

# Childhood Cancer(Leukaemias and Lymphoma) in Basrah- A case-control study-

Hanadi L Obeid\*, Omran S Habib\*\*, Ganan G. Hassan\*\*\*

## **ABSTRACT**

This is a case-control study carried out in Basrah during 2006. It involved 120 cases of leukaemia and lymphoma among children aged less than 15 years. The cases were compared with 180 controls matched for age, sex and area of residence. The study aimed at exploring certain sociodemographic and environmental risk factors.

The results showed significant association between these two cancers and each of probable exposure to radiation, pesticides and chemicals related to automobiles and other sources. No clear association could be elicited between the studied cancers and education, age and occupation of parents.

The study came to the conclusion that leukaemia and lymphoma were important childhood cancers and continuing efforts to register cancer in Basrah is vital for effective planning and research. It is also recommended that this small scale study could be expanded in the near future to confirm or refute the present study findings.

**Key words:** Cancer . Leukaemias .Lymphomas. Basrah

## **INTRODUCTION**

Cancer develops when cells in part of the body begin to grow out of control and function in a manner not useful or even harmful to the body. <sup>(1)</sup> Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries. Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells without known useful function to the body. <sup>(1)</sup>

Cancer cells often metastasize to other parts of the body by the bloodstream or lymph vessels where they begin to grow and replace normal tissue. <sup>(1)</sup>

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not always amenable to repair. People can inherit damaged DNA, which accounts for inherited susceptibility to cancers. <sup>(2)</sup> Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs, and circulate through other tissues where they grow

---

\*Basrah Health Service

\*\* Department of Community Medicine, Basrah College of Medicine

\*\*\* Department of Paediatrics, Basrah College of Medicine

## Childhood Cancer (Leukaemias and Lymphoma) in Basrah - A case-control study-

(3). Risk factors for childhood cancer are numerous. Examples are Alcohol drinking, smoking, genetic diseases like Down syndrome and Klinefelter syndrome, accidental radiation exposure, radiation therapy and chemotherapy, Immune system suppression, certain chemicals, mother's age at birth; mother's use of alcohol, cigarettes, diethylstilbestrol (DES), or contraceptives; father's occupational exposure to chemicals and solvents; and chemical contamination of ground water. (4-6)

### *The Significance Of Childhood Cancer*

Cancer is the second leading cause of death in the United States. Half of all men and one-third of all women in the US will develop cancer during their lifetimes. Today; millions of people are living with cancer, developing new cancer or dying from cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. Although cancer is rare in children, it is still the leading cause of death by disease in children aged 1 to 14.<sup>(7)</sup> The most common childhood cancers include Leukaemias, Hodgkin's and non-Hodgkin's lymphomas, Wilms tumor, Neuroblastoma, Retinoblastoma, Rhabdomyosarcoma, Central nervous system, Bone cancer, Osteosarcoma Ewing sarcoma. As a group, Leukaemias account for about 25% of all childhood cancers and affect about 2,200 American young people each year. Luckily, the chances for a cure are very good with leukemia in well-equipped centres. With treatment, most children with leukemia are free of the disease and safe from relapse<sup>(8)</sup>. But such high cure rate and hence survival rate is only attainable in countries with high quality medical care. Approximately

60% of children with leukemia have ALL, and about 38% have AML. Lymphomas both Hodgkin's and Non-Hodgkin's are receiving increasing attention by researchers because they are growing childhood cancers. In the United States, for example, it was estimated that about 12,156 children under the age of 20 were expected to be diagnosed with cancer in 2005. Of these Hodgkin lymphoma form 8.7% and non-Hodgkin lymphoma 4.7% and represent the third most common cancer in children, following leukemia (24 percent) and brain and nervous system tumors (17 percent). Among very young children a diagnosis of non-Hodgkin lymphoma is more prevalent; whereas adolescents are more commonly diagnosed with Hodgkin lymphoma<sup>(9)</sup>. Most cases of lymphoma have no known cause. The bacterium helicobacter pylori is associated with the development of lymphoma in the stomach wall. Patients with human immunodeficiency virus (HIV) have a much higher risk of developing lymphoma. Burkitt's lymphoma in Africa is associated with prior infection with the Epstein-Barr virus. The virus may play a role in the development of some lymphomas as well. A rural lifestyle and the occupation of farming have been associated with an increased risk of lymphoma. Exposure to certain chemicals contained in herbicides and pesticides in such settings are suspected of playing a role, but these specific relationships are still under study.

### *The Situation In Basrah*

In Basrah, previous studies reported increased risk of both leukemia and lymphoma in children. Two important features were reported:: a rise in the incidence rate of Leukaemias and lymphoma in

children and an age shift towards younger children<sup>(10,11)</sup>. To quote some figures, the incidence rate of Leukaemias has increased from 2.3 to 3.2 per 100 000 population in 1995 and 2005 respectively. Lymphoma has also increased from 2.2 to 4.6 per 100 000 during the same period. However the risk factors associated with such increased disease risk have not been tackled with analytical epidemiological studies. An attempt was made to relate these changes to environmental exposure particularly to depleted uranium but the evidence was inconclusive<sup>(11)</sup>. The present study is an attempt to explore some risk factors for Leukaemias and lymphoma in children in Basrah.

## ***SUBJECTS AND METHODS***

This is a case – control study designed to study the association between childhood cancer (leukemia and lymphoma) and possible risk factors, with some reference to environmental factors.

Cases were children between 1-14 years old with haematological and histological confirmed diagnosis of malignancy (leukaemia and lymphoma). The source of cases was patients attending the oncology wards and oncology clinic in the Basrah Maternity and Children hospital, which provides chemotherapy for all diagnosed cancer cases referred from both public and private hospitals throughout the southern governorates and mainly Basrah governorate. A total of 120 cases were enrolled in the study over a period of 8 months (January-August 2006).

Controls were children free from cancer at the time of the study on clinical basis. A total of 160 controls were included in the study. Cases and controls were matched for age, sex and place of residence at a level of

administrative units. The data from cases and controls were collected by using special questionnaire from designed for the study purpose. The questionnaire was designed to obtain information on sociodemographic characteristics of the patient, type of malignancy, type of treatment, history of exposure to radiation, if there are any inherited diseases which decrease the immunity, history of exposure to pesticides and chemicals, family history of malignancy, father's age, occupation and exposure to radiation. Age of mother, occupation and history of exposure to radiation during pregnancy of the current child. The same information (except those related to current malignancy) was obtained from the controls.

The investigators interviewed the parents of cases and controls directly when they were in the hospital. None of parents of cases and controls refused the interview. Each interview took approximately 20 minutes to be completed.

Statistical analysis of the data was conducted by computer using SPSS (Statistical Package of Social Sciences). Version 11, P values of less than 0.05 were considered significant. Odds ratios (OR) and their confidence intervals (CI) were calculated by using Woolf's methods<sup>(12)</sup> as follows:

OR=ad/bc where:

a=number of exposed cases.

d=number of unexposed controls.

b=number of exposed controls.

c=number of unexposed cases.

The 95% CI of OR  
 $=1n OR \pm 1.96 \sqrt{1/a+1/b+1/c+1/d}$

## ***RESULTS***

A total of 60 males and 40 females were studied, most of the cases were Leukaemias (63 males and 33 females). Lymphomas were 24 cases (17 males and 7 females)

### ***Probable Postnatal exposure of the child to ionizing radiation***

Table 1 shows comparison of cases and controls with respect to potential exposure of the child to ionizing radiation after birth. The percentage of cases exposed was 69.2, which was greater than the percentage of controls exposed which was 56.3. There was a slight increase in the risk of childhood leukemia and lymphoma among those with positive history of exposure to ionizing radiation after birth (odds ratio=1.7, 95% CI=1.06-2.87). The association was statistically significant ( $p<0.05$ ).

### ***Probable exposure of the child to pesticides***

Regarding pesticides exposure, Table 2 shows that the percentage of cases with probable exposure to pesticides was 43.3% which was more than double the percentage of controls with probable exposure (27.5%). The difference was statistically significant ( $p < 0.05$ ), with an Odds ratio of 2.01 and a 95% confidence interval of 1.22-3.33.

### ***Probable exposure of the child to chemicals other than pesticides***

Table 3 shows comparison of cases and controls with respect to probable exposure to chemicals other than pesticides. The percentage of cases with probable exposure was 57.5% which was greater than the percentage of controls with probable exposure (43.1%). Thus children exposed to chemicals of benzene were more likely to develop cancers than not exposed children (odds ratio =1.78, C.I =1.1-2.88) and the difference was statistically significant ( $p<0.05$ ).

### ***Probable preconception exposure of the father to ionizing radiation***

Table 4 shows that the percentage of cases whose fathers were probably exposed to ionizing radiation (67.5%) was greater than the percentage of controls who were probably exposed (50.6%) and the Odds ratio =2.03 confidence interval = 1.24-3.31. The difference was statistically significant ( $p<0.05$ ).

### ***Probable exposure of the mother to ionizing radiation(during pregnancy):***

Table 5 shows that the percentage of cases (15 %) whose mothers were probably exposed to ionizing radiation was about three times greater than the percentage of controls (5.6 %) and the odds ratio = 2.96. with 95 % CI = 1.28 – 6.85 and the difference was statistically significant ( $P< 0.05$ ).

## ***DISCUSSION***

Case control studies are commonly used analytical studies especially in diseases of rare occurrence. They have certain limitations such as bias in the ascertainment of past exposure and confusion of the relationship of exposure and outcome with respect to which have occurred first. However, they are more practical than the cohort studies, less time consuming and need smaller number of participants and thus less costly<sup>(12)</sup>.

The problem of selection was unlikely to have been eliminated totally but it was minimized because the cases included in the study were those with haematological and histopathological ascertained diagnosis of leukemia and lymphoma among patients attending the oncology wards and oncology clinic in the Basrah Maternity and Children

Hospital and represent referred cases from public and private hospitals throughout the southern governorates mainly Basrah governorate. Some cases, though unlikely to be different from those studied, could be treated elsewhere.

A recall bias may be a problem in obtaining information, as history of exposure of parents to radiation before the birth of the child (preconception) might not be completely ascertained. It was at least reduced by: (1) specifying the type of radiation as x-ray examination or probable exposure to radiation as result of war explosions in 2003 and major events of explosions during the nineties. (2) by limiting the recall period to two years before the birth of the child <sup>(23)</sup>. On the other hand some information like date of diagnosis and type of malignancy are taken from medical records and they are very likely to be correct. The completeness of coverage of cases by the study is not easy to guarantee but comparing the number studied with the pooled cases in Basrah. It seems that we have covered more than 50 % of the cases <sup>(10)</sup>.

Age as a strong confounder was removed by the process of matching

In this study cases and controls were matched for age, sex and place of residence. Matching for place of residence has relatively lead to indirect matching for environmental risk factors with wider scope of effect.

Children are considerably more sensitive to the carcinogenic effects of ionizing radiation than adults, and children have a longer life expectancy in which to express risk <sup>(13)</sup>. In the present study, post natal exposure to ionizing radiation whether accidental which happened as result of war explosions or diagnostic x-ray was important risk factor. We found that the percentage of exposed cases was greater than the percentage of

controls. Such results agree with the study had done in Basrah for period from 1990 – 1998 <sup>(11)</sup>, and with studies on victims of Hiroshima and Nagasaki bombing <sup>(14)</sup>.

Several Studies have linked leukemia to pesticides. Use of insecticides in the home and garden was associated with increased risk of ALL <sup>(15,16)</sup>. In the present study it was found that the percentage of cases with probable exposure to pesticides was more than double the percentage of controls and this was comparable to the results of studies carried out in Denver, USA and France <sup>(17,18,19)</sup>.

In the present study there was an association between dwellings neighboring a petrol station, oil refineries car repairing garage and heavy traffic roads which are benzene emitting sources and the risk of childhood leukemia and lymphoma. This result is supported by a study in California <sup>(20)</sup> and in Great Britain <sup>(21)</sup>. Ionizing radiation is a known cause of childhood leukemia.

The association with x-ray is particularly strong <sup>(22)</sup>. In the present study we found that there was strong association between preconception (paternal) exposure to ionizing radiation with leukemia and lymphoma in children. This result is comparable to other study carried out in Shanghai <sup>(22)</sup> and in Germany <sup>(23)</sup>. Intrauterine exposure to ionizing radiation has teratogenic and carcinogenic effects. Most case-control studies have shown a 40-50% increase in the risk of cancer following intrauterine exposure to medical diagnostic radiation <sup>(22)</sup>.

In the present study there was strong association between intrauterine exposure to ionizing radiation and childhood leukemia and lymphoma which is comparable to a study carried out in Germany <sup>(23)</sup> and Shanghai <sup>(22)</sup>.

**Childhood Cancer (Leukaemias and Lymphoma) in Basrah  
- A case-control study-**

**IN CONCLUSION**

, the two childhood cancers; leukaemia and lymphoma are real health problems among children in Basrah. The rising risk could be attributed partly to exposure to certain environmental risk factors including probable exposure to radiation, pesticides and chemicals. It is highly recommended that accurate measurement of the extent of cancer is very necessary for any process of planning of care and research. The cooperation of all partners particularly doctors in cancer registration efforts is vital for the completion of the job. Large scale study is required to

confirm or refute the results of the present study. We suggest continuation of this research work with further improvement of the sample size and comprehensiveness of potential risk factors.

**Table 1: Distribution of cases and controls with respect to probable postnatal exposure to ionizing radiation**

Probable exposure to pesticides	Cases		Controls		Odds ratio	95% CI
	NO.	%	NO.	%		
Exposed	52	43.3	44	27.5	2.01	1.22-3.33
Not exposed	68	56.7	116	72.5		
<b>Total</b>	<b>120</b>	<b>100.0</b>	<b>160</b>	<b>100.0</b>		

$X^2=4.8$

D.F=1

P=0.035

**Table 2: Distribution of cases and controls with respect to probable pesticides exposure**

Probable post natal exposure to radiation	Cases		Controls		Odds ratio	95% C.I
	NO	%	NO	%		
Exposed	83	69.2	90	56.3	1.7	1.06-2.87
Not exposed	37	30.8	70	43.8		
<b>Total</b>	<b>120</b>	<b>100.0</b>	<b>160</b>	<b>100.0</b>		

$X^2 =7.6$

D.F =1

P =.007

**Table 3: Distribution of cases and controls with respect to chemical exposure.**

Probable Chemical exposure	Cases		Control		Odds ratio	95% CI
	NO.	%	NO.	%		
Exposed	69	57.5	69	43.1	1.78	1.1-2.88
Not exposed	51	42.5	91	56.9		
<b>Total</b>	<b>120</b>	<b>100.0</b>	<b>160</b>	<b>100.0</b>		

$$X^2 = 5.67$$

$$D.F = 1$$

$$P = 0.022$$

**Table 4: Distribution of cases and controls with respect to probable exposure of their fathers to ionizing radiation**

Probable exposure of the father to ionizing radiation	Cases		Controls		Odds ratio	95% CI
	NO.	%	NO.	%		
Exposed	81	67.5	81	50.6	2.03	1.24-3.31
Not exposed	39	32.5	79	49.4		
<b>Total</b>	<b>120</b>	<b>100.0</b>	<b>160</b>	<b>100.0</b>		

$$X^2 = 8.008$$

$$DF = 1$$

$$P = 0.005$$

**Table 5: Distribution of cases and controls with respect to probable exposure of the mother to ionizing radiation during pregnancy.**

Mothers' exposure	Cases		Controls		Odds Ratio	95 % C I
	No.	%	No.	%		
Exposed	18	15.0	9	5.6	2.96	1.28 – 6.85
Not exposed	102	85.0	151	94.9		
<b>Total</b>	<b>120</b>	<b>100.0</b>	<b>160</b>	<b>100.0</b>		

$$X^2 = 6.92$$

$$DF = 1 P = 0.013$$

**Childhood Cancer (Leukaemias and Lymphoma) in Basrah  
- A case-control study-**

## ***REFERENCES***

- 1. Robison LL. General principles of the epidemiology of childhood cancer. In: PA Pizzo and DG Poplack (eds). Principles and Practice of Pediatric Oncology. Philadelphia, PA: Lippincott-Raven Publishers, 1997, Pp.1-10.**
- 2. Robison LL, Buckley JD, Bunin G. Assessment of environmental and genetic factors in the etiology of childhood cancers: the Children's Cancer Group Epidemiology Program. Environmental Health Perspective 1995; 103: 111-116.**
- 3. Plon SE, Peterson LE. Childhood cancer, heredity, and the environment. In: PA Pizzo and DG Poplack (eds). Principles and Practice of Pediatric Oncology. Philadelphia, PA: Lippincott-Raven Publishers, 1997, Pp. 11-36.**
- 4. Till M, Rapson N, Smith PG. Family studies in acute leukemia in childhood: a possible association with autoimmune disease. Br J Cancer. 1979;40: 62- 71**
- 5. Reynolds P, Von Behren J, Gunier RB, et al. Childhood cancer incidence rates and hazardous air pollutants in California: an exploratory analysis. Environmental Health Perspectives 2003; 111: 663-66.**
- 6. Menegaux F, Bertrand Y, Lescoeur B et al. Household Exposure to Pesticides and Risk of Childhood Acute Leukemia .Occupational and Environmental Medicine.2006; 63: 131-134.**
- 7. Gurney JG, Davis S, Severson RK et al. Trends in cancer incidence among children in the U.S. Cancer 1996; 78: 532-541 .**
- 8 IARC. International incidence of childhood cancer. IARC Scientific Publication 1998; 2 (144):1–391.**
- 9. Linnet MS, Ries LA, Smith MA et al. Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. J Natl Cancer Inst.1999; 91:1051-1058.**
- 10. Habib OS, Al-Ali JK, Al-Wiswasi MK, Ajeel NAH. The Burden of cancer in Basrah: The state of the art. Basrah 2006. Available on www. Basmedcol.com**
- 11. Yacoub AAH, Al-Sadoon IO, Hassan GG and Muffid Al-Hemadi. Incidence and pattern of malignant disease among children in Basrah with specific reference to leukemia during the period 1990-1998. Medical journal of Basrah University. 1999;17. 27=34.**
- 12. Gordis L. Epidemiology, 3rd edition, USA, Elsevier Saunders, 2004.**
- 13. Kleinerman RA. Cancer risks following diagnostic and therapeutic radiation exposure in children. Pediatric Radiology 2006; 14 :121-5.**



14. Miller RW. Special susceptibility of the child to certain radiation – induced cancers. Environmental Health Perspectives 1995; 103: 41 – 43.
15. Infante – Rivard C, Labuda D, Krajcinovic M, et al. Risk of Childhood leukemia associated with exposure to pesticides and with gene polymorphisms. Epidemiology 1999; 10: 481 – 7.
16. Zahm SH, Ward MH. Pesticides and childhood cancer. Environmental Health Perspectives 1998;106 suppl 3:893-908.
17. Leiss JK, Savitz DA. Home Pesticide use and Childhood cancer: a case-control study. American Journal of public health 1995; 85: 249-52.
18. Bhatia S, Neglia JP. Epidemiology of childhood acute myelogenous Leukemia. Journal of Pediatric Hematology and Oncology 1995; 17: 94-100.
19. Menegaux F, Bertrand Y, Lescoeur B et al. Household Exposure to Pesticides and Risk of Childhood Acute Leukemia .Occupational and Environmental Medicine.2006; 63:131-134.
20. Reynolds P, Von Behren J, Gunier RB, et al. Childhood cancer incidence rates and hazardous air pollutants in California: an exploratory analysis. Environmental Health Perspectives 2003; 111: 663-668.
21. Wilkinson P,Thakrar B,Walls P, et al. Lymphohaematopoietic malignancy around all industrial complexes that include major oil refineries in Great Britain. Ocup Environ Med 1999; 56: 577-581.
22. Shu X.O., Gao Y.T, Brinton L. A. et al.Population-based case-control study of childhood leukemia in Shanghai. Shanghai Cancer institute.1988; Aug: 62:3.
23. –Feuerhake S I, Dannheim B, Heimers A, ET al.Leukemia in the proximity of a German boiling-water nuclear reactor: evidence of population exposure by chromosome studies and environmental radioactivity .Environmental Health Perspectives 1997; 105 suppl 6:1499-504.

## سرطان الطفولة ( ابيضاض الدم وسرطان الغدد اللمفاوية ) في البصرة - دراسة تحليلية-

هنادي لازم عبيد، عمران سكر حبيب، جنان غالب حسن

### الخلاصة

أجريت هذه الدراسة في البصرة في عام ٢٠٠٦. شملت عينة تتكون من ١٢٠ حالة سرطانية (ابيضاض الدم وسرطان الغدد اللمفاوية الأولي) بعمر أقل من ١٥ سنة وعينة ضابطة من ١٨٠ طفلاً مطابقة من حيث العمر والجنس ومنطقة السكن. توخت الدراسة استطلاع العلاقة بين هذين النوعين من السرطان واحتمالية التعرض لمؤثرات بيئية (إشعاع مبيدات او مواد كيميائية أخرى). أظهرت النتائج وجود ترابط معتد إحصائياً بين السرطان وكل من التعرض المحتمل للإشعاع والمبيدات والمواد الكيميائية ولم تظهر علاقات مهمة مع عمر أو مهنة الأبوين. وينصح بضرورة توسيع الدراسات التحليلية بحثاً عن مسببات السرطان وتعزيز التسجيل السرطاني لتكوين قاعدة معلومات رصينة.