

Incidence and Pattern of Childhood Leukaemia in Basrah, Iraq during 2003-2007

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Abstract

Background: Environment of Basrah is seriously contaminated with chemical leukomogens as a result of recent military conflicts. Many studies in the past few years have reported an increase in the incidence of leukemia in Basrah. This study was designed to study the risk and pattern of childhood leukemia in Basrah, Iraq, from 2003 to 2007.

Materials and Methods: This hospital-based cancer registry study was conducted on the hospital registry between June to December 2009. All children with leukemia, aged 1 to 14 years diagnosed from January 2003 to December 2007 in the Pediatrics' Oncology Ward, Maternity and Children Hospital in Basrah, Iraq were included in the study. The records of all confirmed childhood leukemia were retrieved and studied. The specific incidence rates were calculated. The patterns of leukemia classified by age at diagnosis, gender, morphological subtypes and geographical distribution were also determined.

Results: From January 2003 to December 2007, the total number of the cases of childhood leukemia was 159. The overall age standardized incidence rate (ASIR) at this period was 5.45/100000. No temporal increase in incidence rates of childhood leukemia during this 5 year period was observed. The highest incidence rate was observed in the North of Basrah. The most common type of leukemia in this study was acute lymphoblastic leukemia (ALL), followed by acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) respectively. All subtypes of leukemia were more common in males. The highest percentages of ALL and CML were observed at ages between 2 to 5 years. AML occurred more commonly at age of 6 to 14 years.

Conclusion: Leukemia was the most common childhood malignancy in Basrah. Although we observed no temporal increase in the incidence rates of childhood leukemia during the 5 year period from 2003 to 2007, leukemia incidence in children in Basrah was higher in comparison with other countries. There is a need for epidemiological studies to understand the etiology of childhood leukemia in Basrah.

Keywords: Child, Incidence, Leukemia, Basrah.

Introduction

Leukemia is the most common childhood cancer, accounting for 25% to 35% of all incident childhood cancers among most populations^{1,2}.

The common type of childhood leukemia is acute lymphoblastic leukemia (ALL), which constitutes up approximately 80% of children leukemia cases, followed by acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) and with relatively few leukemia cases in other categories³.

The incidence of childhood leukemia incidence shows a trend for higher rates in resource rich countries, which ranges from 4.0 to 4.4 per 100000 per year⁴, and lower in less-developed countries (e.g., 0.9 per 100000 per year in Vietnam)⁵. These variations may reflect the lack of cancer registration in low income-countries⁶. Studies from different parts of the world have indicated an increase in the incidence of childhood leukemia in the recent decades^{7,8} while this incidence stayed largely stable

in the United State ⁹ and Nordic countries ¹⁰. In most countries, the incidence of childhood leukemia is higher in boys than girls ^{11, 12}. Although the etiology of most childhood leukemias is unknown ¹³, several factors have been associated with the disease, including socioeconomic status ^{14, 15}, environmental exposures including ionizing radiation and benzene ¹⁶, infectious agents ¹⁷, and parental exposure risk factors ^{18, 19}. Basrah is the second largest city of Iraq with an estimated

population of 2,426,607 in 2007. It is the country's main port and it is located along Shatt Al-Arab waterway, approximately 545 km southeast of Baghdad and adjacent to Iran and Kuwait borders. Basrah is composed of the flat alluvial plain formed by the combined flood plains and deltas of the Tigris, Euphrates, and Shatt Al-Arab rivers. The area surrounding Basrah has substantial petroleum resources with many oil wells. Basrah has been exposed to massive environmental pollution as a

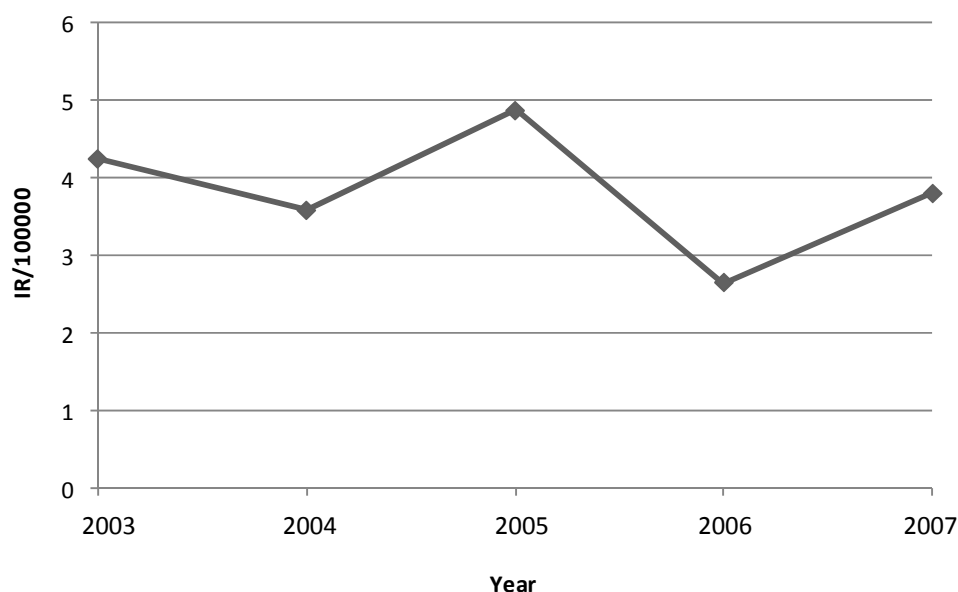


Figure 1. Yearly incidence rate of pediatric leukemia per 100000 in Basrah, Iraq from 2003 to 2007.

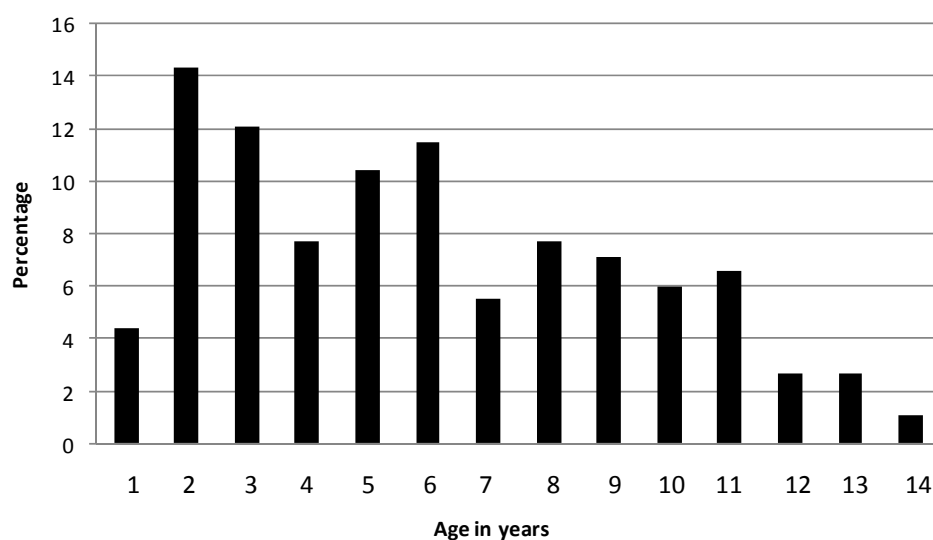


Figure 2. Percentage distribution of leukemia by age among children below 15 years in Basrah, Iraq during 2003 – 2007.

consequence of military conflicts and lack of efficient protective policy from 1980 to 2003. Previous research work and growing impressions among physicians and lay people suggested that childhood leukemia is increasing in Basrah after the Persian Gulf war in 1991²⁰⁻²².

However, these suggestions faced a lot of criticisms for being inadequate to prove a real increase in the risk of childhood leukemia simply because of incomplete case registration and/or inaccurate population denominators. In order to approach the reality, the Basrah Cancer Research Group (BCRG) was established and they initiated a project to improve registration, identify risk factors and improve care. This group (BCRG) achieved good results in registration of cancers including childhood leukemia²³.

The aim of this study was to describe the incidence rates of childhood leukemia and their variations in the population of Basrah, Iraq in the

recent years. Data were available for this study from cancer registry at Pediatrics' Oncology Ward in Maternal and Children Hospital in cooperation with the College of Medicine from the University of Basrah.

Materials and Methods

This hospital-based cancer registry study was based on all new cases of childhood leukemia which were registered in the Pediatrics' Oncology Ward in Basrah Maternity and Children Hospital. The pattern of medical referral in the Basrah governorate channels all childhood leukemia cases to the Pediatrics' Oncology Ward in Basrah Maternity and Children Hospital which is responsible for treatment and registration of childhood malignancies in Southern Iraq. Many of these children are treated outside Iraq but they were diagnosed and registered in Basrah before traveling. Diagnosis was based on histopathology of

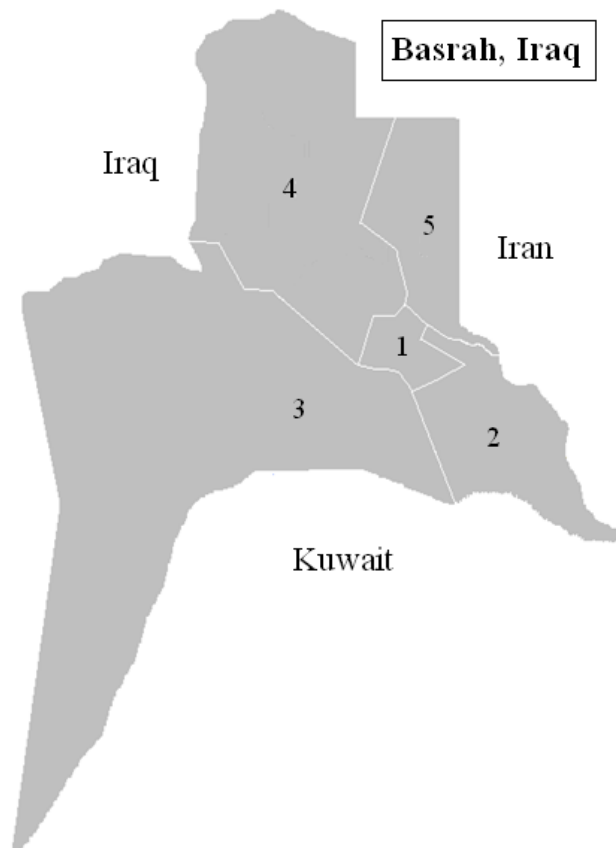


Figure 3. Average rates of childhood leukemia in different areas in Basrah during 2003 – 2007.
(1) Basrah city center, (2) South of Basrah, (3) West of Basrah, (4) North of Basrah, (5) East of Basrah.

Table 1. Distribution of the subtypes of childhood leukemias in Basrah during 2003 – 2007.

Type of leukemia	N (%)
ALL	134 (84)
AML	17 (11)
CML	8 (5)
Total	159 (100)

Table 2. Age distribution and subtypes of childhood leukemia in Basrah during 2003 – 2007.

Age (years)	Type of leukemia		
	ALL N (%)	AML N (%)	CML N (%)
0 – 1	4 (3)	2 (12)	1 (13)
2 – 5	66 (49)	3 (18)	4 (50)
6 – 14	64 (48)	12 (70)	3 (37)
Total	134 (100)	17 (100)	8 (100)

Table 3. Sex distribution and subtypes of childhood leukemia in Basrah during 2003 – 2007.

Sex	Type of leukemia		
	ALL N (%)	AML N (%)	CML N (%)
Male	78 (58)	11 (65)	5 (63)
Female	56 (52)	6 (35)	3 (37)
Total	134 (100)	17 (100)	8 (100)

bone marrow aspirate and complete blood counts. Two hematologists agreed on all diagnoses and no change in diagnostic techniques occurred over the study period. Standard criteria were used to diagnose leukemia, which for the purpose of this analysis have been divided into acute lymphoblastic leukemia, acute myeloblastic leukemia, chronic myeloid leukemia and chronic lymphocytic leukemia.

Information related to population of Basrah was based on data available with Basrah Health Authorities, from the electronic lists and the Statistical Office in Basrah.

According to the modified system used by the health authorities, Basrah governorate was divided into five areas or health sectors. These areas are: Basrah city center, South of Basrah (including Abualkaseeb and Alfao), West of Basrah (including Alzubair), North of Basrah (including Alhartha, Alqurna, and Almudaina) and East of Basrah (including Shatarab) (see map, Figure 3).

Statistical analysis was carried out with the SPSS software ver. 15.0 (Chicago, IL). Some of figures were constructed with Excel (Office 2007) program.

Incidence rate for each year was calculated by dividing incident cases in that year by the population of children aged 0-14 years in that year and then multiplying the result by 100000. Age standardized incidence was derived using the world standard population by the direct method²⁴.

Results

Between January 2003 and December 2007, the total number of the cases of childhood leukemia was 159. This represented 47.2 % of the total number of cancer cases among children in Basrah. The overall crude annual incidence rate among children between January 2003 and December 2007 was 3.98 per 1000000. The overall age standardized incidence rate (ASIR) in this period was 5.45/100000. The yearly incidence rates of leukemia from 2003 to 2007 were 4.25/100000, 3.58/100000, 4.88/100000, 2.64/100000 and 3.80/100000 respectively (Figure 1).

The total reported incidents cases showed that leukemia was predominant in boys (55.3) than in girls (44.7), with a male to female ratio of 124:100. The percentage distribution of leukemia by age is

presented in Figure 2. A clear peak in incidence is observed at ages of 2-6 years.

The subtype of leukemia in Basrah is presented in Table 1. The most common type of leukemia in this study is ALL, followed by AML and CML respectively.

The age distribution according to the subtype of leukemia is present in Table 2. The highest percentages of ALL and CML were observed at ages between 2 to 5 years. AML occurred more commonly at ages between 6 to 14 years. Table 3 shows the sex distribution and the subtypes of leukemia. In the present study, all subtypes of leukemia were more common in males.

The five years crude incidence rates of childhood leukemia in each region in Basrah were presented in Figure 3. The highest incidence rate was observed in the North of Basrah (5.63/100000), followed by the West of Basrah (3.34/100000), Basrah city center (3.27/100000), the South of Basrah (2.37/100000) and the East of Basrah respectively.

Discussion

This paper presents data on the incidence, time trends and regional variations of childhood leukemia in Basrah. Leukemias made up about 47% of pediatric cancers in Basrah whereas international percentages ranged from 27% of pediatric cancers in the United States, 30% in Ireland and France²⁵, 33% in Germany²⁶ and 35% in China (Shanghai)²⁷ and India²⁸. The high percentage of leukemia in the present study may suggest a relatively higher risk of leukemia in Basrah as a result of exposure to many environmental risk factors.

Although, we observed no temporal increase in the incidence rates for childhood leukemia during the 5 year period from 2003 to 2007, leukemia incidence in children in Basrah was higher in comparison with other countries. The rate of leukemia for children <15 years old has been estimated to be 4 per 100000 per year in the developed world and 2.5 per 100000 per year in the developing world²⁹. The percentage distribution of age for childhood leukemia in Basrah has a clear peak between the ages of two and six, with the highest rates at ages of two and three. This is similar to the United State and Great Britain where the peak incidence occurs between ages of 2-5 years and may be downward. The peak is less marked in less developed countries^{30, 31}. However,

it is not certain what specific causes account for the high rate of leukemia and what is the etiology of this age pattern in childhood leukemia in Basrah. This may be attributed to the changes in the life style of the population and/or may be linked to the extensive environmental pollution in Basrah in the recent decades.

Basrah is confronted with a range of environmental problems that are both immediate and severe. Some can be directly linked with the effects of the recent military conflicts. Others have been triggered by internal Iraqi policies and actions and exacerbated by factors such as the impact of economic sanctions³².

In the Persian Gulf War of 1991 and 2003, the US and UK Governments acknowledged that known depleted uranium munitions have been used in Iraq. Many tons of this radioactive substance targeted the Basrah governorate^{20, 33}.

Also, in the Persian Gulf war of 2003, there were reports of oil wells that were deliberately set on fire in the Rumeila oilfield in Basrah where a thick haze of dark smoke could be seen from Kuwait City on the following day. The broad categories of contaminants are volatile hydrocarbons, hydrogen sulfide and naturally occurring radioactivity. Since aromatic hydrocarbons (like benzene), which are known leukemogens, are the most volatile forms of hydrocarbons, exposure even at low levels can be very harmful³⁴.

Studying the leukomogenic nature of war – time exposures is difficult in the welter situation that characterizes warfare. It is known that Basrah region was exposed to environmental insults including pyrophoric depleted uranium³⁵ and leukemogen benzene³⁶, as well as ongoing undifferentiated water and air pollution, but no data are available on the doses of these exposures to the leukemia patients in our study.

The occurrence patterns of the subtypes of leukemia were also analyzed in this study: the most common type of leukemia was ALL. This distribution was similar to that reported in other countries^{37, 38}. The ratio of boys to girls diagnosed with leukemia in our study is 124:100 which is similar to the gender distribution in North America including the United State where the ratio is 120:100. It has also been reported that in many developing countries, the reported number of childhood cancer in boys is

substantially higher than the girls. The ratio of boys to girls registered with childhood cancer, increased with decreasing gross domestic products and with increasing infant mortality, suggesting that boys are increasingly more likely to be affected than girls with increasing economic disadvantages¹². In the present study, childhood leukemia incidence disclosed higher rates in the North of Basrah, an area of low socioeconomic status in comparison with the center of Basrah city. Earlier studies^{1, 31} indicated a geographic place correlation between socioeconomic status and childhood leukemia incidence. These studies have indicated that this characteristic incidence peak emerges with socioeconomic development³⁹, but there is at least one exception⁴⁰. These observations are consistent with the hypothesis that the risk of childhood acute lymphoblastic leukemia can be modified by exogenous factors⁴¹.

Conclusion

Clear increase in the incidence of childhood leukemias in Basrah have been noted recently in comparison with other countries, which cannot be easily explained. It would be interesting to explore whether exposure to environmental pollution and different lifestyle patterns across Iraqi population might be responsible for the observed excess leukemia incidence in governorate such as Basrah, and therefore highlight the need for more research into the etiology of childhood leukemia.

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References

1. Parkin DM, Stiller CA, Draper GJ, Bieber CA. The international incidence of childhood cancer. *Int J Cancer*. 1988; 42:511-20.
2. Pui CH, Schrappe M, Ribeiro RC, Niemeyer CM. Childhood and adolescent lymphoid and myeloid leukemia. *Hematology Am Soc Hematol Educ Program*. 2004;118-45.
3. Linet MS, Devesa S, Morgan GJ. The leukemias. In: Schottenfeld D, Joseph F, Fraumeni J, editors. *Cancer Epidemiology and Practice*. Oxford: Oxford University Press; 2006. p. 841-71.
4. Parkin DM. *Cancer Incidence in Five Continents*. Geneva, Switzerland: International Agency for Researchon Cancer (WHO) International Association of Cancer Registries; 2005.
5. Bunin GR. Nongenetic causes of childhood cancers: evidence from international variation, time trends, and risk factor studies. *Toxicol Appl Pharmacol*. 2004;199: 91-103.
6. Howard SC, Metzger ML, Wilimas JA, Quintana Y, Pui CH, Robison LL, et al. Childhood cancer epidemiology in low-income countries. *Cancer*. 2008; 112:461-72.
7. Hrusak O, Trka J, Zuna J, Polouckova A, Kalina T, Stary J. Acute lymphoblastic leukemia incidence during socioeconomic transition: selective increase in children from 1 to 4 years. *Leukemia*. 2002;16:720-5.
8. McNally RJ, Eden TO. An infectious aetiology for childhood acute leukaemia: a review of the evidence. *Br J Haematol*. 2004;127:243-63.
9. Linet MS, Ries LA, Smith MA, Tarone RE, Devesa SS. Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst*. 1999;91:1051-8.
10. Hjalgrim LL, Rostgaard K, Schmiegelow K, Soderhall S, Kolmannskog S, Vettenranta K, et al. Age- and sex-specific incidence of childhood leukemia by immunophenotype in the Nordic countries. *J Natl Cancer Inst*. 2003;95:1539-44.
11. McNally RJ, Rowland D, Roman E, Cartwright RA. Age and sex distributions of hematological malignancies in the U.K. *Hematol Oncol*. 1997;15:173-89.
12. Pearce MS, Parker L. Childhood cancer registrations in the developing world: still more boys than girls. *Int J Cancer*. 2001;91:402-6.
13. Thompson JR, Gerald PF, Willoughby ML, Armstrong BK. Maternal folate supplementation in pregnancy and protection against acute lymphoblastic leukaemia in childhood: a case-control study. *Lancet*. 2001;358:1935-40.
14. Borugian MJ, Spinelli JJ, Mezei G, Wilkins R, Abanto Z, McBride ML. Childhood leukemia and socioeconomic status in Canada. *Epidemiology (Cambridge, Mass)*. 2005;16:526-31.
15. Raaschou-Nielsen O, Obel J, Dalton S, Tjonneland A, Hansen J. Socioeconomic status and risk of childhood leukaemia in Denmark. *Scand J Public Health*. 2004;32:279-86.
16. Belson M, Kingsley B, Holmes A. Risk factors for acute leukemia in children: a review. *Environ Health Perspect*. 2007;115:138-45.

17. Infante-Rivard C, Olson E, Jacques L, Ayotte P. Drinking water contaminants and childhood leukemia. *Epidemiology* (Cambridge, Mass). 2001;12:13-9.
18. Fear NT, Simpson J, Roman E. Childhood cancer and social contact: the role of paternal occupation (United Kingdom). *Cancer Causes Control*. 2005;16:1091-7.
19. Perez-Saldivar ML, Ortega-Alvarez MC, Fajardo-Gutierrez A, Bernaldez-Rios R, Del Campo-Martinez Mde L, Medina-Sanson A, et al. Father's occupational exposure to carcinogenic agents and childhood acute leukemia: a new method to assess exposure (a case-control study). *BMC cancer*. 2008;8:7.
20. Ciment J. Iraq blames Gulf war bombing for increase in child cancers. *BMJ* (Clinical research ed). 1998;317:1612.
21. Hagopian A, Lafta R, Hassan J, Davis S, Mirick D, Takaro T. Trends in childhood leukemia in Basrah, Iraq, 1993-2007. *Am J Public Health*. Jun;100:1081-7.
22. Yacoub AAH, Al-Sadoon IO, Hassan GG, Al-Hemadi M. Incidence and pattern of malignant disease among children in Basrah with specific reference to leukemia during the period 1990 – 1998. *The Medical Journal of Basrah University*. 1999;17:27-34.
23. Basrah Cancer Research Group. *Cancer in Basrah 2005-2008*. Basrah: Dar Alkutub for Press & Publication, University of Basrah; 2009.
24. Boyle P, Parkin DM. Statistical methods for registries. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG, editors. *Cancer Registration, Principles and Methods*. Lyon: IARC; 1991. p. 126.
25. Desandes E, Clavel J, Berger C, Bernard JL, Blouin P, de Lumley L, et al. Cancer incidence among children in France, 1990-1999. *Pediatr Blood Cancer*. 2004;43:749-57.
26. Spix C, Eletr D, Blettner M, Kaatsch P. Temporal trends in the incidence rate of childhood cancer in Germany 1987-2004. *Int J Cancer*. 2008;122:1859-67.
27. Bao PP, Zheng Y, Wang CF, Gu K, Jin F, Lu W. Time trends and characteristics of childhood cancer among children age 0-14 in Shanghai. *Pediatr Blood Cancer*. 2009;53:13-6.
28. Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990-2001: incidence and survival. *Int J Cancer*. 2008; 122:2607-11.
29. International association of cancer registries. *Cancer Incidence, Mortality and Prevalence Worldwide*. Lyon, France: Globocan; 2000.
30. Plesko I, Somogyi J, Dimitrova E, Kramarova E. Descriptive epidemiology of childhood malignancies in Slovakia. *Neoplasma*. 1989;36:233-43.
31. Stiller CA, Parkin DM. Geographic and ethnic variations in the incidence of childhood cancer. *Br Med Bull*. 1996;52:682-703.
32. United Nations Environment Programme. *Desk Study on the Environment in Iraq* United Nations; 2003. Available at: <http://www.unep.org/pdf/iraq>.
33. Dyer O. WHO suppressed evidence on effects of depleted uranium, expert says. *BMJ* (Clinical research ed). 2006;333:990.
34. Editorial. Assessment of Environmental "Hot Spot" in Iraq. United Nations Environmental Programme, UN. 2005.
35. Mixed messages about depleted uranium. *Lancet Oncol*. 2001;2:65.
36. Austin H, Delzell E, Cole P. Benzene and leukemia. A review of the literature and a risk assessment. *Am J Epidemiol*. 1988;127:419-39.
37. Linabery AM, Ross JA. Trends in childhood cancer incidence in the U.S. (1992-2004). *Cancer*. 2008;112:416-32.
38. Stack M, Walsh PM, Comber H, Ryan CA, O'Lorcain P. Childhood cancer in Ireland: a population-based study. *Arch Dis Child*. 2007;92:890-7.
39. Greaves MF, Colman SM, Beard ME, Bradstock K, Cabrera ME, Chen PM, et al. Geographical distribution of acute lymphoblastic leukaemia subtypes: second report of the collaborative group study. *Leukemia*. 1993; 7:27-34.
40. Fasal E, Jackson EW, Klauber MR. Birth characteristics and leukemia in childhood. *J Natl Cancer Inst*. 1971;47:501-9.
41. Coebergh JW, Reedijk AM, de Vries E, Martos C, Jakab Z, Steliarova-Foucher E, et al. Leukaemia incidence and survival in children and adolescents in Europe during 1978-1997. Report from the Automated Childhood Cancer Information System project. *Eur J Cancer*. 2006;42:2019-36.