DECONVOLUTING & CHARACTERIZING THE NEWLY INCORPORATED GENETIC SUBTYPES & TREATMENT OUTCOMES OF ACUTE LYMPHOBLASTIC LEUKEMIA: A REPORT OF 1,021 INDIAN PATIENTS-5 YEAR STUDY

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INTRODUCTION

Acute lymphoblastic leukemia (ALL), one of the most common pediatric cancers, predominantly occurs in the pediatric age group of 2-10 years. ALL remains the leading cause of morbidity in children and has worse clinical outcomes in adults. ALL is highly heterogeneous and characterized by significant four recurrent cytogenetic/molecular genetic abnormalities and several new entities have been recently incorporated into the genetic landscape of acute lymphoblastic leukemia (ALL), including *DUX4*-rearrangement (r), *MEF2D9*-r, *ZNF384*-r, *PAX*-r, and Ph-like ALL. An extensive search revealed a scarcity of data on the identification, hematological, flowcytometric immunophenotyping (FCM-IP), clinical, & measurable residual disease (MRD) outcomes of prognostically significant B-cell ALL (B-ALL) subtypes from low- and middle-income nations. Evaluating high-risk ALLs at baseline will help hematologists/physicians make alternate curative decisions.

AIM

The aim of the study is to characterize the hematological, clinical, flowcytometric-immunophentyping (FCM-IP) characterization, & treatment outcomes of prognostic significant genetic subtypes of B-ALL cases (n-1021) from developing nations.

METHOD

We examined 1,021 newly-diagnosed B-ALL cases (2016–2023).

A rigorous. panel of FCM-IP, multiplex-RT-PCR, transcriptomic profiling, targeted nCounter NanoString, qPCR-targeted GEP (PHi-RACE), digital droplet (dd)-PCR, FISH, FCM-MRD, LC-MS/MS, & Sanger sequencing for the detection & characterization of four common recurrent gene abnormalities (RGAs) and newly incorporated high-risk Ph-like ALL cases. We built 3 independent logistic regression classifiers for Ph-like ALL detection, CD markers, & clinical symptoms to differentiate prognostically significant genetic subtypes of B-ALL cases.

CONTACT INFORMATION

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RESULTS

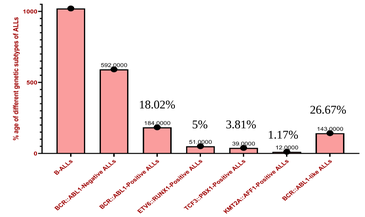


Figure 1: The incidence of four recurrent fusion transcripts (RGAs),.

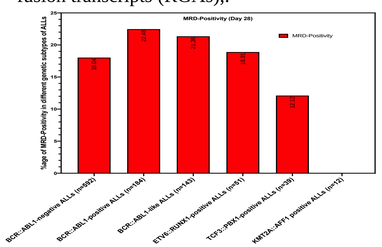


Figure 9:MRD outcomes of different genetic subtypes of B-lineage ALLs.

Figure 2: Heat map showing the clustering of Ph-like ALL cases.

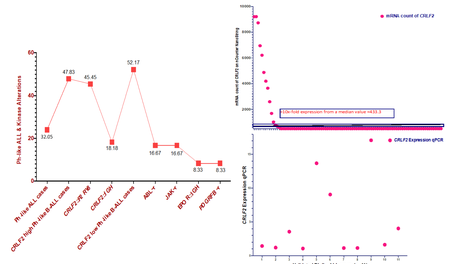


Figure 4: Characterization of *CRLF2* & Kinase alterations in identified Ph-like ALL cases

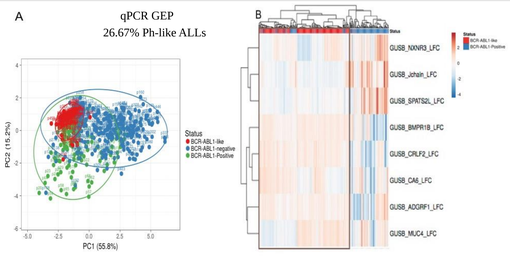


Figure 3:(A, B) PCA & Heat map analysis shows the clustering of Ph-like ALL cases.

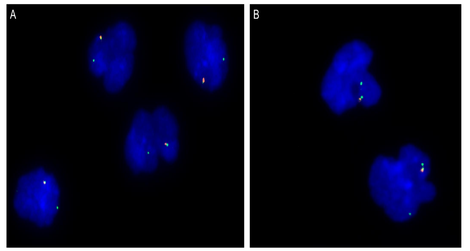


Figure 5: A) FISH using dual color break apart probes showed P2RY8::CRLF2 translocation.

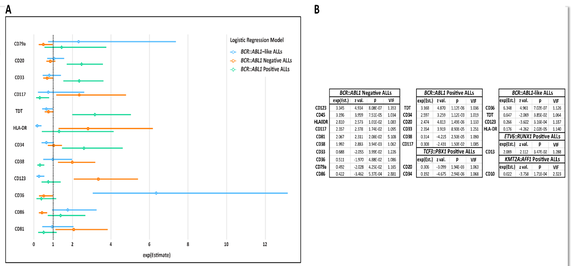


Figure 8: Logistic Regression model of statistically significant CD markers across genetic subtypes of B-ALLs. A & B: Forest plot & Tables of significant predictor CD variables for each of the 6 logistic regression models.

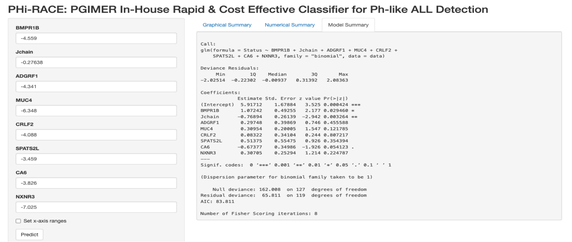


Figure 6: Dynamic Nomogram created using Logistic regression to detect Ph-like ALL cases among RGA^{neg} Ph-negative ALL cases.

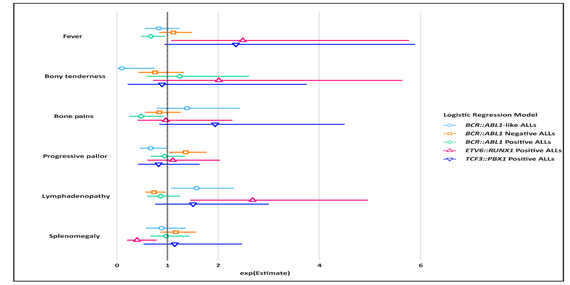


Figure 7: Forest plot of logistic regression coefficients obtained from logistic regression modeling using clinical parameters as predictor variables for the indicated acute lymphoblastic leukemia subtypes.

CONCLUSIONS

This is the first report on the characterization of prognostic significant genetic subtypes & MRD outcomes of a large cohort of Indian B-ALL cases.

ACKNOWLEDGEMENT

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