

Causes of Delayed Presentation of Retinoblastoma in a Tertiary Care Hospital of Pakistan

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ABSTRACT

Purpose: To find out the causes of delayed presentation of Retinoblastoma in a tertiary care hospital.

Study Design: Questionnaire based Survey.

Place and Duration of Study: Pediatric ophthalmology department of The Children's Hospital, Lahore, from January 2018 to December 2019.

Methods: Mothers of patients who presented in the hospital were recruited for this survey. A questionnaire with details of the patient were noted. It included first symptom, time lapse since onset of first symptom, gender, age at presentation to first doctor (general practitioner), time lapse to presentation at tertiary care center (The Children's Hospital & Institute of Child health), gender and laterality. General physical Examination was done by an oncologist and examination under anesthesia was done by a pediatric ophthalmologist. Data was analyzed using SPSS version 20. Pearson Chi Square test was used to find significance of each cause.

Results: Seventy participants were included in the study. Delayed presentation was seen in 42 patients (60%). The various factors identified for delay in diagnosis and treatment in descending order are residence in rural areas 54 %, lack of finances 64%, social pressure 27%, awareness about disease severity 60%, lack of transport 54%, Fear of enucleation 38% and seeking non-medical treatment/ alternate medication 32%. Significance of each factor was calculated using chi-square test.

Conclusion: The causes identified can be highlighted on national level for development of health facilities in rural areas.

Key Words: Retinoblastoma, Cancer, Malignant tumor, Leucocoria.

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INTRODUCTION

Retinoblastoma, the most common intraocular malignancy of infants has an incidence of 1 in 15,000 to 1 in 20,000 live births.¹ This corresponds to almost 9000 new cases per year worldwide. Forty percent of cases have bilateral disease, which are hereditary and are part of a genetic cancer predisposition syndrome.

All children with a bilateral or familial form and 10 to 15% of children with a unilateral form, carry an RB1 gene mutation. Sixty percent retinoblastoma cases are not hereditary.^{2,3} The median age of diagnosis is 24 months in unilateral cases and 9–12 months in bilateral ones.⁴

Leucocoria and strabismus are the most common clinical presentations in the developed world. However, proptosis, buphthalmos and red eye is frequently seen in the retinoblastoma patients of the developing countries.⁵ The management of retinoblastoma requires a multidisciplinary approach by a team of oncologist, ophthalmologist and radiation oncologist. The treatment is highly individualized. The aim of primary treatment is to save the life of the patient, followed by globe saving and any useful

vision if possible with also minimal treatment related complications.

In the last century, a paradigm shift is seen in the management of retinoblastoma. The survival and visual outcome has improved dramatically in the developed world. This can be attributed to early tumor recognition and advances in the management of retinoblastoma. Chemo-reduction followed by adjuvant consolidative treatment has replaced external beam radiotherapy as the primary modality of treatment for intraocular retinoblastoma. Further, histopathological high-risk factors have been identified in enucleated eyes, allowing use of prophylactic chemotherapy to take care of possible micro-metastasis. Intra-arterial chemotherapy (IAC) for retinoblastoma has been adopted as a first-line treatment option by numerous tertiary centers. IAC may be effective in saving eyes of Group D retinoblastoma that have failed in systemic chemotherapy and were destined for enucleation, in addition to group A, B & C.⁶ The survival in case of extraocular retinoblastoma is still low, and the reported survival rate ranges between 50% and 70%. In developing countries, the overall survival of retinoblastoma patients remains low, primarily due to a delayed presentation, resulting in larger proportions of extraocular disease compared with the developed world, where majority of the disease is intraocular.⁷ According to a study, the five-year survival rate for children with unilateral retinoblastoma increased from 85% in 20th century to 97% in 21st century, in London.⁸ The overall survival rate exceeds 95% in Germany per year.⁹ This remarkable improvement cannot be expected in all parts of the world. The reports from Africa predict a disease-free survival of around 20%.¹⁰ An editorial has been written by Kivelia highlighting the advancement in the medical field in the last century. He concluded that, it may take another 200 years for the benefit to spread worldwide.¹¹

The main challenge in treating retinoblastoma effectively in our country is a delay in presentation, resulting in advanced disease and consequently higher treatment-related morbidity and disease-related mortality.

This survey was designed to find out the causes of delayed presentation of the patients of Retinoblastoma at tertiary care centers of Pakistan. This will help in addressing the issue and overcoming the barriers to decrease the morbidity and mortality related with the disease.

METHODS

This survey was conducted in the Pediatric ophthalmology department of the Children's Hospital, Lahore. The new patients who were enrolled for the treatment of retinoblastoma from January 2018 to December 2019 were included in the study. Parental complaint time (lag time 1) was defined as the time starting from the first noticing of the disease by the parent to presentation to the general practitioner/ophthalmologist. Delayed presentation was defined as the lag time 1 if it was more than 2 weeks. Referral time (lag time 2) was defined as the time from the first doctor/general practitioner visit till the presentation to The Children's Hospital and Institute of Child Health, Lahore. Delayed referral was defined if lag time 2 was more than 2 weeks. Total delay (total lag time = lag time 1 + lag time 2) was measured from time of initial parental complaint to the time of the first examination at tertiary care hospital.¹²

The parents (mostly mothers) were source of history in our patients. The details of the patient were noted, namely first symptom, time lapse since onset of first symptom, gender, age at presentation to first doctor (general practitioner), time lapse to presentation at tertiary care center (The Children's Hospital & Institute of Child health), gender and laterality. General physical Examination was done by oncologist and examination under anesthesia was done by a pediatric ophthalmologist.

The staging/grouping of disease at presentation to tertiary care Hospital was done before starting treatment (International Intraocular Retinoblastoma classification and TNM staging). The tumors were classified as intraocular or extraocular based on clinical and radiological evaluation. The new patients of retinoblastoma with group D or E in worse eye or extraocular retinoblastoma were labeled as advanced disease and included in the study.

The mothers were inquired about their hurdles and challenges in the treatment of their children. A questionnaire identifying the major issues was filled by all the parents (with the help of paramedic staff) included in the study. Data was analyzed using SPSS version 20. Pearson Chi Square test was used to find significance of each cause.

RESULTS

Eighty four patients presented to The Children's hospital, Lahore with retinoblastoma from January

2019 to December, 2020. Seventy patients fulfilled the inclusion criteria and were included in the study. Fifty one had intraocular disease and 19 cases had extraocular retinoblastoma.

Two patients had distant metastasis and four had intracranial extension at presentation. Forty five patients had unilateral and 25 had bilateral retinoblastoma. The mean age for bilateral disease was 14 months whereas for unilateral it was 25 months. Delayed presentation was seen in 42 patients (60%). Delayed referral was seen in 47 patients (67.14%). Total Delay was 2 weeks to 13 months. Fifty five patients (79%) had advanced disease at presentation to (Figure 1).

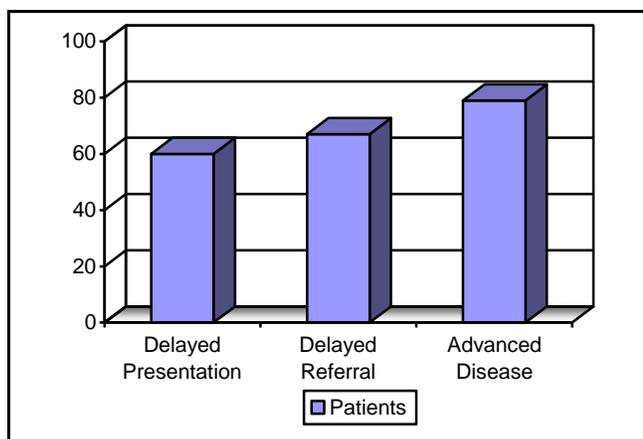


Figure 1: Disease presentation pattern at a tertiary care hospital.

The significance of various factors identified for delay in diagnosis and treatment in descending order is presented in Table 1.

Table 1: Percentage and significance (chi-square test) of various factors responsible for delayed presentation of retinoblastoma.

Factor	Percentage	Significance (Chi-square Test)
Rural areas	54	0.592
Lack of finance	64	0.406
Social pressure	27	0.365
Awareness about nature of disease	60	0.014
Lack of transport	54	0.003
Fear of enucleation	38	0.000

DISCUSSION

Pakistan is a developing country and treatment facility

of intra-arterial chemotherapy, intra-vitreous chemotherapy and focal laser consolidation in addition to intravenous chemotherapy is available at tertiary care hospitals of the country. However, presentation of advanced disease and limited finances leaves no choice for the retinoblastoma team other than enucleation, in most of the cases.^{13,14,15}

Although survival rate is good for advanced intraocular disease, if enucleation is done in time, but fear of eye loss, social norms of our culture and alternative medicine may contribute to a poor outcome. Compliance to treatment is also poor in our country.¹⁶ Timely screening definitely helps in earlier diagnosis of the disease.

The diagnosis of most of the cancers is delayed in developing countries including Pakistan due to many factors.¹⁷ This has been particularly noticed in most of the studies done so far on retinoblastoma in Pakistan, as most of patients in these studies had advanced disease.¹⁸ A rapid advancement took place in terms of availability of advanced treatment options in Pakistan including intra arterial chemotherapy.¹⁹ Little has been done so far in detection of early tumors (IIRC Group A &B) where we can save useful vision in addition to globe and life of the patient. As a result, we are not able to save useful vision in these patients.

The most important factor highlighted in our study for delayed presentation of retinoblastoma is the people living in remote rural areas where adequate health facilities are not available. In Pakistan, 61.4% of the population lives in rural areas, where 21% live below the poverty line.²⁰ The primary health care staff is the front line worker. People have to walk several miles to reach a proper general practitioner. Their poor financial status adds up to their misery. Sometimes they need loan to travel to a nearby district for medical consultation.

The family pressure for people living in close communities also hinder patients from seeking proper medical advice. Ignorance adds up to all the other factors. Sometimes, leucocoria, which is a first sign of retinoblastoma, is taken by parents as a sign of good luck.

There is common practice of seeking non medical treatment for almost all diseases in most of the subcontinent. Lack of trained medical professional coupled with freely available faith healers makes them first choice for treatment in many cases. The faith of community is deep rooted in these people especially

for life threatening diseases, so many people go to them until it is too late.²¹

Another important cause of delayed treatment of retinoblastoma is fear of enucleation. Loss of an organ has a huge impact on human psychology. In many patients, enucleation to save the life of the child is refused by the parents. They go on to search for a person who can treat without enucleation. This leads to wastage of valuable time. Similar reasons have been reported in the past in other developing countries especially India, which has similar demography and social set up.²²

Detection of leucocoria in newborns especially in children at risk can be helpful in better disease outcomes. The role of genetic counseling cannot be denied in early cancer detection and treatment in genetic retinoblastoma. The power of social media can be utilized to spread awareness about life threatening diseases like retinoblastoma. Awareness campaign about retinoblastoma has been taken up in many centers of developing countries, such as India and has helped in early detection of retinoblastoma. It is necessary for us to address these causes at national level. Better medical education and training of health care professionals regarding retinoblastoma diagnosis is essential in this regard.

Considering the importance of the issue, the biggest limitation of this study is the single center survey. Such surveys should be done at national level which will help in making policies in the health sector.

Ethical Approval

The study was approved by the Institutional review board/ Ethical review board (2020-107-CHICH).

Conflict of Interest

Authors declared no conflict of interest.

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Authors' Designation and Contribution

Asma Mushtaq; Assistant Professor: *Concepts, Design, Literature search, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review.*

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