# ATYPICAL BCR-ABL SIGNAL PATTERNS IDENTIFIED BY FLUORESCENCE IN SITU HYBRIDIZATION IN VARIOUS HEMATOLOGICAL DISORDERS & ITS IMPACT ON PROGNOSIS

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## INTRODUCTION

**Background:** BCR-ABL fusion gene, produced by the balanced reciprocal translocation t(9;22)(q34;q11.2), encodes tyrosine kinase BCR-ABL oncoprotein, which is responsible for proliferative signals and leukemogenesis by activating Raf/MEK/ERK, PI3K/AKT, and JAK/STAT pathways[1]. Conventional cytogenetic analysis (CCA) is most commonly used method to confirm the presence of the t (9;22) and/or additional chromosomal abnormalities. However, cryptic translocations or gene rearrangements remain undetectable. Fluorescence in situ hybridization (FISH) with locus-specific BCR-ABL probe, not only confirms the presence of typical BCR-ABL translocation but also shows atypical signal patterns[2].

**Objective:** To determine the frequency and outcome of atypical BCR-ABL signal pattern in newly diagnosed leukemias and suspected myeloproliferative neoplasms.

**Method:** This is a descriptive cross-sectional study performed at the Department of Pathology, Cytogenetics Lab of Shifa International Hospital. Sampling technique used was Non-Probability Purposive Sampling. Data was collected in duration of one year following all ethical considerations. Peripheral blood samples (containing atypical cells or TLC>20,000/UL) or bone marrow aspirate samples were taken in sodium heparin from diagnosed and suspected cases of myeloproliferative disorders meeting the inclusion criteria. FISH for BCR-ABL translocation was performed using Abbott Vysis LSI BCR/ABL Dual Color, Dual Fusion translocation probe. Data was analyzed using SPSS and descriptive statistics were calculated for qualitative and quantitative outcomes.

## RESULTS

Sample size of 204 patients was taken, calculated by WHO sample size calculator. The distribution of patients on the basis of primary Malignancy is shown in Figure 1. The patterns of BCR-ABL signals presented complexity and diversity. A total of 12 BCR-ABL signals were observed in this cohort, including 1R1G2F, 1R1G1F, 2R1G1F, 1R2G1F, 2R2G1F, 1R2G2F, 1R1G3F, 1G3F, 2G3F, 1G4F, 1R1G4F, 1R4F and 3R2G3F. Atypical BCR-ABL signal patterns (≥ two types of signal patterns) were observed in 16.67% of the T-ALL patients, followed by 14.29% of the CML patients, 13.75% of B-ALL, 6.67% of the AML patients and only 5.56% of MPNs patients as shown in Figure 2.

Figure 1: Primary Malignancy

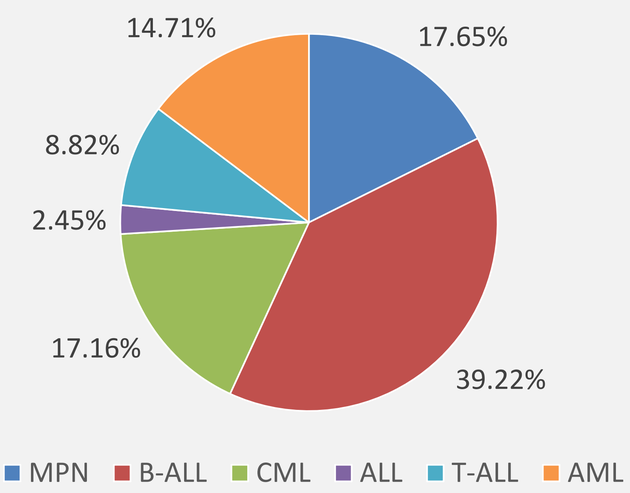
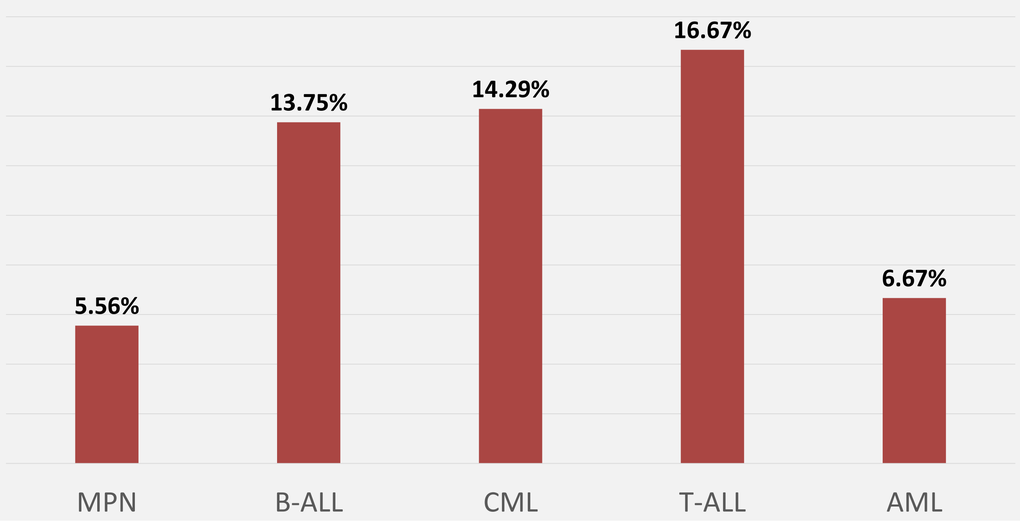
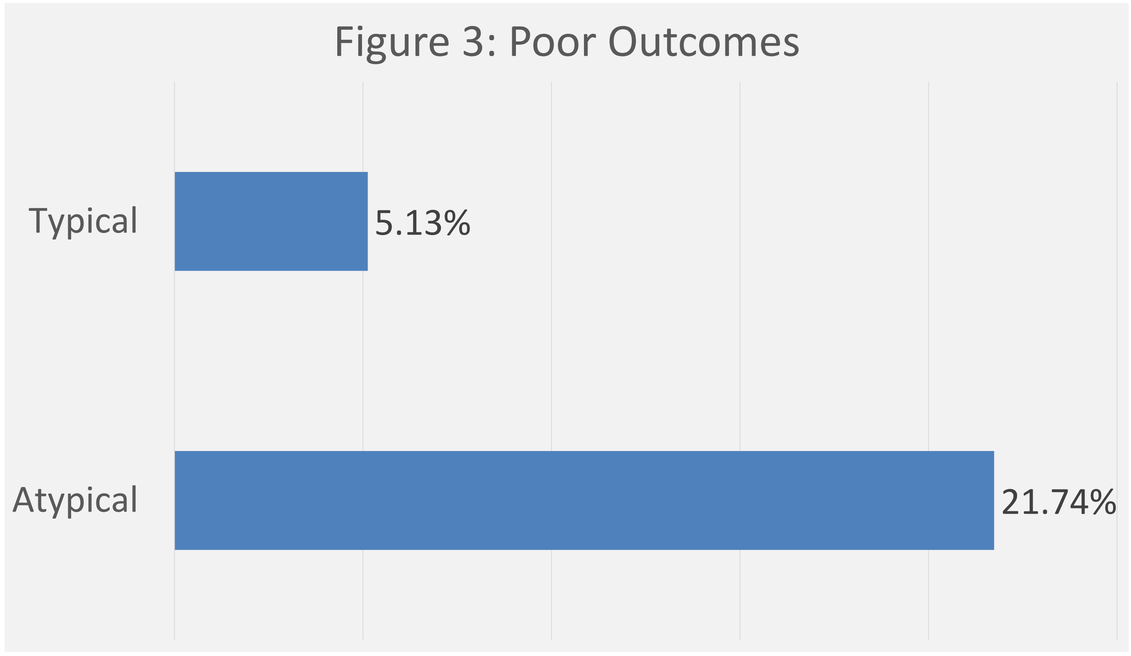



Figure 2: Atypical BCR-ABL Signal Patterns




Out of all the patients positive for BCR-ABL translocations, 63.3% patients had typical patterns while 37.7% had Atypical patterns. Regarding the outcomes of patients having typical versus atypical BCR-ABL translocations, it was observed that 21.74% of patients with atypical translocations had poor prognosis as compared to only 5.13% of patients with typical translocation as shown in Figure 3.

Figure 3: Poor Outcomes




## CONCLUSION

Atypical BCR-ABL signal patterns show poor prognosis, treatment resistance and high risk of relapse even after bone marrow transplant. Monitoring BCR-ABL signal patterns can be an effective mean to provide prognostic guidance and treatment choices for these patients.

## REFERNCES

1. Amarante-Mendes GP, Rana A, Datoguia TS, Hamerschlak N, Brumatti G. BCR-ABL1 Tyrosine Kinase Complex Signaling Transduction: Challenges to Overcome Resistance in Chronic Myeloid Leukemia. Pharmaceutics. 2022 Jan 17;14(1):215.

2. Zhang Z, Chen Z, Jiang M, Liu S, Guo Y, Wan L, et al. Heterogeneous BCR-ABL1 signal patterns identified by fluorescence in situ hybridization are associated with leukemic clonal evolution and poorer prognosis in BCR-ABL1 positive leukemia. BMC Cancer. 2019 Oct 8;19(1):935.