RESEARCH ARTICLE

Epidemiological Characteristics of Acute Leukemia in Child Welfare Hospital in Baghdad

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Abstract

Background: Acute leukemia, the most common form of cancer in children, comprises approximately 30% of all children malignancies, with acute lymphocytic leukemia (ALL) being more common than Acute Myeloid Leukemia (AML) by five times. Objectives: To determine different epidemiological variables associated with acute leukemia& to determine the patterns according to socio demographic data. Patients and Methods: A cross- sectional study and the data collection was carried out for a period of four months, from the 2nd /May/2019 to 2nd /September /2019. Result: The study shows that the majority of patients were ALL & the highest percentage of ALL patients was in the age group (5-9) years, males showed higher percentage than females in both type of leukemia, the highest percentage were from Urban.The majority of patient's parents' education level was primary; while the highest percentage of fathers' occupation was Private sectors & the highest percentage of mothers' occupation were Housewife.The highest percentage of ALL patients were 4th & more Order in family& AML were the 1st child, the highest percentage of patients with Birth space (2-4) years from there brothers.The highest percentage of patients was feed from their mothers (Breast feeding) during their first year & the highest percentage of patients was normal birth weight.Majority of patient's Parent consanguinity were not related, while the lowest percentage of patient's Parent consanguinity were far related.There was an important association between patients' blood group AB & ALL. Conclusions: The study shows that the majority of patients were ALL & the highest percentage of ALL patients was in the age group (5-9) years, males showed higher percentage than females in both type of leukemia, the highest percentage were from Urban. Recommendations: Ensure good MCH system to monitor and ensure the quality of health care practice & demonstrating cultural competency to promoting more effective child health services.

Keywords: *Leukemia, Blood, Cancer, Childhood, Iraq.*

Introduction

Acute leukemia, the most common form of cancer in children [1], comprises approximately 30% of all children malignancies, with acute lymphocytic leukemia (ALL) being more common than Acute Myeloid Leukemia (AML) by 5 times [2].Leukemia is abnormal proliferation of blood cells in the bone marrow and blood formation organs lead to a malignant condition commonly named as leukemia, which can be classified based on the mode of progression [3]. The most common cancers in childhood in Iraq are leukemia, followed by lymphomas and brain and other nervous system tumors, overall, the proportion of leukemia cases were 5.8%, 6.5%, and 3.4% of

all cancer cases in 1998, 1999, 2000 respectively [4]. The incidence of childhood leukemia exhibits wide variation between nations. Annual incidence rates of childhood ALL range from 19 to 56 per million for males and from 12 to 43 per million for females, the incidence rates for ALL are highest in Canada, Finland, and Costa Rica [5].The rates are moderate in most European countries and low in India and China. In contrast, the incidence of AML is highest among the Maori of Costa Rica and New Zealand, with moderate rates in Canada, United States, and the United Kingdom. While Brazil and Kuwait have the lowest reported rates of AML [6].

Geographical variation in leukemia might partly be explained by quality of life, and access to health service linked to economic levels [7, 8], although there is may be a role for etiological factors, including Gene-environment interactions. The observed biological pattern could be because of different risk factors affecting different ages, and might contain a genetic component [9, 10].

Patients and Methods

A cross- sectional study and the data collection was carried out for a period of four months, from the 2nd /May/2019 to 2nd /September /2019.It was performed on pediatric patients with acute leukemia who were diagnosed and treated in pediatric hematology oncology center in children Welfare Teaching Hospital, the patients were less than 14 years old at times of diagnosis. The Sample of the Study were A non-probability (convenient sampling) of (202) cases, and Data were collected through review of case records & direct interview with parents of pediatric leukemic child in outpatients and wards of pediatric disease in Child Welfare Hospital, a structured questionnaire was developed and constructed by the researchers.

Result

A total of 202 patients who diagnosed as acute leukemia and treated in Child Welfare Hospital in Baghdad were studied over the period extending from 2 May until 2 September 2019. As Regarding some demographical characteristics of the patients, the result showed that the age range at the time of the study was between 3month-14 years and the mean age was (7.2) year in both type of disease, the age range in ALL were 9 month -14 years with mean age (8.5) year, while age range in AML was 3month - 14 years with mean age (7.4) year.

The highest percentage of patients was ALL (86.13%) & males showed higher percentage than females in both type of leukemia, in which male consist (60.9%), while female consist (39.1%).In the present study (69.3%) of cases were from urban areas, and (30.7%) rural for both type, ALL were (69%) of cases were from urban areas, and (31%) rural, while AML were (71.4%) of cases were from urban areas, and (28.6%) rural. Regarding level of education for parents we found that the highest percentage of patient's fathers education level was primary (37.2%) for both type of disease, ALL were (36.2%), while AML were (42.9%) of cases.

We found that the highest percentage of patient's mothers education level was primary (35.6%) for both type of disease, ALL were (34.5%) while AML were (42.9%) of cases. Regarding Fathers Occupation we found the highest percentage were work in Private Sectors (55.9%) for both type of disease, ALL were (54.6%) while AML were (64.3%) of cases. Regarding mothers Occupation we found the highest percentage were Housewife (92.1%) for both type of disease, ALL were (90.8%) while AML were (100%) of cases (Table 1).

Table 1: Distribution of the studied sample by socio -demographic   data:

Socio -demographic		Total (n=202)		ALL (n=174)		AML (n=28)		P value
		No	%	No	%	No	%	
Age (years)	<5y	50	24.7	44	25.3	6	21.4	0.164
	5---9y	89	44.1	80	46.0	9	32.2	
	=>10y	63	31.2	50	28.7	13	46.4	
Gender	Male	123	60.9	104	59.8	19	67.9	0.416
	Female	79	39.1	70	40.2	9	32.1	
Living place	Urban	140	69.3	120	69.0	20	71.4	0.793
	Rural	62	30.7	54	31.0	8	28.6	
Father education	Illiterate	31	15.3	25	14.4	6	21.4	0.334
	Primary	75	37.2	63	36.2	12	42.9	
	Intermediate	33	16.3	27	15.5	6	21.4	
	Secondary	14	6.9	13	7.5	1	3.6	
	College & higher	49	24.3	46	26.4	3	10.7	
Mother education	Illiterate	44	21.8	35	20.1	9	32.1	

	Primary	72	35.6	60	34.5	12	42.9	0.339
	Intermediate	37	18.3	34	19.5	3	10.7	
	Secondary	20	9.9	18	10.3	2	7.1	
	College & higher	29	14.4	27	15.5	2	7.1	
Father occupation	Retired	11	5.4	11	6.3	-	-	0.340
	Private sector	113	55.9	95	54.6.	18	64.3	
	Gove. employee	70	34.7	62	35.6	8	28.6	
	Not working	8	4.0	6	3.4	2	7.1	
Mother occupation	Retired	-	-	-	-	-	-	0.247
	Private sector	1	.5	1	.6	-	-	
	Gove. employee	15	7.4	15	8.6	-	-	
	Housewife	186	92.1	158	90.8	28	100	
*Significant difference between proportions using Pearson Chi-square test at 0.05 levels.								

In Table (2) we report that birth Order of child in family, in which the highest percentage of ALL patients were 4th& more (34.4%) while AML were the 1st child (35.7%), and the lowest percentage of patients were in the 2nd Order in both ALL(18.4%) &AML (14.3%). About birth space we found The highest percentage of patients with Birth space (2-4) years from there brothers (44.8%), in both types ALL were (38.5%) while AML were (39.2%), and the lowest percentage of patients were less than 2 years in both types, while ALL were (14.9%), and AML were (10.7%), the Birth space range between (1-11year).Regarding type of feeding, we found the highest percentage of patients were feed from their mothers (Breast feeding) during their first year (38.6%) in both types of disease, AML were (53.6%) while in ALL the highest percentage of patients were feed from their mothers and mixed feeding (36.2% for each). Regarding birth weight we found the highest percentage of patients were normal Birth weight (82.2%) in both types of disease, ALL were (82.2%), while AML were (82.1%). the mean Birth weight were (3.1kg) and range between (1.0-5.0) kg.

Table 2: Distribution of reproductive variable of the studied sample

Reproductive variable		Total (n=202)		ALL (n=174)		AML (n=28)		P value
		No	%	No	%	No	%	
Order of child in family	First	52	25.7	42	24.1	10	35.7	0.596
	2	36	17.8	32	18.4	4	14.3	
	3	47	23.3	40	23.0	7	25.0	
	4+	67	34.2	60	34.4	7	25.0	
Birth space	<2.0	26	14.9	23	13.2	3	10.7	0.291
	2.0---<4.0	78	44.8	67	38.5	11	39.2	
	=>4.0	70	40.3	63	36.3	7	25.1	
Type of feeding	Breast feeding	78	38.6	63	36.2	15	53.6	0.116
	Bottle feeding	56	27.7	48	27.6	8	28.5	
	Mixed	68	33.7	63	36.2	5	17.9	
Birth weight (Kg)	LBW (<2.5)	36	17.8	31	17.8	5	17.9	0.996
	Normal (=>2.5)	166	82.2	143	82.2	23	82.1	
	Mean ±SD (Range)	3.1±0.7 (1.0-5.0)		3.1±0.6 (1.5-4.0)		3.1±0.7 (1.0-5.0)		
*Significant difference between proportions using Pearson Chi-square test at 0.05 levels.								

Regarding patient neonate history we found the highest percentage of patients had no history of Neonatal jaundice (52.5%) at birth in both types of disease, ALL were (52.3%), while AML were (53.6%).Regarding Congenital anomalies we found 7 patients (3.5%) had Congenital anomalies in ALL patients we didn`t found any AML patient with Congenital anomalies. Regarding Down syndrome, we found 4 patients (2%) had Down syndrome in ALL patients we didn`t found any AML patient with Down syndrome. Regarding Mode of delivery we found the highest percentage of patients had normal vaginal delivery (56.4%) in both types of disease, ALL were (54.6%), while AML were (67.9%), & we found the lowest percentage of patients were Forceps delivery(1%) in both types of disease, ALL were (1.1%), while there were no AML child had Forceps delivery. Regarding Duration of pregnancy we found the highest percentage

of patients were full term (81.5%) in both types of disease, ALL were (82.7%) while AML were (93.2%).We found in the present study 39 patients need NCU at day of birth (19.3%) in both types of disease, ALL were 35 patients (20.1%), while AML were 4 patients (14.3%) Regarding Duration of admission to NCU for patients who admits to NCU We found the highest percentage of patients admits for one day (51.3%) in both types of disease, ALL were (54.3%), the mean Duration of admission to NCU was (3.8) day in both type of disease, while it ranged between (1-30) day Table (3).

Table 3: Distribution of neonatal history according to the sample of the study:

Neonatal history		Total (n=202)		ALL (n=174)		AML (n=28)		P value
		No	%	No	%	No	%	
Neonatal jaundice	Yes	96	47.5	83	47.7	13	46.4	
	No	106	52.5	91	52.3	15	53.6	0.900
Congenital anomalies	Yes	7	3.5	7	4.0	-	-	
	No	195	96.5	167	96.0	28	100	0.280
Down syndrome	Yes	4	2.0	4	2.3	-	-	
	No	198	98.0	170	97.7	28	100	0.418
Mode of delivery	Forceps delivery	2	1.0	2	1.1	-	-	
	CS	86	42.6	77	44.3	9	32.1	0.386
	NVD	114	56.4	95	54.6	19	67.9	
Duration of pregnancy	Preterm	13	6.5	11	6.3	2	7.2	
	Full term	164	81.5	143	82.7	21	93.2	
	Late term	25	12.4	20	11.6	5	17.9	0.169
	Mean ±SD (Range)	37.5±1.6 (31-42)		37.7±1.9 (33-42)		37.5±1.6 (31-42)		
Need for NCU at day of birth	Yes	39	19.3	35	20.1	4	14.3	
	No	163	80.7	139	79.9	24	85.7	0.468
Duration of admission to NCU (days)	1	20	51.3	19	54.3	1	25.0	
	2	5	12.8	4	11.4	1	25.0	
	3	4	10.3	2	5.7	2	50.0	0.244
	5	1	2.6	1	2.9	-	-	
	=>7	9	23.2	9	25.8	-	-	
*Significant difference between proportions using Pearson Chi-square test at 0.05 levels.								

Regarding the results which were listed in table (4) we found 20 patient's Mother with history of neonatal death (9.9%) in both type of disease, ALL was 14 patient's Mother with history of neonatal death (8%) while AML were 6 patient's Mother with history of neonatal death (21.4%) of cases. The association of patient's mother history of neonatal death was statistically significant (p=0.028).Regarding Mother History of Stillbirth we found 12 patient's Mother had History of Stillbirth (5.9%) in both types of disease, ALL were 11patient's Mother had History of Stillbirth (6.3%), while AML there were one patient's Mother had History of Stillbirth (3,6%). Regarding Mother History of Abortion we found 59patients Mother had History of Abortion (29.2%) in both types of disease; ALL were 52 patient's Mother (29.9%), while AML were 7patient's Mother (25%).

Table 4: Mother`s neonatal history of the studied sample

		Total (n=202)		ALL (n=174)		AML (n=28)		P value
		No	%	No	%	No	%	
Mother history of neonatal death	Yes	20	9.9	14	8.0	6	21.4	
	No	182	90.1	160	92.0	22	78.6	0.028*
Stillbirth	Yes	12	5.9	11	6.3	1	3.6	
	No	190	94.1	163	93.7	27	96.4	0.568
Abortion	Yes	59	29.2	52	29.9	7	25.0	0.598
	No	143	70.8	122	70.1	21	75.0	
*Significant difference between proportions using Pearson Chi-square test at 0.05 levels.								

Regarding Family Malignant history, we found 32 patients had Family history of leukemia (15.8%) in both types of disease; ALL were 30 patients had Family history of leukemia (17.2%), while AML were 2 patients had Family history of leukemia

(7.1%).Regarding Family history of cancer we found 53 patients had family History of cancer (26.2%) in both types of disease, ALL were 48 patients had family History of cancer (27.6%), while AML were 5 patients had family History of cancer (17.9%).Table4

Table 5: Family Malignant history of the studied sample

Family Malignant history		Total (n=202)		ALL (n=174)		AML (n=28)		P value
		No	%	No	%	No	%	
Family history of leukemia	Yes	32	15.8	30	17.2	2	7.1	0.174
	No	170	84.2	144	82.8	26	92.9	
Family history of cancer	Yes	53	26.2	48	27.6	5	17.9	0.277
	No	149	73.8	126	72.4	23	82.1	
*Significant difference between proportions using Pearson Chi-square test at 0.05 levels.								

Regarding Parental consanguinity we found the highest percentage of patients Parent consanguinity were not related (40.1%) in both types of disease, ALL were (41.4%), while AML were (32.1%), and the lowest percentage of patients Parent consanguinity were Far related (12.9%) in both types of disease, ALL were (12.6%), while AML were (14.3%). Table 6

Table 6: Parental consanguinity of the studied sample

Parental consanguinity		Total (n=202)		ALL (n=174)		AML (n=28)		P value
		No	%	No	%	No	%	
	First degree	62	30.7	54	31.1	8	28.6	0.551
	Second degree	33	16.3	26	14.9	7	25.0	
	Far related	26	12.9	22	12.6	4	14.3	

Discussion

Childhood leukemia is the most common cancer of childhood; the most common type is acute lymphatic leukemia (ALL), while acute myeloid leukemia (AML) is very rare in children accounting for about 15% of all childhood leukemia cases.

Its prevalence varies significantly between and within countries, continents and ethnic groups. This variability could be due to genetic, environmental or socioeconomic factors, our study done in Baghdad and there is no similar study was carried out in Iraq. Many of our results are consistent with many (but not all) prior studies, In the current study 202 cases of Acute leukemia were studied, Acute lymphoblastic leukemia (ALL) occurs more than five times the rate of AML (86.14%), which agree with world estimates of childhood leukemia [11]. Males were more affected than females (60.9%), which agree with a previous study in welfare hospital-Baghdad, males were

(60.6%) &females (39.4 %) [12].In this study, the highest percentage of age group were (5-9) year (44.1%), these results disagree with previous study in Basrah, Iraq, who reported age group (< 5 Years) as highest percentage [13]. The mean age of total patients (7.2years), these results disagree with an epidemiological study in Department of emergency medicine at Aga khan university hospital from January 2009 to December 2013 the median age of the children was (4.75 year) [14].

In regard to the geographical sectors, the majority of cases are in the urban (69.3%), these results agree with population-based case-control study to assess the possibility of an excess risk of childhood leukemia in urban from 1998 to 2011 among residents of two provinces of the northern Italian [15].The risk of leukemia appeared to be elevated in children born to parents with a higher level of education, the highest percentage of Father Education were (College & higher

(24.3%), these results agree with retrospective study was conducted in the Pediatric Hematology Oncology unit of the department of Pediatrics at the Postgraduate Institute of Medical Research, Chandigarh, India which were (39%) [16].

While Mother Education were (14.4%) & highest percentage of Mother Education were Primary (35.6%) which agree with Indian study which were (43%) [16].In regard to the parent's occupation the highest percentage of Father Occupation was Private sector (55.9%) there is no study to be compared. While Mother Occupation the highest percentage were Housewife (92.1%) these results disagree with case-control study in India which reported increased risk of leukemia in children whose mothers were working in agriculture [17].

Regarding Order of child in family the highest percentage of ALL were 4th & more (34.4%),these results disagree with worldwide data pooled from six member population-based birth cohorts in which were the 1st Order were the highest percentage (60 case from 136 total ALL cases) [18]. Regarding Type of feeding at birth, the highest percentage were Breast feeding (38.6%), these results agree with Egyptian study conducted to investigate the impact of breastfeeding on the risk of development of acute leukemia among children Admitted to Alexandria University Children's Hospital [19].

The highest percentage of patients with Birth space (2-4) years from his sibling in ALL were (38.5%) and AML were (39.2%), and the lowest percentage of ALL patients were (14.9%), while AML were (10.7%), these results disagree with study in Denmark at Danish Civil Registration System which was (4 years & more) [20].Regarding Birth weight the highest percentage was Normal Birth weight (82.2%) these results agree with study in Denmark at Danish Civil Registration System [20].

Regarding Neonatal jaundice, the highest percentage of patients were hadn't Neonatal jaundice (52.5%), these results agree with study of risk profile of childhood leukemia in Greece which reported (81.7%) of cases hadn't Neonatal jaundice [21].Regarding congenital anomalies there were 7 cases (3.5%) had Congenital anomalies, all of them ALL, a similar study examined the association between congenital abnormalities and infant leukemia in a case-control study at a Children's Oncology Group institution in the United States &Canada from 1996-2006 reported (69%) from cases were ALL [22].

Regarding Down syndrome there were four cases (2%) of all studying sample, all of them ALL& this results agree with study at Washington State (USA) which reported (1.8%) of total leukemia cases during the years (1981-2002) had Down syndrome [23].

Regarding Mode of delivery, 77cases (44.3%) ALL &9 cases (32.1%) AML were cesarean delivery, it high in comparison with study in California USA which were (22.1%) ALL & (18.3 %) AML [24].In our study, the mean of Duration of pregnancy were (37.5) week & ranged (31-42) week, 13 cases (6.5%) were Preterm birth (PTB), according meta-analysis demonstrated that children born preterm were significantly associated with increased risk of AML [25]. While late term births were 20 cases (11.6%) from total ALL & 5 cases (17.9%) from AML.

In our study, there were 39 case (19.3%), need for NCU at birth with mean (3.8) day ranged (1-30) day, in which 20 case (51.3%) admit for one day, same of them suffering from hyperbilirubinemia. According US study in Northern California which shows that phototherapy use was associated with increased cancer rates (particularly AML) [26].In our study, there were 14 ALL cases (8%) their mothers had history of neonatal death, while AML were 6 cases (21.4%) with positive association.

Regarding patient`s Mother medical History of Stillbirth, there were 11 ALL cases (6.3%) their mothers had history of Stillbirth & AML were one cases (3.6%), while 52(29.9%) cases ALL their mothers had history of Abortion & 7 cases(25%) AML their mothers had history of Abortion, according a systematic review and meta-analysis show Results from the largest ever meta-analysis, on fetal loss history and childhood leukemia risk show a marginally significant association of fetal loss with risk of acute leukemia in subsequent offspring.

This finding pertained to main and sensitivity analyses on ALL, as well as, sensitivity analyses on AML.

By contrast, a marginally significant association of Abortion history with risk of ALL and AML was found [27].Regarding Family history of leukemia (one & second degree only) we found 32 patients (15.8%) had Family history of leukemia while Family history of cancer, we found 53 patients (26.2%) had family History of cancer.

Regarding Consanguinity among ALL patients, 54 cases (31.1%) Consanguinity by First degree (one cousin), 26 cases (14.9%) 2nd degree (two cousin) &22 (12.6%) cases far related (2-4 cousin), which agree with Population-based study in the UAE show that the parents consanguinity rate was higher among ALL cases, The finding of an 80% consanguinity rate among ALL families therefore is highly significant.While Consanguinity among AML patients were 8 cases (28.6%) First degree, 7cases (25%) 2nd degree & 4 cases (14.3%) far related [28].

Conclusions

The study shows that the majority of patients were ALL & the highest percentage of ALL patients was in the age group (5-9) years, males showed higher percentage than females in both type of leukemia, the highest percentage were from Urban& the majority of patient's parents' education level was primary; while the highest percentage of fathers' occupation was Private sectors & the highest percentage of mothers' occupation were Housewife.

Recommendations

Ensure good MCH system to monitor and ensure the quality of health care practice & demonstrating cultural competency to promoting more effective child health services.

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