MATHEWS

Research Article

Mathews Journal of Pediatrics

The Predilection to Age, Sex, Laterally and Treatment of Retinoblastoma: A Retrospective Study at a Tertiary Eye Care Center in Bangladesh

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ABSTRACT

Aim: Retinoblastoma is the most common intraocular malignancy in children, with most cases occurring before the age of five. This study looked at the presentation and treatment of retinoblastoma patients at a tertiary eye care center in Bangladesh. **Methods:** Over a fourteen-year period (01.10.2006 to 31.12.2019), information on gender, age, presenting clinical symptoms, and histopathological results were obtained from the medical records of retinoblastoma patients diagnosed at the Chittagong Eye Infirmary and Training Complex (CEITC), Chittagong, Bangladesh. **Result:** During the study period, one hundred and forty-four cases of retinoblastoma were reported, with 89 (62%) more males being affected than 55 (38%) females. Most children (107, 74.31%) are affected within the first 4 years of their age, with a peak age of 1 and 2 years. Unilateral cases (103, 72%) are more common than bilateral cases (41, 28%). Leukocoria was the most common (83.33%) presenting clinical feature, followed by proptosis. Enucleation and chemotherapy were received by 73 patients (50.69%), followed by enucleation in 54 patients (37.5%). **Conclusions:** To diagnose retinoblastoma as early as possible, health education for parents and healthcare professionals, as well as increased ophthalmologist training, are required. Genetic testing for siblings and children of retinoblastoma patients, as well as detection of high-risk children, would be beneficial, but is currently not financially feasible in underdeveloped countries. Future healthcare planning should prioritize the development of capacity for preschool ophthalmologic screening.

Keywords: Retinoblastoma, Leukocoria, Squint, Enucleation, Chemotherapy

INTRODUCTION

The most common primary intraocular cancer in children is retinoblastoma. It is an uncommon tumor, occurring in around one in every 20,000 live births. The most common presenting symptom is leukocoria (white pupillary reflex), which accounts for almost two-thirds of cases. Other symptoms include strabismus, secondary glaucoma, proptosis, anterior chamber inflammatory changes, and spontaneous hyphema

Vol No: 08, Issue: 01

Received Date: December 19, 2022

Published Date: January 03, 2023

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Citation: Chowdhury EH, et al. (2023). The Predilection to Age, Sex, Laterally and Treatment of Retinoblastoma: A Retrospective Study at a Tertiary Eye Care Center in Bangladesh. Mathews J Pediatr. 8(1):28.

[1]. In underdeveloped countries, the forms of presentation may differ, with late presentation with orbital involvement being the most common (proptosis) and metastasis [2]. Understanding the types of presentation is critical for timely diagnosis because children's survival is strongly reliant on the degree of disease progression.

In Bangladesh, there is a scarcity of published data on the different clinical manifestations of retinoblastoma. As a result, we examined the case records of retinoblastoma patients treated at Chittagong Eye Infirmary and Training Complex (CEITC), Pahartali, a tertiary teaching hospital in Chittagong, Bangladesh, to examine the patient demographics, clinical characteristics, and disease spread at presentation.

MATERIALS AND METHODS

The case records of all retinoblastoma patients treated at CEITC over a fourteen-year period (2006-2019) were reviewed. The age and gender of the patients, the eye, the presenting clinical features, the CT scan findings of the orbits and brain at presentation (to evaluate the spread of the disease into the orbit and brain), the lumbar puncture and bone marrow aspiration results (to assess metastasis) were all recorded in the patients' case records. Clinical examination was used to make the diagnosis, which was corroborated by computed axial tomography scans of the orbits and brain. Patients staged according to International Retinoblastoma Staging System (IRSS). Intraocular tumors were classified as stage I, those with orbital extension as stage II, regional extension (overt orbital or periocular or cervical lymph node extension) as stage III, and those with metastasis (either hematogenous or central nervous system) as stage IV. All intraocular tumors were grouped as A to E according to International Intraocular Retinoblastoma Classification (IIRC) depending on tumor size, location and additional feature. Patients' findings were recorded in the same sort of proforma.

Stata V15 statistical software was used to process and analyze the data.

RESULTS

The demography of patients: During the study period, one hundred and forty-four (144) cases of retinoblastoma were reported, with 89 (62%) more males being affected than 55 (38%) females. Most children (107, or 74.31%) are affected within the first 4 years of their age, with a peak age between 1 year and 2 years, 39 (27.08%);less than 6 months, 16 (11.11%); 6 months to one year, 10 (6.94%);two to three years, 19 (13.19%); three to four years,23(15.97%); four to five years, 15 (10.42%);more than five years, 22 (15.28%). Unilateral cases outnumber bilateral cases by 103 (72%) to 41 (28%). Among them, 59 (41%) are impacted the left side, while 44 (31%) are affected on the right. (Table: 1).

Table 1: Demography and laterality in retinoblastoma patients.

	Number(n=144)	Percentage (%)
Age		
0 m to 6 months	16	11.11
> 6 months to 1 year	10	6.94
> 1 year to 2 years	39	27.08
> 2 years to 3 years	19	13.19
> 3 years to 4 years	23	15.97
> 4 years to 5 years	15	10.42
> 5 years	22	15.28
Sex		
Male	89	61.80
Female	55	38.20
Laterally		
Left	59	40.97
Right	44	30.56
Bilateral	41	28.47

Clinical Features: In our study, leukocoria was the most common (120, 83.33 %) presenting clinical feature, followed by proptosis (4.86 %) and squint (4.86%) (Table: 2). Four complained of vision loss, and two suffered from redness of eyes.

Table 2: Clinical features at a presentation by laterally in retinoblastoma patients (N=144).

Presentations*	Laterally			Total
	Left	Right	Bilateral	
Leukocoria	45	39	36	120 (83.33%)
Proptosis	3	3	1	7 (4.86%)
Squint	3	1	3	7 (4.86%)
Loss of vision and pain	4	0	1	5 (3.47%)
Redness of Eye	2	0	0	2 (1.39%)
Ptosis	1	0	0	1 (0.69%)
Glaucoma	1	0	0	1 (0.69%)
Phthisis Bulbi	0	1	0	1 (0.69%)

*Some of the children had more than one sign at the time of presentation.

Treatment: Enucleation and chemotherapy were given to 73 patients (50.69%), followed by enucleation only 54 patients (37.5%), enucleation and radiotherapy only 6, enucleation with chemotherapy and radiotherapy only 4, enucleation and cryotherapy only 4, enucleation and laser therapy only 1, and chemotherapy only two patients, depending on the stage of the disease at presentation. Bilateral cases, unilateral cases of Group D and E, orbital retinoblastoma cases received neoadjuvant chemotherapy and histopathological (post enucleation) high risk groups received adjuvant chemotherapy.

Table 3: Treatment in retinoblastoma patients.

Treatment	Laterally		Total
	Unilateral	Bilateral	
Enucleation and chemotherapy	42	31	73 (50.69%)
Enucleation only	54		54 (37.50%)
Enucleation and radiotherapy	5	1	6 (4.17%)
Enucleation with chemotherapy and radiotherapy	2	2	4 (2.78%)
Enucleation and cryotherapy	s	4	4 (2.78%)
Enucleation and laser therapy		1	1 (0.69%)
Chemotherapy only		2	2 (1.39%)

Histopathological findings: Histopathological reports were found in only 64 (44.44%) of 144 patients, with Retinoblastoma without Optic Nerve invasion being noted in 27 patients and with Optic Nerve invasion being observed in 20 patients, Retinoblastoma with Optic Nerve and Choroidal invasion being found in 14 patients, with no malignancy being found in 2 patients and Coat's disease and retinal detachment being found in 1 patient which was misdiagnosed as retinoblastoma due to its clinical presentation.

DISCUSSION

The most frequent primary malignant intraocular tumor is retinoblastoma. The incidence varies throughout the world, with around one in every 15,000 live births in the United States of America afflicted, compared to one in every 18,000 live births in Asia [3-5]. According to the findings of this study, most patients (67.63%) had unilateral retinoblastoma, whereas the remainder (28.47%) had bilateral retinoblastoma. This result is consistent with data from other Asian nations [6,7].

Retinoblastoma has no gender preference, and the usual age at diagnosis is 18 months, with the great majority becoming clinically obvious before the age of 3 years. Patients with bilateral tumors were more likely to have them than those with unilateral involvement1. In our study, there was a significant difference in the occurrence of retinoblastoma between boys (62%) and girls (38.0%). Most children (74.31%) are affected within the first four years of their life, with a peak age of between one and two years old (27.08 %).

Worldwide, leukocoria is the most common presenting sign of retinoblastoma, followed by strabismus (Table 4). Figures differ from country to country and from time to time within the same country. This is most likely due to the disease's geographical variation, public awareness of the disease, the availability of medical facilities in that country, and the number of patients examined. The frequency of common retinoblastoma presentation modes in our study is consistent with many other studies from around the world.

At the time of diagnosis, 22.6% to 97.9% of retinoblastoma patients had leukocoria, whereas 5.6% to 26% had strabismus. In addition to the above, Abramson et al. 8 reported many uncommon/rare presenting signs in their study of 1265 retinoblastoma patients, including anisocoria, heterochromia iridis, inflammatory signs, nystagmus, microphthalmia/buphthalmos, proptosis, orbital cellulitis, hyphema, ptosis, aniridia, phthisis bulbi.

However, proptosis as a presenting feature at the time of diagnosis was often recorded in various developing countries, including Nigeria (84.6 %) [9], Pakistan (52.8%) [2], Nepal (44.2 %) [2], Thailand (26.7%) [10], and India (25.3 %) [6]. Proptosis as a presenting symptom was seldom recorded in several affluent nations, such as the United States (0.5%) [8] and South Korea (1.4%) [12], and it was not been found in any patients in Australia [13] or Singapore [14].

Leukocoria is caused by the emergence of a tumor mass or a retinal detachment through the pupil. Strabismus is caused by vision loss because of a tumor or retinal detachment involving the macula and/or optic disc. The tumor's orbital expansion causes proptosis, lid swelling, and ecchymosis, and the illness is thought to be in a fairly advanced stage [15]. The late presentation (proptosis) is most likely owing to a lack of public knowledge about the incidence of cancer in the eye in children. Another factor we discovered in our research is that some parents do not accept the diagnosis of cancer in the eye in their children and hence seek therapy from traditional faith healers. They know, after a few months, that it will not cure the condition. Then, they seek medical assistance from another doctor, by which time the condition has progressed to an advanced level and is incurable.

All children with strabismus should have a thorough fundus examination to rule out retinoblastoma, a potentially fatal condition, as the source of the squint. Although rare indications are present in few children, they should be associated with retinoblastoma. Before identifying a patient with retinoblastoma, all other explanations for similar symptoms/signs should be ruled out. In such cases, the child's life can be preserved by initiating therapy as soon as possible.

Enucleation is a final therapy for retinoblastoma with a low complication risk, but the patient does not have a choice in the afflicted eye's vision.

Although successful, external beam radiation can cause aesthetic deformities, cataracts, or retinopathy, as well as an elevated chance of a second non-ocular cancer in the treatment region. Cryotherapy, laser, and plaque radiation have all been used to treat tiny tumors with no indication of seeding. A combination of focal therapy and chemoreduction has given an alternative to primary enucleation for treating big tumors. Chemoreduction is the use of neoadjunctive chemotherapy to reduce tumor volume and allow for targeted therapy [15].

Table 4: The comparative frequency of common retinoblastoma presenting signs in different parts of the world.

Author	Year	Country	No. of patients	Leuko-coria	Strabismus %	Proptosis %
Abramson DH, et al. [8]	1998	USA	1265	56.1	23.6	0.5
Sahu S, et al. [6]	1998	India	296	97.9	25.3	
Peterson RA. [1]	2000	USA	114	61.4	18.4	
Patikulsila P, et al. [7]	2001	Thailand	30	60.0	10.0	26.7
Kao LY, et al. [13]	2002	Taiwan	96	78.1	12.5	16.7
Dondey JC, et al. [16]	2004	Australia	165	53.3	26.0	
Shanmugam MP, et al. [17]	2005	India	355	74.6	6.2	1.1
Badhu et al. [2]	2005	Nepal	43	32.5		44.2
Chang CY, et al. [18]	2006	Taiwan	54	71.4	14.3	
Berman EL, et al. [19]	2007	Australia	142	72.5	22.5	
Chung SC, et al. [12]	2008	South Korea	70	80.0	8.5	1.4
Aung L, et al. [14]	2009	Singapore	30	50.0	20.0	
Rai P, et al. [2]	2009	Pakistan	53	22.6	5.6	52.8
Present study		Bangladesh	144	83.33%	4.9	4.9

Table 4 shows the comparative frequency of common retinoblastoma presenting signs in different parts of the world.

CONCLUSIONS

Health education for parents and healthcare workers, as well as enhanced ophthalmologist training, is essential to detect retinoblastoma as early as possible. Genetic testing for siblings and offspring of retinoblastoma patients, as well as detecting high-risk children, would be advantageous, but it is presently not financially practical in developing countries. The establishment of capacity for newborn ophthalmologic screening should be prioritized in future healthcare planning.

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