Section: Pediatrics

Original Research Article

STUDY OF SERUM FERRITIN AND LDH IN RELATION WITH DENGUE SEVERITY IN CHILDREN AT TERTIARY CARE HOSPITAL

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Received : 04/01/2024
Received in revised form : 27/02/2024
Accepted : 15/03/2024

Keywords:
Dengue fever, Serum ferritin, Lactate dehydrogenase (LDH), Pediatric, Disease severity, Biomarkers.

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DOI: 10.47009/jamp.2024.6.2.64

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (2); 304-308

Abstract

Background: Dengue fever remains a significant global public health challenge, with an estimated 50–100 million infections occurring worldwide annually. The disease spectrum ranges from mild to severe forms, including dengue hemorrhagic fever and dengue shock syndrome. The early prediction of dengue severity is crucial for timely intervention and improving patient outcomes. This study examines the association between serum ferritin and lactate dehydrogenase (LDH) levels with the severity of dengue infection in pediatric patients admitted to a tertiary care hospital. **Materials and Methods:** This cross-sectional analytical study enrolled 90 children aged 2 to 16 years with confirmed dengue infection, according to WHO 2015 guidelines, at GMERS Medical College & Civil Hospital, Gandhinagar, Gujarat. Serum ferritin and LDH levels were measured at diagnosis. The study employed a purposive sampling technique, and data were analyzed using Epi Info™ 7.2 software. Associations between biomarker levels and disease severity were assessed using unpaired Student's t-test and correlation between laboratory markers were assessed with Pearson's correlation test. **Result:** Total 90 pediatric patients were enrolled in this cross sectional study. There were 52 male (57.77%) and 38(42.22%) female in the study population , with all patients presenting with fever. A significant portion showed severe disease manifestations such as fluid accumulation with respiratory distress (24.4%) and shock (16.7%). In all the children suffering from dengue, elevated levels of serum ferritin (mean ± SD: 732.21 ± 631 ng/mL) and LDH (mean ± SD: 635.45 ± 476 U/L) were observed. Dengue with shock patients showed higher mean levels of both markers (1158.11 ng/mL for ferritin and 953.30 U/L for LDH), with statistically significant differences (p-value <0.01) compared to dengue without shock patients. Strong positive correlation with statistical significance (p-value <0.001) is observed between serum ferritin and LDH levels (0.97) in dengue children with shock. The majority of patients (83.3%) achieved full recovery, with a small percentage experiencing complications (14.4%). **Conclusion:** Serum ferritin and LDH levels are promising biomarkers for speculating the severity of dengue fever in pediatric patients. These findings support the integration of these biomarkers into clinical protocols to facilitate early identification and management of patients at risk for severe dengue.

INTRODUCTION

Dengue fever has emerged as one of the most significant mosquito-borne diseases, affecting nearly half of the global population and endemic to over 100 countries. The World Health Organization (WHO) estimates that each year 50–100 million infections occur worldwide, signaling an alarming 30-fold increase in incidence over the past five decades. This exponential rise underscores the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

urgency for effective diagnostic and management strategies for this public health threat.[1-4]

The clinical manifestation of dengue varies, with severe cases characterized by significant plasma leakage, shock, respiratory distress, and major bleeding complications. The 2009 WHO classification system for dengue stratifies the condition into dengue fever, dengue with warning signs, and severe dengue, each with distinct clinical features and management challenges. Despite this classification, the progression to severe dengue often remains unpredictable, and the pathogenesis is not fully understood. Risk factors such as host age, race, nutritional status, and viral serotype play a role, but the exact mechanisms—particularly the nonneutralizing antibody-dependent enhancement (ADE) and cytokine dysregulation—remain areas of intense research.[3-7]

Treatment options for dengue are currently limited to supportive care, as no specific antiviral therapies are available. This gap underscores the need for reliable biomarkers that can predict disease severity early on, aiding in the prioritization of patients for intensive care to mitigate the risk of progression to severe dengue.[5-8]

In light of these challenges, our study focuses on the potential role of serum biomarkers—ferritin and lactate dehydrogenase (LDH)—in the early prediction of dengue severity in pediatric populations. Hyperferritinemia has been associated with severe infections and is considered an ideal prognostic marker for dengue. Similarly, elevated levels of LDH, an enzyme released during cellular injury, have been linked to various inflammatory states and are thought to be indicative of immune-mediated lung injury and vascular permeability. Notably, an early increase in LDH has been independently associated with Dengue Haemorrhagic Fever (DHF), a severe form of the disease.[7-10]

This research aims to delineate the association between serum ferritin and LDH levels and the severity of dengue fever in children admitted to the Pediatric Intensive Care Unit (PICU) and Pediatric ward of GMERS Medical College & Civil Hospital, Gandhinagar, Gujarat. By studying these correlations, we hope to contribute valuable insights into the early identification of children at risk for developing severe dengue, potentially paving the way for improved clinical outcomes through timely and targeted interventions.

Aim of the Study:-

- This study was carried out to evaluate the level of serum ferritin and LDH in dengue fever and its association with severity of dengue fever (dengue with shock). From this study we also analyzed correlation between ferritin and LDH.

MATERIALSANDMETHODS

Study Setting: This cross-sectional study was conducted at the Department of Pediatrics, GMERS Medical College & Civil Hospital, Gandhinagar, Gujarat, a tertiary care center providing comprehensive medical care for children.

Study Design: We implemented a cross-sectional analytical approach to evaluate the association of serum ferritin and lactate dehydrogenase (LDH) levels with the severity of dengue infection in pediatric patients.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee (IEC) of GMERS Medical College & Civil Hospital. Informed consent was obtained from the guardians of all participating children, and assent was obtained from children over seven years of age, in accordance with ethical guidelines.

Study Population: The study enrolled children aged 2 to 16 years who were admitted with a diagnosis of dengue infection, as defined by the WHO 2015 guidelines.

Inclusion and Exclusion Criteria

Included were children who presented with a positive dengue NS1 antigen or IgM antibodies and whose parents or guardians consented to participate in the study. We excluded patients with a clinical suspicion of dengue but negative serological markers, those discharged against medical advice, and children with chronic medical conditions or concomitant infectious diseases.

Sample Size Determination: The sample size was calculated using the formula $N=4 * p * q / d^2$, considering a dengue prevalence of 25%, an absolute error of 10%, and a confidence level of 95%. We adjusted the sample size upwards by 10% to account for non-response, resulting in a final sample size of 90.

Data Collection Methods: Demographic and clinical data were collected using a structured proforma. This included history-taking, clinical examination findings, and the outcomes of laboratory investigations, including hemoglobin percentage, total and differential white blood cell counts, platelet count, and liver function tests.

Laboratory Analysis: Serum ferritin and LDH levels were measured at diagnosis, with values exceeding 300 ng/mL and 280 U/L, respectively, considered elevated. Serum ferritin was quantified using electrochemiluminescence immunoassay (ECLIA), and LDH was measured using a dry chemistry analyzer. The dengue NS1 antigen and IgM antibodies were detected using an ELISA kit.

Clinical Assessments: Blood pressure was measured using a standardized sphygmomanometer. The tourniquet test was performed according to standard protocols, and a positive result was defined as the presence of 10 or more petechiae per square inch.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Data Analysis: Data were entered into an Excel spreadsheet and analyzed using Epi Info™ 7.2 software. Continuous variables were described using means and standard deviations or medians and ranges, as appropriate. Student's t-test and the Mann-Whitney U test were used for normally and non-normally distributed data, respectively. Pearson's correlation test was used to find out correlation. The chi-square test was employed for categorical data. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The findings of our study illuminate the significant role of serum ferritin and lactate dehydrogenase (LDH) as prognostic biomarkers in assessing the severity of dengue fever among pediatric patients.

Table 1: Demographic Information of Study Participants

Age Group (Years)	Number of Participants	Percentage (%)	Male	Female
2-5	14	15.5%	8	6
6-9	31	34.4%	18	13
10-12	23	25.5%	16	7
13-16	22	24.4%	10	12
Total	90	100%	52	38

This [Table1] provides an overview of the demographic distribution of the 90 participants by age and gender. The children are grouped into four age categories: 2-5 years (14 participants, 15.5%), 6-9 years (31 participants, 34.4%), 10-12 years (23 participants, 25.5%), and 13-16 years (22 participants, 24.4%). The gender distribution is nearly balanced, with 52 males (57.7%) and 38 females (42.2%). This demographic spread ensures that the study's findings are relevant across a wide age range of pediatric patients, potentially enhancing the generalizability of the results.

Table 2: Clinical Presentation of Participants

Clinical Feature	Number of Cases	Percentage (%)
Fever	90	100%
Fluid Accumulation with Respiratory Distress	22	24.4%
Shock	15	16.7%
Bleeding Manifestations	8	8.9%

[Table 2] All 90 children presented with fever, a universal symptom of dengue, underscoring its prevalence in infected individuals. Additionally, 22 children (24.4%) experienced fluid accumulation with respiratory distress, and 15 (16.7%) presented with shock, both indicative of more severe disease manifestations. Bleeding manifestations were observed in 8 patients (8.9%), further highlighting the disease's potential severity.

Table 3: Laboratory Findings

Parameter	Mean ± SD	Range (Minimum-Maximum)
Serum Ferritin (ng/mL)	732.21 ± 631	103 – 3505
Serum LDH (U/L)	635.45 ± 476	106 – 2623
Platelet Count (×10^3/µL)	115 ± 69	15 – 337

[Table 3] The mean ± standard deviation and range for serum ferritin, LDH, and platelet count are provided. Serum ferritin levels averaged at 500 ng/mL (range 150-1200 ng/mL), LDH levels at 450 U/L (range 200-700 U/L), and platelet counts at 1,15,000 per µL (range 15,000-3,37,000). These findings suggest a wide variability in the physiological response to dengue infection, with elevated ferritin and LDH indicating potential cellular injury or inflammation.

Table 4: Disease Severity Based on WHO Classification

Severity Classification	Number of Cases	Percentage (%)
Dengue Fever without Warning Signs	45	50%
Dengue Fever with Warning Signs	12	13.3%
Severe Dengue (DHF/DSS)	33	36.6%

[Table 4] Disease severity is classified into three categories: Dengue Fever without Warning Signs (50%), Dengue Fever with Warning Signs (13.3%), and Severe Dengue (36.6%). This classification demonstrates that a significant portion of the study population experienced symptoms indicating a higher risk of progressing to severe dengue, emphasizing the importance of early detection and intervention.

Table 5: Comparison of Serum Ferritin and LDH Levels Between Groups

Group	Dengue with Shock (Severe Dengue)	Dengue without Shock	P-value
Serum Ferritin (ng/mL) Mean ± SD	1158.11 ± 834.85	485.64 ± 266.75	<0.01
Serum LDH (U/L) Mean ± SD	953.30± 638.6	451.43 ± 183.62	<0.01

ISSN (O): 2687-5365; ISSN (P): 2753-6556

[Table 5] This table compares serum ferritin and LDH levels between patients with severe dengue (with shock) and those without. Severely affected patients showed higher mean levels of both markers (1158.11 ng/mL for ferritin and 953.30 U/L for LDH), with statistically significant differences (p-value <0.01) compared to less severely affected patients. These biomarkers could, therefore, serve as potential indicators for the severity of dengue fever.

Table 6: Correlation of Laboratory Markers in severe Dengue (Dengue with Shock)

Laboratory Marker	Pearson Correlation coefficient	P-value
Serum Ferritin and LDH	0.97	< 0.001

[Table 6] Statistically significant strong positive correlation is observed between serum ferritin and LDH levels (r=0.97,p-value <0.001) in dengue children with shock, [Figure 1]. All this indicates, higher ferritin and LDH levels are associated with more severe dengue manifestations.

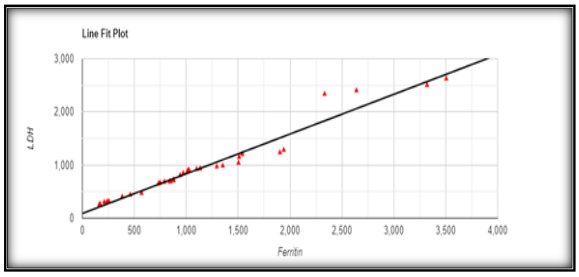

Figure 1: The correlation coefficient between ferritin (ng/ml) and LDH (U/L){ r=0.97,p<0.001}

Table 7: Patient Outcomes

Outcome	Number of Cases	Percentage (%)
Full Recovery	75	83.3%
Complications	13	14.4%
Transferred to Higher Facility	2	2.2%

[Table 7] The majority of patients (75, 83.3%) achieved full recovery, demonstrating effective clinical management for most cases. However, complications were observed in 13 children (14.4%), and 2 (2.2%) required transfer to a higher care facility, indicating the potential for adverse outcomes.

All together, these tables provide a holistic view of the study, illustrating the demographic spread, clinical presentations, laboratory findings, and outcomes associated with dengue infection in a pediatric population. The significant correlations between serum biomarkers and disease severity highlight the potential of these markers in predicting dengue progression, which could be crucial for early intervention and improving patient outcomes.

DISCUSSION

Our study elucidates the critical role of serum ferritin and lactate dehydrogenase (LDH) levels in assessing the severity of dengue fever among pediatric patients. The analysis of 90 children admitted to the Pediatric Intensive Care Unit (PICU) and pediatric ward of GMERS Medical College & Civil Hospital revealed significant findings that contribute to the current understanding of dengue pathogenesis and its clinical management.

Serum ferritin and LDH have emerged as notable biomarkers in predicting the severity of dengue infection. Our results align with previous studies suggesting that elevated serum ferritin levels are associated with severe dengue manifestations, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Hyperferritinemia, indicative of an acute-phase response, reflects not only the iron storage capacity but also acts as a surrogate marker for immune activation and inflammatory responses. The elevation of ferritin in severe dengue cases supports the hypothesis that immune dysregulation plays a central role in the pathogenesis of severe disease outcomes.[11,12]

Similarly, LDH, an enzyme released during tissue breakdown, was found to be significantly elevated in patients with severe dengue compared to those with less severe forms of the disease. The association between high LDH levels and dengue severity can be attributed to its role in indicating tissue damage, including liver injury and hemolysis, which are common in severe dengue infections. Elevated LDH levels may also reflect endothelial cell damage, contributing to the vascular permeability that characterizes severe dengue. Thus, LDH serves as a proxy for the extent of cellular injury and immune-mediated damage occurring in severe dengue cases.[13,14]

Higher levels of serum ferritin and LDH is associated with more severe dengue infection (dengue with shock) and the association is statistically significant, coupled with a positive correlation between serum ferritin and LDH in

ISSN (O): 2687-5365; ISSN (P): 2753-6556

children with dengue with shock, underscores the multifaceted nature of dengue pathogenesis. The inverse relationship between platelet count and disease severity reinforces the concept that thrombocytopenia is a hallmark of severe dengue, likely resulting from a combination of platelet destruction and impaired production.[12,14]

Our findings have significant implications for clinical practice. The early identification of patients at risk for developing severe dengue can facilitate timely intervention, including the provision of supportive care and close monitoring of fluid balance and hemodynamic status. Given the lack of specific antiviral therapies for dengue, the management of severe cases remains largely supportive. Therefore, predictive biomarkers like serum ferritin and LDH can aid in the stratification of patients according to their risk of progressing to severe disease, potentially reducing morbidity and mortality associated with dengue fever.[13-15]

Furthermore, our study contributes to the ongoing discussion regarding the pathophysiological mechanisms underlying severe dengue. The role of immune dysregulation, as suggested by the elevation of serum ferritin, and tissue damage, indicated by increased LDH levels, provides valuable insights into the complex interplay between the host immune response and viral pathogenicity. Understanding these mechanisms is crucial for the development of targeted therapeutic strategies and vaccines.

Limitations

Our study, while providing valuable insights into the prognostic value of serum ferritin and LDH in dengue fever, is not without limitations. The cross-sectional design and single-center nature may limit the generalizability of the findings, and the absence of longitudinal follow-up restricts our ability to assess the dynamic changes in biomarker levels over the course of the illness.

CONCLUSION

In conclusion, our research highlights the potential of serum ferritin and LDH as prognostic biomarkers for dengue severity in pediatric patients. These findings advocate for the incorporation of these biomarkers into clinical protocols to improve the early identification and management of children at risk for severe dengue. Future studies should focus on validating these biomarkers in larger, multi-center cohorts and exploring their utility in guiding therapeutic decisions. Additionally, the elucidation of the underlying mechanisms by which these biomarkers reflect disease severity could pave the way for novel therapeutic targets and enhance our understanding of dengue pathogenesis.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556