

IDH1 mRNA Expression and Exon 4 Transcript-Level Variants in Chronic Myeloid Leukemia

Rashid Ali¹, Hafiza Asma Nawaz¹, Afia Muhammad Akram^{1*}, Amjad Zafar²

¹Department of Zoology, University of Education, Lahore, Pakistan

²Department of Oncology, Allama Iqbal Medical College/Jinnah Hospital, Lahore, Pakistan

*Corresponding author: Afia Muhammad Akram



3.72 vs 2.20

Higher overall *IDH1* expression in CML
($P = 0.030$)



CP 5.06 | AP 0.33 | BP 0.15

Disease-phase expression pattern:
Chronic | AP | Blast



26 / 43 (60.5%)

Patients with transcript variants
(No R132 hotspot alteration)

BACKGROUND

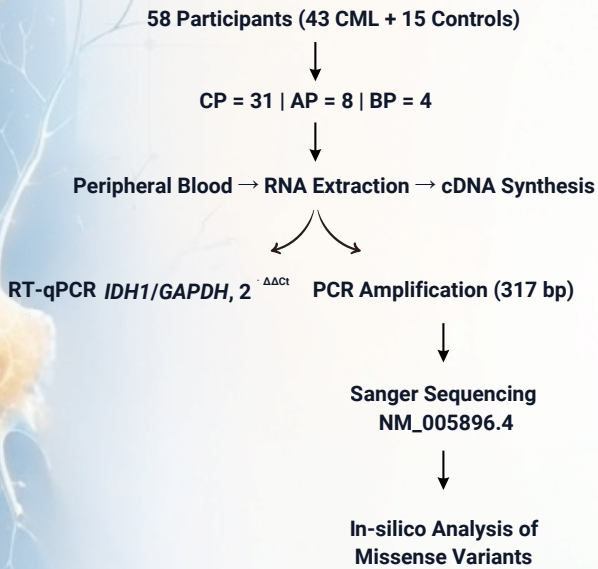
Chronic myeloid leukemia (CML) is driven by *BCR::ABL1*, but additional metabolic alterations contribute to heterogeneity.

IDH1 is an NADP⁺-dependent metabolic enzyme involved in α -ketoglutarate and NADPH production. Evidence regarding *IDH1* expression and sequence variation across CML disease phases remains limited.

OBJECTIVE

Evaluate *IDH1* mRNA expression and cDNA-based transcript variants across CML phases.

METHODS WORKFLOW



Design: Cross-sectional analytical | Stats: t-test / ANOVA ($P < 0.05$)

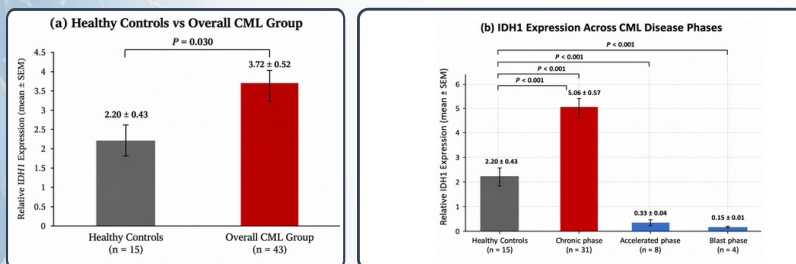


Figure 1. Relative *IDH1* expression in CML overall and across disease phases.

CONCLUSION

IDH1 expression was elevated overall in CML but differed markedly across disease phases, with highest expression in chronic-phase disease. cDNA sequencing identified transcript-level variants without alteration of the canonical R132 hotspot. Genomic and functional validation is required to establish their biological significance.

LIMITATIONS

Modest sample size (particularly AP/BP); cross-sectional design; cDNA sequencing without matched genomic DNA; no protein/metabolite measurements; reliance on computational predictions.

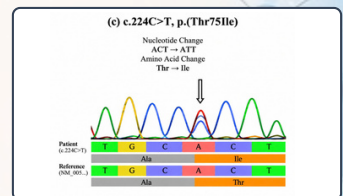
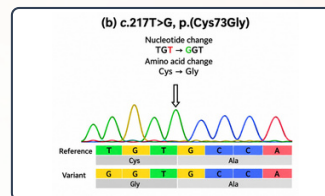
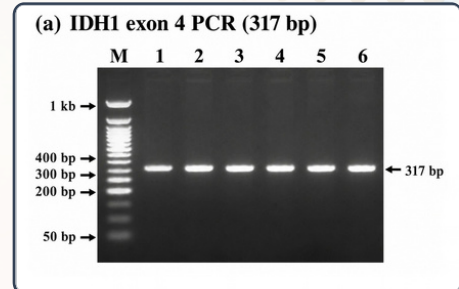


Figure 2. PCR & Sanger chromatograms. PCR yielded expected 317-bp amplicon. Chromatograms show c.217T>G [p.(Cys73Gly)] and c.224C>T [p.(Thr75Ile)].

TRANSCRIPT-LEVEL VARIANTS

Variant	Protein Effect	Type
c.217T>G	p.(Cys73Gly)	Missense
c.224C>T	p.(Thr75Ile)	Missense
c.315C>T	p.(Gly105=)	Synonymous

No sequence alteration affecting the canonical *IDH1* R132 hotspot was detected.

VARIANT FREQUENCY & IN-SILICO SUMMARY

Variant-positive: 26 / 43 (60.5%)

CP: 17/31 (54.8%)

AP: 6/8 (75.0%)

BP: 3/4 (75.0%)

*AP/BP sample sizes were small; percentages do not prove variants drive progression.

In-Silico: Predictions were inconsistent across tools (PolyPhen-2/SNPs&GO = damaging; SIFT/PhD-SNP/FATHMM = neutral).

Functional significance remains unconfirmed.