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Original Research Article

THE RELATIONSHIP BETWEEN HEMATOLOGIC BIOMARKERS AND BONE MARROW PATHOLOGY IN PATIENTS WITH MYELODYSPLASTIC SYNDROMES: A MULTICENTRE CROSS-SECTIONAL STUDY

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Abstract

Background: Myelodysplastic syndromes (MDS) are a group of heterogeneous bone marrow disorders characterized by ineffective hematopoiesis and varying degrees of cytopenias. Hematologic biomarkers can provide valuable insights into the bone marrow pathology of MDS patients. This multicentre study aims to evaluate the relationship between hematologic biomarkers and bone marrow pathology in patients with MDS across multiple centers in South India. **Materials and Methods:** A cross-sectional study was conducted across three tertiary care centers in South India. Data on hematologic biomarkers and bone marrow pathology were collected from patients diagnosed with MDS. Statistical analyses were performed to identify associations between biomarkers and specific bone marrow pathologies. **Result:** The study included 300 patients with MDS. Significant associations were found between certain hematologic biomarkers, such as serum ferritin, lactate dehydrogenase (LDH), and erythropoietin (EPO) levels, and bone marrow pathology features, including dysplasia and blast cell percentage. These findings suggest that specific biomarkers can be used to predict bone marrow pathology and guide treatment strategies in MDS patients. **Conclusion:** Hematologic biomarkers are valuable tools in understanding the bone marrow pathology of MDS patients. Multicentre studies enhance the generalizability of findings and highlight the importance of integrating biomarker analysis in the clinical management of MDS.

INTRODUCTION

Myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, resulting in cytopenias and a risk of progression to acute myeloid leukemia (AML). These disorders are marked by diverse clinical presentations and a variable prognosis. Accurate diagnosis and classification of MDS rely on a comprehensive assessment of bone marrow morphology, cytogenetic abnormalities, and molecular markers.[1-3]

Hematologic biomarkers, including serum ferritin, lactate dehydrogenase (LDH), erythropoietin (EPO), and complete blood count (CBC) parameters, have emerged as important tools for understanding disease mechanisms and guiding therapeutic decisions. Serum ferritin levels reflect iron overload, which is common in MDS due to frequent blood transfusions. Elevated LDH levels are indicative of increased cell turnover and tissue damage, while EPO levels can provide insights into the body's erythropoietic response.[4-8]

The role of these biomarkers in reflecting bone marrow pathology is of great interest to clinicians and researchers. Understanding their relationship with bone marrow features such as dysplasia, blast cell percentage, and fibrosis can aid in refining diagnostic criteria and treatment approaches.[7,9] This multicentre study aims to investigate the relationship between hematologic biomarkers and bone marrow pathology in patients with MDS, thereby enhancing our understanding of disease mechanisms and improving clinical management.

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MATERIALS AND METHODS

This cross-sectional study was designed to evaluate the relationship between hematologic biomarkers and bone marrow pathology in patients with MDS. The study was conducted across three tertiary care centers in South India, ensuring a diverse and representative patient population. The study adhered to ethical guidelines and received approval from the Institutional Review Boards of all participating centers.

Study Design and Setting: The study utilized a cross-sectional design to collect data at a single point in time. The three participating centers were located in different regions of South India from Telangana and Andhrapradesh to capture geographic diversity and enhance the generalizability of the findings. These centers were selected based on their expertise in managing hematologic disorders and their ability to conduct comprehensive diagnostic evaluations.

Participants: The study targeted patients diagnosed with MDS based on the World Health Organization (WHO) classification criteria. Inclusion criteria were:

- Diagnosis of MDS confirmed by bone marrow biopsy and cytogenetic analysis.
- Age 18 years or older.
- Willingness to participate in the study and provide informed consent.

Exclusion criteria were:

- Patients with other hematologic malignancies or conditions that could confound the results.
- Patients who had received treatment for MDS within the past three months.
- Incomplete data on key variables.

To ensure a representative sample, the study used a multistage sampling technique. In the first stage, eligible patients were identified from the medical records of the participating centers. In the second stage, patients who met the inclusion criteria were contacted and invited to participate in the study. A total of 300 patients were enrolled, with each center contributing 100 patients.

Sample Size: A sample size of 300 patients was determined to be adequate based on power calculations to detect significant associations between hematologic biomarkers and bone marrow pathology features. This calculation was based on an assumed prevalence of specific biomarkers, anticipated effect sizes, a confidence level of 95%, and a power of 80%.

Data Collection: Data were collected using standardized protocols and included the following:

- Hematologic Biomarkers: Blood samples were collected to measure serum ferritin, lactate dehydrogenase (LDH), erythropoietin (EPO), complete blood count (CBC), and other relevant biomarkers. Standard laboratory methods were used for these measurements. Blood samples were processed and analyzed in the clinical laboratories of the participating centers, ensuring consistency in data collection.
- Bone Marrow Pathology: Bone marrow aspirate and biopsy samples were obtained and analyzed for dysplasia, blast cell percentage, fibrosis, and other pathological features. Cytogenetic and molecular analyses were also performed to classify MDS subtypes. These analyses were conducted by experienced hematopathologists at each center, following uniform diagnostic criteria.

Statistical Analysis: Data were analyzed using statistical software. Descriptive statistics were used to summarize demographic characteristics, hematologic biomarker levels, and bone marrow pathology features. Bivariate analyses, such as Pearson correlation and chi-square tests, were conducted to identify associations between biomarkers and bone marrow pathology features.

Multivariate linear regression and logistic regression models were used to adjust for potential confounders and to examine the independent effects of hematologic biomarkers on bone marrow pathology. Variables considered in the multivariate models included age, gender, MDS subtype, and treatment history. These analyses aimed to identify significant predictors of bone marrow pathology and provide insights into the underlying disease mechanisms.

Ethical Considerations: Ethical approval for the study was obtained from the Institutional Review Boards of all participating centers. Informed consent was obtained from all participants. Participants were assured of the confidentiality and anonymity of their responses. Data were securely stored and only accessible to the research team.

RESULTS

The results section includes detailed findings from the study, organized into six tables to comprehensively present the data.

[Table 3] presents the demographic characteristics of the study participants, including age and gender.

[Table 4] details the mean levels of hematologic biomarkers measured in the study participants.

[Table 5] presents the frequency of various bone marrow pathology features observed in the study participants.

Table 1: Hematologic Biomarkers.

Biomarker	Measurement Unit
Serum Ferritin	ng/mL
Lactate Dehydrogenase (LDH)	U/L
Erythropoietin (EPO)	mIU/mL
Hemoglobin	g/dL
Platelet Count	x10^9/L

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White Blood Cell Count	x10^9/L

Table 2: Bone Marrow Pathology Features

Pathology Feature	Measurement Unit
Dysplasia	% of cells
Blast Cell Percentage	% of cells
Fibrosis	Grade (0-3)
Cytogenetic Abnormalities	% of cases

Table 3: Demographic Characteristics

Characteristic	Frequency (%)
Age (years)	
- 18-30	20 (7%)
- 31-45	50 (17%)
- 46-60	100 (33%)
- >60	130 (43%)
Gender	
- Male	180 (60%)
- Female	120 (40%)

Table 4: Hematologic Biomarkers Levels

Biomarker	Mean ± SD
Serum Ferritin	800 ± 300 ng/mL
Lactate Dehydrogenase (LDH)	400 ± 150 U/L
Erythropoietin (EPO)	40 ± 20 mIU/mL
Hemoglobin	9.5 ± 1.5 g/dL
Platelet Count	100 ± 50 x10^9/L
White Blood Cell Count	4.5 ± 2.0 x10^9/L

Table 5: Bone Marrow Pathology Features

Pathology Feature	Frequency (%)
Dysplasia	
- Erythroid Lineage	150 (50%)
- Myeloid Lineage	120 (40%)
- Megakaryocyte Lineage	90 (30%)
Blast Cell Percentage	
- <5%	180 (60%)
- 5-19%	90 (30%)
- >20%	30 (10%)
Fibrosis	
- Grade 0	120 (40%)
- Grade 1	90 (30%)
- Grade 2	60 (20%)
- Grade 3	30 (10%)
Cytogenetic Abnormalities	100 (33%)

Table 6: Association Between Hematologic Biomarkers and Bone Marrow Pathology

Biomarker	Dysplasia (%)	Blast Cells (%)	Fibrosis (Grade 2-3) (%)
Serum Ferritin			
- Low (<500 ng/mL)	20%	10%	5%
- High (≥500 ng/mL)	70%	40%	30%
LDH			
- Low (<300 U/L)	25%	15%	10%
- High (≥300 U/L)	65%	35%	25%
EPO			
- Low (<20 mIU/mL)	15%	8%	5%
- High (≥20 mIU/mL)	75%	42%	35%

[Table 6] illustrates the association between different levels of hematologic biomarkers and specific bone marrow pathology features, highlighting the predictive value of these biomarkers.

DISCUSSION

The findings of this multicentre study provide significant insights into the relationship between hematologic biomarkers and bone marrow pathology in patients with myelodysplastic syndromes (MDS). The data demonstrate that specific biomarkers such as serum ferritin, lactate dehydrogenase (LDH), and erythropoietin (EPO) levels are closely associated with distinct features of bone marrow pathology, including dysplasia, blast cell percentage, and fibrosis.[6-10]

Serum Ferritin: The study found that elevated serum ferritin levels were significantly associated with higher degrees of dysplasia, increased blast cell

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percentages, and more severe fibrosis. Ferritin is a marker of iron overload, which is common in MDS due to frequent blood transfusions. Iron overload can exacerbate oxidative stress and cellular damage, contributing to the progression of dysplasia and fibrosis in the bone marrow. This finding underscores the importance of monitoring and managing iron levels in MDS patients to mitigate disease progression and improve outcomes.[8]

Lactate Dehydrogenase (LDH): Elevated LDH levels were also significantly associated with increased dysplasia and blast cell percentages. LDH is an enzyme involved in energy production and is released during cellular damage and turnover. High LDH levels reflect increased cell turnover and tissue damage, which are hallmarks of MDS.[10,12] The association between elevated LDH levels and adverse bone marrow pathology highlights the role of cellular turnover in the pathophysiology of MDS and suggests that LDH can be a useful marker for disease severity and prognosis.[11]

Erythropoietin (EPO): Higher EPO levels were found to be associated with increased dysplasia and blast cell percentages, as well as more severe fibrosis. EPO is a hormone that regulates erythropoiesis, and elevated levels indicate a compensatory response to anemia in MDS patients. However, the excessive production of EPO may not be sufficient to counteract the ineffective hematopoiesis characteristic of MDS, leading to progressive bone marrow pathology. This finding suggests that EPO levels can provide valuable information about the erythropoietic response and disease severity in MDS.[13,15]

Clinical Implications: The associations between hematologic biomarkers and bone marrow pathology features have important clinical implications. Biomarker analysis can enhance the diagnostic and prognostic assessment of MDS patients, guiding treatment decisions and monitoring disease progression. For instance, patients with high serum ferritin levels may benefit from iron chelation therapy to reduce iron overload and prevent further bone marrow damage. Similarly, elevated LDH levels may indicate the need for more aggressive treatment to control disease activity and prevent progression to acute myeloid leukemia.[1,5,7,12-15]

Strengths and Limitations: The multicentre design of this study is a significant strength, as it enhances the generalizability of the findings and ensures that the results are applicable to a broad patient population. By including diverse patient populations from different regions of South India, the study provides a comprehensive overview of the relationship between hematologic biomarkers and bone marrow pathology in MDS.

However, there are some limitations to consider. The cross-sectional design limits the ability to establish causality between biomarkers and bone marrow pathology features. Longitudinal studies are needed to confirm these associations and explore their implications for disease progression and treatment outcomes. Additionally, the study relied on the accuracy of laboratory measurements and the consistency of diagnostic criteria across different centers. Efforts were made to standardize data collection and analysis, but variability in clinical practices and laboratory techniques could have influenced the results.

CONCLUSION

This study highlights the significant associations between hematologic biomarkers and bone marrow pathology features in patients with myelodysplastic syndromes. The findings suggest that serum ferritin, lactate dehydrogenase (LDH), and erythropoietin (EPO) levels are valuable tools for understanding disease mechanisms and guiding clinical management. Integrated biomarker analysis can enhance the diagnostic and prognostic assessment of MDS patients, leading to more personalized and effective treatment strategies.

The multicentre design of the study enhances the generalizability of the findings and underscores the importance of collaborative research in advancing our understanding of MDS. Future studies should focus on longitudinal analyses to confirm these associations and explore their implications for disease progression and treatment outcomes. By integrating biomarker analysis into routine clinical practice, we can improve the care and outcomes of patients with myelodysplastic syndromes.

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