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CLINICAL SIGNIFICANCE OF ROUTINE HEMATOLOGICAL PARAMETERS IN THE PROGNOSTIC STRATIFICATION OF AMYOTROPHIC LATERAL SCLEROSIS

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ABSTRACT

Introduction: *Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder characterized by motor neuron degeneration, leading to muscle weakness, paralysis, and eventual respiratory failure. Systemic inflammation, oxidative stress, and impaired oxygen transport have been implicated in disease progression. Hematological biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), red cell distribution width (RDW), and hemoglobin (Hb), may serve as potential prognostic indicators for ALS.* ***Objectives:*** *This study aimed to evaluate the prognostic value of routine hematological markers (NLR, PLR, RDW, and Hb) in ALS progression.* ***Methodology:*** *A cross-sectional study was conducted in the neurology departments of tertiary care hospitals in Karachi, with 345 ALS patients categorized into early-stage and advanced-stage groups. Independent t-tests and Mann-Whitney U tests were used for group comparisons. Pearson's and Spearman's correlation coefficients assessed relationships between hematological markers and ALS severity. Multivariate logistic regression was applied to identify independent predictors of disease progression.* ***Results & Findings:*** *NLR and PLR were significantly elevated in advanced-stage ALS patients, indicating systemic inflammation. RDW was also higher, suggesting increased oxidative stress, while Hb levels were lower, reflecting impaired oxygen transport. Correlation analyses confirmed significant associations between these markers and disease severity. Logistic regression identified NLR and RDW as independent predictors of ALS progression.* ***Conclusion:*** *Routine hematological markers provide valuable prognostic insight into ALS progression. Their association with inflammation, oxidative stress, and oxygen transport dysfunction suggests their potential role in disease monitoring. Incorporating these biomarkers into clinical assessments may improve patient stratification and therapeutic decision-making. Further longitudinal studies are needed to validate these findings and explore targeted interventions.*

Keywords: Amyotrophic lateral sclerosis (ALS), NLR, PLR, RDW, Hemoglobin, Inflammation, Oxidative Stress, Prognostic Biomarkers, Neurodegeneration, Multivariate Regression.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder primarily affecting motor neurons in the brain and spinal cord, leading to irreversible paralysis, bulbar dysfunction, and ultimately respiratory failure, typically within 3–5 years of onset [1]. The diagnosis of ALS is primarily clinical, supported by neurophysiological assessments, while ancillary investigations such as blood tests, neuroimaging, and cerebrospinal fluid (CSF) analysis serve to exclude alternative diagnoses. Over recent years, there has been a significant focus on identifying novel biomarkers to enhance diagnostic accuracy and facilitate prognostic stratification in clinical practice and research. Among these, neurofilament light chain (NfL) and phosphorylated neurofilament heavy chain (pNfH) have emerged as reliable biomarkers for ALS detection and disease progression assessment [2]. However, the widespread implementation of neurofilament measurement remains limited due to the need for specialized high-sensitivity assays,

restricting its accessibility across ALS centers. Given these limitations, recent investigations have explored the prognostic value of routine blood biomarkers due to their widespread availability and cost-effectiveness. Serum creatinine has demonstrated a strong association with ALS progression, correlating with functional disability, disease severity, and overall survival. Additionally, biomarkers of muscle metabolism, such as creatine kinase, as well as inflammatory markers including serum albumin and C-reactive protein, have been linked to ALS prognosis, although further studies are warranted to validate these findings [3].

Beyond these biochemical markers, hematological parameters have gained attention as potential prognostic indicators in ALS. Alterations in routine hematological indices, including complete blood count (CBC) parameters such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and red cell distribution width (RDW), have been implicated in neuroinflammatory and oxidative stress pathways, both of which play critical roles in ALS pathogenesis [4]. Elevated NLR and PLR have been associated with systemic inflammation and immune dysregulation, which may contribute to disease progression, while increased RDW has been linked to oxidative stress and metabolic dysregulation in neurodegenerative diseases. Furthermore, hemoglobin levels, mean corpuscular volume (MCV), and platelet indices, including mean platelet volume (MPV), have been suggested as potential markers of disease severity and prognosis. In this study, we systematically evaluated the association of a comprehensive panel of routine hematological and biochemical parameters with disease characteristics and clinical outcomes in a large cohort of ALS patients. Specifically, we examined their correlation with disease onset site, markers of upper motor neuron (UMN) and lower motor neuron (LMN) involvement, functional disability, and overall survival. By integrating routine hematological indices into ALS prognostic models, we aim to improve risk stratification and provide insights into the underlying pathophysiological mechanisms contributing to disease progression [5].

METHODOLOGY

This retrospective cohort study was conducted at the Neurology Departments of various tertiary care hospitals in Karachi from January 2023 to December 2024. A total of 345 inpatients diagnosed with Amyotrophic Lateral Sclerosis (ALS) were recruited based on the revised El Escorial Criteria, ensuring the inclusion of individuals with clinically definite [6], probable, and possible ALS. To minimize confounding factors, patients with chronic kidney disease (n = 6) and those presenting with acute inflammatory states (n = 3) at the time of sample collection were excluded. Blood

samples were collected at the time of hospital admission, prior to any medical intervention that could influence hematological parameters. To ensure consistency and reliability, all samples were analyzed in a single accredited laboratory using standardized protocols.

The study focused on hematological parameters, including a complete blood count (CBC) and several derived indices. The CBC panel measured white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin (Hb), platelet count (Plt), polymorphonuclear cells (PMN), lymphocytes (Ly), and monocytes (Mo). Additionally, hematological indices such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), red cell distribution width (RDW), and mean platelet volume (MPV) were assessed to evaluate their potential prognostic significance in ALS. Blood samples were collected through venipuncture and analyzed within two hours using an automated hematology analyzer (Sysmex XN-Series) to maintain accuracy. Internal quality control procedures were followed daily, and external quality assurance measures were ensured through participation in proficiency testing programs.

Statistical analysis was conducted using SPSS version 27.0. Descriptive statistics, including mean and standard deviation, were used to summarize hematological parameters. Comparative analyses between different ALS prognostic groups were performed using independent t-tests for normally distributed data and Mann-Whitney U tests for non-normally distributed variables. Correlations between hematological markers and disease severity were assessed using Pearson's and Spearman's correlation coefficients. Furthermore, multivariate logistic regression was applied to identify independent hematological predictors of disease progression. The study adhered to the ethical guidelines of the Institutional Review Board (IRB) of respective institutes approval were obtained, and patient confidentiality was maintained by anonymizing all collected data.

RESULTS & FINDINGS

This section presents the hematological findings of the study, analyzing their significance in the prognostic stratification of Amyotrophic Lateral Sclerosis (ALS). The results are categorized into descriptive statistics, comparative analyses, correlations, and regression modeling to identify potential hematological markers influencing disease progression.

Demographic information:

The study included a total of 345 patients diagnosed with amyotrophic lateral sclerosis (ALS). The mean age of the participants was 58.6 years with a standard deviation of 10.4 years, indicating a

moderate variation in age distribution within the sample. The median age was 58 years, with an interquartile range (IQR) of 51 to 66 years, suggesting that the majority of patients fell within this age bracket. When categorized into age groups, the highest proportion of patients (36.5%) belonged to the 50–59 years category, followed by 29.6% in the 60–69 years age group. The 40–49 years group constituted 20.9% of the total sample, while only 13.0% of patients were 70 years or older. This age distribution is consistent with global ALS prevalence patterns, where the disease is more commonly diagnosed in middle to late adulthood. Regarding gender distribution, males comprised a significantly higher proportion of the study population, accounting for 61.4% (n = 212) of cases, whereas females represented 38.6% (n = 133). The male predominance in ALS cases aligns with epidemiological trends observed in various studies, where men are generally at a higher risk of developing the disease compared to women.

Table 1: Demographic Characteristics of the Study Population (n = 345)

Characteristic	Mean ± SD / Median (IQR)
Age (years)	58.6 ± 10.4 / 58 (51 - 66)
Age Groups	**n (%)**
40 - 49 years	72 (20.9%)
50 - 59 years	126 (36.5%)
60 - 69 years	102 (29.6%)
≥70 years	45 (13.0%)
Gender	
Male	212 (61.4%)
Female	133 (38.6%)

Descriptive Analysis of Hematological Parameters:

Table 2 provides an overview of the mean, standard deviation (SD), median, and interquartile range (IQR) for key hematological parameters in the study cohort. The data were analyzed for all 345 ALS patients.

Table 2: Descriptive Statistics of Hematological Parameters (n = 345)

Parameter	Mean ± SD	Median (IQR)	Normal Range
White Blood Cells ($\times 10^9$/L)	7.3 ± 1.9	7.2 (6.0 - 8.5)	4.0 - 10.0
Red Blood Cells ($\times 10^{12}$/L)	4.5 ± 0.7	4.6 (4.2 - 5.0)	4.2 - 5.6
Hemoglobin (g/dL)	12.8 ± 1.5	13.0 (11.9 - 14.1)	12.0 - 16.0
Platelet Count ($\times 10^9$/L)	242 ± 65	245 (210 - 280)	150 - 400
Polymorphonuclear Cells (%)	62.5 ± 7.4	63 (58 - 67)	50 - 70

Lymphocytes (%)	28.3 ± 5.8	27 (24 - 32)	20 - 40
Monocytes (%)	6.2 ± 1.4	6.0 (5.0 - 7.0)	2 - 10
Neutrophil-to-Lymphocyte Ratio (NLR)	2.4 ± 0.8	2.3 (1.9 - 2.8)	<3.0
Platelet-to-Lymphocyte Ratio (PLR)	90.5 ± 21.2	88 (75 - 103)	80 - 180
Red Cell Distribution Width (RDW, %)	14.8 ± 1.2	14.7 (14.0 - 15.5)	11.5 - 15.0
Mean Platelet Volume (MPV, fL)	9.6 ± 1.1	9.5 (8.9 - 10.3)	7.4 - 10.4

The white blood cell (WBC) count, red blood cell (RBC) count, and hemoglobin levels were within normal ranges for most patients, while RDW was elevated in a subset, indicating possible erythropoietic stress or anemia-related concerns. The NLR and PLR values, which are markers of systemic inflammation, were slightly higher in some patients, suggesting an inflammatory component in ALS progression.

Comparison of Hematological Parameters Between Early and Advanced ALS Cases:

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder characterized by motor neuron deterioration, leading to muscle weakness, paralysis, and respiratory failure. Based on disease severity, patients in this study were classified into early-stage ALS and advanced-stage ALS. Early-stage ALS included patients with mild motor dysfunction, where muscle weakness was present but did not severely impact daily activities. In contrast, advanced-stage ALS patients exhibited severe motor impairment, significant muscle atrophy, and respiratory involvement, often requiring ventilatory support.

Table 3: Comparative Analysis of Hematological Parameters by ALS Progression

Parameter	Early-stage ALS (Mean ± SD)	Advanced-stage ALS (Mean ± SD)	p-value
White Blood Cells (×10⁹/L)	7.1 ± 1.7	7.6 ± 2.1	0.03
Hemoglobin (g/dL)	13.1 ± 1.4	12.5 ± 1.6	0.02
Neutrophil-to-Lymphocyte Ratio (NLR)	2.1 ± 0.7	2.7 ± 0.9	<0.01
Platelet-to-Lymphocyte Ratio (PLR)	85.2 ± 19.4	96.1 ± 22.5	<0.01
Red Cell Distribution Width (RDW, %)	14.4 ± 1.1	15.2 ± 1.3	<0.01

($p < 0.05$ = statistically significant; $p < 0.01$ = highly significant)

A detailed comparison of hematological parameters between these two groups revealed significant differences, suggesting potential biomarkers for disease progression. White blood cell (WBC) count was slightly elevated in advanced-stage patients ($7.6 \pm 2.1 \times 10^9$/L) compared to early-stage patients ($7.1 \pm 1.7 \times 10^9$/L), with a statistically significant difference ($p = 0.03$). This increase in WBCs may indicate a systemic inflammatory response, which has been associated with neurodegenerative progression. Similarly, hemoglobin (Hb) levels were significantly lower in advanced-stage ALS patients (12.5 ± 1.6 g/dL) than in early-stage patients (13.1 ± 1.4 g/dL, $p = 0.02$). This decline in hemoglobin levels could be linked to chronic inflammation and poor nutritional status, both of which are common in progressive neurodegenerative diseases. Two inflammatory ratios, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), were notably higher in advanced-stage patients. NLR, which reflects systemic inflammation, was significantly increased in advanced ALS (2.7 ± 0.9) compared to early-stage patients (2.1 ± 0.7, $p < 0.01$). Similarly, PLR, another indicator of inflammatory and immune imbalance, was elevated in advanced-stage ALS (96.1 ± 22.5) compared to early-stage patients (85.2 ± 19.4, $p < 0.01$). These findings suggest that inflammation plays a crucial role in disease progression and could be a potential target for therapeutic interventions. Moreover, red cell distribution width (RDW), a marker of erythrocyte variability associated with oxidative stress and inflammation, was significantly higher in advanced-stage ALS patients ($15.2 \pm 1.3\%$) than in early-stage patients ($14.4 \pm 1.1\%$, $p < 0.01$). Elevated RDW levels indicate impaired erythropoiesis and increased oxidative stress, both of which have been implicated in neurodegeneration.

Correlation Analysis Between Hematological Markers and ALS Severity

To further explore the relationship between hematological markers and disease progression in ALS, a correlation analysis was conducted. The results revealed significant associations between various blood parameters and disease severity, with negative correlations indicating worsening conditions as values increased and positive correlations suggesting protective or stabilizing effects. White Blood Cell (WBC) count demonstrated a moderate negative correlation with ALS severity ($r = -0.28$, $p < 0.01$), suggesting that higher WBC levels are associated with more advanced disease stages. This may indicate an underlying inflammatory response contributing to neurodegeneration. Hemoglobin (Hb) levels, on the other hand, showed a moderate positive correlation with disease severity ($r = 0.31$, $p < 0.01$), implying that patients with higher hemoglobin levels tend to have less

severe disease progression. This could be attributed to the role of adequate oxygen transport in maintaining neuronal function and reducing oxidative stress. Inflammatory ratios such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) exhibited strong negative correlations with ALS severity ($r = -0.41$, $p < 0.01$ and $r = -0.37$, $p < 0.01$, respectively). This indicates that higher NLR and PLR values are associated with more severe motor impairment and disease progression. These findings further reinforce the role of systemic inflammation in accelerating ALS pathology. Similarly, Red Cell Distribution Width (RDW) was also negatively correlated with disease severity ($r = -0.35$, $p < 0.01$). Elevated RDW levels suggest increased oxidative stress and impaired erythropoiesis, both of which are known contributors to neurodegeneration in ALS.

Table 4: Correlation of Hematological Parameters with ALS Severity (ALSFRS-R Score)

Parameter	Correlation Coefficient (r)	p-value
White Blood Cells (WBC)	-0.28	<0.01
Hemoglobin (Hb)	0.31	<0.01
Neutrophil-to-Lymphocyte Ratio (NLR)	-0.41	<0.01
Platelet-to-Lymphocyte Ratio (PLR)	-0.37	<0.01
Red Cell Distribution Width (RDW)	-0.35	<0.01

A significant negative correlation was observed between NLR, PLR, RDW, and ALS severity, indicating that elevated inflammatory markers were associated with worse functional impairment. Conversely, higher hemoglobin levels were positively correlated with ALSFRS-R scores, suggesting a potential protective role of optimal oxygen delivery in ALS patients.

Multivariate Regression Analysis to Identify Independent Prognostic Factors

To assess the predictive value of hematological parameters in determining the likelihood of ALS progression, an odds ratio (OR) analysis was performed. The results indicate that inflammatory and hematological markers significantly influence disease severity, with higher odds ratios suggesting increased risk of progression. Neutrophil-to-Lymphocyte Ratio (NLR) was found to be a strong predictor of ALS progression, with an odds ratio of 1.92 (95% CI: 1.35 – 2.72, $p < 0.01$). This means that for every unit increase in NLR, the likelihood of advancing to a more severe stage

of ALS nearly doubles. The strong association between NLR and disease severity underscores the role of systemic inflammation in neurodegenerative progression. Similarly, Platelet-to-Lymphocyte Ratio (PLR) was also significantly associated with ALS severity, with an odds ratio of 1.58 (95% CI: 1.12 – 2.24, p = 0.02). Higher PLR values indicate immune system dysregulation and heightened inflammatory activity, both of which contribute to motor neuron damage. On the other hand, hemoglobin (Hb) levels showed a protective effect against ALS progression, with an odds ratio of 0.79 (95% CI: 0.65 – 0.93, p < 0.01). This suggests that patients with higher hemoglobin levels have a lower risk of severe disease progression, potentially due to better oxygen transport and reduced oxidative stress in neuronal tissues. Red Cell Distribution Width (RDW) was also significantly associated with ALS severity, with an odds ratio of 1.43 (95% CI: 1.19 – 1.86, p < 0.01). Higher RDW values indicate increased variability in red blood cell size, which has been linked to systemic inflammation and oxidative stress—both of which play a role in neurodegenerative diseases.

Table 5: Multivariate Regression Analysis for Predicting Advanced ALS

Parameter	Odds Ratio (OR)	95% Confidence Interval	p-value
Neutrophil-to-Lymphocyte Ratio (NLR)	1.92	1.35 - 2.72	<0.01
Platelet-to-Lymphocyte Ratio (PLR)	1.58	1.12 - 2.24	0.02
Hemoglobin (Hb)	0.79	0.65 - 0.93	<0.01
RDW (%)	1.43	1.19 - 1.86	<0.01

DISCUSSION

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder characterized by the loss of motor neurons, leading to muscle weakness and eventual paralysis. The identification of reliable biomarkers for disease progression is crucial for early diagnosis, prognosis, and therapeutic interventions [7]. This study explored the clinical significance of routine hematological parameters in the prognostic stratification of ALS. The results demonstrated that inflammatory markers, particularly the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), were significantly elevated in patients with advanced-stage ALS [8]. Additionally, red cell

distribution width (RDW) was found to be a predictor of disease severity, whereas higher hemoglobin (Hb) levels were associated with a lower risk of progression. These findings reinforce the role of systemic inflammation, oxidative stress, and hematological disturbances in ALS pathology. Systemic inflammation has been increasingly recognized as a key contributor to ALS pathogenesis [9]. Elevated NLR and PLR levels observed in this study indicate an imbalance between innate and adaptive immune responses, with a predominance of neutrophilic inflammation. NLR was significantly higher in advanced-stage ALS patients compared to early-stage patients, with an odds ratio (OR) of 1.92 (95% CI: 1.35 – 2.72, $p < 0.01$), indicating a nearly twofold increase in the risk of disease progression with rising NLR values. This is consistent with previous studies that have reported increased neutrophilic activity in ALS patients, suggesting an inflammatory-driven neurodegenerative process [10,11]. Neutrophils contribute to neuroinflammation through the release of reactive oxygen species (ROS) and pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which can exacerbate motor neuron damage [12]. Lymphocytes, on the other hand, play a protective role by modulating immune responses and limiting excessive inflammation. A higher NLR reflects a disproportionate increase in neutrophils relative to lymphocytes, suggesting an unchecked inflammatory response that may accelerate disease progression [13]. The strong correlation between NLR and ALS severity ($r = -0.41$, $p < 0.01$) underscores its potential utility as a prognostic biomarker.

Similarly, PLR was also significantly elevated in advanced-stage ALS patients, with an OR of 1.58 (95% CI: 1.12 – 2.24, $p = 0.02$). Platelets play a crucial role in inflammation by releasing inflammatory mediators such as platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF-β), which may contribute to neuroinflammation and vascular dysfunction in ALS [14,15]. Previous studies have suggested that increased PLR is associated with worse clinical outcomes in neurodegenerative diseases, including ALS and multiple sclerosis [16]. The negative correlation between PLR and ALS severity ($r = -0.37$, $p < 0.01$) supports its role as a potential marker for disease progression. RDW, a measure of variability in red blood cell size, has emerged as a significant marker of oxidative stress and inflammation in various diseases, including ALS. In this study, RDW was significantly higher in advanced-stage ALS patients (15.2% ± 1.3) compared to early-stage patients (14.4% ± 1.1), with an OR of 1.43 (95% CI: 1.19 – 1.86, $p <$

0.01). Elevated RDW is indicative of impaired erythropoiesis, chronic inflammation, and increased oxidative stress, all of which are known contributors to ALS pathogenesis [17,18]. Oxidative stress plays a crucial role in motor neuron degeneration in ALS. Studies have shown that increased ROS levels lead to lipid peroxidation, mitochondrial dysfunction, and DNA damage, ultimately contributing to neuronal apoptosis [19]. The strong negative correlation between RDW and ALS severity ($r = -0.35$, $p < 0.01$) suggests that higher RDW levels may reflect ongoing oxidative damage in ALS patients. Additionally, previous research has linked increased RDW to poor survival outcomes in ALS, further highlighting its prognostic significance [20].

Interestingly, hemoglobin levels were found to be significantly lower in advanced-stage ALS patients (12.5 g/dL ± 1.6) compared to early-stage patients (13.1 g/dL ± 1.4), with an OR of 0.79 (95% CI: 0.65 – 0.93, $p < 0.01$). This suggests that higher hemoglobin levels may have a protective effect against ALS progression. Hemoglobin is essential for oxygen transport and delivery to tissues, including the central nervous system. Reduced hemoglobin levels can lead to hypoxia, which exacerbates neuronal damage and accelerates disease progression [21]. Previous studies have reported that anemia is associated with poorer prognosis in ALS, potentially due to reduced oxygenation and increased oxidative stress in motor neurons [22]. The positive correlation between hemoglobin levels and ALS severity ($r = 0.31$, $p < 0.01$) further supports this notion. Maintaining adequate hemoglobin levels through nutritional and medical interventions may help mitigate disease progression in ALS patients.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

The findings of this study have significant clinical implications. First, routine hematological parameters such as NLR, PLR, RDW, and hemoglobin can serve as cost-effective and easily accessible biomarkers for monitoring ALS progression. Unlike advanced imaging or genetic testing, which may be costly and less accessible, these blood parameters can be readily measured in clinical settings. Second, the strong association between systemic inflammation and ALS severity highlights the potential role of anti-inflammatory therapies in disease management. Previous trials with nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids have yielded mixed results; however, targeting specific inflammatory pathways, such as neutrophil activation or platelet aggregation, may offer new therapeutic strategies [21,22]. Third, the

identification of RDW as a marker of oxidative stress further supports the role of antioxidant therapy in ALS management. Antioxidants such as edaravone, which scavenge free radicals and reduce oxidative damage, have been shown to slow disease progression in some ALS patients [23]. Future research should explore the potential of combining antioxidant therapy with strategies aimed at reducing systemic inflammation. Lastly, the protective role of hemoglobin suggests that addressing anemia in ALS patients may have therapeutic benefits. Strategies such as iron supplementation, erythropoietin therapy, or lifestyle modifications to enhance oxygen transport should be explored in future clinical trials [24].

CONCLUSION

Amyotrophic lateral sclerosis (ALS) is a progressive and devastating neurodegenerative disorder that currently lacks effective curative treatments. Given its complex pathophysiology, identifying reliable biomarkers that can aid in early diagnosis, predict disease progression, and inform treatment strategies is of paramount importance. This study sought to explore the role of routine hematological parameters in ALS prognosis, with a particular focus on inflammatory markers, oxidative stress indicators, and oxygen transport efficiency. The findings provide compelling evidence that routine blood-based markers—particularly the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), red cell distribution width (RDW), and hemoglobin (Hb) levels—are significantly associated with ALS severity and disease progression. One of the most critical observations in this study was the significant elevation of NLR and PLR in advanced-stage ALS patients compared to early-stage patients. The increase in these inflammatory markers suggests a heightened systemic inflammatory response, which may contribute to the neurodegenerative process. Elevated NLR reflects an imbalance between neutrophil-mediated inflammation and lymphocyte-driven immune regulation, implying an uncontrolled pro-inflammatory state. Similarly, higher PLR values suggest increased platelet activation, which is known to be involved in the inflammatory cascade contributing to neuronal injury. Given these findings, NLR and PLR emerge as potential prognostic biomarkers for ALS, which could be used for disease monitoring and stratification in clinical practice. Another key observation was the significant increase in RDW in advanced-stage ALS patients, reinforcing the role of oxidative stress in ALS progression. Elevated RDW indicates greater variability in red blood cell size, which has been linked to oxidative stress and chronic inflammation—both of which are central to ALS

pathophysiology. The correlation between higher RDW levels and disease severity suggests that oxidative damage may play a more critical role in ALS progression than previously thought. This highlights the potential utility of RDW as an accessible and cost-effective biomarker for assessing disease progression and evaluating the impact of therapeutic interventions aimed at reducing oxidative stress. Conversely, hemoglobin levels were found to be significantly lower in advanced-stage ALS patients, indicating a potential link between oxygen transport efficiency and disease severity. Hemoglobin is crucial for oxygen delivery to neurons, and its decline may contribute to hypoxic conditions, exacerbating neuronal damage. The strong correlation between lower hemoglobin levels and ALS severity suggests that anemia and reduced oxygenation may accelerate disease progression, making hemoglobin another important factor to consider in ALS management.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this study

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