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The Impact of Immunophenotypes on Some Laboratory Measurements of Acute Lymphoblastic Leukemia Patients

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ABSTRACT

Expression of surface markers (CD) has an impact on the outcome of seventy five cases, where CD34 behaves as a bad prognostic factor, CD1, CD10, CD65 when expressed with hyperdiploidy have a good impact and could be considered as good prognostic factors. In addition to that aberrant expression of myleloid markers had high expression in normal karyotype and low frequency in hyperdiploidy so it had a bad prognostic impact. The T-cell phenotype had good impact in cases with hyperdiploidy but B-precusor behaved as bad prognostic factors with hyperdiploidy. Our study reported that B- precursor**,** and T-cell are good prognostic factor and biphenotypic and B-cell are bad prognostic ones

Key words: lymphoblastic leukemia, immunophenotypes, laboratory measurements

Introduction

Immunophenotypic classification of adult acute lymphoblastic leukemia (ALL) has great importance with respect to characterization of the disease, prognostication, and delineation of therapy (*Le et al.,* 2006).The close association between phenotypic subgroups of ALL with particular cytogenetic and molecular aberrancies accounts in part for the prognostic significance. An example includes myeloid marker co-expression (eg, CD13, CD33) in an older patient with precursor B-cell ALL, which could indicate presence of the Philadelphia chromosome (Ph). The addition of the tyrosine kinase inhibitor imatinib to chemotherapy for patients with Ph positive ALL has dramatically improved outcome. (Long *et al.,* 2013 and Bandyopadhyay *et al.,* 2005).

The incorporation of other targeted agents, such as monoclonal antibodies directed against specific hematopoietic cell surface antigens, has also been explored. Rituximab is a chimeric monoclonal antibody directed at surface CD20, which induces complement-dependent cytolysis, antibody-dependent cell-mediated cytotoxicity, and apoptosis. Rituximab has significant single agent activity in previously treated indolent non-Hodgkin lymphoma (NHL) and hairy cell leukemia.(Kathleen *et al.,* 2003 and Colovic *et al.,* 2012)The incorporation of rituximab into chemotherapy regimens has significantly improved disease-free survival (DFS) rates for certain subsets of NHL and other B-lineage lymphoproliferative disorders, such as Burkitt-type leukemia/lymphoma and mantle cell leukemia/lymphoma. This favorable impact of chemoimmuno therapy regimens on outcome has also extended to diseases such as chronic lymphocytic leukemia, where CD20 expression is even lower than normal B cells. (Pui 2006 and Yip *et al.,* 2006)The CD20 molecule is a B-lineage specific antigen expressed on both normal and malignant cells during nearly all stages of B-cell differentiation, with the exception of stem (precursor)cells and plasma cells. It is a 33 kDa to 37 kDa non glycosylated trans membrane phosphor protein that forms tetramers and functions as a calcium channel, playing an important role in cell-cycle progression and differentiation via downstream signaling pathways. Its role in the apoptosis pathways including regulation of the proapoptotic proteins SERCA3 and Bax/Bak by alterations in intracellular Ca^{++} metabolism has been established. The constitutive activation of the survival pathways involving NF-B and ERK1/2 by CD20 results in overexpression of Bcl-2–and Bcl-2–related gene, which in turn confer drug resistance. Thus, CD20 expression may be of prognostic relevance in addition to serving as a therapeutic target for monoclonal antibody therapy. (Schultz *et al.,* 2007 and Carneiro Borba *et al.,* 2012)
Heterogeneity in expression of CD20 among various B-cell malignancies has been well described. CD20 expression (defined as 20% leukemia cells positive) occurs in approximately 40% to 50% of ALL cases with precursor B-cell immunophenotype. The prognostic implicationsof CD20 expression has been investigated in childhood precursor B-cell ALL with conflicting results. (Borowitz *et al.,* 2005) identifieda worse event-free

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survival (EFS) with a higher fluorescence intensity of CD20, whereas (Jeha *et al.,* 2014 and Borowitz *et al.,* 2005) found that CD20 expression conferred a slightly favorable prognosis (5-year EFS rate of84% ± 2.9% versus 78% ± 3.1%, $p = .08$), suggesting that the intensity of therapy might influence the prognostic significance of CD20 expression. (Colovic *et al.,* 2012 and Zhang *et al.,* 2011)

Acute lymphoblastic leukemia is the most common malignancy of childhood, representing nearly one third of all pediatric cancers and three quarters of pediatric leukemia. Although the pathogenesis of the disease remains largely unknown, several investigations have focused on the role of cytogenetic aberrations, which may contribute to defective apoptosis, dysregulation of cell cycle regulatory genes, consequently expansion of malignant clone (Koehler *et al.,* 2013 and Schultz *et al.,* 2007). Despite its homogeneity at cellular level, ALL is clinically heterogeneous since some patients survive for a long time without therapy, while others progress towards more advanced stages and die despite aggressive treatment. These clinical observations have prompted numerous studies aimed at determining reliable prognostic markers capable of predicting the progression and outcome of the disease (Long *et al.,* 2013 and Yip *et al.,* 2006). Several factors may play a crucial role in monitoring disease prognosis and predicting the possibility of minimal residual disease, such as age, sex, race, leukemic burden, initial TLC, Hb level, platelet count, immunophenotyping and genetic characterization (Le *et al.,* 2006)

The aim of the work come out to study the impact of immunophenotyping on some laboratory measurements of acute lymphoblastic leukemia patients.

Materials and Methods

Seventy five ALL patients with a documented diagnosis of denovo ALL, referring to the Oncology Department, National Cancer Institute, Cairo University were enrolled in this study. All patients were subjected to diagnostic work up which included history and laboratory evaluation as follows:

Immunophenotypic Analyses

Performed on RBC-lysed whole bone marrow aspirate samples. A total of 2 x 10^6 cells per tube were stained, lysed, and then washed before acquisition. Forthe detection of cytoplasmic antigens, fixation and permeabilization steps were taken before staining using the InterPrep kit (Beckman-Coulter, Fullerton, CA) for TdT, and the Fix & Perm kit (Caltag Laboratories, Burlingame, CA) for myeloperoxidase. Three or four color flow cytometric immunophenotypic analysis was conducted using FACScanor FACS Calibur instruments (BD Biosciences, San Jose, CA). The antigens assayed included CD10, CD19, CD20, CD22, CD34, CD38,TdT, CD13, CD15, CD33, CD117, HLA-DR, myeloperoxidase, CD2, CD3, CD5, andCD7. All antibodies were obtained from BD Biosciences, except those directed against myeloperoxidase (Caltag) and TdT (Supertechs, Rockville, MD). Irrelevant monoclonal antibody reagents of the same isotypes, conjugated with the same fluorochromes (change donce during the study period when procedure was modified from3- to 4-color flow cytometry), were used as negative controls. Data were analyzed using Cell Quest (BD Biosciences). An arbitrary cut-off of 20% or more analyzed events brighter than the negative control stain was required for an antigen to be considered positive (Borowitz *et al.,* 2005 and Crist *et al.,* 1989).

Blood Chemistry

Estimation of liver functions:

Measurement of serum Alanine Transaminase (ALT)levels, serum Aspartate transaminase (AST) levels and Bilirubin(Total and direct).By kits supplied by (spectrum diagnostic system, Egypt) Routine tests were measured by microlab 200 semi- analyzer (Olgar *et al.,* 2005).

Estimation of kidney functions:

By kits supplied by (spectrum diagnostic system, Egypt Measurement of serum uric acid level**,** serum creatinine level and serum urea level(Olgar *et al.,* 2005)

Complet blood picture:

Automatic analyzer (agsysmex XT 1800 Provided by BM- Egypt) with 18 parameters and WBC 3 part differential (Hematology Analyzer)

Parameters: WBC, LY%, MO%, NE%, EO%, BA%, LY, MO, NE, EO, BA, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, PCT, MPV, PDW

Follow-up:

By the end of the 120 weeks of continuation therapy, complete re-evaluation was again confirmed by bone marrow analysis, then patients were put under follow-up once monthly by clinical examination + CBC.

Complete remission is defined as the disappearance of organomegaly, normalization of hematological indices and bone marrow normocellularity with <5% lymhoblasts. Early response to chemotherapy demonstrated by clearance of bone marrow or blood of lymphoblasts is accompanied by longer remissions and fewer late relapses(Winick *et al.,* 2004)

Statistical methods:

Data was analyzed using SPSS statistical package version 17 (SPSS INC.,). Numerical data were expressed as mean and stander deviation and median and range as appropriate qualitative data were expressed as frequency and percentage. Chi-square test (fisher's exact test) was used to examine the relations between qualitative and quantitative variable for quantitative data , comparison between two groups was done using (Man-Whitney test) non parametric - test. Comparison of reported measures was done using Friedman test. Spearman-rbo method was used to test correlation between numerical variant.

Results:

Seventy five patients with a diagnosis of ALL were included in this study. Their mean age was 37±15 years with median 40 year , minimum 4 year and maximum 71 years. Patients were divided according to immunophenotype to four groups T-cell, B-cell, B-precursor and biphenotypic. Our study reported that the frequency of male and female patients were respectively 62.7% , 37.3% . In all group, male cases had age mean 36.6± 15 mean Hb% 10.9 ± 0.9 and TLC mean 50 ± 27, on the other hand female cases had age mean 51.6 ± 5.1 mean Hb% 11.1± 0.8 and TLC mean 40± 20. A statistical significant difference was found between the three groups table (1) table (2). The frequency of immunophenotypes among the 75 studied patients was (50.7%) B-precursor, (18.7%)in B-cell cases, (24%) T cell cases and (6.7%)biphenotypic cases. Our study found that 29/75 (38.7%) achieved complete remission (CR) ,23/75 (30.7%) were partial remission(PR) and 23/75 (30.7) showed no response (NR), table (1). The studied cases were divided according to immunophenotype (IPT)to four groups T-cell, B-cell, B-precursor and biphenotypic. The mean age, total leukocytic count (TLC) and Hb% were comparable among the four groups. Patients with T-cell phenotype were 18/75 (24%) with mean age 32.4 ± 19.8, and mean TLC 78.3 with std 12.6; 7/18 (38.9) achieved CR, 5/18 (27.8%) PR and 6/18 (33.3%) showed no response. Patient with B-cell phenotype were 14/75 (18.6%) with mean age 37.7 ± 8.1, TLC 77.6 ± 13.6; 10/14 (71.4%) achieve CR, 4/14 (28.6%) were in PR and 0/14 (0%) showed no response. Patients with B-precursor phenotype were 38/75 (50.7%) with mean age 38.2 ± 14.3, and mean TLC 76.4 ± 12.1, 9/38 (23.7%) achieved CR, 12/38 (31.6%) were in PR and 17/38 (44.7%) showed no response. Patients with biphenotypic phenotype were 5/75 (6.6%) with mean age 51.6± 5.2, mean TLC 80.4 with std 12.7, 3/5 (60%) achieve CR,2/5 (40%) were in PR and 0/5 (0%) showed no response table (6)and table (7). On the other hand the studied cases were classified into three groups: Complete remission group which included 29/75 (38.7%), partial remission were 23/75 (30.7%) and no response group 23/75 (30.7%) table (1).

Table 1. The clinical features of the all the studied cases

	Frequency	Percent
Male	47	62.70%
Female	28	37.30%
T-cell	18	24%
B-cell	14	18.70%
B-precursor	38	50.70%
Biphenotype	5.00	6.70%
CR	29	38.70%
PR	23	30.70%
No response	23	30.70%
Free	49	65.00%
Dead	10	13.30%
Relapse	16	21.30%

Cr: complete remission pr: partial remission

Table 2. Differences between male and female in outcome of ALL patients

	Male		Female		
	Mean		Mean		p-value
Age	36.6	(±15)	51.6	(±5.2)	0.01
Hb%	10.9	(±0.9)	11.1	(±0.8)	0.001
TLC	50	(±27)	40	(±20)	0.05

According to phenotype we found that: Complete remission included T-cell 7/29 (24.1%) ,B-cell 10/29 (34.4%), B-precursor 9/29 (31%) and biphenotypic 3/29 (10.34%), p-value = 0.032.Partial remission included T-cell 5/23 (21.7%) ,B-cell 4/23 (17.3%), B-precursor 12/23(52%) and biphenotypic 2/23 (8.6%), p-value = 0.005. No response included T-cell 6/23 (26%) ,B-cell 0/23 (0%), B- precusor 17/23 (73.9%) and

biphenotypic 0/23 (0%) with p-value = 0.002 table (6).On the other hand , our study determined the frequency of the surface marker expression (CD) also in different groups, the markers studied were (CD34, CD10, CD1, CD 56, DR and aberrant expression marker as follow:CD34 was positive expression in 50/75 (66.7%) and negative in 25/75 (33.3%). CD10 was positive in 46/75 (61.3%) and negative in 29/75 (38.7%). CD56 was positive in 63/75 (84%) and negative in 12/75 (16%).CD1 was positive in 37/75 (49.3%) and negatively in 38/75 (50.6%). DR was negatively in 62/75 (82.7.7%) and positive in 13/75 (17.3%). Aberrant expression was negatively in 70/75 (93.3%) and positive in 5/75 (6.7%) table(5). Also, the study determined some medical measurements of blood chemistry which included liver functions (ALT, AST, Bilirubin (T&D)), kidney functions (urea , creatinine and uric acid), and full blood picture (Hb%, platelets count, WBCs count, differential WBCs count and blast cell count and correlated them to the different groups mentioned above reveal that results regarding response to treatment shows that Complete remission group showed TLC mean $5x10^9$ /L ± 3 , while partial remission group shows TLC mean 26 $x10^9$/L ± 13 , and no response group shows TLC mean 63 $x10^9$/L ± 15.A highly statistical significant difference was found between the three groups (p-value <0.001).Complete remission group shows Hb% mean 10.7g/dL ± 1 , while partially remission group shows Hb% mean 14.5 g/dL ± 1.2 ,and no response group showed Hb% mean 10.1 g/dL ± 0.4, A statistical significant difference was found between the three groups (p-value = 0.038) table (4).

Table 3. The outcome of the different phenotype groups.

	T-CELL		B-CLL		B- precursor		Biphenotypic		
	Mean		Mean		Mean		Mean		p-value
CD34	5.3	(±8)	16.1	(±20.1)	22.2	(±21.7)	5.8	(±4.5)	0.006
CD10	5.3	(±14.5)	1.2	(±1)	33.7	(±21.3)	5.1	(±7.1)	<0.001
CD 1	34.9	(±10.2)	5	(±5)	6.8	(±5.7)	2.8	(±1.3)	<0.001
TLC	35	(±25)	8	(±8)	37	(±28)	8	(±8)	<0.001
Blast	29.3	(±25.7)	8.3	(±8.3)	36.4	(±27.7)	10.6	(±8.6)	0.032
AST	38.6	(±6.1)	26.6	(±12.1)	35.6	(±7.6)	30.2	(±10.4)	0.012

Table 4. The clinico-pathological measurements and response to treatment.

	Complet remission		Partially remission		No response		
	Mean		Mean		Mean		p-value
Hb%	10.7	(±1)	14.5	(±1.2)	10.1	(±0.4)	0.038
Blast cell count	2.8	(±1.3)	23.6	(±5.1)	63.3	(±9.9)	<0.001
TLC	5	(±3)	26	(±13)	63	(±15)	<0.001
AST	28.2	(±9.5)	37.2	(±8.7)	39	(±4.3)	<0.001
ALT	27.4	(±11.5)	40.7	(±4.8)	39.3	(±5.6)	<0.001

Table 5. The frequency of marker expression between ALL patients groups.

	Positive	Negative
HLA-DR DR	13 (17.3%)	62 (82.7%)
CD1	37(49.3%)	38(50.6%)
CD10	46(61.3%)	29(38.7%)
CD34	50(66.7%)	25(33.3%)
CD56	63(84%)	12(16%)
MPO	5(6.6%)	70(93.4)

Table 6. The response of the phenotype groups.

		IPT					
		T-cell	B-cell	B-precursor	Biphenotype	Total	p- value
Response	CR	7 (38.9%)	10 (71.4%)	9 (23.7%)	3 (60%)	29 (38.70%)	0.0032
	PR	5 (27.7%)	4 (28.6%)	12 (31.6%)	2 (40%)	23 (30.70%)	0.005
	No response	6 (33.3%)	0 (0.00%)	17 (44.7%)	0 (0.00%)	23 (30.70%)	0.002
Total		18	14	38	5	75	

IPT: immunophenotyping

Table 7. The frequency of risk features in phenotypes groups.

		AGE		TLC	
		Mean		Mean	
IPT	T-cell	32.4	(±19.8)	78.3	(±12.6)
	B-cell	37.7	(±8.1)	77.6	(±13.6)
	B-precursor	38.2	(±14.3)	76.4	(±12.1)
	Biphenotype	51.6	(±5.2)	80.4	(±12.7)

Complete remission group showed blast cell count mean 2.8% ± 1.3, while partial remission group showed blast cell count mean 23.6% ± 5.1, and no response group showed blast cell count mean 63.3 % ± 9.9, A highly statistical significant difference was found between the three groups (p-value <0.001).Complete remission group showed ALT mean 27.4 U/L ± 11.5, while partially remission group showed ALT mean 40.7 U/L ± 4.8 , and no response group showed ALT mean 39.3 U/L ± 5.6, A highly statistical significant difference was found between the three groups (p-value <0.001). Complete remission group showed AST mean 28.2 U/L ± 9.5, while partial remission group showed AST mean 37.2 U/L ± 8.7 , in addition to no response group showed AST mean 39.2 U/L ± 4.3; A highly statistical significant difference was found between the three groups (p-value <0.001). table (4).In T-cell cases our study found bone marrow relapse (BMR) in 3/18 (16.6%), 0/18(0%) died and 15/18 (83.3%) had free survival, in B-cell cases our study found bone marrow relapse (BMR) in 7/14 (50%), 1/14 (7.10%) died and 6/14 (42.8%) had free survival . In B-precursor cases our study found bone marrow relapse in 4/38 (10.5%), 7/38(18.4%) died and 27/38 (71%) free survival, in biphenotypic cases our study found bone marrow relapse was in 2/5 (40%), 2/5(40%) died and 1/5 (20%) free survival table (8).

Table 8. The frequency of the dead, relapse and free survival between phenotypes groups

		Relapse	Dead	Free
Response	T-cell n= 18	3 (16.6%)	0 (0.00%)	15 (83.30%)
	B-cell n= 14	7 (50%)	1 (7.1%)	6 (42.8%)
	B-precursor n= 38	4 (10.5%)	7 (18.4%)	27 (71%)
	biphenotypic n=5	2 (40%)	2 (40%)	1 (20%)
Total n= 75		16 (21%)	10 (13%)	49 (65%)

Discussion

Acute Lymphoblastic Leukemia (ALL) is a malignant disorder characterized by a clonal expansion of lymphoid progenitor cells arrested at different differentiation steps, whose progressive accumulation causes bone marrow involvement with more than 20% blast cells at diagnosis. The causes of ALL remain largely unknown, although environmental, immunodeficiency and genetic factors were found to play an important role (Pui, 2006)The aim of the current study is to identify major immunophenotypic subgroups in Egyptian ALL patients and to determine its correlation with the clinical presentation .Seventy five patients with ALL in whom immunophenotypic pattern were identified, were included in this study. All patients received a uniform ALL chemotherapy protocol at the Oncology Unit, NCI, Cairo University. Patients were stratified according to their cell surface marker expression. Among our patient population, great variability was observed concerning the incidence of phenotypic markers with the lab measurements. Patients were divided according to immunophenotype to four groups T-cell, B-cell, B-precursor and biphenotypic and the predominant pattern was B- precursor phenotype(Amare *et al.,* 1999).Our study reported that the frequency of male and female patients were respectively 62.7% and 37.3% in all group. Male cases had age mean 36.6 ± 15 year, mean Hb% 10.9 ± 0.9 g/dl and TLC mean $50x10^9$ /L ± 27. On the other hand female cases had age mean 51.6± 5.1 mean Hb% 10.1 g/dl ± 0.8 and TLC mean 40 $x10^9$/L ± 20; A statistical significant difference was found between the three groups (p-value <0.005). Our study approved that gender had a prognostic factor, where female had lower mean TLC and Hb% and male had higher mean TLC and low Hb% , so female gender was a good prognostic factor and this is in agreement (Friedmann and Weinstei *2000).*An increased hemoglobin level is a high risk factor as it indicates extra medullary involvement and high blast count in the proliferative stage of the cell cycle (Pui, 2006).Our finding showed that the frequency of immunophenotypes among the 75 studied patients was (50.7%) B-precursor, (18.7%)in B-cell cases, (24%) T cell cases and (6.7%) biphenotypic cases, so the B-precursor is the predominantphenotype in our cases. The study revealed that 29/75 (38.7%) achieved complete remission (CR), 23/75 (30.7%) were in partially remission (PR) and 23/75 (30.7) had no response (NR).On the other hand we discussed the mean age, total leukocytic count (TLC) and immunophenotypes as prognostic factors. The studied cases were divided according to immunophenotype to four groups: T-cell, B-cell, B-precursor and biphenotypic and the mean age, total leukocytic count (TLC) and response to treatment were comparable among the four groups. The results showed that patients with B-cell phenotype had the higher frequency of achieving CR (71%) and the low frequency was in patients with B-precursor phenotype (23%). the high frequency of PR was in patients with biphenotypic (40%) and low frequency was in patients with T-cell phenotype (27%).(Crist *et al.,*1989).

On the other hand, the high frequency of cases who achieved no response was in cases who had B-precursor phenotype (44%) and the low frequency was in cases with T-cell phenotype (33%). In our study the B-cell phenotype behaved as a good prognostic factor and biphenotypic was a bad prognostic factor and this was in disagreement with (Silva *et al.,* 2002 and.

The difference between our results and other international reports may be due to the presence of high risk features studied among the cases as age and high TLC. This difference also could be due to the low number of patients within each phenotypic group in our study. Alsosignificant differences between the four groups in TLC and age were found. *GroupeFrancais, 1996*) On the other hand, the studied cases were classified into three groups: Complete remission group which included 29/75 (38.7%), partial remission group 23/75 (30.7%) and no response group 23/75 (30.7%). The three groups were classified by their immunophenotype as follows: Complete remission included high frequency in cases with B-cell phenotype 10/29 (34.4%), partial remission included high frequency in cases with B-precursor 12/23 (52%), and no response included high frequency in cases with B-precursor 17/23 (73.9%) On the other hand , our study determined the frequency of the surface marker expression (CD) in the different groups (Amare *et al.,* 1999) The markers studied were (CD34, CD10, CD1, CD 56, DR and aberrant expression markers as follows:CD34 was positive expression in 50/75 (66.7%) and negative expression in 25/75 (33.3%). CD10 was positively expressed in 46/75 (61.3%) and negative in 29/75 (38.7%). CD56 was positively expressed in 63/75 (84%) and negative in 12/75 (16%).CD1 was positively expressed in 37/75 (49.3%) and negatively expressed in 38/75 (50.6%). DR was negatively expressed in 62/75 (82.7.7%) and positive in 13/75 (17.3%). Aberrant expression was negatively expressed in 70/75 (93.3%) and positive in 5/75 (6.7%). Expression of surface markers (CD) was correlated to the disease outcome where CD34 was highly expressed and had a bad prognostic implication. CD1, CD10, CD65 were expressed with high frequency and thusappearing to have a good impact and could consider as good prognostic factors. Aberrant expression had low frequency might have a bad prognostic impact (Crist *et al.,* 1989).

On the other hand , our study determined some medical measurements of blood chemistry which included liver functions (ALT, AST, Bilirubin (T&D) , albumin, alkaline phosphatase and GGT), kidney functions (urea, creatinine and uric acid), and full blood picture (Hb%, platelets count, WBCs count, differential WBCs count and blast cell count and correlated to the different groups mentioned above as follows: according to response to treatment the Complete remission group showed TLC mean $5x10^9/L\pm 3$, while partial remission group showed TLC mean 26 $x10^9/L\pm 13$,and no response group showed TLC mean 63 $x10^9/L\pm 15$(Crist *et al.,*1989). A highly statistical significant difference was found between the three groups (p-value <0.001).Complete remission group showed Hb% mean 10.7 g/dl ± 1 , while partially remission group showedHb% mean 14.5 g/dl ± 1.2 , in and no response group shows Hb% mean 10.1 g/dl ± 0.4. A statistically significant difference was found between the three groups (p-value =0.038) we agree in this with (Pui, 2006) who reported that increased hemoglobin level is a high risk factor as it indicates extra medullary involvement and high blast count in the proliferative stage of the cell cycle (Pui, 2006)Complete remission group showed blast cell count mean 2.8% ± 1.3, while partial remission group showed blast cell count mean 23.6% ± 5.1, and no response group shows blast cell count mean 63.3% ± 9.9. A highly statistical significant difference was found between the three groups (p-value <0.001).Complete remission group showed ALT mean 27.4 u/l ± 11.5, while partial remission group showed ALT mean 40.7 u/l ± 4.8 , and no response group showed ALT mean 39.3 u/l ± 5.6. A statistical significant difference was found between the three groups (p-value <0.001). Schultz *et al.,*2007) Complete remission group showed AST mean 28.2 u/l ± 9.5, while partially remission group showed AST mean 37.2 u/l ± 8.7 , and no response group showed AST mean 39.2 u/l ± 4.3. A statistical significant difference was found between the three groups (p-value <0.001).

High rate of cell turnover produces several metabolic disturbances leading to elevation of serum uric acid and acute renal failure resulting from urate nephropathy may be a presenting feature (Crist *et al.,*1989).T-cell cases in our study showed bone marrow relapse (BMR) in 3/18 (16.6%), 0/18(0%) died and 15/18 (83.3%) showed free survival. In B-cell cases our study found bone marrow relapse) in 7/14 (50%), 1/14 (7.10%) died and 6/14 (42.8%) showed free survival. In B-precursor cases our study found bone marrow relapse in 4/38 (10.5%), 7/38(18.4%) died and 27/38 (71%) showed free survival. In biphenotypiccases our study found bone marrow relapse (BMR) in 2/5 (40%), 2/5(40%) died and 1/5 (20%) showed free survival. Our study reported that B- precursor,andT-cell were good prognostic factors and biphenotypic and B-cell were bad prognostic ones and this is in agreement with (Komrokji *et al.,* 2003) who reported that T-cell behaves as good prognostic factor with hyperdiploidy *cases*. Moreover (Golemovic, 2006) proved that biphenotypicleukemias and B-cell ALL had bad prognosis, also reported that among factors with a negative influence on prognosis is B- precursor phenotype and this was confirmed in our study.

Conclusions:

In conclusion, the results revealed that T-cell phenotype behaves as a good prognostic factor while the biphenotypicleukemias and B-cell behaves as a bad prognostic one. Also B- precursor phenotype was factor

with a negative influence on prognosis. Surface markers (CD) were correlated to the disease outcome where CD34 was highly expressed and had a bad prognostic implication. CD1, CD10, CD65 were expressed with high frequency and appearing thus to have a good impact thus couldbe considered as good prognostic factors. Aberrant expression had low frequency might have a bad prognostic impact

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