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Prospective Study of Liver Function and Lipid Profile Test as Probable Markers of Dengue Fever Severity

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***Abstract*—"Dengue fever" (DF) is a serious public health issue, particularly in South Eastern parts of Asia. Biochemical changes have been proven to be early indicators of DF. This study was done on 90 DF patient to investigate the influence of the disease on liver functions along with lipid profiles and to link the results with the degree of seriousness of the disease.The current cross-sectional and observational study included 90 participants. Frequency and percentage were used to express qualitative data. The experimental investigation comprised a DF test with a quick diagnostic kit, liver function testing, and lipid profile tests. Quantitative data was reported utilizing the "mean standard deviation" as well as "median". The majority of the patients (55.6 percent) were males, with the remainder (44.4 percent) females, for a male to female ratio of 1.25 to 1. Raised "aspartate aminotransferase" (AST) was detected in 84.4% of patients, total bilirubin was found in 15.6%, and serum albumin was found in 56.7%. However, no significant relationship was discovered between ages and the intensity of Dengue. Meanwhile, there was a significant correlation (p0.05) between the result of liver performance tests as well as the severity of Dengue, with impaired liver function rising with increasing severity.**

***Keywords*—Alanine aminotransferase, Dengue fever (DF), Lipid profile, Biochemical alterations, Severity, Bilirubin, Cholesterol.**

INTRODUCTION

"Dengue fever" (DF) is often a self-limiting viral illness transmitted by mosquitos. It occurs by one of the four Dengue virus subtypes. Dengue virus is an RNA virus with a single positive strand. It belongs to the Flaviviridae family, and the genus Flaviviridae is transmitted through "Aedes aegypti" as well as "Aedes albopictus" mosquitos. Fever with limited constitutional symptoms to shock and bleeding tendencies characterize "Dengue shock syndrome / Denguehaemorrhagic fever" (DSS/DHF)[1]. DF has risen considerably in recent years, becoming prevalent in 112 countries in South and North America, Africa, the Mediterranean area and South East Asia.DF threatens roughly 2.5 billion people in tropical and subtropical countries. Every year, around 45-105 million recorded cases of Dengue, 550,000 verified instances of DHF, and at least 13,000 fatalities due to Dengue occur worldwide. 90% of Dengue morbidity occurred in youngsters aged 14 years [2].

Dengue is a self-limiting viral disease, but it can cause life-threatening complications in a considerable proportion of patients, particularly during the crucial phase of the illness. The initial stage of Dengue usually starts with a fever that is similar to that of other abrupt febrile infectious illnesses [3]. It led to underestimate of true incidence and late treatments of a potentially fatal medical disease. With evidence both direct and indirect of metabolic changes associated to the severity of Dengue. According to studies, people with DHF and DSS had higher blood levels for "transaminases aspartate aminotransferase" [SGOT] as well as "alanine aminotransferase" [SGPT][4].

Cross-sectional studies have revealed that DHF and DSS are related with lower blood levels from total cholesterol and triglycerides. These biochemical indicators aren't studied in the beginning stages of Dengue. However, the value of biochemical changes that are more susceptible to DHF due to an earlier diagnosis is uncertain.[2] Close inspection of vital indicators, platelet count, and haematocrit is the usual course of care in the treatment of DF. It has been demonstrated that the majority of DF patients have liver activity in the form of increased serum aminotransferases including transaminases. The increase in enzymes is caused by reactionary hepatitis alongside direct viral harm to hepatocytes. Hepatitis patients are more likely to have renal failure, acalculous cholecystitis, encephalopathy, and bleeding tendencies. In the context of thrombocytopenia, impaired liver function contributes significantly to bleeding. As a result, regular examination of the liver's activity and lipid profiles in DF patients should be performed.

LITERATURE AND REVIEW

Many ideas for the pathophysiology of Dengue virus infection have been proposed, however "antibody dependent enhancement" (ADE) upon infection is thought to play a critical role. It was demonstrated that sera from DHF/DSS patients significantly more likely to display ADE in vitro compared to ordinary DF [5].After viral infection, viral proteins sequester "fatty acid synthase (FASN)" and 3hydroxy3methylglutarylCoA reductase (HMGCR), leading in enhanced cholesterol absorption and triacylglycerol production. Various DENV serotypes (DENV-1, 2, 3, and 4) have also been linked to the

regulation of host lipid droplet breakdown; it has been demonstrated that a viralproteinused the acyltransferase metabolism of AUP1, a lipid dropletlocalized typeIII membrane protein, to initiate lipophagy.Furthermore, several cholesterol absorption receptors in the body such as the low-density lipoprotein receptor (LDLr), have been shown to engaged in DENV infections, allowing researchers to uncover alterations in lipid metabolism following DENV infection that can be utilized to generate novel biomarker to assess disease severity. [6].Ganeshkumar,et al [7], testified mean ALT in DF, DHF and DSS as44.424±17.87, 66.96±15.714 and 287.67±14.216; mean AST in DF, DHF andDSS as 72.64±27.633, 126.36±30.24 and 410.47±190.38; mean total Bilirubin in DF, DHF and DSS as 0.342±0.1332, 0.64±0.108 and 1.375±0.188; and meanserum albumin in DF, DHF and DSS as 3.299±0.28, 3.191±0.068 and1.975±0.05. The difference was significant across all parameters between thegroups (all $p<0.05$).In their study, Shankaraiahand Kiran [8] reported findingswith mean ALTin DF, DHF and DSS as 80 ± 49, 215 ± 123 and 580 ± 211; mean AST as 115± 60, 327 ± 203 and 750 ± 241 and mean total bilirubin as 2.16 ± 1.3, 4.48 ±2.49 and 7.52 ± 2.7 respectively.Lima et al [9]conducted a meta-analysis to study lipid profile as apredictor of DF they concluded that, total- cholesterol ($p< 0.001$) andLDL levels ($p<0.001$) negatively correlated and with severe Dengue infection.HDL ($p=0.07$), VLDL ($p=0.9$) and TG ($p=0.57$) levels, were not significantlycorrelated with Dengue severity.Lodhi et al [64], also reported low total cholesterol in patient with severe Dengue ($p<0.001$).

MATERIALS AND METHODS

This study was done on patients with DF who were hospitalized to Krishna Hospital and Medical Research Centre in Karad over an 18-month period. Duration used for the study lasted 18 months (from October 2018 till March 2020). An ethical clearance was obtained from the college and university committees. Following ethical approval, authorization was obtained from the head of divisions.According to “WHO Fact Sheet dated 13th September 2018” [6], there are 390 million Dengue infections per year, of which 96 million manifests clinically with severe disease [7]. So, the current prevalence of Dengue infected cases is 24.6%.The current cross-sectional and observational study included 90 participants.

Informed consent:Patients who met the criteria for selection were told about the purpose of the study and enrolled in it after providing written and informed permission.

A. Statistical analysis

In the statistical study, IBM Inc.'s "Statistical Package for Social Sciences" (SPSS) trial version 23 was employed. The data was put into statistical software for further analysis afternoted on a research proforma sheet. The qualitative data was expressed using frequency and percentage. The mean +/- standard deviation as well as median were used to depict quantitative data. For frequency analysis, the data was organized into table and graph. The “Chi square test” and the student's “'t' test” were utilized, and a 'p' value of 0.05 was considered statistically significant.Patient who havemet the selection criteria was chosen for the trial. Patients were questioned to acquire demographic information that included age and gender, as well as presenting complaints and being suspected of Dengue viral fever. These individuals were examined clinically, and their results, including vital sign and systemic examinations, were recorded. These finding were documented using a pre-designed along with tested proforma as shown in Figure 1 and table1.Total Blood Count • Liver Function Test • Lipid Profile • Serology for Dengue IgM, IgG, and NS1 Ag Dengue tests were performed using a quick diagnosing kit (Dengue card rapid) from the Mitra business, which used a solid phase immune-chromatographic assay to identify Dengue Ns1 antigen and differentiate IgM/IgG antibodies to Dengue virus. Liver functions tests:Automated (Transasai v2 analyser) liver function tests were performed on the blood sample taken on the day of admission. The calorimetric technique was used to calculate total bilirubin, serum albumin, and alkaline phosphatase. The worldwide association for scientific chemistry evaluated AST and ALT with no pyridoxal phosphate stimulation.

RESULTS

In the study a total of 90 patients detected with Dengue viral fever were included during the study period of 18 months. There were 50 males and 40 females in our study, with male: female ratio of 1.25:1. We had majority of the patients diagnosed with conditions of DF 49 cases, 34 cases had DHF and 7 cases had DSS.

There were 5 patients with platelet numbers less than 20,000, 24 patients with values 20,000-50,000, 44 patients with counts 50,000-1,000,000, and 17 instances with platelets more than 100,000. The average platelet count was 51288.889± 8640.21.

Based on LFT results, we discovered that 67 individuals had elevated ALT, 76 had elevated AST, 14 had elevated Total bilirubin, and 51 had reduced serum albumin.

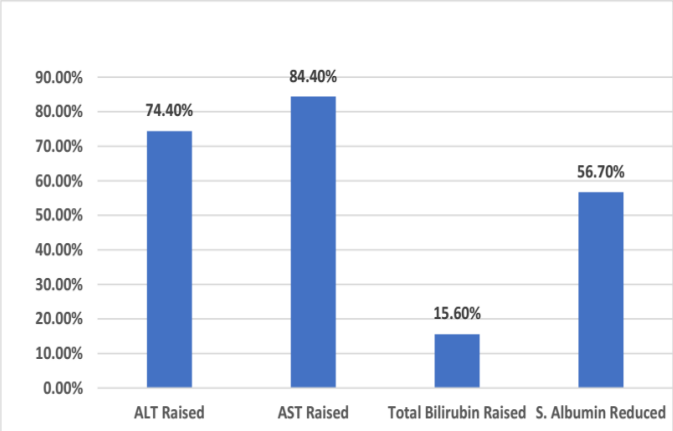

Fig.1. LFT Derangement

Our study found that 67 individuals had lower HDL cholesterol, 40 had lower LDL cholesterol, 35 had lower TG, and 26 had lower total cholesterol.

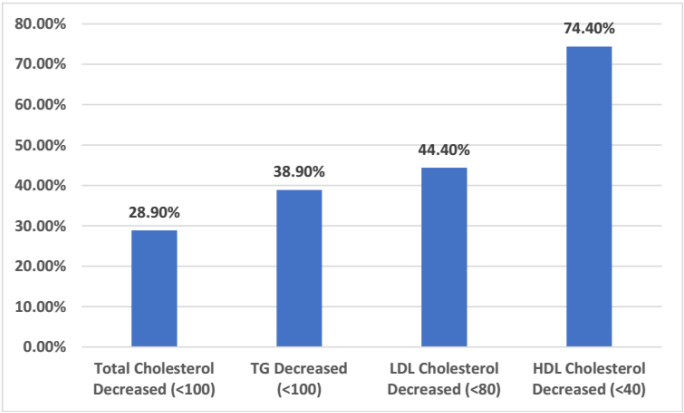

Fig.1- Deranged Lipids Profile

TABLE 1-LAB TEST PARAMETERS

	Minimum	Maximum	Mean	Std. Deviation
ALT	17.0	400.0	106.73	94.24
AST	22.0	486.0	142.58	129.31
T. Bilirubin	0.2	2.6	0.92	0.41
Sr. Albumin	2.4	4.2	3.38	0.48
TC	72.0	186.0	128.61	30.05
TG	18.0	167.0	107.30	23.70
LDL-C	30.0	130.0	83.44	23.64
HDL-C	20.0	56.0	33.61	8.99

Moreover, there was not any significant association between the age and severity of Dengue as shown in Figure 2 (p=0.687).

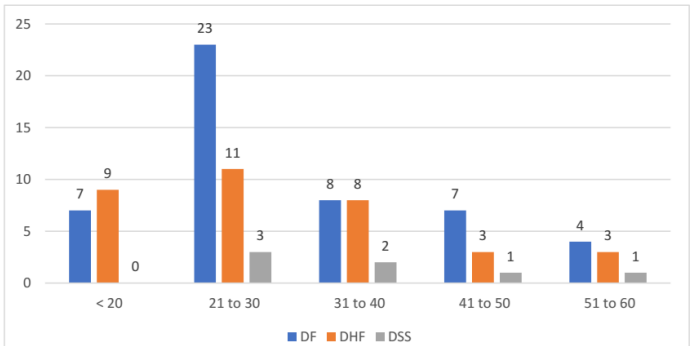

Fig.2. Age & Severity of Dengue

DF affected 27 of the 40 females, whereas DHF affected 9 and DSS affected 4. There were 22 men with DF, 25 with DHF, and three with DSS out of 50. In our study, males were shown to have more DHF cases than females as shown in figure 3.

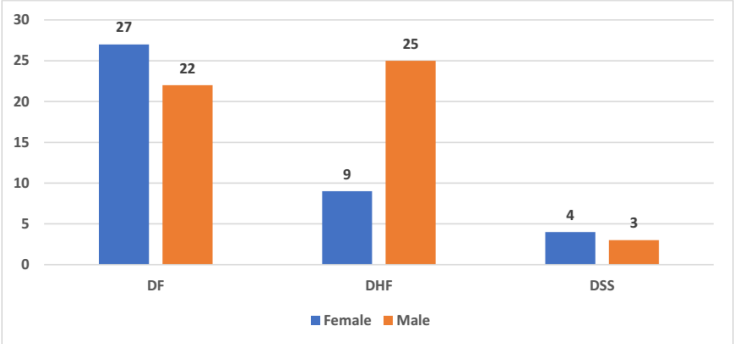

Fig.3. Gender & severity of Dengue

Out of 49 DF patients, 26 had elevated ALT, 35 had elevated AST, and 11 had reduced serum albumin. All 34 patients of DHF had elevated ALT and AST, 8 had elevated total bilirubin, and 33 had reduced serum Albumin. All seven instances of Dengue shock syndrome showed elevated ALT, AST, and decreased Albumin, and six had elevated total Bilirubin as shown in Figure 4, 5 and 6.

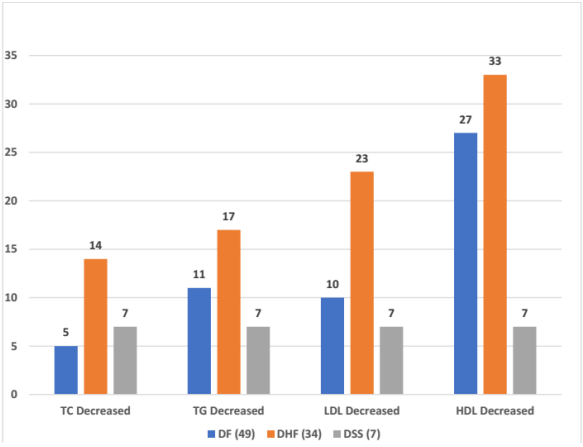

Fig.4. Lipids & Severity of Dengue

Significant difference were seen between the mean values of total cholesterol in Dengue severity groups ($p<0.001$).

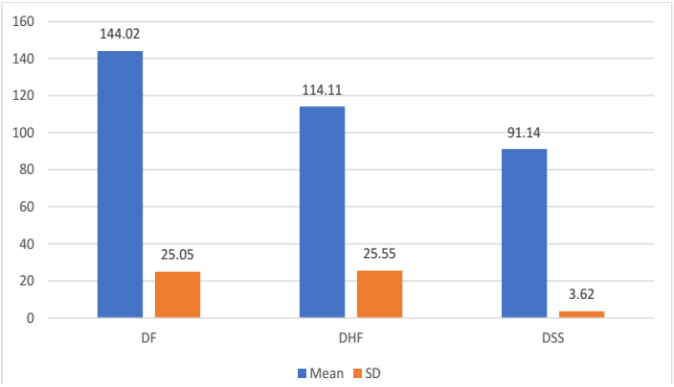

Fig.5. Mean total cholesterol and severity of Dengue

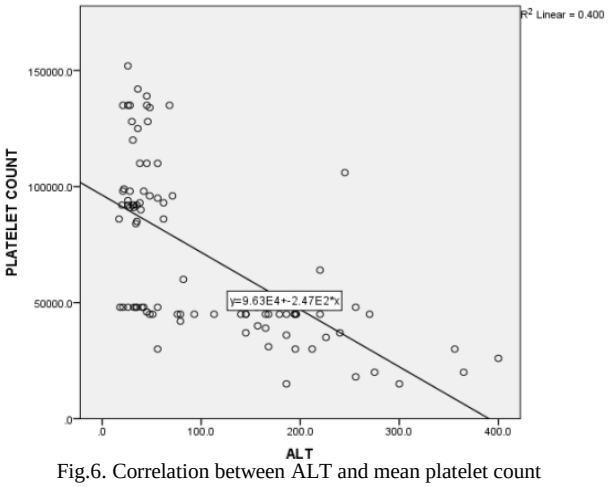

Fig.6. Correlation between ALT and mean platelet count

DISCUSSION

In several studies, there is an increase in AST and ALT, which is more prevalent in DHF and DSS. These levels revert to normal after 14-21 days. Hepatic failure and fulminant hepatitis are more common in DHF/DSS patients and have a dismal prognosis. The fact that AST levels grew faster than ALP levels and AST levels climbed faster than ALT levels might be attributed to AST's shorter half-life. Steatosis, Kupffer cell hyperplasia, hepatocellular necrosis, Councilman bodies, and cellular infiltrates in the portal tract are histological alterations in DF. According to the present study, the age group most impacted was 21-30 years, followed by 31-40 years, 20 years, 41-50 years, and 51-60 years. The majority approximately those receiving treatment were males, with a male:female ratio of 1.25:1. There was no significant relationship discovered between age along with severity of Dengue. DHF was related with a slightly greater proportion of males (p=0.028). Similar results were seen in a research done by Ahmed et al, where "the proportions of DF, DHF, and DSS were 89.82%, 6.79%, and 3.39%, respectively, and the mean age of patients suffering DF was 37.12 ±15.45".

Thrombocytopenia is one of the common findings in Dengue. In this study,mean platelet count was 51288±8640. Majority of patients had platelet countsbetween 50,000 to 1,00,000, followed by 20,000 to 50,000,more than 1,00,000 and less than 20,000. The platelet counts significantly decreased in DHF, DSS ($p < 0.001$). Similar findings were reportedby Mohd. Yaseen et al, where platelet count of < 20,000 was seen in 32%patients and rest had platelet in the range of 20,000-1,00,000. Thrombocytopenia was present in 89% of cases.The fall in platelet count inDHF and DSS was greater as compared to DF. Chaudhuri, N et al., reportedlow platelet count across all groups (DF, DHF and DSS). Thrombocytopeniawas present in 88% of DF and 100% of DHF and DSS. Santhosh et al,reported mean platelet count as 58,800. Rajoo et al. reported mean plateletcount as 48500±2600, Villar-Centeno et al, reported thrombocytopenia in23.6% patients.Further, significantassociation were seen between the liver function tests and severity of Dengue ($p<0.05$) where abnormality of liver function increased with increasing severity.

CONCLUSION

Thebiochemical alterations in form of deranged liver functiontest alteration in fasting lipid profile detected during Dengue infection indicatetowards a more severe infection-DHF and DSS. They can thus, be used asearly marker of Dengue severity and help in early recognition of severe casesand there by aid in better management of complications.It was discovered that during DF, biochemical changes such as increased ALT, AST, bilirubin levels along with reduced levels of serum albumin, high density lipoprotein cholesterol (HDL), total cholesterol, triglycerides levels, low density lipoprotein cholesterol (LDL), and so on indicates a severe infection- DHF and DSS. These markers of severe Dengue infection might therefore aid in the early triaging of Dengue infection patient and so in improved therapy.

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