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# A STUDY ON SERUM LACTATE DEHYDROGENASE AS PROGNOSTIC INDICATOR IN PATIENTS WITH DENGUE FEVER. AN OBSERVATIONAL CROSS-SECTIONAL STUDY IN NORTH DELHI

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**ABSTRACT**

Dengue is a mosquito-borne viral illness caused by one of the four serotypes of the dengue virus (DENV-1 to DENV-4) belonging to the family Flaviviridae. The virus is transmitted to human via Aedes genus, especially Aedes aegypti. The disease is characterized by fever, rash, joint pains, nausea, vomiting, headache, and retro-orbital pain. The disease severity may vary from mild fever which does not require hospitalization to severe disease with features of dengue haemorrhagic fever (DHF)/dengue shock syndrome (DSS) requiring intensive care management. Certain biochemical alterations in dengue may help in early diagnosis and predicting the severity. Studies have reported that patients with DHF have elevated levels of transaminases [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], amylase, lactate dehydrogenase (LDH), and creatine kinase (CK). The serum LDH levels have been reported to be increased in DF and still higher in DHF and DSS cases. LDH is an intracellular enzyme abundantly found in body tissues, e.g., muscles, liver, placenta, RBCs, and reticuloendothelial system. Its serum levels increase after cell injury. Serum lactate may reportedly be used as a marker of tissue hypoxia caused by systemic hypoperfusion. It has been evaluated as a prognostic marker of various inflammatory states like sepsis, infections, myocardial infarction, malignancies, and cardiopulmonary compromise. It is thought to be a marker of vascular permeability in immune-mediated lung injury. However, studies regarding the use of serum lactate level as dengue severity predictor and diagnostic biomarker of plasma leakage are still scarce, therefore further studies are needed.

**Keywords:** Dengue fever, Lactate Dehydrogenase, Aspartate Transaminase, Alanine Transaminase.

## INTRODUCTION

The name “Dengue” was derived from the Swahili word for “bone breaking fever” or the Spanish word for “the walk of a Dandies”.[1] Dengue is a mosquito-borne viral illness caused by one of the four serotypes of the dengue virus (DENV; (DENV-1 to DENV-4) belonging to the family Flaviviridae. The virus is transmitted to human via Aedes genus, especially Aedes aegypti. The disease is characterized by fever, rash, joint pains, nausea, vomiting, headache, and retro-orbital pain.[2] The disease is now endemic in more than 100 tropical and subtropical countries.[1] The clinical spectrum of dengue infection varies from no symptoms to severe dengue with shock. Nearly 100 million cases of dengue fever and between 250,000 and 500,000 cases of severe dengue are annually reported to the

World Health Organization (WHO).[3] Severe dengue is characterized by thrombocytopenia, spontaneous haemorrhages, and plasma leakage that can lead to shock.[4] Approximately 75% of the global populations exposed to dengue reside in the Asia-Pacific region.[5] The disease severity may vary from mild fever which does not require hospitalization to severe disease with features of dengue haemorrhagic fever (DHF)/dengue shock syndrome (DSS) requiring intensive care management.[6] The disease goes through three clinical stages like febrile phase, critical phase, and recovery phase. The febrile phase generally lasts for 2–10 days after which the patient may either enter the recovery phase or progress to a critical phase marked by defervescence and appearance of plasma leakage. Most complications of dengue occur in the above phase. Despite the severity, the acute phase of dengue starts with a fever that is indistinguishable from other acute febrile infections. As per WHO 2007 criteria, patients may be labelled as having dengue fever (DF), DHF, DSS. As per the new terminology recommended by WHO in 2009, the cases are classified into dengue without warning signs, dengue with warning signs (abdominal pain/persistent vomiting/mucosal bleed/increase in haematocrit with decrease in platelet count), and severe dengue (severe plasma leakage, severe bleeding, and severe organ involvement).[7] Dengue causes micro vascular inflammation throughout the body, as evidenced by the increased markers of inflammation e.g. cytokines, chemokines, VEGF and other angiogenic factors. Injury to vascular endothelial cells results from a complex interaction between the circulating proteins of dengue virus and host immune response. Activation of cellular and humoral immune response increases vascular permeability, which may be manifested by ascites, pleural effusion or shock.[8] Certain biochemical alterations in dengue may help in early diagnosis and predicting the severity. Studies have reported that patients with DHF have elevated levels of transaminases [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], amylase, lactate dehydrogenase (LDH), and creatine kinase (CK).[9] The serum LDH levels have been reported to be increased in DF and still higher in DHF and DSS cases. LDH is an intracellular enzyme abundantly found in body tissues, e.g., muscles, liver, placenta, RBCs, and reticuloendothelial system. Its serum levels increase after cell injury. Serum lactate may reportedly be used as a marker of tissue hypoxia caused by systemic hypoperfusion. It has been evaluated as a prognostic marker of various inflammatory states like sepsis, infections, myocardial infarction, malignancies, and cardiopulmonary compromise. It is thought to be a marker of vascular permeability in immune-mediated lung injury. However, studies regarding the use of serum lactate level as dengue severity predictor and diagnostic biomarker of plasma leakage are still scarce, therefore further studies are needed. Dengue has very high rate of admission in tertiary care hospitals. Severe dengue requires aggressive monitoring, thus posing a burden on health system. So, the search for the prognostic factors, may help to reduce the rate of hospitalizations, as well as disease mortality and morbidity. We hypothesized that elevated LDH level might serve as a diagnostic biomarker for identifying tissue hypoperfusion among patients with dengue before clinical manifestations of severe dengue develop. The present study evaluated the prevalence of elevated LDH in patients with dengue fever and the role of LDH as prognostic indicator in dengue severity.

## MATERIALS AND METHODS

**Place of study**: Department of Medicine, Hindu Rao Hospital, Malkaganj, Delhi.
**Study period:** November 2020 to November 2021
**Study design:** An Observational Cross-Sectional Study
**Study subjects:** All the patients with diagnosis of dengue was confirmed by either Dengue NS1 antigen or IgM Dengue serology (ELISA).

**Inclusion Criteria**

• Age > 15 years
• Diagnosis of dengue was confirmed by either Dengue NS1 antigen or IgM Dengue serology (ELISA).

**Exclusion Criteria**

• known case of Chronic liver disease
• known case of chronic kidney diseases
• known case of haemolytic anaemia
• patient on antiplatelets medication
• known case of ITP
• known case of haemolytic anaemia
• known case of pancreatitis

**Methodology**

A total of 100 patients with confirmed Dengue fever meeting inclusion and exclusion criteria were screened for biochemical markers such as Creatinine kinase, LDH, Total cholesterol, HDL, Triglycerides, SGOT, SGPT, Serum albumin through lab investigations and clinical signs and symptoms.

The diagnosed patients of dengue were classified into 3 groups based on their clinical parameters and biochemical studies- group 1-mild, 2- moderate, group 3 -severe. A structured Proforma is developed and used for data collection. The data compared between the three groups by Mann Whitney U test, and chi square test was applied wherever appropriate.

The reagent uses pyruvate and is based on the method of Henry et al.

Pyruvate + NADH → Lactate + NAD+

LDH catalyses the reduction of pyruvate to lactate oxidising reduced nicotinamide adenine dinucleotide (NADH) to NAD. The activity of LDH can be determined by the ratio of decrease in absorbance at 340 nm as NAD is produced.

Specimen Collection and Handling

Use serum, plasma (heparin, EDTA)

It is recommended to follow NCCLs procedures (or similar standardized conditions).

**Diagnostic Criteria**

Dengue Fever:

An acute febrile illness of 2-7 days duration with two or more of the following manifestations:

Headache, retro-orbital pain, myalgia, arthralgia, rash, haemorrhagic manifestations.

**Dengue Haemorrhagic Fever**

a) A case with clinical criteria of dengue Fever plus
b) Haemorrhagic tendencies evidenced by one or more of the following

1. Positive tourniquet test
2. Petechiae, ecchymoses or purpura
3. Bleeding from mucosa, gastrointestinal tract, injection sites or other sites Plus

c) Thrombocytopenia (<100 000 cells per cumm) plus
d) Evidence of plasma leakage due to increased vascular permeability, manifested by one or more of the following:

1 A rise in average haematocrit for age and sex ≥ 20% 2 A more than 20% drop in haematocrit following volume replacement treatment compared to baseline 3 Signs of plasma leakage (pleural effusion, ascites, hypoproteinemia) ≤20%

**Dengue Shock Syndrome**

All the above criteria for DHF with evidence of circulatory failure manifested by rapid and weak pulse and narrow pulse pressure (mm Hg) or hypotension for age, cold and clammy skin and restlessness.

## RESULTS

The study compromised of 100 subjects aged ≥15 years attending the department with dengue fever. All the subjects with dengue fever were from Delhi.

Socio-demographic profile.

**Table 1: Age distribution of the subjects with dengue fever**

| Age group (in years) | No. (n=100) | % |
|---|---|---|
| <20 | 33 | 33.00% |
| 20 - 29 | 29 | 29.00% |
| 30 - 39 | 19 | 19.00% |
| 40 - 49 | 10 | 10.00% |
| 50 - 59 | 3 | 3.00% |
| ≥60 | 6 | 6.00% |

Table 1 shows the distribution of subjects with dengue fever according to age. The majority of subjects were aged between <20 years (33%), followed by 20-29 years (29%), 30-39 years (19%), 40-49 years (10%), 50-59 years (3%) and >=60 years (6%). The mean (SD) age of the included subjects was 29 (14.5) years.

**Table 2: Gender distribution of the subjects with dengue fever**

| Gender | No. (n=100) | % |
|---|---|---|
| Female | 38 | 38% |
| Male | 62 | 62% |

Table 2 shows the distribution of subjects with dengue fever according to gender. The majority of subjects were males (62%).

**Table 3: Diagnosis method among subjects with dengue fever**

| Diagnosis method | No. (n=100) | % |
|---|---|---|
| Ns1Ag | 59 | 59% |
| IgM | 41 | 41% |

Table 3 shows the distribution of subjects with dengue fever according to diagnosis method. The majority of subjects were diagnosed by Ns1Ag (59%), while the proportion of subjects diagnosed by IgM was 41%.

**Table 4: LDH level among subjects with dengue fever**

| LDH level | No. (n=100) | % |
|---|---|---|
| 100 - 199 | 36 | 36.00% |
| 200 - 299 | 23 | 23.00% |
| 300 - 399 | 11 | 11.00% |
| 400 - 499 | 7 | 7.00% |
| 500 - 599 | 6 | 6.00% |

| | | |
|---|---|---|
| 600 - 899 | 7 | 7.00% |
| 900 - 1399 | 10 | 10.00% |

Table 4 shows the distribution of subjects with dengue fever according to LDH level. The majority of subjects had LDH level between 100 – 199 (36%), followed by 200 – 299 (23%), 300 - 399 (11%), 900 – 1,399 (10%), 400 - 499 (7%), 600 – 899 (7%) and 500 - 599 (6%). The mean (SD) and median (IQR) LDH of the included subjects was 380 (299) and 237 (168.5 - 495), respectively.

**Table 5: Duration of dengue fever among the included subjects**

| | Mean (SD) | Median (IQR) |
|---|---|---|
| Duration of dengue fever | 4.38 (2.01) | 4 (3 - 6) |

Table 5 shows the duration of dengue fever among the subjects. The mean (SD) and median (IQR) duration was 4.38 (2.01) and 4 (3 - 6) days, respectively.

**Table 6: Platelet count among the included subjects**

| | Mean (SD) | Median (IQR) |
|---|---|---|
| Platelet count | 34,800 (22,320) | 27,500 (19,000 - 45,800) |

Table 6 shows the platelet count among the subjects with dengue fever. The mean (SD) and median (IQR) platelet count was 34,800 (22,320) and 27,500 (19,000 - 45,800), respectively.

**Table 7: Liver enzymes among the included subjects**

| | Mean (SD) | Median (IQR) |
|---|---|---|
| SGOT | 141.99 (185.52) | 47 (36 - 188) |
| SGPT | 114.27 (147.71) | 36 (28 - 144) |

Table 7 shows the distribution of liver enzymes among subjects with dengue fever. The mean (SD) and median (IQR) SGOT was 141.99 (185.52) and 47 (36 - 188), respectively. The mean (SD) and median (IQR) SGPT was 114.27 (147.71) and 36 (28 - 144), respectively.

**Table 8: Prevalence of high LDH level among subjects with dengue fever**

| | No. (n=100) | % |
|---|---|---|
| High LDH [>280] | 41 | 41.00% |

Table 8 shows the prevalence of high LDH level among subjects with dengue fever. Those with LDH >280 were considered as high LDH level. A total of 41 subjects had LDH >280, therefore the prevalence of high LDH level among subjects with dengue fever was 41%.

**Table 9: Association of dengue haemorrhagic fever with high LDH level among subjects with dengue fever**

| DHF | High LDH | Low LDH | Total | p value | OR (95% CI) |
|---|---|---|---|---|---|
| Yes | 34 (82.9%) | 5 (8.5%) | 39 (39%) | <0.001 | 52.46 (15.41 - 178.61) |
| No | 7 (17.1%) | 54 (91.5%) | 61 (61%) | | |

Table 9 shows the association of dengue haemorrhagic fever with high LDH level among subjects with dengue fever. Those with high LDH had a significantly higher odd of DHF as compared to those with low LDH level [OR (95% CI): 52.46 (15.41 - 178.61); p<0.001].

**Table 10: Association of dengue shock syndrome with high LDH level among subjects with dengue fever**

| DSS | High LDH | Low LDH | Total | p value | OR (95% CI) |
|---|---|---|---|---|---|
| Yes | 16 (39%) | 1 (1.7%) | 17 (17%) | <0.001 | 37.12 (4.665 - 295.346) |
| No | 25 (61%) | 58 (98.3%) | 83 (83%) | | |

Table 10 shows the association of dengue shock syndrome with high LDH level among subjects with dengue fever. Those with high LDH had a significantly higher odd of DSS as compared to those with low LDH level [OR (95% CI): 37.12 (4.66 – 295.35); p<0.001].

**Table 11: Association of mortality with high LDH level among subjects with dengue fever**

| Mortality | High LDH | Low LDH | Total | p value | OR (95% CI) |
|---|---|---|---|---|---|
| Yes | 19 (46.3%) | 0 (0%) | 19 (19%) | | |

| | | | | | |
|---|---|---|---|---|---|
| No | 22 (53.7%) | 59 (100%) | 81 (81%) | <0.001 | 3.682 (2.577 - 5.26) |

Table 11 shows the association of mortality with high LDH level among subjects with dengue fever. Those with high LDH had a significantly higher odds of mortality as compared to those with low LDH level [OR (95% CI):3.68 (2.58 – 5.26); p<0.001].

**Table 12: Association of age and duration of dengue fever with high LDH level among subjects with dengue fever**

| | High LDH [n=41] | | Low LDH [n=59] | | p value |
|---|---|---|---|---|---|
| | Mean (SD) | Median (IQR) | Mean (SD) | Median (IQR) | |
| Age | 28.59 (13.1) | 25 (17.5 - 35) | 29.19 (15.45) | 25 (18 - 34) | 0.842 |
| Duration | 5.07 (2.3) | 5 (4 - 6) | 3.9 (1.65) | 4 (3 - 5) | 0.004 |

Correlation / Association of LDH with different risk factors

Table 12 shows the association of age and duration of dengue fever with high LDH level among subjects with dengue fever. The age of the subjects did not differ significantly among those with high versus low LDH level. However, the mean (SD) duration of dengue fever was significantly higher among those with high versus low LDH level [5.07 (2.3) vs. 3.9 (1.65); p=0.004].

**Table 13: Association of gender with high LDH level among subjects with dengue fever**

| Gender | High LDH | Low LDH | Total | p value | OR (95% CI) |
|---|---|---|---|---|---|
| Male | 24 (58.5%) | 38 (64.4%) | 62 (62%) | 0.552 | 0.78 (0.344 - 1.769) |
| Female | 17 (41.5%) | 21 (35.6%) | 38 (38%) | | |

Table 13 shows the association of gender with high LDH level among subjects with dengue fever. The odds ratio of gender did not differ significantly among those with high versus low LDH level [OR (95% CI): 0.78 (0.344 - 1.769); p=0.552].

**Table 14: Association of diagnosis method with high LDH level among subjects with dengue fever**

| Diagnosis method | High LDH | Low LDH | Total | p value | OR (95% CI) |
|---|---|---|---|---|---|
| IgM | 16 (39%) | 25 (42.4%) | 41 (41%) | 0.738 | 0.87 (0.386 - 1.962) |
| Ns1Ag | 25 (61%) | 34 (57.6%) | 59 (59%) | | |

Table 14 shows the association of diagnosis with high LDH level among subjects with dengue fever. The odds ratio of diagnosis did not differ significantly among those with high versus low LDH level [OR (95% CI): 0.87 (0.386 - 1.962); p=0.738].

**Table 15: Association of platelet count with high LDH level among subjects with dengue fever**

| | High LDH [n=41] | | Low LDH [n=59] | | p value |
|---|---|---|---|---|---|
| | Mean (SD) | Median (IQR) | Mean (SD) | Median (IQR) | |
| Platelet count | 20,100 (9,237) | 19,000 (13,000 - 24,000) | 45,000 (23,100) | 41,000 (29,000 - 58,000) | <0.001 |

Table 15 shows the association of platelet count with high LDH level among subjects with dengue fever. The mean (SD) platelet count was significantly lower among those with high versus low LDH level [20,100 (9,237) vs. 45,000 (23,100); p<0.001].

**Table 16: Association of liver enzymes with high LDH level among subjects with dengue fever**

| | High LDH [n=41] | | Low LDH [n=59] | | p value |
|---|---|---|---|---|---|
| | Mean (SD) | Median (IQR) | Mean (SD) | Median (IQR) | |
| SGOT | 289.1 (217.79) | 201 (148.5 - 374) | 39.76 (10.39) | 38 (34 - 44) | <0.001 |
| SGPT | 235.98 (167.9) | 176 (134 - 340) | 29.69 (7.29) | 30 (26 - 34) | <0.001 |

Table 16 shows the association of liver enzymes with high LDH level among subjects with dengue fever. The mean (SD) SGOT [289.1 (217.79) vs. 39.76 (10.39); p<0.001] and SGPT [235.98 (167.9) vs. 29.69 (7.29); p<0.001] were significantly higher among those with high versus low LDH level.

## DISCUSSIONS

Biochemical alterations detected after 48–96 hours of fever can predict a more severe form of dengue infection. These potential biochemical markers may be used for monitoring illness and predicting severity. Serum LDH levels have been reported to be increased in dengue fever. Liver and kidney are the two main organs in the human body which regulate the lactate level. Changes in hepatic oxygen supply and intrinsic hepatic disorder affect the capacity of the liver to metabolize lactate. In such condition, liver becomes a lactate producing organ rather than using it for gluconeogenesis. Hence, due to dysfunction of these important body organs in dengue infection, blood lactate level increases. While the role of serum lactate in septic patients had been well established, the role of serum lactate as biomarker in dengue patients was understudied, especially in adult patients.

Among the 100 cases of dengue fever in the study, the majority of subjects were aged between <20 years (33%), followed by 20-29 years (29%), 30-39 years (19%), 40-49 years (10%), 50-59 years (3%) and >=60 years (6%). The mean (SD) age of the included subjects was 29 (14.5) years and the majority of subjects were males (62%). The majority of subjects had LDH level between 100 - 199 (36%), followed by 200 – 299 (23%), 300 - 399 (11%), 900 – 1,399 (10%), 400 - 499 (7%), 600 – 899 (7%) and 500 - 599 (6%). The mean (SD) and median (IQR) LDH of the included subjects was 380 (299) and 237 (168.5 - 495), respectively. The mean (SD) and median (IQR) duration of dengue fever was 4.38 (2.01) and 4 (3 - 6) days, respectively and the mean (SD) and median (IQR) platelet count was 34,800 (22,320) and 27,500 (19,000 - 45,800), respectively. The mean (SD) and median (IQR) SGOT was 141.99 (185.52) and 47 (36 - 188), respectively. The mean (SD) and median (IQR) SGPT was 114.27 (147.71) and 36 (28 - 144), respectively.

A total of 41 subjects had LDH >280, therefore the prevalence of high LDH level among subjects with dengue fever was 41%. Those with high LDH had a significantly higher odd of DHF as compared to those with low LDH level [OR (95% CI): 52.46 (15.41 - 178.61); p<0.001]. Also, those with high LDH had a significantly higher odd of DSS as compared to those with low LDH level [OR (95% CI): 37.12 (4.66 – 295.35); p<0.001]. Those with high LDH had a significantly higher odds of mortality as compared to those with low LDH level [OR (95% CI): 3.68 (2.58 – 5.26); p<0.001]. The age of the subjects did not differ significantly among those with high versus low LDH level. However, the mean (SD) duration of dengue fever was significantly higher among those with high versus low LDH level [5.07 (2.3) vs. 3.9 (1.65); p=0.004]. The odds ratio of gender did not differ significantly among those with high versus low LDH level [OR (95% CI): 0.78 (0.344 - 1.769); p=0.552]. The odds ratio of diagnosis did not differ significantly among those with high versus low LDH level [OR (95% CI): 0.87 (0.386 - 1.962); p=0.738]. The mean (SD) platelet count was significantly lower among those with high versus low LDH level [20,100 (9,237) vs. 45,000 (23,100); p<0.001]. The mean (SD) SGOT [289.1 (217.79) vs. 39.76 (10.39); p<0.001] and SGPT [235.98 (167.9) vs. 29.69 (7.29); p<0.001] were significantly higher among those with high versus low LDH level.

In México, Vázquez- Pichardo et al. reported increased activity of LDH (twice as much as the control) was found in the DHF patients for DENV-1 (100±51 U/L), 2 (120±15 U/L) and 3 (94±10 U/L).[10]

In Colombia, Villar-Centeno et al. reported that early alterations of CK (hazard ratio [HR] = 6.98, 95% confidence interval [CI] = 2.34– 20.85, P =0.001), LDH (HR = 3.19, 95% CI = 1.01–10.12, P < 0.05), and albumin (HR = 2.54, 95% CI = 1.09–5.92, P = 0.03) were associated with DHF.[11]

In Saudi Arabia, Ahmed et al. reported elevated levels of serum LDH (33.33%, 16.67%, 4.05%, respectively in consecutive three years, P = 0.040767). Those with high LDH had a significantly higher level of DHF (12.12%) and mortality rate were 4.55%, 25% and 2.7% in consecutive three years.[12]

In India, Mehta et al. reported that LDH > 10000 IU/L and AST > 5000 IU/L were associated with mortality for dengue patients. Average LDH level in non-fatal cases was 4750 IU/L (range: 2500 – 11328 IU/L) while it was 18750 IU/L (range 13500 – 75000 IU/L) in fatal cases.[13] In India, Mittal et al. reported the mean LDH in febrile phase was 550.33 IU/L. The mean LDH in critical phase of the illness was 748.68 IU/L and the mean LDH in the convalescence stage was 406.23 IU/L. The mean LDH level on the day of least platelet count was 608.87 ± 228.67 IU/L.[14] In Thailand, Thanachartwet et al. reported for dengue patients absolute lymphocyte count >2000 cells per µL (p=0.036), absolute atypical lymphocyte count >300 cells per µL (p=0.002), platelet count ≤100×103 per µL (p=0.031), lactate level ≥2.0 mmol/L (p<0.001), albumin level <3.5 g/dL (p<0.001), AST level >120 IU/L (p=0.017), and ALT level >120 IU/L (p=0.032). The median (IQR) duration of hospitalization among patients with severe dengue were significantly longer than those with non-severe dengue (4.8 [2.9–9.8] vs. 3.7 [2.7–4.8] days; p=0.047). Lactate level ≥2.0 mmol/L (OR: 7.340, CI: 2.334– 23.087; p=0.001) was associated with the development of severe dengue. The median (IQR, mmol/L) lactate levels among patients with severe

dengue {2.7 (1.7–3.1)} was significantly greater than patients with non-severe dengue {1.4 (1.2–1.8)} ($p<0.05$) and the extent of elevated lactate was associated with severity of dengue.[15]

In India, Shankar et al. 92.7% had raised levels of LDH with levels more than >600 IU and <3 levels of serum albumin in 32.5% of severe dengue cases with P value of < 0.001, which showed significant association. 62.7% of cases were seen with LDH of 300-600 IU/L and 55.3% had serum albumin levels above 3.5g/dl.[16] In Vietnam, Yacoub et al. reported that patients with recurrent shock had a higher enrolment pulse than those with 1 episode or no shock (median: 114 vs. 100 vs. 100 b/min, P = 0.002), significantly lower Stroke Volume Index (SVI), (median: 21.6 vs. 22.8 vs. 26.8mls/m2, P<0.001) and higher lactate levels (4.2 vs. 2.9 vs. 2.2 mmol/l, P = 0.001). Admission lactate levels predicted patients who subsequently developed recurrent shock (P = 0.004), and correlated positively with the total IV fluid volume received (rho: 0.323, P = 0.001) and also with admission ALT (rho: 0.764, P<0.001) and AST (rho: 0.773, P<0.001).[17]

In China, Huang et al. reported that significant elevated LDH (U/L) levels were observed for both 1st week (297.16±154.33) and 2nd week (309.37±111.52) during primary dengue infections (P<0.001). Similarly, significant elevated LDH (U/L) levels were observed for both 1st week (322.97±170.13) and 2nd week (535.00±502.20) during secondary dengue infections (P<0.001).[18]

In India, Mandal et al. reported that the NS1 antigens were 35.23 ± 5.37 U (normal < 9 U) with 634.67 ± 350.55 U/L LDH (normal ≤250 U/L) (r = -0.57) among 32.33 ±7.13 years patients and IgM antibodies were 52.38 ± 7.68 U with 451.67 ± 119.74 U/L LDH (r = -0.13) among 25.92 ± 5.01 years patients.[19] In Pakistan, Khan et al. reported that LDH was raised to 5949 U/L for dengue patients.[20]

In India, Equebal et al. reported that the median LDH value was 1,133.5 IU [interquartile range (IQR) 640–1,732]. The mean LDH value was significantly higher in patients with severe dengue (2,986.65±3,638.54) as compared to dengue with warning signs (1,209.87±1,370.20) (p = 0.047). The majority (70%) of patients with severe dengue had LDH >1,000 IU and complications like severe bleeding, pleural effusion, ARDS, and shock were higher in this group. Mean hospital stay in patients with LDH >1,000 was 14.685±5.993 days and in those with LDH <1,000 was 8.732±3.312 days (p = 0.000). Mean platelet count was significantly lower in severe dengue (56,405.00 ± 49,918.74) as compared to dengue with warning signs (922,257.50±71,235.44) (p value 0.028) and there was a weak negative correlation between LDH and platelet count which was non- significant (r = Karl Pearson coefficient −0.055; p value 0.676). The case fatality rate was 9%. The mean LDH (4,783±5,131) in non-survivors was much higher than survivors (1,531.1±1,986) though this was not statistically significant.[21]

## CONCLUSION

We found that the majority of subjects had elevated LDH level. A total of 41 subjects had LDH >280, therefore the prevalence of high LDH level among subjects with dengue fever was 41%. Those with high LDH had a significantly higher odd of DHF as compared to those with low LDH level [OR (95% CI):
52.46 (15.41 - 178.61); p<0.001]. Also, those with high LDH had a significantly higher odd of DSS as compared to those with low LDH level [OR (95% CI):
37.12 (4.66 – 295.35); p<0.001]. Those with high LDH had a significantly higher odds of mortality as compared to those with low LDH level [OR (95% CI): 3.68 (2.58 – 5.26); p<0.001]. The mean (SD) platelet count was significantly lower among those with high versus low LDH level [20,100 (9,237) vs. 45,000 (23,100); p<0.001]. Therefore, serum LDH values should be prospectively evaluated in larger studies to assess their usefulness as an early predictor of severity and to determine the cut-off levels so that they can be included in the management guidelines.

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