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CORRELATION OF LIVER FUNCTION TESTS WITH SEVERITY OF DISEASE IN CHILDREN WITH DENGUE FEVER – A PROSPECTIVE STUDY

Paediatrics

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ABSTRACT

Introduction: Dengue has emerged as a notable public health problem in recent decades in terms of mortality and morbidity associated with it. The clinical spectrums of dengue illness range from undifferentiated fever, self-limiting dengue fever (DF) to more severe, life-threatening forms of the illness termed dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Recent reports have demonstrated elevated hepatic transaminases or aminotransferases [Aspartate Transaminase (AST), Alanine Transaminase (ALT)] levels in dengue infection, suggesting that the liver is one of the main targets for the dengue virus.

Aims And Objectives:

- To evaluate the impact of Dengue fever on liver function.
- To determine whether serum transaminases can be of prognostic value in dengue fever.

Materials And Methods: This hospital based prospective study correlated the liver function tests with severity of disease in children with dengue fever. It was conducted in the Department of Pediatrics, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala among 50 children with dengue fever. The liver function enzymes were estimated and correlated with the severity of dengue fever. The student t-test was used for comparing the mean values between the 2 groups whereas chi-square test was applied for comparing the frequency using the SPSS software.

Results: The mean age of the study population was 13.62±3.12 years with 76.0% males and 24.0% females. The mean SGOT and SGPT was significantly more among DSS group at baseline and follow-up. The mean SGOT was significantly more among DSS group at baseline and follow-up (681.38±796.27 and 35.88±10.62 respectively) compared to DF and DHF at baseline (123.62±151.89 and 180.82±99.56 respectively) and follow-up (26.28±3.90 and 30.77±6.19 respectively).

The mean SGPT was significantly more among DSS group at baseline and follow-up (308.13±282.13 and 45.38±14.61 respectively) compared to DF and DHF at baseline (67.93±38.37 and 106.25±49.72 respectively) and follow-up (35.31±4.38 and 38.62±6.64 respectively).

Conclusion: Degree of elevation of SGOT and SGPT levels can be used to predict the severity of dengue. Hence, both elevated SGOT and SGPT level can be used as an early predictor of Severe Dengue fever.

KEYWORDS

INTRODUCTION

Dengue has emerged as a notable public health problem in recent decades in terms of mortality and morbidity associated with it[1]. It is most important mosquito-borne viral disease affecting humans, threatening the health of more than 2.5 billion people of the tropics and subtropics and occurring in over 100 countries. Dengue is endemic in many parts of India and epidemics are frequently reported from various areas within and outside the country[2,3]. Asia, including India, contributes the largest component of dengue infections. Rates of infection have increased 30fold since 1960 probably reflecting a combination of factors including major increase in urban populations, global warming and international travel. Dengue leads to considerable mortality and morbidity whole-world. While it is often thought of as a disease of poorer communities, in reality, the disease does not respect the boundaries of class, age, or wealth[4].

The clinical spectrums of dengue illness are ranging from undifferentiated fever, self- limiting dengue fever (DF) to more severe, life-threatening forms of the illness termed dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which are characterized by plasma leakage as a result of increased vascular fragility and permeability[5]. In the early phase, this illness often shows similar clinical features of other febrile illnesses, such as headache, myalgia, arthralgia, and rash[6].The main characteristics of DHF such as retro-orbital pain, petechiae or other clinical signs of bleeding, and plasma leakage are not seen in the early phase of illness in many patients. They typically appear after the third or fourth day of fever[7].Definitive early dengue diagnosis is difficult and requires laboratory tests based on viral or antigen detection, such as real time polymerase chain reaction (RT-PCR), and virus isolation[8].There are 4 distinct, but closely related, serotypes of the virus that cause dengue (DEN- 1, DEN-2, DEN-3 and DEN-4). Recovery from infection by one provides lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary. Subsequent infections by other serotypes increase the risk of developing severe dengue[9,10].DF/DHF/DSS are caused by four serotypes (DEN 1-4) transmitted from viremic human beings to susceptible mainly by bites of Aedes Aegypti and Aedes Albopictus mosquito species. The case fatality rate with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) is 44%, seen mostly among children. Appropriate clinical management can save the lives of DHF and 16 DSS patients and mortality can be reduced to less than 1%.

As early recognition and prompt initiation of appropriate supportive treatment can decrease the morbidity and mortality. Most of the data reported on abnormal liver functions in dengue are retrospective. To evaluate the impact of dengue fever on liver function by assessing the patterns elevation of AST and ALT in a hospital setting and to assess whether these estimations will be of 18 prognostic value in a dengue positive child.

Hence present study is done to find the correlation of liver function tests with severity of disease in children with dengue fever – A Prospective study.

AIMS AND OBJECTIVES

- To evaluate the impact of Dengue fever on liver function.
- To determine whether serum transaminases can be of prognostic value in patient with dengue.

METHODS:-

This was a hospital based prospective study which included 50 Patients with Dengue conducted between January, 2020 till June, 2021 in NICU at MMIMSR, Mullana.

Inclusion Criteria

WHO Criteria Of Dengue Fever –

Fever > 5 days plus 2 or more of the following: Headache, retro-orbital

pain, myalgia, arthralgia, nausea/vomiting, skin rash and supportive serology or occurrence at the same location and time as other confirmed cases.

WHO Criteria For Dengue Hemorrhagic Fever:
Fever of 2-7 days. Bleeding manifestations indicated by positive tourniquet test/petechiae, ecchymoses, purpura/bleeding per mucosa/hematemesis, melena. 2. Platelet count 20%, fall in PCV by 20% after IV Fluids, Pleural effusion, ascites, hypoalbuminemia.

WHO Criteria For DSS:
DHF + weak pulse, hypotension, narrow pulse pressure and cold dry skin, restlessness.

Exclusion Criteria
1.Age group 18 years. 2. Children having scrub typhus, malaria, enteric fever, dengue like illness. 3. Children with other disease which affect the Liver. 4. Children having drug induced toxicity.

A prior approval of The Institutional Ethics committee was obtained. The study didn't impose any financial burden on the parents or guardians of the study group and an informed written consent was taken from the parents/guardians of the participants before conducting the study. All participants were ensured confidentiality. The study was not funded by any agency.

Blood sample was collected for serological testing of Dengue infection and Liver function test.

For Serology test, the blood sample (2ml) was drawn after clinical examination using red vial.

Intended use- Dengue Day 1 Test is rapid solid phase immune-chromatographic test for the qualitative detection of dengue NS1 antigen and differential detection of IgM and IgG antibodies to dengue virus in human serum/plasma. Conformed by ELISA (Enzyme – Linked immunosorbent assay).

Liver Function Test:
A Blood sample (3 ml) was drawn after an overnight fast for Liver function test using red vial. Alanine Aminotransferase – Alanine aminotransferase catalyzes the transamination of L-alanine to Alpha-ketoglutarate forming lactate dehydrogenase and pyruvate. The pyruvate formed is reduced to lactate-by-lactate dehydrogenase with simultaneous oxidation of reduced NADH.

Aspartate Aminotransferase – Aspartate aminotransferase catalyzes the transamination from L-aspartate to alpha – ketoglutarate, forming L-glutamate and oxalacetate. The oxalacetate formed is reduced to malate-by-malate dehydrogenase with simultaneous oxidation of reduced NADH.

STATISTICALANALYSIS:
The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS version 25.0. The Quantitative (Numerical variables) were present in the form of mean and SD and the Qualitative (Categorical variables) were present in the form of frequency and percentage.

The student t-test was used for comparing the mean values between the 2 groups whereas chi-square test was applied for comparing the frequency. The p-value was considered to be significant when less than 0.05.

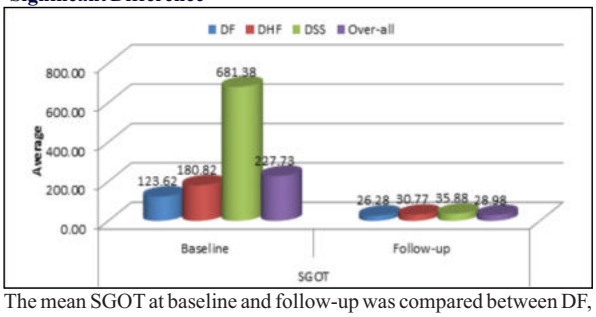
RESULTS:
Table 1: Demographic profile of the study participants

Variable	Mean		
	DF	DHF	DSS
Mean age (in years)	13.55±3.03	13.85±2.67	13.50±4.38
Gender Male Female	 21(72.4%) 8(27.6%)	 12(92.3%) 1(7.7%)	 5(62.5%) 3(37.5%)

Distribution Of Mean SGOT At Baseline And Follow-up Among Study Population

SGOT		Mean	Std. Deviation	F-value	p-value
Baseline	DF	123.62	151.89	8.984	0.001*
	DHF	180.82	99.56		
	DSS	681.38	796.27		
	Total	227.73	383.13		
Follow-up	DF	26.28	3.90	8.895	0.001*
	DHF	30.77	6.19		
	DSS	35.88	10.62		
	Total	28.98	6.86		

*Significant Difference

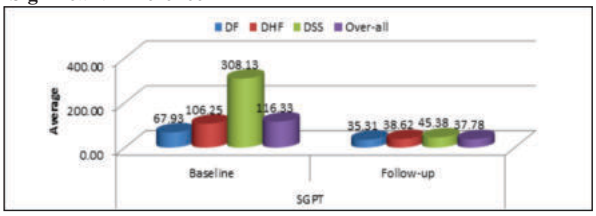


The mean SGOT at baseline and follow-up was compared between DF, DHF and DSS. The mean SGOT at baseline and follow-up was significantly more among DSS group compared to DF and DHF.

Distribution Of Mean SGPT At Baseline And Follow-up Among Study Population

		Mean	Std. Deviation	p-value
SGPT Baseline	DF	67.93	38.37	0.001*
	DHF	106.25	49.72	
	DSS	308.13	282.13	
	Total	116.33	142.26	
Follow-up SGPT	DF	35.31	4.38	0.005*
	DHF	38.62	6.64	
	DSS	45.38	14.61	
	Total	37.78	8.09	

*Significant Difference



The mean SGPT at baseline and follow-up was compared between DF, DHF and DSS. The mean SGPT at baseline and follow-up was significantly more among DSS group compared to DF and DHF.

DISCUSSION
Dengue infected patients present with acute febrile illness without localized signs and symptoms and the clinical presentations may resemble other infections hence it is difficult to distinguish it from other infections such as tropical infection (rickettsial disease, leptospirosis or malaria), other viral infection and primary bacteremia. Our study identified the significant differences of clinical features and liver function tests to facilitate the distinguishing of dengue infection from other causes[10].

The clinical presentations in dengue infection are fever, headache, loss of appetite, nausea, bleeding diathesis, myalgia, abdominal pain, sore throat and diarrhea. These symptoms are not specific and can be found in other infections. In the index study, we found that headache, nausea, loss of appetite and bleeding diathesis were commonly found in dengue patients but chills presented significantly more frequently in the control group. Therefore, these clinical presentations may be helpful in distinguishing dengue infection from the other infections at presentation[10].

In current study, the mean SGOT and SGPT at baseline and follow-up was significantly more among DSS group compared to DF and DHF. The liver enzymes were elevated among children with Dengue fever. Elevated SGOT level, SGPT level were observed in 96.0% and 68.0% subjects respectively.

Similar to our study, **Kuo and colleagues**[11] reported elevated levels of AST and ALT were found in 93.3% and 82.2% of cases respectively.

While the majority of patients had only mildly or moderately elevated levels of these transaminases, some 10% (11% and 7% for AST and ALT respectively) of patients had levels elevated by 10-fold or greater. **DeSouza and colleagues**[12] observed alterations of AST and ALT levels in 63% and 45% of patients respectively. They noted that the average levels of AST and ALT were significantly higher in DHF patients than in DF patients, an observation supported by other studies. Several authors have noted that the levels of serum AST are greater than serum ALT which is in contrast to the normal finding with viral hepatitis[11].

Roy A and Sarkar D[13] also observed 84.4% and 93.75% ALT and AST elevation respectively in DHF and 94.5% and 95.9% ALT and AST elevation respectively in DSS. **Jagadish Kumar et al.**[14] observed elevated ALT in 69.4% DF, 84.6% in DHF and 92% DSS and raised AST in 88% of DF,100% DHF and 96% of DSS group similar to other studies.

A similar result has been shown by **Fernando et al**[15]in 55 adult patients of dengue, where highest AST levels were seen on day 6 of illness and it was higher in patients with DSS.

Jagdish kumar et al[14] observed elevated ALT in 69.4% of DF, 84.6% of DHF and 92% of DSS, and raised AST in 88% of DF, 100% of DHF and 96% of DSS group. The hepatic enzymes were elevated significantly in DSS and DHF when compared to DF group which is similar to other studies.

CONCLUSION:

Elevated SGOT level was found in majority of the study population and is found to have significant association with IgM Dengue positivity. Hence elevated SGOT levels during the first week of admission can be reliably used as an early predictor of Severe Dengue fever. Degree of elevation of SGOT levels can be used to predict the severity of dengue. Degree of elevation of SGPT was also found to have a significant linear correlation with the severity of dengue fever. Hence both elevated SGOT and SGPT level can be used as an early predictor of Severe Dengue fever.

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Conflicts of interest: There are no conflicts of interest

Limitations:

In our study, the participants were relatively small in number. Thus, the result of this thesis cannot be generalized for a larger population. Therefore, complementary studies with larger sample size and diverse demographic profile are needed.

REFERENCES

1. WHO report on global surveillance of epidemic prone infectious disease. (GAR)
2. WHO resources for prevention, control and outbreak response dengue/DHF.
3. WHO Dengue: guidelines for diagnosis, treatment, prevention and control new edition, 2009.
4. Messina, J.P., Brady, O.J., Golding, N. et al. The current and future global distribution and population at risk of dengue. Nat Microbiol. 2019; 4:1508-15.
5. Ferreira GL. Global dengue epidemiology trends. Rev Inst Med Trop Sao Paulo. 2012;54(18): S5-6.
6. Setiati TE, Wagenaar J FP, de Kruif MD, Mairuhu A TA, van Gorp E CM, et al. (2006) Changing epidemiology of dengue hemorrhagic fever in Indonesia. Dengue Bull 30: 1-14.
7. Chaterji S, Allen JC Jr, Chow A, Leo YS, Ooi EE. Evaluation of the NS1 rapid test and the WHO dengue classification schemes for use as bedside diagnosis of acute dengue fever in adults. Am J Trop Med Hyg. 2011;84(2):224-8
8. Dutra NR, de Paula MB, de Oliveira MD, de Oliveira LL, De Paula SO. The laboratorial diagnosis of dengue: applications and implications. J Glob Infect Dis. 2009;1(1):38-44.
9. Achalkar GV. Dengue-A clinicopathological study. J Evolution of Medic Dent Sci. 2013;2(48):9380-5
10. Chaloemwong J, Tantiworawit A, Rattanathammethee T, Hantrakool S, Chai-Adisaksopha C, Rattarittamrong E, et al. Useful clinical features and hematological parameters for the diagnosis of dengue infection in patients with acute febrile illness: a retrospective study. BMC Hematol. 2018; 18:20.
11. Nimmannitya S, Thisyakorn U, Hemsrichart V. Dengue hemorrhagic fever with unusual manifestations. Southeast Asian J Trop Med Public Health 1987;18(3):398-405.
12. De Souza LJ, Nogueira RM, Soares LC, Soares CE, Ribas BF, Alves FG, et al. The impact of dengue on liver function as evaluated by aminotransferase levels. Braz J Infect Dis. 2007;11(4):407-10.
13. Roy A, Sarkar D, Chakraborty S, Chaudhuri J, Ghosh P, Chakraborty S. Profile of hepatic involvement by dengue virus in dengue infected children. N Am J Med Sci. 2013;5(8):480-5.
14. Jagadishkumar K, Jain P, Manjunath VG, Umesh L. Hepatic involvement in dengue Fever in children. Iran J Pediatr. 2012;22(2):231-6.
15. Fernando S, Wijewickrama A, Gomes L, Punchihewa CT, Madusanka SD, Dissanayake H, et al. Patterns and causes of liver involvement in acute dengue infection. BMC Infect Dis. 2016; 16:319.