A Study On The Etiologies, Clinical And Biochemical Profile Of Liver Abnormalities In Dengue Patients In A Tertiary Care Centre

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Abstract

Background: Dengue is one of the most important arboviral diseases which has a significant impact on human lives in terms of both morbidity and mortality.

Aim of the study: To find out the clinical profile among patients with dengue. To identify the biochemical profile of liver abnormalities in dengue patients in a tertiary care center.

Methods: A prospective study was done at Sri Muthukumaran Medical College Hospital and Research Centre, Chennai. A total of 50 serologically confirmed cases of dengue who were aged more than 14 years were included in the study. A detailed history was collected from all the patients. Clinical examination was performed and investigations like complete blood count, serum bilirubin, liver enzyme assessment for SGOT, SGPT, ALP, and ultrasound assessment were done. They were followed up for 7 days. Informed written consent was obtained from all study participants. The data were analyzed using SPSS software and the variables with a p-value <0.05 was considered to be significant.

Results: A total of 50 patients were included in the study. The mean age of the patients was 39.8 years and the majority (72%) were males. Fever and myalgia were the common symptoms that were present in all patients. Signs of liver failure were found in 66% of the patients. The average red blood cell count was 4.48 million and the mean platelet count was 91280. Serum bilirubin increased with an increase in age among these patients, yet it was not statistically significant. 50% of the patients had elevated serum bilirubin levels. SGOT was elevated in 82% of patients with an average of 114.3 and age had a significant association with SGOT. The mean SGPT level among the patients was 71.3. Among the 50 study participants, 36 (72%) had elevated SGPT. A higher proportion of females had elevated SGPT than males. The average ALP level was 118.4 with elevated values of 16%. Platelet count had a significant negative correlation with SGOT and SGPT levels. Serum bilirubin and ALP did not have any association with platelet count.

Conclusion: Dengue virus infection significantly affects liver function and this impact increases with a reduction in platelet count.

Keywords: biochemical investigations, clinical features, dengue, etiology, liver functions

Introduction

Dengue otherwise known as break bone fever is one of the most common causes of febrile illness mainly in tropical and subtropical countries. It is the second most common mosquito-borne disease after malaria.[1] The most common vector in the transmission is Aedes aegypti and Aedes Albopictus in.[2] The incidence of dengue has increased globally

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over years and almost 50% of the world's population is at risk of dengue. As per World Health Organization, 100 to 400 million infections are estimated to occur every year. Among the total cases of dengue, 80% of the cases are usually mild and asymptomatic.[3] Hence, the disease is often under-reported and it was also found that dengue is misinterpreted as other causes of febrile illness.[3] Previous studies have estimated that 390 million dengue virus infections are occurring every year and 3.9 billion people worldwide are at risk of dengue virus infection.[5] Nearly 70% of the estimated cases are in Asia.[4] The actual number of cases of dengue reported to WHO by various countries has increased from 505,430 cases during the year 2000 to 2.4 million in the year 2010 and 5.2 million in 2019. The reported number of deaths has also increased from 960 in the year 2000 to 4032 in 2015.[6] A wide range of risk factors are involved in the occurrence and transmission of dengue viz., increasing urbanization with improper town planning, poor standard of living, availability of an artificial collection of water in and around the household, increase in travel leading to global spread, inadequate health infrastructure has increased the disease burden globally.[7,8] Dengue should be suspected in an individual presenting with fever and 2 of the associated symptoms like severe headache, pain behind the eyes, nausea, vomiting, muscle, and joint pain, swollen glands, and rash. About 3 to 7 days following the onset of illness patient enters into a critical phase.[9] Warning signs of severe dengue include severe pain abdomen, rapid breathing, restlessness, persistent vomiting, fatigue, liver enlargement, bleeding gums, and blood in vomitus and stool.[10] Dengue is one of the diseases reported to cause multi-organ involvement. The dengue virus is reported to have few hepatotoxic effects. The available previous literature has stated that hepatocytes and Kupffer cells are the prime targets of dengue virus infection in the liver which are confirmed using biopsy and autopsy findings.[11] Other mechanisms for involvement of the liver due to immunological hyperactivity through T cell medicated cytokine storm and decreased hepatic perfusion due to circulatory failure.[12] Dengue leads to derangement in liver functions which includes elevated levels of serum bilirubin, elevated liver enzymes, and a reduction in serum albumin levels.

Though liver involvement is asymptomatic in most patients, some patients may present with clinical features like jaundice, nausea, vomiting, anorexia, and other signs of liver failure.[13] Some studies have also reported the occurrence of acute liver failure with dengue. Since there is no specific treatment available for dengue, early detection of the disease, its severity, associated complications, and organ involvement might help in reducing the mortality associated with dengue. [14]

Methods: This Prospective study was done on 50 patients with the dengue Department of General Medicine, Sri Muthukumaran Medical College Hospital and Research Centre. Patients who are admitted with signs of dengue and further confirmed as having dengue serologically at the Department of General Medicine, Sri Muthukumaran Medical College Hospital and Research Centre.

Inclusion Criteria:

1. Patients with dengue aged ≥14 years
2. Both genders
3. Patients who provide informed written consent to participate in the study
4. Patients with a duration illness of fewer than 5 days were included.

Exclusion Criteria:

1. Patients admitted with other causes of fever
2. Patients who did not provide informed consent.
3. Known case of chronic liver disease
4. Patients with a history of renal disease
5. Patients on oral steroids for more than 7 days
6. Patients treated with NSAIDs before admission

Study procedure: Detailed history was collected from all the patients including name, age, gender, date of onset of illness, and symptoms. Complete clinical examination was done for all the patients that included a general examination to identify pallor, icterus, signs of liver failure, etc. Systemic examination was also done to identify the presence of abdominal distension, pleural effusion, and other complications. Routine investigations including complete blood counts, platelet count, serum bilirubin, and liver enzyme assessment for SGOT, SGPT, and ALP were done. To identify the timeline of liver involvement, clinical examination and blood investigations were done daily for 1 week. The duration of follow-up in this study was 7 days after

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admission to the study center. A serial ultrasound examination was also done to identify the presence of peritoneal fluid for fluid leakage.

Statistical analysis: The statistical analysis was done using SPSS software version 21. Descriptive and inferential statistical analysis was done. Chi-square and Pearson Correlation tests were the statistical tests used to find the association between the outcome and independent variables. For all statistical tests, a p-value of <0.05 was taken as significant.

Results

A total of 50 patients with confirmed dengue were included in the study. The mean age of the patients infected with dengue included in the study was 39.8±15.9 years. The age of the participants was ranging from 14 and 67 years.

Among the total 50 study participants, 36 were males which accounted for 72% and the rest 14 (28%) were females.

Table 1: Clinical profile of dengue patients

Clinical finding	Number of participants	Percentage
Fever	50	100
Myalgia	50	100
Abdominal distension	29	58
Pleural effusion	6	12
Jaundice	32	64
Icterus	29	58
Signs of liver failure	33	66

Among the total 50 patients, everyone had a fever. Similarly, all the patients had complaints of myalgia. Out of the total 50 patients with dengue, 29 of them had abdominal distension which accounted for 58%. Six patients i.e., 12% of the patients with dengue had pleural effusion. Thirty two patients (64%) infected with dengue had jaundice. Signs of liver failure were observed among a total of 33 patients accounting for 66%. (Table 1)

The pulse rate of the patients was ranging from 70 to 100 per minute. The temperature of the patients was ranging between 99 and 101. The mean pack cell volume was 40.6±8.4 with a minimum of 16 and a maximum of 55. The average red blood cell count was 4.48±0.81 million which was ranging from 1.32 to 5.95 million. The mean platelet count was 91280±31516 and it was ranging from 30000 to 148000.

Table 2: Factors associated with elevated bilirubin level

Variables	Elevated n (%)	Normal n (%)	Total	Chi-square value	p-value
Age					
14 to 29 years	5 (31.2%)	11 (68.8%)	16 (100%)	5.1	0.07
30 to 49 years	8 (47.1%)	9 (52.9%)	17 (100%)		
≥ 50 years	12 (70.6%)	5 (29.4%)	17 (100%)		
Gender					
Female	8 (57.1%)	6 (42.9%)	14 (100%)	0.39	0.52

| Male | 17 (47.2%) | 19 (52.8%) | 36 (100%) | | |

*p values not significant

The mean serum bilirubin level was 1.79±1.5 with a minimum level of 0.3 and a maximum level of 6.7. Of the total 50 patients studied, 25 (50%) had normal serum bilirubin levels and the rest 25 (50%) had elevated levels of serum bilirubin.

The proportion of patients with elevated serum bilirubin increased with an increase in age. However, this difference was not significant. Though bilirubin was elevated more among females, the difference in proportion was not significant. (Table 2) With the use of the Pearson correlation test, there was no significant association between platelet count and serum bilirubin level.

Table 3: Factors associated with elevated SGOT

Variables	Elevated n (%)	Normal n (%)	Total	Chi-square value	p-value
Age					
14 to 29 years	16 (100%)	0	16 (100%)	6.9	0.031*
30 to 49 years	11 (64.7%)	6 (35.3%)	17 (100%)		
≥ 50 years	14 (82.4%)	3 (17.6%)	17 (100%)		
Gender					
Female	12 (85.7%)	2 (14.3%)	14 (100%)	0.18	0.67
Male	29 (80.6%)	7 (19.4%)	36 (100%)		

*p value significant

SGOT values was ranging between 21 and 332 with an average value of 114.3±95.5. Regarding SGOT levels, among the total dengue patients, only 9 (18%) had normal SGOT levels and in the remaining 41 (82%) patients it was elevated.

Table 3 describes the factors associated with elevated SGOT among dengue patients. SGOT was significantly elevated in both younger and older patients. Similar to serum bilirubin, SGOT was also higher in females without statistical significance. Pearson correlation test showed that SGOT was increased with a reduction in platelet count with an r-value of -0.48 and p-value of 0.0001.

Table 4: Factors associated with elevated SGPT

Variables	Elevated n (%)	Normal n (%)	Total	Chi-square value	p-value
Age					
14 to 29 years	13 (81.2%)	3 (18.8%)	16 (100%)	4.6	0.09
30 to 49 years	9 (52.9%)	8 (47.1%)	17 (100%)		
≥ 50 years	14 (82.4%)	3 (17.6%)	17 (100%)		
Gender					
Female	14 (100%)	0	14 (100%)	7.5	0.006*

Male	22 (61.1%)	14 (38.9%)	36 (100%)		

* p value significant

The mean SGPT level among the dengue patients included in the study was 71.3±41.3 which was ranging from 22 to 236. Among the 50 study participants, 14 (28%) had normal levels of SGPT and 36 (72%) of the patients had elevated SGPT.

Similar to the SGOT level, elevated SGPT level was noticed among young and older age groups compared to middle-aged patients. SGPT was elevated in all females compared to only 61% among males. (Table 4) Similar to SGOT, SGPT also increased with a reduction in platelet count with an r-value of -0.29 and a p value of 0.035.

Table 5: Factors associated with elevated ALP

Variables	Elevated n (%)	Normal n (%)	Total	Chi-square value	p-value
Age					
14 to 29 years	2 (12.5%)	14 (87.5%)	16 (100%)	1.09	0.58
30 to 49 years	2 (11.8%)	15 (88.2%)	17 (100%)		
≥ 50 years	4 (23.5%)	13 (76.5%)	17 (100%)		
Gender					
Female	2 (14.3%)	12 (85.7%)	14 (100%)	0.04	0.83
Male	6 (16.7%)	30 (83.3%)	36 (100%)		

*p values not significant

The mean level of the ALP enzyme was 118.4±115.7. The ALP level was ranging from 38 to 629. A total of 42 patients (84%) had normal ALP levels and the remaining 8 (16%) had elevated ALP levels. There was no significant association between age, gender, and ALP level. (Table 5) Pearson correlation did not show any significant association between platelet count and ALP.
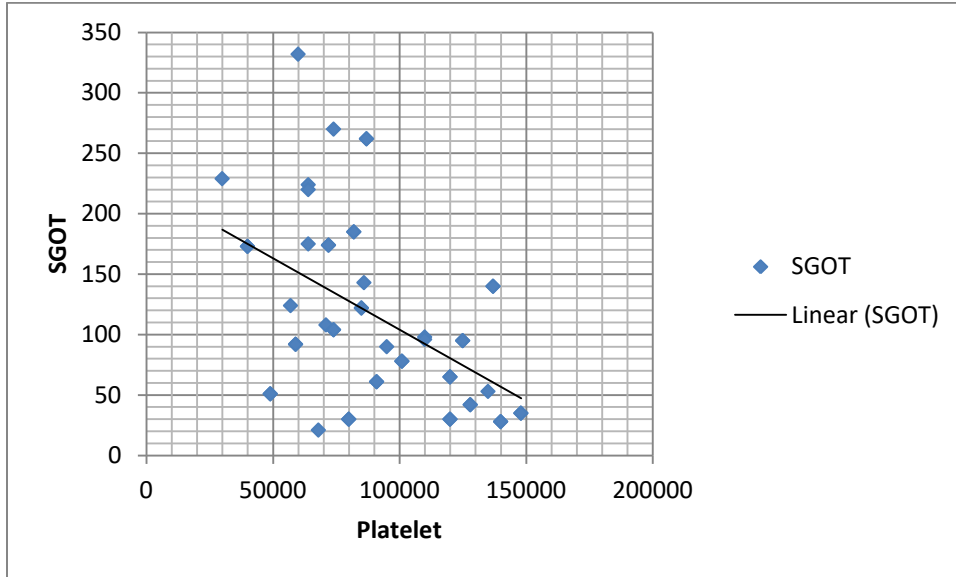
Scatter Plots

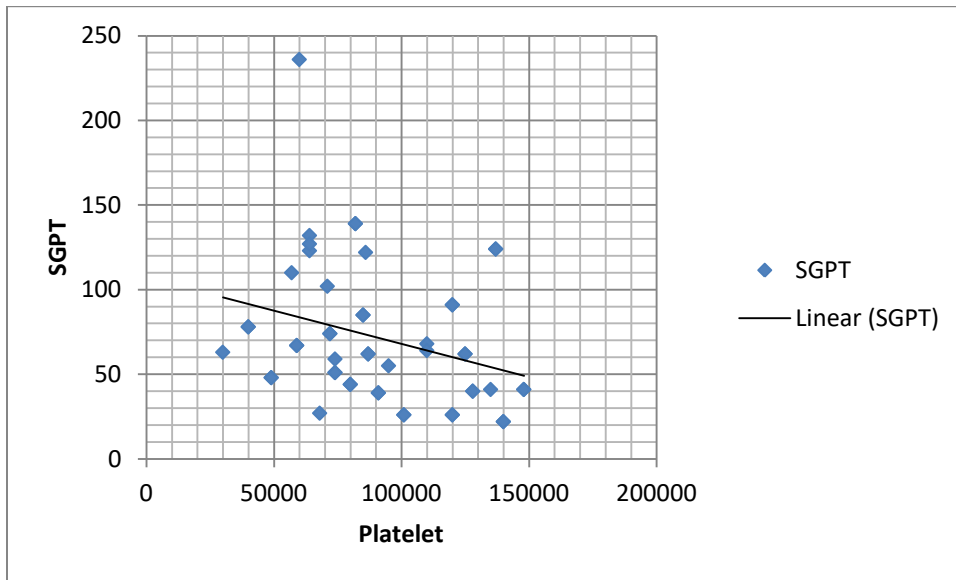**Graph :1 Association Between Platelet And Bilirubin Level**
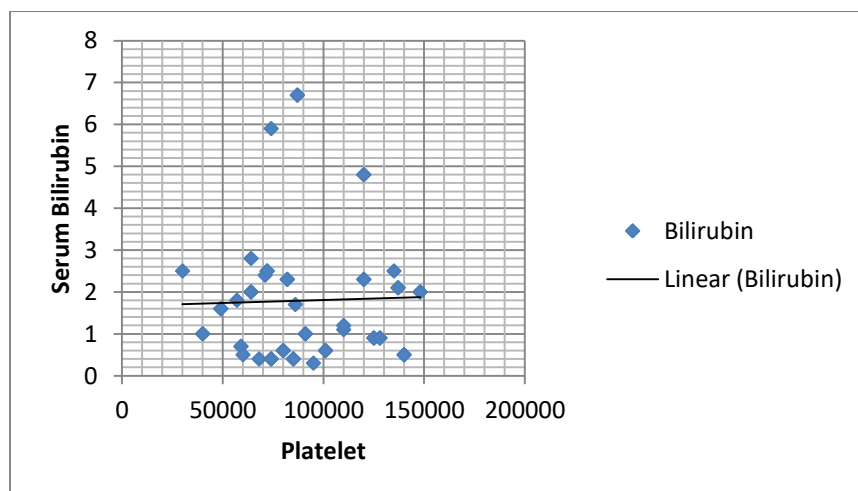
***p value not significant**

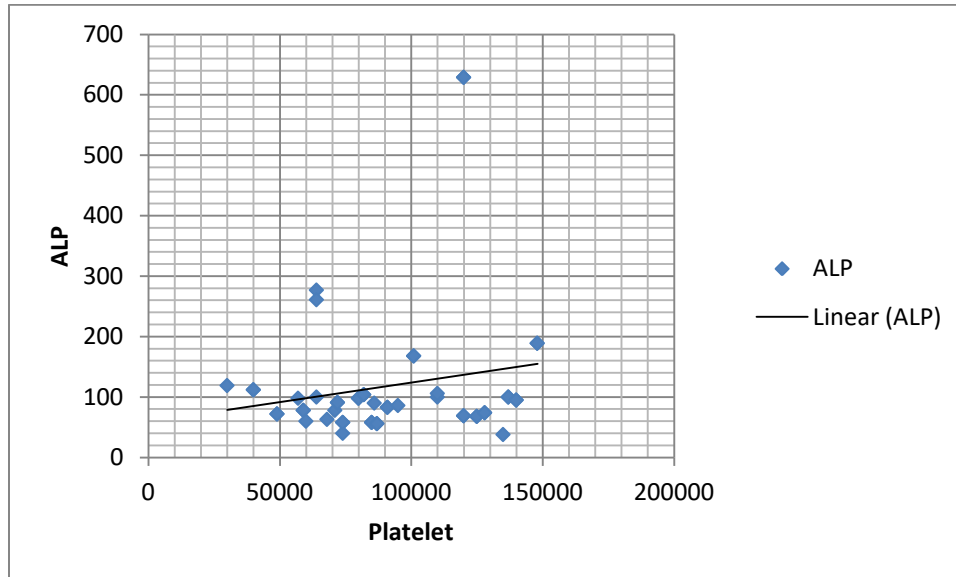**Graph :2 Association Between Platelet And Sgot**

*p value not significant

Graph :3 Association Between Platelet And Sgpt

*p value significant

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Graph :4 Association Between Platelet And Alp

*p value not significant

Discussion

The present study included 50 patients with dengue admitted to a tertiary care teaching hospital and they were assessed for the effect of dengue on liver function. In the present study, the mean age of the dengue patients was 39.8 years. In another study by Swamy et al, the mean age reported was 34.8 years which was lower than our study.[15] Similarly, another study done in India by China et al also reported lower mean age among dengue patients which was 31.6 years. In the current study, the majority of the dengue patients were males. Similarly, other studies by Swamy et al, Chhina et al also found a higher male preponderance.[15,]In the current study all patients presented with fever as reported by China et al.[16] In our study, myalgia was reported by 100% of patients which was higher than the proportion of 43%. This study found elevated serum bilirubin in 50% of the patients. The proportion is much higher than the studies by China et al, Narasimhan et al, Kuo et al, Itha et al, Wong et al, Trung et al, Saha et al where 5%, 19.5%, 7.2%, 30%, 13.4%, 1.7%, and 16.9% respectively had elevated bilirubin.[16-22]In the present study, SGOT was elevated in 82% of patients. Another study by Chhina et al reported a higher incidence of elevated SGOT levels which was found in almost 97%.[16] The proportion of dengue patients with elevated SGOT levels was ranging from 63% to 97%. However, most of the previously published studies reported elevated SGOT levels among more than 90%. We could also find such results in our study. We found elevated SGPT levels among 72% of the patients which was lower than the proportion reported by Chhina et al in which almost 94% has elevated SGPT.[16] Elevated SGPT levels as reported by Kuo et al, Wong et al, Souza et al, Lee et al, Parkash et al and Trung et al were 45%, 46%, 71.7%, 82.2%, 86%, and 97% respectively.18,20,24,25,26,21] Thus, the findings of our study correlate with the findings of other such studies. Elevated ALP level was present in 16% of patients with dengue in our study which was lower than the proportion of 32% reported by Chhina et al.[16]The most common derangement in liver function parameters found in this study was SGOT compared to SGPT, ALP, and bilirubin (82% vs 72% vs 16% vs 50%). This result is consistent with the findings of other study reports published by Kuo et al, Itha et al, Trung et al, Parkash et al, Wong et al, Karoli et al, lee et al and Souza et al who also noticed the highest elevation in SGOT compared to other parameters.[18-21, 23-25] In our study, we could find that liver enzyme were elevated among patients with low platelet count. This is concurrent with the findings of Swamy et al who also reported such findings.[15]

Conclusion

In the present study it was found that liver function was affected in dengue patients with an increase in

serum bilirubin, and elevated liver enzymes like SGOT, SGPT, and ALP. This elevation in liver enzymes and bilirubin was high when the platelet count was less which indicated that when the disease severity is more, dengue leads to a higher impact on liver function. The cause of liver failure in acute dengue infection may include hypoxic injury due to decreased perfusion, direct damage by the virus, and immune-mediated injury. Other causes can include pre-existing liver injury and hepatotoxic drugs. Hence, it is advisable to perform liver function tests among dengue patients when their platelet counts are reducing.

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