DECODING MYELOID NEOPLASMS: THE TRANSFORMATIVE ROLE OF NGS IN HEMATOLOGY ONCOLOGY-REAL WORLD DATA FROM RESOURCE-CONSTRAINED SETTINGS

Memoona Khan[1], Nadia Sial[1], Hamza Irshad [1], Maryam Khan [2], Haider Nisar [3], Mehreen Ali Khan[2]

1. Molecular Department, Armed Forces Bone Marrow Transplant Center, CMH, Rawalpindi, Pakistan
2. Adult Stem Cell Transplant Department, Armed Forces Bone Marrow Transplant Center, CMH, Rawalpindi, Pakistan
3. Paediatric Stem Cell Transplant Department, Armed Forces Bone Marrow Transplant Center, CMH, Rawalpindi, Pakistan

Introduction

The genetic landscape of myeloid neoplasms encompasses a complex molecular profile that plays a significant role in both diagnosis and prognosis [1]. In resource-constrained settings, applying next-generation sequencing (NGS) has the potential to revolutionize clinical decision-making. This study highlights the real-world utility of NGS in diagnosing and risk-stratifying myeloid malignancies.

Aim

To investigate the clinical impact of next-generation sequencing (NGS) in enhancing diagnostic accuracy, prognostic stratification, and disease reclassification in patients with suspected or confirmed myeloid malignancies.

Objectives

- To assess the diagnostic utility and effectiveness of NGS in stratifying acute myeloid leukemia (AML) cases using ELN risk guidelines.
- NGS role in reclassifying cases initially suspected to be secondary to infection or reactive cytopenias into primary hematological disorders.
- To describe the mutation spectrum of myeloid disorders detected through a 58-gene NGS panel in a real-world, resource-constrained clinical setting.

Methods

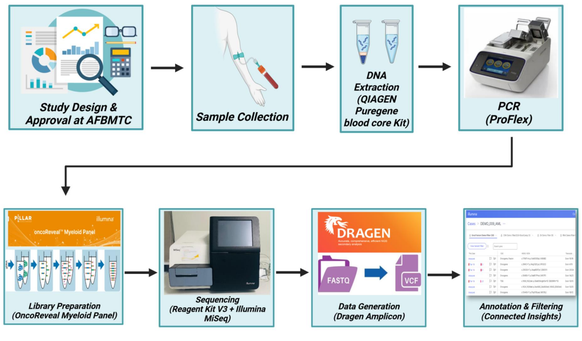
Period: January 2024-December 2024
Center: Molecular Department, Armed Forces Bone Marrow Transplant Center, Rawalpindi.
Sample Size and Selection: Total 52 Samples

Table 1: Sample selection

Sample Size	Purpose	Clinical Conditions
38 cases	Diagnosis	Transfusion-dependent anemia, unexplained cytopenias, leukocytosis / thrombocytosis, inadequate marrow findings
10 cases	Prognosis	Acute Myeloid Leukemia (AML) – ELN Risk Stratification
4 cases	Risk Stratification	Known Myelodysplastic Syndrome (MDS) and Myeloproliferative Neoplasms (MPN)

The methodology and workflow used in this study are depicted in Figure 1.

Fig 1: Workflow



Results

Fig 2: Frequency of Positive Cases on NGS

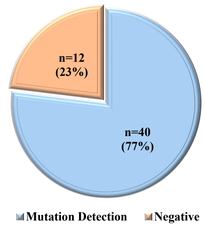
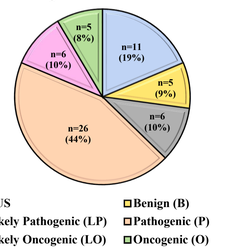


Fig 3: Variant Classification



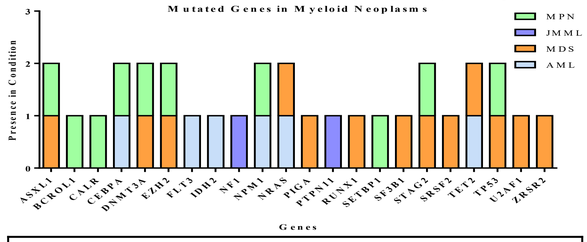


Table 2: Disease-Wise Mutation Distribution

Variant Classification	Disease Subtype	Genes
Pathogenic (P)	AML	*NPM1, CEBPA, IDH2, NRAS*
	MDS (suspected)	*SF3B1, DNMT3A, ASXL1, RUNX1, TP53, NRAS, TET2*
	JMML	*PTPN11, NF1*
	MPN	*CALR, ASXL1, DNMT3A, SETBP1, NPM1*
Likely Pathogenic (LP)	AML	*FLT3, TET2*
	MDS (suspected)	*U2AF1*
Likely Oncogenic (LO)	MDS (suspected)	*EZH2*
Oncogenic (O)	MDS (suspected)	*RUNX1, EZH2, TET2, PIGA, STAG2*
	MPN	*STAG2, EZH2*
Variant of Unknown Significance (VUS)	AML	*TET2*
	MDS	*TET2, SRSF2, RUNX1, ZRSR2,*
	MPN	*CEBPA, TP53, ASXL1, BCROL1*

Summary

This study highlights the clinical utility of NGS in accurately diagnosing and risk-stratifying myeloid neoplasms, even in resource-constrained settings. NGS reclassified multiple cases, revealing its transformative role in hematology-oncology practice.

Discussion

- NGS demonstrated high diagnostic yield, identifying mutations in over 77% of cases, including many PCR negative cases.
- It enabled accurate ELN-based risk stratification in AML and reclassified undiagnosed cases such as those with unexplained cytopenias and fibrosis into definitive myeloid neoplasms [2].
- These findings support the integration of NGS into routine diagnostics, even in resource-limited settings, due to its impact on diagnosis, prognosis, and clinical decision-making.

References

1. A Brief Overview of the Molecular Landscape of Myelodysplastic Neoplasms (Current Oncology)
2. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN (Blood)