One-year survival of children with malignant diseases in Basrah

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ABSTRACT

Background: **Childhood cancer represents an important health problem in Basrah with an incidence rate as high as rates in western countries. Little is known about the prognosis and survival of children diagnosed with malignancy after initiation of treatment.**

Objectives: **to estimate the one-year survival of children diagnosed with malignant diseases in Basrah and to identify non–medical risk factors for the risk of death during the first year following diagnosis.**

Methods: **This is a hospital-based follow up study of 352 children aged less than 15 years diagnosed with any sort of malignant disease. The study was conducted in Basrah Specialized Hospital for Children over the period (1st of October 2012 to 31st December 2013) and enrolled all newly diagnosed cases during two calendar years (2011-2012 inclusive). The fate of each and every case was ascertained chronologically during and at the end of the 12 months after diagnosis.**

Results: **The results showed that, of the 352 cases followed up, 102 (29.0%) completed their treatment courses at the end of 1st year while 105 (29.8 %) of them were still continuing on treatment , 19 (5.4%) relapsed and still on treatment and 89 (25.3 %) of the cases died by the end of first year. The remaining have stopped treatment 25 (7.1%), refused treatment in Basrah 10 (2.8%) or transferred elsewhere on medical advice 2 (0.6%).**

The one year survival rate for all the studied children was 74.7%, Thus the one year mortality was 25.3%). Among a set of variables, three "female gender, better mother education and modern type of family accommodation" were significant predictors of one year survival of a child with cancer.

Conclusions: **Childhood cancer is major health problem in Basrah in terms of incidence and burden on the health care system. Despite all efforts the one year survival rate was much lower than corresponding figures in many other countries.**

Key word: **Childhood cancer, Survival, mortality, Basrah**

فرصة البقاء حيا بعد سنة من التشخيص للأطفال المصابين بالسرطان في البصرة

الخلفية: يمثل سرطان الأطفال مشكلة صحية مهمة في البصرة وتضاهي نسب حدوث المرض المستويات في الدول الغربية ولا تتوفر معلومات كافية عن تطور المرض وفرصة الحياة للمرضى بعد بدء العلاج.

الهدف: قياس نسبة البقاء على قيد الحياة بين الأطفال المصابين بالسرطان بعد سنة من التشخيص واستطلاع العوامل غير الطبية التي تؤثر في احتمال الحياة والموت.

الطرائق: الدراسة الحالية أجريت في مستشفى الأطفال التخصصي في البصرة على ٣٥٢ طفلا دون سن الخامسة عشرة من العمر ممن شخصوا بإصابتهم بأي نوع من أنواع السرطان. استغرقت الدراسة في مرحلة جمع البيانات خمسة عشر شهرا من الأول من شهر تشرين الأول ٢٠١٢ الى الحادي والثلاثين من شهر كانون الأول ٢٠١٣. وكان الغرض الرئيسي للدراسة قياس نسبة البقاء على قيد الحياة بعد سنة من تشخيص المرض ومعرفة حال الطفل عند تلك النقطة الزمنية.

ولتحقيق هذا الغرض تمت متابعة كل طفل أدرج في الدراسة لمدة ١٢ شهرا في الأقل من تاريخ التشخيص. وتأشير اي حالة وفاة أثناء السنة الأولى من تاريخ التشخيص.

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النتائج: بالنسبة للعينة التي تمت متابعتها فقد كان موقفهم عند نهاية السنة الأولى بعد التشخيص كالآتي: ١٠٢(٢٩%) أكملوا العلاج و ١٠٥ (٢٩.٨%) مستمرين على العلاج و١٩ (٥.٤%) انتكسوا وأعيدوا إلى العلاج و ٨٩ (٢٥.٣%) توفوا خلال السنة الأولى وهناك ٢٥(٧.١%) لم ينتظموا في اخذ العلاج و١٠ (٢.٨%) رفضوا أصلا البدء في العلاج في البصرة و٢ (٠.٦%) أرسلوا الى مراكز أخرى للعلاج، وبذلك تكون نسبة البقاء على الحياة بعد سنة من التشخيص ٧٤.٧% وهو ما يعني ان نسبة الوفيات خلال السنة الأولى كانت ٢٥.٣%. ويبدو من النتائج أن فرصة الحياة كانت أفضل نسبيا وبدرجة معتدة إحصائيا للأطفال الإناث ولمن كانت أمهاتهم على درجة أفضل من التعليم وللأسر ممن يملكون دور سكن حديثة.

الاستنتاج: إن سرطان الأطفال يمثل مشكلة صحية كبيرة في البصرة من حيث نسب الإصابة واحتمالية الوفاة مبكرا للأطفال المصابين. بالرغم من الجهود الكبيرة لخدمة المرضى فان نسبة الوفاة عالية مما يستدعى جهدا اكبر في توفير خدمات أفضل جودة ومسؤولية.

الكلمات المفتاحية: سرطان الأطفال، فرصة الحياة، الوفيات، البصرة

INTRODUCTION

Cancer is locally destructive and invasive and often metastasizes to distance sites, via the lymphatic system or through the bloodstream. [1] Cancer, which is relatively common disease in adults, is rare in children and adolescents. However, childhood cancer is increasing in recent decades. The incidence rates in the United States of America, for example, increased slightly by 0.6% per year over the five-year period 2005 to 2009. [2] In developed countries, cancer is the second most common cause of death among children between the ages of 1 and 14 years, exceeded only by accidents.[3] In developing countries, incidence, mortality and survival trends for childhood cancers are much more difficult to analyze due to inadequate reporting and registration and competing causes of death such as infectious diseases (HIV, malaria and tuberculosis), poverty and malnutrition and political conflicts.[4] Both the ever increasing incidence rates and the absolute burden of childhood cancer is growing in developing countries, due mainly to the populations in these countries are younger and expanding. As a result, more than 2% of all cancers in developing countries arise in children compared to much smaller proportions in Europe and North America. [5] In Basrah, the picture of childhood cancer for both sexes is taking shape in the recent few years as a result of better facilities for diagnosis, registration and epidemiological analysis. According to data published by Basrah Cancer Research Group[6] the incidence rates for children aged less than 15 years ranged from 12.4 per 100000 females aged 10-14 years to as high as 21.0 per 100000 males aged less than five years. These figures seem a bit higher than the corresponding figures in some other developed countries. Also, it is suggested that the risk of childhood malignancies and leukaemias in particular was rising in Basrah over the last two decades.[7-8] In addition, cancer specific mortality rates for the year 2005 was reported in southern Iraq to be around 4.3 per 100000 children. [6] But very little is known about survival after specific period of time following diagnosis and treatment. It is good to provide medical care but also it is good to know whether such medical care is achieving intended objectives. In cancer medical care, it is empirical and very desirable to expect treated children to survive with or without the residuals of disease. The results in Basrah are not very clear on survival. The present study is an attempt to provide profile on one year survival of children with cancer.

PATIENTS AND METHODS

The study population consisted of all children presented to Basrah Children Specialized Hospital with clinical features suggestive of malignant disease. Any child, who is confirmed by various available diagnostic methods to have

any childhood malignancy/Brain tumour, was included in the study. All identified cases during the years 2011-2012 inclusive were included and followed up for one calendar year from the date of diagnosis. A total of 352 cases were successfully followed up and included in the statistical analyses. It was planned initially to include all children diagnosed with malignancy and treated at Basrah Specialized Hospital for Children during the two year-study period. The choice of this hospital was based on the assumption that it enroll majority of children suffering from cancer for the purpose of diagnosis, treatment and registration. The estimated number of new cases registered in Basrah for the two years 2011-2012 was around 500 cases. [9] A planned approximate sample was calculated on the basis of the following formula:

$$N = \frac{(Z)^2 \times P\,(1-P)}{SE^2}$$

Where **N** is the desired sample size,

Z = 1.96 the level of significance at 95%,

P= 0.80 the expected survival after one year of diagnosis

SE = is the level of error tolerated at 0.05 level. We assume to tolerate 4% (0.04) error around the one year survival estimate.

The calculated sample was 384 cases. It was the target for the study. However the actual number of cases studied in the present study was 352. Thus the effective sample was 91.7% of the planned sample and the proportion of children studied out of total expected cases was around 70.4%. A special questionnaire form was constructed and used to gather data on cases. Extensive set of variables were covered (demographic characteristics, social, economic and environmental conditions, type of cancer with date of diagnosis, fate/outcome of patients by the end of first year after diagnosis, in addition to other potential risk factors) were ascertained for every child studied. Outcome was defined for the purpose of this study as "the state of the child at the end of the first 12 months after diagnosis". For calculation of one year survival, the number of children who were alive at the end of the first year after diagnosis were divided by the total number of children in the cohort which was followed up for one year.

$$\text{One-year survival rate} = \frac{\text{No. of children alive at the end of one year}}{\text{No. of children followed up for one year}} \times 100$$

For describing the fate, the status of cases at the end of one year after diagnosis was categorized as follows:

a. Alive and included:

- Completed treatment and considered initially cured.
- Still on treatment and follow up.
- Relapsed and still on treatment and follow up.
- Discontinued treatment after initiation at the hospital.
- Refused treatment from the start.
- Transferred to other centers/preferred other treatment centers.

b. Died any time during the year following diagnosis

Data obtained on each and every patient enrolled in the study were fed on two computer statistical programmes. An excel file which was used as data base from which the data were transferred to an SPSS programme (Statistical Package for Social Science-Version 15). Data were checked on both files for consistency and any visible errors and corrected accordingly. Analysis was made on SPSS to present the data in the form of tables and diagrams. Relevant statistical tests were used when needed.

RESULTS

Characteristics of the studied children (Age, gender and governorate of residence)

(Table-1), shows the distribution of the studied cases by age, gender and governorate of residence. Children aged less than five years represented 44.6% followed by children aged 5-9 years who accounted for 32.1% and the least frequent group was those aged 10-14 years

accounting for 23.3%. Gender-wise, male cases represent 192 (54.5%) and female cases 160 45.5%). The majority of cases 235 (66.8%) were from Basrah governorate. The rest were mainly from neighbouring governorates.

Table 1. Distribution of the studied children by age groupings.

Variable	No. of cases	% out of total
Age		
<5	157	44.6
5-9	113	32.1
10-14	82	23.3
Gender		
Male	192	54.5
Female	160	45.5
Governorate of residence		
Basrah	235	66.8
Thi Qar	70	19.9
Missan	36	10.2
Others	11	3.1
Total	352	100.0

Type of childhood cancer

(Table-2), shows the distribution of the studied cases according to the type of childhood malignancy by gender. The main groups of the studied cases were leukaemias representing 42.3% followed by lymphomas both Hodgkin and Non-Hodgkin (19.0%) and neuroblastoma (7.7%), then other cancers: Renal tumours (5.7%), brain tumours and soft tissue tumours (4.8% each), followed by retinoblastoma (4.0%) and malignant bone tumours (3.7%). Regarding the distribution among gender groups, no statistical association could be detected between gender and type of cancer despite the fact that some types were not equally distributed between male and female cases. Male cases predominate in most of the types.

Table 2. Distribution of studied children by type of cancer and gender

Cancer main types	Male		Female		Total		% out of total
	No.	%	No.	%	No.	%	
Leukaemias	73	49.0	76	51.0	149	100.0	42.3
Lymphomas	43	64.2	24	35.8	67	100.0	19.0
Malignant brain tumours	10	58.8	7	41.2	17	100.0	4.8
Neuroblastoma	16	59.2	11	40.7	27	100.0	7.7
Retinoblastoma	7	50.0	7	50.0	14	100.0	4.0
Renal tumors	12	60.0	8	40.0	20	100.0	5.7
Hepatic tumors	3	50.0	3	50.0	6	100.0	1.7
Malignant bone tumors	7	53.8	6	46.2	13	100.0	3.7
Soft tissue tumors	9	52.9	8	47.1	17	100.0	4.8
Germ cell tumors	2	40.0	3	60.0	5	100.0	1.4
Other malignant epithelial neoplasm	4	66.7	2	33.3	6	100.0	1.7
Other and unspecified malignant neoplasm	1	50.0	1	50.0	2	100.0	0.6
Histeocytosis (not included in ICCC-3)	5	55.6	4	44.4	9	100.0	2.6
Total	192	54.5	160	45.5	352	100.0	100.0

Statistical testing for the first five types and all others merged together
X^2 = 4.855 5 df P=0.434

Fate of children after one year of diagnosis

Overall one- year (status) of all studied children

(Table-3) shows the fate / status of the studied children at the end of first year from the date of diagnosis. About 29.0% of the studied cases completed their treatment courses without problems, while 29.8% of cases were still continuing on treatment and 5.4% of the cases have relapsed and still on treatment as well. In the meantime, 25.3% died by the end of first year.

Table 3. Fate/Status of the studied children at the end of first year from diagnosis

Fate/status at the end of first year from diagnosis	No. of cases	% out of total
Complete treatment courses	102	29.0
Still on treatment	105	29.8
Relapsed and on treatment	19	5.4
Died	89	25.3
Stopped treatment	25	7.1
Refused treatment	10	2.8
Transferred/ preferred other treatment centers	2	0.6
Total	352	100.0

One year survival by age and gender

(Table-4), explains the one year survival of the studied children according to the age group in which children less than 5 years showed the least one year survival rate (69.4%) while the other two older age groups (5-9 and 10-14 years) had relatively higher one year survival year 77.9% and 80.5% respectively. A slightly better survival among females cases is noticed. The association of one year survival with each of age and gender was statistically not significant (P > 0.05).

Table 4. One year survival by age and gender

Variable	No. of children studied	No. Alive at one year	One year survival rate (%)
Age in years			
<5	157	109	69.4
5-9	113	88	77.9
10-14	82	66	80.5
Gender			
Male	192	140	72.9
Female	160	123	76.9
Total	352	263	74.7

One year survival by type of cancer

(Table-5), presents one year survival rates of the studied children according to the type of cancer. It is difficult to draw a clear pattern of one year survival for different types of cancer given that some numbers are small. However it is possible to identify cancers with survival lower (poorer prognosis) than overall average. Leukaemia, brain tumours, neuroblastoma, retinoblastoma, soft tissue tumours and histiocytosis all have one year survival rate lower than the overall average of 74.7%. All others have survival rate higher than the average.

Table 5. One year survival by type of cancer.

Type of cancer	No. of children studied	No. Alive at one year	One year survival rate (%)
Leukaemia	149	101	67.8
Lymphomas	67	57	85.1
Malignant brain tumours	17	12	70.6
Neuroblastoma	27	18	66.7
Retinoblastoma	14	10	71.4
Renal tumours	20	18	90.0
Hepatic tumours	6	6	100
Malignant bone tumours	13	11	84.6
Soft tissue tumours	17	12	70.6
Germ cell tumours	5	4	80.0
Other malignant epithelial neoplasm	6	6	100.0
Other and unspecified malignant tumours	2	2	100.0
Histeocytosis	9	6	66.7
Total	352	263	74.7

Logistic regression analysis to predict one year survival

In order to identify significant and independent predictors of survival, we carried out logistic regression analysis to predict one year survival using a set of probable explanatory variables. Some of these explanatory variables were examined in the bivariate analysis above, some others were not. The dependent variable was state of the child at the end of first year after diagnosis (Alive versus dead for all types of cancer). The explanatory variables were mixture of quantitative variables (Age, father education, mother education) and qualitative variables

(gender, type of house, ownership of house, history of cancer, of chronic disease, child birth order and no. of siblings). Three variables could be shown to predict better survival. These were female gender, better mother education and modern type of accommodation (Table-6). All other variables were not significant predictors of survival.

Table 6. Logistic regression analysis to predict one year survival

Significant predictors	B	S.E.	WALD	DF	SIG.	EXP (B)	95% C.I. FOR EXP (B)	
							lower	upper
Female Gender	1.425	0.574	6.169	1	0.013	4.159	1.351	12.805
Better mother education	1.413	0.667	4.486	1	0.034	4.109	1.111	15.192
Living in modern house	0.836	0.423	3.900	1	0.048	0.434	0.189	0.994

DISCUSSION

Significance of the study: The present study is an attempt to quantify the risk of death following affliction with any sort of childhood malignant disease in Basrah. No reliable documents on childhood survival/mortality after getting cancer could be found in Basrah. Few previous attempts were made to present data on mortality. [10-13] No doubt that studying survival of children after cancer is one of the means to scrutiny of the effectiveness of diagnosis and treatment. A high quality care in terms of early diagnosis and adequate treatment should lead to reduction in the risk of death and improving the chance for survivorship. The size of the sample in this study and the very close and high rate of follow up of each and every child in the study must give some degree of credibility to the results reported in this piece of work and hence the documented survival is a product of complex set of factors including quality of medical care.

Adequacy and representativeness of the sample/Generalization of the results: The results in terms of fate after one year represent, in the strict sense, the children included in the study. However, given the relatively large sample size and the successful follow up, it is possible to generalize the results to the whole situation of childhood cancer in Iraq on the assumption that level of care in major treatment centres is not different. This assumption and the tendency to consider the results of the present study as representative sample for fate of childhood cancer cases is supported by the results of Al-Hadad et al [14] who also found high mortality rates/ low survival rates among children they have treated. Thus, the one year survival year of 74.7 or a relative one year mortality rate of 25.3% could be taken as a true figure and a worrying figure in the light of the increasing risk of childhood cancer in Basrah and in the light of the much better outcome of care in many treatment centres across the world. Actually the one year survival rate in the present study is almost similar to five-year survival in England and the United States [15-16] for most of childhood cancers. This means simply that the expected five year survival in Basrah will be much lower than the corresponding figures in Western medical centres. The calculated sample was 384 cases. It was the minimal target for the study to be fairly adequate at least for the estimation of the overall one-year survival rate in this study. However the total number of cases studied in the present study was 352. Thus the effective sample was 91.7% of the planned sample and the proportion of children studied out of total expected cases was around 70.4%. This is fairly high to consider the studied sample as being representative of the reference

cases. However, it must be stressed that this sample size is adequate for the statistical analysis regarding general features, one year survival or one year outcome at the level of the sample as a whole. The sample size might not be adequate for some detailed statistical analysis. Therefore, detailed results need to be interpreted with caution and generalizations in this context are limited with this inherited deficiency in the study.

How accurate the data collection are? Most of the cases studied and most of the data on each case were obtained directly by the investigators from patients or their relatives supported by views of specialist oncologists and evidence documented by records. Therefore, the data about these children were undoubtfully accurate enough to rely on in results and conclusions made out of them. The fate and other related outcomes were carefully verified from records, medical staff, interviews and phone contacts with parents.

Fate of children: In the present study, the overall mortality of children due to childhood cancer within one year from the diagnosis is higher than overall rates even after 5 year from diagnosis in many studies in developed countries.[17] None of the childhood cancers studied was exceptional to this finding of high one year mortality except few of them. Even the types which are known now to have better prognosis under good quality medical care such as leukemia, lymphomas and retinoblastoma**[15,18]** had high one year mortality/low one year survival in Basrah. The level of one year mortality/survival demonstrated in the present study is worrying and deserves further critical analysis and appropriate action to improve survival.**[19]**

Survival*:* The estimated one year survival rate in this study was 74.7% which means that 25.3% of the cases of childhood cancer diagnosed, treated and registered at the Basrah Children Specialty Hospital; the best treatment centre in southern Iraq, died before they celebrated their first year after diagnosis. This figure of 25.3% is high by all means and standards. Actually it is higher than the five year mortality among children treated in most American, European and Australian cancer centres. [15,17-18, 20] The high one year mortality is universal to all childhood cancer types except for few types with fewer cases like hepatic cancers. The pattern of the relative low survival rate was also universal to cases regardless of age, gender or type of cancer. This universal pattern could pinpoint to problems with late diagnosis and/or defected medical care and client adherence to prescribed treatment protocol. We did not attempt to make an in-depth inquiry about the factors which augment the risk of first year death of cases but absence of marked variation among various subgroups may support our above stated conclusion. Despite that, minor variation in one year survival were documented. Just to quote examples: the survival rates were better in children aged 5-9 years and in females. This is similar to the survival pattern in the United States, according to the SEER data 2003-2009.[21] Similarly when the one year survival rates for leukaemia and lymphoma in the present study are compared with the five year survival rates in Great Britain, they are unfavourable and it is expected that the five year survival among cases in Basrah would be much lower than the corresponding figures in Britain.[15,21] Survival rate for leukemia and lymphomas are being less than 5 year survival in Great Britain, this may reflect a deficit in facilities for childhood cancer management in our country. However lymphomas, with few other cancers like Wilms tumour, showed one of the most favourable survival rates in the present study. This result was supported by similar previous results in India for example where Hodgkin's lymphoma and Wilms tumour had the best five year survival rates. [22] Gender-wise, our study results showed that females have somewhat better one year survival rates comparing with males and the best one year survival is being in the younger age group less

than 5 years old for all cancers and for leukaemia, this does not agree with SEER data (2003-2009) in which there is slight gender differences in survival of lymphomas and the very young (less than one year age) children have the worst survival percentage. [23,24] One year survival of malignant brain tumour is relatively higher as compared to survival rates in other cancers and might look favourable in the light of results reported for Europe, [25] but this should be carefully interpreted as the cases treated in the hospital and included in the present study were selective. Probably those who came for chemotherapy in the hospital were the surviving ones and originally have better prognosis. In general the trend in survival among cases studied in the present study does not differ from the trends in other studies for various types of childhood cancers[26-29] but the outcome in Basrah is much unfavourable and deserves a lot of consideration to improve quality of diagnosis as early as possible, effective and comprehensive treatment.

In Conclusions, cancer of children in Basrah represent a real challenge to policy makers, health care providers and the community in terms of extent and outcome. The one year survival rate was 74.7%. Thus the one year relative mortality rate (one year case-fatality ratio) was 25.3% was very high compared to figures in many other countries. Indeed, the one year mortality in Basrah is almost equivalent to five year relative mortality in European countries. The determinants of the high relative mortality seems to lie within the network of social response to illness, quality of suspicion by doctors and the adequacy of diagnostic and treatment care received by cases. The study of survival of children with cancer for a period longer than one year is feasible in the light of the remarkable response to follow up obtained in the present study.

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