq)		<0.001 (ANOVA)

Table 6: Factors predictive of increased parental, diagnosis, and treatment lag time in multivariate logistic regression analysis

Factor	Parental lag time		Diagnosis lag time		Treatment lag time	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Demographic Profile						
Father's education: illiterate/primary education	1.22 (0.76–1.95)	0.402	1.56 (0.96–2.50)	0.069	1.07 (0.64–1.78)	0.784
Mother's education: illiterate/primary education	3.06 (0.149–6.11)	0.002	0.87 (0.37–2.41)	0.768	0.59 (0.28–1.32)	0.172
Socioeconomic status: Lower/Lower middle	1.72 (1.17–2.52)	0.006	1.89 (1.27–2.82)	0.002	1.32 (0.88–1.98)	0.180
Distance travelled for treatment						
Distance >500 km	2.04 (1.34–3.13)	0.001	1.36 (0.88–2.10)	0.166	1.26 (0.83–1.93)	0.276
Family History						
Family history of cancer	4.36 (1.30–20.24)	0.031	0.87 (0.32–2.70)	0.799	0.71 (0.29–1.94)	0.481
Family history of blindness	0.44 (0.16–1.33)	0.132	0.62 (0.21–2.11)	0.409	0.40 (0.15–1.09)	0.062
Religion	2.00 (0.83–4.64)	0.112	1.46 (0.49–3.74)	0.461	1.37 (0.51–3.29)	0.501
Maternal Health and birth history						
Age at pregnancy: less than 20 years	2.47 (1.46–4.16)	0.001	1.60 (0.94–2.68)	0.078	1.67 (0.94–2.89)	0.073
Birth weight 2.5 Kg	0.82 (0.56–1.18)	0.286	0.88 (0.60–1.27)	0.487	0.90 (0.66–1.40)	0.852
Hospital Delivery	0.70 (0.40–1.19)	0.197	0.88 (0.50–1.50)	0.651	1.32 (0.75–2.23)	0.319
Laterality and symptom						
Bilateral retinoblastoma	1.08 (0.75–1.56)	0.697	1.04 (0.71–1.54)	0.836	1.49 (1.00–2.24)	0.053
Symptom: Leucocoria vs non leukocoria	0.73 (0.46–1.14)	0.177	1.22 (0.77–1.90)	0.388	1.56 (1.00–2.39)	0.044
Gender	1.03 (0.74–1.44)	0.860	1.17 (0.82–1.67)	0.390	1.00 (0.70–1.42)	0.989
First healthcare provider consulted						
Non-specialist	0.50 (0.33–0.75)	0.001	0.39 (0.25–0.61)	0.000	0.50 (0.31–0.82)	0.005

OR - Odds ratio, CI - Confidence interval

percent of children in this study presented with a red, painful eye and orbital inflammation, which may also involve proptosis but was not counted as presenting symptom and could account for the low incidence of proptosis in this study. Leukocoria not being the presenting symptom was associated with increased treatment lag time. Tumors affecting the macula can cause early vision loss and sensory strabismus, which might not prompt urgent medical consultation by the caregivers, risking delayed diagnosis and disease progression. Dilated fundus examinations should therefore be standard for all children with strabismus and should be reinforced in all RB awareness and training sessions for healthcare workers. Advanced RB often presents with proptosis, cellulitis, or fungating masses, where the treatment protocol involves chemoreduction, surgery, and radiotherapy, necessitating referral and travel to specialized centers to access these treatment facilities. This complexity—especially in bilateral cases needing chemotherapy, focal therapy, and other complex treatment modalities—could contribute to longer treatment delays in bilateral patients, unlike advanced unilateral cases where enucleation is the primary treatment approach.

Diagnosis of RB for the majority of children in this study was made either by an ophthalmologist or pediatrician, and a correct diagnosis at the first consultation was made by 61.3% of ophthalmologists and 50.5% of pediatricians. However, a correct diagnosis was made in only 12.7% patients when the first consultation was with a nonspecialist. The mean lag time for diagnosis was also significantly higher when a nonspecialist was the first consultation, compared to ophthalmologists and pediatricians. Hence, there is need for strengthening RB awareness initiatives among ophthalmologist, pediatricians, as well as general physicians and traditional medicine practitioners. Community awareness programs should also incorporate these aspects and encourage early consultation with an ophthalmologist or pediatrician for any ocular symptoms suggestive of RB.

Parental lag time was less than 3 months in 86.8% of patients indicating that the majority of families had sought early consultation for ocular symptoms. Despite this, 25.18% of patients in this study had extraocular RB at presentation. This indicates that early RB can be asymptomatic, and strategies to improve RB outcome should also adopt screening strategy for the target age group before the onset of symptoms, alongside awareness initiatives. Screening can be done by trained healthcare providers, specifically eliciting a history of white reflex from the family or looking for a subtle white reflex during red reflex screening in a child's eye. Piggybacking on community-based pediatric eye screening programs and training the involved healthcare providers about the early symptoms of RB and the white pupillary reflex can be an effective screening strategy. Paediatric eye screening, especially for children under 5 years, can also be incorporated during routine healthcare visits like immunization. Several smartphone-based applications can become potential screening tools for community-based healthcare workers, thus aiding early diagnosis.[24,25] Interestingly, in this study, 15.4% of children who presented with extraocular RB had a total lag time of less than 1 month. This aggressive tumour behavior and rapid progression despite a short diagnosis lag time suggests a possible role of aggressive tumour biology and need further evaluation with molecular and genetic studies. A comparative study of RB patients from European countries versus African countries found African patients presenting with advanced disease despite shorter travel time and improved access to care, possibly suggesting a similar role of aggressive tumour biology in these cohorts.[26]

The geographical distribution of the patients showed variation across different zones of the country, with the majority of extraocular RB patients concentrated in the densely populated states of Northern and Eastern India, which rank poorly on socio-economic indicators like education and poverty compared to the states of the South Zone. This disparity reinforces the co relation of delay in diagnosis with socio-economic status and the need to direct RB awareness, screening, and access to care services to the areas of greatest need. Improved maternal education level is a predictor of reduced lag time and early diagnosis in this study. A zone-wise comparison of the maternal education level of the study participants showed the highest maternal illiteracy rate in the North Zone (29.5%) and the lowest in the South Zone (2.3%), as shown in Fig. 3. Improved maternal education and increased awareness about the early symptoms likely led to early diagnosis, resulting in the majority of children presenting with intraocular RB in the South Zone of the country. Not all RB treatment centers in the country were part of this study, and this potential limitation in depicting the complete clinicodemographic profile can be addressed in the future by ensuring more complete participation of all RB treatment centers.

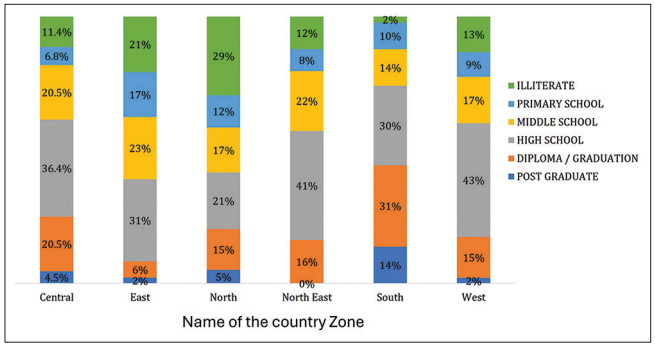

Figure 3: Analysis of maternal education level of the study patients among the different geographical zones of the country

Unlike previous studies from India, the current research did not find older age at diagnosis to be a significant predictor of increased lag time. Meel *et al*.[27] reported a mean lag time of over 9 months for older RB patients (>6 years), with 45% presenting with extraocular disease. In contrast, this study found no correlation between age at presentation or unilateral disease and lag time. This suggests that alongside delayed presentation, disease biology may influence disease progression and requires further investigation.

In conclusion, this is the first prospective multicentric study from India involving major RB treatment centers across the country, providing a representative overview of the sociodemographic profile and presentation of RB in India. The vast majority of RB cases presented and were appropriately diagnosed in <3 months. Whilst this can be optimized, there appears to be delayed recognition by the parents. Efforts for earlier diagnosis, therefore, need to be directed towards community awareness and routine screening during contact with healthcare professionals, such as at immunization. First consultation with a nonspecialist other than an ophthalmologist or pediatrician was associated with delayed diagnosis. Hence, training and awareness initiatives should be directed towards all cadres of healthcare workers and not be limited to specialists.

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List of abbrebiations

RB	Retinoblastoma
TTD	Time to diagnosis
HIC	High income countries
LMIC	Low middle income countries
ICIR	International Classification of Intraocular Retinoblastoma
IRSS	International Retinoblastoma Staging System

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