ORIGINAL ARTICLE

Evaluation of CD30 expression in B ALL and its correlation with MRD(Minimum Residual Disease)

Amirhossein Kazemian, Pardis Nematollahi
Department of Pathology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Background: This study was conducted to evaluate CD30 expression in minimum residual disease after chemotherapy in B-acute lymphoblastic leukemia (B-ALL). **Materials and Methods:** This was a cross-sectional study on 30 new cases of B-ALL between 2018 and 2019. We checked CD30 expressions in fresh bone marrow aspirates by flow cytometry. After 28 days of routine chemotherapy, we calculated minimal residual disease in CD30 positive and negative patients and compare them by Kolmogorov–Smirnov test. **Results:** Thirty patients with B-ALL with a mean age of 15.62 ± 20.488 were included in the study. CD30 marker was positive in about 10 patients and was negative in about 20 participants. Mean blast count in baseline in CD30 positive group was 77 ± 7.88%, in negative group was 76.3 ± 17.78 % (P = 0.292). After 28 days of chemotherapy mean minimal residual disease (MRD) was 1.07 ± 3.754 in the negative group, 0.12 ± 0.034 in the positive group (P = 0.025). **Conclusion:** Lower MRD on day 28 after chemotherapy was seen in B-ALL patients with baseline CD30 expression.

Keywords: Acute lymphoblastic leukemia, B lymphoblastic leukemia, CD30, flow cytometry, minimum residual disease

How to cite this article: Kazemian A, Nematollahi P. Evaluation of CD30 expression in B ALL and its correlation with MRD(Minimum Residual Disease). J Res Med Sci 2021;26:90.

INTRODUCTION

CD30, known as K1-antigen, is a member of tumor necrosis factor α-receptors.[1] It is expressed in some hematologic malignancies including B-cell and T-cell leukemia.[2] Due to its estimated role in the pathogenesis of refractory cases of acute lymphoblastic leukemia (ALL), several therapies such as brentuximab vedotin are now targeted this receptor.[3] In ALL patients, the remaining blastic leukemic cells in the bone marrow after chemotherapy regimens which are known as a minimal residual disease (MRD) are defined as a marker of treatment response and are probably an indicator of following relapse.[4]

Some studies hypothesized that CD30 expression in primary bone marrow aspiration (BMA) samples might have some relation with the after chemotherapy MRD cells so it could be an indicator of the ongoing remission and relapse.[5] We designed this study to declare whether CD30 positivity at the baseline has any relation with posttreatment MRD or not.

MATERIALS AND METHODS

This is a cross-sectional study which had been done on fresh BMA samples of 30 definitely diagnosed B-ALL new patients in Isfahan medical university (IUMS) from April 2018 to March 2019. Convenience time-based sequential sampling method was used as our sampling method. We exclude patients whom could not be examined for MRD (due to misplaced marker expression); Participants without BMA samples for flow cytometry and patients with diluted samples. This study is approved by the medical ethics committee of IUMS (IR. MUI. MED. REC.1398.045). BMA was collected after assigning informed consent by patients of his/her parents.

Access this article online

Quick Response Code:

Website: www.jmsjournal.net

DOI: 10.4103/jrms.JRMS_1024_20

Address for correspondence: Dr. Amirhossein Kazemian, No 149, Bahar 3, Mehran, Mehr, Salman Farsi St. Isfahan, Iran.
E-mail: a.h.kazemian69@gmail.com
Submitted: 28-Aug-2020; **Revised:** 17-Mar-2021; **Accepted:** 14-Apr-2021; **Published:** 18-Oct-2021

All BMA samples from the posterior superior iliac spine (PSIS) were obtained by hematologist through Jamshidi cannula (15G mm × 79 mm). BMA samples were collected in EDTA impregnated tubes. The samples were adjusted to approximately 500,000 cells/100 µL with Phosphate-buffered Saline (PBS). Samples were added to 4-color flow cytometry panel of CD30 marker; APC anti-human CD30 antibody, from Biolegend Co.

The samples were analyzed after being centrifuged twice and PBS washing by CyFlow software and a minimum of 30,000 events were acquired and analyzed. The cutoff point for CD30 positivity was 20%. After 28 days of routine anti-ALL therapy[6] another BMA was obtained again from PSIS and MRD was calculated, with blastic markers expression, flow cytometry analyzer.

The collected data were entered into SPSS version 25 (SPSS Corp., Chicago, IL, USA). $P < 0.05$ was considered as the minimum value for statistical significance. Finally, we compare MRD between CD30 positive and negative samples by one-sample Kolmogorov–Smirnov test.

RESULTS

Finally, 30 patients with B-ALL were included, 12 (40%) were females and 18 (60%) were males. The mean age was 15.62 ± 20.488. Table 1 summarizes demographic findings.

The cases were categorized with flow cytometry findings into early pre-B ALL (14 patients), pre-B ALL (15 patients), and pro-B ALL (1 patient). CD30 expression in early pre-B was 17.35 ± 17.989, Pre-B was 15.01 ± 23.441, in Pro-B was 0.6 and totally was 15.62 ± 20.488. There were no significant differences in CD30 in B-ALL Immunophenotypes ($P = 0.323$). Expression of CD 30 in males was 17.06 ± 22.431 and in females was 13.48 ± 17.90 ($P = 0.465$). There were no significant differences between CD30 expression in different age groups ($P = 0.465$). The blood indices were not significantly difference with CD30 expression [Table 2].

CD30 was positive in 20 participants and negative in 10 patients. The mean blast count in baseline in CD30 positive group was 77 ± 7.88, in the negative group was 76.3 ± 17.78%. After 28 days of chemotherapy mean MRD was 1.07 ± 3.754 in the CD30 negative group, 0.12 ± 0.034% in the positive group [Figure 1]. Total MRD count was 0.75 ± 3.073in participants. MRD levels were statistically different two groups ($P = 0.025$).

DISCUSSION

This study was conducted to show any relation between baseline CD30 positivity in B-ALL patients and their posttreatment MRD level.

Table 1: CD30 marker expression in terms of age, sex, and acute leukemia immunophenotyping of the patients

Variables	CD30 expression, mean (percentage)±SD	P
Sex		
Male	17.06±22.431	0.465
Female	13.48±17.90	
Total	15.62±20.48	
Age (years old)		
<10	17.30±20.651	0.800
10-20	18.11±29.970	
20-30	12.75±17.890	
30-40	2.00±00.00	
>40	2.80±3.818	
Total	15.62±20.488	
ALL immune phenotyping		
Early preB	17.35±17.989	0.323
Pre-B	15.01±23.441	
Pro-B	0.60±00.00	
Total	15.62±20.488	

ALL=Acute lymphoblastic leukemia; SD=Standard deviation

Table 2: Levels of blood indices in terms of the CD30 marker being positive or negative

Variables	Mean±SD		P
	CD30 negative	CD30 positive	
WBC	37441.00±50944.10	22982.00±32995.90	0.713
Hb	9.23±2.05	8.19±1.99	0.267
PLT	78350.00±68172.59	80100.00±54726.49	0.619
MCV	85.61±9.47	84.10±8.33	0.779
MCH	27.52±2.69	26.67±2.24	0.397
RDW	17.56±3.19	16.23±1.57	0.198
Blast	76.30±17.789	77.00±7.88	0.307

SD=Standard deviation; WBC=White blood cells; Hb=Hemoglobin; PLT=Platelet; MCV=Mean corpuscular volume; MCH=Mean corpuscular hemoglobin; RDW=Red cell distribution width

Kalinova *et al*.[7] concluded that using the CD30 molecule to determine MRD is not a viable method. This finding is not consistent with the results of the present study. Elafifi *et al*. showed that an increase in MRD was not statistically significant in ALL relapsing cases compared to new cases. Accordingly using the CD30 molecule to identify and diagnose MRD was not opted to be a viable option.[8] Levels of MRD have a prognostic value in many hematologic malignancies.[9-15]

A meta-analysis study also found that high serum CD30 levels were a predictor factor of poor prognosis in patients with Hodgkin's lymphoma which is quite different from our study.[16] The serum CD30 level decreases with the treatment of the disease and returns to its highest levels in case of relapse.[17] As we showed CD30 positive patients had lower MRD, it might be a good prognostic factor and a positive indicator of treatment response.

Limitation of this study was the limited sample size and short clinical follow-up time which were due to budget

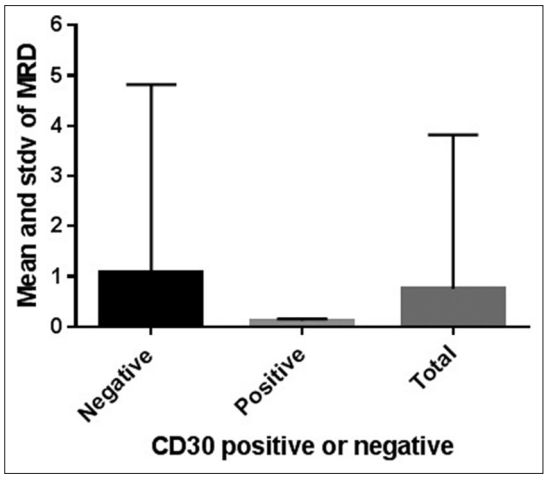

Figure 1: Number of blasts on day 28 after starting the treatment (minimal residual disease) by a multicolored flow cytometry method

constraints, resulting in a need for further studies with higher sample size and extended follow-up to obtain more valid and established evidences.

CONCLUSION

Lower MRD on day 28 after chemotherapy was seen in B-ALL patients with baseline CD30 expression.

Financial support and sponsorship

This study was supported by Isfahan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Li M, Liu ZS, Liu XL, Hui Q, Lu SY, Qu LL, *et al.* Clinical targeting recombinant immunotoxins for cancer therapy. Onco Targets Ther 2017;10:3645-65.
2. Suri A, Mould DR, Song G, Kinley J, Venkatakrishnan K. Population pharmacokinetics of brentuximab vedotin in adult and pediatric patients with relapsed/refractory hematologic malignancies: Model-informed hypothesis generation for pediatric dosing regimens. J Clin Pharmacol 2020;60:1585-97.
3. Wagner SM, Melchardt T, Egle A, Magnes T, Skrabs C, Staber P, *et al.* Treatment with brentuximab vedotin plus bendamustine in unselected patients with CD30-positive aggressive lymphomas. Eur J Haematol 2020;104:251-8.
4. Tsukasaki K, Marçais A, Nasr R, Kato K, Fukuda T, Hermine O, *et al.* Diagnostic approaches and established treatments for adult T cell leukemia lymphoma. Front Microbiol 2020;11:1207.
5. Landry M, Bienz MN, Sawan B, Temmar R, Beauregard P, Chaunt F, *et al.* Bone marrow immunohistochemistry and flow cytometry in the diagnosis of malignant hematologic diseases with emphasis on lymphomas: A comparative retrospective study. Appl Immunohistochem Mol Morphol 2020;28:508-12.
6. Kato M, Manabe A. Treatment and biology of pediatric acute lymphoblastic leukemia. Pediatr Int 2018;60:4-12.
7. Kalinova M, Krskova L, Brizova H, Kabickova E, Kepak T, Kodet R. Quantitative PCR detection of NPM/ALK fusion gene and CD30 gene expression in patients with anaplastic large cell lymphoma – residual disease monitoring and a correlation with the disease status. Leuk Res 2008;32:25-32.
8. Elafifi AM, Said RM, AbdElbary HM, Abdulrahman R, Ali K. Flow cytometric assessment of CD30 expression in adult patients with acute leukemia. Egypt J Haematol 2019;44:1.
9. Anderson KC. Novel biologically based therapies for myeloma. Cancer J 2001;7 Suppl 1:S19-23.
10. Herrera AF, Armand P. Minimal residual disease assessment in lymphoma: Methods and applications. J Clin Oncol 2017;35:3877-87.
11. Chase ML, Armand P. Minimal residual disease in non-Hodgkin lymphoma – Current applications and future directions. Br J Haematol 2018;180:177-88.
12. Schwind S, Jentzsch M, Bach E, Stasik S, Thiede C, Platzbecker U. Use of minimal residual disease in acute myeloid leukemia therapy. Curr Treat Options Oncol 2020;21:8.
13. Steger B, Floro L, Amberger DC, Kroell T, Tischer J, Kolb HJ, *et al.* WT1, PRAME, and PR3 mRNA expression in acute myeloid leukemia (AML). J Immunother 2020;43:204-15.
14. Wang J, Li F, Ma Z, Yu M, Guo Q, Huang J, *et al.* High expression of TET1 predicts poor survival in cytogenetically normal acute myeloid leukemia from two cohorts. EBioMedicine 2018;28:90-6.
15. Gökbuget N, Dombret H, Giebel S, Bruggemann M, Doubek M, Foà R, *et al.* Minimal residual disease level predicts outcome in adults with Ph-negative B-precursor acute lymphoblastic leukemia. Hematology 2019;24:337-48.
16. Nigm DA, Abd El Hameed ZA, AbdElrahman MZ. CD30 expression vs. serum soluble CD30 (sCD30) level: Role in prognosis and treatment of acute myeloid leukaemia. J Clin Cell Immunol 2017;8:51.
17. Leoncini L, Ambrosio M, Lazzi S, Rocca B, Tosi P. CD30 expression in lymphoid neoplasms: From diagnostic marker to target of therapy. Drugs Cell Ther Hematol 2014;2:279-300.