

METHODS

Participation in community screening and hospital-based multidisciplinary treatment for early detection and life and globe salvage of patients with retinoblastoma in developing countries: Authors' experiences

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Nearly 8000 new retinoblastoma cases occur every year worldwide. Although revolutionary management strategy had increased the survival rate of retinoblastoma to more than 95%, it remains a deadly kind of cancer. The survival rate for retinoblastoma patients depends on the income of an individual (>90% vs. 40% in high- to low-income countries), and metastasis is higher in low-income countries. Forty-three percent of global disease burden are found in six countries of Asia. An estimated worldwide death rate is more than 40%, with the majority of cases reported from Asia and Africa. In Bangladesh, retinoblastoma constitutes 83% of all pediatric cancer among children below 4 years of age. Early detection and timely referral of cases may decrease the risk for advanced-stage disease, and this can be achieved through strong awareness program. To save life and vision, a multidisciplinary team approach is important. Chittagong Eye Infirmary is a tertiary eye care center with good chemotherapy facilities serving retinoblastoma patients with a multidisciplinary team approach since 2017. This center started screening and local community training program in order to detect the disease easily, and in 2019, it has upgraded treatment facility. From January 2017 to June 2021, a total of 284 retinoblastoma patients were diagnosed, of which 104 received chemotherapy and 53 underwent enucleation with long optic nerve. A total of 256 children were screened. From July 2019 to February 2021, 169 primary school teacher and 408 health worker were trained about the causes and symptoms of retinoblastoma. This helps in early treatment of white pupillary reflex, which is an early sign of retinoblastoma. The hospitals also take care for visual and psychosocial rehabilitation of the retinoblastoma survivals.

Keywords: retinoblastoma, awareness program, early detection, team approach, timely referral

Introduction

Retinoblastoma is the most protectcommon primary intraocular malignancy in the pediatric population, with an incidence of 1:16,000 to 1:18,000 live births, and represents 11% of cancer that develop in the first year of life (1, 2). According to a Retinoblastoma International Collaborative

Study, 90% of cases are diagnosed in children under the age of 6 years and approximately 99% under the age of 10 years. The median age at diagnosis is 1.5 years (3).

The delayed presentation is common in developing and underdeveloped countries. This could be due to a lack of awareness, lack of organized treatment facilities, and economic factors. More than 50% of patients died due

to late presentation (4). Like other developing countries, Bangladesh is also facing the problem in management of RB patients.

Left untreated, RB is fatal. However, due to improved treatment modalities, it has become one of the highest survival cancer among all pediatric malignancies (1, 5, 6). In developed countries, the survival rate is about 95% with a high ocular salvage (7). However, it remains a deadly kind of cancer worldwide, with an estimated death rate of more than 40% and the majority reported from Asia and Africa. In developing countries, the focus should be on early detection and the development of advanced treatment facilities and referral system. Chittagong Eye Infirmary is a tertiary eye care center in Bangladesh which provides services for RB patients since 2017. It has multidisciplinary treatment facilities. To detect early cases of RB and other childhood vision-related diseases, awareness program is a must. For this reason, in 2019, this center has started field-level awareness program and upgraded the treatment facilities. We now discussed our hospital- and field-level activities.

Retinoblastoma: present-day status

Nearly 8000 new RB cases occur every year worldwide, with more than 1400 cases in India (8). Although it affects various socioeconomic groups equally, the lower socioeconomic groups present with more advanced stages. The mortality rate in different regions of the world is different. Africa had the highest mortality rate (70%). The estimated rate in other regions includes 39% in Asia (excluding Japan), 3% in Japan, 3% in North America, 20% in Latin America, and 10% in Oceania (7). Survival rate in developed countries is highly good. One survey shows the percentage of survival rate in high- and low-income countries is 90% and 40%, respectively (9). Literature also shows that the occurrence of metastasis is higher in low-income countries compared with middle-income ones (32% vs. 12%) (10). One study showed that approximately 43% of global burden lives are found in six countries of Asia (i.e., India, China, Indonesia, Pakistan, Bangladesh, and Philippines) (9).

Bangladesh and retinoblastoma

According to Sarwar et al., the most common childhood cancer types in Bangladesh were leukemia, RB, and malignant bone tumor, mostly found in 0–14 years age group. RB constitutes 25% of all pediatric and adolescent cancers, with 83% occurring in 0–4 years age group (11).

In our country, only few tertiary centers provided the treatment for RB, but not total care. For this reason, patients move to different centers for further treatment. Most of the patients are lost in this way and ultimately endangers the life of infected children. In addition, parents lack awareness

about the white pupil and as a result patients delayed in seeking treatment assistance and this further creates difficulties to health facilitators. These problems are almost the same in other developing and underdeveloped countries of Asia and Africa. Some difficulties that these countries faced are as follows:

- Delay in seeking medical attention – due to lack of awareness about RB
- Lack of National Screening Program on eye diseases
- Lack of trained personnel specialized in treating RB
- Presence of less well-equipped treatment centers
- Lack of information
- Socioeconomic factors, financial issues, religious belief, gender bias
- Poor compliance to treatment
- Lack of one-stop multidisciplinary team in one roof
- Lack of proper counseling and support group
- Poor referral system

Current management protocol of retinoblastoma

RB needs multidisciplinary management in a team approach. The team consists of ocular oncologist, oculoplastic surgeon, retina specialist, pediatric ophthalmologist, pediatrician, pediatric oncologist, radiation oncologist, anesthesiologist, histopathologist, ophthalmologist, and counselor.

The management includes:

- Proper diagnosis of the disease
- Treatment
- Timely follow-up
- Genetic and general counseling
- Sibling screening
- Rehabilitation of RB survivor

Treatment plan of RB depends on presentation of the disease, either bilateral or unilateral; grading and staging of tumor; and the extent of metastasis.

The management of RB has dramatically changed over the past two decades, from previous radiotherapy methods to current chemotherapy strategies. Chemotherapy has become the first choice of treatment. Intravenous chemotherapy for six cycles at an interval of 3–4 weeks is accepted as an international treatment standard by most centers of the world (12, 13). Combination of systemic chemotherapy with local treatments, also called sequential aggressive local therapy (SALT) (14), is the most popular conservative treatment for intraocular tumor. But enucleation still remains the gold standard for some cases of unilateral RB.

The treatment options are shown in **Table 1**.

TABLE 1 | Current treatment options for retinoblastoma.

Treatment options	
Local therapy	Laser photocoagulation (Green laser) Transpupillary thermotherapy (diode laser) Cryotherapy
Chemotherapy	Local chemotherapy Intravitreal Periocular Intracameral Intravenous chemotherapy Intra-arterial chemotherapy Intrathecal chemotherapy
Radiation therapy	Plaque radiation therapy (brachytherapy) External beam radiation therapy Proton beam therapy
Surgery	Enucleation (intraocular) Exenteration (extraocular)

Retinoblastoma and role of chittagong eye infirmary

Chittagong Eye Infirmary and Training Complex is a tertiary eye care and referral center in Bangladesh. This institute treats RB and its team consists of ocular oncologist, oculoplastic surgeon, retina specialist, pediatric ophthalmologist, pediatrician, oncologist, anesthesiologist, histopathologist, and ocularist. In addition to chemotherapy and surgical treatment, the hospital also provides sibling screening, general and genetic counseling, timely follow-up of the patients, visual and cosmetic rehabilitation of RB survivors, awareness programs, field-level screening and training programs, reliable histopathological services, and proper data preservation.

From January 2017, the hospital started chemotherapy services for RB children with the support of a German NGO named Children Eye Cancer Foundation, and up to June 2021, 284 cases were diagnosed, of which 88 children had received vincristine, etoposide, carboplatin (VEC) chemotherapy and 14 are still receiving. Also, 53 children underwent enucleation with long optic nerve.

Due to high cost of treatment, which is a burden to a family, the hospital is providing services at free or minimal cost. The Children Eye Cancer Foundation gives support for chemotherapeutic medicine and the hospital provides support for surgery and local therapy. Schedule of chemotherapy, physical conditions of patients, and reports related to patients are monitor regularly by telephone or using different apps. Many children need blood transfusion as adverse effect of chemotherapy. For managing these situations, we have blood donor team also. Besides, junior doctors and midlevel ophthalmic assistants are trained about the chemotherapy preparation and management of complication.

From 2019, the Chittagong Eye Infirmary along with International Rotary Club has started screening and field-level awareness program for RB by providing training to primary school teacher and health worker under “Fighting Small Children Blindness and Death under 6” project. Under this program, from July 2019 to February 2020, a total of 169 primary school teacher and 408 health workers were trained about the features and signs of RB. In addition, 256 children were screened at different schools and EPI centers of Chittagong district. Due COVID pandemic, the field activities are stopped, but not the hospital activities. The hospital also started transpupillary thermotherapy (TTT), which is the most commonly used adjuvant therapy. Treatment can also be undertaken as a primary task (15). This awareness program has increased the referral to our center and new treatment modalities have given new strength to the surgeons to fight against this deadly tumor (Table 2).

Future plan

- Spreading the awareness program for early detection of cases countrywide
- Extend the RB screening program
- Strengthening the existing oncology services
- Start genetic screening test for RB

TABLE 2 | Hospital and field-level activity of chittagong eye infirmary and training complex.

Hospital activity			Field activity		
Time period 2017 Jan to 2021 June	Diagnosis	284	Time period 2019 Aug to 2021 Feb	Screening	256
	Chemotherapy	102		Training of school teacher	169
	Enucleation with long optic nerve	53		Training of health worker	408
	Transpupillary thermotherapy and Cryotherapy	76			



FIGURE 1 | Field activity. **(A)** Training program. **(B)** Screening of under 6 children.



FIGURE 2 | Hospital activity. **(A)** Chemotherapy. **(B)** Counselling. **(C)** TTT Application.

Conclusion

Since the management of RB is long, the cumulative treatment cost is high. Most of the patients of developing countries are from low- and middle-income families and so it is a burden for families to bear the whole treatment and follow-up cost. Strong awareness program and timely referral will help detect the cases early, which will save both life and treatment cost. The multidisciplinary team approach will increase the patient compliance. All these efforts will decrease the economic burden of countries. To make this effort successful, donation and support from individuals, institutions, government, and different NGOs are needed.

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