



HOSPITAL BASED STUDY OF CLINICAL SEVERITY AND ITS RELATIONSHIP WITH BIOCHEMICAL MARKERS IN DENGUE PATIENTS

General Medicine

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ABSTRACT

Background: Dengue fever is an acute febrile infectious disease in subtropical and tropical areas transmitted by *Aedes aegypti* mosquitoes. Early prediction of severity helps in reducing complications and mortality.

Objectives: To determine the prognostic efficacy of biochemical markers i.e. S. lactate and LDH in predicting severity of dengue.

Methodology: Tertiary hospital based observational test study during Dec 2015 to May 2017 where 150 patients above 18 years of age with Dengue fever were included.

Results: As per severity of Dengue, two third of the cases (66.7%) were of dengue fever while 27.3% and 6% were of dengue hemorrhagic fever and dengue shock syndrome (severe dengue) respectively.

KEYWORDS

Dengue Fever(DF), Lactate, LDH

INTRODUCTION:

Dengue fever is an acute febrile infectious disease in subtropical and tropical areas that is progressively making its way from being "one of the great neglected diseases of mankind"¹. In the last 50 years, incidence of dengue has increased 30-fold with increasing geographic expansion to new countries and from urban to rural settings. An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries².

The clinical manifestations of dengue vary with the age and immunity of the patient. It can present as 1) In apparent infection 2) non-specific febrile illness, 3) classic dengue fever (DF), 4) dengue hemorrhagic fever (DHF), 5) Dengue shock syndrome (DSS) and 6) encephalopathy and fulminant liver failure³. Early identification of patients at risk of developing severe dengue is critical to provide timely supportive care, which can reduce the risk of mortality to < 1%. There is evidence suggesting an early association of elevated levels of S. lactate and lactate dehydrogenase (LDH) with dengue complications. Severe dengue hemorrhagic fever (DHF) patients also develop shock and experience a certain degree of hepatic injury, implicating that serum lactate and LDH may be elevated in Dengue shock syndrome (DSS)⁴.

The present study aims at studying the clinical severity in dengue patients and to determine the correlation of biochemical markers i.e. S. lactate and LDH in predicting severity of dengue.

METHODS:

This hospital based observational study was carried out in department of General medicine for the period of 18 months. The purpose of this study was explained to patients, and they were included in the present study only on their willingness.

The present study involved adult patients with acute febrile disease diagnosed as positive dengue (NSI, IgM, or positive IgG) or dengue-hemorrhagic fever and dengue-shock syndrome cases. The present study excluded positive cases of malaria, typhoid or any other infectious fever.

Detailed patient history was elicited at the time of admission from the patient or relatives or those who accompanied the patient. History included age, sex, fever, retro-orbital pain, headache, arthralgia, bodyache, nausea and vomiting, abdominal pain, respiratory symptoms, rash, hemorrhagic manifestations, altered sensorium and convulsion.

All patients were subjected to Routine laboratory tests (as part of the standard hospital protocol), S. LDH and S. Lactate. The final outcome after management at the end of 1 week was noted as: survived, died or LAMA (leave against medical advice). All the data was recorded on a pre-structured proforma.

RESULTS:

Table 1. Distribution of study subjects as per Age group

Age group (yrs)	N	%
<20 yrs	16	10.7%
21-30 yrs	44	29.3%
31-40 yrs	24	16.0%
41-50 yrs	37	24.7%
> 50 yrs	29	19.3%
Total	150	100.0%
Mean age - 30.32 +/- 11.16 years		

Mean age of the study cases was 30.3 years with over half of them were between 18-40 years of age. Male predominance was seen in study cases with 59.3% males to 40.7% females.

Table 2. Distribution of study subjects as per severity of Dengue infection

Severity of Infection	N	%
DF	100	66.7%
DHF	41	27.3%
DSS	9	6.0%
Total	150	100.0%

As per severity of Dengue, two third of the cases (66.7%) were of dengue fever while 27.3% and 6% were of dengue hemorrhagic fever and dengue shock syndrome (severe dengue) respectively.

Table 3. Clinical manifestations as per severity of Dengue infection

Clinical Manifestations	DF (n-100)		DHF (n-41)		DSS (n-9)		Total
Fever	100	100.0%	41	100.0%	9	100.0%	150
Nausea and vomiting	49	49.0%	35	85.4%	7	77.8%	91
Headache	36	36.0%	33	80.5%	9	100.0%	78
Body ache	21	21.0%	39	95.1%	9	100.0%	69
Abdominal pain	21	21.0%	17	41.5%	7	77.8%	45
Retro orbital pain	19	19.0%	16	39.0%	9	100.0%	44
Hepatomegaly	15	15.0%	17	41.5%	9	100.0%	41
Hemorrhagic manifestations	0	0.0%	41	100.0%	9	100.0%	50
Arthralgia	16	16.0%	13	31.7%	9	100.0%	38
Rash	3	3.0%	25	61.0%	5	55.6%	33
Conjunctival congestion	14	14.0%	13	31.7%	6	66.7%	33
Respiratory symptoms	7	7.0%	18	43.9%	4	44.4%	29
Decreased urine output	0	0.0%	15	36.6%	7	77.8%	22

Splenomegaly	2	2.0%	9	22.0%	6	66.7%	17
Convulsion	0	0.0%	0	0.0%	7	77.8%	7
Altered sensorium	0	0.0%	0	0.0%	6	66.7%	6

Mortality rate observed in present study was 2.7% with all of them had Dengue shock syndrome and developed DIC.

Table 4. Association of severity of Dengue infection with Biochemical Parameters

Variables	Group	N	Mean	SD	p- value
LDH Levels (U/L)	DF	100	313.21	78.21	<0.01
	DHF/ DSS	50	612.70	84.33	
Lactate Levels (U/L)	DF	100	1.62	0.59	<0.05
	DHF/ DSS	50	2.51	0.92	

Among biochemical parameters, mean LDH levels (612 U/L vs 313 U/L) and Lactate levels (2.51 U/L vs 1.62 U/L) were significantly higher in cases with severe dengue ($p < 0.05$).

Table 5. Association of severity of Dengue infection with LDH Levels

LDH Levels (U/L)	Group		Total
	DF	DHF/ DSS	
< 600	94	15	109
	94.0%	30.0%	77.9%
≥ 600	6	35	41
	6.0%	70.0%	29.3%
Total	100	50	150
	100.0%	100.0%	100.0%
p- value - 1.0			

Among 50 cases with severe dengue, 35 had LDH levels above 600 U/L (70%) as compared to only 6 out of total 100 cases of dengue fever. The sensitivity and specificity of LDH to predict severity of dengue infection at this cut-off is 70% and 94% respectively with overall diagnostic accuracy of 86%.

Table 6. Association of severity of Dengue infection with Lactate Levels

Lactate Levels (U/L)	Group		Total
	DF	DHF/ DSS	
< 2	84	19	103
	84.0%	38.0%	73.6%
≥ 2	16	31	47
	16.0%	62.0%	33.6%
Total	100	50	150
	100.0%	100.0%	100.0%
p- value - 1.0			

Among 50 cases with severe dengue, 31 had lactate levels above 2.0 U/L (62%) as compared to only 16 out of total 100 cases of dengue fever. The sensitivity and specificity of Lactate to predict severity of dengue infection at this cut-off is 62% and 84% respectively with overall diagnostic accuracy of 76.7%.

DISCUSSION:

• DEMOGRAPHY

Mean age of the study cases was 30.3 years with over half of them were between 18-40 years of age.

STUDY	Male	Female
Our study	59.3%	40.7%
Perveen S et al ⁵	66.1%	33.9%
Laul et al ⁶	57%	43%
Gandhi K et al ⁷	63%	37%

These findings showed that dengue fever affects younger population with relatively higher incidence in males. This can be attributed to more involvement of younger population especially males in outdoor activities as compared to females

• SEVERITY OF DENGUE

STUDY	Dengue fever	DHF	DSS
Our study	66.7%	27.3%	6%
Perveen S et al ⁵	61.3%	39.7%	-
Narayanan M et al ⁸	72.8%	18.8%	8.4%
Bhatt et al ⁹	67%	39%	4%

• CLINICAL PRESENTATION

Most common symptom in each group was fever followed by nausea/ vomiting in dengue cases and headache/ body ache in severe dengue cases. Fever is the most common presenting complaint in cases of dengue fever associated with body ache/ headache as reported by previous studies.

Hemorrhagic manifestations were seen in 27.3% cases overall which is exclusively associated with severe dengue. Similar results were observed by Laul et al.⁶ and Bhatt N et al.⁹ where bleeding manifestations were found in 21% and 34.6% of the cases respectively.

• MORTALITY

Most deaths from dengue occur in patients with profound shock, particularly if the situation is complicated by fluid overload. In present study too, mortality rate of 2.7% was observed with all the mortality was associated with cases of dengue shock syndrome.

• PROGNOSTIC MARKERS

LDH & Lactate

In present study, mean LDH (612 U/L vs 313 U/L) and lactate levels (2.51 U/L vs 1.62 U/L) were significantly higher in cases with severe dengue i.e. DHF & DSS cases ($p < 0.05$). Mean LDH levels were also significantly higher in cases with DSS as compared to DHF cases (659.2 U/L vs 526.3 U/L; $p < 0.05$). In the study by Perveen S et al.⁵, LDH levels were higher in patients with DHF (mean 618.38 U/L ± 219) as compared to the patients with dengue fever (mean 316.45 U/L ± 104). Authors concluded that High LDH (> 600 U/L) can be used to predict outcome in dengue patients.

Sirikutt P et al.¹⁰ in their study observed the mean serum lactate levels on Day 0 to be higher in DSS patients (2.26 U/L) as compared to DF patients (1.63 U/L; $p < 0.05$). Their study concluded that Lactate may be used as a predictor of severe dengue if the level is > 2 U/L on Day 0, similarly LDH can also be used to differentiate patients with or without dengue in the early febrile phase, if the level is > 500 IU.

It was observed that an early increase in LDH (three times the normal value) is an independent predictor of DHF. Various studies show that Lactate & LDH levels are higher in DHF and DSS patients.

CONCLUSION:

The present study confirms the prognostic importance of novel markers like S. LDH and lactate levels. Both serum lactate and LDH levels were found to be elevated in DHF and DSS patients as compared to dengue fever cases. A cut off value of more than 600 U/L for LDH and more than 2 U/L for Lactate was observed to have good diagnostic accuracy in prediction of severe dengue infection.

The prediction of dengue severity through these markers can help clinicians in controlling disease and reduction in morbidity and mortality caused by this disease.

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