

## A Study of Serum Lipid Profile as a Prognostic Marker In Dengue Infection.

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### I. INTRODUCTION

The word dengue came from denga or dyengo which in Africa means hemorrhage. The first definite clinical report of Dengue is attributed to Benjamin Rush in 1789.<sup>1</sup> He coined the term “break- bone fever” because of the symptoms of myalgia and arthralgia.<sup>2</sup> Dengue fever is distributed world-wide, involving nearly all tropical and subtropical countries, and hence has many names like-dandy fever, Denguero, denga, dunga, break-bone fever, bouguet, seven day fever, bonon, chapenonada, Knieuble, Tokkive-ana, Mal de genoux, homanguu, and coup-d barre.<sup>3</sup>

Dengue virus (DENV) is an arthropod-borne single stranded RNA virus of genus Flavivirus. It is comprised of 4 closely related but antigenically distinct serotypes, DENV-1, -2, -3, and 4. Presently no specific therapies or vaccines are available to treat diseases or to prevent DENV transmission. Illnesses caused by DENV infection include undifferentiated fever, dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS).<sup>4</sup> Dengue ranks as the most important mosquito-borne viral disease in the world. Current estimates report that, at least 112 countries are endemic for Dengue and about 40% of the world populations (2.5-3 billion people) are at risk in tropics and sub-tropics. Annually 100 million cases of dengue fever and half a million cases of dengue haemorrhagic fever occurs worldwide.<sup>5</sup>

In India, the first major epidemic illness clinically compatible with dengue was reported from Madras in 1780, which later spread all over the country. Later, an outbreak of dengue like illness was reported in 1956 from Vellore, Tamil Nadu and since then, it has persisted in various parts of the country.<sup>6</sup>

There are number of study on serum lipid profile and its correlation with severity of dengue fever, but results are conflicting. We want to study serum lipid profile and its correlation with various complications of dengue like bleeding, DIC, hepatitis, shock etc.

We would also like to evaluate whether lipid profile recovers after the acute event or not.

### II. AIMS AND OBJECTIVES

- To document the changes in lipid profile in adult patients of Dengue Infection.
- To document the association between changes in lipid profile and complications in DF, DHF and DSS.
- To document the changes in lipid profile during recovery from the acute event.

### III. MATERIALS AND METHODS

The study was conducted to know the prognostic significance of lipid profile for predicting severity of dengue infection in a sample of adult patients admitted in a tertiary care center.

#### (I) Study Design-

Study design is prospective observational study. The study participants were longitudinally followed up at 5 and 10 days to identify lipid abnormalities along with their progression in dengue infection.

#### (II) Study Duration-

April 2017 to April 2018. Considering the seasonal fluctuations in dengue infection, more patients were admitted during the rainy season. A period of 15-18 months was required to attain the desired sample size.

#### (III) Study setting-

In patient Department of Medicine ward of tertiary care hospital

#### (IV) Study Population-

The target population was all patients of dengue infection in Surat City during the study period. The accessible population for our study purpose was dengue patient presenting to In-patient department of our tertiary care hospital and the study population was a purposively chosen sample of 100 patient admitted in ward.

**INCLUSION CRITERIA:-**

The study was on patients of tertiary care hospital who are:-

1. All adult patients (more than 18 years) admitted with Dengue viral infection.
2. All patients satisfying WHO Criteria for confirmatory diagnosis as DF, DHF & DSS.<sup>7</sup>
3. All Dengue patients admitted within 5 days of onset of fever.
4. All patients who give informed consent to participate in this study.

**EXCLUSION CRITERIA:-**

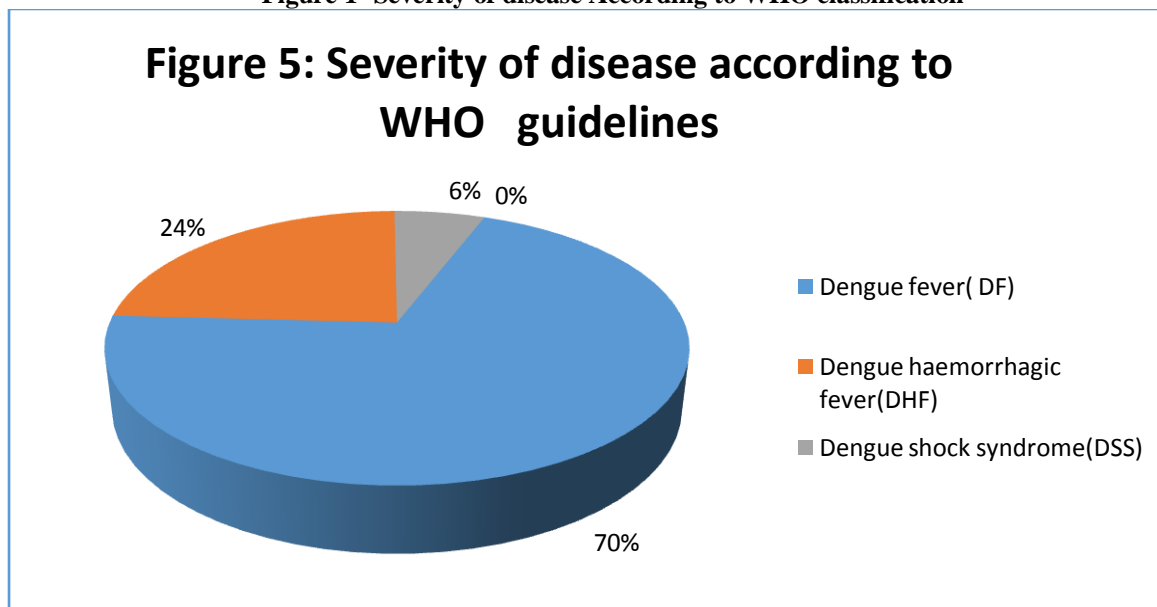
1. Patients having fever other than dengue or mixed infection.
2. Pregnant women.
3. Patient having CRF, DM, HTN, HIV, Liver disease and other immune-compromised status

**(V) Sample and Sampling techniques:**

- During the study period of January 2017 to June 2018, all patients satisfying the inclusion criteria were invited to participate in the study. Patients were provided with all information about the study in the form of PIS (Patient Information Sheet) in their local language. Those patients who gave written informed consent were formally enrolled in the study. The sampling technique used was non-probability purposive sampling in which all consecutive patients of dengue infection were enrolled till the adequate sample size was achieved.
- A structured clinical proforma was used for data collection in which all pertinent details of the patients were recorded. Information regarding chief complaints, history of present illness, personal history etc. was recorded. The demographic variables collected were age, gender, occupation, religion etc. General physical examination was done to record variables like pulse rate, blood pressure, respiratory rate, temperature, pallor, icterus etc.
- All routine investigations like CBC, LFT, RFT, Lipid profile, NS 1 antigen, IgM dengue, Chest X-Ray and USG abdomen were done in all the patients.
- Exposure variables collected were age, gender, symptoms like fever, rash, headache, myalgia, petechiae etc. and levels of serum lipids (Cholesterol, HDL, LDL, TGs.)
- Outcomes variable collected were severity of dengue infection (DF, DHF, DSS diagnosed on the basis of WHO 2011 criteria)<sup>7</sup>
- Serum lipids were measured first during the acute phase of infection when the patient presented for admission (first 5-6 days of illness). The lipid investigation was performed again during the recovery phase (at 8-10<sup>th</sup> day of illness). The paired measurements were used to identify lipid abnormalities as prognostic markers of clinical progression of dengue infection.

**IV. OBSERVATION AND RESULTS**

**Figure 1- Severity of disease According to WHO classification**



In present study, out of 100 cases, most of cases were having dengue fever (70%), followed by dengue hemorrhagic fever (24%) and 6% were having dengue shock syndrome.

**Table 1- Mean increase in lipid profile levels during recovery phase compare to acute phase in patients of dengue infection.**

Lipid profile	Acute phase(within 5 day)		Recovery phase(at 8-10 days)		P value
	Mean	SD	Mean	SD	
<b>Total cholesterol</b>	84.97	21.83	112.95	21.79	< 0.05
<b>HDL</b>	27.39	5.485	34.5	4.54	< 0.05
<b>LDL</b>	85.64	66.51	99.72	25.33	< 0.05
<b>TGs</b>	115.76	44.76	148.59	45.44	< 0.05

The above comparison table shows that the mean lipid profile levels of total cholesterol, HDL, LDL, and TGs increased from acute phase of infection to the recovery phase. On applying paired t-test, the mean increase in lipid profile was found to be statistically significant (p value<0.05)

**Table 2- Percentage increase in lipid profile levels during recovery phase compare to acute phase in patients of dengue infection.**

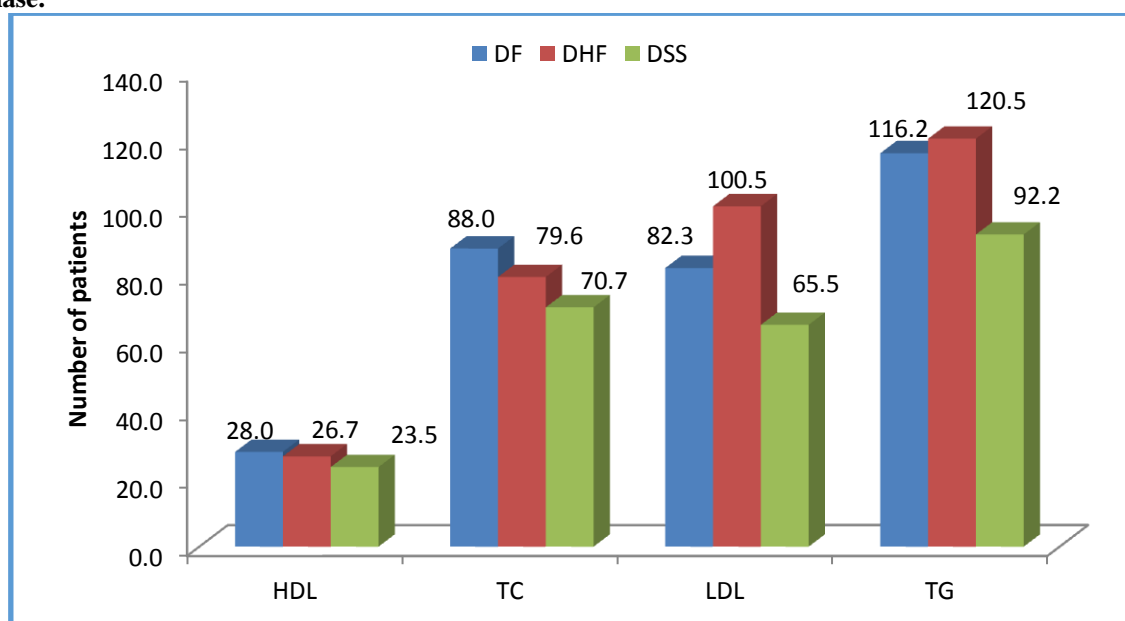
Lipid profile	<20%	21-40%	41-60%	>60%
<b>Cholesterol</b>	27	35	19	19
<b>HDL</b>	38	40	12	10
<b>LDL</b>	44	31	11	14
<b>TGs</b>	45	26	11	18

Out of 100 patients 73% had significant rise in total cholesterol >20%, 62% had similar rise in HDL, 56% in LDL and 55% in TGs. This shows that change in total cholesterol was much more than the other lipid components.

**Table 3- Pattern of lipid profile among patients of dengue viral infection according to their clinical severity during ACUTE phase of infection (within 5 days of illness) [n=100]**

Severity	T. Cholesterol		HDL		LDL		TGs	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<b>DF</b>	88.03	22.85	27.97	5.48	82.27	19.35	116.17	45.38
<b>DHF</b>	79.63	16.99	26.67	4.65	100.5	131.97	120.46	43.26
<b>DSS</b>	70.67	19.57	23.5	7.56	65.5	24.5	92.16	43.18
<b>P value</b>	0.066		0.12		0.38		0.38	

**Figure 2- Bar chart showing comparison of lipid profile levels on the basis of severity of dengue in acute phase.**



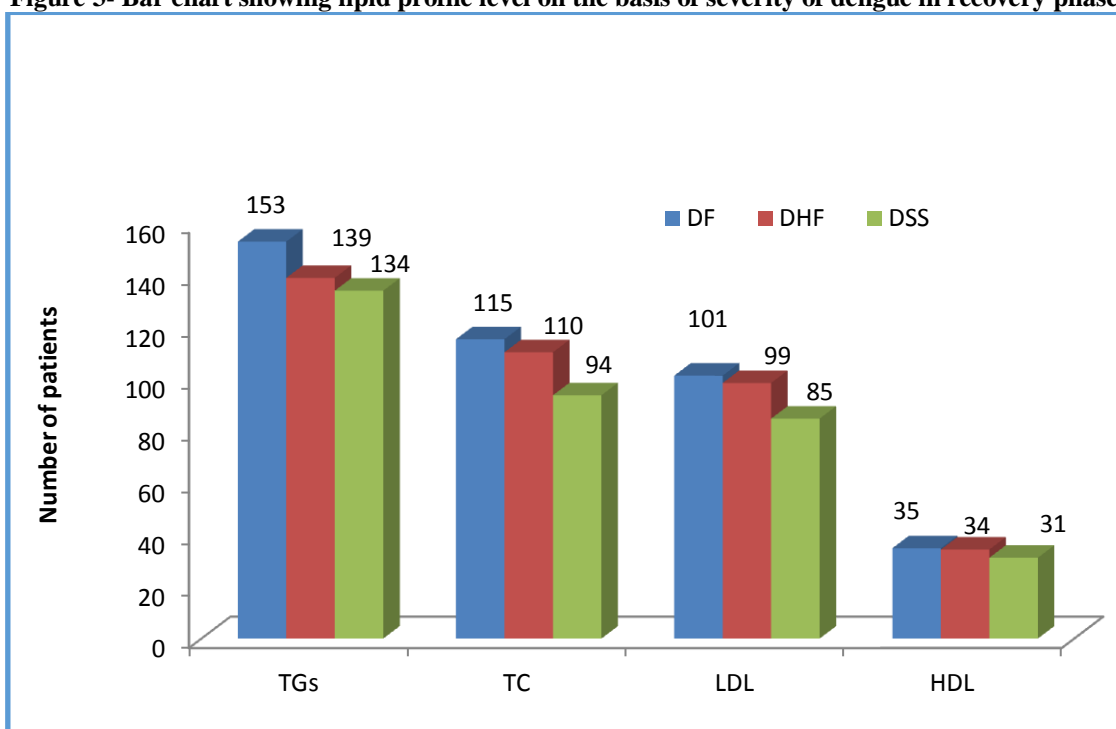
Mean values of lipid profile parameters during acute phase were compared on the basis of severity of dengue infection among the patients using One-way Anova test on MS Excel software.

It was found that the mean total cholesterol and HDL decreased linearly with rising severity of dengue infection from DF, DHF to DSS. Although the decrease was not statistically significant (p value >0.05), it was clinically significant. Conversely, levels of LDL and TGs increase from DF to DHF but decreased in patients of DSS.

**Table 4- Pattern of lipid profile among patients of dengue viral infection according to their clinical severity during RECOVERY phase of infection (at 8-10th days of illness)**

Severity	T. Cholesterol		HDL		LDL		TGs	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<b>DF</b>	115.46	20.77	34.84	4.44	101.38	25.76	153.07	48.16
<b>DHF</b>	110.42	21.71	34.33	3.16	98.58	22.86	139.12	40.42
<b>DSS</b>	93.83	26.79	31.16	8.63	84.83	29.48	134.17	19.96
<b>P value</b>	0.051		0.16		0.30		0.32	

**Figure 3- Bar chart showing lipid profile level on the basis of severity of dengue in recovery phase.**



Mean values of lipid profile parameters during recovery phase were compared on the basis of severity of dengue infection among the patients using One-way Anova test on MS Excel software.

It was found that the mean total cholesterol, HDL, LDL & TGs decreased linearly with rising severity of dengue infection from DF, DHF to DSS.

As compare to acute phase, rise in total cholesterol, HDL, LDL and TGs during recovery phase well correlated with severity of dengue fever. The rise was least in DSS and maximum in DF. Although it was not statistically significant (p value >0.05), it looked clinically significant.

**Strength of the study:**

Our study being a longitudinal study demonstrated a change from acute to recovery phase in lipid levels. Being a hospital based study in a tertiary care referral hospital; we could enroll patients with different stages & severity of dengue. Our study also enrolled adult patients in comparison to previous studies which focused mostly on pediatric age-group.

**Limitation of study:**

The main limitation might be referral bias so that only patients with greater severity sought treatment in our hospital. Further, considering the high mortality in dengue infection, most of the patients who presented with complications could not be followed up till the recovery phase. Most of these patients eventually died during the

acute phase only, hence paired estimates of lipid levels were not available. These patients had to be excluded from the final analysis. This might explain the lesser number of patients of DSS & DHF in our study.

Our study identified an association between lipids and dengue severity; however, there can be other prognostic factors as well like age, sex, nutrition, immunity, etc. which have an influence on the natural history of dengue infection.

#### **Implication for future study:**

Our study was a hospital based study and hence the results could not be extrapolated to general population. Further community based studies are required to determine the true level of plasma lipids in patient suffering from dengue infection in the general population.

In addition to plasma lipids, there are other prognostic factors as well which influence the severity in dengue infection; further studies are required to identify these predictors of dengue severity other than serum lipid profile.

### **V. SUMMARY**

- The study was carried out at a tertiary care center in Surat over the duration of one year in which, study of lipid profile and its correlation with severity of dengue fever was studied and analyzed.
- Total 100 cases were studied during 1 year period.
- Most of the patients (64%) were between 18-27 years. The second common age groups of patients (21%) were from the age group of 28-37 years. Mean age of the study population was 27.9±10.09 years.
- In our study, out of 100 cases, 64 (64%) were male and 34 (34%) were female.
- Most common presenting clinical features were fever (100%) followed by body ache (99%), anorexia (90%), nausea (90%), abdominal pain (81%), and vomiting (47%). Other presenting features were bleeding, rash, patechiae, free fluids, breathlessness, and convulsion.
- Out of 100 cases, 70 (70%) were having dengue fever, 24 (24%) were having dengue hemorrhagic fever (DHF), and 6(6%) were having dengue shock syndrome (DSS).
- In present study 83(83%) cases were having normal bilirubin levels (<1mg/dl). Increased bilirubin was not commonly seen in dengue fever and dengue hemorrhagic fever. It was significantly increased only in dengue shock syndrome patients.
- Most of the patients of dengue were having mild elevation of liver enzymes. 67% were having mildly elevated SGOT levels (41–300 IU/L), and 60% were having mildly elevated SGPT levels between 41–300 IU/L. Patients having SGOT/SGPT levels <1000 completely recovered, and 1 (1%) patient with SGOT/SGPT >1000 IU/L expired.
- Half of the patients were having normal hemoglobin concentration in the range of 13 – 17 gm/dl (51%). Rest of the patients were anemic.
- The mean hematocrit value of dengue cases in our study was 38.54 ± 5.57 %. In DHF and DSS, an increase in hematocrit levels was noted. Hematocrit value >45% was found in 10% patients. Hemoconcentration was not commonly seen with severe dengue fever in the present study.
- No mortality was seen in patients having WBC count between 4000-11000. A patient who expired, was having WBC count >11000cmm.
- Most of the patients (63%) were having low platelet count (<1 lakh) with a mean platelet count of 83,538 cells/cmm.
- In the present study total cholesterol, HDL, LDL, and TGs decreased in acute phase (within 5 days of infection) which increased during recovery phase (at 8-10 day of illness). This was statistically significant (p value <0.05)
- In the present study around 73% of the patient were having significant (>20%) rise in total cholesterol, 62% had similar rise in HDL, 56% in LDL and 55% in TGs. This shows that change in total cholesterol level was much more than the other lipid components.
- Mean total cholesterol, HDL, LDL, and TGs levels well correlated with severity of DF, DHF, and DSS in acute as well as recovery phase.
- The decrease in lipid component level was maximum in DSS and least in DF. Similarly rise in lipid component level during recovery phase was maximum in DF and least in DSS.

## VI. CONCLUSION

There is significant decrease in lipid component levels during acute phase of dengue infection which improves during recovery phase. All the lipid components (HDL, LDL, TGs, and total cholesterol) showed a significant rise from acute to recovery phase. Decrease in lipid component levels were maximum in DSS and least in DF, which may guide about prognosis and therapy in DF, DHF and DSS.

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