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CORRELATION BETWEEN HEMATOLOGICAL PARAMETERS AND DISEASE SEVERITY IN ACUTE LEUKEMIA PATIENTS

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ABSTRACT

Background: Aim: This study aimed to evaluate the correlation between hematological parameters and disease severity in patients diagnosed with acute leukemia, focusing on their prognostic significance and utility in clinical risk stratification.

Material and Methods: A cross-sectional study was conducted on 90 newly diagnosed acute leukemia patients aged 18 years and older. Data collection included demographic information, clinical history, and laboratory investigations such as complete blood count (hemoglobin, total leukocyte count, platelet count, and differential leukocyte count), peripheral blood smear examination, and bone marrow biopsy. Disease severity was categorized into mild, moderate, and severe based on clinical and laboratory criteria, including blast count, and organ involvement. Statistical analysis was performed using SPSS Version 25.0, with p-values <0.05 considered statistically significant.

Results: The mean age increased significantly with disease severity (p=0.045). Hemoglobin levels decreased significantly (p<0.001), while total leukocyte count, Peripheral blood blast percentage, serum LDH, CRP, and ESR levels increased with disease severity (p<0.001 for all). Platelet count showed a significant decline with severity (p<0.001). Bone marrow findings revealed higher blast counts, increased fibrosis. ROC curve analysis showed high predictive accuracy for Peripheral blood blasts (AUC=0.93), total leukocyte count (AUC=0.91), and serum LDH (AUC=0.90).

Conclusion: This study demonstrated strong correlations between hematological parameters, biochemical markers, and disease severity in acute leukemia patients. Hemoglobin, total leukocyte count, platelet count, Peripheral blood blasts, serum LDH, CRP, and ESR emerged as reliable indicators of disease severity. These findings emphasize the importance of routine hematological assessments for effective risk stratification, disease monitoring, and personalized treatment strategies.

Keywords: Acute leukemia, Hematological parameters, Disease severity, Peripheral blood blasts, Biomarkers.

INTRODUCTION

Acute leukemia is a group of aggressive hematological malignancies characterized by the rapid proliferation of immature blood cells, primarily affecting the bone marrow and peripheral blood. It is broadly classified into acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL), depending on the lineage of the affected cells. Despite advancements in diagnostic and therapeutic strategies, acute leukemia remains a significant global health burden due to its heterogeneity, rapid progression, and high mortality rates. The severity of the disease varies greatly among patients, ranging from indolent forms to aggressive subtypes associated with multi-organ failure and poor prognosis.[1] Hematological parameters, including hemoglobin levels, total leukocyte count, platelet count, and peripheral blood blast percentage, play a crucial role in the diagnosis,

classification, and prognostic evaluation of acute leukemia. These parameters are reflective of bone marrow function, leukemic cell burden, and the extent of disease progression. Changes in hematological parameters often serve as key indicators for disease severity and are closely linked to clinical outcomes. Therefore, an in-depth understanding of their correlation with disease severity can provide valuable insights for early diagnosis, risk stratification, and therapeutic decision-making.[2] Hemoglobin levels, a marker of oxygen-carrying capacity in the blood, are frequently reduced in patients with acute leukemia due to bone marrow suppression, ineffective erythropoiesis, and increased consumption by proliferating leukemic cells. Severe anemia is often associated with higher disease burden and poor prognosis. On the other hand, total leukocyte count serves as a reflection of the leukemic cell load in circulation. Extremely high leukocyte counts are frequently observed in aggressive subtypes of leukemia and are associated with leukostasis, a potentially fatal complication arising from microvascular obstruction by circulating blasts. Similarly, thrombocytopenia, characterized by a significant reduction in platelet count, is a common finding in acute leukemia and is closely linked to bleeding risk and disease severity.[3]

Peripheral blood blasts, the hallmark of acute leukemia, represent immature leukemic cells released prematurely into the bloodstream. The percentage of Peripheral blood blasts correlates directly with disease burden and reflects the aggressiveness of leukemia. A higher blast percentage in peripheral blood is often associated with advanced disease stages and poor clinical outcomes. In addition to traditional hematological parameters, several biochemical markers, such as serum lactate dehydrogenase (LDH), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), have gained attention as potential indicators of disease severity. LDH is an enzyme released during cellular breakdown, and elevated levels are commonly observed in leukemia due to rapid cellular turnover. Similarly, CRP and ESR, markers of systemic inflammation, are often elevated in acute leukemia patients and are indicative of disease activity and immune response.[4] Bone marrow findings, including blast percentage, cellularity, and fibrosis are integral components in assessing disease severity. Bone marrow hypercellularity is frequently observed in aggressive leukemia subtypes due to the rapid proliferation of immature leukemic cells. These findings provide valuable information about disease biology and aid in risk stratification.[5] Understanding the correlation between hematological parameters and disease severity in acute leukemia is not only important for prognosis but also for therapeutic decision-making. Patients presenting with severe hematological derangements often require more aggressive treatment strategies, including intensive chemotherapy, targeted therapies, or hematopoietic stem cell transplantation. Additionally, identifying key hematological and biochemical markers associated with disease severity can help clinicians predict treatment response, monitor disease progression, and identify patients at higher risk of relapse.[6] Despite significant advancements in leukemia research, there remains a gap in our understanding of how specific hematological and biochemical markers interact with disease severity. The heterogeneity of leukemia, coupled with variations in genetic and environmental factors, often complicates the interpretation of hematological findings. Moreover, resource-limited settings face additional challenges in implementing advanced diagnostic tools, making hematological parameters an even more critical component of disease assessment.[7] Early identification of high-risk patients based on hematological and biochemical parameters can improve clinical outcomes by enabling timely interventions and personalized treatment approaches. Hematological parameters are not only easily accessible and cost-effective but also provide real-time insights into the disease state. Therefore, they have the potential to serve as reliable biomarkers for disease severity, treatment response, and prognosis in acute leukemia patients.[8] This study aims to evaluate the correlation between hematological parameters and disease severity in acute leukemia patients. By analyzing key hematological markers, including hemoglobin, leukocyte count, platelet count, and Peripheral blood blast percentage, along with biochemical markers such as LDH, CRP, and ESR, this study seeks to identify reliable predictors of disease severity. Additionally, bone marrow findings, including blast percentage, cellularity and fibrosis, will be examined to provide a comprehensive understanding of their association with disease severity.

MATERIALS AND METHODS

This cross-sectional study was conducted to evaluate the correlation between hematological parameters and disease severity in patients diagnosed with acute leukemia. A total of 90 patients diagnosed with acute leukemia were included in the study. The study was approved by the Ethical Review Board of the institute. Written informed consent was obtained from all participants prior to enrollment in the study. The research adhered to the principles outlined in the Declaration of Helsinki.

Inclusion Criteria

1. Patients aged 18 years and older.
2. Newly diagnosed cases of acute leukemia (both acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML)).
3. Patients who provided informed consent for participation.

Exclusion Criteria

1. Patients with chronic leukemia or other hematological malignancies.
2. Patients undergoing treatment for acute leukemia prior to the study.
3. Individuals with comorbid conditions likely to affect hematological parameters (e.g., severe liver disease, chronic kidney disease).

Methodology

Demographic data, clinical history, and laboratory findings were meticulously collected from each participant to ensure a comprehensive analysis of factors contributing to disease severity in acute leukemia. The demographic data included age, gender, and other relevant baseline characteristics, while the clinical history focused on the duration and progression of symptoms, presence of organ involvement such as splenomegaly, hepatomegaly, and lymphadenopathy, and any previous medical conditions or treatments. Laboratory investigations formed a crucial component of the assessment and included a complete blood count (CBC), which measured hemoglobin (Hb) levels, total leukocyte count (TLC), platelet count, and differential leukocyte count. These parameters provided insight into the hematopoietic status and functional integrity of the bone marrow.

Peripheral blood smear examination was performed to identify and quantify leukemic blasts and other morphological abnormalities in circulating blood cells, which are indicative of disease progression and burden. Bone marrow biopsy, a gold standard in leukemia diagnosis, was carried out to confirm the diagnosis, evaluate the degree of blast cell infiltration, and assess bone marrow architecture, cellularity, and fibrosis.

The severity of the disease was categorized based on a combination of clinical and laboratory criteria, including blast percentage in both peripheral blood and bone marrow, degree of anemia, thrombocytopenia, leukocyte counts, and the extent of organ involvement. Patients were classified into three distinct groups: mild, moderate, and severe. The mild group included patients with relatively stable hematological parameters, lower blast counts, and minimal or no organ involvement. The moderate group consisted of patients showing intermediate levels of blast proliferation, hematological derangement, and some degree of organ infiltration. In contrast, the severe group included patients with markedly elevated blast counts, profound hematological abnormalities, significant organ involvement.

This multi-faceted approach to data collection and classification ensured a holistic assessment of each patient's disease state, allowing for a more nuanced understanding of the relationship between hematological parameters and disease severity. These parameters not only facilitated risk stratification but also served as potential biomarkers for predicting disease progression and treatment response in acute leukemia patients.

Statistical Analysis

The data were analyzed using SPSS, Version 25.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The correlation between hematological parameters and disease severity was assessed using Pearson or Spearman correlation coefficients, as appropriate. Group differences were analyzed using one-way ANOVA or Kruskal-Wallis test, depending on the data distribution. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Demographic and Clinical Characteristics of Study Participants

The demographic and clinical characteristics of the 90 acute leukemia patients were compared across three disease severity groups: mild, moderate, and severe. The mean age increased progressively with disease severity (35.40 ± 10.20 in the mild group, 40.10 ± 11.50 in the moderate group, and 42.80 ± 12.70 in the severe group), showing a statistically significant difference (p=0.045). Although the male gender was predominant in all groups, the difference in gender distribution was not statistically significant (p=0.523).

The mean Body Mass Index (BMI) also increased with disease severity (23.50 ± 3.20 in mild, 24.80 ± 4.10 in moderate, and 26.10 ± 4.50 in severe), with a significant difference (p=0.042). Regarding the type of leukemia, the distribution of ALL and AML was not significantly different across the severity groups (p=0.410 and p=0.389, respectively).

The duration of symptoms increased significantly with disease severity (p=0.001), indicating a delay in diagnosis or a rapid progression in severe cases. Splenomegaly, hepatomegaly, and lymphadenopathy were significantly more common in severe cases (p=0.004, p=0.003, and p=0.002, respectively). These findings suggest that organ involvement is directly related to disease severity and should be considered a marker for progression.

Table 2: Hematological Parameters Across Disease Severity Groups

Hematological and biochemical parameters demonstrated a clear trend correlating with disease severity. Hemoglobin levels decreased significantly as disease severity increased, from 11.50 ± 1.80 g/dL in the mild group to 9.40 ± 2.00 g/dL in the moderate group, and further down to 7.80 ± 1.50 g/dL in the severe group (p<0.001). Conversely, the total leukocyte count increased significantly across the groups (p<0.001), indicating a higher leukemic burden in severe disease.

Platelet counts also declined significantly with increasing severity (p<0.001), suggesting impaired bone marrow function in advanced disease stages. Peripheral blood blast percentage was substantially higher in the severe group (65.40 ± 12.50%)

compared to the mild group (20.50 ± 8.10%) ($p<0.001$).

Biochemical markers, such as serum Lactate Dehydrogenase (LDH), C-Reactive Protein (CRP), and Erythrocyte Sedimentation Rate (ESR), increased significantly with disease severity ($p<0.001$). Serum LDH levels, in particular, rose from 320.50 ± 50.20 U/L in mild cases to 730.40 ± 120.50 U/L in severe cases, indicating extensive cellular turnover and tissue damage. CRP and ESR also showed significant elevation, reflecting increased inflammatory activity in severe disease.

Table 3: Correlation Between Hematological and Biochemical Parameters with Disease Severity

Correlation analysis revealed significant relationships between disease severity and multiple hematological and biochemical parameters. Hemoglobin levels were inversely correlated with disease severity ($r = -0.654$, $p<0.001$), while total leukocyte count ($r = 0.721$, $p<0.001$), Peripheral blood blast percentage ($r = 0.781$, $p<0.001$), and serum LDH levels ($r = 0.742$, $p<0.001$) showed strong positive correlations. Platelet count had a significant negative correlation with severity ($r = -0.612$, $p<0.001$), reflecting bone marrow suppression in severe cases.

Inflammatory markers, including CRP ($r = 0.689$, $p<0.001$) and ESR ($r = 0.695$, $p<0.001$), also demonstrated significant positive correlations with disease severity. These findings underscore the utility of both hematological and biochemical parameters in assessing and predicting disease progression in acute leukemia.

Table 4: Comparison of Bone Marrow Findings Among Disease Severity Groups

Bone marrow findings were analyzed to further elucidate the relationship with disease severity. Bone marrow blast percentage increased significantly with severity, ranging from 30.50 ± 10.30% in mild cases to 75.60 ± 15.40% in severe cases ($p<0.001$). Hypercellularity was more prevalent in moderate and severe groups, reflecting increased leukemic cell proliferation.

Bone marrow fibrosis, another marker of disease progression, increased from 12.00% in mild cases to 38.00% in severe cases ($p=0.010$). Myeloperoxidase activity was also significantly higher in severe cases (75.20 ± 20.10%) compared to mild cases (42.50 ± 12.20%) ($p<0.001$). These findings suggest that bone marrow findings, including blast count and fibrosis, are strongly associated with disease severity.

Table 5: Predictive Value of Hematological and Biochemical Parameters for Disease Severity

Receiver Operating Characteristic (ROC) curve analysis demonstrated the predictive value of various hematological and biochemical parameters for disease severity. Hemoglobin levels ≤9.50 g/dL had a sensitivity of 84.30% and specificity of 78.10%, with an AUC of 0.89 (95% CI: 0.82–0.95). Total leukocyte count ≥20.00 $\times 10^3/\mu L$ showed excellent predictive accuracy with an AUC of 0.91 (95% CI: 0.85–0.96).

Peripheral blood blasts (≥50.00%) demonstrated the highest predictive value, with a sensitivity of 90.20% and specificity of 85.00% (AUC: 0.93, 95% CI: 0.88–0.97). Serum LDH ≥500.00 U/L and CRP ≥20.00 mg/L also showed strong predictive values, with AUCs of 0.90 (95% CI: 0.83–0.94) and 0.88 (95% CI: 0.81–0.92), respectively.

These findings indicate that Peripheral blood blasts, serum LDH, and total leukocyte count are highly accurate markers for predicting disease severity in acute leukemia patients.

Table 1: Demographic and Clinical Characteristics of Study Participants

Variable	Mild (n=30)	Moderate (n=30)	Severe (n=30)	p-value
Age (mean ± SD)	35.40 ± 10.20	40.10 ± 11.50	42.80 ± 12.70	0.045*
Gender (Male, %)	18 (60.00%)	20 (66.67%)	22 (73.33%)	0.523
BMI (mean ± SD)	23.50 ± 3.20	24.80 ± 4.10	26.10 ± 4.50	0.042*
Type of Leukemia				
- ALL	16 (53.33%)	14 (46.67%)	12 (40.00%)	0.410
- AML	14 (46.67%)	16 (53.33%)	18 (60.00%)	0.389
Duration of Symptoms (weeks, mean ± SD)	3.20 ± 1.10	4.50 ± 1.50	5.80 ± 1.80	0.001**
Splenomegaly (%)	6 (20.00%)	12 (40.00%)	20 (66.67%)	0.004**
Hepatomegaly (%)	5 (16.67%)	10 (33.33%)	18 (60.00%)	0.003**
Lymphadenopathy (%)	8 (26.67%)	15 (50.00%)	22 (73.33%)	0.002**

Table 2: Hematological Parameters Across Disease Severity Groups

Parameter	Mild (n=30)	Moderate (n=30)	Severe (n=30)	p-value
Hemoglobin (g/dL)	11.50 ± 1.80	9.40 ± 2.00	7.80 ± 1.50	<0.001**
Total Leukocyte Count (x10³/µL)	15.40 ± 5.20	22.10 ± 6.40	28.70 ± 8.10	<0.001**
Platelet Count (x10³/µL)	120.50 ± 30.20	85.30 ± 25.50	60.20 ± 20.70	<0.001**
Peripheral blood blasts (%)	20.50 ± 8.10	45.20 ± 10.70	65.40 ± 12.50	<0.001**
Serum Lactate Dehydrogenase (U/L)	320.50 ± 50.20	520.70 ± 80.30	730.40 ± 120.50	<0.001**
C-Reactive Protein (mg/L)	12.50 ± 5.20	22.10 ± 8.40	35.20 ± 10.10	<0.001**
Erythrocyte Sedimentation Rate (mm/hr)	22.10 ± 8.10	35.50 ± 10.40	50.30 ± 12.70	<0.001**

Table 3: Correlation Between Hematological and Biochemical Parameters with Disease Severity

Parameter	Correlation Coefficient (r)	p-value
Hemoglobin	-0.654	<0.001**
Total Leukocyte Count	0.721	<0.001**

Platelet Count	-0.612	<0.001**
Peripheral blood blasts	0.781	<0.001**
Serum LDH	0.742	<0.001**
C-Reactive Protein	0.689	<0.001**
ESR	0.695	<0.001**

Table 4: Comparison of Bone Marrow Findings Among Disease Severity Groups

Variable	Mild (n=30)	Moderate (n=30)	Severe (n=30)	p-value
Bone Marrow Blast Count (%)	30.50 ± 10.30	55.10 ± 12.70	75.60 ± 15.40	<0.001**
Bone Marrow Cellular Density	Normocellular	Hypercellular	Hypercellular	-
Bone Marrow Fibrosis (%)	12.00%	24.00%	38.00%	0.010**
Myeloperoxidase (%)	42.50 ± 12.20	58.10 ± 15.70	75.20 ± 20.10	<0.001**

Table 5: Predictive Value of Hematological and Biochemical Parameters for Disease Severity

Parameter	Cut-off Value	Sensitivity (%)	Specificity (%)	AUC (95% CI)
Hemoglobin (g/dL)	≤ 9.50	84.30	78.10	0.89 (0.82-0.95)
Total Leukocyte Count	≥ 20.00	88.50	81.70	0.91 (0.85-0.96)
Platelet Count (x10³/µL)	≤ 80.00	82.40	76.50	0.87 (0.79-0.93)
Peripheral blood blasts (%)	≥ 50.00	90.20	85.00	0.93 (0.88-0.97)
Serum LDH (U/L)	≥ 500.00	85.30	79.10	0.90 (0.83-0.94)
CRP (mg/L)	≥ 20.00	83.10	75.50	0.88 (0.81-0.92)

DISCUSSION

In our study, the mean age of patients increased significantly with disease severity, with severe cases showing a mean age of 42.80 ± 12.70 years (p=0.045). This finding aligns with a study by Sakr et al. (2023), which reported that older patients were more likely to present with advanced stages of acute leukemia.[8] Similarly, a study by Cheng et al. (2024) observed a higher prevalence of severe disease in older patients, suggesting that age might be a surrogate marker for disease aggressiveness.[9]

Regarding gender distribution, no significant difference was observed across severity groups (p=0.523). This finding supports research by Cheng et al. (2024), where gender showed no significant association with disease severity.[9] However, some studies, such as one by Abdelrahman et al. (2021), reported a slight male predominance in severe cases, suggesting possible regional or genetic influences.[10]

The BMI showed a statistically significant increase with disease severity (p=0.042). While this association is less frequently studied in acute leukemia, a recent study by Al-Rashid et al. (2022) indicated that higher BMI might affect chemotherapy outcomes and leukemic cell proliferation rates, warranting further investigation.[11]

Clinical parameters such as splenomegaly, hepatomegaly, and lymphadenopathy were significantly more common in severe cases (p=0.004, p=0.003, and p=0.002, respectively). These findings align with results from Sakr et al. (2023) and Abdullah et al. (2020), who reported higher rates of organ involvement in severe disease. The presence of organomegaly often indicates leukemic cell infiltration and poor prognosis.[8,12]

In our study, hemoglobin levels decreased significantly with increasing disease severity (p<0.001). Similar results were observed in a study by Gupta et al. (2022), where hemoglobin levels below 9.5 g/dL were strongly associated with poor outcomes. This relationship can be attributed to bone marrow suppression caused by leukemic infiltration.[13]

The total leukocyte count increased significantly across the severity groups (p<0.001). This finding is consistent with the results of Zhao et al. (2021), who reported elevated leukocyte counts as a marker of disease burden and leukostasis. Elevated leukocyte counts in acute leukemia often indicate rapid disease progression and an increased risk of complications.[14]

The decline in platelet count observed in our study (p<0.001) also corroborates findings by Al-Sabbagh et al. (2019), where thrombocytopenia was identified as a significant predictor of disease severity and bleeding complications in acute leukemia patients.[15]

Peripheral blood blasts showed a substantial increase with disease severity (p<0.001). Cheng et al. (2024) similarly reported a strong association between higher Peripheral blood blast percentages and poor outcomes. Elevated Peripheral blood blasts indicate inadequate marrow response and increased leukemic proliferation.[9]

Serum LDH levels showed a marked increase with disease severity (p<0.001). A study by Khan et al. (2022) demonstrated similar findings, associating elevated LDH with increased cellular turnover and tissue damage. LDH is widely recognized as an independent prognostic marker in leukemia.[16]

CRP and ESR also showed significant elevation with increasing disease severity (p<0.001). These findings are supported by studies by El-Fakharany et al. (2021) and Mahmoud et al. (2023), who observed higher CRP and ESR levels in severe cases, indicating the inflammatory and immunological responses involved in disease progression.[17,18]

Correlation analysis revealed significant associations between disease severity and hematological/biochemical parameters. Hemoglobin (r=-0.654) and platelet count (r=-0.612) showed

strong negative correlations with disease severity, consistent with observations made by Zhao et al. (2021).[14] Total leukocyte count (r=0.721) and Peripheral blood blasts (r=0.781) had strong positive correlations, supporting findings by Gupta et al. (2022).[13]

Serum LDH (r=0.742), CRP (r=0.689), and ESR (r=0.695) also exhibited strong positive correlations with disease severity. These results echo the findings of El-Fakharany et al. (2021), who reported similar correlation coefficients for LDH and inflammatory markers, underscoring their value in assessing disease burden and progression.[17]

The percentage of bone marrow blasts increased significantly with disease severity ($p<0.001$). This observation is in line with findings from Singh et al. (2020), who reported higher blast percentages in severe leukemia cases.[19]

Bone marrow fibrosis increased significantly with disease severity ($p=0.010$), which was also noted in studies by Al-Sabbagh et al. (2019).[15] Myeloperoxidase activity was significantly higher in severe cases ($p<0.001$), correlating with findings by Gupta et al. (2022), who suggested its role as a diagnostic and prognostic marker in acute myeloid leukemia.[13]

ROC curve analysis demonstrated that Peripheral blood blasts, total leukocyte count, and serum LDH had the highest predictive accuracy for disease severity, with AUCs of 0.93, 0.91, and 0.90, respectively. Similar findings were reported by Cheng et al. (2024) and Zhao et al. (2021), where Peripheral blood blasts and LDH levels showed robust predictive accuracy for advanced disease.[9,14]

CRP and ESR also demonstrated strong predictive value (AUCs of 0.88 and 0.87, respectively). Studies by Mahmoud et al. (2023) confirmed that inflammatory markers have a valuable role in predicting adverse outcomes in acute leukemia patients.[18]

CONCLUSION

In conclusion, this study highlights the significant correlation between hematological parameters, biochemical markers, and disease severity in acute leukemia patients. Parameters such as hemoglobin levels, total leukocyte count, platelet count, Peripheral blood blast percentage, serum LDH, CRP, and ESR demonstrated strong associations with disease progression and severity. Bone marrow findings, including blast percentage, cellularity, and fibrosis, further reinforced their prognostic value. These findings underscore the importance of routine hematological and biochemical assessments for early risk stratification, monitoring disease progression, and guiding therapeutic interventions. Incorporating these parameters into clinical practice can enhance patient outcomes through timely and personalized management strategies.

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