



Evaluation of Role of Serum Lactate as a Marker of Dengue Infection Severity

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ABSTRACT

Background: Dengue infections, caused by four distinct serotypes of the dengue virus (DENV1, DENV2, DENV3, DENV4) from the Flaviviridae family, represent one of the most widespread arboviral diseases in humans, leading to significant morbidity and mortality globally.

Objective: The aim of this study was to evaluate serum lactate levels in dengue patients and determine their correlation with disease severity.

Methodology: This prospective observational study was conducted among indoor patients admitted to the General Medicine Department at Hitech Medical College and Hospital in Bhubaneswar. The study spanned 9 months.

Results: The study included 154 patients, with the majority (83 cases, 53.9%) being under 30 years of age. A higher number of cases were male (96 cases, 62.3%). The most common symptom was fever, reported in 39% (39 cases), while 66 cases (42.7%) showed elevated lactate dehydrogenase (LDH) levels. A comparison of serum LDH levels with dengue severity revealed that the mean serum LDH for non-severe dengue was 148.45 ± 11.81 , whereas severe dengue had a significantly higher mean LDH of 388.23 ± 99.47 ($p = 0.001$), indicating statistical significance.

Conclusion: This study suggests that monitoring serial lactate levels, rather than relying on a single lactate measurement, is beneficial in assessing dengue severity.

credible interval 304-537 million), leading to approximately 20,000 deaths and 500,000 cases of severe dengue. The Aedes mosquito transmits the virus from one person to another. Dengue can present as a mild febrile illness, often referred to as "dengue fever," or escalate to "severe dengue," also known as dengue hemorrhagic fever (DHF), which involves capillary leakage resulting in hypovolemic shock, organ dysfunction, and bleeding. Currently, dengue is managed primarily through careful fluid replacement in severe cases, as there are no antiviral drugs or vaccines available [2].

Each year, approximately 36 million cases of dengue fever are reported globally. While the exact prevalence remains unclear, an estimated 2.1 million cases of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) are documented annually, representing 5–10% of all cases [3]. Of these 36 million cases, 6% (around 2.1 million) will progress to DHF, which has a case-fatality rate of 1%, resulting in approximately 21,000 deaths [4]. Dengue affects over 100 countries, including nations in Europe and the United States [5]. The first confirmed dengue outbreak in India occurred in Calcutta and along the Eastern Coast in 1963–1964, though the first recorded instance of dengue-like illness in India dates back to 1780 in Madras [6]. Reducing dengue-related mortality requires a thorough understanding of warning signs, clinical symptoms, changes in biochemical markers, and patterns of multisystem involvement.

The primary mechanism underlying DHF is plasma leakage, which generally occurs as the fever subsides during the critical phase, typically peaking five days after the onset of fever [7][8]. In cases of shock or hypotension, anaerobic metabolism takes over, resulting in increased lactate production, which serves as a key marker of tissue hypoperfusion. Numerous studies have examined the relationship between venous lactate levels and the severity of dengue fever.

Our investigation aims to explore the correlation between venous lactate levels and various dengue complications, including the need for platelet transfusions, ventilator support,

I. INTRODUCTION

Dengue infections, caused by four distinct serotypes of the dengue virus (DENV1, DENV2, DENV3, DENV4) from the Flaviviridae family, are the most significant arboviral diseases in humans in terms of geographic spread, morbidity, and mortality. Currently, around 2.5 billion people are at risk of contracting dengue, marking a fourfold increase in the global burden of the disease over the past 30 years [1]. Annually, over 100 countries report an estimated 99 million symptomatic cases (with a 95% credible interval of 71-137 million) and 404 million asymptomatic infections (95%



inotrope administration, and the length of hospital stay.

II. MATERIALS AND METHODS

After receiving approval from the ethics committee, a prospective observational study was conducted among inpatients admitted to the General Medicine Department at Hitech Medical College and Hospital in Bhubaneswar. The study spanned a period of 9 months. Written informed consent was obtained from each participant, and the inclusion criteria were as follows: adult patients meeting the WHO criteria for dengue fever (DF), dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS), and those presenting within five days of fever onset. Patients who agreed to participate were excluded if they had hyperlactatemia caused by conditions other than sepsis, including ethanol poisoning, aluminum phosphate poisoning, cardiogenic shock, hemorrhagic shock, diabetic ketoacidosis (DKA), trauma, burns, seizures, or mixed infections. The sample size was calculated based on the dengue fever prevalence in Bhubaneswar between 2018 and 2024, which was recorded at 16.6%. Using the formula $N = z^2 \alpha / 2pq / I^2$, where P is the dengue fever proportion in Bhubaneswar, Q is (p-1), and L represents the allowable error (6%), the calculated sample size was 154.

Confirmed dengue fever patients were admitted to the medical wards, where venous lactate levels were measured using the ABL 800 analyzer at baseline, and on days three and five of

hospitalization. Each patient underwent routine examinations, including a complete blood count (CBC), liver function tests (LFT), renal function tests (RFT), lipid profile, chest X-ray, and abdominal ultrasound (USG). All patient data were recorded using a structured clinical proforma, capturing details such as the presenting complaints, disease history, and personal information. Demographic data including age, gender, occupation, religion, and other relevant factors were also collected. A general physical examination was performed, assessing parameters like temperature, pallor, icterus, respiratory rate, pulse rate, and blood pressure.

Throughout the hospital stay, patients were monitored for the number of platelet transfusions received, the volume of intravenous fluids administered daily, and the need for ventilator or inotrope support from admission to discharge. Data were collected and entered into an MS Excel spreadsheet. Descriptive statistics were analyzed using frequencies and percentages, while quantitative data were presented as means with standard deviations. Comparisons between groups were made using an unpaired t-test.

III. RESULTS

The demographic characteristics of the 154 cases are summarized in Table 1. A majority of the patients, 83 (53.90%), were under 30 years of age. Among the total cases, 96 (62.34%) were male. Nearly half of the patients (47.4%) had a fever duration of 2 to 3 days.

Variables	Patients (%)
Age in years	
< 30	83 (53.9%)
31-45	40 (25.97%)
46-60	24 (15.58%)
>60	7 (4.55%)
Gender	
Male	96 (62.34%)
Female	58 (37.66%)
Duration of fever in days	
One	12 (7.79%)
Two	39 (25.32%)
Three	34 (22.08%)
Four	36 (23.38%)
Five	33 (21.43%)

Table 1: Demographic variables of dengue cases in the study participants.

Table 2 presents the serological findings for the cases. Of the 154 patients, 66 (42.66%) exhibited elevated LDH levels, 57 (37.01%) had elevated creatine kinase levels, and 58 (37.66%) showed low total cholesterol. Additionally, 72 (46.75%) patients had low levels of high-density

lipoprotein (HDL), 44 (28.57%) had low triglyceride levels, 82 (53.25%) had elevated SGOT levels, 78 (50.65%) had elevated SGPT levels, and 63 (40.91%) had low serum albumin levels.



Variables	Patients (%)
Lactate dehydrogenase	
High	66 (42.86%)
Normal	88 (57.14%)
Creatinine kinase	
High	57 (37.01%)
Normal	97 (62.99%)
Total cholesterol	
Low	58 (37.66%)
Normal	96 (62.34%)
High density lipoprotein	
Low	72 (46.75%)
Normal	82 (53.25%)
Triglycerides	
Low	44 (28.57%)
Normal	110 (71.43%)
SGOT	
High	82 (53.25%)
Normal	72 (46.75%)
SGPT	
High	78 (50.65%)
Normal	76 (49.35%)
Serum albumin	
Low	63 (40.91%)
Normal	91 (59.09%)

Table 2: Serological variables of dengue cases in the study participants.

Table 3 illustrates that 39 (25.32%) of the cases had severe dengue, 79 (51.30%) experienced complications, 56 (36.36%) required blood

transfusions, 22 (14.29%) patients died, and 11 (7.14%) cases had encephalitis.

Variables	Patients (%)
Type of dengue	
Without warning signs (DNWS)	66 (42.86%)
With warning signs (DWWS)	49 (31.82%)
Severe dengue (SD)	39 (25.32%)
Complications	
Present	79 (51.3%)
Absent	75 (48.7%)
Blood transfusion	
Yes	56 (36.36%)
No	98 (63.64%)
Death	
Yes	22 (14.29%)
No	132 (85.71%)
Death (n=22)	
Encephalitis	11 (7.14%)
Severe bleeding	9 (5.84%)
Respiratory failure	2 (1.3%)

Table 3: Clinical variables of dengue cases in the study participants.

Table 4 presents the comparison of clinical variables with dengue severity. The mean age of patients without severe dengue was 26.27 years (SD = 12.96), while the mean age of those

with severe dengue was 33 years (SD = 20.71). A comparison of age between the two groups revealed a p-value of 0.203, which was not statistically significant.



Type of dengue	DNWS (n=66)	DWWS (n=49)	Severe Dengue (n=39)	P Value
Age	26.27 ± 12.96	30.19 ± 13.52	33 ± 20.71	0.203
Lactate dehydrogenase	148.45 ± 11.81	219.32 ± 30.74	388.23 ± 99.47	<0.001
Creatinine kinase	169.22 ± 22.17	233.48 ± 64.3	403.66 ± 61.57	<0.001
Total cholesterol	178.02 ± 9.04	157.35 ± 28.64	96.19 ± 9.3	<0.001
High density lipoprotein	46.08 ± 5.44	39.06 ± 6.4	31 ± 4.2	<0.001
Triglycerides	142.18 ± 13.71	132.25 ± 25.95	94.66 ± 7.93	<0.001
SGOT	31.12 ± 5.58	72.38 ± 23.4	137.95 ± 51.66	<0.001
SGPT	31.08 ± 5.94	75.16 ± 28.42	135 ± 50.57	<0.001
Serum albumin	4.55 ± 0.48	3.55 ± 0.46	3.02 ± 0.28	<0.001

DNWS - Dengue without warning signs; DWWS - Dengue with warning signs

Table 4: Comparison of clinical variables with severity of dengue.

The comparison of serum lactate dehydrogenase (LDH) levels with dengue severity showed a mean LDH level of 148.45 (SD = 11.81) in patients without severe dengue, compared to 388.23 (SD = 99.47) in those with severe dengue. This difference had a p-value of 0.001, indicating statistical significance. Regarding serum creatine kinase (CK), the mean CK level for non-severe dengue was 169.60 (SD = 22.70), whereas for severe dengue, it was 403.66 (SD = 61.57). The p-value for this comparison was 0.001, which was statistically significant. When comparing serum total cholesterol, the mean for non-severe dengue was 178.02 (SD = 9.04), while it was 96.19 (SD = 9.03) for severe dengue. The p-value for this comparison was also 0.001, showing statistical significance. For high-density lipoprotein (HDL), the mean for non-severe dengue was 46.08 (SD = 5.44), and for severe dengue, it was 31 (SD = 4.2),

with a p-value of 0.001, indicating statistical significance. In the case of serum triglycerides, the mean for non-severe dengue was 142.18 (SD = 13.71), while in severe dengue, it was 94.66 (SD = 7.93). The p-value for this comparison was 0.001, showing statistical significance. For SGOT, the mean for non-severe dengue was 31.12 (SD = 5.58), compared to 137.95 (SD = 51.56) in severe dengue, with a p-value of 0.001, indicating statistical significance. Similarly, for SGPT, the mean for non-severe dengue was 31.08 (SD = 5.94), while for severe dengue, it was 135 (SD = 50.57), with a p-value of 0.001, which was statistically significant. Finally, for serum albumin, the mean level for non-severe dengue was 4.55 (SD = 0.48), while for severe dengue, it was 3.02 (SD = 0.28). The comparison revealed a p-value of 0.001, indicating statistical significance.

Table 5 shows a significant association between the severity of dengue and complications, the need for blood transfusion, and mortality across all cases.

Study Variables	DNWS (n=66)	DWWS (n=49)	Severe Dengue (n=39)	P Value
Gender				
Male	45 (68.18%)	31 (63.27%)	20 (51.28%)	0.181
Female	21 (31.82%)	18 (36.73%)	19 (48.72%)	
Duration of fever in days				
One	11 (16.67%)	1 (2.04%)	0 (0%)	0.614
Two	16 (24.24%)	14 (28.57%)	9 (23.08%)	
Three	16 (24.24%)	8 (16.33%)	10 (25.64%)	
Four	16 (24.24%)	9 (18.37%)	11 (28.21%)	
Five	7 (10.61%)	17 (34.69%)	9 (23.08%)	
Complications				
Present	0 (0%)	40 (81.63%)	39 (100%)	0.001
Absent	66 (100%)	9 (18.37%)	0 (0%)	
Blood transfusion				
Yes	0 (0%)	34 (69.39%)	22 (56.41%)	0.001
No	66 (100%)	15 (30.61%)	17 (43.59%)	
Death				
Yes	0 (0%)	0 (0%)	22 (56.41%)	0.001
No	66 (100%)	49 (100%)	17 (43.59%)	

DNWS - Dengue without warning signs; DWWS - Dengue with warning signs

Table 5: Association between clinical variables with dengue warning signs.



IV. DISCUSSION

Dengue fever, one of the most significant arboviral infections, has emerged as a major global public health threat. It is the most prominent tropical infectious disease, with outbreaks occurring more frequently in countries like India. An increase in the frequency of epidemics and the involvement of younger age groups are indicative of a rising prevalence of infection. While most cases of dengue are mild, a small percentage can progress to dengue hemorrhagic fever (DHF), a much more severe form of the illness compared to the classic acute febrile dengue fever. Early detection and proper management are essential to reduce mortality from this life-threatening disease.

In a study by Sirikutt P et al., 253 patients were enrolled, including 28 non-dengue cases, 120 with dengue fever (DF), 75 with dengue hemorrhagic fever (DHF), and 30 with dengue shock syndrome (DSS). The study showed that aspartate aminotransferase (AST) levels were significantly elevated in dengue patients (94.9%) compared to non-dengue patients (68.6%), suggesting that the majority of dengue patients experienced liver dysfunction. Initially, dengue patients did not exhibit high serum lactate levels, whereas non-dengue patients did. However, in DSS patients, blood lactate levels increased towards the end of the feverish period, peaking at Day 0 (2.2 U/L), while the non-dengue group showed decreasing lactate levels. On Day 0, DSS patients had significantly higher mean blood lactate levels (2.26 U/L) compared to DF patients (1.63 U/L), DHF patients (1.79 U/L), and non-dengue patients (1.68 U/L), with a p-value of <0.05. Early in the disease, all patient groups had elevated serum lactate dehydrogenase (LDH) levels, but to varying extents. The mean LDH levels in DF, DHF, DSS, and non-dengue patients were 709.2 IU, 1,873 IU, 654.5 IU, and 434 IU, respectively. Dengue patients had LDH levels higher than 500 IU, compared to non-dengue patients. Only DHF and DSS patients demonstrated a significant increase in LDH levels toward the end of the febrile period, with mean levels of 1,060.7 IU in DHF, 1,180.7 IU in DSS, 787.2 IU in DF, and 423.8 IU in non-dengue patients [7].

Another study by Thanachartwet V et al. analyzed 153 hospitalized patients with confirmed dengue infections. Among them, 133 patients (86.3%) had non-severe dengue, including 7 patients (5.3%) with dengue without warning signs and 125 patients (94.7%) with dengue accompanied by warning signs. The remaining 21 patients (13.7%) had severe dengue, which included severe clinical bleeding (8 patients, 38.1%), severe organ

involvement (16 patients, 76.2%), and severe plasma leakage (16 patients, 76.2%). A stepwise multivariate logistic regression analysis identified several clinical factors independently associated with the development of severe dengue, including age over 40 years (odds ratio [OR]: 5.215, 95% confidence interval [CI]: 1.538–17.689), persistent vomiting (OR: 4.817, CI: 1.375–16.873), and the presence of more than 300 cells per L of absolute atypical lymphocytes (OR: 3.163, CI: 1.017–9.834). Additionally, elevated levels of lactate and atypical lymphocytes were found to be strongly associated with the severity of dengue ($p < 0.05$) [8].

This study had a few limitations, including a small sample size and a short follow-up period. Additionally, it was a single-center study, and only patients who were admitted to the hospital were included in the analysis.

V. CONCLUSION

The current study suggests that higher serum lactate levels at baseline are associated with an increased likelihood of dengue complications. It highlights the importance of monitoring serial lactate levels rather than relying on a single lactate measurement. Falling lactate levels over time were linked to a reduced risk of complications.

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