Trends in Childhood Leukemia in Basrah, Iraq, 1993–2007

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Objectives. Through a sister-university relationship between the University of Basrah and the University of Washington, we analyzed Ibn Ghazwan Hospital's leukemia registry data to evaluate trends in childhood leukemia since 1993.

Methods. We documented leukemia cases among children aged 0 to 14 years for each of the last 15 years. Population data were obtained from a 1997 census and various subsequent estimates to calculate rates.

Results. We observed 698 cases of childhood leukemia between 1993 and 2007, ranging between 15 cases (2.6 per 100 000 annual rate) in the first year and 56 cases (6.9 per 100 000 annual rate) in the final year, reaching a peak of 97 cases in 2006 (12.2 per 100 000 annual rate).

Conclusions. Childhood leukemia rates in Basrah more than doubled over a 15-year period. The test for trend was significant (P=.03). Basrah's childhood leukemia rate compared unfavorably with neighboring Kuwait and nearby Oman, as well as the United States, the European Union, and other countries. (*Am J Public Health.* 2010;100:1081–1087. doi:10.2105/AJPH.2009.164236)

The hematologic malignancy leukemia is the most common childhood cancer. Incidence rates in higher-income countries range from 4.0 to 4.4 per 100 000 per year, typically higher than in lower-income countries (e.g., 0.9 per 100 000 per year in Vietnam),[1,2] although these disparities may simply reflect the lack of cancer registries in low-income countries.[3] The most common type of childhood leukemia is acute lymphoblastic leukemia (ALL), which makes up approximately 80% of leukemia cases, followed by acute myeloid leukemia (AML) and chronic myeloid leukemia (CML), with relatively few in other categories.[4] Childhood leukemia rates increased in Europe 1.4% per year from 1975 to 1995[5] while staying largely stable in the United States during this period.[6] Males typically have higher rates of leukemia than do females.[1] Although the etiology of most childhood leukemias[7] is unknown, several factors in addition to socioeconomic status[8] have been associated with the disease, including Hispanic population affiliation,[1] ionizing radiation,[9] environmental exposures including chemicals and infectious agents,[10] chromosomal abnormalities,[11] perinatal influences,[12] birth weight,[13] and parental exposure factors.[14–17] The variation in incidence between countries is less for childhood leukemia than for adult cancers, which suggests the same or equipotent risk factors for childhood leukemia in different countries.[2]

Basrah is the most southern governorate in Iraq, containing the country's third largest city and its only major port. Its strategic location, on the Shatt al Arab waterway below the confluence of the Tigris and Euphrates rivers and short distances from Iran and Kuwait, has made it a focal point for the last three of Iraq's major wars from 1980 to the present (see map, Figure 1). This study was initiated as part of a sister-university relationship between the University of Basrah and the University of Washington following reports by a University of Basrah pediatric oncologist (J.H.) of increasing rates of childhood malignancies in the Basrah oncology referral hospital. University of Washington researchers (A.H., T.T., and S.D.) then engaged an experienced Iraqi epidemiologist (R.L.) to assist in the assessment of the cancer rates in the governorate of Basrah. The purpose of this study was to assess changes in the rates of childhood leukemia in Basrah, Iraq, from 1993 through 2007.

METHODS

This hospital-based cancer registry study used the complete set of children's medical records from the oncology service at Basrah's Ibn Ghazwan Women and Children's Hospital, which is affiliated with the University of Basrah, spanning 15 years (1993–2007). Ghazwan Hospital is the only pediatric cancer treatment hospital in the region, and as such, its records constitute a pediatric cancer registry for the Basrah governorate. R.L. made 2 trips to Basrah to collect data according to the research design. Our focus was on confirmed diagnoses over this time period, not etiology, treatment, stage, or outcome of disease.

The pattern of medical referral in the Basrah governorate channels all childhood leukemia cases to the Ibn Ghazwan pediatric oncology ward, because it provides the only access to chemotherapeutics for pediatric cancers. None of the other 4 hospitals in the community treat pediatric cancer. The lead pediatric oncologist for the clinic (J.H.) has been in her position at Basrah since 1992. We queried several Basrah hematologists and oncologists about geographic referral patterns and determined that it is only in rare cases that patients bypass Basrah for care in Baghdad or Kuwait.

Study inclusion criteria specified all children aged 0 through 14 years with any leukemia type in the Basrah governorate during the 15 years of the study. All children in the study were admitted to the Ibn Ghazwan pediatric oncology ward. Diagnoses were based on histopathology of bone marrow and complete blood counts. Two hematologists agreed on all diagnoses, and no changes in diagnostic technique occurred over the study period.

Demographic data for the population of the Basrah governorate, which were used to calculate rates, were obtained from a variety of sources, as detailed in Table 1. The 1997 population data were obtained from Iraq's Central Organization for Statistics and Information Technology (COSIT), as published by

Source. United Nations Cartographic Section map of Iraq used by permission, no. 3835 Rev. 4 January 2004. Available at: http://www.un.org/Depts/Cartographic/english/htmain.htm. Accessed June 30, 2009.

FIGURE 1—Map of Iraq.

TABLE 1—Population by Year: Basrah, Iraq, 1993–2007

Year	Source of Data	Total Iraq Population	Total Basrah Population	Basrah Population Aged 0–14 Years (0.433071)
1993	Interpolated from 1997[a]	. . .	1 324 530	573 616
1994	Interpolated from 1997[b]	. . .	1 364 266	590 825
1995	Interpolated from 1997[c]	. . .	1 405 194	608 549
1996	Interpolated from 1997[d]	. . .	1 447 350	626 806
1997	1997 Iraq Census[e]	19 442 780	1 490 770	645 610
1998	Interpolated from 1997[d]	. . .	1 554 873	673 416
1999	ICMMS in-depth analysis[f]	23 382 068	1 621 233	702 110
2000	Interpolated from 1999[g]	. . .	1 655 279	716 854
2001	Interpolated from 1999[h]	. . .	1 690 040	731 908
2002	Interpolated from 1999[i]	. . .	1 725 531	747 278
2003	From Table E-2[f]	26 388 081	1 762 453	763 268
2004	Burnham et al. 2006 and ILCS[f]	26 769 584[j]	1 773 249[j]	767 944
2005	Interpolated and adjusted for migration[f]	27 597 117[j]	1 801 110[j]	780 009
2006	COSIT, figures were used to calculate the Iraq Family Health Survey study sample base weights and were adjusted for migration[f]	28 514 649[j]	1 835 030[j]	794 699
2007	Interpolated by using growth rate between 2005 and 2006 of 1.018833	29 051 657	1 869 588	809 665

Note. COSIT = Central Organization for Statistics and Information Technology; ICMMS = Iraq Child and Maternal Mortality Survey; ILCS = Iraq Living Conditions Survey I.
[a]Basrah population in 1994 × 0.970874 (or 1/1.03). We used the figure 3.1% per year to decelerate the population from 1997–1993 on the basis of the statement on the COSIT Web site that the "population reached 16.3 million in 1987 with an annual growth rate of 3.1% during the period 1977–1987 and then reached 22 million according to the population census in 1997, with an annual growth rate of 3% during the period 1987–1997." The portion of the population aged 0 to 14 years was 43.31% from the 1997 census.
[b]Basrah population in 1995 × 0.970874.
[c]Basrah population in 1996 × 0.970874.
[d]Basrah population in 1997 × 0.970874.
[e]Conducted by COSIT, as published by IPUMSI (Integrated Public Use Microdata Series International) of the Minnesota Population Center at the University of Minnesota.
[f]From Table E-2 in Iraq Family Health Survey Study Group et al.[18]
[g]Basrah population in 1999 × 1.021.
[h]Basrah population calculated for 2000 × 1.021.
[i]Basrah population calculated for 2001 × 1.021.
[j]Population accelerator factor adjusted for migration, as reported in Table E-2 in Iraq Family Health Survey Study Group et al.[18] We applied the country-wide factor to the Basrah population, lacking any other indication that the factor would be different.

the Integrated Public Use Microdata Series International of the University of Minnesota's Minnesota Population Center. Population estimates from 1999 and 2003 through 2006 were extracted from the supplement to a *New England Journal of Medicine* article estimating violence-related mortality in Iraq (2002–2006).[18] The remaining years of population estimates (1993–1996, 1998, 2000–2002, and 2007) were extrapolated by using the most appropriate population escalation multiplier, based on growth rates between the years during which we had anchor numbers, as detailed above. Note that this estimate accounted for an outward migration of 1.49 million persons from Iraq secondary to the conflict in the country, which reduced the population multiplier for the years 2003 through 2007. Without other information, we assumed Basrah's outward migration was similar to that for the rest of the country. We examined hospital birth and death rates for 2003 through 2007 and saw no particular patterns of utilization change.

Incidence data were reported for each year. Rate calculations were made using SAS version 9.1 (SAS Institute, Cary, NC) by dividing the incidence by the population (aged 0–14 years) for each year, then multiplying by 100 000. To assess whether the increase in leukemia rates over time was statistically significant, we calculated rates for five 3-year time periods spanning 1993–2007 and used standard linear regression to test whether the slope of the line between each of the five 3-year average rates was different from 0. This method is similar to that used by Linet et al.[6] in their study of the changes in leukemia rates in the United States.

RESULTS

There were 698 cases of leukemia in children aged 0–14 years registered at the Ibn Ghazwan pediatric oncology ward from 1993–2007. The number of cases ranged from 15 cases in the first year to 56 cases in the final year and reached a peak of 97 cases in 2006 (Table 2). Distribution of the cases among the 3 study periods showed that 54 were registered in the period from 1993 through 1995, 72 in the period from 1996 through 1998, 160 in the period from 1999 through 2001,

TABLE 2—Leukemia Rates for Children Aged 0 to 14 Years by Year: Basrah, Iraq, 1993–2007

Year	No. of leukemia cases[a]	Population[b]	Rate per 100 000 population
1993	15	573 616	2.615
1994	14	590 825	2.370
1995	25	608 549	4.108
1996	24	626 806	3.829
1997	24	645 610	3.717
1998	24	673 416	3.564
1999	30	702 110	4.273
2000	60	716 854	8.370
2001	70	731 908	9.564
2002	85	747 278	11.375
2003	94	763 268	12.315
2004	33	767 944	4.297
2005	47	780 009	6.026
2006	97	794 699	12.206
2007	56	809 665	6.916

Source. Case data collected from Basrah's Ibn Ghazwan Maternal and Child Hospital pediatric cancer registry, affiliated with the University of Basrah.
[a]For acute lymphoblastic leukemia, acute myeloid leukemia, and chronic myeloid leukemia.
[b]Population aged 0 to 14 years.

212 in the period from 2002 through 2004, and 200 in the period from 2005 through 2007. The rates we found among children under the age of 15 years in Basrah's hospital-based registry grew from 3.03 per 100 000 (average annual rate for 1993–1995) to 8.4 per 100 000 (average annual rate for 2005–2007).

The test for trend using untransformed 3-year rates was significant, with P=.03. To assess whether the increase in the leukemia rate was dependent on the shape of the "dose-response" relation between 3-year rates and time, we also fitted a regression model by using the natural log transformation of the average rates for each 3-year period as well as the natural log transformation of annual rates. The P values for log-transformed 3-year rates and annual rates remained approximately the same. With use of the parameter estimate from the regression model of untransformed values, leukemia rates increased by approximately 1.6 cases per 100 000 during each 3-year period (B=1.63; SE=0.43). Leukemia rates in children aged 0 to 14 years more than doubled over the 15-year period (ratio of 2005–2007 rate to 1993–1995 rate=2.7; 95% confidence interval=1.437, 5.124).

We also investigated the square root transformation of both the annual rates and the 3-year average rates; the results were essentially unchanged. The purpose of applying either the square root or log transformations was to explore whether the variance changed with the mean, a situation that would violate the assumption of standard normal distribution used in linear regression. We were satisfied that the presentation of the 3-year average rates in Figure 2 was a robust finding of a significant increase in childhood leukemia in Basrah over the period of our study.

In the period of from 1993–1995, there were 43 cases of ALL, 9 cases of AML, and 2 cases of CML. These case numbers reflect rates of 1.8 per 100 000 children for ALL, 0.4 for AML, and 0.1 for CML. By the period of 2005–2007 period, the case counts and rates had increased to 162 for ALL, 27 for AML, and 11 for CML, reflecting rates of 6.8, 1.1, and 0.5 per 100 000, respectively (data not shown).

Younger children had a higher rate of leukemia than did older ones; this pattern persisted over the study period. In the 1993–1995 period, children ages 0 through 4 had overall annual leukemia rates of 2.9 per 100 000, compared with 2.7 for children aged 10 to 14 years. In the 2005–2007 period, children ages 0 through 4 had an annual rate of 10.0 per 100 000, compared with 5.0 for children aged 10 to 14 years (data not shown).

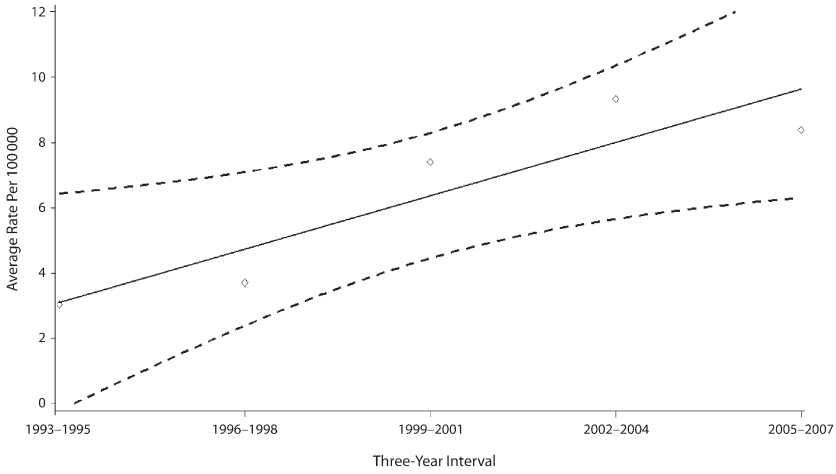
The total leukemia rate among boys was 4.8 per 100 000 during the years 1993–1995 and 9.2 per 100 000 for 2005–2007. For girls, the rates were 1.6 during the earlier period and 7.6 during the most recent 3-year period (data not shown). This pattern of higher rates for boys mimics international patterns.

The patterns of age by gender for all 3 types of leukemia are shown in Table 3, which also includes nonleukemia pediatric cancers in the registry for 2006. During that year, there were 211 recorded cases of all malignancies; of these, 97 were leukemia cases. In the 2006 data, 45 of the leukemia cases were among children under 5 years, 36 were among children aged 5 to 9 years, and 16 were in the age category of 10 to 14 years. ALL made up 82% of all leukemia cases, or 38% of total cancers, whereas AML made up 13% of all leukemia cases and 6% of total cancers. CML made up 4% of leukemia cases for the year 2006.

DISCUSSION

The purpose of this article was to report changes in childhood leukemia rates for the population of the Basrah, Iraq, governorate. Data were available for this study from a cancer registry at Ibn Ghazwan Women and Children's Hospital, affiliated with University of Basrah, since 1993. We found that recorded childhood leukemia rates in Basrah more than doubled over the 15-year period of 1993–2007. The surge was particularly concentrated in the age group of 0 to 4 years.

The governorate of Basrah has endured almost 30 years of conflict and turmoil, dating to 1980. The city was repeatedly shelled during the Iran–Iraq war, between 1980 and 1986.[19] In the summer of 1990, Iraq invaded its southern neighbor, Kuwait, followed by a 1991 US military operation to eject Iraqi troops from Kuwait.[20] Basrah was exposed to byproducts of the petroleum fires that occurred during the latter conflict, because of its location on the Kuwaiti border.[21] Following the relatively brief 1991 Gulf War, about 10 years of sanctions were imposed on Iraq,[22] resulting in a deterioration of infrastructure, nutrition, and population



Source. Case data collected from Basrah's Ibn Ghazwan Maternal and Child Hospital pediatric cancer registry, affiliated with the University of Basrah.

FIGURE 2—Average leukemia rates and 95% confidence intervals among children aged 0 to 14 years in the governorate of Basrah, Iraq, by 3-year intervals: 1993–2007.

health.[23] In March of 2003, the United States invaded Iraq, resulting in heavy fighting in Basrah.

Studying the leukemogenic nature of wartime exposures is difficult in the chaotic situations that characterize warfare. It is known that the Basrah region was exposed to environmental insults including chemical weapons agents,[24] pyrophoric depleted uranium,[25] and the known leukemogen benzene,[26] as well as ongoing undifferentiated water and air pollution, but no data are available on the doses of those exposures to the leukemia patients in our study. Our findings could also be consistent with a theory of an infectious etiology posited by Kinlen, who found elevated childhood ALL in occupational sectors where population-mixing (e.g., the level of contact with different people seen in construction and trucking) might have contributed to the risk.[27,28]

A point of comparison is the cancer registry for the neighboring country of Kuwait, as published by the International Association of Cancer Registries.[1] Kuwait's cancer registry reported rates separately for native Kuwaitis and nonnatives working in the country. We looked at the rates for the period from 1988 through 1993, although data for 1990 to 1991 are not provided because "reliable incidence and population data for the years 1990–1991 are not available due to the disruption brought about by the occupation of the country in 1990."[1] For non-Kuwaitis, whose demographic distribution was heavily skewed toward working-aged males, the rates for all leukemias (all ages) were 2.1 per 100 000 for males (4.6 when age-adjusted) and 2.0 for females (3.6 when age-adjusted). No summative number for the rates for children aged 0 to 14 years was provided in the Kuwaiti registry report. Unfortunately, cancer registry data are not reported for other countries in the Middle East region.

An article describing the incidence of leukemia in the Sultanate of Oman[29] (1994–1996) offered an approximate registry from a university hospital detailing rates for children aged 0 to 4 years (with type ALL only) as 3.9 per 100 000 for males and 2.8 per 100 000 for females. The rates for ages 5 to 14 years were 1.95 for males and 1.7 for females (summary data not reported). Summary rates for AML type leukemia were reported at 0.64.

Registry data from European Union countries show that children aged 0 to 14 years had leukemia incidence rates of 4.2 per 100 000 between 1994 and 2000, compared with 5.09 per 100 000 reported by the US national cancer registry.[30] Another article reporting US

TABLE 3—Leukemia Cases Among Children Aged Less Than 15 Years, by Age and Sex: Basrah, Iraq, 2006

	Age < 5 Years			Age 5–9 Years			Age 10–14 Years			
Type of leukemia	Male, No. of cases	Female, No. of Cases	Total No. of Cases	Male, No. of cases	Female, No. of Cases	Total No. of Cases	Male, No. of cases	Female, No. of Cases	Total No. of Cases	Total No. of Cases (%)
Leukemia										
ALL	21	18	39	18	10	28	9	4	13	80 (82)[a]
AML	0	3	3	3	4	7	2	1	3	13 (13)[a]
CML	3	0	3	0	1	1	0	0	0	4 (4)[a]
Total	24	21	45	21	15	36	11	5	16	97 (47)[b]
Other cancer	33	22	55	20	20	40	13	6	19	114 (53)[b]
Total cancer			100			76			37	211

Note. ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; CML = chronic myeloid leukemia.
Source. Case data collected from Basrah's Ibn Ghazwan Maternal and Child Hospital pediatric cancer registry, affiliated with the University of Basrah.
[a]Percent of total leukemia.
[b]Percent of total cancer.

registry data suggested the incidence for children aged 0 to 20 years in the United States to be a little lower, at 4.19 per 100 000 between 1992 and 2004.[31] Reports from India, Greece, and Mexico reported childhood rates similarly, between 4 and 5.5.[32–34]

Our data show that the average annual incidence of all types of leukemia in Basrah (per 100 000 children aged 0–14 years) has risen substantially. The rates for the most recent 3-year periods (7.40, 9.33, and 8.38) compare unfavorably to neighboring Kuwait and nearby Oman, as well as to the United States, the European Union, and other countries.

Our study had several limitations. Childhood cancers are rare, and therefore evaluating trends even in a robust data set such as this is difficult. In a war zone environment, reduced case ascertainment may also have affected the rates. Our comparisons with rates in Kuwaiti and other international rates may be misleading, because methods of data collection and the completeness of population denominators vary widely.

Although there is a well-developed and stable data set for cancer cases presenting at Ibn Ghazwan, in recent years, population displacement by the violence may have affected both the total population and referral patterns in Basrah in ways for which we did not accurately account. We applied the outward migration percentage calculated by Alkhuzai for the entire nation of Iraq as if it were the same for Basrah (2004–2006),[18] although it was probably higher in the border province of Basrah. The consequence of these limitations, however, would be to understate the leukemia rate, rather than overstate it.

A strength of the study was that the leukemia registry in Basrah is a natural byproduct of referral patterns and the concentration of resources and physicians in one facility.

This research project came about as the result of a sister-university affiliation between the University of Washington and the University of Basrah, a partnership initiated after the US invasion of Iraq in 2003 as an effort to bring academic public health professionals together despite the political environment. We were initially interested in all pediatric cancers, as well as birth defects, because all these pediatric conditions were described anecdotally as being elevated. We elected to focus on leukemia because it is the most common pediatric cancer and could be histologically proven. A clearer understanding of leukemia may offer opportunities for future studies of etiology and prevention, especially in populations with suspected higher risk exposures. ■

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Contributors

A. Hagopian and T. Takaro originated and designed the research project after meeting J. Hassan, who collected the data on which the article is based and participated in editing the article. R. Lafta traveled to Basrah, Iraq, to collect data from the cancer clinic and participated in the data analysis and writing and editing of the article. S. Davis was the lead epidemiologic advisor on the project and designed the approach to the statistical analysis. D. Mirick was the lead statistician on the project.

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Human Participant Protection

The protocol of the study was approved by the Human Subjects institutional review board of the University of Washington. Although there was no similar institution functioning in Iraq from which to seek approval at the time we began this study, a data user agreement was signed by an official at Mustansiriya University to authorize the study.

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