Exploring the Genetic Landscape of B-ALL: A Comparative Analysis of Copy Number Alterations in Adults and Paediatrics

P. Sharma[1], G. Leons[1], S. Gupta [1], S. Bakhshi [2], R. Gupta [1], S. Gajendra [1], A. Roy [3], R. Sahoo [2], D. Pushpam [2]

1 Laboratory Oncology Unit, Dr BRA IRCH, All India Institute of Medical Sciences (AIIMS), New Delhi, INDIA.

2 Department of Medical Oncology, Dr BRA IRCH, All India Institute of Medical Sciences (AIIMS), New Delhi, INDIA.

3 Kusuma School of Biological Sciences, Indian Institute of Technology (IIT), New Delhi, INDIA

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INTRODUCTION

- ✓ B-cell acute lymphoblastic leukemia (B-ALL) primarily affects the pediatric and young adult populations.
- ✓ Generally, pediatric patients have better prognostic outcomes compared to adults.
- ✓ However, there is a lack of comparative data on copy number alterations (CNAs) in adult and pediatric B-ALL patients.

AIM

- ✓ To study the genetic landscape or CNAs of B-ALL in adult and pediatric B-ALL patients

METHOD

- ✓ Overall, 281 B-ALL patients were retrospectively analyzed and divided into pediatric (≤18 years) and adult (≥19 years) cohorts for comparison.
- ✓ Genomic DNA from bone marrow/ peripheral blood samples underwent Multiplex ligation-dependent probe amplification (MLPA) for CNAs using P335 kit (MRC, Holland).
- ✓ The CNAs of genes, namely EBF1, IKZF1, JAK2, CDKN2A, CDKN2B, PAX5, ETV6, BTG1, RB1 and the Xp22.33/Yp11.31 region (PAR1), comprising CRLF2, CSF2RA, and IL3RA genes were detected.
- ✓ The cases were risk categorized using the Moorman's criteria and IKZF1plus criteria given by Stanulla et.al .
- ✓ The final risk category of MR-2 (High risk), MR-1 (Intermediate risk), and MR-0 (Standard risk), were obtained by adding both risk scores [1].

RESULTS

- ✓The analysis incorporated a cohort of 281 patients comprising 171(60.85%) pediatric and 110 (39.15%) adult cases diagnosed with B-ALL.
- ✓Patients in the adult cohort had a median age of 33.5 years (range 19–61 years), and patients in the pediatric cohort had a median age of 7 years(range 8mth–18 years).
- ✓CNAs were identified in 216 (77%) cases in the overall cohort;94(85%) cases in the adult group and 122(71%) cases in the pediatric group (p-value =0.006).
- ✓ The most frequently affected genes associated with CNAs were CDKN2A/B, observed in 98 cases(35%), IKZF1-94 cases(33%), and PAX5-92 cases(33%).
- ✓Among the patients in the adult cohort, the most affected genes were IKZF1- 62cases(56%), CDKN2A/B- 46 cases(42%), and PAX5- 46 cases(42%).
- ✓In the pediatric group, the most frequently affected genes were CDKN2A/B-52 cases(30%), PAX5-46 cases(27%), and IKZF1-32 cases(19%).
- ✓ The adult cohort had 23(20.90%), 18(16.36%), 53 (48.18%) cases and the pediatric cohort had 41(23.98%), 27(15.79%), 53(31%) cases with 1,2 and >=3 CNAs respectively.

CONCLUSIONS

- ✓ Our findings indicate an overall higher proportion of ≥3CNAs (48.18% vs 31%) in the adult B-ALL patients as well as much higher prevalence of IKZF1 alterations (56% vs 19%) as compared to the pediatric cohort.

Fig1.: Oncoprint of all cases

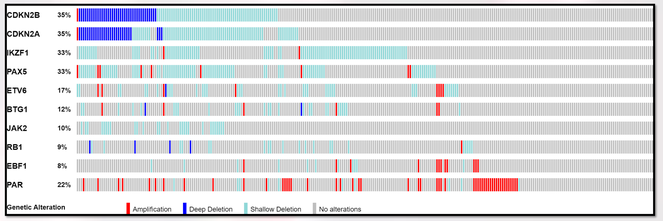


Fig2.: Oncoprint of adult cases

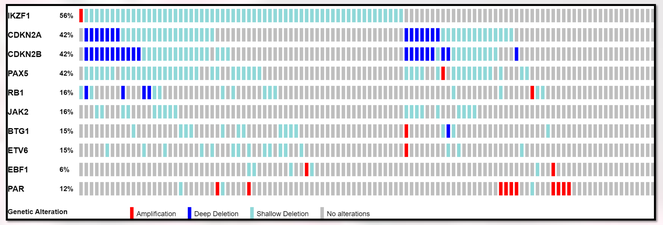
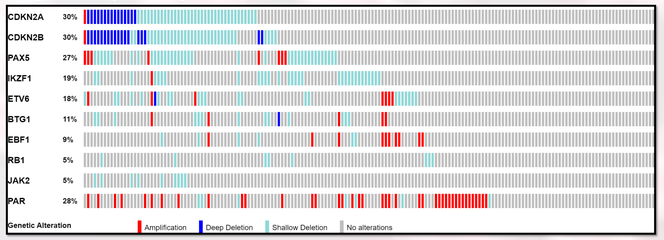


Fig3: Oncoprint of pediatric cases



GENES	Total (N=281)		Adult (N=110)		Pediatric (N=171)	
	Del N(%)	Amp N(%)	Del N(%)	Amp N(%)	Del N(%)	Amp N(%)
CDKN2A/B	97 (35)	1(0.4)	46(42)	0	51(30)	1(0.58)
IKZF1	92(33)	2(0.71)	61(55)	1(0.9)	31(18)	1(0.58)
PAX5	83(30)	9(3.20)	45(41)	1(0.9)	38(22)	8(4.68)
ETV6	39(14)	8(2.8)	16(14)	1(0.9)	23(13)	7(4.09)
EBF1	11(4)	12(4.3)	5(15)	2(1.8)	6(4)	10(5.85)
BTG1	29(10)	6(2.13)	15(16)	1(0.9)	14(8)	5(2.92)
RB1	25(9)	1(0.4)	17(15)	1(0.9)	8(5)	0
JAK2	27(10)	0	18(16)	0	9(5)	0
PAR	10(4)	51(18.14)	3(3)	10(9.01)	7(4)	41(23.98)

RISK- Stratification	Total (N=281) N(%)	Adult (N=110) N(%)	Pediatric (N=171) N(%)
High risk (MR-2)	51(18.14)	33(30)	18(10.52)
Intermediate Risk (MR-1)	112(39.86)	53(48.18)	59(34.50)
Standard Risk (MR-0)	118(42)	24(21.81)	94(54.97)

REFERENCES

1. Gupta SK et al. Proposal and clinical application of molecular genetic risk scoring system, "MRplus", for BCR-ABL1 negative pediatric B-cell acute lymphoblastic leukemia- report from a single centre. Leuk Res. 2021 Dec;111:106683. doi: 10.1016/j.leukres.2021.106683.

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CONTACT INFORMATION

Preity Sharma
Preity.sharma11@aiims.edu
+91 8949690573