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Incidence and mortality rates for childhood acute lymphoblastic leukemia in Puerto Rican Hispanics, 2012–2016

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Abstract

Background: Acute lymphoblastic leukemia (ALL) accounts for 80% of all leukemias diagnosed in children. Although ALL age patterns are consistent across racial/ethnic groups, their incidence and mortality rates are highly variable.We assessed the age-standardized ALL incidence and mortality rates of Puerto Rican Hispanic (PRH) children and compared them with those of US mainland Hispanics (USH), non-Hispanic whites (NHW), non-Hispanic blacks (NHB) and Non-Hispanic Asian or Pacific Islanders (NHAPI).

Methods: Differences between racial/ethnic groups were assessed by estimating the Standardized Rate Ratio (SRR) for 2010–2014. Secondary data analyses of the Puerto Rico Central Cancer Registry and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) databases were performed for the 2001–2016 period.

Results: PRH children had 31% lower incidence rates than USH, but 86% higher incidence rates than NHB. In addition, the incidence trends of ALL increased significantly from 2001 to 2016 among PRH and USH, with 5% and 0.9% per year, respectively. Moreover, PRH have a lower 5-year overall survival (81.7%) when compared to other racial/ethnic groups.

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Conclusions: PRH children were found to have disparities in ALL incidence and mortality rates compared to other racial/ethnic groups in the US. Additional research is warranted to identify the genetic and environmental risk factors that may be associated with the disparities observed.

Impact: This is the first study reporting the incidence and mortality rates of childhood ALL for PRH and making comparisons with other racial/ethnic groups in the US.

Keywords

Childhood leukemia; Puerto Rico; Hispanic; epidemiology; leukemia subtypes

INTRODUCTION

Acute Lymphoblastic Leukemia (ALL) is the most common cancer in children and adolescents in the United States (US). This malignancy accounts for approximately 26% of all cancers occurring in children younger than 20 years (>3,000 new cases per year)[1–4] and causes approximately 25% of cancer-related deaths in children[5]. According to the Centers for Disease Control and Prevention (CDC), the overall incidence of pediatric ALL in the US during 2001–2014 was 34.0 cases per million persons. In the past decades, ALL incidence rates have increased by approximately 1% per year for all races/ethnicities in the US, suggesting that risk factors may have become more prevalent[1, 6].

The incidence and mortality rates of childhood leukemia vary according to the molecular subtype, race/ethnicity, age at diagnosis, sex and socioeconomic status[7–15]. US Hispanics have the highest incidence rates of childhood ALL and have poorer survival rates than other non-Hispanic ethnic groups[7, 9, 13, 16–18]. However, the term Hispanic is often used as a broad category to refer to subpopulations of Mexican, Cuban, Puerto Rican, South or Central America, Dominican, or other individuals of Spanish descent living in mainland US[18, 19]. According to 2021 data from the US Census, people of Mexican origin were the largest Hispanic group (63.0% of total Hispanic population), followed by other Hispanic (14.9%) and Puerto Rican (8.8%)[20]. Therefore, the cancer data reported for Hispanics are aggregated, which may mask important differences between these subpopulations. However, because the Puerto Rico Cancer Registry (PRCCR) is not a part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, the Hispanic cancer data reported by SEER in the US does not include data from Hispanics living in Puerto Rico.

During 2010–2014, the Puerto Rico Cancer Registry (PRCCR) reported that leukemia was the most common cancer diagnosed in Puerto Rican Hispanic children, accounting for 26.0% and 26.4% of all cancers diagnosed in boys and girls, respectively[21]. From 2000 to 2016, childhood cancer incidence rates in boys increased by 3% per year, whereas in girls, they increased by an average of 4.8% per year in Puerto Rico. Higher cancer incidence rates were observed in children between 15 and 19 years of age than in children between 5 and 14 years of age. Moreover, children aged 15–19 years were reported to have higher mortality rates than children under 9 years of age[21]. Unfortunately, the PRCCR report combined all leukemia cases. Therefore, incidence and mortality data from childhood ALL cases, the most common type of leukemia diagnosed among children, in Puerto Rican Hispanic children are lacking. This study is the first to address this knowledge gap by assessing the

incidence and mortality of childhood ALL for Puerto Rican Hispanics and to compare this data with ALL incidence and mortality rates among racial/ethnic groups in mainland US.

MATERIALS AND METHODS

This study involved secondary data analysis of the Puerto Rico Central Cancer Registry (PRCCR) and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. The PRCCR gave us access to ALL pathology reports to extract information, including genetic tests, when available. Data from PRCCR were provided to us without personal identifiers and through a Secure File Transfer Protocol. Data from the SEER program are of the public domain, contain no personal identifiers of the cancer cases included, and are available online on the following website: http://seer.cancer.gov/. This study was approved by the Institutional Review Board of the University of Puerto Rico, Medical Sciences Campus (protocol number 0150118).

Data sources

Puerto Rico Central Cancer Registry (PRCCR): Incident cases of childhood ALL in Puerto Rico for the period 2008–2016 were obtained from the PRCCR. PRCCR (RRID: SCR_023507), one of the oldest population-based cancer registries in the world, is responsible for collecting, analyzing, and publishing information on all cancer cases diagnosed and/or treated in Puerto Rico. Reporting of cancer cases to the PRCCR by public and private medical institutions is required by law. Since 1997, the PRCCR has been part of the CDC's National Program of Cancer Registries and uses the Surveillance, Epidemiology, and End Results (SEER) Program and the North American Association of Central Cancer Registries (NAACCR) standards for coding data. Partially supported by the CDC's National Program of Cancer Registries, the PRCCR must meet national standards like completeness of case ascertainment and information recorded, limits on death certificate only cases, duplicate primary cases, and passing standard edits. The PRCCR acquires information from island-wide hospitals, outpatient clinics, pathology laboratories, and radiotherapy/chemotherapy sites. In addition, linking the PRCCR database to Medicaid, Medicare, and private insurance data for PR residents, the PRCCR-Health Insurance Linkage Database (HILD) provides information about treatment, medical procedures, comorbidities, costs, and provider information. Over the years, the PRCCR improved data collection of cancer cases through electronic reporting, achieving a completeness of more than 95% of all cases since 2010, an important achievement that resulted in obtaining the NAACCR's Gold Certification and maintaining the PR cancer data in the CDC's report "United States Cancer Statistics"[22]. Mortality information for PR from 2008–2016 was obtained from the PRCCR, as reported by death certificates prepared by the Demographic Registry of the Puerto Rico Department of Health.

Incident cases of childhood ALL for US Hispanic (USH), non-Hispanic White (NHW), non-Hispanic Black (NHB) and Non-Hispanic Asian or Pacific Islanders (NHAPI) individuals in the US for the period 2008–2016 were obtained from the SEER*Stat 8.3.4 software (National Cancer Institute Surveillance Program, Bethesda, MD). The SEER program is a national cancer surveillance database that collects and reports incidence and survival

data from a sample of the US population. Data collected by SEER include demographic characteristics, anatomical and histological characteristics of the specific cancer, stage of diagnosis, diagnostic techniques used, treatment received within four months of diagnosis, and patient outcomes. Cancer mortality information for NHW, NHB, USH and NHAPI from 2008–2016 was obtained from the SEER program as reported by the National Center for Health Statistics (NCHS). Puerto Rico mortality cases were not included in the NCHS data source.

Study Population: All reported cases of childhood (0–19 years) Acute Lymphoblastic Leukemia (ALL) in Puerto Rican Hispanics (PRH) and in the US, specifically for the NHW, NHB, and USH groups, during 2008–2016 were analyzed.

Statistical Analysis

Incidence and mortality rates: For each racial/ethnic group, we applied the indirect method to compute childhood ALL age-standardized incidence and mortality rates per 100,000 persons during 2012–2016, using the incidence and mortality of 2000 US rates as standard risks. These rates were identified by the IASI for incidence and IASM for mortality, as follows:

$$IASI_j(IASM_j) = C * \frac{o_j}{\sum_i R_{i*} P_{ij}} = C * \frac{observed}{Expected}$$

where C indicates the crude incidence or mortality in the study population; $O_j$indicates the total number of incident cases or deaths in our study population with the *j*-th ethnic group; $R_i$indicates the age-specific incidence or mortality rate in the *i*-th age group of the standard population; and P_{ij}indicates the number of persons in the *i*-th age group for *j*-th ethnic group. IASI and IASM incidence trends were summarized annual percent change (APC).

Trends: Age-standardized incidence (IASI) and age-standardized mortality (IASM) incidence trends for the period 2001–2016 were summarized with the annual percent change (APC) and estimated by ethnic group. The APCs were calculated using the Joinpoint Regression Program of the NCI[23, 24].

Risk differences: To assess racial/ethnic group differences, the IASI/IASM were grouped from 2012 to 2016 as follows: $IASI/IASM_i = \sum_{j=1}^{4} w_j \frac{\sum_{k=2012}^{2016} d_{ij}^k}{\sum_{k=2012}^{2016} n_{ij}^k}$. Where $w_j$is the proportion of children in the *j*-th age group of the US 200 standard population, $d_{ij}^k$is the number of cases (new cases or deaths) in the *j*-th age group for the *i*-th ethnic group in the *k*-th year, and $n_{ij}^k$is the population in the *j*-th age group of the *i*-th ethnic group in the *k*-th year.

Then, the ratio of two standardized rates $\left[IASI/IASM_{group_i} / IASI/IASM_{group_j}\right]$ between two different groups was estimated with their 95% confidence interval,[21] to assess significant differences in ALL children incidence and mortality rates between USH, NHW, NHB, and

NHAPI compared with PRH. This ratio was denoted as the Standardized Rate Ratio (SRR), and we used USH, NHW, NHB, and NHAPI as the reference racial/ethnic groups.

Relative Survival: One, three, and five-year relative survival rates were calculated for children with PRH. Follow-up was performed to 2017. The relative survival rate represents the ratio of the observed survival of cancer patients divided by the expected survival for a group of people in the general population that is similar to that of the patient group with respect to sex, age, and calendar period of observation.

Data Availability

The datasets generated and analyzed during the current study are not publicly available due to the confidentiality policy of the Puerto Rico Central Cancer Registry but are available from the corresponding author on reasonable request.

RESULTS

Incidence and Mortality

To assess racial/ethnic group differences of Puerto Rican Hispanic (PRH) children with ALL with US Hispanics (USH), non-Hispanic-white (NHW), non-Hispanic-black (NHB) and non-Hispanic Asian or Pacific Islander (NHAPI), we estimated the incidence and mortality Standardized Rate Ratio (SRR) for 2012–2016. The overall Age-standardized rates (ASR) of childhood ALL incidence and mortality per 100,000 by racial/ethnic group from 2012–2016 are shown in Table 1. USH had the highest age-standardized incidence rate overall, followed by NHW, PRH, NHAPI, and NHB. Similar trends were observed when analyzing age-standardized incidence according to sex, with the exception that PRH girls had higher incidence than NHW. For PRH and NHAPI, we observed that girls had a slightly higher incidence of ALL than boys, in contrast to the other racial/ethnic groups. Our data showed that overall, PRH children had a 31% lower incidence of ALL (SRR = 0.69, 95% CI = 0.57, 0.81) and 86% higher incidence (SRR = 1.86, 95% CI = 1.50, 2.28) than USH and NHB, respectively. PRH male children had a 39% lower incidence (SRR = 0.61, 95% CI = 0.47, 0.77) compared to USH, but a 69% higher incidence (SRR = 1.69, 95% CI = 1.25, 2.24) compared to NHB. PRH girls had an 86% higher incidence (SRR = 1.86, 95% CI = 1.50, 2.28) compared to NHB. No significant differences in incidence rates were observed between PRH and NHW or NHAPI. For age-standardized mortality rate overall, USH had the highest rate, followed by PRH, NHAPI, NHW, and NHB. The same trend was observed when analyzing age-standardized mortality according to sex, with the exception that NHW and NHB girls had the same value. In addition, no significant differences ($p<0.05$) were observed in mortality rates between PRH children and those from other racial/ethnic groups in the US.

From 2001 to 2016, distinct patterns in ALL incidence trends were observed according to race/ethnicity (Figure 1A). The incidence of ALL increased significantly ($p<0.05$) from 2001 to 2016 among children with ALL for PRH and USH, with 5% and 0.9% per year, respectively. The mortality rates for NHW and USH decreased significantly during this

period, with APC=−4.1% and −3.92%, respectively (Figure 1B). The mortality rate for PRH could not be calculated for this period because there were fewer than seven deaths per year.

Table 2 shows the 1-, 3- and 5-year survival estimate for PRH children with ALL for the 2008–2012 period, with overall survival estimate of 92.4% (95% CI, 86.2% - 95.9%), 83.2% (95% CI, 75.6% - 88.6%), and 81.7% (95% CI, 73.9% - 87.4%), respectively. Males have higher 1-year survival estimates when evaluated by age, however the 3- and 5-year survival rates were similar. The age distribution and number of deaths of PRH children diagnosed with ALL between 2008–2016 are shown in Figure 2. During this period, 231 cases of childhood Acute Lymphoblastic Leukemia were identified and a total of thirty-three deaths were recorded.

DISCUSSION

Acute lymphoblastic leukemia (ALL) accounts for 80% of all leukemias diagnosed in children[25]. In the United States (US), ALL accounts for 27% of cancers diagnosed in children aged 0–19 years, disproportionately affecting children between 2 and 5 years[4]. Even though the age patterns of ALL are consistent across racial and ethnic groups, the incidence and survival rates are highly variable[7, 26]. Several studies have reported higher incidence and lower survival rates for some Hispanic subpopulations in the US [1, 3, 18, 19, 27]. However, to date, there have been no reports on childhood ALL in Hispanics living in Puerto Rico (PRH). According to the United States Census Bureau Puerto Rico: 2020 Census, the population of Puerto Rico is 98.9% Hispanic or Latino (RRID: SCR_011587). In this study, we report the first estimates of childhood acute lymphoblastic leukemia incidence, mortality, and survival rates in PRH and compare them with other racial/ethnic groups in the US. The information revealed in our study will serve as a guide for future research on this minority population.

Consistent with what has been published, the majority of the diagnosed cases of ALL in PRH were between the ages of 2 and 4 years [4, 27]. In addition, we observed that PRH girls had a slightly higher incidence of ALL than PRH boys, which is in contrast with other racial/ethnic groups in this study and what has been previously reported[4, 9, 28, 29]. The reasons behind sex differences in childhood ALL risk are unknown, but studies have suggested that sex-specific factors and single nucleotide polymorphism (SNPs) in the regulatory regions of *RASSF2* and *HLA-DQB1* genes may explain sex-specific effects[30, 31]. However, further studies are needed to evaluate genetic variation in PRH children and how they may explain the slightly higher incidence observed in girls from Puerto Rico.

The overall ALL age-standardized incidence reported in this study for PRH children is similar to that of non-Hispanic White (NHW) children and non-Hispanic Asian or pacific Islander (NHAPI) living in the US. Nevertheless, there are significant differences in childhood ALL incidence between PRH children and US Hispanics (USH) and non-Hispanic Blacks (NHB). PRH children have a lower risk (31%) of ALL compared to USH. This is not unexpected given that several studies have reported that USH children have the greatest incidence of childhood leukemia in the country, with incidence rates more than 20% higher than those for non-Hispanic children[1, 32, 33]. For instance, Marcotte *et al.* evaluated

the incidence by single year of age and reported that USH children have a 46% higher risk of developing ALL than NHW, whereas NHB and NHAPI have a lower risk than NHW[33]. Similarly, Giddings *et al.* reported that Hispanics in California had 32% higher risk (32%) of ALL when compared to NHW, while NHB and NHAPI had 45% and 9% lower risk than NHW, respectively[29]. In contrast, PRH children have a higher risk (86%) of ALL than NHB children, which have the lowest childhood ALL incidence in the US[1, 33].

This report also documents an increasing incidence of childhood ALL in PRH and USH children during the 2001–2016 period, with PRH children having the highest annual percent change (5.3% versus 0.9%, respectively). Childhood leukemia cases in Puerto Rico, like those on the mainland, are diagnosed using the National Comprehensive Cancer Network (NCCN) guidelines, and patients have been participating in National Cancer Institute-sponsored clinical trials since 1980 (Cancer Therapy Evaluation Program (CTEP) ID: PR018 and CTEP ID: PR038), ruling out the possibility that the high annual percent change for PRH is due to differences in diagnosis methodologies. Siegel *et al.*[1], stated that although there was an increasing trend in childhood ALL rates during 2001–2008 for USH, it was followed by a subsequent period (2008–2014) of stable trends. We included data of cases of childhood ALL for USH from two additional years (2015–2016) that may explain the slight increase in incidence observed for this group. Similarly, previous reports have described the increased in incidence among USH during the past decades[28]. Even though the underlying basis of the increased risk of childhood leukemia in USH remains unknown, GWAS performed with Hispanic in California identified a risk loci in *IKZF1* which was significantly associated with both global and local Indigenous American ancestry[34]. Among the risk factors for childhood ALL are cesarean delivery, advanced maternal age, infant birthweight, and as well as germline variants located within or near cancer predisposition genes[35–38]. Furthermore, occupational and/or residential exposure to organic solvents and pesticides has been linked to an increased risk of childhood leukemia in the United States and other Latin American countries[39–42]. However, none of these factors have been studied in PRH. Due to the small number of deaths per year, it was not possible to assess the mortality trend for PRH children for the 2001–2016 period, but a significant decrease in mortality was observed for the NHW and USH.

Despite the fact that the 5-year survival for ALL has improved significantly over the past decades due to increased participation of patients in clinical trials, improved supportive care, and risk stratification implementations[2, 9, 43–50], this study reported a lower 5-year overall survival (OS) for PRH children (81.7%) when compared to the ones reported for USH, NHB, NHAPI and NHW in other studies. For instance, Khan *et al.*[18] reported that the 5-year OS rates for USH and non-Hispanic patients from 2005 to 2011 were 89.2% and 92.7%, respectively. On the other hand, for the 2000–2005 period, Hunger *et al.*[17] estimated that the 5-year OS rates for USH, NHW, and NHB were 87.6%, 91.4%, and 87.4%, respectively. In the US, the 5-year OS rate is slightly higher for girls than for boys, and survival rates vary according to age group and leukemia subtype[4, 51, 52]. In contrast to other ethnic groups living in the US, where survival rates have been generally higher for girls, PRH girls and boys have similar 5-year OS rates of 81.6% vs. 81.8%, respectively. Additionally, PRH girls and boys have lower 5-year OS rates than those reported for other groups in the US: 85.1% and 83.0% for USH girls and boys, 85.6 % and 82.7% for NHB girls and boys,

89.3 % and 86.3% for NHAPI girls and boys, and 91.6 % and 88.9% for NHW girls and boys, respectively[15]. There was also a marked difference in the 1-year survival rates for PRH boys (96.1%) and girls (87.1%), which differs from the US, where the reported 1-year net survival rates for boys and girls are 95.9% and 95.5%, respectively[52]. Age at diagnosis has been demonstrated to be an important prognostic factor for both the incidence and survival of pediatric ALL and has been incorporated into the NCI risk group classification. Most of the deaths in children with ALL in PR were reported for infants <1 year of age, followed by children >12 years of age. This is in agreement with what has been reported in the literature for childhood ALL survival distribution by age in the US, where children diagnosed during infancy have higher mortality rates, followed by those diagnosed between ages 10–14 and 15–19[2, 51, 52]. Treatment failure is one of the factors associated with a decrease in ALL survival, since one out of five children with ALL experience relapse and have an overall survival rate of only 30%[53–59]. It has been reported that USH and NHB have a higher likelihood of relapse and lower 5-year disease-free survival than other ethnic groups[16]. An increased risk of neurotoxicity as a result of methotrexate chemotherapy for USH has been reported, which is associated with relapse, hospitalization, and changes in leukemia therapy[60].

It is known that the genetic composition of different racial and ethnic groups varies dramatically, and ancestry-related genetic variations may contribute to the racial and ethnic disparities observed in childhood ALL incidence and mortality [27–29, 61–63]. Hispanics are known to have a complex population structure resulting from more than 500 years of genetic admixture of European, Native American, and African individuals, and at the same time, these populations exhibit ancestry variation within countries themselves[64–66]. PRH have an average ancestral composition of 15.2%, 21.2%, and 63.7% from Native American, African, and European populations, respectively[66]. Correlations between ancestry and risk of ALL have been established for Hispanic populations [64], indicating that a higher proportion of Native American genetic ancestry is associated with a higher risk of ALL[26, 67–69]. For example, for B-ALL (that accounts for 80–85 % of childhood ALL[46]), higher proportions of African and Native American genetic ancestry have been correlated with lower survival for NHB and USH, respectively[70]. Moreover, genetic ancestry has been associated with ALL molecular subtypes showing that Native American ancestry is associated with *CRLF2* rearrangements and *ETV6-RUNX1*-like ALL. African ancestry has been associated with T-cell ALL and *TCF3-PBX1* gene fusion. All of these genetic alterations are linked with poor prognosis based on the functional effect on the affected genes and other coexisting mutations[71–74]. Higher levels of Native American ancestry have also been linked to an increased risk of relapse in children with ALL of self-declared Hispanic ethnicity[26]. However, for PRH children diagnosed with ALL, further analysis must be conducted to assess how ancestral genetic composition may be associated with the incidence and lower survival rates reported in this study.

The genetic basis of childhood ALL susceptibility is likely polygenic[75]. Cumulative evidence suggests that genetic variation among Hispanic subpopulations is correlated with an increased risk of childhood ALL. For example, several studies have identified that variations in certain genes [62, 69, 76–80] are associated with an increased risk of childhood ALL development in USH. Quiroz *et al.*[67] carefully postulated that the differential ancestral

proportions among Central and South America are correlated with the variable incidence of childhood ALL, stating that regions with higher indigenous ancestry have higher incidence, while those with higher African American ancestry have lower incidence. Furthermore, variability in the incidence and mortality rates of colorectal, endometrial, breast, prostate, liver, thyroid, and cervical cancers between Puerto Ricans (living in the US and on the main island) and other Hispanic subpopulations has also been observed[8, 81–84]. Studies focused on the molecular biology of childhood ALL based on the ancestral proportions among Hispanic subpopulations are needed to shed light on the disparities observed in incidence and mortality rates for children with PR.

In conclusion, the disparities observed among children with PR when compared to other ethnic groups in the US, especially with USH, may be attributed to factors such as the frequency of high-risk leukemia subtypes, environmental exposures, reduced access to care, and compliance to chemotherapy[3, 7, 16]. However, ancestry-related genetic variations may also play an important role in the risk of childhood ALL. The increasing evidence of how ancestral contributions among the admixed Hispanic subpopulations correlate with the incidence and survival of childhood ALL underscores the need for further studies to assess the impact of genetics in the Puerto Rican pediatric population to attain personalized treatment to improve survival.

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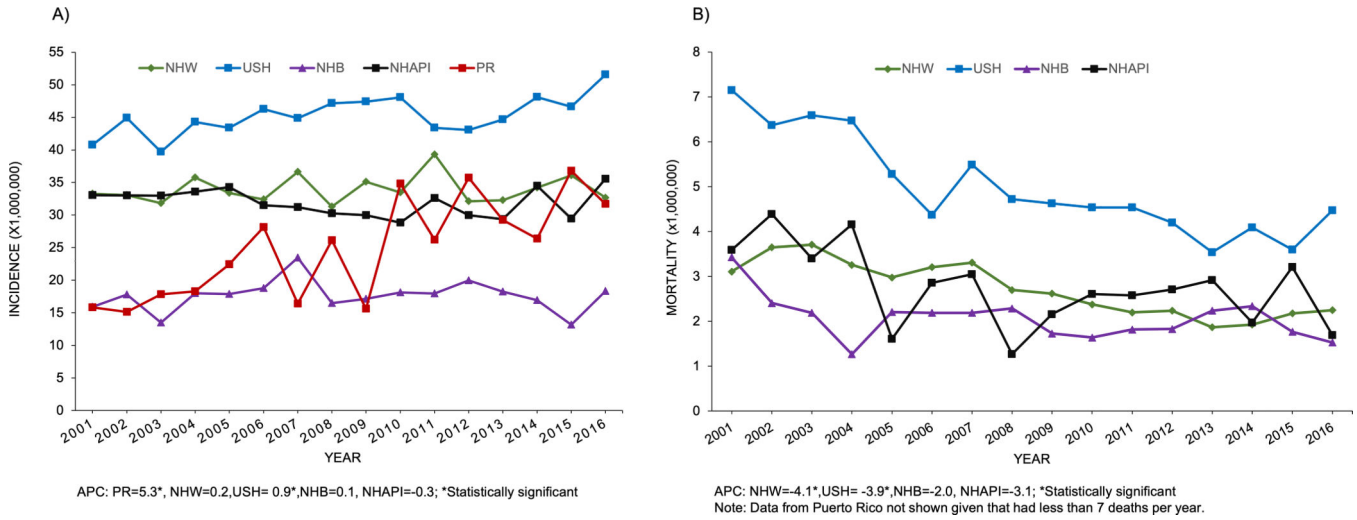

Figure 1.

Trends for age-standardized (using 2000 US population) incidence **(A)** and mortality **(B)** rates (per 1,00,000) for children (0–19 years) with acute lymphoblastic leukemia (ALL) for Puerto Rican Hispanics (PRH) and among Non-Hispanic Whites (NHW), Non-Hispanic Blacks (NHB), US Hispanics (USH) and Non-Hispanic Asian or Pacific Islanders (NHAPI), 2001–2016.

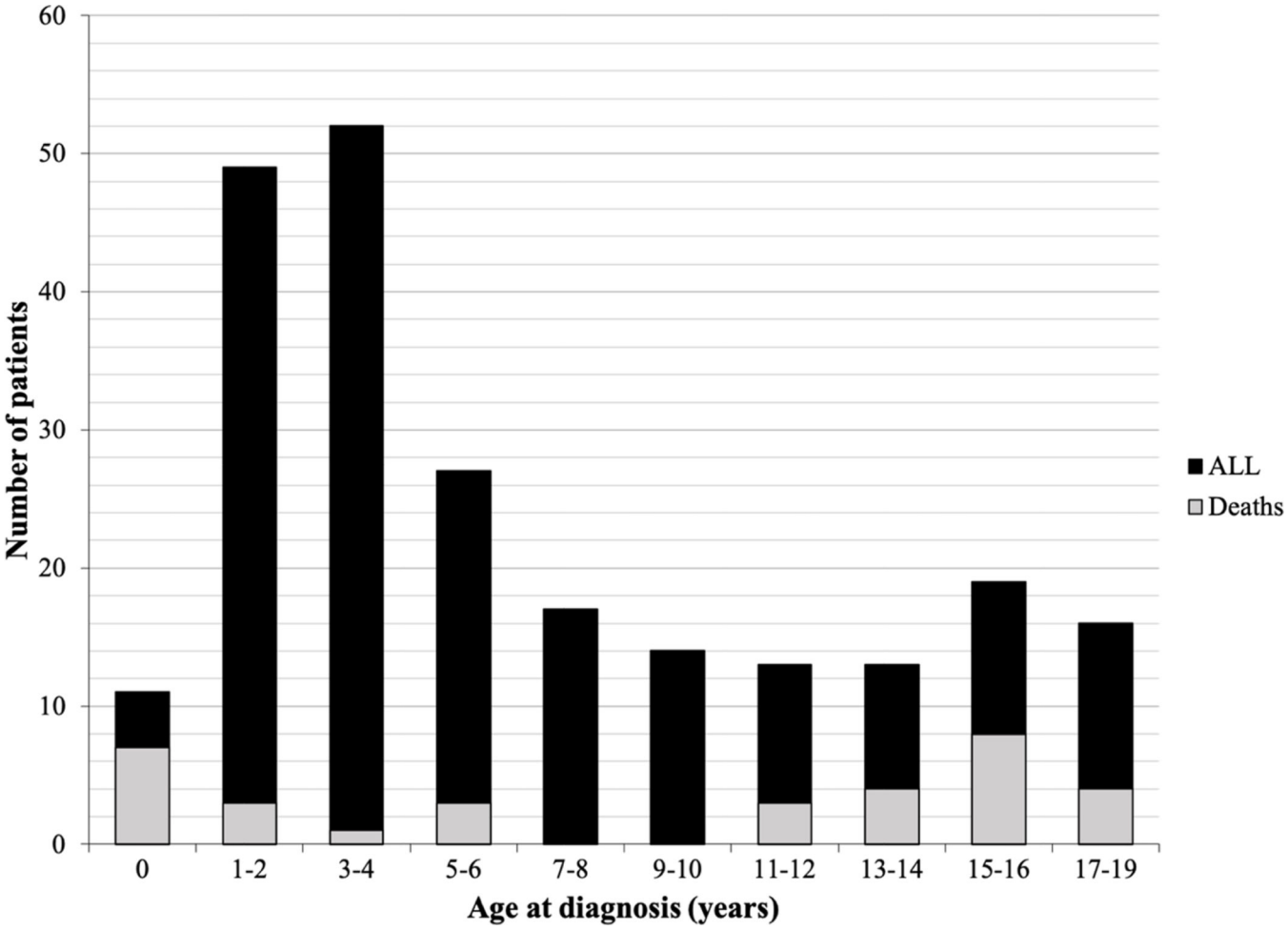

Figure 2.

Age distribution of Puerto Rican Hispanics ALL patients at diagnosis (n = 231 patients, diagnosed during 2008–2016 period). Black columns represent patients diagnosed with ALL by age; gray columns represent reported deaths by age.

Table 1.

Age-standardized* Incidence and Mortality Rates (per 100,000) for Children with Acute Lymphoblastic Leukemia (ALL) from 2012 to 2016

	Age-standardized rates						SRR (95% CI)				
	PRH	**NHW**	**USH**	**NHB**	**NHAPI**	**US overall**	**PRH vs NHW**	**PRH vs USH**	**PRH vs NHB**	**PRH vs NHAPI**	**PRH vs US overall**
Incidence											
Overall	3.21	3.32	4.68	1.73	3.15	3.55	0.97 (0.80–1.15)	**0.69 (0.57–0.81)**	**1.86 (1.50–2.28)**	1.02 (0.83–1.24)	0.90 (0.75–1.07)
Boys	3.16	3.59	5.19	1.87	3.12	3.87	0.88 (0.68–1.12)	**0.61 (0.47–0.77)**	**1.69 (1.25–2.24)**	1.01 (0.76–1.33)	0.82 (0.63–1.03)
Girls	3.26	3.03	4.14	1.58	3.19	3.23	1.08 (0.82–1.37)	0.79 (0.60–1.00)	**1.86 (1.50–2.28)**	1.02 (0.76–1.35)	1.01 (0.78–1.28)
Mortality											
Overall	0.29	0.21	0.40	0.19	0.25	0.25	1.38 (0.73–2.21)	0.73 (0.38–1.17)	1.48 (0.77–2.45)	1.16 (0.59–2.00)	1.13 (0.60–1.81)
Boys	0.34	0.24	0.46	0.22	0.28	0.30	1.41 (0.61–2.51)	0.74 (0.32–1.32)	1.57 (0.66–2.90)	1.20 (0.49–2.39)	1.16 (0.50–2.05)
Girls	0.23	0.17	0.33	0.17	0.21	0.21	1.33 (0.43–2.63)	0.70 (0.23–1.39)	1.37 (0.43–2.83)	1.08 (0.34–2.46)	1.09 (0.35–2.14)

*Age-standardized rates using the US 2000 standard population;

**SSR indicated standardized rate ratio with 95% confidence interval. PRH=Puerto Rican Hispanics, NHW=non-Hispanic White, USH=US Hispanics, NHB=non-Hispanic Black, NHAPI=non-Hispanic Asian or Pacific Islander, US overall=All US racial/ethnic groups.

Table 2.

Net Survival (%) at 1, 3, and 5 years after diagnosis for Puerto Rican Hispanic children (0–19 years) diagnosed with Acute Lymphoblastic Leukemia for the 2008–2012 period.

	Year	Survival (%)	95% CI
Overall	1	**92.4**	86.2 – 95.9
	3	**83.2**	75.6 – 88.6
	5	**81.7**	73.9 – 87.4
Boys	1	**96.1**	88.3 – 98.8
	3	**83.0**	72.5 – 89.8
	5	**81.8**	71.1 – 88.9
Girls	1	**87.1**	74.8 – 93.7
	3	**83.4**	70.5 – 91.1
	5	**81.6**	68.4 – 89.7