ORIGINAL ARTICLE

Serum Lactate as a Predictor of Severity in Dengue Infection

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ABSTRACT

Background Dengue infections caused by the four antigenically distinct dengue virus serotypes (DENV1, DENV2, DENV3, DENV4) of the family Flaviviridae are the most major arboviral diseases in humans in terms of geographic spread, morbidity, and mortality.

Objective: The study was conducted to assess serum lactate in cases of dengue and correlate it with severity in dengue infection.

Methodology: A prospective observational study was carried out among indoor patients admitted to the general medicine department of the tertiary care hospital SMIMER Surat. The study's duration was 15 to 18 months.

Result: our study found out of total 154 cases; majority of cases were belonged from 83(53.90%) cases were from less than 30 years. male was contributed 96 (62.34%), majority of cases had duration of fever 39(25.32%), 66 (42.66%) case had high LDH, comparison of serum lactate dehydrogenase with severity of dengue mean lactate dehydrogenase of dengue without severity was mean was 148.45 and SD 11.81, while in severe dengue mean serum lactate dehydrogenase 388.23 and SD 99.47 with p value 0.001 which was statically significant.

Conclusion According to this study, it is preferable to monitor serial lactate levels as opposed to using a single lactate number.

INTRODUCTION

In terms of geographic distribution, morbidity, and mortality, dengue infections brought on by the four antigenically different dengue virus serotypes (DENV1, DENV2, DENV3, DENV4) of the family Flaviviridae are the most significant arboviral diseases in humans. There are currently 2.5 billion people at risk of dengue, a fourfold rise in the disease's global burden over the past three decades. [1] Each year, more than 100 nations experience an estimated 99 million (95% credible interval 71-137 million) symptomatic and 404 million (95% credible interval 304-537 million) asymptomatic dengue infections, with 20 000 fatalities and 500 000 severe dengue cases. Aedes mosquitoes spread the virus from person to person. From a mild febrile illness known as "dengue fever" to "severe dengue," also known as dengue hemorrhagic fever (DHF), which is characterized by capillary leakage leading to hypovolemic shock, organ impairment, and bleeding complications, dengue virus infections can cause a wide clinical spectrum of disease. [2] Dengue is currently managed by prudent fluid replacement in severe cases because there are no antiviral medications or vaccines available.

There are 36 million dengue fever cases each year. Alt-

hough the precise prevalence is unknown, an estimated 2.1 million cases of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which account for 5–10% of all cases, are recorded each year. [3] Of the 36 million cases annually, 6% (2.1 million) will progress to DHF, which has a 1% case-fatality rate (21,000 deaths). [4] More than 100 nations, including those in Europe and the United States, are affected by dengue infection (USA). [5] The first virologically confirmed dengue fever outbreak in India occurred in Calcutta and the Eastern Coast of India in the years 1963–1964; the first instance of dengue-like sickness to be documented in India was in Madras in 1780. [6] To decrease mortality from dengue, it is essential to understand the warning signs and symptoms, changes in biochemical parameters, and multisystem involvement pattern.

The primary mechanism in DHF is plasma leakage. Plasma leakage typically happens when a fever decreases during the crucial phase and peaks five days after a fever begins [7] [8]. Because anaerobic metabolism takes over in shock or hypotension and results in an excess generation of lactate, lactate is a key indicator of tissue hypoperfusion. There have been several investigations on the relationship between venous lactate levels and the severity of dengue fever.

We wanted to investigate the relationship between venous lactate levels and numerous dengue complications, including the number of patients who require platelet transfusions, ventilator support, inotrope support, and length of hospital stay.

METHODOLOGY

After obtaining approval from the ethics council, a prospective observational study was carried out among indoor patients admitted to the general medicine department of the tertiary care hospital SMIMER Surat. The study's duration was 15 to 18 months. After obtaining written authorization from each case, we included any that met the following criteria. All adult patients who meet the WHO criteria for DF, DHF, and DSS diagnoses. All adult Dengue patients who arrived within five days of the fever's start. All adult patients who provide informed consent to participate in this study are not included if any of the following conditions apply. Patients with hyperlactatemia due to any cause other than sepsis, such as ethanol poisoning, aluminum phosphate poisoning, cardiogenic shock, hemorrhagic shock, DKA, trauma, burns, seizures, or mixed infection sample size was calculated by considering the proportion of dengue fever in Surat city between 2002-2016 and data recorded is 16.6%. The sample size was calculated using formula

$N = z^2_{\alpha/2}pq/l^2$, where P is proportion of dengue fever in Surat city; Q is (p-1); and L is Allowable error (6%). The calculated sample size was 154.

Dengue fever patients that have been confirmed have been admitted to these medical wards. After that, the

ABL 800 was used to test the venous lactate level at baseline, on days three and five of hospital admission. Each patient underwent all standard examinations, including CBC, LFT, RFT, Lipid profile, chest X-ray, and USG abdomen. All patient information was documented on a structured clinical proforma used for data collection. The main complaints, the history of the current disease, personal information, etc. were all noted. Age, gender, occupation, religion, and other demographic factors were collected. A general physical examination was performed to measure things like temperature, pallor, icterus, respiration rate, pulse rate, and blood pressure. the number of patients who received platelets each day, the amount of intravenous fluid administered each day, the number of patients who required ventilator support, and the number of patients who required inotropes from the time of admission through the time of discharge, patients were evaluated. Information was collected and recorded into an MS Excel spreadsheet. Descriptive statistics were then examined using frequency and percentages, while quantitative data were given as a mean and standard deviation and were then contrasted using an unpaired t test.

RESULT

Demographic profile of the 154 cases was shown in table 1. Majority of cases, 83 (53.90%) were less than 30 years old. Out of 154, 96 (62.34%) cases were male. Nearly half of the cases (47.4%) had duration of fever between 2 to 3 days.

Table 2 shows serological profile of the cases. Out of total 154 cases, 66 (42.66%) case had high LDH, 57 (37.01%) cases had high creatine kinase, 58 (37.66%) cases had low total cholesterol,72 (46.75%) cases had low high-density lipoprotein level, 44 (28.57%) case had low triglycerides level, 82 (53.25%) cases had high SGOT, 78 (50.65%) cases had high SGPT, and 63 (40.91%) cases had low serum albumin level.

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

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 2: Serological variables of dengue cases in the study participants

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 3: Clinical variables of dengue cases in the study participants

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 shows that 39 (25.32%) cases had severe dengue, 79 (51.30%) cases had complication, 56 (36.36%) cases needed blood transfusion, death occurred in 22 (14.29%), and 11 (7.14%) cases had encephalitis.

Table 4 show that comparison of clinical variables with severity of dengue, mean age of dengue without severity was mean age 26.27 years and SD 12.96 was of severe dengue was 33 years and SD 20.71, comparison of age with severity of dengue shows p value 0.203 which was statistically not significant.

Comparison of serum lactate dehydrogenase with severity of dengue mean lactate dehydrogenase of dengue without severity was mean was 148.45 and SD 11.81, while in severe dengue mean serum lactate dehydrogenase 388.23 and SD 99.47, compaction of both group shows p value 0.001 which was statically significant.

Comparison of serum creatinine kinase with severity of dengue mean creatinine kinase of dengue without severity was mean was 169.60 and SD 22.70, while in severe dengue mean serum creatinine kinase 403.66 and SD 61.57, compaction of both group shows p value 0.001 which was statically significant.

Comparison of serum total cholesterol with severity of dengue mean total cholesterol of dengue without severity was mean was 178.02 and SD 9.04, while in severe dengue mean serum total cholesterol 96.19 and SD 9.03, compaction of both group shows p value 0.001 which was statically significant.

Comparison of serum high density lipoprotein with severity of dengue mean high density lipoprotein of dengue without severity was mean was 46.08 and SD 5.44, while in severe dengue mean serum high density lipoprotein 31 and SD 4.2, compaction of both group shows p value 0.001 which was statically significant.

Comparison of serum triglycerides with severity of dengue mean triglycerides of dengue without severity mean was 142.18 and SD 13.71, while in severe dengue mean serum triglycerides 94.66 and SD 7.93, compaction of both group shows p value 0.001 which was statically significant.

Comparison of SGOT with severity of dengue mean SGOT of dengue without severity mean was 31.12 and SD 5.58, while in severe dengue mean serum tri SGOT 137.95 and SD 51.56, compaction of both group shows p value 0.001 which was statically significant.

Comparison of SGPT with severity of dengue mean SGPT of dengue without severity mean was 31.08 and SD 5.94, while in severe dengue mean serum tri SGPT 135 and SD 50.57, compaction of both group shows p value 0.001 which was statically significant.

Comparison of serum albumin with severity of dengue mean serum albumin of dengue without severity mean was 4.55 and SD 0.48, while in severe dengue mean serum albumin 3.02 and SD 0.28, compaction of both group shows p value 0.001 which was statically significant.

Table 5 shows that there was a significant association between dengue severity and complications, blood transfusion, and death in all cases.

Table 4: Comparison of clinical variables with severity of dengue

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 5: Association between clinical variables with dengue warning signs

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

DISCUSSION

The most significant human arboviral illness, dengue fever, has emerged as a serious global public health issue. The most significant tropical infectious illness in the world is this one. Epidemics are happening increasingly frequently in India. Younger age groups' involvement and an increase in epidemic frequency are signs of a higher prevalence of infection. A tiny percentage of dengue infections result in DHF, a more severe disease than classical dengue fever, which is an acute febrile sickness. To prevent this deadly disease from taking valuable lives, early detection and careful management are crucial.

As per Sirikutt P et al study there were 253 patients enrolled, including 28 non-dengue patients and 120 DF, 75 DH, 30 DSS patients. Aspartate aminotransferase (AST) levels were significantly higher in dengue patients (94.9%) than in non-dengue patients (68.6%), indicating that the majority of dengue patients had liver impairment. Patients with dengue did not initially have high serum lactate levels, although non-dengue patients did. In DSS patients, the mean blood lactate levels increased towards the end of the feverish period and peaked on Day 0 (2.2 U/L). On the other hand, it was discovered that the non-dengue group's serum lactate levels were falling. DSS patients had higher mean blood lactate levels on Day 0 (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) (p 0.05). In the early stages of the disease, mean serum LDH levels were raised in all patient groups, but at varying amounts. In DF, 1,873 DHF, 654.5 DSS, and 434 IU in non-dengue patients, the mean serum LDH levels were 709.2, 1,873, and 705 respectively. In contrast to non-dengue patients, those with dengue had mean LDH levels > 500 IU. Only DHF and DSS patients showed increased mean LDH levels towards the end of the febrile episode; DF and non-dengue patients did not. In DHF, DSS, DF, and non-dengue patients, the mean LDH levels on Day 0 were 1,060.7, 1,180.7, 787.2, and 423.8 IU, respectively. [7]

As per Thanachartwet V et al study one hundred and thirty-three (86.3%) of the 153 hospitalized patients with confirmed dengue virus infections had non-severe den-

gue, including dengue without warning signals in seven patients (5.3%) and dengue with warning signs in 125 patients (94.7%). The remaining individuals (21, 13.7%) all had severe dengue, including severe clinical bleeding (8, 38.1%), severe organ involvement (16, 76.2%), and severe plasma leakage (16, 76.2%). Stepwise multivariate logistic regression was used to identify the clinical factors that were independently associated with the development of severe dengue, including age >40 (odds ratio [OR]: 5.215, 95% confidence interval [CI]: 1.538-17.689), persistent vomiting (OR: 4.817, CI: 1.375-16.873), the presence of >300 cells per L of absolute atypical lymphocytes (OR: 3.163, CI: 1.017-9.834), (OR: 7.340, CI: 2.334-23.087). Furthermore, elevated levels of lactate and absolute atypical lymphocytes were associated with severe dengue (p 0.05). [8]

LIMITATIONS OF THE STUDY

There were few shortcomings in this study including the small sample size and short follow up, it was single centre study. Only admitted patients were included in the study.

CONCLUSION

According to the current study, dengue complications were more likely when serum lactate levels were high at baseline. According to this study, it is preferable to mon-itor serial lactate levels as opposed to using a single lactate number. Serial lactate levels that were falling were linked to less complications.

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