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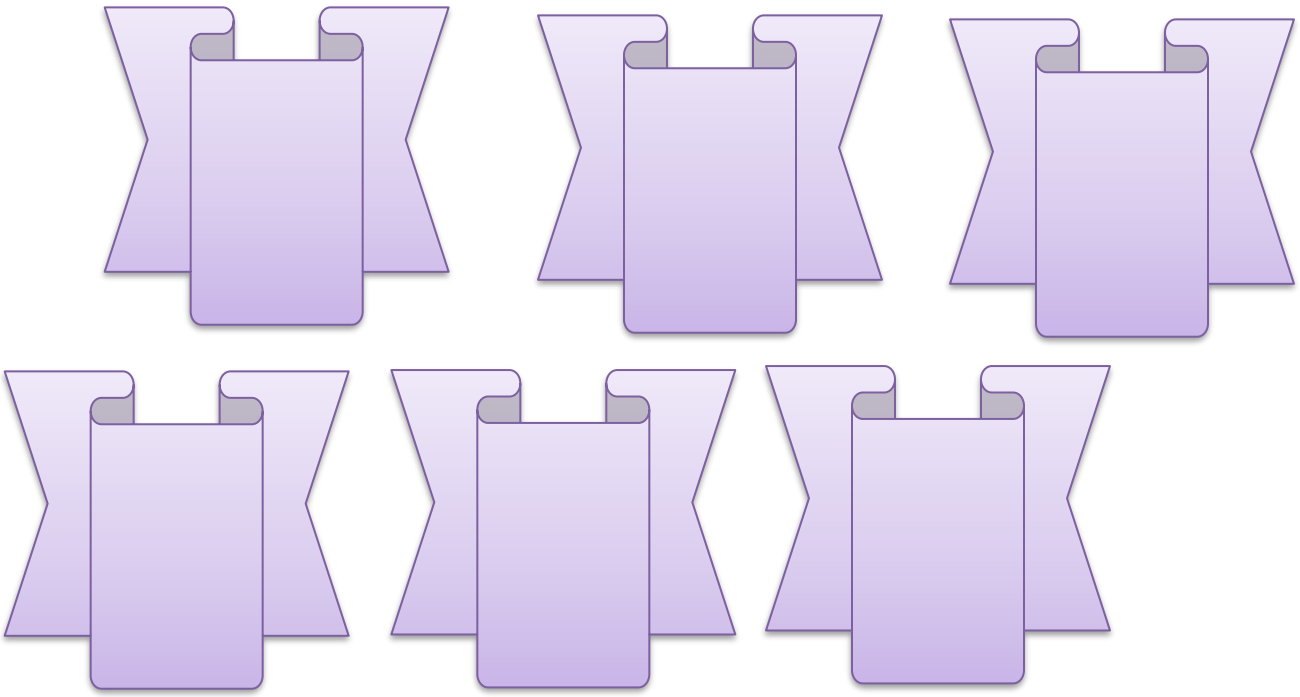

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Original Article

Detection of Aberrant Phenotypes in Acute Leukemia Patients in Relation to Some Hematological Parameters

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ABSTRACT

Background: Patients with acute leukemia [AL] may express aberrant antigens that are normally restricted to a different lineage. We evaluated the frequency of aberrancy in AL patients.

Aim of the work: Evaluation and analysis of the incidence of aberrant phenotypes in mononuclear cells in AL patients and their relation to hematological parameters.

Patients and Methods: This observational descriptive study was conducted on 150 newly diagnosed cases of AL over the period from August 2017 to March 2021. Flow cytometry was performed by Becton Dickinson [BD] FACS Calibur/BD FACS Canto flow cytometers using monoclonal antibodies against cell markers.

Results: The overall frequency of aberrancy was 38.7% [58/150] in all AL patients. Aberrant antigenic expression was more frequent in acute lymphoblastic leukemia [ALL] than acute myeloid leukemia [AML], T-ALL with aberrant expression was 66.6% of all T-ALL patients, while B-ALL with aberrant expression was 45.8% of all B-ALL patients, and AML with aberrant expression was 31.1% of all AML patients.

Conclusion: Aberrant phenotypes were found with considerable frequency in AL patients, and the implication of aberrant markers can help in disease monitoring, detecting measurable residual disease, and determining risk stratification and treatment intensity.

Keywords: Acute Leukemia, AML, Flow cytometry, Aberrant phenotypes

INTRODUCTION

Acute leukemia [AL] is a heterogeneous group of hematological malignancies with clonal expansion of neoplastic myeloid/lymphoid cells in blood and bone marrow [1].

According to the blast cell lineage, AL is primarily divided into acute lymphoblastic leukemia [ALL] and acute myeloid leukemia [AML]. In each type of AL, blast cells express a characteristic pattern of molecules known as cluster of differentiation antigens [CD]. Classification of AL depends on the expression of lineage-specific markers on blast cells. In several cases of AL, blasts of one lineage do not exhibit the markers of normal differentiation but express unusual markers in which myeloid-associated antigens are expressed in lymphoblasts and lymphoid-associated antigens are expressed in myeloblasts. This phenomenon is called aberrant phenotypes [2].

Aberrant expression of antigen is an abnormal expression of antigens by blasts that are normally not expressed by a particular lineage [Myeloid, B-lymphoid, and T-lymphoid] and do not fulfill the World Health Organization [WHO] criteria for mixed phenotype acute leukemia [MPAL]. This aberrant leukemia-associated immunophenotype [LAIP] can be used to monitor measurable residual disease [MRD]. Aberrant antigens in certain leukemias may indicate the presence of a genetic event or may affect the prognosis [3].

Flowcytometric immunophenotyping plays an important role in the identification of the lineage of AL along with the detection of aberrant antigens, which help in treatment monitoring and MRD analysis [4].

The aim of this study was to evaluate and analyze the incidence of aberrant phenotypes in mononuclear cells in AL patients and their relation to hematological parameters.

PATIENTS AND METHODS

This prospective observational study was approved by the Research Ethical Committee. Oral and written consents were obtained from all patients after a full explanation of the study.

The present study was conducted on 150 patients suffering from AL. Patients were referred to the clinical pathology department from the pediatric and internal medicine departments, Al Hussein Hospital, Al-Azhar University, over the period from August 2017 to March 2021 at the time of initial diagnosis, before induction therapy. Patients' clinical and laboratory information was reviewed from their medical records.

Inclusion criteria: All newly diagnosed cases of AL are diagnosed based on morphology.

Exclusion criteria: Secondary leukemias evolved from myeloproliferative neoplasms and myelodysplastic syndromes, and AL cases who received treatment.

All patients were subjected to a full history, clinical examination, and laboratory investigations as complete blood picture [CBC], coagulation prolife and flow cytometry [FCM] Immunophenotyping.

Two milliliters [ml] of peripheral blood/bone marrow samples were collected from each patient on an EDTA vacutainer tube. Also, two ml of peripheral blood samples were collected from each patient on a citrated vacutainer tube for the coagulation profile.

Samples for immunophenotyping were processed within 6 hours of collection at room temperature.

Immunophenotypic analysis of leukemic cells was performed by flowcytometry using a large panel of fluorochrome-labeled monoclonal antibodies. The monoclonal antibodies used in this study included early non-lineage specific markers [CD34, HLA-DR, and nuclear terminal deoxynucleotidyl transferase [TdT]], myeloid markers [cytoplasmic myeloperoxidase [MPO], CD13, CD33, CD15, and CD117], monocytic markers [CD14, CD64, and CD11c], B cell markers [CD19, cytoplasmic CD79a, CD22, CD20, and CD10], T cell markers [cytoplasmic CD3, CD7, and CD2], megakaryoblastic markers [cytoplasmic CD41 and cytoplasmic CD61] and erythroid marker [glycophorin A]. Mouse anti-IgG1 labelled with fluorescein isothiocyanate [FITC]/ IgG2 labelled with phycoerythrin [PE] were used as isotype controls.

Reagents

1] Phosphate buffered saline [PBS]: used for washing the sample during preparation. PBS was prepared by adding NaCl: 1.37 mMol, KCl: 26.8

mMol, NaPO4: 0.1mMol, KPO4: 17.6 to 800ml purified water, then addition of 1N HCL for adjustment of PH [7.4], **2]** BD FACS Lysing solution, **3]** BD FACS Cytofix/Cytoperm [fixation & permealization Solution], **4]** Cytometer Setup and Tracking beads [CS&T beads] and **5]** BD compensation beads.

Sample preparation

A] Surface staining [Stain-Lyse-Wash method] of CDs [CD34, HLADR, CD13, CD33, CD15, CD117, CD14, CD64, CD11C, CD19, CD22, CD20, CD10, CD7, CD2, and glycophorin A]

Each test tube [BD falcon 5ml polystyrene sterile test tubes] was labelled properly and was sequentially placed. 20-100 µl of the specimen [whole EDTA peripheral blood/bone marrow] were added to each test tube. 5µl of the corresponding labelled monoclonal antibody were added to each test tube. The tubes were incubated in a dark area for 30 minutes at room temperature. FACS Lyse was prepared in distilled water at a 1:10 dilution. 2 ml of prepared FACS Lyse solution was added to each test tube and incubated for 10 minutes at room temperature in a dark area. The contents of the tube were centrifuged after incubation for five minutes at 2000 round per minute [RPM] at room temperature, and after discarding the supernatant, the residual fluid was thoroughly mixed for re-suspension of cells. This was followed by adding 2 ml of isotonic PBS to each test tube and centrifuging for 5 minutes at 2000 RPM. The supernatant was discarded again. Washing with PBS was repeated twice and centrifuged for 5 minutes at 2000 RPM. The supernatant was discarded again. The cells were re-suspended in 200–400 µl of sheath fluid solution for final flow cytometric analysis.

B] Cytoplasmic and nuclear staining [Lyse-Stain-Wash method] of CDs [cytoplasmic MPO, nuclear TdT, cytoplasmic CD3, cytoplasmic CD79a, cytoplasmic CD41 and cytoplasmic CD61]

Each test tube was labelled properly and was sequentially placed. 20-100 µl of the specimen [whole EDTA peripheral blood/bone marrow] were added to each test tube. FACS Lyse was prepared in distilled water at a 1:10 dilution. 2 ml of prepared FACS Lyse solution was added to each test tube and incubated for 10 minutes at room temperature in a dark area. The contents of the tube are centrifuged after incubation for five minutes at 2000 RPM at room temperature, and after wasting the supernatant, the residual fluid was thoroughly mixed for re-suspension of cells. This was followed by adding 2 ml of isotonic PBS to each test tube and centrifuging for 5 minutes at 2000 RPM. The supernatant was discarded again. 250 µl of BD FACS Cytofix/Cytoperm Solution were added to each tube and incubated for 20 minutes at room temperature in a dark area. This was followed by adding 2 ml of PBS to each test tube and centrifuging for 5 minutes at 2000 RPM. The supernatant was discarded again. 5 µl of the corresponding labelled monoclonal antibody were added to each test tube. The tubes were incubated in a dark area for 30 minutes at room temperature. Unbound monoclonal antibodies were removed by washing the cells twice in 4 ml of PBS buffer and centrifuging for 5 minutes at 2000 RPM. The supernatant was discarded again. The cells were re-suspended in 200–400 µl of sheath fluid solution for final Flow cytometric analysis.

Immunophenotyping of samples was done using Flow cytometer Becton Dickenson [BD] FACS Calibur/BD FACS Canto and analyzed by BD CellQuest Pro and FacsDIVA software, respectively.

Statistical analysis: The data were analyzed using the Statistical Program for Social Science [SPSS] version 24. Quantitative data were expressed as mean ± SD for normally distributed data and median with Interquartile range [IQR] for not normally distributed data. Qualitative data were expressed as frequency and percentage. The Mann-Whitney U test [MW] was done for comparing two continuous variables. Probability [P-value] was also used. A P-value < 0.05 was considered significant.

RESULTS

According to the description of age and sex of 150 newly diagnosed AL patients, regarding age, the mean age of all studied patients was 34.08 ± 24.4 years, and regarding sex, there were 93 males [62%] and 57 females [38%] in all studied patients, as shown in table [1].

The overall frequency of aberrancy was 38.7% in all AL patients; some patients express more than one aberrant marker, as demonstrated in table [2].

In table [3], aberrant antigenic expression was more frequent in ALL than AML; T-ALL with aberrant expression was 66.6% of all T-ALL patients, while B-ALL with aberrant expression was 45.8% of all B-ALL patients, and AML with aberrant expression was 31.1% of all AML patients. Regarding aberrant expression in AML cases, cytoplasmic CD79a was the most frequently expressed antigen [16.7%], followed by CD10 and CD22 [5.6% and 1.1%, respectively], while expression of CD7 in AML cases was 12.2% of all AML cases. In B-ALL cases, CD33 was the most aberrantly expressed antigen [25%], followed by CD13 [20.8%], while expression of CD7 was 8.3% of all B-ALL cases. In T-ALL cases, CD10 was the most expressed antigen [50%], followed by cytoplasmic CD79a [25%] in all T-ALL cases, while no myeloid antigens were expressed in T-ALL cases.

There was not a statistically significant [p-value > 0.05] relation between aberrancy and FAB classification of AML patients except for CD10, as there was an increased percentage of expression in M5 [2 patients, 33.3%] and M7 [1 patient, 33.3%] when compared with other FAB categories, as shown in table [4].

There was not a statistically significant [p-value > 0.05] difference between aberrant AML patients and non-aberrant AML patients regarding the studied hematological manifestations demonstrated in table [5].

Comparison of hematological variables versus [vs.] aberrancy in B-ALL was illustrated in table [6], platelet [PLT] count was statistically significantly [p-value = 0.016] decreased in aberrant B-ALL patients when compared with non-aberrant B-ALL patients; also, APTT was statistically significantly [p-value = 0.003] increased in aberrant B-ALL patients [33.2 ± 4.6] when compared with non-aberrant B-ALL patients [29.2 ± 3.5]. There was not a statistically significant [p-value > 0.05] difference between aberrant and non-aberrant B-ALL patients with regard to other studied hematological manifestations.

In table [7], comparison of hematological variables vs. aberrancy in T-ALL, hemoglobin was statistically significantly [p-value = 0.048] decreased in non-aberrant T-ALL patients [8.2 ± 1.11] when compared with aberrant T-ALL patients [9.8 ± 0.97], PLT count was statistically significantly [p-value = 0.048] increased in aberrant T-ALL patients when compared with non-aberrant T-ALL patients; also, APTT was statistically significantly [p-value = 0.008] increased in non-aberrant T-ALL patients [42 ± 5.2] when compared with aberrant T-ALL patients [32.1 ± 4.6], but there was no statistically significant [p-value > 0.05] difference between aberrant T-ALL and non-aberrant T-ALL patients as regard other studied hematological manifestations.

Table [1]: Description of age and sex in all acute leukemia patients

Demographic data		Studied patients [N = 150]	
Sex	Male	93	62%
	Female	57	38%
Age [years]	Mean ±SD	34.08 ± 24.4	
	Min - Max	2 – 76	

Standard deviation [SD], Minimum [Min], Maximum [Max], Number [N]

Table [2]: Description of aberrant expression in all acute leukemia patients

Aberrancy		Studied patients [N= 150]	
Aberrant expression	No	92	61.3%
	Yes	58	38.7%
Markers of aberrant expression [N = 66]	CD79a	17	29.3%
	CD10	11	19%
	CD13	10	17.2%
	CD33	12	20.7%
	CD7	15	25.9%
	CD22	1	1.7%

*Some patients expressed more than one aberrant marker. Number [N]

Table [3]: Comparison of aberrant expression markers in AL patients

Aberrant expression markers in AL		Diagnosis						X^2	P-value
		AML [N= 28/90]		B-ALL [N = 22/48]		T-ALL [N = 8/12]			
B- lymphoid markers	CD79a	15	16.7%	-	-	3	25%	22.4	< **0.001**
	CD10	5	5.6%	-	-	6	50%	36.4	< **0.001**
	CD22	1	1.1%	-	-	0	0%	0.67	0.715
Myeloid markers	CD13	-	-	10	20.8%	0	0%	22.7	< **0.001**
	CD33	-	-	12	25%	0	0%	27.7	< **0.001**
T- lymphoid markers	CD7	11	12.2%	4	8.3%	-	-	1.97	0.372

*Some patients expressed more than one aberrant marker, Number [N]

Table [4]: Frequency of aberrant expression markers according to FAB classification of AML

FAB classification	AML patients [N = 90]														P-Value
	M0 [N=3]		M1 [N = 24]		M2 [N=21]		M3 [N=15]		M4 [N = 18]		M5 [N=6]		M7 [N =3]		
Aberrancy	2	66.7%	7	29.2%	8	38.1%	3	20%	4	22.2%	3	50%	1	33.3%	0.567
CD79a	0	0%	3	12.5%	5	23.8%	3	20%	4	22.2%	0	0%	0	0%	0.678
CD10	0	0%	2	8.3%	0	0%	0	0%	0	0%	2	33.3%	1	33.3%	**0.01**
CD13	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-----
CD33	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-----
CD7	2	66.7%	4	16.7%	3	14.3%	0	0%	1	5.6%	1	16.7%	0	0%	0.058
CD22	0	0%	1	4.2%	0	0%	0	0%	0	0%	0	0%	0	0%	0.836

Table [5]: Comparison of hematological variables versus aberrancy in AML

Hematological variables		AML patients [N= 90]			
		Non-aberrant [N = 62]	Aberrant [N = 28]	MW	P-value
Hb [g/dl]	Mean ± SD	8.3 ± 1.7	7.6 ± 1.5	668.5	0.082
TLC [x 10^3/ul]	Median [IQR]	24.8 [12.1 – 35.8]	23.6 [14 – 36.9]	803.5	0.574
PLTs [x 10^3/ul]	Median [IQR]	34.5 [26 – 67.3]	44.5 [27 – 83]	779	0.438
PB Blast [%]	Median [IQR]	40 [24 – 60]	52.5 [35 – 63]	706	0.158
BM Blast [%]	Median [IQR]	73 [42 – 86]	71.5 [51.7 – 84.8]	798	0.542
INR	Mean ± SD	1.57 ± 0.56	1.63 ± 0.65	865	0.979
APTT [sec]	Mean ± SD	44.4 ± 11.9	45.7 ± 15.6	858	0.934
D-Dimer [ng/ml]	Median [IQR]	0.6 [0.45 – 1.33]	0.5 [0.41 – 1.1]	747.5	0.292

Standard deviation [SD], Number [N], Interquartile range [IQR], Mann-Whitney U test [MW], Hb [Hemoglobin], Total leucocytic count [TLC], Platelets [PLTs], Peripheral blood [PB], Bone marrow [BM], International normalized ratio [INR], Activated partial thromboplastin time [APTT].

Table [6]: Comparison of hematological variables versus aberrancy in B-ALL

Hematological variables		B-ALL patients [n = 48]			
		Non-aberrant [n = 26]	Aberrant [n = 22]	MW	P-value
Hb [g/dl]	Mean ± SD	8.9 ± 1.3	9.2 ± 1.3	255	0.521
TLC [x 10^3/ul]	Median [IQR]	26.1 [19.2 – 32.2]	18.6 [14.4 – 28]	197	0.065
PLTs [x 10^3/ul]	Median [IQR]	79.5 [43 – 114.2]	53 [30 – 70.2]	169.5	**0.016**
PB Blast [%]	Median [IQR]	46 [39 – 59]	57.5 [42 – 67]	214	0.136
BM Blast [%]	Median [IQR]	72.5 [61 – 83]	79 [73 – 86.3]	199	0.072
INR	Mean ± SD	1.05 ± 0.08	1.04 ± 0.09	253.5	0.487
APTT [sec]	Mean ± SD	29.2 ± 3.5	33.2 ± 4.6	141.5	**0.003**
D-Dimer [ng/ml]	Median [IQR]	0.3 [0.29 – 0.4]	0.3 [0.3 – 0.4]	278.5	0.874

Standard deviation [SD], Number [N], Interquartile range [IQR], Mann-Whitney U test [MW], Probability [P-value], Hb [Hemoglobin], Total leucocytic count [TLC], Platelets [PLTs], Peripheral blood [PB], Bone marrow [BM], International normalized ratio [INR], Activated partial thromboplastin time [APTT].

Table [7]: Comparison of hematological variables versus aberrancy in T-ALL

Hematological variables		T-ALL patients [N = 12]			
		Non-aberrant [N = 4]	**Aberrant [N = 8]**	**MW**	**P-value**
Hb [g/dl]	Mean ± SD	8.2 ± 1.11	9.8 ± 0.97	4.0	**0.048**
TLC [x 10^3/ul]	Median [IQR]	13.4 [10.1 – 17.3]	15.1 [12.4 – 19.8]	11.5	0.461
PLTs [x 10^3/ul]	Median [IQR]	23.5 [23 – 70.5]	82 [55.2 – 112]	4	**0.048**
PB Blast [%]	Median [IQR]	36 [28.5 – 37.5]	51 [26.5 – 72.5]	11	0.461
BM Blast [%]	Median [IQR]	39 [31.5 – 43.5]	43 [31.5 – 48]	12	0.570
INR	Mean ± SD	1.17 ± 0.07	1.12 ± 0.09	9.5	0.283
APTT [sec]	Mean ± SD	42 ± 5.2	32.1 ± 4.6	1.0	**0.008**
D-Dimer [ng/ml]	Median [IQR]	0.4 [0.36 – 0.45]	0.4 [0.27 – 0.4]	12	0.570

Standard deviation [SD], Number [N], Insignificant [NS], significant [S], Interquartile range [IQR], Mann-Whitney U test [MW], Hb [Hemoglobin], Total leucocytic count [TLC], Platelets [PLTs], Peripheral blood [PB], Bone marrow [BM], International normalized ratio [INR], Activated partial thromboplastin time [APTT].

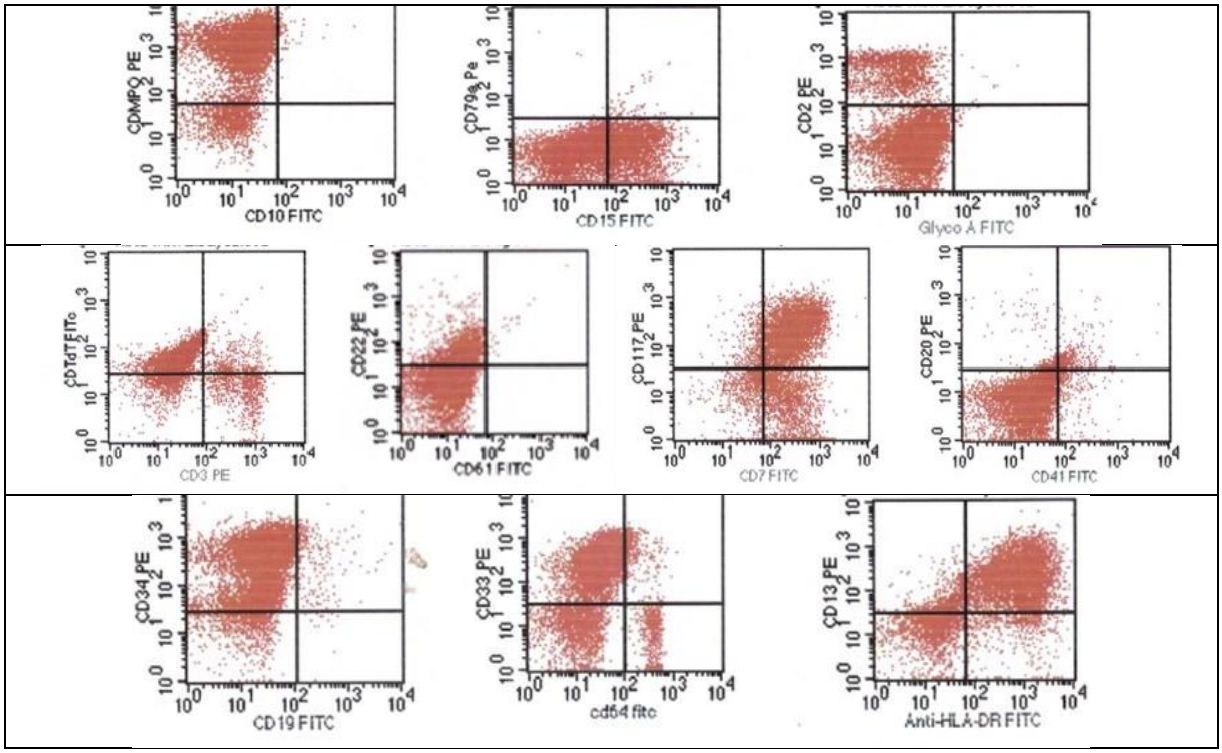

Figure [1]: Histograms of AML case with aberrant expression of CD7. *****CD2 expression [17%] resembles normal T-lymphocytes

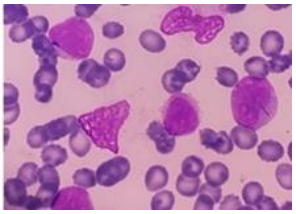

Figure [2]: Auer rods

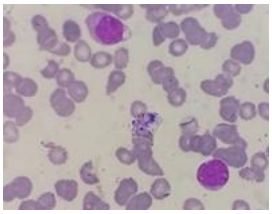

Figure [3]: AML M1

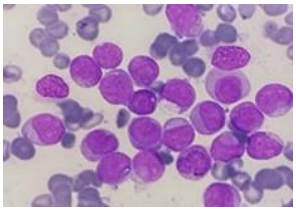

Figure [4]: AML M4

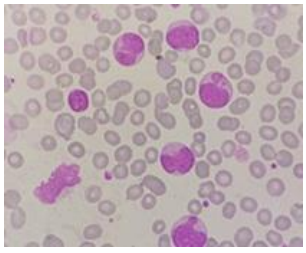

Figure [5]: Hypogranular M3

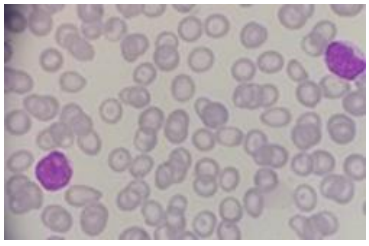

Figure [6]: T-ALL

DISCUSSION

FCM immunophenotyping plays an important role in the diagnosis and classification of AL. It also provides prognostic as well as predictive information, aiding in modulating therapy appropriately. The apparently morphologically similar blast cells can be easily differentiated by immunophenotyping based on the expression of different CD markers. One of the important advantages of FCM immunophenotyping is its ability to analyze many cells, which improves the accuracy of leukemia diagnosis. This analysis can be completed within hours and is often sufficient [5].

In our study, there was an adult predominance in AL; this may be because AML was more common than ALL. In accordance with these findings, others noted that the frequency of AL was higher in adults than pediatrics [6] but this was contrary to the results of other studies [7].

The prevalence of aberrancy in our study was 38.7% [58/150] of all AL cases. Aberrant antigenic expression is more frequent in T-ALL 66.6% [8/12] and B-ALL 45.8% [22/48] than in AML cases 31.1% [28/90].

The frequency of aberrant expression in AML in our study was 31.1%. Other studies found that the aberrant expression ranged from 11.1% to 26.4% in AML cases [6, 8]. Other studies were like ours; they reported a frequency of aberrant expression among their AML patients between 30% and 67.5% [9, 10].

In the present study, aberrant expression of B markers in AML patients showed that CD79a was the most frequently expressed marker at 16.7% [15/90] of all AML patients, followed by CD10 and CD22 at 5.6% [5/90] and 1.1% [1/90], respectively, while expression of T marker CD7 in AML patients was 12.2% [11/90]. Other studies noted different distributions of aberrant marker expression, and many of them reported that CD7 was the most common lymphoid-associated antigen in AML, followed by CD19 [11, 12].

Chang *et al.* [13] demonstrated CD7 to be an independent prognostic factor adversely affecting disease-free survival [DFS] and Post-remission survival in AML patients with a normal karyotype at diagnosis. If confirmed, CD7 expression may inform the decision to consolidate AML patients with a normal karyotype who have achieved first remission with chemotherapy, autologous, or allogenic transplantation.

Chang *et al.* [14] showed a correlation between CD7 expression and chromosome 5/7 anomalies but found that when all the cytogenetic groups were included, CD7 expression did not affect the prognosis.

A study carried out by **El-Sissy *et al.*** [15] suggested that CD7 expression in AML should be interpreted with cytogenetics as it may be associated with an unfavorable outcome.

In our study, 45.8% [22/48] of B-ALL patients had aberrant expression, which was like a study carried out in Sohag University Hospital by **Abdullah *et al.*** [16] who noted that the aberrancy was seen in 46% out of 15 B-ALL cases. Also, **Sarma *et al.*** [4] noted that 59.2% of cases of B-ALL had aberrant phenotypes.

In the present study, regarding aberrant expression of myeloid antigens in B-ALL cases, CD33 was the most expressed antigen [25%, 12/48] of all B-ALL cases, followed by CD13 [20.8%, 10/48], while expression of T antigen CD7 in B-ALL was 8.3% [4/48].

Momani *et al.* [7] conducted a study in Jordan and noted that CD33 was the commonest aberrant marker in B-ALL patients with aberrant expression [60.5%], followed by CD13 [50%] and CD7 was expressed in only one case [3%]. These findings were also found in another study done by **Alkayed *et al.*** [17] on Jordanian children with B-ALL. In accordance with us, other studies reported that CD33 was more common than CD13 [18, 19].

Aberrant expression in T-ALL patients was 66.66% [8/12]; CD10 was the most expressed marker at 50% [6/12], followed by cytoplasmic CD79a at 25% [3/12] of all T-ALL cases, while no myeloid markers were expressed in T-ALL cases.

In contrast to ours, other studies noted that aberrant expression of myeloid markers in T-ALL was more common than B-cell markers [20]. In controversy with all these results, including ours, others reported that there were no aberrant B-cell markers in T-ALL cases [21, 22].

Chromosomal aberrations are of high prognostic significance in ALL. In ALL with

rearrangements of MLL [poor prognosis], ALL blasts with MLL rearrangements frequently express myeloid-associated antigens CD15 and/or CD65. Several of the other myeloid antigens [CD13, CD33, and CD66c] are only occasionally positive. TEL/AML1pos ALL [Favorable diagnosis] are often CD33-positive and/or CD13-positive. The expression of CD13 and/or CD33 may be heterogeneous and, in many cases, clearly negative. ALL with numerical chromosomal changes: high hyperdiploidy represents the most common numerical chromosomal abnormality in ALL [a favorable diagnosis]. Myeloid antigens CD13, CD33, and CD65 were typically negative for this type. BCR/ABL fusion gene, the product of t[9;22] [q34;q11] [unfavorable diagnosis], most of the cases present distinct aberrant features; blasts usually display high CD10 and are CD34, but expression of CD13 and/or CD33 is frequent [23].

In our study, Platelet count was statistically significantly [p-value = 0.016] lower in aberrant B-ALL patients than in non-aberrant B-ALL patients, but it was statistically significantly [p-value = 0.048] higher in aberrant T-ALL patients than in non-aberrant T-ALL patients.

The hemoglobin level was statistically significantly [p-value = 0.048] decreased in non-aberrant T-ALL patients [8.2 ± 1.11] as compared to aberrant T-ALL patients [9.8 ± 0.97].

Considering the examined hematological features, there was no statistically significant [p-value > 0.05] difference between aberrant and non-aberrant AML patients.

Similar results were reported by **Vitale *et al.*** [24] in ALL patients, who discovered that patients with aberrant myeloid expression had higher platelet counts. This investigation also revealed that the group with greater myeloid expression had higher platelet values. In contrast to our findings, **Silva *et al.*** [25] reported no statistically significant difference between ALL patients with and without aberrancy regarding platelet count.

Determining the platelet count when treating children with ALL is important. Because of the lifetime of platelets in the circulation [8-10 days], lower platelet counts in the blood of patients diagnosed with AL show the high proliferative power of the leukemic clone. In addition, because of changes in capillary fragility secondary to inflammation, fewer than 50,000 platelets/mm^3 in patients with infection can lead to hemorrhage, characterized by epistaxis, gingival bleeding, gastrointestinal bleeding, and CNS bleeding, leading to the need for transfusion therapy and supportive care for children with ALL [26].

Conclusion: We concluded that aberrant phenotypes were found with considerable frequency in AL patients, but further studies on larger scales are needed to confirm the correlation of aberrancy to diagnosis, prognosis, and therapeutic response.

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