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Demographical study of acute lymphoblastic leukemia in Basrah

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***Abstract*---**Background: Leukemia is a complex and biologically separate group of hematological cancer. Aim: Studying the association between demographical factors, hematological tests with type of ALL. Method: A cross-sectional study conducted during the period between 2020 and 2022, fifty children with acute lymphoblastic leukemia (ALL) and their ages ranged from < 2 year - 15 years have been included. The patients diagnosed by specialist physicians based on clinical, histological and immunophenotypic procedures carried out locally at the Oncology Unit in Basrah Children Specialty Hospital. The cases of ALL distributed according to type of ALL, sex, age groups, and residency. Hematological parameters were studied in all those 50 patients before and after chemotherapy; Hb, platelets, WBC, peripheral blood blasts, and bone marrow blasts. Patient who showed WBC count equal to 50.000/ mm^3, considered as standard-risk patient and who showed WBC count > 50.000/ mm^3 considered as high-risk patient. Results: Out of 50 ALL patients, 45 were B-ALL and 5 were T-ALL. Males with B-ALL were 55.6% and females were 44.4% with no statistical differences. Males with T-ALL (80.0%) showed higher percentage than females (20.0%) with no statistical significant. Regarding to distribution of age groups in these two types of ALL, age group (2-5 y) showed higher frequencies in T-ALL (60.0%) The age group (2-5 Y) showed high frequency in B-ALL (48.9%). Age group (<2 Y) showed (20.0%) with B-ALL The age group (6-12 Y) showed high frequency in T-ALL (40.0%) while B- ALL was (22.2%). Age group (13-15 Y) showed (8.9%) B-ALL Type of leukemia and age groups showed no statistical significant. Distribution of ALL patient in urban regions

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showed highest percentage of T-ALL (60.0%) while rural regions showed lower frequencies with no statistical significant. Regarding to hematological tests, Blast cells were absent after chemotherapy while Hb, Platelets, and WBC were significantly higher after chemotherapy with (P value <0.05). The distribution of risk was not significantly different in relation to type of leukemia (P value >0.05). Conclusion: No statistical differences observed regarding to sex, age groups residency, and risk in Types of ALL while hematological tests after chemotherapy showed statistical differences (P value < 0.05).

***Keywords*---**Acute lymphoblastic leukemia, T-ALL, B-ALL, residency, blasts, platelets, WBC, risk.

Introduction

Leukemias are a complex and biologically separate group of hematological cancers (Petridou et al., 2008) and it is the most frequent malignancy in children, as well as the leading cause of mortality due to disease (Wheatley et al., 2009). The most common childhood cancer is ALL that representing nearly 30% of all tumors in white children and 80% of all leukemias (Feltbower et al., 2009), which is up to twice as prevalent in males as it is in females (Doreset et al., 2012). In most cancer registries, Acute Lymphoblastic Leukemia (ALL), Acute Myeloid Leukemia (AML), Chronic Lymphoblastic Leukemia (CLL), and Chronic Myeloid Leukemia (CML) are the four primary subtypes of leukemia (Xie et al., 2003). The French American British (FAB) morphological criteria, which differentiated ALL into 3 categories (L1, L2, and L3) depending on the cell size, cytoplasm, nucleoli, vacuolation, and basophile, were the first attempt to define ALL (Bennett et al., 1976). Adults and children are affected by acute leukemias, although adults are mostly affected by chronic leukemia (Petridou et al., 2008). The accumulation of malignant, poorly differentiated lymphoid cells in the bone marrow, peripheral blood, and extra medullary locations is the most common clinical presentation of ALL. With a combination of clinical symptoms and markers of bone marrow loss, the presentation might be heterogeneous (anemia, thrombocytopenia, leukopenia), Fever, weight loss, night sweats, easy bleeding or bruising, weariness, dyspnea, and infection are all common symptoms. Extra medullary site involvement is widespread, and in 20% of patients, it might result in lymphadenopathy, splenomegaly, or hepatomegaly (Alvarnas et al., 2015). ALL is caused by a clonal population of lymphoid cells that proliferates and differentiates abnormally. Down syndrome, Fanconi anemia, Bloom syndrome and Nijmegen breakdown syndrome have all been identified as genetic abnormalities that predispose to a minority of occurrences of ALL in children (Shah et al., 2013). There are other risk factors which may be the causative agent such as ionizing radiation, chemicals, some solvents, and viruses like the Epstein-Barr Virus and the Human Immunodeficiency (Sehgal et al., 2010). The ability to accurately assess prognosis is important in the treatment of ALL. The clinician can use risk stratification to establish the most appropriate initial treatment regimen as well as when allogeneic stem cell transplantation should be considered. Patients were previously risk categorized based on their age and white blood cell count at the time of diagnosis. Long-term survival rates for patients over the age of 60 are just

10–15 percent (Rowe et al., 2010). Age, initial White Blood Cell (WBC) count, time to complete remission, immunophenotype (T and B cell), aberrant karyotypes, and cytogenetics have all been found to have an impact on the disease's outcome (Hilden et al., 2006). Two risk groups can be identified according to WBC count as either standard risk or high risk group (Schultz *et al.,* 2007).

Methods

In this cross-sectional study which conducted during the period between (2020-2022) fifty children with acute lymphoblastic leukemia (ALL) and their ages ranged from < 2 year - 15 years have been included. The patients diagnosed by specialist physicians based on clinical, histological and immunophenotypic procedures carried out locally at the Oncology Unit in Basrah Children Specialty Hospital. Identifying type of ALL based on the results of flow cytometry which done in private laboratories. Using multi-color flow cytometry and panel of markers, data collected from these reports for the current study. Moderate to bright CD45 expression with low SSC, $cCD3^+$, sm. $CD3^+$, TdT^+, $CD34^-$, $CD10^+$, $CD2^+$, $CD5^+$, $CD7^+$, $CD4^-$, $CD8^+$ suggested picture of T-ALL. Dim or negative CD45 expression with low SSC, $CD19^+$, $CD10^+$ (moderate and heterogeneous), HLA-DR+, $cCD79a^+$, $cIgM^-$, $CD2^-$, $CD33^-$, $cCD3^-$ and MPO^- was suggestive picture of B-ALL. The cases of ALL distributed according to type of ALL, sex, age groups, and residency. Hematological parameters were studied in all those 50 patients before and after chemotherapy; Hb, platelets, WBC, peripheral blood blasts, and bone marrow blasts. Patient who showed WBC count less than 50.000/ mm^3, considered as standard-risk patient and who showed WBC count > 50.000/ mm^3 considered as high-risk patient.

Results

Out of 50 ALL patients, 45 were B-ALL and 5 were T-ALL. Males with B-ALL were 55.6% and females were 44.4% with no statistical differences. Males with T-ALL (80.0%) showed higher percentage than females (20.0%) with no statistical significant. Regarding to distribution of age groups in these two types of ALL, age group (2-5 y) showed higher frequencies in T-ALL (60.0%) followed by B-ALL (48.9%). The age group (6-12 Y) showed high frequency in T-ALL (40.0%) while B-ALL was (22.2%). Age group (<2 Y) showed (20.0%) with B-ALL and no patient within this age group have T-ALL. The age group (13-15 Y) age showed (8.9%) B-ALL while no patient within this age group have T-ALL. Type of leukemia and age groups showed no statistical significant. Distribution of ALL patient in urban regions showed highest percentage of T-ALL (60.0%) followed by B-ALL (53.3%) while rural regions showed lower frequencies; B-ALL (46.7%) and T-ALL (40.0%). No statistical significant observed between residency and type of ALL. Regarding to hematological tests, Blast cells where absent after chemotherapy both in the peripheral blood and in the bone marrow. Regarding to hematological tests, Hb was significantly higher after chemotherapy with the average moved from 7.6 to 11.0 mg/dl (P value <0.05). Similarly platelets were significantly higher after chemotherapy where they were raised from a mean of 83.5 to a mean of 249.7*1000 (P value <0.05). WBC showed significant elevation from a mean of 2.4 to 3.4 (P value <0.05) (Table.2). Distribution of ALL patients regarding to risk showed that Majority of patients had standard risk (76%) compared to 24% with

high risk. However, the distribution of risk is not significantly different in relation to type of leukemia (P value >0.05) (Table.3).

Discussion

Leukemia is the 15th most often diagnosed cancer and the 11th leading cause of cancer-related mortality worldwide (Bispo *et al.*, 2020). ALL is an important disease among children and adolescent,where several studies have found an increase incidence of ALL, especially in the province of Basrah, has compared to other provinces(Airudainy, Salih and Aldorky, 2009; Habib *et al.*, 2010; Hagopian *et al* .,2010).

Leukemia is a group of hematological malignancies characterized by aberrant leukocyte growth and differentiation. Depending on the degree of cell development, they might be classed as chronic or acute. It can alternatively be classed as myeloid or lymphoid depending on the cell type (Lyengar and Shimanovsky, 2021). Studying the rearrangement pattern of Ig and TCR gene rearrangement in ALL children has not performed yet in Iraq, so the results of the present study compared with studies done in other countries.Detection of Immunoglobulin and T-cell receptor gene rearrangements is considered an important tool for clonality diagnostic in patients with T- cell and B-cell lymphoproliferation besides its role in the identification of PCR targets by DNA-based multiplex PCR method used in Minimal Residual Disease (Van Dongen *et al.*, 2003).

The most dependable way to understand how rearrangement happens during the course of disease is by the detailed sequencing analysis of Ig/TCR rearrangements (Mous *et al.*, 2009). In this study the sample was divided into four age groups: < 2 years, 2-5 years, 6-12 years, and >12 years. There is no significant difference between cases group regarding age distribution *(P =0.542)*. The peak age incidence in this study ranges from (2-5) years, with a percentage of (50%), And there are several studies that agree with the results of this study, where the majority of patients' ages range are between 2 to 5 years (Chiaretti *et al*,. 2013; Orkin *et al.*, 2014; Hassan, 2020), while there are other studies that conflict with the results of this study, where the majority of patients ages range between 6 to 12 years (Khan *et al.*, 2020; Badr *et al.*, 2021; Dai *et al.*, 2021). With regard to the sex distribution between the two groups participating in this study, there was no significant differences were noticed (*P = 0.293*). The number of male patients was higher than the female percentage; male (58%) and female(42%). This results agreed with a study done by Bader et al which occurs in the same hospital, they reported a similar ratio of male and female (Badr *et al.*, 2021).

The impact of socioeconomic class on the prevalence and patterns of pediatric leukemia is a subject of discussion among researchers. A study done by Dockerty and Draper et al which reported a relationship between leukemia in children and medium and upper socioeconomic groups. Poor nutrition may lead to an increase in childhood leukemia in low socioeconomic groups by affecting the immune system and predisposing children to recurring infections. ALL is a clonal malignant illness of lymphoblasts, the immature progenitors of the lymphoid lineage. The excessive proliferation of lymphoblasts in the bone marrow reduces

normal cell synthesis, resulting in symptoms such as pallor, weariness, bleeding, fever, and infection (Hasting *et al.*, 2012).

Acute leukemias have a confusing and diverse clinical appearance such as fever, pallor and bleeding making diagnosis challenging. The mechanism of leukemia as a maturation suppression of erythroid and megakaryocytic cells may be described by increased blast cell production, which results in decreased synthesis of normal leucocytes (fever), erythrocytes (anemia/pallor), and platelets (resulting in bleeding) (Fasseh and Fazli 2014). Pancytopenia is defined as a reduction in hemoglobin, platelets, or leukocyte count. The majority of children with pancytopenia have ALL, as well as blast cells in their peripheral blood (Llano, 2017). Furthermore, aberrant hematologic parameters such as low hemoglobin (Anemia), leukopenia, and thrombocytopenia in people who have received induction chemotherapy may signal remission failure. To enhance the possibilities of remission, it is important to determine the corresponding components. In this study Hb was significantly higher after chemotherapy with an average moved from 7.6 to 11.0 mg/dl. This result agrees with (Kong *et al.*, 2014), whom they found the mean hemoglobin level of ALL patient was 8.91g/dL and (Gupta *et al.*, 2021) which reported that the mean hemoglobin level of newly diagnostic ALL children was 7.3 g/dL.

Conclusion

No statistical differences observed regarding to sex, age groups residency, and risk in Types of ALL while hematological tests after chemotherapy showed statistical differences (P value <0.05).

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Tables:

Table 1: Distribution of ALL cases regarding to type of ALL, sex, Age and residency

			Leukemia		Total	P value*
			B-ALL	T-ALL		
sex	Male	Frequency	25	4	29	0.293
		Percent	55.6%	80.0%	58.0%	
	Female	Frequency	20	1	21	
		Percent	44.4%	20.0%	42.0%	
Age	<2	Frequency	9	0	9	0.542
		Percent	20.0%	0.0%	18.0%	
	2-5	Frequency	22	3	25	
		Percent	48.9%	60.0%	50.0%	
	6-12	Frequency	10	2	12	
		Percent	22.2%	40.0%	24.0%	
	13 and more	Frequency	4	0	4	
		Percent	8.9%	0.0%	8.0%	
Residence	Rural	Frequency	21	2	23	0.777
		Percent	46.7%	40.0%	46.0%	
	Urban	Frequency	24	3	27	
		Percent	53.3%	60.0%	54.0%	

*Chi squared test

Table 2: Parameters before and after chemotherapy

	Before (mean ± SD (median)	After (mean ± SD (median)	P value*
Hb	7.6 ± 2.4 (8.0)	11.0 ± 1.5 (11.0)	0.0001
Platelets	83.5 ± 85.8 (57.0)	249.7 ± 86.4 (233.5)	0.0001
WBC	2.4 ± 2.5 (1.0)	3.4 ± 1.2 (3.0)	0.0001
PB blast	52% ± 29% (70%)	0	**
BM blast	84% ± 14% (90%)	0	**

*Mann Whitney's test

**No comparison because the values after chemotherapy were zero.

Table 3: Distribution of ALL patients regarding to Risk

			Leukemia		Total	P value*
			B-ALL	T-ALL		
Risk	Standard risk	Frequency	35	3	38	0.377
		Percent	77.8%	60.0%	76.0%	
	High risk	Frequency	10	2	12	
		Percent	22.2%	40.0%	24.0%	

*Chi squared test