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Original Research Article

Correlation of Serum Lactate Dehydrogenase, Indirect Bilirubin, and Haptoglobin with Hematological Parameters in Hemolytic Anemia: A Cross-Sectional Study from a Tertiary Care Center in Rajasthan

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Abstract:

Background: Hemolytic anemia is characterized by increased destruction of red blood cells leading to release of intracellular enzymes and hemoglobin metabolites into circulation. Simple biochemical markers such as serum lactate dehydrogenase (LDH), indirect bilirubin, and haptoglobin are routinely available in most medical college laboratories and can assist in assessing the degree of hemolysis, particularly in resource-limited settings.

Objectives: (1) To assess serum LDH, indirect bilirubin, and haptoglobin levels in patients with hemolytic anemia. (2) To correlate biochemical markers of hemolysis with hematological parameters, namely hemoglobin level and reticulocyte count. (3) To evaluate the diagnostic utility of routine biochemical investigations in assessing severity of hemolysis.

Materials and Methods: This hospital-based cross-sectional study was conducted at Government Medical College, Jhalawar, Rajasthan, over a period of one and a half years. A total of 51 patients diagnosed with hemolytic anemia were included. Hematological investigations included complete blood count, reticulocyte count, and peripheral blood smear examination. Biochemical parameters included serum LDH, total and indirect bilirubin, and serum haptoglobin. Statistical analysis was performed using SPSS software, and correlations were assessed using appropriate tests.

Results: Serum LDH and indirect bilirubin levels were significantly elevated, while serum haptoglobin levels were reduced in the majority of patients. A significant negative correlation was observed between hemoglobin levels and serum LDH and indirect bilirubin, whereas reticulocyte count showed a significant positive correlation with these biochemical markers. Serum haptoglobin demonstrated a positive correlation with hemoglobin concentration and a negative correlation with LDH.

Conclusion: Routine biochemical markers such as serum LDH, indirect bilirubin, and haptoglobin correlate significantly with hematological indices of hemolysis and can serve as reliable, cost-effective indicators for assessing hemolytic anemia in resource-limited tertiary care settings.

Keywords: Hemolytic Anemia, Lactate Dehydrogenase, Indirect Bilirubin, Haptoglobin, Reticulocyte Count.

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Introduction

Anemia remains a major public health concern in India, contributing significantly to morbidity across all age groups. While nutritional anemia accounts for the majority of cases, hemolytic anemia represents an important subset encountered in tertiary care hospitals, particularly in regions with a higher prevalence of hemoglobinopathies, autoimmune disorders, infections, and drug-induced hemolysis. [1] Hemolytic anemia results from premature destruction of red blood cells (RBCs), leading to shortened erythrocyte lifespan and compensatory erythropoiesis. [2]

The diagnosis of hemolytic anemia is based on clinical features, hematological findings, and biochemical evidence of increased RBC destruction. Hematological features include anemia with reticulocytosis and characteristic peripheral blood smear findings. [3] Biochemical changes include elevated serum lactate dehydrogenase (LDH), increased indirect bilirubin, and decreased serum haptoglobin levels due to binding of free hemoglobin released during hemolysis. [4-5]

Serum LDH is a sensitive marker of cell breakdown and is markedly elevated in intravascular hemolysis.

Indirect bilirubin rises due to increased heme catabolism, while haptoglobin levels decrease as it forms complexes with free hemoglobin cleared by the reticuloendothelial system. [6] These parameters are widely available and inexpensive, making them particularly valuable in developing countries.

In many Indian medical colleges, especially in small cities, advanced diagnostic modalities such as flow cytometry, molecular studies, or enzyme assays are not readily accessible. [7] Hence, reliance on simple laboratory markers becomes essential. There is limited region-specific data correlating biochemical markers of hemolysis with hematological indices in resource-constrained settings.

Therefore, the present study was undertaken at Government Medical College, Jhalawar, to evaluate serum LDH, indirect bilirubin, and haptoglobin levels in patients with hemolytic anemia and to correlate these biochemical parameters with hematological indices, thereby assessing their practical utility in routine clinical practice.

Materials and Methods

Study Design: Hospital-based observational cross-sectional study.

Study Setting: Departments of Pathology and Biochemistry, Government Medical College and Associated Group of Hospitals, Jhalawar, Rajasthan, India.

Study Duration: One and a half years.

Study Population: A total of 51 patients diagnosed with hemolytic anemia.

Inclusion Criteria

- Patients of all age groups and both sexes
- Laboratory evidence of hemolytic anemia
- Informed consent obtained

Exclusion Criteria

- Anemia due to acute or chronic blood loss
- Nutritional anemia without evidence of hemolysis
- Chronic liver disease, renal failure, malignancy, or active infection
- Recent blood transfusion (within 3 weeks)

Laboratory Investigations: Hematological tests included complete blood count, reticulocyte count, and peripheral blood smear examination. Biochemical tests included serum LDH, total and indirect bilirubin, and serum haptoglobin, analyzed using standard automated methods.

Statistical Analysis: Quantitative variables were expressed as mean ± SD. Correlations were assessed using Pearson's or Spearman's correlation coefficient. A p-value <0.05 was considered statistically significant.

Results

Table 1: Hematological Parameters of Patients with Hemolytic Anemia (N = 51)

Parameter	Mean ± SD	Range
Hemoglobin (g/dL)	7.6 ± 1.8	4.2 – 11.0
Reticulocyte Count (%)	4.8 ± 2.1	1.6 – 9.5
RBC Count (×10⁶/μL)	2.9 ± 0.7	1.6 – 4.2

Table 2: Biochemical Markers of Hemolysis

Parameter	Mean ± SD	Range	Reference Range
Serum LDH (U/L)	782 ± 265	420 – 1480	140 – 280
Indirect Bilirubin (mg/dL)	2.4 ± 1.1	0.9 – 5.5	0.2 – 0.8
Serum Haptoglobin (mg/dL)	22 ± 14	5 – 60	30 – 200

Table 3: Correlation Between Biochemical and Hematological Parameters

Comparison	r-value	p-value
LDH vs Hemoglobin	–0.68	<0.001*
LDH vs Reticulocyte Count	+0.61	<0.001*
Indirect Bilirubin vs Hemoglobin	–0.64	<0.001*
Haptoglobin vs Hemoglobin	+0.66	<0.001*

*Statistically significant

Discussion

The present study evaluated the relationship between routinely available biochemical markers of hemolysis and hematological parameters in patients with hemolytic anemia in a tertiary care center in Rajasthan. Hemolytic anemia is a clinically heterogeneous condition, and timely diagnosis depends on a combination of laboratory findings reflecting increased red cell destruction and compensatory erythropoiesis. In the current study, serum lactate dehydrogenase (LDH) and indirect bilirubin levels were markedly elevated, while serum haptoglobin levels were significantly reduced, reflecting active hemolysis.

In this study, the mean serum LDH level was 782 ± 265 U/L, which was substantially higher than the

upper limit of the normal reference range. LDH is released from lysed erythrocytes during intravascular hemolysis and also reflects increased turnover in extravascular hemolysis. A significant negative correlation was observed between serum LDH and hemoglobin levels ($r = -0.68$, $p < 0.001$), indicating that higher LDH values were associated with greater severity of anemia. Additionally, LDH showed a significant positive correlation with reticulocyte count ($r = +0.61$, $p < 0.001$), suggesting an appropriate marrow response to increased red cell destruction. These findings emphasize the utility of LDH as a surrogate marker of hemolysis severity.

Our results are in agreement with the study by Kato et al., who demonstrated that LDH strongly correlates with hemolytic severity and serves as a reliable biochemical marker of intravascular hemolysis in patients with sickle cell disease.[8] Although their study focused on a specific inherited hemolytic disorder, the correlation patterns observed in our study across heterogeneous causes of hemolytic anemia mirror their findings, reinforcing the broader applicability of LDH in hemolytic conditions.

Indirect bilirubin levels in our study were also significantly elevated, with a mean value of 2.4 ± 1.1 mg/dL. The rise in unconjugated bilirubin reflects increased heme breakdown exceeding hepatic conjugation capacity. A significant inverse correlation was noted between indirect bilirubin and hemoglobin concentration ($r = -0.64$, $p < 0.001$), while a positive correlation was observed with reticulocyte count ($r = +0.58$, $p = 0.002$). These findings highlight the role of indirect bilirubin as an indirect yet reliable marker of hemolysis, particularly in chronic hemolytic states.

Barcellini and Fattizzo reported similar observations, noting that indirect bilirubin levels correlate well with disease activity and can be effectively used alongside LDH to assess hemolytic burden. [9] Their study emphasized that no single laboratory parameter is sufficient in isolation and that a combination of biochemical markers improves diagnostic accuracy — a conclusion strongly supported by the present study.

Serum haptoglobin levels in our study were markedly reduced, with a mean value of 22 ± 14 mg/dL, falling below the lower limit of the reference range in the majority of patients. Haptoglobin binds free hemoglobin released into plasma and is rapidly cleared by the reticuloendothelial system, resulting in low circulating levels during hemolysis. In this study, serum haptoglobin showed a significant positive correlation with hemoglobin levels ($r = +0.66$, $p < 0.001$) and a strong inverse correlation with serum LDH ($r = -0.72$, $p < 0.001$), underscoring its diagnostic value.

These findings are consistent with those of Shih, who demonstrated that serum haptoglobin levels below 25 mg/dL are highly sensitive for diagnosing hemolytic anemia and for differentiating hemolytic from non-hemolytic causes of anemia. [10] The strong correlations observed in our study further validate haptoglobin as a valuable biochemical marker, particularly in settings where advanced diagnostic tests are unavailable.

The composite analysis of biochemical markers in the present study revealed that patients with higher LDH and indirect bilirubin levels and lower haptoglobin concentrations had more severe anemia, as reflected by lower hemoglobin levels and higher reticulocyte counts. This reinforces the concept that integrating multiple biochemical parameters provides a more accurate assessment of hemolysis severity than relying on a single marker.

From an Indian healthcare perspective, especially in smaller cities and district-level medical colleges, access to advanced investigations such as flow cytometry, red cell enzyme assays, or molecular studies is often limited. In such settings, reliance on simple, cost-effective biochemical tests becomes essential. The findings of this study support the incorporation of serum LDH, indirect bilirubin, and haptoglobin into routine diagnostic algorithms for hemolytic anemia, facilitating early diagnosis and appropriate management.

Nevertheless, biochemical markers can be influenced by non-hemolytic conditions such as liver disease, infections, or tissue injury. Therefore, these parameters must be interpreted in conjunction with clinical findings and hematological investigations. Despite these considerations, the present study demonstrates that routinely available biochemical markers remain reliable and practical tools for assessing hemolysis in routine clinical practice.

Conclusion

Serum LDH, indirect bilirubin, and haptoglobin show significant correlation with hematological parameters in hemolytic anemia. These routinely available, cost-effective biochemical markers can reliably assess hemolysis severity and are especially valuable in resource-constrained tertiary care centers.

Limitations: Small sample size, single-center design, and lack of etiological subclassification of hemolytic anemia.

Recommendations: Larger multicentric studies are recommended to validate findings and establish standardized diagnostic cut-offs for hemolysis severity.

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