

Lactate dehydrogenase and Serum Albumin As Prognostic Markers of Dengue: An Observational Study

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Conflict of interest: Nil

Abstract:

Background: Dengue fever is the most significant arboviral infection affecting humans and poses significant public health challenges in tropical and subtropical regions worldwide. The clinical manifestations of dengue range from mild flu-like symptoms to severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), both of which can be fatal if not managed properly.

Aim: To explore the significance of lactate dehydrogenase (LDH) and serum albumin as prognostic markers in dengue fever.

Material & Methods: This observational study involved the recruitment of 60 patients aged over 15 years who were admitted to the Department of Medicine at our hospital between August 2024 and December 2024. The patients were categorized according to the WHO guidelines from 2009 based on their clinical presentations into dengue with warning signs (DNWS), dengue without warning sign (DWWS), or severe dengue (SD) and were compared to a control group of 40 healthy individuals.

Results: The mean LDH levels showed a marked increase with disease severity in Dengue, with values of 237.59 ± 58.31 U/L in DNWS, 576.47 ± 285.22 U/L in DWWS, and 764.58 ± 178.39 in Severe Dengue ($p < 0.05$). Conversely, the mean albumin levels demonstrated a significant decrease as the disease severity escalated, being highest in DNWS (4.65 ± 0.35 g/dl) and significantly lower in both DWWS (3.08 ± 0.48) and Severe Dengue (3.05 ± 0.32).

Conclusion: The judicious application of biochemical markers has the potential to alleviate economic strain, as well as reduce morbidity and mortality associated with severe Dengue cases.

Keywords: Dengue Fever, Prognostic Marker, Lactate Dehydrogenase, Albumin.

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Introduction

Dengue fever, caused by the dengue virus, is a mosquito-borne illness that poses significant public health challenges in tropical and subtropical regions worldwide. The clinical manifestations of dengue range from mild flu-like symptoms to severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), both of which can be fatal if not managed properly. [1] Accurate early diagnosis and effective monitoring of disease progression are crucial for improving patient outcomes. Among the various laboratory markers used in the clinical management of dengue, lactate dehydrogenase (LDH) and serum albumin have gained attention as potential prognostic indicators.[2]

Lactate dehydrogenase is an enzyme involved in cellular metabolism, catalyzing the conversion of lactate to pyruvate and vice versa. It is widely distributed across body tissues, and its levels in the blood rise significantly during cellular injury or metabolic stress. Elevated LDH levels have been

reported in various conditions, including viral infections like dengue, and are associated with tissue damage and the severity of the disease. In dengue, high LDH levels are indicative of extensive cellular damage, especially in organs such as the liver, heart, and muscles, which may signal the onset of more severe disease forms like DHF or DSS. Thus, LDH has been studied as a potential marker for assessing disease severity and predicting outcomes in dengue patients.[3]

Serum albumin, a major protein produced by the liver, plays a vital role in maintaining osmotic pressure and transporting various molecules in the bloodstream. In the context of dengue, hypoalbuminemia (low serum albumin levels) is commonly observed, especially in patients with severe manifestations. The drop in albumin levels is often attributed to increased vascular permeability, a hallmark of severe dengue, which leads to fluid leakage from blood vessels and contributes to shock. As a result, low serum

albumin levels are frequently correlated with poor prognosis, indicating a higher risk of complications such as organ failure and death.[4]

The use of LDH and serum albumin as prognostic markers in dengue provides valuable insights into disease progression and severity. By monitoring these markers, healthcare providers can potentially identify high-risk patients early, allowing for timely interventions and better management strategies. This article aims to explore the significance of lactate dehydrogenase and serum albumin in predicting the clinical outcomes of dengue fever, highlighting their potential role in improving patient prognosis and reducing mortality rates.

Material & Methods

This observational study involved the recruitment of 60 patients aged over 15 years who were admitted to the Department of Medicine at our hospital between August 2024 and December 2024. The inclusion criteria encompassed patients presenting with fever lasting three days, those in the febrile phase of dengue fever, or individuals experiencing complications related to dengue fever. Conversely, patients in the afebrile phase of dengue fever, those with negative NS1 antigen tests, and individuals with a history of hepatic, cardiac, or hematological disorders, as well as other comorbidities, were excluded from the study. Ethical approval was obtained from the institution, and written informed consent was secured from all participants.

A comprehensive case history was documented, and blood samples were collected to assess Hemoglobin (Hb%), Packed Cell Volume (PCV%), platelet count, dengue serology, serum LDH, and serum albumin levels following the confirmation of dengue fever (NS1 Ag-positive). The patients enrolled were categorized according to the WHO guidelines [6] from 2009 based on their clinical

presentations into dengue with warning signs (DNWS), dengue without warning signs (DWWS), or severe dengue (SD) and were compared to a control group of 40 healthy individuals.

Statistical Analysis

Data collection and compilation were performed using Microsoft Excel, with analysis conducted via SPSS version 23.0. Continuous data were expressed as mean \pm standard deviation. For continuous variables, frequency, percentage, means, and standard deviations (SD) were calculated, while ratios and proportions were determined for categorical variables. A p-value of less than 0.05 was considered statistically significant. The Student's t-test was utilized to evaluate the significance of differences between two means.

Results

The study observed that the largest proportion of participants (35%) belongs to the 15-30 age category, followed by those aged 31-40 (25%), over 50 years (22%), and under 20 years (18%). The male population represented 65%, while females accounted for 35%. The average duration of fever recorded was 3.24 ± 1.24 days.

Additionally, the mean levels of lactate dehydrogenase (LDH) exhibited a significant increase in correlation with the severity of the disease, with recorded values of 237.59 ± 58.31 U/L in DNWS, 576.47 ± 285.22 U/L in DWWS & 764.58 ± 178.39 U/L in Severe Dengue ($p < 0.05$). Conversely, the mean albumin levels demonstrated a significant decrease as the disease severity escalated, being highest in DNWS (4.65 ± 0.35 g/dl) and considerably lower in both DWWS (3.08 ± 0.48 g/dl) and Severe Dengue (3.05 ± 0.32 g/dl) ($p < 0.05$). Table 1 Serum LDH & Serum albumin levels in Dengue patients.

Parameter		DNWS	DWWS	Severe Dengue	P value
Serum LDH levels	Normal (135-450 U/L)	30 (50%)	4(6.66%)	2(3.33%)	<0.05
	Abnormal (>450 U/L)	0(0%)	10(16.66%)	14(23.33%)	<0.05
	Mean \pm SD	237.59 ± 58.31	576.47 ± 285.22	764.58 ± 178.39	<0.05
Serum Albumin levels	Normal (3.5-5.5 g/dl)	30 (50%)	4(6.66%)	2(12.5%)	<0.05
	Abnormal (<3.5 g/dl)	0(0%)	10(16.66%)	14(87.5%)	<0.05
	Mean \pm SD	4.65 ± 0.35	3.08 ± 0.48	3.05 ± 0.32	<0.05

Discussion

Dengue fever represents the most significant arboviral infection affecting humans and has emerged as a critical global public health concern. It ranks among the foremost tropical infectious diseases worldwide.[7] In India, the frequency of epidemics is on the rise, with a notable involvement of younger populations, indicating an

increased incidence of infection. While classical dengue fever manifests as an acute febrile illness, a small percentage of cases progress to a more severe form known as dengue hemorrhagic fever (DHF). Timely identification and careful management are essential to protect lives from this potentially fatal disease.[8]

Biochemical changes observed within 48 to 96 hours of fever onset can serve as predictors for more severe dengue infections, indicating that early pathogenic alterations may precede the onset of complications. These biochemical markers hold promise for monitoring the disease and forecasting its severity. Elevated serum levels of lactate dehydrogenase (LDH) have been documented in cases of dengue fever.[9]

In the present study, the majority of participants (35%) were in the 21-30 age group, followed by those aged 31-40 (25%), over 50 years (22%), and under 20 years (18%). Males comprised 65% of the sample, while females accounted for 35%. The average duration of fever recorded was 3.24 ± 1.24 days. These results align with findings from previous research conducted by Priya et al. in 2024[5]. The patients were classified according to WHO guidelines 2009, as with 30 patients in DNWS, 14 in DWWS, and 16 in SD. The mean LDH levels showed a marked increase with disease severity in Dengue, with values of 237.59 ± 58.31 in DNWS, 576.47 ± 285.22 in DWWS, and 764.58 ± 178.39 in Severe Dengue. ($p < 0.05$) The mean albumin levels showed a marked decrease with disease severity, it was highest in DNWS (4.65 ± 0.35) and significantly lower in both DWWS (3.08 ± 0.48) and Severe Dengue (3.05 ± 0.32). ($p < 0.05$)

In the present study, 24 patients exhibited serum albumin levels below the normal range. The average albumin concentration in cases of severe dengue was found to be 3.05 ± 0.32 g/dl. These findings align with the research conducted by Priya et al. in 2024.[5] Additionally, the study by Kularatnam et al. noted that patients with diminished albumin levels during critical phases of illness progressed to severe dengue. Plasma leakage, which signifies that dengue induces hypoalbuminemia, serves as a marker of disease severity. [10] According to the research by Shankar P et al., albumin levels below 3 g/dl were linked to a higher occurrence of severe dengue. Typically, elevated albumin levels may indicate the integrity of the vascular endothelium, while levels falling below 3 g/dl could serve as an early sign of changes in vascular permeability. Consequently, this parameter may act as an early indicator of plasma leakage and a valuable prognostic marker.[8]

In a study conducted by Shankar P et al. in 2017 involving 150 children, measurements of serum lactate dehydrogenase (LDH) and serum albumin levels were taken. The findings indicated that patients suffering from severe dengue exhibited elevated LDH levels and reduced serum albumin levels.[8] Equebal A et al. reported the mean LDH level in the study cohort to be 1,802 IU [9], while similar results were noted by Sirikutt and

Kalayanarooj, who found a mean LDH of 1,873 IU. They also noted that dengue patients had mean LDH levels exceeding 500 IU, in contrast to non-dengue patients, who had levels below 500 IU.[11] Furthermore, an increase in LDH levels was observed towards the conclusion of the febrile phase in cases of dengue hemorrhagic fever (DHF) and dengue shock syndrome. Lactate dehydrogenase is an intracellular enzyme that is prevalent in various body tissues, including muscles, liver, placenta, red blood cells, and the reticuloendothelial system.[12] Its serum concentration rises following cellular injury and has been assessed as a prognostic indicator in numerous inflammatory conditions such as sepsis, infections, myocardial infarction, malignancies, and cardiopulmonary issues. [13] Additionally, it is considered a marker of vascular permeability in immune-mediated lung injuries. An early elevation in LDH levels, specifically three times the normal value, has been identified as an independent predictor of DHF, as noted by Praveen et al. in 2014.[14]

Conclusion

The research identified a notable correlation between the biomarkers Lactate Dehydrogenase (LDH) and albumin in relation to dengue fever. Increased serum levels of LDH were observed in cases of severe dengue and Dengue with Warning Signs (DWWS), underscoring the necessity for effective triage and ongoing monitoring of patients. The judicious application of biochemical markers has the potential to alleviate economic strain, as well as reduce morbidity and mortality associated with severe dengue cases.

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