Association Between Somatic Mutation Burden and Anemia Severity in Lower-Risk Myelodysplastic Syndromes: A Cross-Sectional Analysis from an Indian Cohort

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BACKGROUND

- Lower-risk myelodysplastic syndromes (MDS are marked by clonal hematopoiesis and ineffective erythropoiesis[1].
- Next-generation sequencing (NGS) plays a central role in the diagnosis of MDS[2].
- The clinical relevance of baseline mutation burden—particularly in predicting anemia severity—remains underexplored in Indian populations[3].

AIM

To evaluate the association between baseline somatic mutation burden—quantified by variant allele frequency (VAF)—and anemia severity in patients with very low, low, or intermediate-risk myelodysplastic syndromes (MDS).

METHODS

A cross-sectional analysis using baseline data from a prospective Indian cohort of adults diagnosed with lower-risk MDS was conducted. A targeted amplicon-based NGS to detect myeloid-specific mutations and quantified VAF was applied. Patients were stratified by hemoglobin (Hb) levels (<8 g/dL, 8–9 g/dL, >9 g/dL) and transfusion dependence (≥3 units in prior 16 weeks). associations between VAF, number of mutations, and anemia severity were assessed using Spearman correlation and multivariable logistic regression.

RESULTS

Of 40 enrolled patients, 85% harbored ≥1 somatic mutation with VAF ≥5%. The most prevalent mutations were SF3B1 (42.5%), ASXL1 (27.5%), and TET2 (22.5%). Patients with multiple mutations (≥2) had significantly lower median Hb (7.6 g/dL) compared to those with one or no mutation (8.9 g/dL, p = 0.004). A strong inverse correlation was found between cumulative VAF and baseline Hb (r = –0.51, p < 0.01). Transfusion-dependent patients had a significantly higher clonal burden (p = 0.03). Notably, patients with SF3B1 mutations had higher Hb and lower transfusion need than those with ASXL1 or TET2 mutations.

DISCUSSION

- In treatment-naïve, lower-risk MDS patients, baseline somatic mutation burden and mutation profile are significantly associated with anemia severity and transfusion dependence.
- Higher clonal burden (measured by VAF) correlates with more severe anemia and increased likelihood of transfusion dependence.
- These findings underscore the prognostic value of molecular profiling at diagnosis.

Number of Patients	N=40
Median Age (years)	68 (42-84)
Male	62.50%
ECOG at baseline	
1	8
2	22
3	10
Baseline Hb (g/dL)	8.2 ± 0.9
Transfusion Dependence (%)	60%
RS > 15% or SF3B1+	100%

Table 1: Baseline characteristics- most of the patients were in ≥ 2 ECOG and were transfusion dependent. RS-Ring Sideroblasts

Gene Mutation	Prevalence n(%)	Median Hb (g/dL)	Transfusion-Dependent (%)
SF3B1	17 (42.5)	9.1	25
ASXL1	11 (27.5)	7.4	85
TET2	9 (22.5)	7.8	70

Table 2 Mutation Frequencies with Hemoglobin and Transfusion Dependency. Note- No mutations detected in 3 participants (N=37)

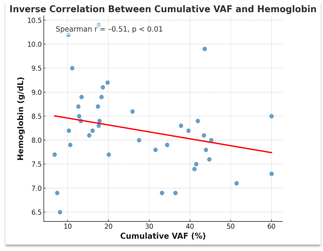


Figure 1- Correlation between cumulative VAF and baseline hemoglobin. VAF-Variant Allele Frequency

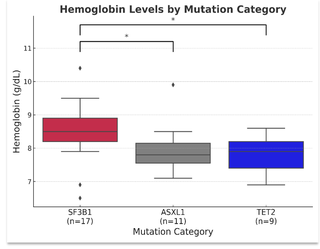


Figure 2: SF3B1 mutations had higher Hb than those with ASXL1 or TET2. Note- No mutations detected in 3 participants (N=37

CONCLUSION

- Incorporating VAF-based risk stratification into early MDS evaluation may aid physicians in identifying high-risk patients sooner.
- This approach can support more personalized treatment decisions and timely interventions in lower-risk MDS.

REFERENCES

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