Comparative Inflammatory Landscapes of Lower- and Higher-Risk Myelodysplastic Syndromes Across Demographics and Geographic Regions

Bishal Tiwari MBBS , Nassau University Medical Center, NY, USA
Prashant Chaulagain MBBS, Sinai Hospital of Baltimore, MD, USA



Introduction

•MDS is a heterogeneous clonal disorder with varying immune phenotypes.
•LR-MDS typically exhibits heightened inflammatory activity.
•HR-MDS often reflects immune suppression and progression risk.
•Geographic and demographic influences on immune signatures remain underexplored.
•Immunological profiling may guide personalized therapeutic decisions.
•This study reviews immune landscapes of LR- and HR-MDS across global cohorts.

Objectives

To compare immune signatures (cytokines, inflammasome markers, checkpoint expression) between LR- and HR-MDS.
To analyze demographic (age, sex) and geographic consistency in findings.
To identify potential immune targets for risk-adapted therapy.

Methods

•Narrative review and synthesis of peer-reviewed studies (2009–2025).
•Included immune profiling of T-cell subsets, cytokines, inflammasome activity.
•Studies spanned North America, Europe, Asia; cohort sizes 30–200 per risk group.
•Supplemented with gene expression and flow cytometry data when available.
•No interventions; observational data only.

Figure 1: Comparative Cytokine and Immune Marker Expression in LR-MDS vs HR-MDS

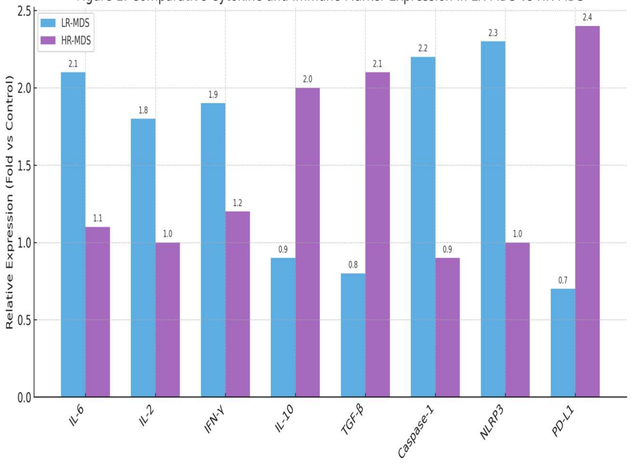
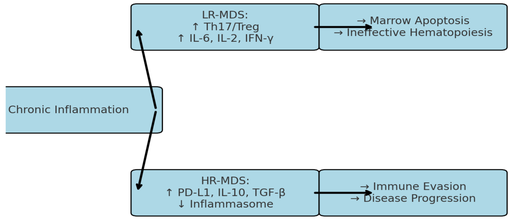


Figure 2: Divergent Immune Pathways in LR-MDS and HR-MDS



Results

•**LR-MDS**:
  • Elevated Th17/Treg ratio (~1.5–2x vs controls)
  • ↑ IL-6, IL-2, IFN-γ (P<0.01)
  • ↑ Caspase-1 and NLRP3 (>2-fold vs controls)
  • ↓ PD-L1 expression
•**HR-MDS**:
  • Immunosuppressive profile (↑ IL-10, TGF-β; P<0.05)
  • ↓ inflammasome markers
  • ↑ PD-L1 expression
•Immune differences were **consistent across age, sex, and geography**.

Conclusion

•**LR-MDS** is defined by a pro-inflammatory bone marrow microenvironment.
•**HR-MDS** reflects immune suppression and potential for immune escape.
•Immune landscapes **are stable across demographic/geographic strata**.
•Tailored therapy:
  • LR-MDS → anti-inflammatory agents
  • HR-MDS → checkpoint inhibitors, hypomethylating agents
•Validates need for prospective, multicenter immune profiling studies.

References

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