

Relationship Among Alanine Amino-Transferase (ALT), Partial Thromboplastin (APTT) and Electrolyte Levels in Dengue Fever Positive Patients of Rawalpindi District

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Abstract: Dengue fever (DF) has become a major public problem in recent years and it is more frequent in tropical and subtropical regions and most commonly in urban and peri-urban areas, caused by Dengue virus which belongs to the family Flaviviridae. The present study was designed to find out relationship among blood biochemical parameters i.e. ALT, APTT and electrolytes and to study their association with age. Blood of serology positive Dengue fever patients was collected for measurement of values of ALT, APTT and electrolytes. The data was analyzed by using SPSS 16 and cross tabulation and Pearson Chi-Square test was employed to find out significant relationship among variables. Laboratory hematological findings in dengue fever were thrombocytopenia, leucopenia, neutropenia, APTT and raised hematocrit values. There was significant rise in blood biochemical parameter like ALT which is suggestive liver damage in disease. It was observed that ALT levels were significantly related ($P=0.01$) with age while there was no significant relationship between age and APTT values. Similarly ALT and APTT levels were significantly correlated ($P=0.001$) with each other. A significant relationship ($P=0.03$) was observed between Sodium ions and ALT/APTT levels and between Potassium ions and APTT levels ($P=0.04$) while no significant relationship was observed between Potassium and ALT levels and similarly Chloride with ALT/APTT levels. It is concluded that patients of middle and higher age and having previous history of liver disease should be especially monitored for liver functioning when admitted with confirmed Dengue fever.

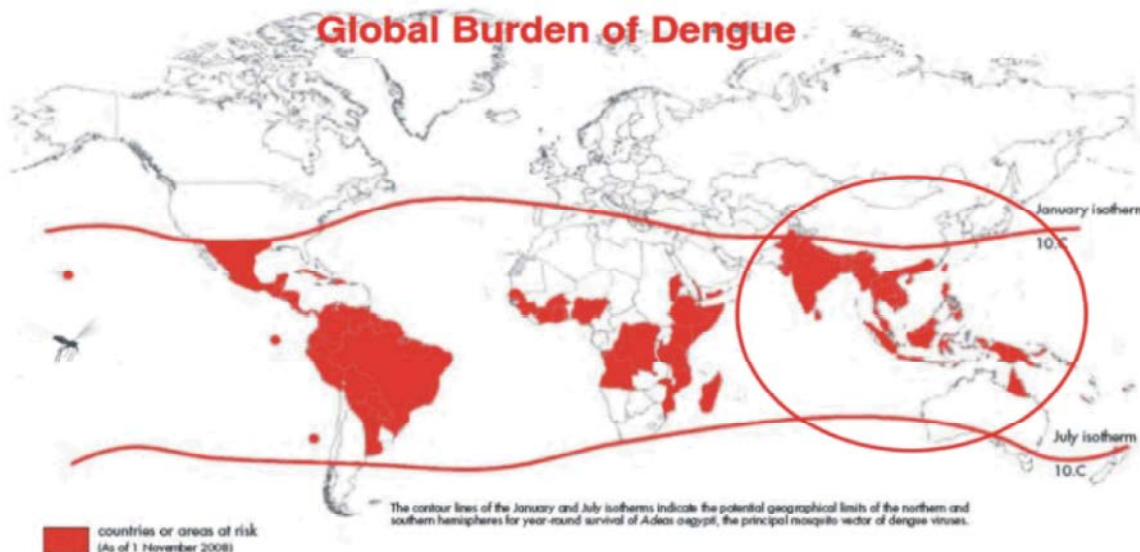
Key words: Dengue • ALT • APTT • Hematocrit • Thrombocytopenia

INTRODUCTION

Pakistan is one of the WHO East Mediterranean Region country in which dengue fever is a major public health issue and has faced first confirmed outbreak of dengue haemorrhagic in 1994, later on DEN-3 and DHF was first reported in 2005. Dengue outbreak has been reported with expansion of infection with increased frequency and severity from the large cities of Pakistan in

2008. Ministry of health Pakistan reported 1500 laboratory confirmed cases of dengue fever including the 15 deaths to WHO on 25 October 2010 [8].

Dengue fever is caused by Dengue virus which belongs to the family Flaviviridae and genus Flavivirus. It has four different serotypes DEN-1, DEN-2, DEN-3, DEN-4 which are antigenically similar to each other with some exception [4]. A person recovers from the infection of any one serotype of dengue virus become immune



Global distribution of Dengue Fever (WHO, 2009)

permanently for that serotype and may become partially immune, temporarily immune or both for the other serotypes [5].

Hematological abnormalities among the dengue patient are varying from mild to severe. Laboratory hematological findings associated with dengue fever are thrombocytopenia (Platelet count below 50,000/ul) leucopenia (Leukocyte count 4000/ul or below) and neutropenia, prolonged activated partial thromboplastin time and raised hematocrit values. Mean hemoglobin and hematocrit values are usually normal. In dengue fever patients there is significant rise in biochemical parameters of the blood like ALT, APTT and electrolytes. Alanine Amino-transferase is related with liver parenchymal destruction and results in Acute Liver failure. Dysfunctioning of liver results in decreased production of protein and clotting factor due to which APTT may be observed [6].

Acute liver failure in association with Dengue haemorrhagic fever was initially reported during the epidemics in Indonesia in the 1970s. Later, it was reported during the 1987 epidemic in Thailand and the 1990 epidemic in Malaysia. Dengue virus serotypes DEN-1, 2 & 3 have been isolated from the patients dying from liver failure with both primary and secondary dengue infections. Dengue antigens have been detected in hepatocytes, in Kupffer cells and occasionally in acute inflammatory cells in these patients [7].

A research reported that in DHF the average levels of AST and ALT are greater than in classic dengue fever. There is greater hepatic injury among patients with

sequential infections of dengue virus (IgG positive) and in cases of hemorrhagic dengue [9]. The main objective of the current study is to study relationship among Alanine Amino-transferase (ALT), APTT and electrolyte levels in Dengue Fever serology positive patients and its correlation with age. This relationship will help to understand the progression of disease in age groups.

MATERIAL AND METHODS

Place of Research: The study was carried out in Tertiary Care hospitals of Rawalpindi.

Population Concerned: Study was focused on patients with febrile condition admitted as suspected Dengue Fever patients.

Sample Size: Data of 115 patients admitted as serology tests confirmed dengue fever cases in Tertiary Care hospitals of Rawalpindi was taken.

Inclusion Criteria: Patients with Dengue Fever confirmed by ELISA test were included in this study.

Exclusion Criteria: Patient with symptoms like dengue fever and not confirmed by ELISA test were excluded from the study.

Sample Collection: Blood samples were collected by venipuncture technique and blood collected in APTT and gel tubes.

Sample Processing: Blood serum of suspected dengue fever patients was collected for confirmation of Dengue Fever employing immunosorbant assay (ELISA) [10]. Furthermore, blood serum was analyzed for Alanine Amino-transferase (ALT) Spectrophotometry (kinetic method) to investigate effect of dengue virus on liver functioning [11] and serum Electrolyte by using (Equipment: BACKMAN COULTER CX-9). Citrated plasma was used for the analysis of partial thromboplastin time analyze on Semi-automated instrument KC 4 Amelung (Biotech) [6].

Statistical Analysis: SPSS 16 a statistical tool was used for analysis of data, and cross tabulation and chi-square test were employed to find out association between the study variables having significance level at $\alpha=0.05$ and 95% confidence interval.

RESULTS AND DISCUSSION

Total 115 No. (N=115) serology test positive patients were included in this study and out of these 92 patients (80%) were males and 23 patients (20%) were females. Proportion of patients in different age groups is shown in (Table 1).

Fever was most common symptom of presentation found in 115 patients (100%), body pain was present in 73 patients (63.56%) and vomiting was found in 67 patients (58.3%) (Table 2).

Pearson Chi-square test was used to find out association among age and ALT levels of the patients with 95% confidence interval and $\alpha=0.05$. Analysis of the study data showed highly significant association among the age and ALT levels (Table 3-a). Patients having 21-40 years of age had higher level of ALT as compared with other age groups. (Figure 1 indicates different age groups and corresponding level of ALT). While no significant relationship between age and APTT was observed (Table 3-b).

Statistical analysis of study data of ALT and APTT levels with help of Pearson Chi-Square test showed highly significant association ($P=0.01$) between ALT and APTT levels (Table 4). Figure 2 illustrates significant association between ALT and APTT Levels. It was observed that with the increase of ALT levels APTT levels also increase.

According to the WHO, Acute Liver failure was reported initially in Indonesia in 1970s. Later, it was reported in Thailand in 1987 dengue epidemic and in 1990 epidemic in Malaysia. WHO 1997 reported that Dengue antigens had detected in hepatocytes and in Kupffer cells,

Table 1: Distribution of gender in age groups

Age and Sex Crosstabulation			
		F	M
Age	1-20 years	7	17
	21-40 years	12	63
	41-60 years	4	11
	60-Above years	0	1
Total		23	92

Table 2: Clinical symptom

Symptom	Count	Percentage %
Fever	115	100
Body Pain	73	63.5
Vomiting	67	58.3
Bleeding	43	37.4
Headache	4	3.5

Chi-Square Tests

Table 3a: Association between the age and ALT levels of patients

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	15.486 ^a	6	.017
Likelihood Ratio	15.859	6	.015
N of Valid Cases	115		

Table 4: ALT and APTT association

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	82.159 ^a	4	.001
Likelihood Ratio	80.965	4	.001
N of Valid Cases	115		

Table 5: Sodium and ALT levels association

Chi-Square Tests			
	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.842 ^a	2	.012
Likelihood Ratio	8.909	2	.012
N of Valid Cases	115		

Table 6: Sodium and APTT association

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.941 ^a	2	.031
Likelihood Ratio	7.354	2	.025
N of Valid Cases	115		

Table 7: Potassium and ALT association

Chi-Square Tests	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.326 ^a	2	.115
Likelihood Ratio	4.545	2	.103
N of Valid Cases	115		

Table 8: Potassium and APTT association

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.484 ^a	2	.039
Likelihood Ratio	7.526	2	.023
N of Valid Cases	115		

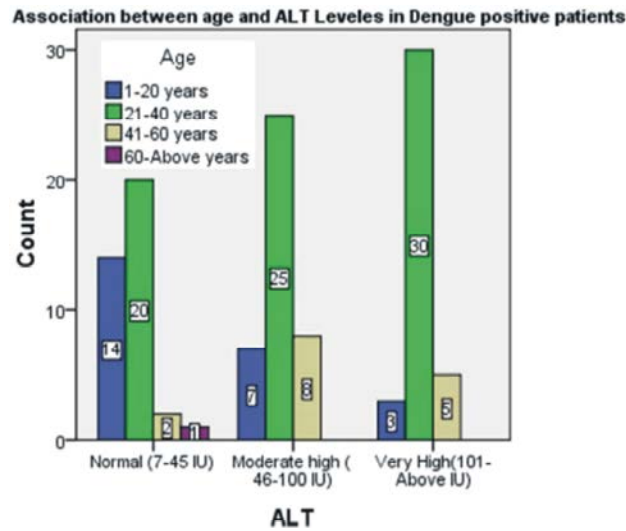


Fig. 1: ALT association with age

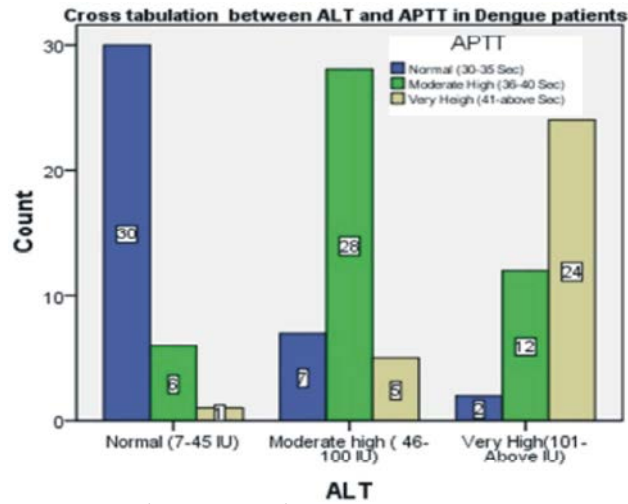


Fig. 2: Cross tabulation between ALT and APTT Levels2

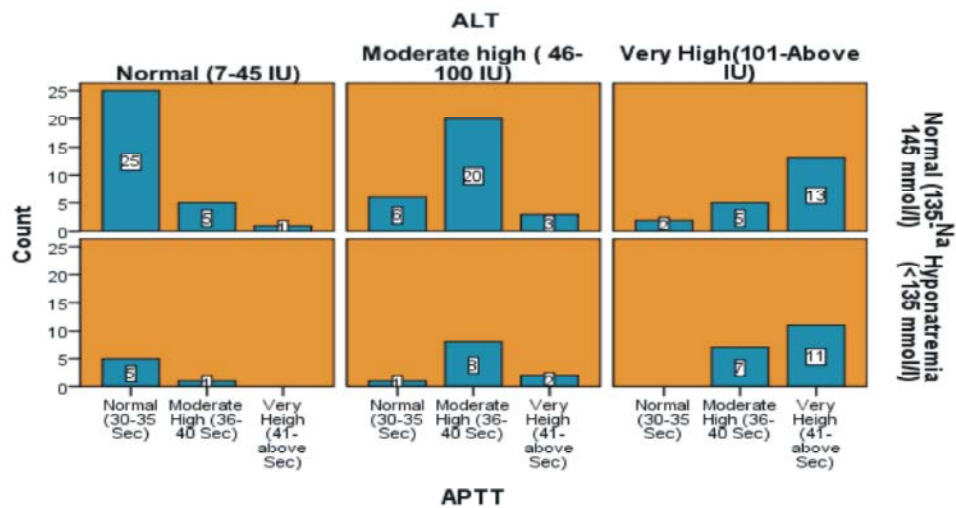


Fig. 3: Sodium Correlation with APTT and ALT

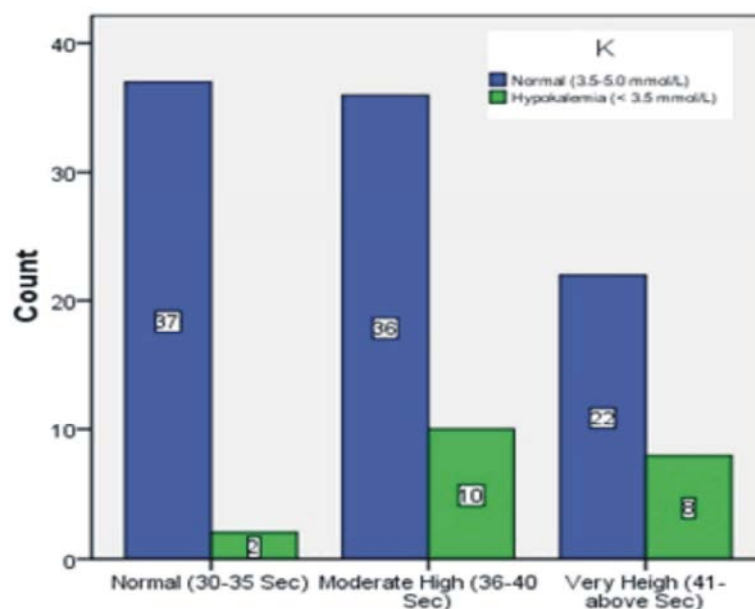


Fig. 4: Association between APTT and Potassium

similar studies were carried out by “Vinodh *et al.*,” “Pichardo *et al.*” and “Seneviratne *et al.*” [12-14]. The finding of our study sure that levels of ALT are higher which means that Liver is also affected with Dengue virus infection that result in increased level of APTT, These results are in line with other researcher carried out in different parts of world.

Among blood electrolytes Sodium ions (Na⁺) showed significant relationship with ALT and APTT levels (Table 5 & 6) and Figure 3 shows significant association (P=0.03) of ALT and APTT levels in the patients with hyponatremia. In 38 patients ALT levels were very high and out of these 18 patients (47.4%) showed hyponatremia. While in 40 cases ALT levels were moderately high and out of these 11 patients (27.5%) were present Hyponatremia. APTT levels were very high in total 30 patients out of which in 13 patients (43.3%) were hyponatremic and total 46 cases showed moderate levels of APTT out of which 16 patients (34.8%) were present with Hyponatremia.

There was no significant association between Potassium ions (K⁺) and ALT levels (Table 7) but there was significant association (P=0.04) between K⁺ and APTT levels (Table 8). The level of confidence interval was 96%.

It is hypothesize the low levels of Na⁺ and K⁺ due to infusion which were given immediately after the admission of the patients. So due to haemodilution Sodium levels were decreased that have association with ALT and APTT (Fig. 2). Hypokalemia have significant association with APTT because it is one of the clotting factors that

why APTT was observed high in hypokalemia patients. The Figure 4 shows significant association of Potassium ions and APTT levels. Out of total 30 patients with very high values of APTT 08 patients showed hypokalemia and out of 46 patients with moderate levels of APTT 10 patients (21.7%) were presented with hypokalemia, Chloride ions (Cl⁻) has no significant association with ALT and APTT and other variables. Normal chloride level found in 91 patients (79.1%) of total population (N=115), 19 patients (16.5%) were hyperchloremic and 5 patients (4.3%) were having hypochloremia (<96 mmol/l) (Figs. 2, 3).

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