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ORIGINAL RESEARCH RETINOBLASTOMA AND STUDY OF ITS POOR PROGNOSTIC FACTORS

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ABSTRACT

Aim: -To study Retinoblastoma (RB) and its prognostic factors for its poor outcome.
Purpose: The aim is to carry out prospective study in a group of diagnosed cases of retinoblastoma (RB) along with variable prognostic factors. There are many socio economic and demographic aspects which impose serious effect on prognosis of retinoblastoma. Outcome includes poor prognostic factors related to RB.
Design: Prospective study
Method: Here, we have a case series of six patients diagnosed with RB from January 2020 to July 2020 and discuss their clinical features, treatment, outcome and its prognostic factors. Detailed examination will be carried out and assessment will be done.
Result: 6 patients were studied for 6 months and prognostics factors were evaluated. 66% patients had delayed presentation, 33% belonged to lower socioeconomic class,16% were having associated family history.
Conclusion: Delayed presentation is related to RB which is a risk factor for poor outcome. Poor literacy, low socioeconomic condition, treatment abandonment, and high clinical grading is found poor prognostic for RB outcome.

Keywords: Retinoblastoma, prognosis, chemotherapy, presentation

INTRODUCTION

Retinoblastoma is the most common malignant intraocular tumour of childhood and the second most common primary intraocular malignancy of the eye with a reported incidence ranging from 1 in 15,000 to 1 in 18,000 live births. Approximately 1% of all deaths caused by cancer before 15 years of age have been attributed to retinoblastoma. [(1)] There is no racial or gender predisposition for the incidence of retinoblastoma. Retinoblastoma is bilateral in about 25–35% of cases. [(2)] The average age at diagnosis is 18 months, unilateral cases being diagnosed at around 24 months and bilateral cases before 12 months. Globally, mortality is considerably higher due to delayed diagnosis, poor access to multidisciplinary retinoblastoma-specific health care and pathology, lack of genetic testing and counselling, and socioeconomic factors.[(3)] International Intraocular Retinoblastoma classification has classified Retinoblastoma into groups A–E, represent, to the extent possible, eyes containing sequential phases of normal tumour progression with time.[(4)] Leukocoria is the most frequent

symptom at presentation, and other symptoms include poor vision, redness, squint,hyphema, vitreal hemorrhage or proptosis.[5]
Here, we have a case series of six patients diagnosed with retinoblastoma (RB) from January 2020 to July 2020 and discusstheirclinicalfeatures, treatment, outcome and its prognostic factors.

MATERIAL AND METHOD

6 patients presenting to a private hospital with Retinoblastoma from January 2020 to July 2020 were taken for the study.
Detailed history regarding clinical features along with **socioeconomic status**, **literacy of parents**, **travel time from home to hospital**, **screening at the time of birth, previous consultation** for any ophthalmic complains was taken. **Family history regarding consanginous** marriages, **affection of the siblings** and other relatives was recorded.
Detailed examination was done involving the vision, pupillary reaction, symptoms and signs such as white reflex, watering, pain, redness, protrusion of eyeball, squint and hyphema were obtained. [6]

EUA (Examination Under Anaesthesia) was done for all 6 cases to evaluate fundus, ocular tension and grading of retinoblastoma. Investigations included X-ray chest, computed tomography scan of orbit and brain, B-scan. Enucleated eyes were sent to histo-pathology examination (HPE), serum and aqueous lactate dehydrogenase. Radiotherapy, cryotherapy, chemotherapy and enucleation are modalities of treatment for retinoblastoma. All the patient was followed up. The empty socket and the other apparently normal eye were examined carefully at each visit for recurrence or secondary tumors.

Case 1: RE Group A, LE Group E with ONI
A Male patient was first time diagnosed as RB at age of **28 months. Patient presented with** complain of squint on left eye. Patient had first consulted at primary health center before 6 months for left eye squint and was advised eye drops but his parents didn't pay attention. Condition become worse and developed white reflex with squint. Finally, patient consulted in tertiary eye hospital where he was diagnosed as a retinoblastoma. There was significant **lag period** between onset of symptoms and diagnosis of retinoblastoma.
Tumour didn't respond well to treatment and there was intracranial extension. Patient **died** after intracranial extension of tumour.

Case 2: RE group E, LE group C
A Female patient first presented to a village quack for red eye and white glow in right eye. Due to lack of vigilance and literacy, continued treatment given by quack for 4 months. After no improvement patient consulted tertiary hospital and retinoblastoma was diagnosed at age of 26 months. Again, there was found significant **lag period** between onset of symptoms and diagnosis.
After initial few weeks treatment tumour **spread to CNS** and patient died after 2 cycles of chemotherapy.

Case 3: LE stage C
A female patient belonging to an educated family was screened at time of birth and advised ophthalmic screening 6 monthly. At the age of 11 months consulted to tertiary hospital ophthalmologist for complain of red eye in left eye. On further evaluation, Retinoblastoma diagnosed and treatment started.
Retinoblastoma **responded well to treatment** and patient is evaluated on routine follow-up.

Case 4: LE Group D

A male patient consulted a general practitioner for white reflex in left eye. General practitioner referred the patient to ophthalmologist. at age of 1.6 years. On detailed examination and after investigation, stage D retinoblastoma was diagnosed, and treatment started.
Retinoblastoma **regressed well after treatment** and patient is on regular follow up.

Case 5: RE Group E
A male patient consulted at general practioner for complain of right eye white reflex at age of 24 months. Patient was referred to tertiary hospital where patient diagnosed as retinoblastoma and treatment started.
After 2 cycles of chemotherapy **CNS spread** and intracranial metastasis was found.
At present patient is **on palliative chemotherapy treatment.**

Case 6: RE Group E with ONI
A female Patient presented at age of 30 months at primary health center where right eye protrusion and white reflex was noticed for which they advised for tertiary hospital consultation. But patient consulted tertiary hospital after worsening symptoms. After all required investigations diagnosis of RB was made. And patient was advised for enucleation followed by chemotherapy. But due to **financial constraints**
and hesitancy to enucleate eye **patient** abandoned treatment.

RESULT

PROGNOSTIC FACTORS	**CASE1**	**CASE2**	**CASE3**	**CASE4**	**CASE5**	**CASE6**
Time lag between noticing symptoms and diagnosis	**+(6 months)**	**+(4 months)**	**-**	**-**	**-**	**+(6 months)**
Age at presentation	**28 months**	**26 months**	**11 months**	**18 months**	**24 months**	**36 months**
Sex	**Male**	**Female**	**Female**	**Male**	**Male**	**Female**
Socio-economic status	**Poor**	**Poor**	**Good**	**Good**	**Poor**	**Poor**
Literacy of parents	**Poor**	**Poor**	**Good**	**Average**	**Average**	**Poor**
Group	**Right eye- A, lefteye-E with ONI**	**Right eye-E, left eye-C**	**Left eye-C**	**Left eye-D**	**Right eye-E**	**Right eye–E With ONI**
Unilateral / bilateral	**Bilateral**	**Bilateral**	**Unilateral**	**Unilateral**	**UnilateralL**	**Unilateral**
Family history	**Absent**	**Absent**	**Present**	**Absent**	**Absent**	**Absent**
Screening at time of birth	**-**	**-**	**+**	**-**	**-**	**-**

Presentation	**Squint with white reflex**	**White reflex**	**Red eye**	**White reflex**	**White reflex**	**White reflex With proptosis**
Travel time from home to tertiary hospital	**3 hours**	**5 hours**	**4 hours**	**2 hours**	**3 hours**	**5 hours**
Intraorbital / extraorbital	**Intraorbital**	**Intraorbital**	**Intraorbital**	**Intraorbital**	**Intraorbital**	**Extraorbital**
TREATMENTOUTCOME						
Globe salvage	+	+	+	+	+	**TA***
Metastasis [10]	+	+	-	-	+	+
Treatment abandoned	-	-	-	-	-	+
Outcome	**Death**	**Death**	**Good (Tumour respond to treatment)**	**Good (Tumour responed to treatment)**	**Poor (On palliative treatment)**	**TA`**

(TA: treatment abandoned)

DISCUSSION

RB usually manifests between the ages of 3 months to 5 years. [6] The diagnosis of neonatal RB may be three times more frequent in developed countries compared to developing countries. This difference could be attributed to increased awareness among parents about genetic transmission of the disease and importance of screening of neonates in developed countries compared to developing countries. Most of the cases are diagnosed at the time of routine fundus screening at or immediately after birth in cases with a positive family history of RB.
In this prospective case study, we have studied 6 case of retinoblastoma with median age of 24 to 28 months. We investigated and studied demographic, socioeconomic, clinical features of these patient. The majority of our patients presented at advanced stage. Socioeconomic disparities exist among children with retinoblastoma. [11]

- **Time lag** between noticing of symptoms and diagnosis is also found prognostic for this study. [7] 3 cases have time lag for final diagnosis. All they came out with poor prognosis. Mostly due to not getting lack of awareness and improper guidance. [9]

- 2 cases in the study has **bilateral** and 4 of them had **unilateral** involvement. Bilateral cases had worse outcomes and poor prognosis. Both bilateral presented cases came out to death after initial treatment.

- Most of them has lower **economic level**, only 2 out of 6 patients (33%) belonged to good socioeconomic status that shifted them to good prognostic outcome.

- Cases with lower **educational standard of parents** also shown poor outcome.

- 4 patients showed **delayed presentation**s (66%) at age >2 years with advanced stages. All late presented cases had poor prognosis.

- 1 patient had **family history of** retinoblastoma (16%) in sibling, undergo early diagnosis and get good outcome.

- Considering the travel **time from home to hospital**, all these patients has different duration. On comparing the result based on this factor, no significant difference was seen on prognosis.

- 5 cases had **intraocular** growth with different grading at presentation with different prognosis. 1 **extraocular** RB case advised to enucleate with adjuvant chemotherapy abandoned treatment due to hesitancy to enucleate eye and financial constraints.

CONCLUSION

Delayed presentation is related to extraocular RB which is a risk factor for poor outcome. Poor literacy, low socio-economic condition, treatment abandonment, and high clinical grading are found poor prognostic for RB outcome [(12)]. Recently, adjuvant chemotherapy was widely used for RB patients, which increased the eye salvage. Rural background, financial constraints and hesitancy to enucleate were important causes behind treatment abandonment.

Education for parents and general physicians for the early signs of RB such as leukocoria, therapy strategy of RB may promote early diagnosis, improve the compliance and outcome. Literacy cannot affect outcome of the disease if we guide each case in proper way.

Screening at birth time with regular follow up if done, that will give early diagnosis and good outcome for inherited cases.

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