RESEARCH ARTICLE

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Frequency and Prognostic Impact of Aberrant Antigens Expression among Egyptian Adult Acute Leukemia

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Abstract

Objective: Aberrant antigen expression was reported to be due to genetic and epigenetic dysregulation. This study aimed to address aberrant antigen expression and its link to poor prognostic genetic markers in acute leukemia patients. **Methods:** This study included 432 newly diagnosed acute leukemia patients (AML, B-ALL). For all included patients blast cells expression for line assignment CD33 *CD13* on B-All and *CD7* on cytogenetically normal-AML blasts was assessed by flow cytometry in parallel to FLT3 and Philadelphia and philadelphia like chromosome in B-ALL. **Results:** From the total 432 cases of acute leukemia, the most frequent aberrant antigen expressed in B acute lymphoid leukemia (ALL) was *CD33* (23.3%) followed by *CD13*(16.7%); while the most frequent one in AML was CD7 (16.7%). Aberrant myeloid phenotype in B-ALL was associated with lower mean total leukocytes count (TLC), low platelets count, positive Philadelphia like chromosome, shorter overall survival compared to the B-ALL without. Aberrant lymphoid phenotype (*CD7*) in AML was associated with a higher platelets count, *FLT3* mutation, shorter disease-free and overall survival compared to those patients without. **Conclusion:** CD7 aberrant antigen expression is frequently detected in patients with CN-AML and frequently associated with FLT3 mutation. While in patients with B-ALL the most frequently detected ones are *CD33* and *CD13* which are frequently associated with Philadelphia like chromosome.

Keywords: CD7- *CD33*- *CD13*- CN-AML- B-ALL

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Introduction

Acute leukemia (AL) is a disease of clonal hematopoietic stem cells in which cell growth and differentiation are not regulated. AL is divided into acute lymphocytic leukemia (ALL), and acute myeloid leukemia (AML) based on the expression of certain surface molecule named cluster of differentiation (CD). Flow cytometric immunophenotyping has a crucial role in the identification of leukemic lineage characteristics as well as aberrant antigen expression (Ahuja and Malviya, 2022). Aberrant antigen expression was attributed to abnormal genetic process that makes precursor cells retain features of one lineage, which should be lost during differentiation to another lineage (Sarma et al., 2015; Gupta et al., 2021). The specific phenotypic pattern and aberrancies on leukemic cells can be used in monitoring minimal residual disease (MRD) after chemotherapy (Gupta et al., 2021).

Previous studies reported wide variation in frequency of these aberrancies in both B-ALL and CN-AML. These immunophenotypic aberrancies could predict treatment outcome in acute leukemia. Some studies report poor prognostic effect, while other failed to get any association between aberrant antigen expression and patients' outcome (Hussein et al., 2021).

The aim of our study was to assess the frequency of aberrant antigens expression in both CN-AML and B-ALL patients and determine their prognostic impact on patients' outcome.

Materials and Methods

Subjects

This study included 432 newly diagnosed patients with acute leukemia (156 females and 276 males, median age 45 years, range 18 to 81years); attending to Mansoura University Oncology Center (MUOC). Patients were diagnosed according to 2016 WHO specification using morphological, immunophenotypic, and cytogenetic molecular evaluations. The included patients were subcategorized into 252 patients with CN-AML and 180 patients with B-ALL.

All included patients were observed for up to 36 months. We have received informed written consent from all participants. Patients were excluded (leukemic patients under 18 years, patients with other malignancies, patients who received prior treatment). All patient clinical data including age, sex, complete hemogram, and course of

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disease were recorded. For all included acute leukemia patients complete immunophenotyping panel were done. For B-ALL patients both Philadelphia chromosome (*BCR/ABL 190* fusion gene) was identified by Real time PCR and *CRLF2* expression was assessed by flow cytometry. *FLT3-ITD* mutation was identified in CN-AML.

CN-AML patients were treated by cytarabine based intensive chemotherapy regimen with different dosages during induction therapy based on performance status, while B-ALL patients were treated with pediatric inspired protocol plus tyrosine kinase inhibitors (only for Philadelphia chromosome positive cases) and Hyper-CVAD for adult patients. Relapsed/ refractory cases were treated by either HAM (high dose cytarabine and mitoxantrone) or FLAG (fludarabine, cytarabine and G-CSF) protocol.

Response was defined as complete response (CR) no circulating blasts or extramedullary disease, trilineage hematopoiesis (TLH) and < 5% blasts, absolute neutrophil count (ANC) > 1000/uL, platelets > 100,000/uL and no recurrence for 4 weeks. Refractory disease was failure to achieve CR at the end of induction. Induction death (ID) was defined as occurrence of death during induction phase. Relapsed disease was defined as reappearance of blasts in the blood or bone marrow (> 5%) or in any extramedullary site after a CR.

Identification of leukemic blast cells immunophenotyping by flowcytometry

Fresh BM EDTA samples were processed within 2hs from sampling. Flowcytometric analysis was done using different monoclonal antibodies labeled with different flourochromes on bone marrow samples using standard stain/lyse/wash method. Acquisition of minimum of 50,000 events was done employing (Navios EX Flow Cytometer (Beckman coulter).

Blast cells were gated after initial gating by forward scatter area on X-axis versus forward scatter height on Y-axis to exclude doublets, then another gate was done using *CD45* versus forward scatter (FSC) to include only viable cells, then blast population were gated as low side scatter (SCC) in dim *CD45* and calculated as a percentage of the total number of gated events. Expression of various surface and cytoplasmic markers was analyzed on blast population.

FLT3-ITD mutation detection

One milliliter EDTA bone marrow sample was collected. DNA extraction was done using QIAmp DNA blood mini kit QIAGEN. Two µL of DNA was extracted followed by thermal amplification (95oC for 5 minutes), 40 cycles of the next steps: denaturation 95°C for 30 seconds, annealing (56°C for 45 seconds) and extension (72°C for 30 seconds). The final extension was done at 72°C for 10 minutes. The primers used for *FLT3-ITD* gene mutation detection were as follow: forward primers: 14F: 5'-GCAATTTAGGTATGAAAGCCAGC-3' and reverse primers: 15R: 5'- CTTTCAGCATTTTGACGGCAAC -3'. *FLT3-ITD* type will produce a single band of 329 bp, while mutant *FLT3-ITD* produced additional band larger than 329 bp.

Immunophenotyping CRLF2 staining

The *CRLF2* expression was identified using the following combination of MoAb: *CD45* Amcyan, *CD34 PECy7, CD3 PerCP, MPO PE, CD13* or *CD7 FITC*, and *CRLF2 APC* (BD, Franklin Lakes, NJ, USA). Incubate the fresh BM sample (50 µL) with surface MoAb (10 µL) for 20 minutes at room temperature. Then, 2mL of the diluted FACS Lysing Buffer (BD Biosciences, CA, USA) was added to the samples and incubated for 10 minutes at room temperature. The samples were washed two times in phosphate-buffered saline (PBS) and then the pellet was resuspended in the PBS. As a minimum 50,000 events per tube were acquired on the BD FACSCanto II™ (BD Biosciences, CA, USA) and analyzed using the FACS DIVA software (BD, Franklin Lakes, NJ, USA. The negative control for the CRLF2 staining was defined as the mature lymphocytes in BM samples analyzed. A 10% limit of CRLF2-positive cells was used to identify positive samples in blast sub clones.

Philadelphia chromosome detection

The RNA extraction was performed by phenol/ chloroform method from fresh BM EDTA samples. The cDNA was used to PCR, using specific primers for *BCR-ABL* genes and quantified by Real time PCR. Primer sequences used for qualitative RT-PCR (Forward primer: BCR E-12 AGA ACA TCC GGG AGC AGC AGA AGA A; Reverse primer: ABL-2 TCC AAC GAG CGG ATT CAC T).

Statistical analysis

Statistical analysis was conducted using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent and compared by using Chi square test. Non-normally distributed continuous variables were presented as median (min-max). Mann Whitney test (for comparing non-parametric data between two groups) was used. Kaplan- Meier test was used for survival analysis and statistical significance of differences among curves was determined by Log-Rank test. For all above mentioned statistical tests done, the results were considered significant when the $p \leq 0.05$.

Results

Patient's characteristics

252 patients were categorized as CN-AML (58.3%) aged from (18 to 81 years), (156 males, 96 females) and rest 180 patients were subtyped as B-ALL (41.7%) aged from (18 to 73 years), (120 males, 60 females).

Immunophenotypic analysis

In CN-AML, *CD7* was the most frequent aberrant antigen expression (16.7%). In B-ALL, 42/180 (23.3%) cases had *CD33* aberrant antigen expression and followed by *CD13* (16.7%) (Figure 1).

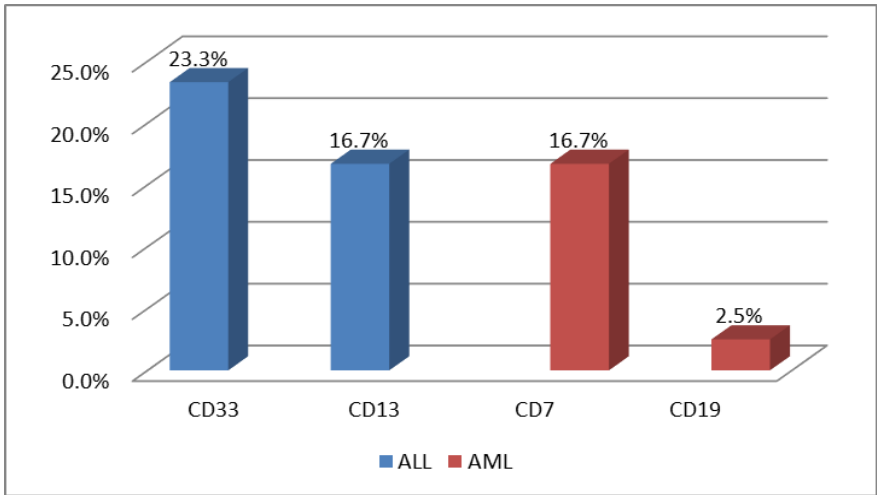

Figure 1. Displayed the Frequency of Aberrant Antigens Expression in Patients with B-ALL and CN-AML. The most frequent ones in B-ALL are *CD33* (23.3%) and *CD13*(16.7%), and in patients with CN-AML is CD7 (16.7%).

Impact of aberrant antigen expression on clinicopathological characteristics

Regarding the effect of *CD13* and *CD33* aberrant antigen expression on clinicopathological characteristics of B-ALL patients, B-ALL patients with *CD13* aberrant antigen expression are significantly older than B-ALL patients without *CD13* aberrant antigen expression. Platelet is significant reduced in B-ALL with *CD13* aberrant antigen expression compared to B-ALL patients without *CD13* aberrant antigen expression, while WBC was significantly higher in B-ALL with *CD13* aberrant antigen expression compared to B-ALL patients without *CD13* aberrant antigen expression. Non-CR and dead are more frequent in B-ALL with *CD13* aberrant antigen expression compared to B-ALL patients without *CD13* aberrant antigen expression. Relapsed and dead B-ALL patients are more frequent in B-ALL patients with *CD33* aberrant antigen expression compared to B-ALL patients without *CD33* aberrant antigen expression. Unfavorable risk stratification is more frequent in B-ALL patients with *CD33* or *CD13* aberrant antigen expression compared to B-ALL patients without aberrant antigens expression (Table 1). Philadelphia chromosome-like and unfavorable risk stratification is more frequent in B-ALL patients with *CD33* or *CD13* aberrant antigen expression compared to B-ALL patients without aberrant antigen expression

Table 1. Effect of Aberrant Expression of *CD13* and *CD33* on Clinicopathological Characteristics in B-ALL Patients.

Parameter		CD33		CD13		P[1]	P[2]
		Negative	positive	Negative	positive		
Age* (years)	Median (Min-max)	38.0 (18-73)	49.0 (18-61)	30.0 (18-73)	48.0 (40-68)	0.327	0.001
Gender	Male	96 (69.6%)	24 (57.1%)	102 (68.0%)	18 (60.0%)	0.135	0.396
	Female	42 (30.4%)	18 (42.9%)	48 (32.0%)	12 (40.0%)		
Hb g/dl*	Median (Min-Max)	8.0 (3.0-13.8)	8.9 (5.0-12.1)	8.7 (3-13.8)	7.9 (7.4-11.0)	0.542	0.213
WBCS $\times 10^9$/L*	Median (Min-Max)	5.5 (2.7-150)	66.0 (2.7-125.0)	5.5 (2.7-150.0)	42.2 (4.0-125.0)	0.088	0.003
PLT $\times 10^9$/L*	Median (Min-Max)	32.0 (7-289)	28.0 (18-111)	32.0 (7-289)	18.0 (7-92)	1	0.027
BM blast cells%*	Median (Min-Max)	90.0 (35-95)	87.0 (48-98)	87.0 (35-95)	90.0 (35-98)	0.214	0.105
Philadelphia and Philadelphia like Chromosome	Negative	96 (96.6%)	18 (42.9%)	102 (68.0%)	12 (40.0%)	0.002	0.004
	Positive	42 (30.4%)	24 (57.1%)	48 (32.0%)	18 (60.0%)		
Response	CR	114 (82.6%)	30 (71.4%)	126 (84.0%)	18 (60.0%)	0.113	0.003
	Non-CR	24 (17.4%)	12 (28.6%)	24 (16.0%)	12 (40.0%)		
Relapse	Non-relapsed	96 (84.2%)	12 (40.0%)	96 (76.2%)	12 (66.7%)	<0.001	0.383
	Relapsed	18 (15.8%)	18 (60.0%)	30 (23.8%)	6 (33.3%)		
Outcome	Alive	84 (60.9%)	18 (42.9%)	90 (60.0%)	12 (40.0%)	0.039	0.044
	Dead	54 (39.1%)	24 (57.1%)	60 (40.0%)	18 (60.0%)		
Risk stratification	Favorable	84 (60.9%)	12 (28.6%)	90 (60.0%)	6 (20.0%)	<0.001	<0.001
	Unfavorable	54 (39.1%)	30 (71.4%)	60 (40.0%)	24 (80.0%)		
Cumulative incidence of OS**		57.80%	42.90%	55.80%	40.00%	<0.001	0.025
Cumulative incidence of DFS**		82.80%	26.70%	72.40%	66.70%	<0.001	0.491

Continuous variables are expressed as median (min-max).* data are compared using Mann-Whitney tests, Chi square test, log rank test ** P^1, between *CD33* groups, P^2, between *CD13* groups. **significant (P value < 0.05).

Table 2. Effect of Aberrant Epression of *CD7* on Clinicopathological Characteristics in CN-AML Patients

Parameter		CD7		P
		Negative	positive	
Age* (years)	Median (Min-Max)	44.0 (18-81)	50.0 (19-70)	0.06
Gender	Male	126 (60.0%)	30 (71.4%)	0.164
	Female	84 (40.0%)	12 (28.6%)	
Hb g/dl*	Median (Min-Max)	7.8 (4-11.9)	7.0 (6-9.6)	0.087
WBCs $\times 10^9$/L*	Median (Min-Max)	20.0 (1-281)	21.0 (0.8-56)	0.646
PLT $\times 10^9$/L*	Median (Min-Max)	33.0 (5-529)	29.4 (12-49)	0.008
BM blast %*	Median (Min-Max)	70.0 (24-98)	70.0 (30-90)	0.165
FLT3 mutation	Negative	176 (83.8%)	14 (33.3%)	<0.001
	Positive	34 (16.2%)	28 (66.7%)	
Induction remission Response	CR	150 (73.5%)	24 (57.1%)	0.034
	Non-CR	54 (26.5%)	18 (42.9%)	
Relapse	Non-relapsed	108 (72.0%)	6 (25.0%)	<0.001
	Relapsed	42 (28.0%)	18 (75.0%)	
Outcome	Alive	90 (42.9%)	6 (14.3%)	0.001
	Dead	114 (54.3%)	36 (85.7%)	
Cumulative incidence of OS**		40.30%	14.30%	<0.001
Cumulative incidence of DFS**		54.40%	0.00%	<0.001

Continuous variables are expressed as median (min-max).* data are compared using Mann-Whitney tests, Chi square test, log rank test ** P^1, between *CD33* groups; P^2, between *CD13* groups. **significant (P value < 0.05)

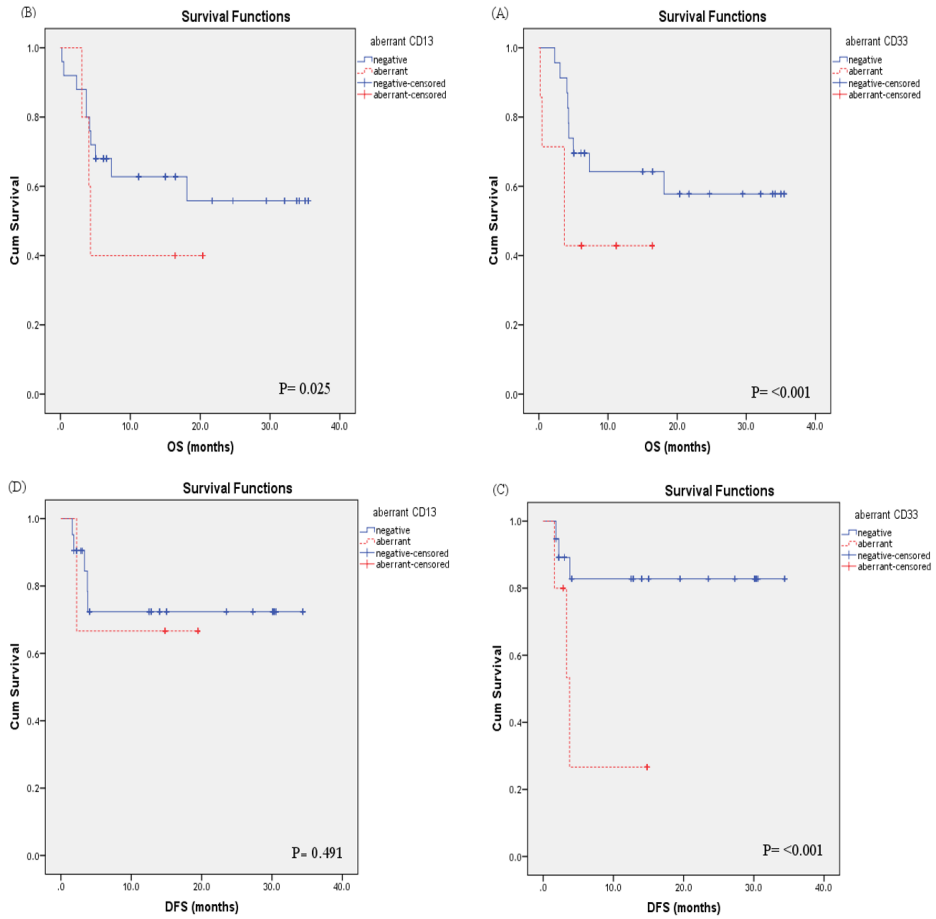

Figure 2. Kaplan-Miere Curve for Impact of Aberrant *CD33* Expression and Aberrant *CD13* Expression on OS and DFS of B-ALL Patients. Figure (2A,2B) showed that Patients with aberrant *CD33* expression and aberrant *CD13* expression had shorter cumulative OS survival as compared to those without aberrant expression (P=<0.001, and =0.025 respectively). Figure (2C) showed that Patients with aberrant *CD33* expression had shorter cumulative DFS as compared to those without aberrant expression (P= <0.001),While DFS (Figure 2D) was not significantly different between those with and without *CD13* aberrant expression (P= 0.491).

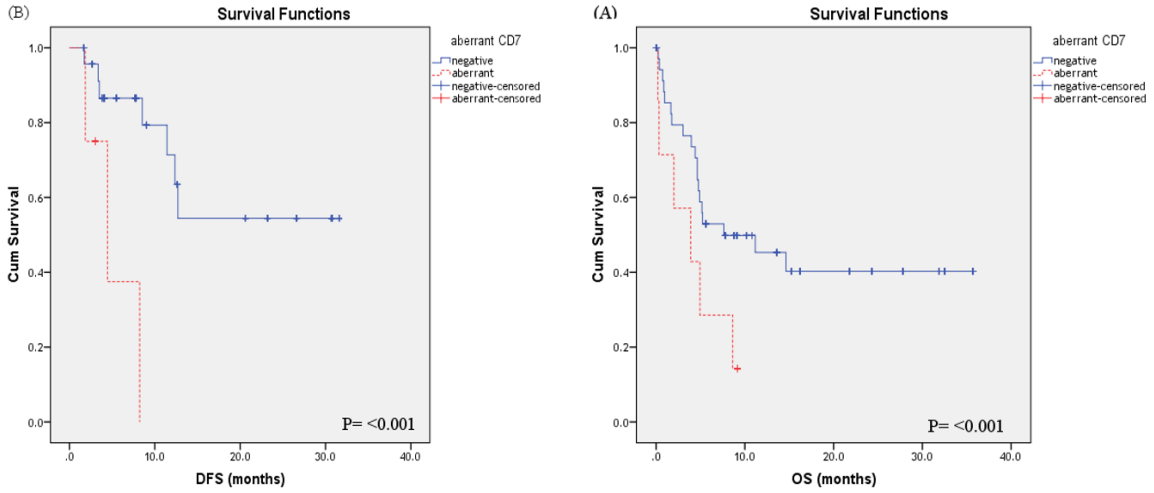

Figure 3. Kaplan-Miere Curve for Impact of Aberrant *CD7* on OS and DFS of CN-AML Patients. Figure (3A) showed that Patients with aberrant CD7 expression had shorter cumulative OS survival as compared to those without aberrant expression (P=<0.001). Figure (3B) showed that Patients with aberrant *CD7*expression had shorter cumulative DFS as compared to those without aberrant expression (P= <0.001).

(Table 1).

Regarding the effect of *CD7* aberrant antigen expression on clinicopathological characteristics of CN-AML patients, platelet is significant reduced in CN-AML with CD7 aberrant antigen expression compared to CN-AML patients without *CD7* aberrant antigen expression. Non-CR, relapsed cases, dead cases are more frequent in CN-AML with *CD7* aberrant antigen expression compared to CN-AML patients without *CD7* aberrant antigen expression (Table 2). FLT3 mutation and Poor risk stratification are more frequent in CN-AML patients with *CD7* aberrant antigen expression compared to CN-AML patients without aberrant expression (Table 2).

Impact of aberrant antigen expression on OS and DFS

B-ALL patients were classified as regard aberrant antigen expression into B-ALL patients with and without *CD33* aberrant antigen expression and also B-ALL patients with and without *CD13* aberrant antigen expression. CN-AML patients were classified as those with and without *CD7* aberrant antigen expression.

In B-ALL, patients with *CD33* and *CD13* aberrant antigens expression had significantly shorter OS compared to patients without *CD33* aberrant antigen expression and without *CD13* aberrant antigen expression (P=<0.001, P=0.025 respectively), as regard DFS those with aberrant *CD33* expression had significantly shorter DFS (P=<0.001) (Figure 2). CN-AML patients with *CD7* aberrant antigen expressions had significantly shorter OS and DFS compared to patients without aberrant *CD7* (P=<0.001 for both) (Figure 3).

Discussion

Proper risk categorization of acute leukemia is essential in management and can be only obtained if patients are thoroughly investigated with various technical tools. One of these tools is flow cytometry that allows identification of immunophenotypic profile and assessment of frequency of aberrant phenotype (Rashed et al., 2020).

Regarding the frequency of aberrant antigen expression, the present study revealed that *CD7* was the most predominant aberrant antigen expressed in CN-AML patients and *CD33* and *CD13* were the most frequent aberrant antigens expressed in B-ALL patients which was in agreement with majority of studies (Al Anizi and Al Mashta, 2017; Cruse et al., 2005; Rodríguez Rodríguez et al., 2016). In contrary to these results, (Bhushan et al., 2010; Aparna and Murugesan, 2018; Gupta et al., 2019) observed CD19 as the most frequent aberrant marker in AML. The present study noted that the most common aberrant markers in B-ALL was *CD33* followed by *CD13*. These results go in harmony with previous studies (Bhushan et al., 2010; Kamal et al., 2016; Sivakumar et al., 2021) while another studies reported that *CD13* was the most common aberrant marker in B-ALL (Mazher et al., 2013; Chaudhary et al., 2018; Sharma et al., 2016).

In the present study *CD13* aberrant antigen expression in B-ALL cases were associated with higher median WBCs and lower median platelet count. This is in line with the finding reported by Sivakumar and Basu (2021). However, Lopes et al., (2014), demonstrated higher platelets count and Sharma et al., (2016) reported lower TLC and Bhushan et al., (2010) didn't find any statistical significance among hematological parameters between B-ALL with and without aberrant expression. In the current study, we found lower platelet count in CN-AML patients with *CD7* aberrant antigen expression. Similar results were identified by Sharma et al., (2016). On the contrary Bhushan et al., 2010; Aparna and Murugesan, 2018 stated that there is no significant association between any of hematological parameters and aberrant lymphoid antigen in CN-AML cases.

The molecular genetics (Philadelphia and Philadelphia chromosome-like) findings were more frequently detected in B-ALL patients with *CD33* or *CD13* aberrant antigens expression compared to B-ALL patients without

aberrant expression. Similar finding was reported by Sivakumar and Basu (2021); Vitale et al., (2014) but did not reach the levels of significance. No previous study evaluated the association between aberrant antigens expression and Philadelphia like chromosome. Furthermore, CN-AML patients with *CD7* aberrant expression is frequently associated with FLT3 mutation. On contrary to these result, Bhushan et al., (2010); Rai et al., (2014) founded no significant association between the frequency of FLT3 mutation and aberrant *CD7* expression in CN-AML patients. Analysis the impact of aberrant antigens expression on CR and relapse, the present study demonstrated that CR was more frequent in B-ALL patients without *CD13* or *CD33* aberrant antigens expression but the difference did not reach the level of significance. while relapse was more frequent in B-ALL patients with aberrant *CD33* expression compared to patients without aberrant expression. Similar results reported by Mohamed et al., (2021) who noted that B-ALL patients without aberrant expression achieved significant higher CR rates that patients with aberrant expression, also relapse occurred more in B-ALL patients with aberrant expression. As regard AML patients with *CD7* aberrant antigen expression had significant lower CR rates and higher relapse rate compared to patients without aberrant expression. These result in agreement with Mohamed et al., (2021) who reported that CR was higher in AML patients without aberrant expression but without statistical significance, while significance higher relapse rates in AML patients with aberrant expression detected.

Regarding the impact of aberrant expression on OS and DFS. B-ALL patients with *CD33* and *CD13* aberrant antigens expression had shorter OS compared to B-ALL patients without aberrant expression, while only ALL patients with *CD33* aberrant antigen expression had shorter DFS compared to patients without aberrant expression. These results are in harmony with that reported by Dalal et al., (2014), who stated that adult B-ALL patients with *CD13* aberrant antigen expression had shorter OS and RFS. Contrary to these results Abdulateef et al., (2014) documented a significant difference was detected in ALL group with and without aberrant. CN-AML patients with aberrant *CD7* expression had significant shorter OS and DFS compared to patients without aberrant expression. Similar results reported by Rai et al., (2014) who stated that *CD7* aberrant expression in AML patients had significant bad impact on OS and DFS, moreover Sadek et al., (2020) documented that *CD7* aberrant antigen expression in CN-AML patients showed significant shorter OS. On contrary to these results Abdulateef et al., (2014) documented that on significance difference between AML patients with and without aberrant expression with respect to OS or DFS.

In conclusion, *CD7* is the most frequent aberrant antigen expression in patients with CN-AML and frequently associated with FLT3 mutation. While in patients with B-ALL the most frequent aberrant antigens expression is *CD33* which is frequently associated with philadelphia like chromosome.

Author Contribution Statement

Conception: Salah Aref, Nadia El Menshawy; Interpretation and analysis of data: Omnia Khaled, Mohamed Ayed, Mohamed Aref; Preparation of the manuscript: Omnia Kahaled, Mohamed Aref, Mohamed Ayed; Revision for important intellectual content: Omnia Khaled, Mohamed Ayed; Supervision: Salah Aref, Nadia, El Menshawy

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Ethical aspects

This study was approved by the local Mansoura Faculty of Medicine Ethics Committee. Informed consent from all included subjects were taken prior to recruitment. The authors declare that there is no conflict of interest.

Availability of data

The data available upon request to the corresponding author

*Conflict of interes*t

The authors declare that there is no conflict of interest.

References

Abdulateef NA, Ismail MM, Aljedani H (2014). Clinical significance of co-expression of aberrant antigens in acute leukemia: a retrospective cohort study in Makah Al Mukaramah, Saudi Arabia. *Asian Pac J Cancer Prev*, **15**, 221-7.

Ahuja S, Malviya A (2022). Spectrum of immunophenotypic aberrancies in acute leukemia along with their correlation with adverse hematological parameters. *Indian J Health Sci Biomed Res*, **15**, 76-80.

Al-Anizi W, Al-Mashta M (2017). The frequency of aberrant lymphoid antigens expression in 202 Iraqi patients with de novo acute myeloid leukemia. *Iraq J Hematol*, **6**, 49-54.

Aparna S, Sharmila M (2018). Aberrant phenotypes in acute myeloid leukemia in India. *Int J Adv Med*, **5**, 361.

Bhushan B, Chauhan PS, Saluja S, et al (2010). Aberrant phenotypes in childhood and adult acute leukemia and its association with adverse prognostic factors and clinical outcome. *Clin Exp Med*, **10**, 33-40.

Chaudhary A, Attri SK, Mohini S (2018). Aberrant CD markers in patients with acute leukemia and response to induction remission therapy. *Int J Healthc Biomed Res*, **6**, 107 21.

Cruse JM, Lewis RE, Pierce S, et al (2005). Aberrant expression of *CD7*, CD56, and CD79a antigens in acute myeloid leukemias. *Exp Mol Pathol*, **79**, 39-41.

Dalal BI, Al Mugairi A, Pi S, et al (2014). Aberrant expression of *CD13* identifies a subgroup of standard-risk adult acute lymphoblastic leukemia with inferior survival. *Clin Lymphoma Myeloma Leuk*, **14**, 239-44.

Gupta M, Monga L, Mehrotra D, et al (2021). Immunophenotypic Aberrancies in Acute Leukemia: A Tertiary Care Centre Experience. *Oman Med J*, **36**, e218.

Gupta N, Pawar R, Banerjee S, et al (2019). Spectrum and Immunophenotypic Profile of Acute Leukemia: A Tertiary Center Flow Cytometry Experience. *Mediterr J Hematol Infect Dis*, **11**, e2019017.

Hussein G, Jawad A (2021). Impact of aberrant antigens expression on remission rate after first induction course of chemotherapy in de novo adult acute myeloid leukemia. *Iraq J Hematol*, **10**, 118-22.

Kamal N, Khasawneh R, Momani A (2016). Aberrant Antigen Expression in Patients with Acute Leukemias : Experience of King Hussein Medical Center in Jordan. *J R Med Serv,* **23**, 59-67.

Lopes TC, Andrade KN, Camelo NL, et al (2014). Influence of aberrant myeloid expression on acute lymphoblastic leukemia in children and adolescents from Maranhão, Brazil. *Genet Mol Res*, **13**, 10301-7.

Mazher N, Malik N, Imran AK, et al (2013). Aberrant Expression of CD Markers in Acute Leukemia. *Cancer Biomark*, **15**, 501-5.

Mohamed MA, Shafik EA, Ahmed AO, et al (2021). Expression of aberrant markers in acute leukemia at South Egypt Cancer Institute: A retrospective study. *SECI Oncol J*, **9**, 53-63.

Rai S, Singh S, Gupta R (2020). Prognostic significance of CD56 and *CD7* in acute myeloid leukaemia and their outcome. *Am J Blood Res*, **10**, 109-17.

Rashed A, Tarafder S, Sattar H, et al (2020). Hossain S, Expression of Aberrant Antigens in Adult Acute Leukemia: A Study in Bangladesh. *Int J Cancer Res*, **16**, 28-34.

Rodriguez S, Pomerantz A, Demichelis R, et al (2016). Impact of Aberrant Antigens in the Outcome of Patients with Acute Leukemia at a Referral Institution in Mexico City. *Rev Invest Clin*, **68**, 305-13.

Sadek N, Abd-eltawab S, Assem N, et al (2020). Prognostic Value of Absolute Lymphocyte count, Lymphocyte percentage, Serum albumin, Aberrant Expression of CD7, CD19 and the Tumor Suppressors (PTEN and p53) in Patients with Acute Myeloid Leukemia, *Asian Pac J Cancer Biol*, **5**, 131-40.

Sarma A, Hazarika M, Das D, et al (2015). Expression of aberrant CD markers in acute leukemia: a study of 100 cases with immunophenotyping by multiparameter flowcytometry. *Cancer Biomark*, **15**, 501-5.

Sharma M, Sachdeva MU, Varma N, et al (2016). Characterization of immunophenotypic aberrancies in adult and childhood acute lymphoblastic leukemia: A study from Northern India. *J Cancer Res Ther*, **12**, 620-6.

Sharma M, Varma N, Singh Sachdeva MU, Bose P, Varma S (2020). Clinical and hematological correlates of aberrant immunophenotypic profiles in adult and pediatric acute myeloid leukemia at presentation. *J Cancer Res Ther*, **16**, 105-9.

Sivakumar M, Basu A (2021). Aberrant immunophenotypic expressions in acute lymphoid leukemia: an observational analytical study. *Int J Res Med Sci*, **9**, 804.

Sivakumar M, Basu A (2021). Aberrant immunophenotypic expressions in acute lymphoid leukemia: an observation, Analytical study. *Int J Res Med Sci*, **9**, 804.