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Original Research Article

Descriptive Study of Retinoblastoma Survivors in Tertiary Care Center in 2019

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Abstract: ***Purpose:*** Retinoblastoma is rare disease but potentially fatal if left untreated. This study aimed to evaluate demographic profile, treatment and complications in survivors of retinoblastoma in tertiary care center in 2019. ***Method:*** This is multicentric hospital based cross sectional study conducted from January 2019 to December 2019 after ethical clearance from National Health Research Council. All post-treatment cases of retinoblastoma who had completed at least 1-year follow-up examination in any of our retinoblastoma (RB) center in 2019 were included whereas newly diagnosed and ongoing treatment cases and those failed to consent were excluded. Data based on demographic profile, ethnic and geographical distribution of RB survivors was collected and entered into Microsoft Excel 2016. Statistical analysis was performed using Statistical Package for Social Sciences version 20. ***Result:*** A total of 37 RB survivors that included 24(64.9%) female and 13(35.1%) male. Of the total, 34 (91.8%) survivors had unilateral (Right Eye 18, Left Eye 16) involvement whereas 3(8.1%) bilateral involvement. The mean age at diagnosis and study time was 38.65 ± 37.43 months (3-214 months) and 93.46 ± 65.58 months (16-252 months) respectively. Primary enucleation was commonest mode of treatment (64.9%). Majority of survivors belonged to upper caste group 20(54.1%) and mostly from Bagmati 15(40.5%) followed by province-2 (21.6%). ***Conclusion:*** Descriptive study showed that most of survivors had undergone enucleation due to delayed presentation with poor prognosis. Early diagnosis and appropriate treatment modality are prerequisite for salvaging life of child, sight and eyeball.

Keywords: Descriptive, Enucleation, Ethnicity, Retinoblastoma, Survivors.

INTRODUCTION

Retinoblastoma is the most common intraocular malignancy of infancy and childhood with a survival rate exceeding 95% in high-income countries [1]. With advanced technology and treatment modality in developed countries, the goals of retinoblastoma treatment have been diverted to save sight and eye; however, developing countries like Nepal are struggling to save child life due to delayed presentation and inadequate conservative modality of treatment. More recently, the use of targeted chemotherapy allowed the salvage of even more advanced cases [2, 3]. So, early diagnosis and appropriate treatment are crucial in achieving the primary goals of treatment i.e. saving life and eye with vision as much as possible.

In the context of developed countries, newer effective systemic chemotherapeutic agents and newer local treatment modalities such as laser photocoagulation, cryotherapy, brachytherapy, thermotherapy, and Intravitreal chemotherapy have been implicated to preserve vision [4] while the majority of patients in developing countries present in advanced stages when enucleation remains the only treatment of choice.

To our knowledge, none of the studies in Nepal revealed the demographic profile, geographical distribution of survivors of retinoblastoma living in this country. Herein, we present this study to report the demographic profile, treatment modality and complications treatment of survivors living in our country.

METHODOLOGY

This is a multicentric hospital-based cross-sectional study conducted by the tenets of the Declaration of Helsinki from January 2019 to

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December 2019 after ethical approval from the National Health Research Council (NHRC) Ethical Review Board (Ref. no 1768). Twenty –seven Retinoblastoma centers were selected for the study based on location, patient flow. Retinoblastoma patients who completed treatment and one-year follow-up examination attending RB centers in the year 2019 were included. Other newly diagnosed and ongoing treatment patients who failed to consent for the study were excluded. The retinoblastoma survivors were defined as those retinoblastoma patients who completed treatment and 1-year follow-up examination. Retinoblastoma survivors were classified based on their clinical records as either unilateral or bilateral, familial or sporadic, grouping and staging as per the International Classification of Retinoblastoma groups (ICRB). An ethnicity code was provided to each patient as per the health management information system (HMIS) [5] and ethnic and geographical distribution of survivors were evaluated.

Data entered into Microsoft Excel 2010 and analyzed using Statistical Package for Social Sciences version 20 (SPSS, Inc. Chicago, IL, USA). For descriptive statistics, percentage, mean, standard deviation was computed and presented in the graphical and tabular presentation.

RESULTS

Thirty-seven survivors of retinoblastomas attended RB centers during the said study period. Of the total, 24(64.9%) survivors were female and 13(35.1%) male with a male: female ratio of 1: 1.85. The majority of cases were unilateral involving the right eye (48.6%) and left eye (43.2%) whereas only 8.1% of cases were bilateral. The mean age at the time of study and diagnosis was 93.46 ± 65.58 months (16-252 months) and 38.65 ± 37.43 months (3-214 months) respectively. Detailed demographic characteristics of survivors are as shown in **Table 1.**

Table-1: Demographic characteristics of study participants.

Characters	**Number (%)**
Mean Age at Diagnosis Mean ± SD* (range)	38.65 ± 37.43 months (3-214 months)
Mean Age at study time Mean ± SD(range)	93.46 ± 65.58 months (16-252 months)
Sex	
Male	13 (35.1%)
Female	24 (64.9%)
Family History of RB	
Positive	1 (2.7%)
Negative	36 (97.3%)
Consanguinity	
Yes	1(2.7%)
No	36(97.3%)
Health insurance	
Yes	1(2.7%)
No	36(97.3%)
Laterality	
Right eye	18 (48.6%)
Left eye	16 (43.2%)
Both eye	3 (8.1%)

Values expressed in Numbers and %
*SD, Standard Deviation

More than half of survivors 20 (54.1%) were from the Upper caste group whereas no survivors were reported from religious minorities Muslims. Disadvantaged Janjatis and non-Dalit terai caste groups had 5(13.5%) survivors each while advantaged Janjatis and Dalits had 4(10.8%) and 3(8.1%) survivors. Bagmati province had 15(40.5%) survivors followed by province-2 8(21.6%), Lumbini province 5(13.5%), Province-1 5(13.5% and Gandaki 3(8.1%). All the detailed ethnical and geographical distribution of survivors are as shown in **Table 2**.

Table-2: Distribution of survivors by Ethnicity and Geography.

Characteristics	Number (%)
Ethnicity	
Dalits	3 (8.1%)
Disadvantaged janjatis	5 (13.5%)
Disadvantaged non dalit terai caste	5 (13.5%)
Religious minority Muslims	0
Relatively advantaged janjatis	4(10.8%)
Upper caste	20 (54.1%)
Geography	
Province 1	5 (13.5%)
Province 2	8 (21.6%)
Bagmati	15(40.5%)
Gandaki	3 (8.1%)
Lumbini	5(13.5%)
Karnali	1 (2.7%)
Province 7	0

The majority of survivors had undergone enucleation only 24(64.9%) followed by enucleation plus systemic chemotherapy 10(27%). However, only 1(2.7%) survivor from province-2 was provided all modalities of conservative treatment. The treatment modalities distribution by geography is as shown in **Table 3.** The majority of patients received treatment in Nepal 35(94.6%) and only 2(5.4%) had received treatment in India. Almost all survivors (97.3%) attended for socket evaluation and prosthesis cleaning up. None of the survivors reported complications.

Table-3: Treatment modalities distributed by Geography.

Treatment	**Province**							**Total**
	1	**2**	**Bagmati**	**Gandaki**	**Lumbini**	**Karnali**	**7**	
Enucleation	4	4	9	2	4	1	0	24
Systemic CT + Enucleation	1	4	4	0	1	0	0	10
Enucleation + CT+ Laser	0	0	1	0	0	0	0	1
Enucleation + Laser	0	0	0	1	0	0	0	1
Systemic CT+ Cryo+ TTT+ Laser	0	0	1	0	0	0	0	1
Total	5	8	15	3	5	1	0	37

DISCUSSION

Retinoblastoma management has been evolved over a century, from >95% mortality to > 95% survival in high-income countries [6]. However, developing countries are still in the phase of saving the life of a child rather than vision and eyeball due to delayed presentation and limited treatment options. In the context of Nepal, no study has been carried out revealing the demographic profile of survivors, the treatment they received, and complications related to disease and treatment. Herein, we conducted a descriptive study of RB survivors in our country in 2019.

In our study, there was a female preponderance in contrast to previously published literature. [7, 8] However, female preponderance was reported similar to our study in various studies [1, 9, 10]. The mean age of survivors at the time of diagnosis was 38.65 months which is higher than other studies [7, 11]. The late presentation of RB in our country is probably due to ignorance, illiteracy, and poverty that lead to an advanced stage with a poor prognosis. The mean age of survivors at the time of the study was 93.46 months with a range of 16-252 months which is much lesser than other studies with long-term follow-up examination [12–16]. Here we have included all survivors who had completed at least 1 year of follow-up examination after treatment. However, long-term follow-up is required for assessing health-related problems associated with the disease itself and treatment.

More than 95% of survivors reported a negative family of retinoblastoma and parental marriage consanguinity. Similar to our study, previous studies done in Nepal showed there is no role of consanguinity in retinoblastoma among Nepalese children [17]. However, consanguinity is closely related to the occurrence of bilateral retinoblastoma as shown in the literature [7, 10, 13].

While concerning laterality, more than 90% of survivors had unilateral retinoblastomas among which right eye involvement was predominant (48.6%). Only

a few survivors were bilaterally involved (8.1%). Similar unilateral involvement predominantly right eye was reported in the studies published in Nepal and abroad [7, 18]. However, bilateral retinoblastoma survivors were predominant in some other studies [18, 19].

In our study, the majority of survivors had undergone enucleation only (>60%) due to late presentation to illiteracy, poverty, and lack of appropriate treatment modalities. Only 27% of survivors were treated with systemic chemotherapy followed by enucleation. Another focal therapy like TTT, Cryotherapy, and laser was given to very few survivors. In developing countries like Nepal, primary enucleation was a commonly used treatment modality [17, 18, 21, 22]. In contrast to developing countries, conservative treatment modalities have been adopted to save eyeball and vision in developed countries due to advances in diagnostic technology and the availability of modern treatment.

The presenting study showed that the most of survivors were found in Province-1 (35.3%) and Bagmati province (23.5%). The possible reason could be the availability of retinoblastoma care services and increased awareness among the people in these provinces. Most of the retinoblastoma cases remained undiagnosed and presented at an advanced stage with a poor prognosis of life and sight in the remote areas. The previous studies conducted in our country revealed that 50% of retinoblastomas were from Terai followed by the hilly regions (46%) [17, 23]. However, no studies have been carried out so far revealing the causes for the higher prevalence of retinoblastoma in the Terai region of Nepal. The possibility of consanguineous marriage among Muslims and positive family history of cancer are reported and suggested for the higher prevalence in terai. Further prospective study regarding the variation of prevalence of retinoblastoma among different provinces is needed.

In this study, most survivors belonged to the so-called upper caste group comprising Chhetri and Brahmin (>50%). The marginalized groups encompassing Dalits, disadvantaged Janjatis, and disadvantaged non-dalit Terai caste groups constituted the rest of the survivors. Surprisingly, religious minority Muslims and Churaute had no survivors in our study. Although retinoblastoma has no racial and gender predilection, a larger number of survivors in the upper-caste group is due to a larger proportion of the population of Chhetri and Brahmin in Nepal [24]. We found neither positive family history, nor marriage consanguinity, and Muslim religion has a statistically significant role in the incidence and survival rate of retinoblastoma. However, accessibility, affordability, and availability of treatment of RB have a great impact on survival and disease burden.

Almost 95% of survivors were treated in one tertiary eye care center in Nepal, while 2 cases had a history of treatment in the neighboring country. Most of the survivors presented for routine socket evaluation and prosthesis care. There were no other complications or evidence of secondary tumor reported by survivors. However, the quality of life of RB survivors wasn't studied.

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Conflict of Interest: None

CONCLUSION

In summary, this multicentric multiethnic hospital-based study showed the demographic profile of RB survivors including type and place of treatment provided. The high degree of clinical suspicion, easy referral network, and availability of modern treatment modalities are important for increasing the survival rate of life, sight, and eyeball. However, the quality of life of retinoblastoma survivors was not studied. Further prospective study on the quality of life of RB survivors is recommended.

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