Determining the Incidence of Retinoblastoma and Survival Rate of Retinoblastoma Patients in Puerto Rico using the Cancer Registry of Puerto Rico (1985-2012)

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Objective: To determine the incidence of retinoblastoma (Rb) and the survival rate of patients with Rb in Puerto Rico.

Methods: This was a retrospective review of data from the Puerto Rico Central Cancer Registry (1985 – 2012).

Results: There were a total of 57 patients with Rb, with an overall incidence of 3.6 per 100,000 live births. By birth cohort, the incidence was 1 of every 29,393 live births. The mortality rate was 14.04% at 5 years. The incidence and the survival rate did not change over the 2 time periods that were compared: 1985 through 1998 and 1999 through 2012.

Conclusion: The incidences of Rb are similar in Puerto Rico and the continental United States. However, our data indicate that the survival rate is lower in the former than it is in the latter. The incidence and the survival rate remained stable over the time studied. [*P R Health Sci J 2022;41(3):149-152*]

Key words: Retinoblastoma, Incidence, Survival rate, Hispanic

Retinoblastoma (Rb) is the most common primary ocular malignancy in the world, with incidence rates reported to be around 1 per 14,000 to 34,000 live births (1-4). Although the general consensus is that there is no difference in incidence between races (5), previous studies have reported that in the United States, the incidence of Rb in Hispanic children is higher than that in non-Hispanic white children of the same age (6). This warrants an investigation into the incidence of Rb in Hispanic patients, which we did using the database of the Central Cancer Registry of Puerto Rico (RCCPR, by its abbreviation in Spanish)

Recent data published by the RCCPR suggest that the incidence of cancer in Puerto Rico increased from 1987 to 2009 (7). Data also show that mortality rates decreased in Puerto Rico during the same time period (7). No reports specific to Rb in Puerto Rico have been published and this study assesses whether Rb trends are consistent with the general cancer trends on the island.

The survival of Rb patients fluctuates considerably between developed and developing nations. In some parts of Asia and Africa, mortality has been reported to be as high as 70%, while in the United States and Europe it has been found to be from 3 to 5% (8-11). We compared the survival rate of Rb patients in Puerto Rico to those rates reported worldwide to see where Puerto Rico lies in terms of the care quality for Rb patients. We hope this study will provide a basis for comparison for future screening and treatment modalities of Rb in Puerto Rico so that we can see whether the techniques employed are giving us the desired results.

To our knowledge, to date, there has not been a study like this one performed in Puerto Rico.

Methods

The data were obtained through the Puerto Rico Central Cancer Registry (RCCPR), a program of the Department of Health established on March 20th, 1951, making it one of the oldest registries in America (12). The RCCPR forms part of the Surveillance Epidemiology and End Results program of the National Cancer Institute. All the Rb cases reported to the RCCPR from 1985 through 2012 were included for analysis in this study. The study was approved by the Institutional Review Board (IRB) of the University of Puerto Rico Medical Sciences Campus.

The RCCPR collects the demographical information of all cancer patients, which includes age, sex, ethnicity, municipality of residence, and occupation. Diagnostic information includes the type of cancer, its localization and size, the date of diagnosis, and the disease extent at the time of diagnosis. Finally, information about the dates and types of treatment is collected as well (12). This information allowed us to estimate survival

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rates for all patients and compare them to the survival rate based on age at diagnosis and other important measures.

We hope this information will provide both primary physicians and ophthalmologists with clues as to how to improve patient and ocular survival in Rb patients in Puerto Rico and allow us to assess whether the current screening and treatment techniques on the island are up to par with those of developed countries.

Various methods exist to estimate the incidence of Rb. The first is a population-based method, which is calculated as the number of people who develop Rb in a given period of time divided by the total person-time risk in that same period. We used the population of children aged 0 to 4 years as the population at risk since a diagnosis of Rb at an older age is rare. The second, standard annual analysis, is the incidence estimated as the number of people who developed Rb in a given period of time divided by the number of live-born children in that period. Finally, birth cohort analysis estimates the incidence of Rb as the number of people who developed Rb among the people born in a given period of time divided by the total number of live-born children in that period. Seregard and coworkers (13) recommend using birth cohort analysis because there is less variability in the incidence rate results. Here, we present all 3 methods of calculating incidence.

To determine the survival durations of patients with Rb, we looked at the intervals between the date of the initial diagnosis and the date of death, the date of loss to follow-up, or the follow-up closing date, whichever applied. We also compared survival rates between age at diagnosis and bilateral and unilateral tumors.

A 95% CI of the incidence rate was estimated based on Poisson distribution. P values less than 0.05 were considered statistically significant.

Results

From 1985 through 2012, there were a total of 57 patients diagnosed with Rb in Puerto Rico. By population at risk (children aged 0 to 4 years), the overall incidence was 8.18 per 1,000,000 person-years. By standard annual analysis, it was 3.59 per 100,000 live births. By birth cohort, incidence was 1 of every 29,393 live births.

The analysis was divided into 2 time periods: from 1985 through 1998 and from 1999 through 2012. By birth cohort, the incidence during the first period was 1 of every 30,987 live births. For the second period, the incidence was 1 of every 27,540 live births. The difference in incidence between the 2 time periods was not statistically significant (P = 0.33) (Table 1).

Survival analysis was conducted on all 57 patients diagnosed during the periods of interest. The mortality rate was 14.04% (8 of 57 cases) at 5 years (Figure 1A). Mortality for the 2 periods were 13.79% and 14.29% respectively. This difference was not statistically significant (P = 0.41) (Figure 1B). Diagnosis at 1 year old or younger resulted in a survival rate of 91.7%. Patients diagnosed at 2 years of age or older had a survival rate of 76.2% (Figure 1C).

The mortality rate for the 41 unilateral cases was 17.07%. For the 13 bilateral cases, the mortality rate was 7.69%. This finding was not statistically significant (P = 0.20).

When calculating the age at diagnosis, we did not consider 3 cases in which the birth date data were limited to the year that the patient was born. Additionally, we did not consider 1 patient who was diagnosed with Rb at 33 years old, as the patient was a significant outlier and would have skewed our statistics because of the small size of the cohort. For the other 53 patients, the average age at diagnosis was 24.21 months. The average age at diagnosis for the 38 unilateral cases included in the analysis was 24.11 months. For the 13 bilateral cases, the average age at diagnosis was 14.31 months.

Discussion

This study evaluated the incidence of Rb and the survival rate of patients diagnosed with Rb from 1985 through 2012 using the database of the Puerto Rico Central Cancer Registry (RCCPR). Under law 28 of 1951, all the physicians and all the hospitals, private clinics and other institutions providing health services must report all the cases of cancer diagnosed and/or treated in their institution. Audits by the CDC have reported that, at 95%, the RCCPR registration rate is comparable to the median in the continental United States (12). Therefore, we believe its data serves as a reliable tool to elicit the incidence of Rb.

There were a total of 57 patients diagnosed with Rb reported to the Puerto Rico Central Cancer Registry from 1985 through 2012. The overall incidence of Rb during the entire period of interest was similar to that reported by previous studies, regardless of the method used (1-4, 6, 11). As revealed previously, for example, by standard annual analysis, the incidence in Puerto Rico was 3.59 per 100,000 live births or 1 per 27,855 live births; and by birth cohort, the incidence was 1 of every 29,393 live

Table 1. Incidence rate of Retinoblastoma in Puerto Rico during the period of interest (1985-2012).

Period	Incidence per Live Birth (95% CI)	Incidence from Birth Cohort Analysis (95% CI)	Incidence by Population at Risk (95% CI)
1985-1998	3.2 (2.2-4.6) per 100,000 live births or 1 per 30,987 (21,739-45,455) live births	3.2 (2.2-4.6) per 100,000 live births or 1 per 30,987 (21,739-45,455) live births	8.1 (5.6-11.7) per 1,000,000 person-years
1999-2012	4.1 (2.8-5.9) per 100,000 live births or 1 per 24,631 (16,949-35,714) live births	3.6 (2.5-5.3) per 100,000 live births or 1 per 27540 (18,868-40,000) live births	8.3 (5.6-12.4) per 1,000,000 person-years
1985-2012	3.6 (2.8-4.7) per 100,000 live births or 1 per 27,855 (21,739-45,455) live births	3.4 (2.2-4.6) per 100,000 live births or 1 per 29,393 (22,727-38,462) live births	8.2 (6.2-10.7) per 1,000,000 person-years

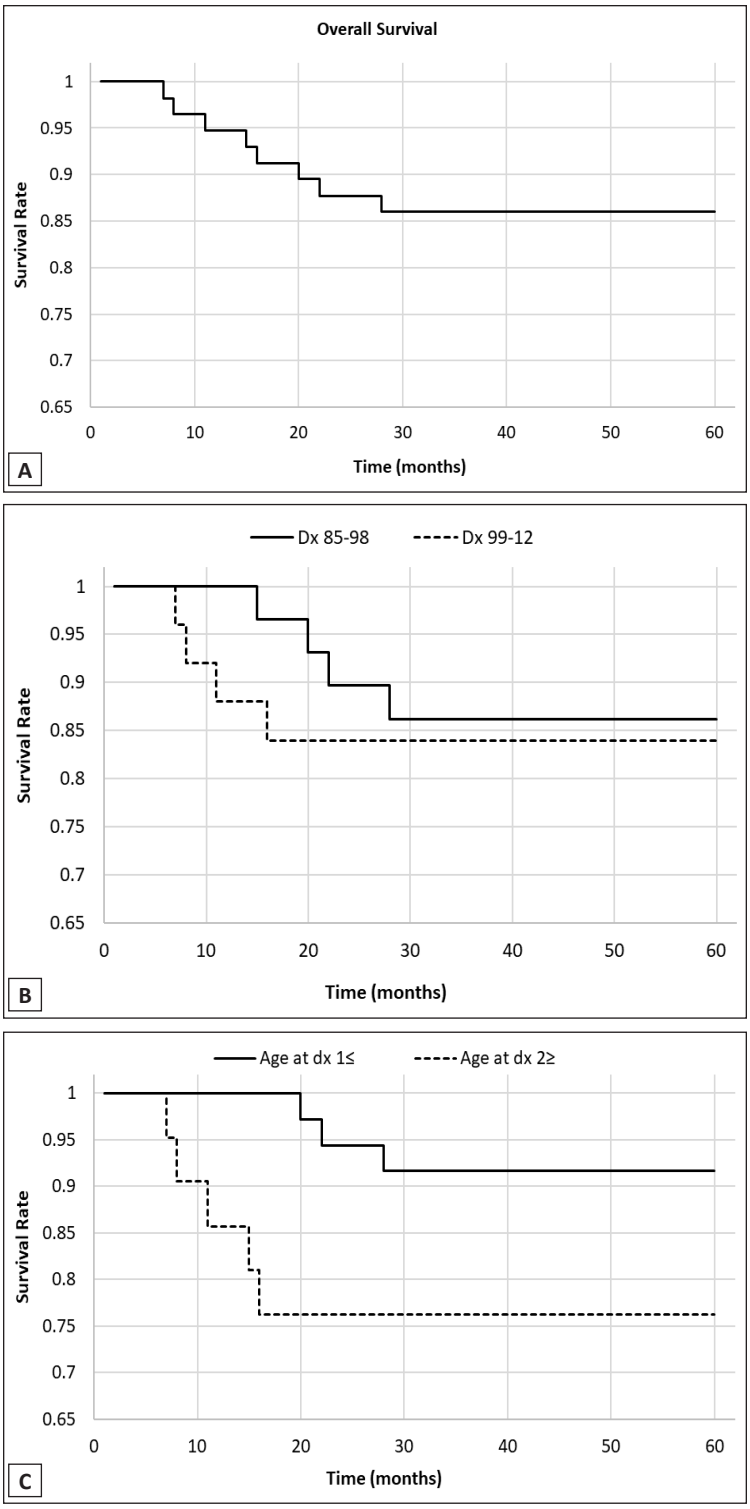

Figure 1. (A) The 5-year survival rate (including all-cause mortality) of patients in Puerto Rico diagnosed with retinoblastoma from 1985 through 2012. (B) The 5-year survival rates (including all-cause mortality) of patients in Puerto Rico diagnosed with retinoblastoma from 1985 through 1998 (continuous line) and 1999 through 2012 (fragmented line). The survival rates were similar. (C) The 5-year survival rates (including all-cause mortality) of patients in Puerto Rico diagnosed with retinoblastoma at age ≤1 (continuous line) and ≥2 years old (fragmented line) from 1985 through 2012.

births. These numbers are comparable to the already established incidence of Rb in the United States, which ranges from 1 of 18,000 to 1 of 34,000 live births (6, 11). The incidence did not change over the studied time period.

The mortality rate of Rb for cases diagnosed from 1985 through 2012 was 14.04%. This rate was higher than the one found by Broaddus and colleagues (11) and the difference was statistically significant (P = 0.0037), which indicates a higher mortality of Rb in Puerto Rico compared to the continental United States and other developed countries.

Treatment for cancer in Puerto Rico has improved significantly as shown by the decreased mortality rates for all types of cancer (12). However, our study shows that the Rb mortality rate did not improve, as both time periods had similar mortality rates.

There were a total of 41 unilateral cases, 13 bilateral cases and 3 cases in which laterality was unknown. Although we found an increase in mortality in unilateral cases in our study, which is inconsistent with what has already been established in the literature (1), this finding was not statistically significant. Given no abnormalities in the average age at diagnosis of our study, this finding can be attributed to chance and the small sample size of our study.

It has been well documented that the delayed diagnosis of Rb leads to a poorer prognosis and a lower survival rate. In our study, diagnosis at 1 year old or younger resulted in a survival rate of 91.7% versus 76.2% in patients diagnosed at 2 years of age or older. This led us to consider that delayed diagnosis might explain the increased mortality in Puerto Rico compared to the continental United States. However, the age at diagnosis in our study was consistent with already established averages of age at diagnosis in the United States (1, 11). Furthermore, the percentage of patients diagnosed at 1 year or younger in our study was similar to the percentages seen in other studies that have reported higher survival rates (4). All these data argue that the increased mortality of Rb patients in Puerto Rico is not caused exclusively by their being diagnosed at a higher age. We theorize that other factors, such as a lack of availability or access to treatment options and insufficient follow-up and surveillance of comorbidities may be responsible for the increased mortality. Further studies are needed to try to elicit the possible reasons for increased mortality in Puerto Rico compared to the continental United States.

The present study had several limitations. The RCCPR database is incomplete for many patients,

especially regarding treatment. Therefore, we were unable to compare treatment options and their effects on mortality. This limited our ability to assess whether the increased mortality in Puerto Rico compared to the continental United States was more strongly associated with screening techniques or with available treatment options.

This study will provide a basis for comparison for the future analysis of Rb diagnosis and patient results in Puerto Rico. This study also sets up further studies that can elicit the reasons for the decrease in survival rate of Rb patients in Puerto Rico compared to the continental United States. This may lead to improved screening techniques, genetic diagnosis and the co-management of patients with Rb in Puerto Rico.

Conclusions

To our knowledge, this is the first report on Rb incidence and patient survival rate in Puerto Rico. Even though the incidence of Rb in Puerto Rico is similar to that of the continental United States, our data show that the survival rate in Puerto Rico is lower. The incidence and the survival rate remained stable over the studied period. More studies are needed to determine the reasons for the increased mortality of patients with Rb in Puerto Rico compared to the continental United States.

Resumen

Objetivo: Determinar la incidencia de retinoblastoma (Rb) y la tasa de supervivencia de pacientes con Rb en Puerto Rico. Métodos: Revisión retrospectiva de datos del Registro Central de Cáncer de Puerto Rico. (1985 – 2012). Resultados: Hubo un total de 57 pacientes diagnosticados con Rb. La incidencia fue de 3.59 por cada 100,000 nacimientos vivos, o 1 de cada 29,393 nacimientos vivos. La tasa de mortalidad fue 14.04% a 5 años. Ni la incidencia ni la tasa de supervivencia cambiaron en los diferentes periodos estudiados: 1985 a 1998 y 1999 a 2012. Conclusiones: A pesar de que la incidencia de Rb en Puerto Rico fue similar a la de los Estados Unidos continentales, nuestros datos sugieren que la tasa de supervivencia en Puerto Rico fue más baja que en los Estados Unidos continentales. La incidencia y la tasa de supervivencia permanecieron estables a través del periodo de estudio.

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