Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(5), 2993-2998 | ISSN:2251-6727

Study of Role of Serum Lactate Dehydrogenase as a Prognostic Marker in Patients of lymphoma

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(Received: 25 August 2025 Revised: 27 September 2025 Accepted: 14 October 2025)

KEYWORDS

Lymphoma, Hodgkin lymphoma, Non-Hodgkin lymphoma, Lactate dehydrogenase

ABSTRACT:

Introduction: Lymphomas are malignant neoplasms of the lymphatic system, broadly categorized into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). These entities differ in clinical behavior, histopathology, and prognosis. Serum lactate dehydrogenase (LDH), an intracellular enzyme released during cellular turnover and tissue breakdown, has been proposed as a prognostic biomarker in lymphoproliferative disorders. Elevated LDH levels may reflect tumor burden, disease aggressiveness, and metabolic activity, making it a valuable adjunct in staging and risk stratification. This study investigates the correlation between serum LDH levels and lymphoma subtype and stage, aiming to validate its prognostic utility.

Materials and Methods: A retrospective observational study was conducted on 100 histopathologically confirmed lymphoma cases at a tertiary care center. Demographic details, lymphoma subtype (HL or NHL), clinical stage (Ann Arbor classification), and serum LDH levels were recorded. LDH values were categorized into four ranges: ≤200 U/L, 201–400 U/L, 401–600 U/L, and >600 U/L. Patients with concurrent malignancies, hepatic dysfunction, hemolytic anemia, or incomplete records were excluded. Statistical analysis was performed using SPSS version 25.0. Chi-square tests were applied to assess associations between LDH levels and lymphoma type and stage, with $p < 0.05$ considered statistically significant.

Observations and Results: Out of 100 patients, 60% were male and 40% female. The majority belonged to the age group ≥41 years. NHL was more prevalent (80%) than HL (20%). HL cases were predominantly in early stages (Stage I and II), while NHL cases spanned all stages. LDH levels were significantly higher in NHL compared to HL ($p = 0.003$). A strong association was observed between LDH elevation and advanced disease stage ($p = 0.00008$). Stage IV patients showed the highest LDH levels (>600 U/L), while early-stage cases had predominantly normal or mildly elevated LDH.

Conclusion: Serum LDH levels demonstrated a significant correlation with both lymphoma subtype and disease stage. Elevated LDH was more common in NHL and advanced-stage disease, supporting its role as a surrogate marker of tumor burden and disease progression. LDH estimation is a cost-effective, accessible tool that can aid in prognostic assessment and clinical decision-making, especially in resource-limited settings.

Introduction

Lymphomas represent a diverse group of hematological malignancies originating from lymphoid tissues, broadly classified into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). These neoplasms exhibit variable clinical behavior, ranging from indolent to highly aggressive forms, necessitating reliable biomarkers for early diagnosis, risk stratification, and therapeutic monitoring. Among the biochemical parameters evaluated in oncologic practice, serum lactate dehydrogenase (LDH) has emerged as a potential surrogate marker of tumor burden, cellular turnover, and disease progression[1,2,3].LDH is a

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cytoplasmic enzyme involved in anaerobic glycolysis, catalyzing the interconversion of pyruvate and lactate[4]. Elevated serum LDH levels have been associated with increased tumor proliferation, tissue necrosis, and poor prognosis in various malignancies, including lymphomas[5,6,7]. Its inclusion in prognostic indices such as the International Prognostic Index (IPI) for NHL underscores its clinical relevance[8]. However, the extent to which LDH correlates with lymphoma subtype and disease stage remains a subject of ongoing investigation, particularly in resource-limited settings where advanced imaging and molecular diagnostics may not be readily accessible[9].This study aims to evaluate serum LDH levels in patients diagnosed with HL and NHL and to assess its association with disease stage. By elucidating the prognostic utility of LDH, the study seeks to reinforce its role as a cost-effective, accessible biomarker that may aid clinicians in stratifying disease severity and guiding treatment decisions[10].

Aim & objectives

1. To assess LDH enzyme levels in lymphoma patients
2. To assess prevalence of Stage of lymphoma
3. To correlate LDH enzyme levels withStage of lymphoma
4. To correlate LDH enzyme levels with Type of lymphoma

Material and Methods

This retrospective observational study was conducted at a tertiary care hospital in India. The objective was to evaluate serum lactate dehydrogenase (LDH) levels in patients diagnosed with Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), and to assess their correlation with disease stage.

Study Population

A total of 100 patients with histopathologically confirmed lymphoma were included in the study. Patient records were reviewed over a defined period to extract relevant clinical and biochemical data.

Inclusion Criteria

- Patients of any age and gender with a confirmed diagnosis of HL or NHL.
- Availability of serum LDH values at the time of initial diagnosis.
- Complete staging information based on clinical, radiological, and pathological findings.

Exclusion Criteria

- Patients with concurrent malignancies or metastatic disease from non-lymphoid origin.
- Presence of conditions known to elevate LDH independently, such as hemolyticanemia, myocardial infarction, hepatic dysfunction, or skeletal muscle injury.
- Incomplete medical records or missing LDH/staging data.

Data Collection

Demographic variables (age, gender), lymphoma subtype (HL or NHL), disease stage (I–IV), and serum LDH levels were extracted from hospital records. Staging was performed using the Ann Arbor classification system, supplemented by the Lugano criteria for response assessment.

LDH Estimation

Serum LDH levels were measured using an enzymatic colorimetric method on an automated biochemistry analyzer. LDH values were categorized into four groups for analysis:

- ≤200 U/L
- 201–400 U/L
- 401–600 U/L
- 600 U/L

These thresholds were based on institutional reference ranges and prior literature[8].

Statistical Analysis

Data were compiled in Microsoft Excel and analyzed using SPSS version 25.0. Descriptive statistics summarized demographic and clinical variables. Chi-square tests were used to assess associations between LDH levels and lymphoma type, and between LDH levels and disease stage. A p-value <0.05 was considered statistically significant.

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Observation and Result

Table 1: Demographic Variables

Sr No	Age (Years)	Male n (%)	Females n (%)	Total N (%)
1	**≤20**	3 (3 %)	10 (10 %)	**13 (13 %)**
2	**21 to 40**	18 (18 %)	8 (8 %)	**26 (26 %)**
3	**41 to 60**	18 (18 %)	13 (13 %)	**31 (31 %)**
4	**>60**	21 (21 %)	9 (9 %)	**30 (30 %)**
Total N (%)		**60 (60 %)**	**40 (40 %)**	**100 (100 %)**

Table 1 presents the age and gender distribution of the 100 lymphoma patients. The largest age group was 41–60 years (31%), followed closely by those over 60 years (30%). This suggests lymphoma is more prevalent in middle-aged and older adults.Males comprised 60% of the cohort, while females made up 40%, indicating a male predominance in this sample.The 21–40 age group accounted for 26%, and ≤20 years for 13%, showing lower prevalence in younger individuals.Lymphoma appears more common in males and in patients aged above 40, aligning with known epidemiological trends.

Table 2: Type of lymphoma

Sr No	Type of lymphoma	Stage 1	Stage 2	Stage 3	Stage 4	Total N (%)
1	**Hodgkinlymphoma (HL)**	11 (11 %)	8 (8 %)	0 (0 %)	1 (1 %)	20 (20 %)
2	**Non-Hodgkins lymphoma (NHL)**	29 (29 %)	18 (18 %)	17 (17 %)	16 (16 %)	80 (80 %)
Total N (%)		**40 (40 %)**	**26 (26 %)**	**17 (17 %)**	**17 (17 %)**	**100 (100 %)**

Table 2categorizes patients by lymphoma type and stage. Hodgkin lymphoma (HL) accounted for 20% of cases, with most patients in early stages (Stage 1: 11%, Stage 2: 8%). Only one HL case was in Stage 4. Non-Hodgkin lymphoma (NHL) was more prevalent (80%), with a broader stage distribution: Stage 1 (29%), Stage 2 (18%), Stage 3 (17%), and Stage 4 (16%). NHL is significantly more common than HL and tends to present across all stages, including advanced ones, suggesting a more heterogeneous progression pattern.

Table 3: levels of LDH Vs Type of lymphoma

Sr No	Type of lymphoma	≤200 (U/L) n (%)	201 to 400 (U/L) n (%)	401 to 600 (U/L) n (%)	>600 (U/L) n (%)	Total N (%)	Chi square	P value
1	**Hodgkin lymphoma (HL)**	9 (9 %)	10 (10 %)	1 (1 %)	0 (0 %)	20 (20 %)	**13.84**	**0.003 (S)**

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2	**Non-Hodgkins lymphoma (NHL)**	10 (10 %)	44 (44 %)	9 (9 %)	17 (17 %)	80 (80 %)		
Total N (%)		19 (19 %)	54 (54 %)	10 (10 %)	17 (17 %)	100 (100 %)		

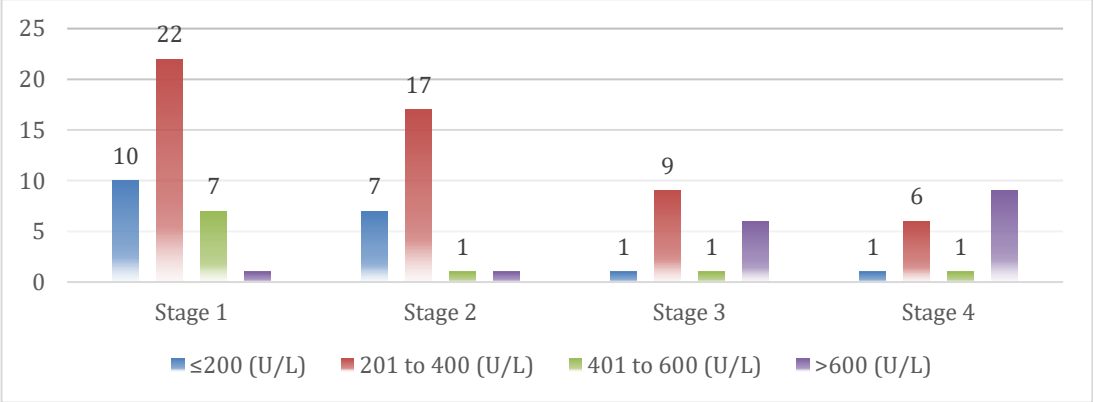
Table 3compares LDH levels across HL and NHL. HL patients mostly had LDH levels ≤400 U/L, with 9% ≤200 and 10% between 201–400. Only 1% had levels between 401–600, and none exceeded 600. The chi-square value of 13.84 and a p-value of 0.003 indicate a statistically significant association between LDH levels and lymphoma type. HL tends to be associated with lower LDH levels, while NHL (data in Table 4) shows higher LDH values, reinforcing LDH as a potential marker for disease aggressiveness and type differentiation.

Table 4: levels of LDH Vs Stage of lymphoma

Sr No	Stage of lymphoma	≤200 (U/L) n (%)	201 to 400 (U/L) n (%)	401 to 600 (U/L) n (%)	>600 (U/L) n (%)	Total N (%)	Chi square	P value
1	**Stage 1**	10 (10 %)	22 (22 %)	7 (7 %)	1 (1 %)	**40 (40 %)**	**34.10**	**0.00008 (S)**
2	**Stage 2**	7 (7 %)	17 (17 %)	1 (1 %)	1 (1 %)	**26 (26 %)**		
3	**Stage 3**	1 (1 %)	9 (9 %)	1 (1 %)	6 (6 %)	**17 (17 %)**		
4	**Stage 4**	1 (1 %)	6 (6 %)	1 (1 %)	9 (9 %)	**17 (17 %)**		
Total N (%)		**19 (19 %)**	**54 (54 %)**	**10 (10 %)**	**17 (17 %)**	**100 (100 %)**		

Table 4correlates LDH levels with disease stage. LDH levels ≤200 U/L were most common in Stage 1 (10%) and Stage 2 (7%), but dropped sharply in Stage 3 and 4 (1% each).LDH >600 U/L was predominantly seen in Stage 4 (9%), followed by Stage 3 (6%), with minimal presence in early stages.The chi-square value of 34.10 and p-value of 0.00008 confirm a highly significant association.LDH levels rise with advancing stage, supporting its role as a prognostic biomarker. Elevated LDH correlates with disease severity and may reflect tumor burden or cellular turnover.

Graph1: levels of LDH Vs Stage of lymphoma



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Discussion

Lymphomas, encompassing Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), are biologically diverse malignancies of the lymphatic system. Prognostic stratification is essential for guiding treatment and predicting outcomes. Serum lactate dehydrogenase (LDH), a ubiquitous intracellular enzyme released during cellular turnover, has been proposed as a surrogate marker for tumor burden and disease aggressiveness[6].The study revealed a male predominance (60%) and a higher prevalence of lymphoma in patients aged ≥41 years (61%). These findings align with epidemiological data from Shaikh et al.[6] and Armitage et al.[11], which report increased lymphoma incidence in middle-aged and elderly males. The lower representation in younger age groups may reflect the natural age-related risk gradient for lymphoproliferative disorders.NHL constituted 80% of cases, with a broader distribution across all stages, while HL accounted for 20%, predominantly in early stages (Stage I and II). This pattern is consistent with the WHO classification[5] and Lugano staging observations[10], where HL often presents with localized disease and NHL with disseminated involvement. The higher frequency of advanced-stage NHL underscores its heterogeneous and often aggressive nature.HL patients predominantly exhibited LDH levels ≤400 U/L, whereas NHL cases showed a wider range, including elevated levels >600 U/L. The statistically significant association ($p = 0.003$) supports findings by Thieblemont et al.[9]and Shaikh et al.[6], who reported elevated LDH in aggressive NHL subtypes. This reinforces LDH's role in differentiating lymphoma types based on metabolic activity and proliferation rates.A clear trend emerged: LDH levels increased with advancing stage. Stage IV patients had the highest proportion of LDH >600 U/L, while early-stage cases showed predominantly normal or mildly elevated levels. The strong statistical association ($p = 0.00008$) mirrors results from the International Prognostic Index (IPI) study[4], where LDH was a key predictor of poor prognosis. Similar trends were observed in follicular lymphoma cohorts studied by Thieblemont et al.[9].

LDH is released during anaerobic glycolysis and cellular lysis. In lymphoma, elevated LDH reflects increased tumor cell turnover, hypoxic microenvironments, and necrosis within bulky or aggressive lesions[6]. NHL subtypes, particularly diffuse large B-cell lymphoma (DLBCL), exhibit rapid proliferation and metabolic reprogramming, leading to elevated LDH levels. Advanced-stage disease further exacerbates LDH release due to widespread tissue infiltration and systemic inflammation.Moreover, LDH elevation may correlate with cytokine-driven metabolic shifts and angiogenic activity, contributing to tumor progression. The observed association between LDH and disease stage in this study supports its utility as a non-invasive biomarker for disease burden, complementing imaging and histopathological assessment[10].

Conclusion

Present study highlights the prognostic significance of serum lactate dehydrogenase (LDH) in lymphoma, demonstrating a clear association between elevated LDH levels and advanced disease stage. LDH values were significantly higher in non-Hodgkin lymphoma (NHL) compared to Hodgkin lymphoma (HL), and progressively increased with disease advancement, reinforcing its role as a surrogate marker of tumor burden and aggressiveness. Given its accessibility and cost-effectiveness, LDH serves as a valuable adjunct to clinical staging, particularly in resource-limited settings. Integrating LDH assessment into routine diagnostic and prognostic workflows may enhance early risk stratification and guide therapeutic decision-making in lymphoma management.

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JCHR (2025) 15(5), 2993-2998 | ISSN:2251-6727

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