High Lifetime Incidence of Adult Acute Lymphoblastic Leukemia among Hispanics in California

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Abstract

Background: **The higher incidence of acute lymphoblastic leukemia (ALL) among Hispanic children relative to that in other racial/ethnic groups is well-known. We evaluated the incidence patterns of ALL in adults.**

Methods: **We analyzed the incidence patterns of ALL (International Classification of Diseases for Oncology 3 codes 9835-9837) among all patients diagnosed from 1988 to 2004 in California using data from the California Cancer Registry to determine whether adult Hispanics also had higher incidence rates of ALL compared with non–Hispanic Whites (Whites). Age-adjusted incidence rates (AAIR), incidence rate ratios (IRR), and 5-year survival rates were obtained using SEER*Stat. AAIRs of other leukemia subtypes and IRRs relative to non–Hispanic Whites were also examined as references for ALL.**

Results: **AAIRs of ALL in Hispanic males and females ages 20 to 54 years were higher compared with those in White males and females (IRR, 1.99; 95% confidence interval, 1.74-2.28 and IRR, 1.91; 95% confidence interval, 1.60-2.25, respectively). A higher AAIR of ALL was also observed among older (55+ years) Hispanic females (IRR, 1.84; 95% confidence interval, 1.52-2.21), but not in males (IRR, 1.07; 95% confidence interval, 0.84-1.34). Among Hispanics, low socioeconomic status was associated with a higher AAIR compared with high/middle socioeconomic status (IRR, 1.33; 95% confidence interval, 1.04-1.70). The respective 5-year survival rates among ALL patients were 38% and 30% for Whites and Hispanics ages 20 to 54 years, and 8% and 12% for patients 55 years of age or older. Compared with other racial/ethnic groups, Hispanics did not have an increased IRR of the other major leukemia subtypes.**

Conclusion: **Hispanics experience a higher incidence of ALL throughout life, but not other subtypes.** (Cancer Epidemiol Biomarkers Prev 2009;18(2):611–5)

Introduction

Acute lymphoblastic leukemia (ALL) is a neoplasm that arises from clonal expansion of lymphoblasts, the majority of which arise from B-lymphoblasts and a small subset from T-lymphoblasts (1). Although childhood ALL has been well-studied epidemiologically, the incidence pattern of ALL in adults has not, probably because of the relatively low incidence. Population-based studies of ALL in children have consistently reported higher incidence among Hispanics compared with other ethnic groups in the United States (2-5). Using data from the California Cancer Registry, we performed the current study to examine whether adult Hispanics also experience higher incidence rates of ALL. We also examined relative survival among ALL patients according to racial/ethnic group.

Patients, Materials and Methods

Source of Subjects. The source of data for the study was the California Cancer Registry, the legally mandated system of regional cancer registries reporting to the California Department of Health Services, which consists of three population-based cancer registries designated as part of the National Cancer Institute Surveillance, Epidemiology, and End-Results Program (SEER; ref. 6). Data from these California registries contains, at the minimum, 98% of all incident cancers diagnosed in the state for any given year.

Cases were defined as California residents diagnosed with ALL [International Classification of Diseases for Oncology (ICD-O-3) morphology codes 9835-9837, according to the accepted WHO/REAL classification system], during the years 1988 to 2004 (1). Diagnoses were verified by pathology report for 99% of the cases. Age-adjusted incidence rates (AAIR) and incidence rate ratios (IRR) of ALL by race/ethnicity were compared

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with other leukemia subtypes diagnosed during the same period, and classified as B-cell chronic lymphocytic leukemia (ICD-O-3 morphology codes 9823 and 9670), acute myelogenous leukemia (9840, 9861, 9866, 9867, 9870-9874, 9891, 9895-9897, 9910, 9920, 9930, and 9931), and chronic myelogenous leukemia (9863, 9875, and 9876). Adults were defined as subjects who were 20 years of age and older at diagnosis.

Classification of Demographic Factors. Demographic information collected by the registries includes age at diagnosis, sex, block group residence at diagnosis [to assign socioeconomic status (SES)], race/ethnicity and birthplace. Patients were categorized into the following racial/ethnic groups: non–Hispanic White (White), non–Hispanic African American (African American), non–Hispanic Asian/Pacific Islander/American Indian/Alaskan Native (Asian/PI/AI/AN), and Hispanic. Assignment of Hispanic race/ethnicity was based on an algorithm that included information from the hospital record, birthplace, and surname (from the 1980 U.S. Census). Information on birthplace was collected from ~74% of all Hispanic cancer patients during the time period under study.

SES is based on census block group characteristics of the case residence at the time of diagnosis, incorporating information on median education, proportion unemployed, occupation, proportion with incomes below twice the poverty level, median household income, median rent and median home value obtained from the 1990 and 2000 U.S. Census and incorporated into a single socioeconomic indicator as described previously by Yost et al. (7). Each block group in California was assigned a score and the scores ranked into quintiles irrespective of race or ethnicity. Each patient received an SES classification based on the quintile of the block group of his/her residence at the time of diagnosis. For this analysis, the time period was limited to the 5-year time period surrounding the 2000 census (1998-2002) because the census block group populations were not available for intracensal years (between census counts). To estimate our population-at-risk denominator for analyses by SES, the 2000 population counts were multiplied by 5 (8). SES quintiles were collapsed into two groups: high/middle (quintile 3-5) and low (quintile 1-2).

Statistical Methods. SEER*Stat software[5] was used to calculate the average annual AAIR and 5-year relative survival rates by sex, race/ethnicity, and age (<19 years old, 20-54 years old, and 55 years or older) for cases diagnosed between 1988 and 2004; AAIRs are reported as the number of cases per 100,000 people, and age-adjusted (within the broad age ranges) to the 2000 U.S. population standard. IRRs were obtained based on the AAIRs using the same software, with Whites as the reference group. Tests of statistical significance are two-sided, with $P = 0.05$ considered statistically significant. For some analyses, all diagnoses in persons >19 years old were considered together as ''adult'' cases. Incidence rates and IRRs by SES were also obtained using SEER*Stat software.[5]

[5] Surveillance Research Program, NCI, http://seer.cancer.gov/seerstat.

Because population-based denominator data is not available by birthplace, we assessed the risk of ALL among adult Hispanics born outside of the United States versus those born in the United States (reference group) in case-case comparisons with two ''control'' groups: all other Hispanic leukemia patients and all other Hispanic cancer patients, excluding ALL patients. Both birthplace comparisons were limited to Hispanic patients diagnosed at 20 years of age or older. Proportional odds ratios for risk by birthplace were then calculated using a multivariable unconditional logistic regression model which included sex (male/female), age at diagnosis (continuous), and SES (high, middle, low; ref. 9). Logistic regression analyses were calculated using SAS version 9.1.3 (10).

Results

A total of 5,203 males and 3,972 female residents of California were diagnosed with ALL during the period 1988 to 2004 (Table 1). Incidence rates were highest during childhood among all sex-specific and racial/ethnic–specific groups, decreased during young adulthood, and increased again slightly at older ages, demonstrating a bimodal pattern (Table 1A and B).

AAIRs for ALL were highest in male and female Hispanics within each age category compared with those in other racial/ethnic groups (Table 1A and B). The greatest difference in incidence rates relative to Whites was observed among Hispanics ages 20 to 54 years. In the oldest age group of Hispanics, the incidence rate in older Hispanic males was not much higher than that in older White males; Hispanic female incidence remained quite high relative to that of White females. Among all racial/ethnic groups combined, males had a 1.3-fold or greater AAIR of ALL compared with females (data not shown), with some variation by age and racial/ethnic group.

Among adult Hispanics, the AAIR of ALL was modestly higher in those of low SES relative to those of high/middle SES. No such difference by SES was seen among White ALL patients (Table 2).

Adult Hispanics with ALL were more likely to be born outside of the United States (relative to within the United States) when compared with other Hispanic leukemia patients (proportional odds ratios, 1.31; 95% confidence interval, 1.12-1.55), and to all other (non-leukemia) Hispanic cancer patients (proportional odds ratios, 1.57; 95% 1.36-1.81) diagnosed in California during the time period 1988 to 2004. Hispanic adults did not have higher incidence rates of any other major leukemia subtypes compared with other racial/ethnic groups, thus the excess incidence is specific only for ALL (Table 3).

Five-year relative survival was highest in the youngest age group, and dropped precipitously with older age at diagnosis, a pattern evident across all ethnicities (Fig. 1). Survival rates among Hispanics were slightly lower than those of Whites among children (77% in Hispanics versus 84% in Whites), and young adults 20 to 54 years old (30% in Hispanics versus 34% in Whites). Among the oldest age group, Hispanic ALL patients had slightly higher 5-year relative survival rates compared with Whites (12% in Hispanics versus

Table 1. Average annual AAIR and IRR of ALL in California according to gender, race/ethnicity, and age group

(A) Average annual AAIR and IRR of ALL* in California males by race/ethnicity and age group (1988-2004)

	N	AAIR† (95% CI)‡	IRR§ (95% CI)‡
Ages 0-19			
White	1,292	3.68 (3.48-3.89)	1.00
African American	113	1.66 (1.37-1.99)	0.45 (0.37-0.55)
Hispanic	1,715	4.77 (4.55-5.01)	1.30 (1.21-1.40)
Asian/PI/AI/AN‖,¶	287	3.00 (2.66-3.37)	0.82 (0.72-0.93)
Ages 20-54			
White	441	0.60 (0.55-0.66)	1.00
African American	54	0.57 (0.43-0.75)	0.95 (0.70-1.26)
Hispanic	533	1.20 (1.09-1.32)	1.99 (1.74-2.28)
Asian/PI/AI/AN‖,¶	115	0.70 (0.57-0.84)	1.16 (0.93-1.43)
Ages 55+			
White	474	1.57 (1.43-1.72)	1.00
African American	19	0.82 (0.48-1.32)	0.52 (0.30-0.85)
Hispanic	106	1.68 (1.35-2.06)	1.07 (0.84-1.34)
Asian/PI/AI/AN‖,¶	54	1.27 (0.95-1.68)	0.81 (0.59-1.09)

(B) Average annual AAIR and IRR of ALL* in California females by race/ethnicity and age group (1988-2004)

Ages 0-19			
White	954	2.86 (2.68-3.04)	1.00
African American	97	1.48 (1.20-1.80)	0.52 (0.42-0.64)
Hispanic	1,253	3.65 (3.45-3.86)	1.28 (1.17-1.39)
Asian/PI/AI/AN‖,¶	222	2.46 (2.15-2.80)	0.86 (0.74-1.00)
Ages 20-54			
White	310	0.43 (0.39-0.49)	1.00
African American	43	0.44 (0.32-0.60)	1.01 (0.71-1.40)
Hispanic	311	0.83 (0.73-0.93)	1.91 (1.61-2.25)
Asian/PI/AI/AN‖,¶	87	0.50 (0.40-0.61)	1.15 (0.89-1.46)
Ages 55+			
White	457	1.13 (1.03-1.24)	1.00
African American	25	0.79 (0.51-1.18)	0.70 (0.45-1.05)
Hispanic	167	2.08 (1.77-2.43)	1.84 (1.52-2.21)
Asian/PI/AI/AN‖,¶	46	0.82 (0.60-1.10)	0.73 (0.52-0.99)

*ICD-O-3 codes 9835 to 9837.
†Rates are expressed per 100,000 population and age-adjusted according to the percentage of distribution in 5-year age groups.
‡Ninety-five percent confidence interval.
§IRRs using Whites as the reference group.
‖Asian/Pacific Islanders/American Indians/Alaskan Natives.
¶White, African American, Hispanic, and Asian/PI/AI/AN are mutually exclusive groupings of race and ethnicity.

8% in Whites). Female Hispanics had slightly higher survival rates as children and teenagers, but slightly lower survival rates as adults compared with male Hispanics (data not shown). None of these differences were statistically significant.

To ensure that our results were not biased due to the inclusion of data prior to the adoption of the new classification of ALL, we restricted the analyses to the time period 1994 to 2004, and found essentially identical results (data not shown).

Discussion

Hispanics have the highest incidence rates of ALL, but not other types of leukemia, throughout life. There is some evidence to support an association between low SES and increased ALL incidence rates among Hispanics. Hispanic ALL patients diagnosed up to 54 years of age had a 5-year survival rate that was marginally lower than that of Whites, but among those diagnosed at 55 years of age or older, the survival rate was marginally higher.

Table 2. Average annual AAIR and IRR of ALL in California Hispanic and White adults diagnosed at ≥20 y of age, by SES and race/ethnicity (1998-2002)

Race/ethnicity	SES	*N*	AAIR* (95% CI)†	IRR‡ (95% CI†
Hispanic§	High/Middle	128	1.19 (0.97-1.45)	1.00
	Low	287	1.58 (1.38-1.81)	1.33 (1.04-1.70)
White§	High/Middle	354	0.74 (0.66-0.82)	1.00
	Low	102	0.67 (0.54-0.81)	0.90 (0.71-1.13)

NOTE: ICD-O-3 codes 9835 to 9837.
*Rates are expressed per 100,000 population and age-adjusted according to the percent distribution of 5-year age groups.
†Ninety-five percent confidence interval.
‡IRRs using high/middle SES as the reference group.
§White and Hispanic are mutually exclusive groupings of ethnicity.

Table 3. Average annual AAIR and IRR for major leukemia subtypes by race/ethnicity among California residents ≥20 y of age (1988-2004)

Leukemia subtype	Race/ethnicity	*N*	AAIR* (95% CI)†	IRR‡ (95% CI)†
Acute lymphoblastic§	White	1,682	0.76 (0.72-0.80)	1.00
	Hispanic	1,117	1.29 (1.20-1.38)	1.69 (1.55-1.84)
	African American	141	0.60 (0.50-0.71)	0.78 (0.65-0.94)
	Asian/PI/AI/AN‖,¶	302	0.72 (0.64-0.81)	0.95 (0.83-1.08)
Acute myeloid**	White	12,295	5.35 (5.25-5.44)	1.00
	African American	2,515	4.14 (3.96-4.33)	0.77 (0.74-0.81)
	Hispanic	898	4.62 (4.32-4.95)	0.87 (0.81-0.94)
	Asian/PI/AI/AN‖,¶	1,492	4.18 (3.96-4.40)	0.78 (0.74-0.83)
B-cell chronic lymphocytic††	White	18,529	7.95 (7.83-8.06)	1.00
	Hispanic	1,737	3.86 (3.67-4.05)	0.49 (0.46-0.51)
	African American	1,154	6.31 (5.95-6.70)	0.79 (0.75-0.84)
	Asian/PI/AI/AN‖,¶	632	1.92 (1.77-2.08)	0.24 (0.22-0.26)
Chronic myeloid‡‡	White	4,152	1.82 (1.77-1.88)	1.00
	Hispanic	1,152	1.70 (1.59-1.82)	0.93 (0.87-1.00)
	African American	414	1.98 (1.79-2.19)	1.09 (0.97-1.20)
	Asian/PI/AI/AN‖,¶	537	1.38 (1.26-1.51)	0.76 (0.69-0.83)

*Rates are expressed per 100,000 population and age-adjusted according to the percent distribution of 5-year age groups from the 2000 U.S. population (U.S. Census Bureau).
†Ninety-five percent confidence interval.
‡IRRs using White as the reference group.
§ICD-O-3 code: 9835-9837.
‖Asian/Pacific Islanders/American Indians/Alaskan Natives.
¶White, African American, Hispanic, and Asian/PI/AI/AN are mutually exclusive groupings of race and ethnicity.
**ICD-O-3 codes: 9840, 9861, 9866, 9867, 9870-9874, 9891, 9895-9897, 9910, 9920, 9930, and 9931.
††ICD-O-3 codes: 9823 and 9670.
‡‡ICD-O-3 code: 9863, 9875, and 9876.

Although the higher incidence rates of ALL among Hispanic children is well-known (2-5), only one published report and one book have examined the pattern in adults (11, 12). An examination of incidence patterns for 85 different types of cancer in Los Angeles County from 1972 to 1998 also showed an excess of ALL among Hispanics throughout life (11). In another study, Matasar et al. (12) reported that the excess incidence rates for Hispanics leveled off at older ages. We saw a similar pattern among Hispanic males only; the incidence rate among the oldest female Hispanics was still the highest of any ethnic group.

Previous studies have examined the relationship between SES and leukemia incidence rates with variable results but the relationship has rarely been examined in adults. In an extensive review of the literature, Poole and colleagues (13), summarized 47 studies on the relationship between SES and childhood leukemia incidence and concluded that there was no clear-cut evidence of an association. Because the inverse association of SES with AAIR of ALL was observed among Hispanics but not among non–Hispanic Whites, it is likely that different etiologic pathways are responsible for disease in different age and ethnic groups.

Our finding of lower survival of ALL in Hispanic children compared with White children is consistent with a previous report based on SEER data from other geographic areas in the United States (14). There are no other reports of variation in survival rates by ethnicity for adults with ALL. The slightly higher survival rates of Hispanics compared with Whites in the oldest group of patients is surprising and cannot be easily explained; however, the overall survival rates and the number of patients in this age group are so low that the differences are not statistically significant.

The limitations of our study include reliance on ecological data at the population level rather than individual data for some exposures such as SES, which could result in nondifferential misclassification. There may be some misclassification of Hispanic ethnicity (15) because information on ethnicity was obtained from the medical records as part of the cancer reporting process. Furthermore, because California has a large number of undocumented Hispanics (estimated at 2,575,000 in 2005; ref. 16), which the census may not count accurately, the incidence rates may be inflated due to an artificially low denominator. However, because the higher incidence rate among Hispanics was observed only for ALL and not other types of leukemia, this is not a likely

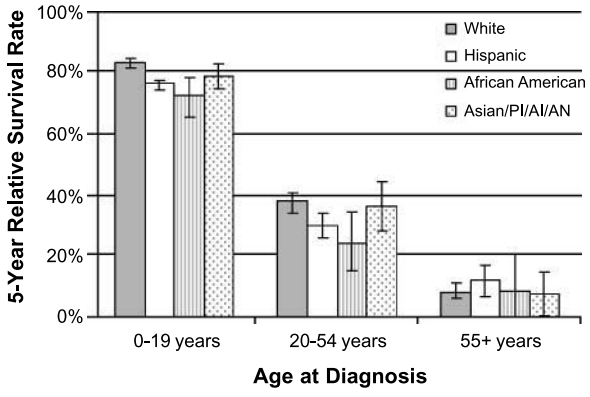

Figure 1. Five-year relative survival rate for California ALL patients by ethnicity/race and age group (1988-2004), California Cancer Registry.

explanation and the effect may be real. In addition, we observed a similar high IRR of ALL among adult Hispanics when the analysis was restricted to Los Angeles County and when it was expanded to include 16 U.S SEER registries (data not shown).

Because data on the population at risk by birthplace are unavailable, we used all other Hispanic cancer patients and all other Hispanic leukemia patients as comparison groups. This type of case-case analysis can produce biased results depending on the distribution of the exposure in the comparison group. However, the consistency of the association across the two comparisons suggests a true birthplace effect. Finally, we also confirmed the bimodal incidence peak for ALL reported by others (12, 13). A similar bimodal incidence peak was not seen in the United Kingdom (17). The persistent higher incidence rate among Hispanics throughout life suggests that the disease may have etiologic factors in common when diagnosed at different ages.

There is evidence of both genetic and environmental risk factors in the etiology of childhood ALL, including *in utero* folate deficiency, parental exposure to radiation and pesticides, infections, and certain genotypes involved in oxidative stress and folate metabolism (18). Latency from prenatal exposures up to 10 years has been suggested (18), but the period is unlikely to extend through adulthood. Chemotherapy is associated with an increased relative risk of acute myelogenous leukemia, but not ALL, in adulthood (19). Little has been published on risk factors for adult ALL, but one group of investigators have reported evidence of a protective association between variants of the folate-metabolizing gene methylenetetrahydrofolate reductase and adult ALL (20, 21); however, Hispanics were not included in these studies based primarily on European origin populations. A recent National Health and Nutrition Examination Survey reported a lower prevalence of the protective C677T methylenetetrahydrofolate reductase genotype in Mexican-Americans compared with non–Hispanic Whites (22), which offers a possible line of inquiry. One of the purposes of descriptive epidemiologic studies is to identify associations between demographic factors and disease which can be used for hypothesis generation. This study raises an important observation worthy of further follow-up.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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