Association of Myeloid Aberrant Antigens and the Presence of BCR-ABL Gene Re-arrangements in ALL Patients

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rearrangements in ALL patients of our population, so that we can predict presence of BCR-ABL rearrangements beforehand.

ABSTRACT

Background: BCR-ABL translocation is the most common genetic abnormality associated with adult Acute Lymphoblastic Leukaemia (ALL) with poor outcome. **Objective:** The aim of the study was to determine the association of myeloid aberrant antigens and the presence of BCR-ABL gene rearrangements in acute lymphoblastic leukaemia (ALL) patients in our context. **Method:** A total of 38 ALL patients were included in this cross-sectional study from August 2018 to July 2019 according to selection criteria. BCR-ABL was detected by Real-Time Polymerase Chain Reaction (RT-PCR). **Results:** The median age at diagnosis was 28 years with male (76.3%) predominance. Aberrant myeloid markers, e.g. CD13 was present in 9 (64.3%) patients who were BCR-ABL positive which was statistically significant ($p < 0.05$). **Conclusion:** Early suspicion about BCR-ABL positivity can be made in ALL patients who show aberrant myeloid expression.

Key words: Acute Lymphoblastic Leukaemia, BCR-ABL.

Introduction

Acute lymphoblastic leukaemia (ALL) is a haematological malignancy characterized by abnormal proliferation and accumulation of immature lymphoid cells in the bone marrow and lymphoid tissues.^{1,2} It is the most common malignant disease in childhood but accounts for approximately 20% of acute leukaemia in adults.² BCR-ABL translocation is the most common genetic abnormality associated with adult ALL.³ BCR-ABL positive ALL has an aggressive clinical course with a variable leukocyte count at presentation and is associated with a poor prognosis.⁴ Moreover, these patients require addition of a TKI for their treatment.⁵ Prompt recognition and timely management of this disorder can ensure a better outcome. This study was done to determine the association of myeloid aberrant antigens and the presence of BCR-ABL

Materials and Methods

This was a cross sectional observational study conducted in the department of Haematology, Bangabandhu Sheikh

Mujib Medical University (BSMMU), from August 2018 to July 2019. Ethical permission was taken from the institutional review board of BSMMU and the issue was addressed to every patient. Thirty-eight diagnosed cases of acute lymphoblastic leukaemia were enrolled following selection criteria. All patients were interviewed by semi structured questionnaire. Informed written consent was taken from the subjects prior to enrolment. Samples of peripheral blood (5 ml) and bone marrow were collected from each study subject following standard procedures. Sample was reported in the Department of Microbiology, BSMMU and in abroad in well reputed diagnostic and molecular laboratory. The identification of the BCR-ABL gene rearrangements was performed by reverse transcription polymerase chain reaction (RT-PCR). Quality assurance measures were taken. All data were checked after collection and then entered into computer software. The statistical analysis was done by using Statistical Packages for Social Science (SPSS-version-23).

Results

This study included a total of thirty-eight diagnosed cases of ALL among them 14 (36.9%) were positive BCR-ABL cases and 24 (63.1%) were negative BCR-ABL cases. In myeloid markers, CD13 was found 5 (35.7%) in BCR-ABL positive group and 2 (8.3%) in BCR-ABL negative group. The expression of CD13 in BCR-ABL positive group was found to be statistically significant ($p < 0.05$). (Table I)

Table I: Association between BCR-ABL and aberrant myeloid marker (n:38)

Immunophenotyping findings	BCR-ABL; n (%)		P- value
	Positive; n:14	Negative; n:24	
CD13	5 (35.7)	2 (8.3)	0.049
CD33	2 (14.3)	3 (12.5)	0.619
CD117	2 (14.3)	1 (4.2)	0.302

Among the positive BCR-ABL cases, 64.3% patients expressed aberrant myeloid markers. Among them, CD13 was positive in 55.6% patients, CD33 was positive in 22.2% cases and CD117 was positive in 22.2% cases. (Table II)

Table II: Distribution of the BCR-ABL positive patients according to aberrant myeloid marker. (n:14)

Type of aberrant myeloid marker	n (%)
Absent	5 (35.7)
Present	9 (64.3)
CD13	5 (55.6)
CD33	2 (22.2)
CD117	2 (22.2)

Validity test was done for aberrant myeloid antigen. It was found that in case of CD13, the sensitivity was 35.7%, specificity was 91.3%, positive predictive value was 71.4% and negative predictive value was 70% for BCR-ABL positive ALL patients. (Table III)

Table III: Association of myeloid aberrant antigens and the presence of BCR-ABL gene rearrangements in ALL patients

Validity test	Markers		
	CD13	CD33	CD117
Sensitivity	35.7	14.3	14.3
Specificity	91.3	87.0	95.7
Accuracy	70.3	59.5	64.9
Positive predictive value	71.4	40.0	66.7
Negative predictive value	70.0	62.5	64.7

Discussion

In this cross-sectional observational study, a total of 38 ALL patients were included for BCR-ABL assessment. Regarding immunophenotyping findings it was observed that Myeloid marker CD13 positivity was found in 5 (35.7%) cases. Among other markers TdT was positive in 10 (71.4%) cases. CD13 and TdT were significantly ($p < 0.05$) higher in BCR-ABL positive group than negative group. However, other immunophenotype findings were not statistically significant ($p > 0.05$). In a study by Corrente et al. stated high expression of CD19, CD79a, CD22, CD10 among the BCR-ABL positive group.⁶ These findings were consistent with our study. We have observed that aberrant myeloid marker was found in 9 (64.3%) patients who were BCR-ABL positive for ALL. Among them 5 (55.6%) patients had positive CD13 marker, 2 (22.2%) had positive CD33 and 2 (22.2%) had positive CD117 marker. Corrente et al. also found greater frequency of myeloid aberrant antigens positivity in BCR-ABL positive cases compared with BCR-ABL negative cases.⁶ They found aberrant myeloid markers CD13 by 42.5%, CD33 by 30.5% and CD66 by 63.2% were positive among BCR-ABL positive ALL cases.⁶ Our study showed sensitivity of CD13 was 35.7%, specificity 91.3%, positive predictive value 71.4% and negative predictive value 70%. These findings were consistent with the previous study.

Conclusion

It is found that a significant number of BCR-ABL positive ALL patient expressed aberrant myeloid antigen in immunophenotype. So, an early suspicion about BCR-ABL positivity can be made in ALL patients who show aberrant myeloid expression.

Limitations

1. The study population was selected from one selected hospital – BSMMU, Dhaka. So, the results of the study may not reflect the exact picture of the country.
2. The present study was conducted at a short period of time.
3. Small sample size was also a limitation of the present study.

Recommendation

Further multi-centered prospective analytical study with larger sample size is recommended.

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