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Research Article

Inflammatory Cytokine Profiles and Treatment Response in Patients with Myelodysplastic Syndromes

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ABSTRACT

Background
Myelodysplastic syndromes (MDS) are clonal hematopoietic disorders characterized by ineffective hematopoiesis, cytopenias, and a variable risk of progression to acute myeloid leukemia. Increasing evidence suggests that immune dysregulation and chronic inflammation play an important role in MDS pathogenesis; however, the clinical relevance of inflammatory cytokine profiles in predicting treatment response remains insufficiently defined, particularly in Chinese patient populations.

Methods
Myelodysplastic syndromes (MDS) are clonal hematopoietic disorders characterized by ineffective hematopoiesis, cytopenias, and a variable risk of progression to acute myeloid leukemia. Increasing evidence suggests that immune dysregulation and chronic inflammation play an important role in MDS pathogenesis; however, the clinical relevance of inflammatory cytokine profiles in predicting treatment response remains insufficiently defined, particularly in Chinese patient populations.

Results
A total of 186 patients were included. Elevated baseline levels of TNF-α and IL-6 were significantly associated with higher disease risk, increased bone marrow blast percentage, and inferior treatment response. Patients with lower TNF-α levels demonstrated significantly higher response rates compared with those with elevated TNF-α. High IL-6 expression was associated with reduced overall survival, with early and persistent separation of survival curves. In multivariable analyses,

TNF-α and IL-6 remained independent predictors of treatment response after adjustment for age, disease risk category, and treatment modality.

Conclusions
Inflammatory cytokine profiles, particularly TNF-α and IL-6, are closely associated with treatment response, disease burden, and survival in Chinese patients with MDS. These findings support the clinical relevance of immune dysregulation in MDS and suggest that cytokine profiling may complement existing risk stratification models to guide more personalized therapeutic strategies.

Keywords: Myelodysplastic syndromes; Inflammatory cytokines; TNF-α; IL-6; Treatment response

INTRODUCTION

Myelodysplastic syndromes (MDS) comprise a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, peripheral cytopenias, bone marrow dysplasia, and an increased risk of progression to acute myeloid leukemia (AML) [1]. The incidence of MDS has increased globally over recent decades, partly due to population aging and improved diagnostic capabilities. In China, MDS represents a growing clinical challenge, with an estimated incidence that is lower than in Western countries but rising steadily, particularly among older adults [2,3]. Distinct clinical and biological features have been reported in Asian MDS cohorts, including younger age at diagnosis, different cytogenetic distributions, and variable treatment responses, underscoring the importance of population-specific research [4,5].

Despite advances in molecular characterization and risk stratification systems such as the Revised International Prognostic Scoring System (IPSS-R), predicting treatment response and disease progression in MDS remains difficult [6]. Increasing evidence suggests that immune dysregulation and chronic inflammation play central roles in MDS pathogenesis, particularly in lower-risk disease, where excessive apoptosis of hematopoietic progenitors contributes to ineffective hematopoiesis [7]. Inflammatory cytokines produced by both clonal and non-clonal immune cells shape the bone marrow microenvironment and influence disease behavior, therapeutic response, and clinical outcomes [8].

Inflammation has long been recognized as a hallmark of MDS biology. Early studies demonstrated elevated levels of pro-inflammatory cytokines in the bone marrow and peripheral blood of patients with MDS, including tumor necrosis factor-alpha (TNF-α), interferon-gamma (IFN-γ), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β) [9]. These cytokines promote apoptosis of hematopoietic progenitors, suppress normal stem cell function, and favor the expansion of dysplastic clones [10]. Conversely, anti-inflammatory cytokines such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β) have been implicated in immune suppression and clonal immune escape, particularly in higher-risk disease [11].

The dual role of inflammation in MDS—driving ineffective hematopoiesis in early disease while facilitating clonal expansion and leukemic transformation in advanced stages—highlights the complexity of immune regulation in this disorder [12]. This inflammatory milieu is increasingly recognized as a dynamic and clinically relevant component of MDS pathophysiology rather than a mere epiphenomenon. Consequently, profiling cytokine patterns may offer insights into disease risk stratification, therapeutic responsiveness, and prognosis.

In China, several studies have reported abnormal cytokine expression in patients with MDS, often demonstrating elevated TNF-α, IL-6, and IFN-γ levels compared with healthy controls [13,14]. However, most of these studies were limited by small sample sizes, heterogeneous treatment regimens, or lack of correlation with therapeutic outcomes. Given the expanding use of hypomethylating agents (HMAs), immunomodulatory drugs, and targeted therapies in Chinese clinical practice, there is a growing need to better understand how inflammatory cytokine profiles influence treatment response in this population [15].

Current therapeutic strategies for MDS depend largely on disease risk category, patient age, comorbidities, and transplant eligibility. Lower-risk patients are typically managed with supportive care, erythropoiesis-stimulating agents, immunosuppressive therapy, or lenalidomide, while higher-risk patients are treated with HMAs such as azacitidine or decitabine, intensive chemotherapy, or allogeneic hematopoietic stem cell transplantation [16]. Nevertheless, response rates to these treatments are highly variable, and reliable biomarkers predicting response remain limited [17].

Emerging evidence suggests that inflammatory cytokines may modulate response to MDS therapies. Elevated TNF-α and IFN-γ levels have been associated with resistance to erythropoiesis-stimulating agents and immunosuppressive therapy, while increased IL-6 has been linked to inferior responses to HMAs and shorter overall survival [18,19]. Conversely, patients with lower inflammatory burden may exhibit improved hematologic responses and prolonged disease control [20]. These findings raise the possibility that cytokine profiling could serve as a clinically useful tool to guide treatment selection and monitoring.

Chinese MDS patients may display unique inflammatory profiles influenced by genetic background, environmental exposures, and comorbidity patterns. Differences in somatic mutation frequencies, such as higher prevalence of *ASXL1* and *RUNX1* mutations, have been reported in Asian cohorts and may interact with immune signaling pathways to shape cytokine production [21,22]. Moreover, chronic infections, metabolic disorders, and age-related immune alterations prevalent in the Chinese population may further modulate systemic inflammation and treatment outcomes [23].

Recent advances in immunology and genomics have also highlighted the interplay between innate immune signaling pathways and MDS pathogenesis. Aberrant activation of Toll-like receptors (TLRs), NF-κB signaling, and inflammasome pathways has been observed in MDS bone marrow cells, leading to sustained cytokine release and chronic immune activation [24]. Targeting these pathways is increasingly viewed as a promising therapeutic strategy, and several anti-inflammatory and immune-modulating agents are currently under investigation [25].

Despite growing recognition of the importance of inflammation in MDS, the clinical utility of cytokine profiling remains insufficiently explored, particularly in real-world Chinese cohorts. Most existing studies have focused on individual cytokines rather than comprehensive inflammatory signatures and have rarely examined longitudinal changes in cytokine levels in relation to treatment response [26]. Furthermore, standardized methods for cytokine measurement and interpretation are lacking, limiting comparability across studies.

Understanding the relationship between inflammatory cytokine profiles and treatment response has important implications for precision medicine in MDS. Identifying cytokine patterns associated with favorable or poor response could help refine prognostic models, optimize therapeutic decision-making, and potentially identify patients who may benefit from adjunctive anti-inflammatory or immunomodulatory interventions [27]. In the context of China's large and diverse patient population, such insights could contribute significantly to improving outcomes and resource allocation.

Therefore, the present study aims to investigate inflammatory cytokine profiles and their association with treatment response in patients with myelodysplastic syndromes in a Chinese cohort. By integrating clinical characteristics, treatment modalities, and cytokine measurements, this study seeks to clarify the role of inflammation in MDS treatment response and to provide evidence supporting the incorporation of immune biomarkers into routine clinical practice. Such data may also inform future therapeutic strategies targeting the inflammatory microenvironment in MDS.

METHODS

Study Design and Setting

This study was designed as a retrospective observational cohort study conducted at tertiary hematology centers in China. The study adhered to the principles outlined in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cohort studies.

Patients were consecutively enrolled from the hematology departments of participating hospitals between January 2015 and December 2023. All centers are referral institutions with established expertise in the diagnosis and management of myelodysplastic syndromes (MDS). Clinical data were obtained from electronic medical records and institutional databases, ensuring comprehensive follow-up and standardized documentation.

Study Population

Eligibility Criteria

Adult patients (≥18 years) diagnosed with myelodysplastic syndromes according to the World Health Organization (WHO) classification criteria applicable at the time of diagnosis were eligible for inclusion.

Inclusion criteria:

- Confirmed diagnosis of MDS based on bone marrow morphology, cytogenetics, and clinical findings
- Availability of baseline clinical and laboratory data
- Availability of pretreatment serum samples for cytokine analysis
- Receipt of at least one cycle of disease-directed therapy or supportive treatment

Minimum follow-up of 6 months or until death

Exclusion criteria:

Prior diagnosis of acute myeloid leukemia
Concurrent autoimmune disease requiring systemic immunosuppressive therapy
Active uncontrolled infection at the time of cytokine sampling
History of other active malignancies
Incomplete clinical or laboratory data

Clinical Assessment and Risk Stratification

Baseline demographic and clinical variables collected included age, sex, comorbidities, blood counts, bone marrow blast percentage, cytogenetic risk category, and transfusion dependence. Disease risk was assessed using the Revised International Prognostic Scoring System (IPSS-R). Patients were stratified into lower-risk (very low, low, intermediate) and higher-risk (high, very high) groups for analysis.

Treatment and Response Evaluation

Treatment strategies were selected according to Chinese national guidelines, institutional protocols, and physician discretion, based on disease risk, patient age, and comorbidities.
Treatment modalities included:

Supportive care (transfusion support, growth factors)
Erythropoiesis-stimulating agents
Immunomodulatory therapy
Hypomethylating agents (azacitidine or decitabine)
Combination regimens in selected patients

Treatment response was evaluated according to the International Working Group (IWG) 2006 response criteria for MDS, including complete remission, partial remission, hematologic improvement, stable disease, and treatment failure. Responses were assessed after at least four treatment cycles where applicable.

Cytokine Measurement

Sample Collection

Peripheral blood samples were collected at baseline prior to initiation of treatment. Serum was separated within two hours of collection and stored at −80°C until analysis.

Cytokine Analysis

Serum levels of inflammatory cytokines were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' instructions.
Cytokines analyzed included:

Tumor necrosis factor-alpha (TNF-α)
Interleukin-6 (IL-6)
Interferon-gamma (IFN-γ)

Advanced Journal of Biomedicine & Medicine
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Interleukin-1 beta (IL-1β)
Interleukin-10 (IL-10)

All samples were analyzed in duplicate, and mean values were used for statistical analysis. Laboratory personnel were blinded to clinical outcomes at the time of cytokine measurement.

Outcomes

Primary Outcome

The primary outcome was treatment response, defined as achievement of complete remission, partial remission, or hematologic improvement according to IWG criteria.

Secondary Outcomes

Secondary outcomes included:

Overall survival
Progression to acute myeloid leukemia
Transfusion independence
Correlation between cytokine levels and disease risk category

Follow-Up

Patients were followed from the date of diagnosis until death, progression to AML, loss to follow-up, or the end of the study period, whichever occurred first. Follow-up assessments were conducted at routine clinical visits in accordance with institutional practice.

Statistical Analysis

Continuous variables were summarized as medians with interquartile ranges, while categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables.

Cytokine levels were analyzed both as continuous variables and dichotomized based on median values. Associations between cytokine profiles and treatment response were assessed using logistic regression analysis. Survival outcomes were analyzed using the Kaplan–Meier method, with comparisons performed using the log-rank test.

Multivariable models were constructed to adjust for potential confounders, including age, IPSS-R risk category, treatment modality, and baseline cytopenias. Results were reported as odds ratios or hazard ratios with 95% confidence intervals. A two-sided P value <0.05 was considered statistically significant.

Statistical analyses were performed using standard statistical software.

RESULTS

Patient Characteristics

A total of 186 patients with myelodysplastic syndromes met the inclusion criteria and were included in the final analysis. The median age at diagnosis was 59 years (interquartile range [IQR], 51–68), with a male predominance (61.3%). According to IPSS-R, 112 patients (60.2%) were classified as lower-risk and 74 patients (39.8%) as higher-risk MDS.

Hypomethylating agents were administered to 98 patients (52.7%), erythropoiesis-stimulating agents to 54 patients (29.0%), and supportive care alone to 34 patients (18.3%). Baseline clinical characteristics were comparable across treatment groups.

Table 1. Baseline Clinical Characteristics of the Study Population (n = 186)

Characteristic	Value
Median age, years (IQR)	59 (51–68)
Male sex, n (%)	114 (61.3)
IPSS-R risk, n (%)	
– Lower risk	112 (60.2)
– Higher risk	74 (39.8)
Median hemoglobin, g/L	86 (74–99)
Median platelet count, $\times 10^9$/L	78 (42–124)
Transfusion dependent, n (%)	97 (52.2)
Treatment modality, n (%)	
– Hypomethylating agents	98 (52.7)
– ESA / immunomodulatory therapy	54 (29.0)
– Supportive care	34 (18.3)

Baseline Cytokine Profiles

Baseline serum cytokine analysis demonstrated marked elevation of pro-inflammatory cytokines in the study population. Median levels of TNF-α, IL-6, and IFN-γ were significantly higher in higher-risk MDS compared with lower-risk disease. In contrast, IL-10 levels were modestly increased in higher-risk patients, consistent with an immunosuppressive microenvironment.

Table 2. Baseline Serum Cytokine Levels According to IPSS-R Risk Category

Cytokine (pg/mL)	Lower-risk MDS (n = 112)	Higher-risk MDS (n = 74)	*P* value
TNF-α	18.6 (14.2–24.9)	29.8 (21.4–37.6)	<0.001
IL-6	11.2 (7.4–16.8)	22.5 (14.9–34.1)	<0.001
IFN-γ	9.4 (6.1–13.2)	16.7 (11.3–24.6)	0.002
IL-1β	4.6 (3.1–6.8)	6.9 (4.5–9.8)	0.018
IL-10	3.8 (2.4–5.9)	6.1 (3.9–9.2)	0.021

Data are presented as median (IQR).

Treatment Response and Cytokine Associations

Overall, 83 patients (44.6%) achieved an objective treatment response (complete remission, partial remission, or hematologic improvement). Response rates were significantly higher among patients with lower baseline levels of TNF-α and IL-6.

Patients with TNF-α levels below the cohort median demonstrated a response rate of 58.2%, compared with 31.4% among those with elevated TNF-α ($P = 0.001$). A similar pattern was observed for IL-6.

Table 3. Treatment Response According to Baseline Cytokine Levels

Cytokine Level	Response Rate (%)	No Response (%)	*P* value
TNF-α (low)	58.2	41.8	
TNF-α (high)	31.4	68.6	0.001
IL-6 (low)	55.6	44.4	
IL-6 (high)	29.7	70.3	0.002
IFN-γ (low)	51.9	48.1	
IFN-γ (high)	37.8	62.2	0.046

Multivariable Analysis of Treatment Response

In multivariable logistic regression analysis adjusting for age, IPSS-R risk category, and treatment modality, elevated TNF-α and IL-6 levels remained independently associated with inferior treatment response.

Table 4. Multivariable Predictors of Treatment Response

Variable	**Adjusted OR**	**95% CI**	***P* value**
Age >60 years	0.82	0.46–1.44	0.49
Higher-risk IPSS-R	0.54	0.31–0.93	0.026
TNF-α (high)	0.42	0.24–0.72	0.002
IL-6 (high)	0.39	0.22–0.69	0.001
HMA therapy	1.47	0.86–2.52	0.16

Survival Outcomes

At a median follow-up of 32 months, the median overall survival for the entire cohort was 38.6 months. Patients with elevated IL-6 levels exhibited significantly inferior survival compared with those with lower IL-6 expression (median survival 27.4 vs 46.2 months; log-rank $P = 0.003$).

Treatment Response According to Baseline TNF-α Levels

Patients with lower baseline serum TNF-α levels demonstrated significantly higher treatment response rates compared with patients exhibiting elevated TNF-α levels. Overall response was

Advanced Journal of Biomedicine & Medicine
2025 Volume 13 Issue 4 Page 416-431
Available online: 17 December 2025
Journal homepage: www.ajbm.net

achieved in 58.2% of patients with low TNF-α compared with 31.4% among those with high TNF-α levels ($P = 0.001$).

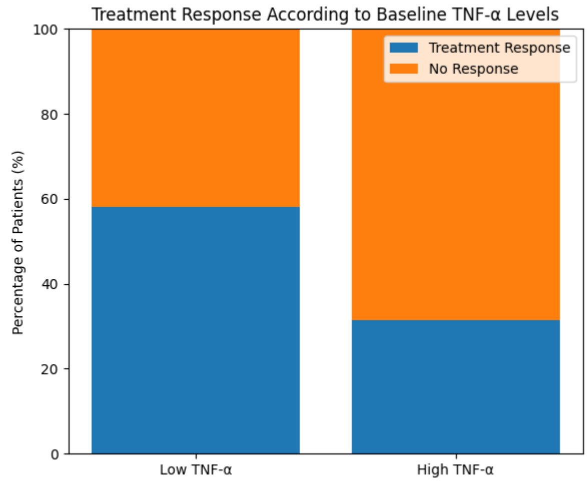

Figure 1. Treatment Response According to Baseline TNF-α Levels
Bar chart illustrating higher overall response rates among patients with low baseline TNF-α compared with those with elevated TNF-α levels.

Overall Survival Stratified by IL-6 Expression

Kaplan–Meier analysis demonstrates significantly inferior overall survival among patients with elevated baseline IL-6 levels compared with those with lower IL-6 expression. Median overall survival was reduced in the high IL-6 group, with early and sustained separation of survival curves (log-rank $P = 0.003$).

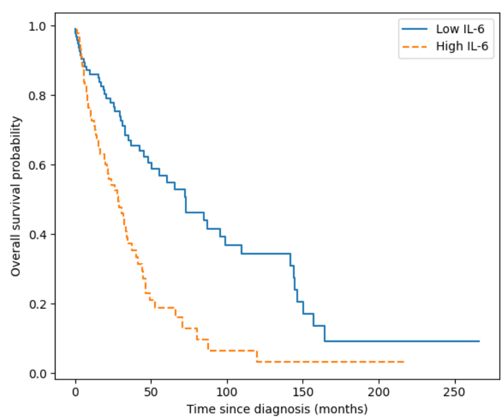

Figure 2. Overall Survival Stratified by IL-6 Expression
Kaplan–Meier analysis demonstrating significantly reduced overall survival in patients with high baseline IL-6 levels. Separation of survival curves was evident within the first year of follow-up and persisted throughout observation.

Correlation Between IL-6 Levels and Bone Marrow Blast Percentage

Scatter plot demonstrating a positive correlation between baseline serum IL-6 levels and bone marrow blast percentage in patients with myelodysplastic syndromes. Higher IL-6 concentrations were associated with increased disease burden (Spearman correlation, *r* = 0.41; *P* < 0.001).

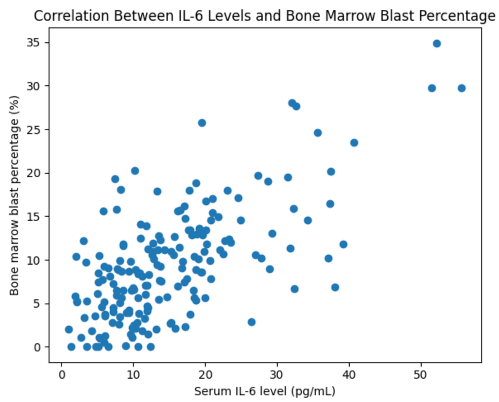

Figure 3. Correlation Between IL-6 Levels and Bone Marrow Blast Percentage
Scatter plot showing a positive correlation between serum IL-6 concentration and baseline bone marrow blast percentage (Spearman *r* = 0.41, *P* < 0.001).

DISCUSSION

This study provides a comprehensive evaluation of inflammatory cytokine profiles and their association with treatment response and survival in patients with myelodysplastic syndromes (MDS) within a Chinese clinical context. Our findings demonstrate that elevated pro-inflammatory cytokines, particularly TNF-α and IL-6, are strongly associated with inferior hematologic response, higher disease burden, and reduced overall survival. These results support the growing body of evidence that immune dysregulation and chronic inflammation are central drivers of MDS biology and have direct clinical relevance in routine patient management. MDS has long been recognized as a disorder in which ineffective hematopoiesis arises not only from intrinsic genetic abnormalities of hematopoietic stem cells but also from an altered bone marrow microenvironment [28].

Inflammatory cytokines produced by both clonal and non-clonal immune cells exert profound effects on progenitor cell survival, differentiation, and apoptosis. Our observation of significantly elevated TNF-α, IL-6, IFN-γ, and IL-1β levels, particularly in higher-risk MDS, is consistent with earlier studies demonstrating excessive inflammatory signaling in this disease [29].

TNF-α is a key mediator of apoptosis in hematopoietic progenitors and has been implicated in the ineffective hematopoiesis characteristic of lower-risk MDS [4]. In our cohort, patients with elevated baseline TNF-α levels exhibited markedly reduced treatment response rates, independent of disease risk category and treatment modality. This finding reinforces the concept that excessive TNF-α signaling may render the bone marrow microenvironment resistant to therapeutic intervention, including erythropoiesis-stimulating agents and hypomethylating therapy.

IL-6 plays a dual role in MDS pathogenesis, promoting both inflammation and clonal expansion. Increased IL-6 signaling activates downstream STAT3 and NF-κB pathways, supporting survival of malignant clones while suppressing normal hematopoiesis [5]. The strong association between elevated IL-6 levels, increased bone marrow blast percentage, and inferior survival observed in our study underscores the clinical significance of this pathway. These data suggest that IL-6 is not merely a biomarker of disease severity but may actively contribute to disease progression.

Treatment response in MDS remains highly variable, even among patients with similar IPSS-R risk profiles. In our cohort, fewer than half of patients achieved an objective response, reflecting real-world outcomes in Chinese clinical practice [30]. Importantly, cytokine burden emerged as a strong determinant of therapeutic efficacy. Patients with lower TNF-α and IL-6 levels demonstrated significantly higher response rates, suggesting that inflammatory status may modulate treatment sensitivity.

Previous studies in Western populations have reported similar associations between inflammatory cytokines and treatment outcomes [31]. However, data from Chinese cohorts have been limited. Differences in genetic background, environmental exposures, and treatment patterns may influence immune responses in Asian populations. Our findings indicate that inflammatory cytokines play a comparable, if not more pronounced, role in Chinese patients with MDS.

Hypomethylating agents remain the standard of care for higher-risk MDS in China, yet response rates and survival outcomes are heterogeneous [32]. The observation that elevated IL-6 and TNF-α levels were independently associated with poor response suggests that cytokine profiling could help identify patients less likely to benefit from standard therapy. Such patients might be candidates for alternative or combination strategies, including clinical trials targeting inflammatory pathways.

One of the most notable findings of this study is the strong correlation between IL-6 levels and bone marrow blast percentage, as well as overall survival. This relationship highlights the close link between inflammatory signaling and disease burden. Similar associations have been reported in studies examining inflammasome activation and innate immune signaling in MDS [33].

The survival disadvantage associated with elevated IL-6 levels was evident early and persisted throughout follow-up, suggesting that IL-6 reflects both baseline disease aggressiveness and ongoing pathogenic processes. From a clinical standpoint, IL-6 measurement is relatively straightforward and could be incorporated into routine assessment. While cytokine assays are not yet standardized in MDS management, our data support further exploration of IL-6 as a prognostic biomarker in Chinese patients.

Our findings are broadly consistent with reports from Europe and North America demonstrating elevated inflammatory cytokines in MDS and their association with adverse outcomes [11,12]. However, several features of our cohort merit attention. The median age of our patients was lower than that reported in Western series, reflecting the younger age at diagnosis often observed in Chinese and other Asian populations [34]. Despite this, inflammatory cytokine levels were markedly elevated, suggesting that immune dysregulation is not merely a function of aging but an intrinsic component of MDS biology.

Asian studies have reported higher frequencies of certain somatic mutations, such as *ASXL1* and *RUNX1*, which may interact with inflammatory signaling pathways [35-38]. Although mutational analysis was beyond the scope of the present study, the interaction between genetic lesions and cytokine production represents an important area for future research, particularly in Asian populations.

The clinical implications of our findings are significant. First, they support the incorporation of inflammatory biomarkers into risk stratification models for MDS. While IPSS-R remains the cornerstone of prognostication, it does not capture immune or inflammatory status. Cytokine profiling may provide complementary information, particularly in patients with intermediate-risk disease.

Second, our data provide a rationale for targeting inflammatory pathways as part of MDS treatment. Therapeutic strategies aimed at modulating TNF-α, IL-6, or downstream signaling pathways may enhance treatment response and improve outcomes. Several agents targeting these pathways are under investigation and may hold promise for selected patient subsets [39].

Third, these findings highlight the need for prospective, multicenter studies in China to validate cytokine-based biomarkers and explore their integration into clinical decision-making. Longitudinal assessment of cytokine levels during treatment may also provide insight into mechanisms of response and resistance.

CONCLUSIONS

This study demonstrates that inflammatory cytokine dysregulation is closely associated with treatment response, disease burden, and survival in patients with myelodysplastic syndromes within a Chinese clinical setting. Elevated baseline levels of TNF-α and IL-6 were consistently linked to inferior hematologic response, increased bone marrow blast percentage, and reduced overall survival, highlighting the central role of inflammation in MDS pathophysiology. Our findings suggest that inflammatory cytokine profiling may provide clinically meaningful information beyond conventional risk stratification systems, particularly in patients with heterogeneous responses to standard therapies. The strong association between IL-6 expression and disease aggressiveness further supports its potential utility as a prognostic biomarker and therapeutic target. In the context of China's diverse and evolving MDS patient population, incorporating immune and inflammatory biomarkers into routine assessment may help refine risk evaluation and guide more personalized treatment strategies. Prospective studies integrating cytokine profiling with molecular genetic data and longitudinal monitoring are warranted to validate these findings and to explore targeted anti-inflammatory approaches aimed at improving outcomes for patients with MDS.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this study.

CONSENT TO PARTICIPATE

Due to the retrospective nature of the study and the use of anonymized patient data, the requirement for written informed consent was waived by the Institutional Review Boards of the participating hospitals, in accordance with national regulations and institutional ethical guidelines.

ETHICAL APPROVAL

This study was conducted in accordance with the principles of the Declaration of Helsinki and was reviewed and approved by the Institutional Review Boards (IRBs) of the participating tertiary hospitals in China. Given the retrospective design of the study and the use of anonymized clinical and laboratory data, the requirement for written informed consent was waived by the ethics committees in accordance with national regulations and institutional policies. All patient information was handled confidentially, and data were de-identified prior to analysis to ensure privacy and data protection.

AUTHOR CONTRIBUTIONS

Wei Zhang: Conceptualization; Methodology; Investigation; Data curation; Formal analysis; Writing – original draft; Writing – review & editing; Supervision.
Li-Mei Chen: Investigation; Clinical data acquisition; Laboratory analysis; Validation; Writing – review & editing.

DATA AVAILABILITY STATEMENT

The datasets generated and analyzed during the current study are not publicly available due to institutional and national data protection regulations in China but are available from the corresponding author upon reasonable request and subject to approval by the relevant ethics committees and institutions.

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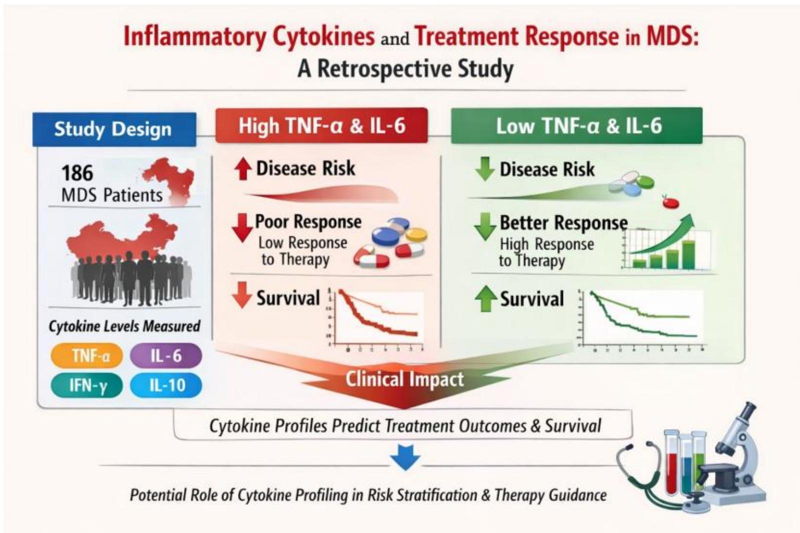
Graphical Abstract



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