
The constitution of the Family in Childhood Leukemia

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Abstract

Background: There is evidence that leukemia in general is higher among children whose mothers had previous abortions, knowing that there are many other factors which participate in increasing incidence of leukemia among certain families.

Objective: To find out the relationship between the consanguineous marriage and the history of family cancer with the number of maternal abortions and the birth order of the leukemic child.

Patient & Method: one hundred twenty children with acute leukemia and 150 children as a control attending out patient clinic in Central teaching Hospital for Children for the period 1st Dec 2002- 1st May2003 were randomly selected . Questionnaire about family history of any type of cancer, number of maternal fetal loss, birth order of the leukemic child and the consanguinity between the parents in both patients and control had been obtained

Results: Forty three (43%) of acute leukemia in this study have positive consanguineous marriage while the control group is (40%). For maternal history of abortions 33.3% of the leukemic mothers had history of abortion (28 mother had one abortion, 3mother had 2 abortion, 7 had 3 abortion, and2 more than 3), while in the control there is 30%. Family history of cancer is positive in 25 (20.8%) family of leukemic children and as such,11 leukemia,1 lymphoma, 3 CA breast, 1 brain tumor ,3renal , 1 uterine, and 5 unknown. While family history of malignancy among control group is 22 (14.3%) and most of them were of solid tumor like CA stomach, larynx, prostate.

Children after 1st child and before the last one had higher incidence of leukemia in the family setting and constitute 61.6%.

Conclusion: Family history of cancer was statically higher in leukemic families with more incidence of leukemia than in the control group. Regarding history of no. of abortion there is no significance difference. Being of consanguineous marriage there is no significant difference from the control knowing that there is frequent consanguineous marriage among Iraqi people. Birth order seems to involve those follow 1st child and before last one. This explains the viral theory and other postnatal genetic alteration behind etiology of leukemia.

Key wards: acute leukemia, risk factors, children.

Introduction:

The etiology of ALL (acute lymphocytic leukemia) is unknown, several genetic and environmental factors are associated with childhood leukemia.up to 5% of acute leukemia ^[1,2] , both acute lymphocyte and acute myeloid leukemia (ALL&AML) are associated with inherited predisposing genetic syndromes ^[3], AML occur only rarely in familial form^[4].

Siblings of children with ALL have 2-3 fold increased risks of developing ALL than children in the general population ^[2,5]. Combination of rearranged chromosomes may be transmitted to offspring's resulting in high frequency of miscarriage ^[6].

There is increased incidence of cancer, lymphoma, and leukemia in families of women experiencing spontaneous recurrent abortions ^[7].

Being the 1st born baby or the only child was one of the 1st identified risk factor for childhood leukemia, decreasing risk with increasing birth order ^[8, 9, 10].

ALL is associated with small family size, the greater the number of previous births the lower the child risk of ALL ^[10, 11].

Patient &Methods:

One hundred twenty children diagnosed as acute leukemia both ALL & AML in central teaching hospital for children were selected randomly from in & out patients, 150 children as a control group matched for sex and age attending the out patient clinic for common diseases where complete blood picture was taken and systemic examination was done. The history of the number of maternal abortions ,being of consanguineous marriage or not as well ,the history of any cancer in parents or close relatives with its type &site then the birth order of patients in their families as well the size of each family were taken.

T Test used for statistical analysis and P value of <0.05 was considered of significance.

Results:

The number of children in an Iraqi family range from 1-10 children, with an average 4.5 child per family, and the spacing between siblings is not more than 2-3 years.

M: F 1.4: 1 ALL: AML was 4:1 Mean age 5.4y

Family cancer history in both ALL & AML 1: 2.1 & 1: 3.6 respectively. First degree consanguineous marriage is 52 (43%) in the

leukemia & 60 (40%) in the control group as seen in table (1).

Table (1&2) showing maternal abortions as 40 (33.3%), 45 (30%) in the leukemia & the control group, table 2 giving the detail of each group as ,28

mothers had 1 abortion ,3 had 2 abortions, 7 had 3 abortions, 2 had more which is of no statistical importance in comparison to abortions of the normal mothers

Table1: Characteristics of family with leukemia

	Leukemia (n=120)		Control (n=150)		P-Value
	No.	%	No.	%	
Consanguinity	52	43	60	40	0.581 *
Positive					
Negative.	68	57	90	60	
Maternal Abortions	40	33.3	45	30	0.558 *
positive					
Negative	80	66.7	105	70	
FH Cancer positive	25	20.8	22	14.3	0.184 *
Negative	95	79.2	128	85.7	

NS * not significant

Table2: Maternal abortions:

History of abortions in mothers of children with acute Leukemia	History of abortions in mothers of normal children
No. 40 (33.3%)	45 (30%)
28 → 1 abortion	35 → 1 abortion
3 → 2 abortion	4 → 2 abortion
7 → 3 abortion	4 → 3 abortion
2 → >3 abortion.	1 → >3 abortion.

Table (3) showing the family history of cancer, it is present in 25 (20.8%) family of leukemic children as such; 11 leukemia ,1 lymphoma ,3 CA breast , 1 CA brain ,3 renal , 1 uterine , 5 unknown. While family history of malignancy among the control group is 22 (14.3%) most of them are of solid tumors like CA stomach, pharynx & prostate.

Table (4) describing children according to birth order, children after the 1st child & before the last sibling constitute 61.6% which is the highest than the latest children in the family (23.3%) , while the 1st child constitute (15.8%) in the family setting of the leukemia children.

Table3: Family history of cancer (F.H.C)

F.H.C in children with acute leukemia	F.H.C. in normal children
No. 25 (20.8%)	22 (14.3%)
11 acute leukemia	4 CA Bladder
1 lymphoma	1 CA Stomach
3 CA Breast	2 CA Larynx
1 brain tumor.	5 CA Prostate
3 renal tumor	1 CA Pancreas
1 uterine malignancy	1 CA Liver
5 unknown	1 CA Thyroid
	1 CA Spinal cord
	1 leukemia
	2 Hodgkin lymphoma.

Table4: Birth order in children with acute leukemia:

1st birth order	19 (15.8%)
2^{nd-4th} or more birth order	74 (61.6%)
Late birth order	27 (32.3%)

Discussion:

Family history of high incidence of cancer is an important consideration, unusual susceptibility to leukemia has been associated with certain inheritable chromosomal disorder like Fanconi anemia .and ataxia telangictasia [3,5]. Li & Fraumine (LFS) observed close relatives of children with soft tissue sarcoma, leukemia, brain tumor and cancer of breast had high frequency of cancer [3,5].

The frequency of leukemia is higher than expected in families of leukemia patients; it makes (2.5%-5%) [12], in our study the family history of leukemia is more (table 3) although the number of patient is small.

The over all risk for 1st degree relatives is 2-3 time higher than that of the general population [5,12], in our study the incidence of family cancer in leukemia children is (20,8%) while of the control group is (14,5%), which is about 1.5: 1 table (3).

Potter et al 1991 ;showed that 5-10% from the close relatives of patients had family history of cancer compared to 1-2% of similarly affected families of healthy persons [13]the type of cances were mainly leukemia ,breast ,brain tumor while of the control group were mainly solid tumor table(3)

LFS confirmed that 1st degree relative of such patients do demonstrate a significant cancer excess (5,14,15) , in our study it is also higher but of no statically significant table (1)

In our community the consanguineous marriage is widely familiar, and it was encountered in 48(40%), of leukemia children and 72(48%) of the control group, which is of no statistical significance table (1) (p value 0.581), this mean that there is no role for the consanguinity in the causation of leukemia in childhood.

Prior fetal loss appear to be one of the most consistent risk factors [6, 7,15], maternal history of two or more fatal loss may increasing the relative risk for infant ALL and AML up to 25 time compared to the healthy control [3,6].in this study table (2) shows the leukemia mothers are 40(33,3%) had history of abortions ,which is consistent with US study of children cancer group case control study [7] which show 1/3 of the mothers patients have a history of spontaneous abortions, while the control group only 48(30%) (p value .558 which is not significant).

One study had found lower risk associated with prior fetal loss in a Chinese population and other

studies failed to find any association in ALL [6, 7, 16], in our study the two group had comparable results though it is small study sample size.

Prior fetal loss suggests a number of optional mechanisms including chronic environmental exposure and or genetic predispositions in varying effects on the fetus [7]; increased HLA-DR sharing between parent in both ALL&AML and recurrent abortions [17,18].

Greaves suggest no specific infectious agents is involved in the etiology of leukemia but reduced antigenic challenge in infant can lead to increased proliferation of pre leukemic clone when a later infection occur [19].

The occurrence of infection in early childhood is in some way protective for later development of ALL [20, 21]. Children who have no or few older siblings may be especially likely to have delayed exposure to infection [10].

Delayed exposure to common infection can behave differently from the earlier exposure [19].

Birth order may be a surrogate measure for timing of exposure to infectious agents [22], increased birth orders reflect lower age for exposure to infection which support delayed exposure to infection hypothesis of leukemia development [21].

Dockerty group by Faith detected a statistically strong effect of increasing parity or higher birth order in protecting against ALL, a child with 5 siblings or more was 50% less likely to have ALL than 1st born child [10]. it is not only being 1st child but being the only child and a longer interval (>5y) between propend and the preceding siblings is another risk factor and being of small family size. Child born after another sibling is more likely to develop leukemia by age 2-3 y than the 1st born or an only child [23], this is consistent with our study where most affected group are the mid group, table(4) and the peak age incidence was 5.4 year and consistent with Tine [23] who says that later born children may have less ability than their siblings to fight off the infection against when exposed.

Fourth child in the family is at higher risk, the explanation is unknown, may be related to combination of genetic mutation with viral triggers [23].

Iraqi family doesn't consider small family, average 4-5 children. / one family ,the spacing between siblings is less obvious 2-3 year apart ,the 1st first born child in order constitute 19(15.8%), in between 1st and latest child is 74(61.6%),the latest child is 27(23.3%). For our children in this study, the peak age incidence is 5.4 y which is similar to other studies [4,,15].

For children diagnosed in childhood peak of leukemia ,primary infection may occur shortly before diagnosis while for other ages attention focused on gestational /neonatal exposure leading

to persistent infection [3,24], this is consistent with Faith [10] who mentioned that children who have no or few siblings may be especially likely to have delayed exposure to infection .

Conclusion:

Positive family history of cancer ,is of great importance , while being of a consanegenouse marriage was not a risk factor , history of maternal abortions showed no relation to leukemia as risk factor , while the most significant birth order affected are in between the 1st birth order group and latest in the family setting , further large epidemiological study is recommended for detecting more risk factors.

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