

Pattern of leukaemia in Basrah

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ABSTRACT

Background: In Basrah, previous studies reported increased risk of certain cancers including leukaemia. Two important features were reported: a rise in the incidence rate of leukaemias in children and an age shift towards younger children. These studies were limited by the incompleteness of data they used.

Objectives: This paper is intended to present a profile of leukaemia in Basrah over the years 2005-2008.

Methods: The cases of leukaemia presented in this paper represent all cases diagnosed, treated and registered in Basrah during the years 2005-2008. The cases were drawn from the pool of cancer registries in various health care institutions dealing with cancer using a case series study design. All available and verifiable cases were included in the study. Relevant incidence rates were calculated by dividing the average annual number of cases by mid-period population for each category used.

Results: During the four – year study period, it was possible to identify 608 cases of leukaemia; 56.4% were among males and 43.6% were among females. More than half of the cases (52.8%) were from Basrah, 26.5% were from Thi Qar, 13.6% were from Missan, and 7.1% were from other governorates. The age-specific incidence rate in Basrah showed a bimodal distribution with higher rates at extreme ages. The crude incidence rate was 3.6 per 100000 population (3.9 per 100000 males and 3.2 per 100000 females). The age standardized incidence rate was 4.3 per 100000 males and 3.9 per 100000 females.

Conclusion: Leukaemia is a significant malignant disease in Basrah. The figures of incidence rate point towards an upward trend, but still comparable to the figures from other Gulf countries.

Keywords: Leukaemia, incidence, Basrah

طراز إبيضاض الدم في البصرة

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الخلاصة

الخلفية: أشارت دراسات سابقة في البصرة الى زيادة في الإصابات ببعض أنواع السرطان، ومنها إبيضاض الدم. وقد تمت الإشارة الى نقطتين: الأولى زيادة في نسبة الإصابة بين الأطفال، والثانية تغير في نمط العمر للمصابين باتجاه الأعمار الأصغر، إلا أن تلك الدراسات استندت الى بيانات ناقصة مما حدد دقة نتائجها.

الأهداف: يهدف البحث الحالي الى إعطاء لمحة عن إبيضاض الدم في البصرة للسنوات ٢٠٠٥-٢٠٠٨.

الطرائق: تمثل البيانات المعروضة في البحث جميع حالات إبيضاض الدم الجديدة المشخصة والمعالجة والمسجلة في محافظة البصرة خلال السنوات ٢٠٠٥-٢٠٠٨. وقد تم الحصول عليها من جميع مصادر تسجيل البيانات، حيث تم تدقيقها وتوثيقها تباعاً. ولغرض حساب نسب الإصابة تم تقسيم المعدل السنوي للإصابات على عدد سكان محافظة البصرة في منتصف سنوات الدراسة.

النتائج: تم توثيق ٦٠٨ حالات جديدة (٤,٥٦% منهم من الذكور، ٤٣,٦% من الإناث) خلال السنوات الأربع ٢٠٠٥-٢٠٠٨، وكان ٥٢,٨% من الإصابات من سكان محافظة البصرة فيما مثلت الإصابات من محافظة ذي قار ٢٦,٥%، ومن محافظة ميسان ١٣,٦%، والمحافظة الأخرى ساهمت بنسبة ٧,١%.

أظهرت نسبة الإصابة حسب العمر وجود ثنائية المنوال حيث الإصابة أعلى في طرفي العمر، وكانت نسبة الإصابة الخام ٣,٦ لكل ١٠٠٠٠٠ نسمة وهي أعلى في الذكور (٣,٩) منها في النساء (٣,٢)، أما النسبة المعيارية فكانت ٤,٣ لكل ١٠٠٠٠٠ من الذكور و٣,٩ لكل ١٠٠٠٠٠ من الإناث.

الاستنتاجات: يمثل إبيضاض الدم مرضاً خبيثاً مهماً في البصرة، ومن المحتمل أن تكون نسب الإصابات قد ازدادت في السنوات الأخيرة ولكن المستوى العام مازال ضمن مستويات الإصابة في المنطقة العربية.

كلمات دالة: إبيضاض الدم، إصابات، البصرة، وبائيات السرطان.

INTRODUCTION

Haematological malignancies comprise a collection of heterogeneous conditions, all originating from cells of the bone marrow and the lymphatic system. There are three major groups: leukaemias, lymphomas, and plasma cell neoplasms.¹ Leukaemia is a disease resulting from the neoplastic proliferation of haemopoietic or lymphoid cells. It results from a mutation in a single stem cell, the progeny of which form a clone of leukaemic cells. Often there is a series of genetic alterations rather than a single event. Genetic events contributing to malignant transformation include inappropriate expression of oncogenes and loss of function of tumor suppressor genes. The cell in which the leukaemic transformation occurs may be a lymphoid precursor, a myeloid precursor or a pluripotent stem cell capable of differentiating into both myeloid and lymphoid cells.²

Leukaemias are broadly divided into: (i) acute leukaemia, which, if untreated, leads to death within weeks or months; and (ii) chronic leukaemia, which, if untreated lead to death within months or years. They are further subdivided according to which kind of blood cells is affected into lymphoid or myeloid.² Accordingly, the major four types are acute lymphoblastic leukaemia (ALL), acute myeloblastic leukaemia (AML), chronic lymphoblastic leukaemia (CLL) and chronic myeloblastic leukaemia (CML).

Worldwide, over 250 000 people are diagnosed with leukaemia each year, accounting for 2.5% of all cancers. The incidence of leukaemia, however, is variable across the world. The lowest incidence rate is reported in Sub-Saharan Africa and the highest in Australia and new-Zealand. All age groups can be affected; leukaemias are the most

common pediatric tumors (35% of cancers in children aged 0-14 years). Most cases, however, occur in older adults; more than half after 65 years of age.^{1,3}

In the Arab areas of Asia, studies are limited on leukaemia particularly regarding risk factors but it seems an important and a growing problem.⁴

Suspensions of increased leukaemia incidence in the region of Basrah have been raised since 1995, presumably as consequence of the use of ammunition with depleted Uranium in the Gulf wars. Previous studies reported increased risk of certain cancers including leukaemia. Two important features were reported: a rise in the incidence rate of leukaemia and lymphoma in children and an age shift towards younger children.^{5,6} To quote some figures, the incidence rate of leukaemia has increased from 2.3 in 1995 to 3.2 per 100 000 population in 2005. 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.⁶

The present study is an attempt to present a profile on all cases of leukaemia diagnosed, treated or registered in Basrah over a four-year period 2005-2008.

PATIENTS AND METHODS

The cases of leukaemia presented in this paper represent all cases diagnosed, treated and registered in Basrah during the years 2005-2008. The cases were drawn from the pool of cancer registries in various health care institutions dealing with cancer. The study is part of a comprehensive

project on “cancer and environment in Basrah”.⁷ From the pool of cases available to the Basrah Cancer Research Group (BCRG), all verifiable cases with definite diagnosis of any subtype of leukaemia were compiled and entered into an SPSS computer programme for statistical analysis. A total of 608 cases were identified and used in this paper. Included are cases with verified and ascertained diagnosis from first week of January 2005 up to December 31st, 2008.

Cases identified by various sources were typed first on excel sheets in most centers or identified from their original documents and typed by members of BCRG on excel sheet. Then, all the excel files were pooled together in one file and matched and checked for any repetition resulting from cases being reported by more than one source.

The ascertainment of cases was based on morphological methods of diagnosis. The results are presented for all registered cases first, then specific rates are presented for cases from inhabitants of Basrah province.

Information related to population of Basrah was based on data available from Basrah Health Authorities and from the Statistical Office in Basrah. Incidence rates were calculated by dividing the average annual number of new cases by mid-period population for each category used, then multiplying by 100000. Age standardized incidence was derived using the World standard population by the direct method.³

RESULTS

Characteristics of cases

The distribution of cases registered in Basrah is shown in **Table 1**. Male cases were more frequent than female cases accounting for 56.4% and 43.6% respectively. (Male:Female ratio= 1.29:1). More than half of the cases (52.8%) were from Basrah, 26.5% were from Thi Qar, 13.6% were from Missan, and 7.1% from other governorates.

Regarding years of registration, the percentage of cases registered during 2005 was the lowest (18.8%). In both 2006 and 2007, a relatively higher registration was reported (28.5% and 28.6% respectively). The percentage declined in 2008 to 24.2%.

Table 1. Characteristics of leukaemia cases registered in Basrah during 2005-2008.

Characteristics	No. of cases	(%)
Sex		
Male	343	56.4
Female	265	43.6
Place of residence		
Basrah	321	52.8
Thi Qar	161	26.5
Missan	83	13.6
Other governorates	43	7.1
Year of Registration		
2005	114	18.8
2006	173	28.5
2007	174	28.6
2008	147	24.2
Total	608	100.1*

The main types of leukaemia

Figure 1 shows that the most frequent type of leukaemia is ALL which represents 69% of all registered cases followed by AML representing 16% and the lowest frequent type is CLL forming 5%.

Figure 2 shows a comparison of the relative frequency of types for children and adults. The most frequent type of leukaemia in children is ALL which constituted 82% followed by AML 13%. Among adults, ALL again is the most frequent type (60%) followed by AML (16%), CML (14%) and the lowest is CLL (10%).

Age by type of cases

The mean and median ages are different according to the different types of leukaemia as shown in **Table 2**.

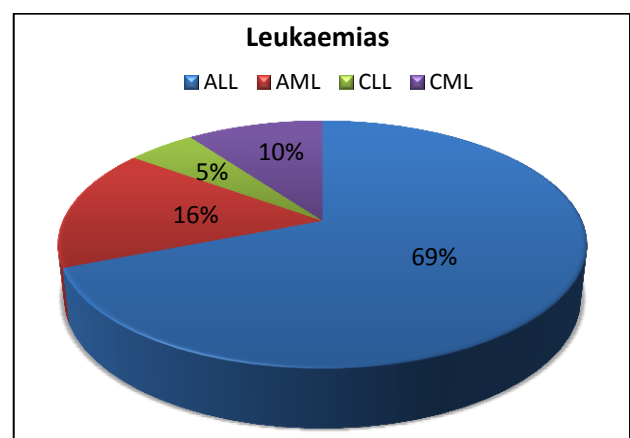


Figure 1. The-percentage distribution of the main 4 types of leukaemia.

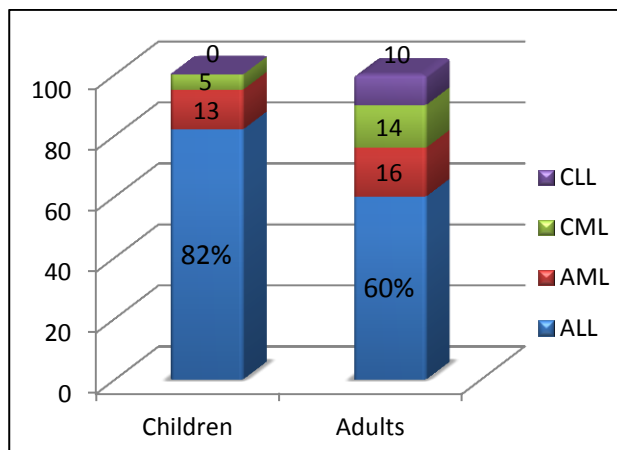


Figure 2. The percentage distribution of the four types of leukaemia in children (below 15 year) and adults.

Table 2. Mean and median age (years) by types of leukaemia.

Type of leukaemia	Mean Age+ SD	Median age
ALL	19.6+18.5	14
CLL	58.3+16.2	60
AML	28.4+21.9	22
CML	38.6+22.5	40

Leukaemia in Basrah: Risk by sex

Table 3 shows the distribution of incidence rate of leukaemia in Basrah according to age and sex. A total of 178 cases were registered among males over the period 2005-2008 and the average number per year was about 45 cases. This gives a crude annual incidence rate of 3.9 per 100000 males and an age standardized incidence of 4.3 per 100000 males. The incidence rate is high in male children aged less than 15 years then it declines with advancing age until the middle of the fifth decade when it rises again reaching a maximum rate of 29.2 per 100000 males aged 75 years and older. For females a total of 143 cases were registered over the period 2005-2008 and the average number per year was about 36 cases. This gives a crude annual incidence rate of 3.2 per 100000 females and an age standardized incidence rate of 3.9 per 100000 females. The incidence rate is high in children aged less than 15 years then it declines with advancing age until the middle of the fifth decade when it rises again with advancing age reaching a peak of 16.8 per 100000 in the age group 70-74 years. The results suggest a bimodal distribution in both sexes. The major mode is in the 8th decade of age and less prominent mode is seen in children aged less than 10 years.

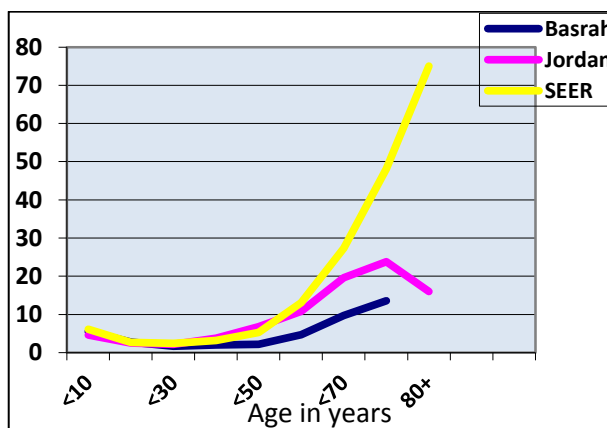
Subtypes of leukaemia in Basrah in comparison to selected countries

Table 4 presents a comparative data on subtypes in Basrah, Kuwait and Saudi Arabia (Riyadh). Although the overall pattern is more or less similar, clear discrepancies do exist particularly in ALL which is much more common in Basrah. The age-specific incidence rates in Basrah are similar to those in Jordan and America in children and young adults but lower in Basrah compared to Jordan and America from the fifth decade of age onwards as shown in Figure 3.

Table 3. Incidence rates (IR) of leukaemia in Basrah during 2005-2008 by age and sex.

Age in years	Males		Females	
	No. of cases in 4 years	IR per 100000 per year	No. of cases in 4 years	IR per 100000 per year
<5	32	5.6	25	4.6
5-9	38	7.0	25	4.6
10-14	19	3.6	11	2.2
15-19	14	2.9	11	2.4
20-24	10	2.2	7	1.6
25-29	6	1.4	8	1.8
30-34	7	1.8	3	0.9
35-39	7	2.4	10	3.5
40-44	2	1.0	3	1.2
45-49	9	4.7	4	2.3
50-54	6	4.1	8	4.4
55-59	6	5.7	6	5.4
60-64	9	9.4	8	12.0
65-69	2	3.6	6	15.0
70-74	3	8.2	6	16.8
75 and above	8	29.2	2	5.0
Total	178	3.9	143	3.2

Age standardized incidence rate per 100000 (Male=4.3, Female =3.9)



SEER= statistical and epidemiological end results.

Figure 3. Comparison of age specific incidence rates in three registries.

Table 4. Relative frequency (%) of subtypes of leukaemia in Basrah, Kuwait and Riyadh.

Region	ALL (%)	CLL	AML	CML
Basrah (2005-2008)	69.0	5.0	16.0	10.0
Kuwait (1994)	44.2	8.6	32.4	14.8
Riyadh (1991)	24.23	18.77	37.54	19.11

DISCUSSION

In Basrah, which was subjected to massive environmental damage from wars, economic embargo and local events, cancer and its determinants became a hot issue. Claims and counter claims are plenty.⁸⁻¹³ Three basic questions remained unanswered; what is the incidence rate of cancer (including leukaemia) in Basrah? Is there an adequate evidence that cancer has increased in Basrah during the last two decades? If there is increasing cancer risk with time, what are the possible explanations?

Leukaemia is one of the top ten cancers both in males and females.⁷ This study took the advantage of a unique registry of almost all cases diagnosed and treated in Basrah over the period of 2005-2008, to provide an epidemiological profile of leukaemia in Southern part of Iraq and in particular to present a reliable estimates of incidence of leukaemia in Basrah. These results may be considered as the basis for comparison in any attempt to examine the time trend of cancer in the past or in the future.

Leukaemia in Southern part of Iraq, as other haematological malignancies worldwide, showed slightly male preponderance (M:F was 1.29:1). The registered cases were distributed geographically mainly over three provinces with more than half of the cases (56.4%) from Basrah. During the period 2005-2008, the median age at diagnosis for leukaemia was 18 years for males and 22 years for females. This clearly points out to the distinct feature of younger age affected as compared with, for example, 67 years median age at diagnosis of leukaemia in US.¹³ It, in turn, reflects two facts; the first is the structure of population at risk of leukaemia in general, people aged 50 years and older represent just above 10% of all leukaemia cases as compared to more than 70% of statistical and epidemiological end results (SEER) population,¹³ the second fact is that the risk of leukaemia is high in children younger than 15 years.

The occurrence of subtypes of leukaemia was analyzed in the present study also. Acute lymphoblastic leukaemia was the most frequent type overall and both in children and adult population (69%, 82% and 60% respectively), followed by AML (16%, 13% and 16%), CML (10%, 5% and 14%). The lowest fraction was for the subtype CLL (5%). This finding also could add supporting evidence that the risk of leukaemia is higher in younger ages than in elderly. In Kuwait,¹⁴ Al-Bahar *et al*, during the 1980s also reported that ALL as the most frequent subtype (44.2%) followed by AML (32.4%), CML (14.8) and the least was CLL (8.6%), the pattern of occurrence is somewhat different from Saudi Arabia.¹⁵ In the UK, almost one third of the cases were AML and around a further third were CLL; CML and ALL each accounted for one tenth of the cases.¹⁶ Chronic lymphoid leukaemia which constitutes more than 30% of all leukaemia in western countries, is extremely rare in Asian countries like Japan and China (10% of all leukaemias).¹⁷ If the age structure of the present study population was considered as compared to longevity of East Asian countries, the figure of 5% seems to be acceptable. However, the true incidence and the relative frequency of CLL are slightly higher because of the initial benign clinical course of the disease and probably some of the patients were not seeking medical advice and thus have not been registered. This also may be true in developed countries, for example in the USA the actual incidence of CLL could be higher than the estimated from tumor registries.¹⁷ However, CLL is a disease of elderly in the present study which is comparable with Western countries.

Acute myeloid leukaemia (AML) is the commonest acute leukaemia in adults and is rare in children and young adults. The incidence of AML increases with age and ranges from 0.7 to 3.9 cases per 100 000 between 0 and 60 years and from 6.7 to 19.2 cases per 100 000 above 60 years with a median of more than 70 years.¹⁸ In the present study, it ranked second after ALL with interestingly low median age of 22 years as compared with average age of 30 among Omanis adults and children¹⁹ and 34 years of adult Egyptians.²⁰

The incidence of CML is variable but increases with age. The median age differs between cancer

registries and clinical trials by 10-20 years.²¹ The median age of CML patients in the present study is 40 years.

Leukaemia in Basrah, as in other Gulf countries²² (R GCC) is more common when compared with the worldwide incidence. It is the 5th most common cancer⁷ and accounts for 4.3% of all cancers in Basrah with male:female ratio of 1.24:1. The age standardized incidence rates were 4.3 and 3.9 per 100000 population for males and females respectively. This rate is intermediate among other Gulf States; Bahrain had the highest incidence among males with ASR of 8.1 followed by Qatar and Kuwait. The lowest incidence was in UAE males (ASR was 2.9). In females, Qatar had the highest incidence (ASR was 4.7) followed by Bahrain and Kuwait with 4.6 each. The lowest incidence was among Saudi women (ASR was 2.9).^{7,22}

According to age-specific incidence rates, leukaemia in Basrah has bimodal distribution with first peak at pediatric age group of < 15 year and the highest peak after age of 70 and this is true for both males and females. However, the incidence rate is still similar to the figures from neighbouring countries like Jordan as well as SEER until the forties and then it declines,²³ as shown in **Figure 3**.

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