Distribution and Basic Hematological parameters of Acute Leukemia (Myeloid & Lymphoid type) in Thamar City, Yemen

1. Original Research Article

Abstract:

***Background*:** Acute hyper leucocytic leukemia (AHL) is a commonly occurred type of acute leukemia that represent a special variant in acute leukemia. Laboratory evidence of acute hyper leucocytic leukemia requires particular attention with special care in the diagnosis and treatment.

Objective: The aim of this study is to identify changes in several basic hematological parameters in patients with acute leukemia. Also assess hematologic parameters in patients with acute leukemia with and without laboratory evidence of leukocytosis. ***Materials and Methods*:** A total of 113 patients with newly diagnosed acute leukemia were included. Diagnosis was based on criteria for leukemic cells found in both blood and bone marrow samples.

Results: Of the total 113 patients studied, 72 (63.7%) were male, 41 (36.3%) were female, and (61.1%) patients had ALL [50 (72.5%) children and 19 (27.5%) adults] and (38.9%) had AML, [15 (34%) children and 29 (66%) adults]. The mean age of acute leukemia patients in this study was 17.2±15.3 years. The mean age of ALL patients ranged from 12.1±11.8 years and that of AML patients ranged from 25.1±16.8 years. Leukopenia was seen in (10.6%) patients and neutropenia in (71.7%) patients. Leukemic cells were present in the peripheral blood of patients (58.4%), and the other (27%) patients had the leukemic subtype. There was a statistically significant difference in total white blood cell count (*P. value*=0.03) following anemia severity for hemoglobin concentration (*P. value* =0.007). A statistically significant (*P. value* = 0.019) lower hemoglobin concentration was detected in patients with leukocytosis than in patients without leukocytosis. AML patient had lower hemoglobin concentrations than those with

ALL types identified (*P. value* = 0.03). There was a statistically significant (*P. value*=0.0001) direct relationship between total white blood cell count and absolute peripheral blood blast cell count, and there is a significant relationship between total white blood cell count and absolute neutrophil count (*P. value*=0.0001).

Conclusions: AHL has lower hemoglobin concentrations compared to patients with acute leukemia without leukocytosis and affects younger age groups than adult patients. AHL occurs more frequently in the myeloid than in the lymphoblastic leukemia type and more frequently in the monocyte subtype. The main form of anemia is (mild to moderate normochromic-normocytic anemia).

Keywords: Acute Hyper leucocytic Leukemia, Anaemia, AML, ALL, Thamar, Yemen.

Introduction:

"Acute myeloid leukemia (AML) is the result of somatic mutations in pluripotent stem cells or poorly differentiated progenitor cells. As mutant cell progeny proliferates to form approximately 10 billion or more cells, normal hematopoiesis is disrupted and normal blood levels of red blood cells, neutrophils, and platelets are reduced. Diagnosis is made by counting blood cells and examining cells in the blood and bone marrow and is based on finding blasts in the bone marrow and blood" **[1].** "Acute lymphoblastic leukemia (ALL) is a malignancy derived from a single B or T lymphocyte progenitor cell. It is a neoplastic disease resulting from somatic mutations in a single lymphoid progenitor in one of several discrete developmental stages. Blast proliferation and accumulation in the bone marrow leads to suppression of hematopoiesis and subsequent anemia, thrombocytopenia and neutropenia. The disease is most common in children but can occur at any age. ALL has many subtypes and can be classified using morphological, immunological, cytogenetic, and molecular genetics methods" **[1]. "**The main complications of acute leukemia of any type are due to suppression of normal hematopoiesis. A very high blast count can cause an increase in blood viscosity (hyperleukocytosis with leukocytosis). Disseminated intravascular coagulation (DIC) may occur. In addition, sometimes leukemic cells may infiltrate tissues and form a mass, which may impair organ function" **[2].** "A very high blast count particularly myeloblasts, may increase the blood viscosity. Patients may develop a leukocytosis syndrome characterized by altered mental status, respiratory failure, and congestive heart failure.

Leukocytosis can occur with blast counts ≥50 $X10^9$/L, and the risk increases significantly with blast counts ≥100 $X10^9$/L. Symptoms include dyspnea, headache, confusion and stupor. Intraocular hemorrhages may be present. Leukocytosis is most common with AML, particularly cases with monocytic differentiation, but can also be seen with ALL, chronic myeloid leukemia (CML), and, rarely, chronic lymphocytic leukemia (CLL). Hyperleukocytosis syndrome (WBC count ≥50 x 109/L), acute leukemia may present with extremely high blast counts; a phenomenon known as hyper-leukocytosis" **[2].** Hyper leukocytic syndrome (white blood cell 50≥count x 109/l) Absolute leukocyte counts have been found to have a significant impact on microcirculatory blood viscosity at levels of 50 x 109/l **[3,4,5,6].** "However, in capillary and precapillary microcirculation, increased blood viscosity may be less important than the very high intrinsic viscosity and low deformability of individual leukemic blasts" **[6].** However, lung injury can occur secondary to the toxicity of cellular components of leukemic blasts **[7,8].** For endothelium and other tissues **[4].** "In addition, excessive leukocyte counts can impair pulmonary circulation flow by blocking micro channels and forming aggregates and white thrombi in small veins. However, leukemia cells are invasive and can damage blood vessel walls" **[9].** "The large amount of fibrin degradation products may directly damage the pulmonary vasculature, leading to respiratory distress syndrome" **[10].** "Respiratory failure, intracranial hemorrhage, and severe metabolic abnormalities are common in acute hyper leukocytic leukemia (AHL) and are the major causes of high premature mortality (20% to 40%)". **[11].** "Leukocytosis was previously thought to be the presence and increased viscosity of a significant leucocratic (percentage of leukocyte volume), but now it is believed that endothelium-blast interactions lead to aggregation of blasts in the microcirculation. There is growing evidence that they are connected. This is due to the differential expression of adhesion molecules on lymphoblast and myeloblast cell surfaces. Adhesion molecules expressed on leukemic blasts and chemotactic responses to cytokines in the vascular microenvironment are more important than cell number" **[9,10].**

Severe complications and even death can occur in cases of acute or chronic significant leukocytosis above 25x109/mL. Leukemia, lymphoma, and myeloproliferative disorders all exhibit a hyper viscosity type syndrome, which can be brought on by WBC counts of

25 x 10-9/mL and higher. This oncological emergency can present with vision changes, bleeding, stroke or neurological changes, infarction, ischemia, and/or multi-organ failure. The extent of the organ system involvement and its long-term effects can influence the complications associated with the hyper viscosity syndrome. Rehydration, phlebotomy, and plasmapheresis are some of the treatments that can help prevent death and lessen long-term complications when they are recognized and administered promptly. In particular, hematologic malignancies, which are sometimes the cause of leukocytosis, can result in tumor lysis syndrome (TLS), a very dangerous side effect of patients receiving treatment for cancer [11].

The aim of this study is to identify changes in several basic hematological parameters in patients with acute leukemia. Also assess hematologic parameters in patients with acute leukemia with and without laboratory evidence of leukocytosis.

Materials and methods:

Study design:

This is a cross-sectional study aimed to identify changes in several basic hematological parameters in patients with acute leukemia.

Study area:

Cases were distributed according to different geographical areas in Yemen (according to the governorates including patient's resident in the towns and the districts officially following that governorate). Al-Jomhori, and Al Thawra Educational Hospitals is one of the largest hospitals in Sana'a, the capital of the Yemen Republic. The Hematology unit was established within the medical department to deal with hematological diseases including hematological malignancies. We have limited diagnostic facilities and inadequate facilities for standard management.

Study population:

The main source of the patient data studied was collected from the Hematology Unit at Al-Jomhori, and Al Thawra Teaching Hospital in Sanaa-Yemen.

Inclusion criteria:

All patients included in the study are Yemenis and came from different regions of Yemen and were newly diagnosed with acute leukemia.

Exclusions criteria:

Patients who were previously diagnosed or have received treatment.

Sample size:

113 patients with newly diagnosed acute leukemia.

Methods:

Basic Hematological Parameters:

The diagnosis of leukemia was identified according to the standard practice and based on at least peripheral blood and bone marrow morphology. All the basic hematological tests (CBC) were done using an automated blood cell analyzer with morphological study done by a hematopathologist. The blood is measured in cells per liter (cells/L) or grams per deciliter (grams/dL). These instruments provide accurate, precise, low-cost differential counts with fast turnaround times.

Data analysis:

All collected data were analyzed using SPSS for Windows, version 16. Paired Student t-test was used for calculating the degree of variation, with *P. value* (≤ 0.05) considered as significant.

Results:

Table 1: It shows the distribution of acute leukemia, of the 113 (100%) patients, 72 (63.7%) were male and 41 (36.3%) were female. (61.1%) patients had ALL [50 (72.5%) children and 19 (27.5%) adults] and (38.9%) had AML [15 (34%) children and 29 (66%) adults]. The mean age of patients with acute leukemia in this study was ($\overline{X} \pm$ SD) 17.2 ± 15.3 (range = 1-75) years. The mean age of ALL patients was 11.8±12.1 (range = 1-65) years and that of AML patients was 16.8±25.1 (2-75) years. **Table 2:** It shows that leukocytosis was present in 78 (69%) patients, of whom (31%) had WBC counts ranging from 12-50 × 109/L. Of the 113 patients, 43 (38%) had hyperleukocytosis (≥50 × 109/L), of which 26 (23%) had hyperleukocytosis (≥100 × 109/L). Leukopenia was seen in (10.6%) patients and neutropenia (absolute neutrophil count < 2 x 109/L) was seen in

(58.4%) patients. Leukemia cells were present in the peripheral blood of patients (73.5%), and the other (27%) patients had the leukemic subtype. **Table 3:**A statistically significant difference in the total white blood cell count follows the severity of anemia (for hemoglobin concentration (*P. value*=0.007) was noticed (*P. value* =0.03). **Table 4:** Patients with hyperleukocytosis show statistical significance (*P. value*=0.019) for lower hemoglobin concentrations than those without. **Table 5:** Shows the statistical significance (*P. value* = 0.03) of lower hemoglobin concentrations in AML patients than in ALL-type patients. **Table 6:** There was a statistically significant (*P. value* = 0.0001) direct relationship between total WBC counts and absolute peripheral blast counts, and a significant (*P. value* = 0.0001) between total WBC counts and absolute neutrophil counts(*P. value*=0.0001) indicates that there is a relationship. **Table 7:** Leukocytosis is seen in ALL patients (28.9%) but in AML patients (50%). **Table 8:** Normochromic normocytic anemia type was the predominant type of anemia in both leukemia type (64%) AML and (65%) ALL. Macrocytic anemia has been shown in AML patients (36%) and ALL patients (18%). Hypochromic microcytic anemia (18%) is seen in all cases Undetermined red blood cell morphology studies in (43%) of AML and (51%) of ALL cases. **Table 9:** Leukocytosis, if present, detected in (45%) of patients with M1-M3 AML in (62%) of M4-M5 AML patients.

Table (1):

TYPE	***No (%)***	***Age (yrs.)***	***No (%)***	***Sex***	***No (%)***
ALL	69(61.1%)	< 15	50(72.5%)	M	29(58%)
				F	21(42%)
		≥ 15	19(27.5%)	M	12(63.2%)
				F	7(36.8%)
AML	44(38.9%)	< 15	15(34%)	M	12(80%)
				F	3(20%)
		≥ 15	29(66%)	M	19(65.5%)
				F	10(34.5%)
Total	113(100%)	< 15	65(57.5%)	M	41(63.1%)
				F	24(36.9%)
		≥ 15	48(42.5%)	M	31(64.6%)
				F	17(35.4%)

Distribution of Acute Leukemia Patients studied According to the Type, Age and Sex.

Table (2): Leucocyte Parameters of Acute Leukemia

LEUCOCYTE PARAMETERS		ALL No (%) 69 (61.1%)	AML No (%) 44 (38.9%)	TOTAL No (%) 113 (100%)
Total WBC count ($\times 10^9$/L)	< 4	6(8.7%)	6(13.6%)	12(10.6%)
	4 – 11	20(29%)	3(6.8%)	23(20.4%)
	12 – 49	22(31.9%)	13(29.5%)	35(31%)
	50 – 100	5(7.2%)	12(27.3%)	17(15%)
	> 100-528	16(23.2%)	10(22.7%)	26(23%)
Hemoglobin (g/dL)	< 6	13(18.8%)	11(25%)	24(21.2%)
	6-9	27(39.1%)	18(40.9%)	45(39.8%)
	> 9	24(34.7%)	13(29.5%)	37(32.7%)
	Normal	5 (7.2)	2(4.5)	7(6.19)
Platelet count ($\times 10^9$/L)	< 10	6(8.7%)	3(6.8%)	9(8%)
	10 – 50	44(63.8%)	26(59.1%)	70(61.9%)
	51 – 100	5(7.2%)	11(25%)	16(14.1%)
	> 100	14(20.3%)	4(9.1%)	18(15.9%)

Table (3): Comparison between Hematological Parameters According to hemoglobin in Acute Leukemia

PARAMETER	HAEMOGLOBIN LEVEL			*P. value*
	(Hb: < 6 g/dl) NO. (%) 24(21.2%) ($\overline{X}$ ± SD.)	(Hb: 6-9 g/dl) NO. (%) 45(39.8%) ($\overline{X}$ ± SD.)	(Hb: >9 g/dl) NO. (%) 44(38.9%) ($\overline{X}$ ± SD.)	
Hb (g/dl)	(4.397± 1.017)	(7.39± 1.25)	(10.59± 1.35)	0.007
Total WBC count ($\times 10^9$/L)	(92.26± 149.74)	(69.38± 78.40)	(65.42± 93.15)	0.03
Platelet count ($\times 10^9$/L)	(23.53± 14.919)	(52.11± 84.88)	(107.45±171.48)	0.18

Table (4): Relationship between hyperleukocytosis and Hematological Parameters of Acute Leukemia.

PARAMETER	**HYPERLEUCOCYTOSIS (Total WBC count: more than 50 ($\times 10^9$/L)**		***P- value*** **(t-test)**
	Present	Absent	
	No (%)	No (%)	
	43/113(38.1%)	70/113(61.9%)	
	$\overline{X}$ ± SD.	$\overline{X}$ ± SD.	
Hemoglobin (g/dl)	7.76± 2.48	8.25± 2.63	0.019
Total WBC count ($\times 10^9$/L)	164.71± 115.93	16.06± 13.51	0.4
Platelet count ($\times 10^9$/L)	57.57± 95.38	73.74± 138.57	0.1
Age (Years)	22 ± 18	14 ± 12	

Table (5): Relationship between Hematological Parameters according to the Acute Leukemia type.

PARAMETER	Acute leukemia Type		P- value (t-test)
	ALL	AML	
	NO. (%)	NO. (%)	
	69/113(61.1%)	44/113(38.9%)	
	$\overline{X}$ ± SD.	$\overline{X}$ ± SD.	
Hemoglobin (g/dl)	(8.31± 2.67)	(7.69± 2.41)	0.03
Total WBC count ($\times 10^9$/L)	(73.94± 114.75)	(70.75± 80.05)	0.9
Platelet count ($\times 10^9$/L)	(81.98± 153.77)	(45.02± 40.15)	0.7

Table (6): Relationship between the total WBC count and differential cell count in acute leukemia.

PARAMETER	Differential Cell Count		P- value (t-test)
	Absolute blast cell count	Absolute neutrophil count	
	$\overline{X}$ ± SD.	$\overline{X}$ ± SD.	
Total WBC count ($\times 10^9$/L)	42 ± 77.6	4.4 ± 9.1	0.0001

Table (7): Relationship between hyperleukocytosis and Acute Leukemia.

PARAMETER	HYPERLEUCOCYTOSIS (Total WBC count: more than 50 ($\times 10^9$/L))		*P. value* (t-test)
	ALL	AML	
	No (%)	No (%)	
	21/ 69(30%)	22/44(50%)	
	$\overline{X}$ ± SD.	$\overline{X}$ ± SD.	
Hemoglobin (g/dl)	8.1 ± 2.7	7.3 ± 2.3	0.05
Total WBC count ($\times 10^9$/L)	217±127	122.6 ±84.9	0.13
Platelet count ($\times 10^9$/L)	76 ± 136	42.3 ± 24.8	0.3
Age (Years)	16 ± 16	26 ± 19	0.03

Table (8): Distribution of Acute Leukemia According to the Red Cell Morphology Study.

Leukemia Type	Red Cell Morphology Study (cases with determined morphology study)			Undetermined RBCs morphology
	Normochromic normocytic RBCs	Normochromic macrocytic RBCs	Hypochromic microcytic RBCs	
	No. (%)	No. (%)	No. (%)	No. (%)
AML	16/25 (64%)	9/25 (36%)	0	19/44(43%)
ALL	22/34 (65%)	6/34(18%)	6/34 (18%)	35/69 (51%)

Table (9): Distribution of those with hyperleukocytosis and those without in Acute Myeloid Leukemia According to the Subtype.

Parameter Of AML cases	AML Subtype		
	M1-M3 Granulocytic leukemia 31/44 (70%)	M4-M5 Monocytic Leukemia 13/44 (30%)	M6 & M7 Erythro & Megaloblastic 0
AML With hyperleukocytosis	14/31 (45%)	8/13 (62 %)	0
Mean WBC count	114.5	136.6	0
AML Without hyperleukocytosis	17/31 (55%)	5/13 (38 %)	0
Mean WBC count	15	29	0

Discussion:

In this study, AL distribution showed a predominance of ALL type compared to AML, with ALL to AML being the predominant AL type in children included in this study (72.5%). Furthermore, most of the AML patients (66%) were adults. The gender distribution of AL patients was male to female, and ALL patients had a male-to-female ratio of 1.6:1, and AML patients had a 3:1 ratio **[3,4].** Normochromic-normocytic anemia was the predominant type of anemia in both leukemia types (64%) AML and (65%) ALL. Macrocytic anemia was identified in AML (36%) and ALL (18%) patients investigated. Hypochromic microcytic anemia was found in (18%) ALL cases. These results suggest that the normochromic normocytic morphology of erythrocytes is the most common type of anemia in leukemia, and hypochromic microcytic or macrocytic deformities of erythrocytes contribute to dysplastic processes or general nutritional deficiencies. It is

consistent with the notion that in younger patients. All types of acute leukemia are more common **[1,3,4].**Undetermined red blood cell morphology studies in (43%) of AML and (51%) of ALL cases. These results are due to incomplete reporting of acute leukemia patients and the fact that the RBC index calculated by automated hematology analyzers is imprecise and affected by blood samples with high leukocyte counts. Leukocytosis (white blood cell count 50≥ x 109/L) was found in (38%) of the patients in this study. This is similar to figures in other studies by Würthner, andLichtman**[4,12].** (23%) had leukocytosis (≥100×109/L) similar results reported by Gayathri with his colleagues, and other studies **[3,13,14].** There was a statistically significant difference in total white blood cell count (*P. value* =0.03) following anemia severity (for hemoglobin concentration (*P. value* =0.007). This may be due to the degree of bone marrow infiltration and the degree of suppression of erythropoiesis following the severity of the leukemia burden. Discovered in the current study. The latter finding may reflect a compensatory effect in which reduced red blood cell mass in patients with leukocytosis reduces blood viscosity, ensuring microcirculation, especially blood flow in vital organs. A statistically significant (*P. value* = 0.03) lower hemoglobin concentration was seen in AML patients than in those with ALL types. This may be due to the involvement of the erythropoietic lineage in the myeloid leukemia process. It is not directly involved in its lymphatic counterpart. This phenomenon is associated with or suggests disease progression, as indicated by higher leukemia counts. There was a statistically significant (*P.value* = 0.0001) direct relationship between total WBC and absolute peripheral blood blast counts, and a significant (*P.value* = 0.0001) relationship between total WBC and absolute neutrophil counts *(P. value*= 0.0001), the latter in which the absolute neutrophil count is directly affected by the total white blood cell count. This association explains the fact that granulopoiesis is specifically reduced by the process of leukemic invasion, in addition to being arrested at maturity as an essential part of the leukemic process. Statistically, patients with ALL leukocytosis were found to be significantly younger than those with AML leukocytosis (*P.value* =0.03). This follows commonly accepted the occurrence of ALL in the younger age group. Leukocytosis was seen in ALL patients (30%) and (52.7%) of AML patients. Leukocytosis in AML was more common than in ALL. The monocyte subtype was the highest leukocyte patient type (62%) compared to the non-

high leukocyte group (38%). This result is consistent with other studies done by Wald and MaSk with colleagues **[15,17].**

The mean total leukocyte count was lower in granulocytic AML (M1-M3) (114.4 x 109/L) than in the monocytic subtype (136.6 x 109/L). Thismay reflect the influence of blast cell morphology and size on the development and clinical significance of leukocytosis. Leukocytosis in AML is an ominous sign associated with the development of intravascular leukemic cell thrombosis(leukocytosis) in the lung and brain, which can lead to lung and brain infection and infarction, and early death **[17].**Also, the study observed no statistically significant differences between ALL and AML cases in total white blood cell and platelet counts in patients with and without experimental evidence of leukocytosis **[3].**This supports the finding in the present study of a significantly lower hemoglobin concentration in those with laboratory evidence of hyperleukocytosis (7.76 ± 2.48 g/dL) than those without (8.25 ± 2.63 g/dL) *(P. value*=0.019). Some patients with acute leukemia without hyperleukocytosis (<50 x109/L) may develop leukocytosis **[18].** Excess white blood cell counts can impair pulmonary circulation by blocking microchannels and by forming aggregates and white thrombi in small veins. However, leukemic cells are invasive and can damage blood vessel walls **[9].**

Among oncologic emergencies, tumor lysis syndrome is the most frequent. Although it can also happen on its own, this condition is common in both adult and pediatric oncology patients who are receiving chemotherapy. The majority of the symptoms experienced by patients with tumor lysis syndrome are caused by the release of intracellular chemicals that impair the target organs' ability to function. Acute kidney injury (AKI), fatal arrhythmia, and even death may result from TLS [11]. Unfortunately, we did not include this in our study and therefore, we recommend to include tis issue in the further studies.

Conclusions:

AHL has lower hemoglobin concentrations compared to patients with acute leukemia without leukocytosis and affects younger age groups than adult patients. AHL occurs more frequently in the myeloid than in the lymphoblastic leukemia type and more

frequently in the monocyte subtype. The main form of anemia is (mild to moderate normochromic-normocytic anemia).

Ethical approval and consent:

Ethical approval for the study was obtained from the Board of the Faculty of Medical Laboratory Sciences at Thamar University. The written informed consent form was obtained from each guardian of the participant as well as from the subject himself before recruitment into the study. All protocols in this study were done according to the Declaration of Helsinki (1964).

Sources of Funding:

There was no specific grant for this research from any funding organization in the public, private, or nonprofit sectors.

Conflict of Interest:

The author has declared that no competing interests exist.

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