

Study of Liver and Renal Dysfunction in Hospitalised Dengue Patients in a Tertiary Health Care Facility of Odisha

Ganeswar Sethy¹, Abinash Swain², Abinash Panda³, Geetanjali Sethy⁴

^{1,2} Department of Medicine, MKCG Medical College & Hospital, Berhampur, Odisha, India.

³Department of Pharmacology, MKCG Medical College, Berhampur, Odisha, India.

⁴Department of Paediatrics, PRM Medical College, Baripada, Odisha, India.

ABSTRACT

BACKGROUND

Dengue is an acute viral haemorrhagic fever with large number of fatalities worldwide. According to WHO, 50 - 100 million infections occur annually, out of which 5 lakhs are dengue haemorrhagic fever. India is no way better like any other tropical country. Southern part of Odisha shows high prevalence of dengue cases which are referred to MKCG Medical College, Berhampur. Dengue is a vector borne disease, which is of much epidemiological importance throughout India. No clinical study has been undertaken in recent past on this disease as regard to clinical parameter, course and outcome. Hence, it was decided to carry out a study to assess the epidemiological profile of dengue patients, the prevalence and pattern of liver and kidney dysfunction and outcome of hospitalized patients in MKCG Medical College and Hospital.

METHODS

This cross-sectional study was carried out on laboratory confirmed dengue patients admitted to hospital in Department of Medicine, MKCG Medical College & Hospital, Berhampur from January 2018 to December 2018.

RESULTS

More number of patients (58 %) were male and from rural area (72 %). Alanine aminotransferase (ALT) and aspartate aminotransaminase (AST) were elevated in 68 % of cases to more than 3 times of normal. Mortality is 4 % among the admitted patient. More death observed with high international normalized ratio (INR) value.

CONCLUSIONS

Mortality is high in patients of dengue with deranged liver function and kidney function. Early screening of dengue patients by clinical and laboratory parameter will help clinicians to predict mortality for dengue cases. Dengue cases with liver and kidney dysfunction need aggressive monitoring and appropriate management to prevent complications and death.

KEYWORDS

Severe Dengue, Early Parameters, AST / ALT, Outcome, Mortality

Corresponding Author:

Dr. Geetanjali Sethy,

Professor & HOD,

Department of Paediatrics,

QR No- 4R/402, Staff Quarters 3,

PRM MCH, Baripada, Mayurbhanj,

Odisha, India.

E-mail: geetanjalisethy@gmail.com

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BACKGROUND

Dengue is an acute febrile disease of viral aetiology. The etiologic agent belongs to the flaviviridae family and genus flavivirus. The viruses of this family are Arbo viruses (RNA virus) and are transmitted by *Aedes mosquito*.¹ Approximately 2.5 billion people (40 % of the world's population) live in urban areas of tropical and subtropical regions with risk of acquiring dengue infection. The world health organization (WHO) estimates that 50 - 100 million infections occur annually out of which 5 lakhs are dengue haemorrhagic fever. This accounts for 22,000 paediatric deaths. Among 100 endemic countries, most cases are reported from South-East Asia and the western Pacific regions (WHO 2013). Dengue is one of the major re-emerging viral infections. In recent years, dengue has become a major global public health concern. Approximately 2.5 billion people (40 % of the world's population), living mainly in urban areas of tropical and subtropical regions, are estimated to be at risk of acquiring dengue infection.

The WHO estimates that 50 - 100 million infections occur yearly including 5 lakhs DHF cases and 22,000 deaths, mostly among children. While dengue is endemic in more than 100 countries, most cases are reported from South-East Asia and the western Pacific regions (WHO 2013). The resurgence of dengue has been observed in India. Dengue outbreaks have been frequently reported from different parts of the country in both urban and rural populations.² The various manifestations of dengue may not have a distinct line of demarcation. Apart from the classic features, reports of rare presentations have recently become more frequent.³ In Odisha, increasing number of cases are reported since 2010. Several outbreaks have been reported from various parts of the state but mainly from the coastal districts. Eighty percent of people infected with dengue virus are asymptomatic: Five percent proceed to severe illness and in some it is life-threatening.⁴ Dengue haemorrhagic fever and dengue shock syndrome are associated with high mortality up to 20 %.⁵ The disease affects various organ of body including liver, haematological system, respiratory system, brain, kidney etc. It causes liver dysfunction including a preferential rise of SGOT, hepato-splenomegaly, ascites, pleural effusion and leucopenia. Liver injury is nearly universal in adult dengue patients. It is a sign of bad prognosis in dengue patients. Hepatic involvement in dengue can be a major contributing factor in morbidity and mortality of dengue patients. Acute kidney injury is one of the least studied complication of dengue. There is no data on hepatic & renal involvement in adult dengue patients, so it is a priority area of research to know the prevalence as well as pattern of liver & kidney involvement in dengue patients. As a large number of patients from southern Odisha come to this referral center, it was decided to carry out the study with following objectives.

Objectives

1. To observe the epidemiological profile of admitted dengue patients.

2. To estimate the prevalence and pattern of liver and kidney dysfunction and outcome of hospitalized dengue patients.

METHODS

It is a hospital based cross sectional study carried out using convenient sampling method. Hundred dengue patients admitted in dengue ward or other wards of Medicine Department of MKCG Medical College were observed during a period of 1 year from January 2018 to December 2018. Institutional ethics committee (IEC number 459) approved the study.

Patients admitted to medicine ward with history of acute onset of fever were identified. Consent was taken from all subjects before enrolment into the study. Patients coming from area of high dengue prevalence were the study subjects. Convenient sampling method was adapted. A detailed history was taken & clinical examination was done in all cases. Patient particulars including age, gender, detailed address, presenting complaint were recorded in a prescribed proforma. All cases were subjected to thorough clinical examination including sensorium, temperature, pulse, blood pressure, oxygen saturation, respiration and urine output. Detailed physical examination was also carried out and noted in the proforma. Sick and hemodynamically unstable patients were stabilized before enrolment. All clinically suspected dengue cases were subjected to various laboratory investigations like complete blood count, with differential count, reticulocyte count, comment on peripheral smear, slide for malaria parasite and immunochromatographic test for malaria was done to exclude malaria infection. Liver function test (LFT), renal function test (RFT), NS1 antigen and/or dengue IgM antibody was done in all cases. All laboratory confirmed cases were enrolled into the study. Those patients who had a mild degree of infection not requiring hospitalization were excluded from the study. Patients with confirmed dengue & requiring hospitalization were shifted to dengue ward and observed for any evolving signs of severity. As per WHO 2009 dengue guidelines, Severe dengue is defined as evidence of severe plasma leakage (shock (DSS) or Fluid accumulation with respiratory distress) and/or severe bleeding and/or severe organ involvement as evaluated by clinician [Liver: AST/ALT CNS: Impaired consciousness, heart & other organs]

Inclusion Criteria

1. All clinically suspected & laboratory confirmed dengue cases between age group 15 - 65 years.

Exclusion Criteria

1. Patients with fever due to other infections like malaria, enteric fever.
2. Alcoholic liver disease and/or chronic kidney/liver disease were excluded.

Statistical Analysis

All the data was analysed by statistical package for social sciences (SPSS) 20.0 statistical software. Non-random association between categorical variables like LFT (AST/ALT) & PT-INR was determined by Fisher’s exact test.

RESULTS

Majority of the patients were above 45 - years of age (38 %). Males were 58 in number (58 %) and maximum were from rural area (72 %). About 64 % of the patients were without BPL card (Table 1). 68 (68 %) and 51 (51 %) of patients had abnormal AST and ALT respectively at the time of hospitalization. 69 cases (69 %) have either AST or ALT elevation. Eighteen (18) cases had elevated creatinine at presentation. Sixteen (16) cases had elevated PT INR at the time of presentation. (Table 3)

AST and ALT elevation has a linear relation among themselves. Patients having high AST also have high ALT value and vice versa. (Figure 1) The mean AST levels of the study participants was 125.79 ± 52 whereas the mean ALT levels were 124.88 ± 59.96 . Median ALT value was 137 with maximum and minimum value being 309 and 19 respectively. Likewise, median AST value was 118.5. Maximum AST value was 340 and minimum value is 18. Creatinine levels showed a mean of 1.034 ± 0.38 . Median creatinine value being 1 with maximum and minimum value of 4.2 and 0.5 respectively. Mean PT INR was 1.036 ± 0.248 . Median PT INR elevation was 1.0 with maximum and minimum being 1.9 and 0.9 respectively (Table 2).

LFT was repeated after 48 hours in those who had abnormal LFT at the beginning. Persistent abnormal LFT is associated with higher mortality in this study (table 4). Both abnormal LFT & abnormal INR were associated with disease severity and mortality (P value < 0.0001) [table 5].

This proves the hypothesis that there is a significant association between liver function as depicted by Serum AST/ALT and PT INR values and the disease severity as well as mortality in hospitalized dengue patients. (null hypothesis

that there are no such association stands rejected). Those who recovered clinically showed improved liver function, which is statistically significant. There is a linear relation between hepatic dysfunction and abnormal INR. (Figure 2) Out of 69 cases with abnormal LFT, one case (1.4 %) died whereas out of 59 new cases of abnormal LFT, 1 case (2 %) died. (Table 4) The mortality with abnormal creatinine level and abnormal PT INR was 5.5 % and 6.2 % respectively.

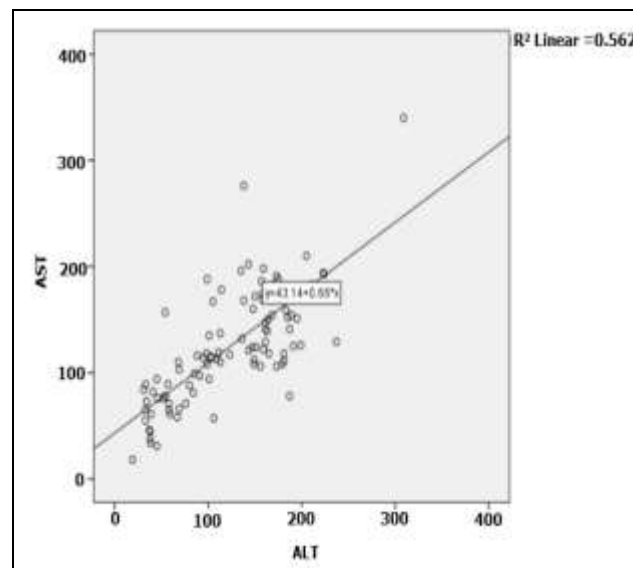


Figure 1. Correlation of AST and ALT Levels

DISCUSSION

This prospective study was conducted to assess the prevalence and pattern of liver and kidney dysfunction as well as overall outcome of hospitalized dengue patients in MKCG Medical College and Hospital.

The study showed that the mean AST and ALT was $125.79 + / - 5.2$ and $124.4 + / - 5.4$ respectively. AST was found to be elevated more than three times of upper limit of normal in 68 % of patients.

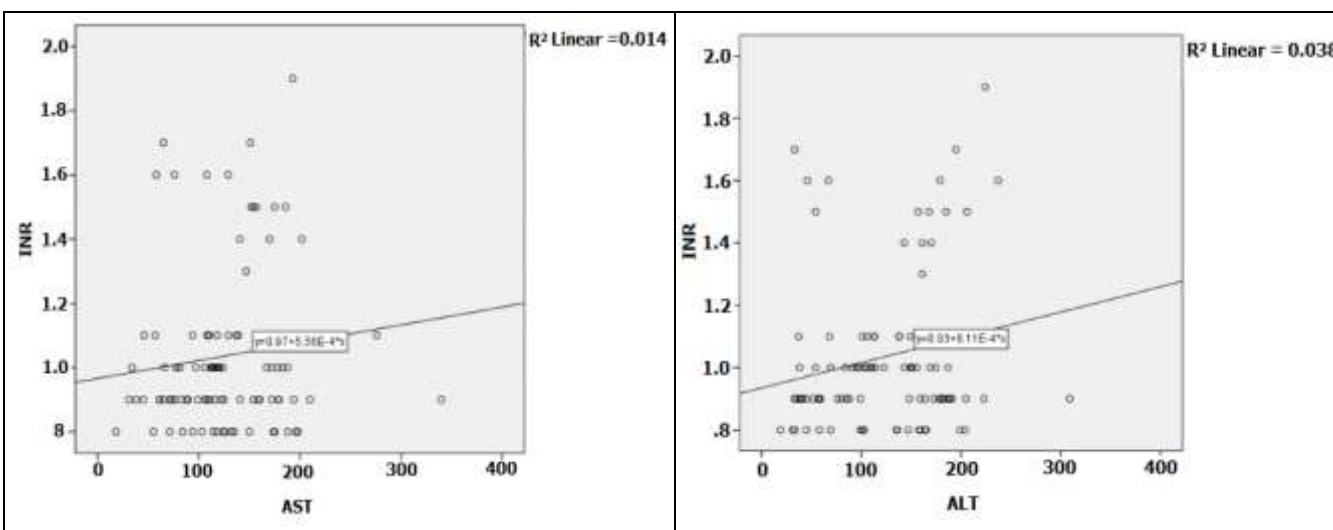


Figure 2. Correlation of AST and ALT Levels with INR

Similarly, ALT was elevated, more three times of upper limit normal in 51 % of patients. Either AST or ALT is elevated in 69 % of patients. At the same time, both AST and ALT are elevated in 50 % of cases. This type of AST and ALT elevation has been reported in several other studies. A similar type of study among 1585 dengue patients, conducted by Souza et al.⁶ published in Brazilian journal of infectious disease in 2004. In this study, Souza et al.⁶ found that AST and ALT were elevated in 63.4 % and 45 % respectively. Another study by Saha et al.⁷ in 2012 showed that 52 % of patients had elevated AST and 50 % of patients had raised ALT.

	Profile	No.	%
Age	< 15	25	25
	15 - 45	37	37
	> 45	38	38
Sex	Male	58	58
	Female	42	42
Residence	Rural	72	72
	Urban	28	28
SES	With BPL	46	46
	Without BPL	64	64

Table 1. Socio Demographic Profile of the Study Population

Parameter	Mean	Median	SD	Minimum	Maximum
AST	125.79	118.5	52	18	340
ALT	124.88	137	59.96	19	309
Creatinine	1.034	1.0	0.38	0.5	4.2
PT INR	1.036	1.0	.248	0.8	1.9

Table 2. Liver Dysfunction and Serum Creatinine in the Study Population

Elevation of Parameter	%
AST	68
ALT	51
Creatinine	18
INR	16
LFT	69

Table 3. Abnormal Parameter Detected (Percentage)

Abnormality	No. of Cases	No. of Deaths	%
LFT	69	1	1.4
LFT New	51	1	2
Creatinine	18	1	5.5
INR	16	1	6.2

Table 4. Mortality Profile of Patients with Various Lab Abnormalities

	Survived (%)	Death (%)	P Value (Fischer's Exact Test)
Abnormal LFT	86	16	< 0.0001
Elevated PT-INR	31	69	< 0.0001

Table 5. LFT & PT-INR Levels in Patients at Admission and Mortality

Patients with elevated AST who also had high ALT values showed a linear relation. Mortality rate is 1.4 % among patients with hepatic dysfunction with either AST or ALT or both elevated and 2 % among patients with both AST and ALT elevation. Similar results were also detected by Soeksiam Tan et al.⁸ in the year 2012. Mean INR was found to be 0.958 ± 0.03 and elevated [> 1.1] in 16 % of patients. INR elevation has linear relation with hepatic dysfunction. About 16 % of patients with both AST and ALT elevated have INR elevation with a P value of 0.029. High INR value coincides with high liver enzyme value. Mortality is 6.2 % among patients with elevated INR.

High creatinine was observed in 18 % of patients in our study. It contributed to mortality in significant number of

cases. Similar results were found in a study-conducted by Khalil et al.⁹ in the year 2012. They found that the prevalence of AKI among dengue patients was 13.3 %. Another retrospective study conducted by T H Mallhi et al.¹⁰ in the year 2013, revealed that prevalence of AKI among dengue patients was 14 %. Mortality among patients with elevated creatinine in our study was 5.5 %.

CONCLUSIONS

Significant hepatic and renal dysfunction were found in almost all admitted dengue patients in this study. The elevations of AST, ALT & INR had a linear correlation with each other in all of these patients. Dengue patients showing abnormal LFT are classified under severe dengue. So, these tests must be done upfront to predict future course of disease during hospital stay and thus managed aggressively to prevent further complication such as dengue shock syndrome and multiorgan dysfunction. Clinical recovery is associated with laboratory improvement. These patients landed up in higher mortality as compared to those with no hepatic dysfunction. Similarly, high creatinine was associated with higher mortality in these patients. Thus, both LFT (including PT-INR) and serum creatinine can be considered as poor prognostic factors and indicator of higher mortality among dengue patients.

So, it is concluded that early detection of abnormal laboratory parameters like LFT, PT-INR, creatinine can be used to prognosticate the outcome, hence these patients should be kept under strict supervision & managed appropriately to prevent death. However, further study with greater sample size needs to be performed for establishment of the above results.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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