

RESEARCH ARTICLE

Epidemiological Characteristics of Retinoblastoma in Children Attending Almuassat University Hospital, Damascus, Syria, 2012-2016

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Abstract

Retinoblastoma (Rb) is a malignant tumor that originates from the developing retina. Diagnosis is based on clinical signs and symptoms and usually children under the age of five years are affected. Early diagnosis and treatment of Rb and non-ocular tumors can reduce morbidity and increase longevity. Treatment in the early stages may allow a good prognosis and salvage of visual function. The aim of this study is to present descriptive epidemiological aspects of retinoblastomas in children seen at Almuassat University Hospital (AUH) in Damascus, Syria from 1 January 2012 to 31 October 2016. In this retrospective, observational hospital survey, medical records of 37 retinoblastoma cases were reviewed. The male/female (M/F) ratio was 1.6. The most frequent presenting sign was leukocoria (56.7%) and 81% of cases were diagnosed between the ages of 4 months and 3 years. More than 73% of cases were diagnosed early at stages I and II.

Keywords: Retinoblastoma- epidemiology- children - Syria

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Introduction

Retinoblastoma is the most common primary ocular malignancy in children (Eagle, 2013; Wongmas et al., 2015). Unfortunately, it is not detected until advanced stages in developing countries (Ajaiyeoba et al., 1993; Zygulska-Mach et al., 1994; Sahu et al., 1998). About 90% of cases feature a germline mutation in the RB1 gene and these will develop retinoblastoma during their early childhood. An association between mutations in germline cells and aging has been demonstrated. This suggests a higher incidence of childhood cancer including retinoblastoma among children of older parents (Saremi et al., 2014). Retinoblastoma morbidity and mortality are improved as the diagnosis and management of this condition is improving, also success rates for conservative therapies are greater when therapy is administered in earlier stage disease (Ramirez-Ortiz et al., 2014).

To detect the incidence rate of retinoblastoma, many population-based studies have been conducted in several countries, such as the USA (Broaddus et al., 2009), Great Britain (MacCarthy et al., 2009a; MacCarthy et al., 2009b; MacCarthy et al., 2009c), Europe (Arndt et al., 2007), Singapore (Lim et al., 2013), and Japan (Azuma, 2007; Araki et al., 2011). According to these studies the incidence rates of retinoblastoma were 40–60 per million

live births worldwide (1 per 16,000–24,000 live births). However in Syria till now there is no accurate information regarding the frequency and clinical characteristics of RB.

Currently, most patients diagnosed in early stages can achieve long time disease free survival (Kalita et al., 2014; Liu et al., 2014; Soliman et al., 2015). The overall 5-years survival rate in USA increased from 92.3% to 96.5% over a period of 30 years (1975–2004) (Broaddus et al., 2009). In less-developed countries, there is a much lower mean survival rate ranging from 40% (23–70%) in lower-income countries to 79% (54–93%) in upper-middle-income countries (Houston et al., 2013).

The management of retinoblastoma previously aimed to save the life, eye, vision and cosmetics of the child, respectively. Currently, retinoblastoma is treated with various procedures including enucleation (eye removal), external beam radiotherapy, systemic chemotherapy and focal therapies, such as thermotherapy, cryotherapy, laser photocoagulation and plaque radiotherapy (Bhavsar et al., 2016; Tuncer et al., 2016).

Treatments vary from person to person. Trend of metastasis, risks of second malignancy, sizes and locations of the tumors, systemic conditions, visual prognosis estimates and other specific situations should be taken into consideration comprehensively (Liu et al., 2014).

Over the last two decades, intravenous chemotherapy

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combined with focal treatments has played a pivotal role in the management of retinoblastoma worldwide (Shields and Shields, 2010), With this treatment approach, ocular salvage was favourable in eyes with less advanced tumours , while enucleation is still unavoidable and is the preferred treatment in eyes with advanced tumours in most countries worldwide (Mourits et al., 2016).

In Syria, there is no accurate information regarding the frequency and clinical characteristics of RB, and we aim to document all retinoblastomas seen at Al Mouassat University Hospital (AUH) in the period between January 2012 and October 2016, as AUH is a central hospital in Syria that could deal with this type of conditions.

Materials and Methods

A retrospective, observational hospital survey during the period from 1 January 2012 to 31 October 2016. Cases were identified by searching the records of the hospital computerized databases. We included all lesions diagnosed as retinoblastoma by fundus examination using the direct and indirect ophthalmoscope, ultrasonography, and MRI. Each patient underwent a thorough history and clinical examination. All clinical records of patients with retinoblastoma histopathological diagnosis, attended by Al Mouassat University Hospital (AUH) in Damascus, Syria, were reviewed. AUH has precise records of the population that receive medical care. The overall number was 37 cases.

Study variables

The variables collected for this study included family history of retinoblastoma, sex, age at diagnosis, unilateral and bilateral retinoblastoma, presenting signs and symptoms, metastases and extraocular extensions.

Statistical analysis

The frequency of cases with retinoblastoma with family history and the frequency of unilateral and bilateral cases of retinoblastoma without a family history of retinoblastoma were obtained. In addition, the average annual retinoblastoma incidence (AAI) from each year

of the study was obtained.

Results

A total of 37 retinoblastoma cases were reviewed, of which three (8.1%) were with a family history of retinoblastoma; the remainder were with no family history of retinoblastoma. There were 9 (24.3%) bilateral cases and 28 (75.6%) unilateral cases. 23 male cases were diagnosed, and 14 female cases, leading to 1.6 Male/Female ratio.

Retinoblastoma incidence in children <4 months was 3 cases (8.1) and it was associated with the family history of retinoblastoma. in children between 4 months and three years there were 30 cases (81%). There were only 4 cases (10.8%) of retinoblastoma in children older than three years.

The most presenting sign of retinoblastoma was Leukocoria (white pupillary reflex) with 19 cases (51.4%), followed by strabismus; 7 cases (18.9%), then there were ocular inflammation in 5 cases (13.5%), and only 2 cases presents with anisocoria at the time of diagnosis.

The stage at diagnosis was established for all cases, depending on the American Joint Committee on Cancer (AJCC); 72.9% (n=27) of cases were diagnosed at stages I and II. Among the 37 cases there was no metastases,

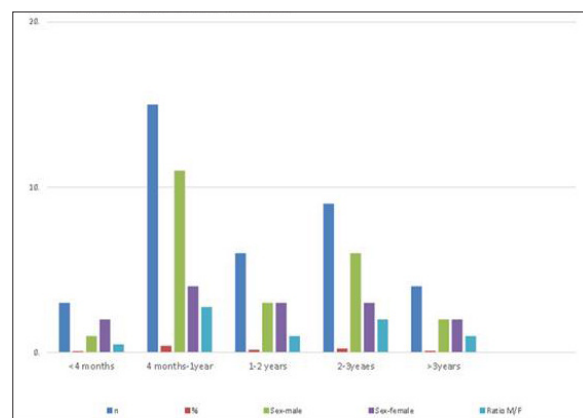


Figure 1. Average Annual Incidence of Retinoblastoma by Age and Sex and Trend

Table 1. Average Annual Incidence of Retinoblastoma by Age and Sex and Trend

Age	n	%	Sex-male	Sex-female	Ratio M/F
<4 months	3	8.1%	1	2	0.5
4 months-1 year	15	40.6%	11	4	2.75
1-2 years	6	16.2%	3	3	1
2-3 years	9	24.3%	6	3	2
>3 years	4	10.8%	2	2	1
	37		23	14	1.6

Table 2. Stages of Retinoblastoma at the Time of Diagnosis

Stage	<4 months	4 months-1 year	1-2 years	2-3 years	>3 years	Total
I	2	7	2	1	-	12
II	1	6	3	5	-	15
III	-	2	1	2	1	6
IV	-	-	-	1	3	4

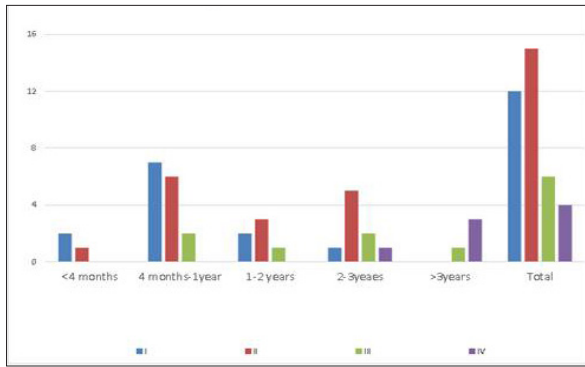


Figure 2. Stage of Retinoblastoma at the Time of Diagnosis

although there were 3 cases (13.5%) of extraocular extensions and were diagnosed by Ultrasonography, CT and MRI.

Discussion

It has been difficult to determine retinoblastoma in Syria. There needs to be a thorough documentation of cases in the population and a better record keeping of their origin.

The data on incidences by family history, age, sex, stage and retinoblastoma bilaterality here offer an extensive epidemiological analysis of retinoblastoma in Syria. The sex ratio in our study was 1.6 (M/F) which is consistent with the Mexican study (Amozorrutia-Alegria et al., 2002) with a ratio of 1.6 too; however this ratio was about 1 in the European countries (MacCarthy et al., 2006). The percentage of cases with family history was 8.1%, which is close to what Amir P. found in his study of RB in Saudi Arabia that 12% of cases was with a family history (Pirouzian, 2014).

Given that bilateral cases are usually hereditary, the frequency we found (24.3%) was similar to the cases in studies from other countries, 21.2% in Mexico City (Amozorrutia-Alegria et al., 2002) and 26% in USA (Pirouzian, 2014). These findings suggest that inherited cases have the same prevalence in Syria as in other countries.

We had three cases (13.5%) with an extra-ocular extension, which is a low percentage compared to 37.1% in Indian children (Sethi et al., 2013) and 52% in a Malaysian study (Menon et al., 2009; Subramaniam et al., 2014), this low percentage is probably due to the routine check-up system applied in the country in the last decade.

According to the age of diagnosis, there were tendencies for early incidences as compared to other studies with 48.7% of the cases that were diagnosed before one year of age, while in the Mexican study 38% of cases were under the age of one year (Amozorrutia-Alegria et al., 2002), and the percentage was 37.6% in the European countries.

The frequency of cases in stages III and IV diagnosed at AUH is (27%), which is similar to Mexican study with 25% of cases in stage III and IV (Amozorrutia-Alegria et al., 2002). This is because most cases were discovered early <1 year.

The most common presenting sign was Leukocoria

followed by strabismus; these results are the same as the one Abramson DH got in his study on 1265 patients (leukocoria 56.2% and strabismus 23.6%) (Abramson et al., 2003).

In conclusion, it is very important to make future studies about the true incidence of RB in Syrian population, and to determine the management methods and survival rates in the country.

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