ORIGINAL ARTICLE

Use of Alanine Aminotransferases Level and Platelet Count to Predict Dengue Fever Severity

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ABSTRACT

Objective: To determine the use of raised Alanine Aminotransferases and low platelet count as predictors of dengue fever severity.

Study Design: Cross sectional observational study.

Place and Duration of Study: Department of Medicine District Headquarter Hospital Rawalpindi, from 1st August 2014 to 31st December 2014.

Materials and Methods: Diagnosed cases of dengue fever based on history, examination and positive non structural protein 1(NS 1) antigen were included consecutively. Platelet count and Alanine Aminotransferases level were performed on admission. Patients were classified into different groups on the basis of Alanine Aminotransferases level and Platelet count. Disease severity and outcome was observed as; having dengue without complications, dengue hemorrhagic fever and dengue shock syndrome. The relationship of Aminotransferases levels and Platelet count were studied with the disease severity. The statistical analysis of data was done in SPSS version 20.

Results: Among 124 confirmed dengue fever cases, 66.9% were males and 33.1% females with mean age of 30.79+13.78 years. Mean duration of fever was 5.59+1.32 days and mean duration of hospital stay was 3.74+1.04 days. Elevated Alanine level was found in 89.5%. Thrombocytopenia was observed in 99.58% patients. Most of our patients were found to have dengue fever without complications, only 20.2% developed dengue hemorrhagic fever and 11.3% developed dengue shock syndrome.

Conclusion: Neither Alanine Aminotransferases, nor low platelet count can predict the severity of Dengue fever.

Key Words: *Alanine Aminotransferases, Dengue Fever, Platelet Count.*

Introduction

Dengue fever is an acute febrile illness of viral etiology, and currently it is the most common cause of arthropod borne viral disease globally.[1] Dengue virus belongs to the Flaviviridae family with 4 serotypes. The disease is endemic in over 100 countries, including Pakistan; around 2.5 billion people are at increased risk of infection worldwide.[2,3] About 390 million cases of Dengue fever occur annually and 96 million develop severe Dengue[4], causing 20,000 deaths every year in developing countries.[5] Mortality is high in patients developing dengue hemorrhagic fever or dengue shock syndrome, mortality is as high as 20% in severe dengue if untreated.[6] It is thought that development of severe dengue and evolution to death is related to some clinical and laboratory findings that are still not fully understood.[7] Its first outbreak in Pakistan was reported in 1994 and it has become a major health problem in Southeast Asia with 2-3 epidemics every year.[8]

Dengue virus is transmitted to humans by bites of infected female Aedes mosquito.[1] Infection with dengue virus can present after 5-7 days of mosquito bite with high grade fever, rash, severe headache.[9] Other symptoms include severe joint and muscular pain, nausea, vomiting, and eye pain. Illness ranges from a mild, non-specific febrile syndrome to classic dengue fever (DF), to the severe forms of the disease, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[10] In 2009 WHO classified dengue according to levels of severity based on clinical and laboratory parameters.[11] This classification may help in clinical management of patients but the parameters of the severity used in this classification

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may vary according to different epidemiological settings.[12]

The identification of some clinical as well as laboratory parameters that can serve as early predictors of severe Dengue is important to reduce the morbidity and mortality of Dengue fever. Many studies has been conducted to find the predictors of mortality in severe Dengue, gastrointestinal bleeding, hematuria, thrombocytopenia, dyspnea at rest, late presentation in hospital, age ≥ 50 years and high hematocrit were found as risk factors for increased mortality in severe Dengue.[13,14,15] Few studies has also been conducted to indentify the early predictors of severe Dengue, high Lactate Dehydrogenase, high Lactate[16] and Ferritin[17] levels were found as early predictors of severe Dengue at the time of hospital admission.

Raised Alanine Aminotransferases levels (ALT) and low platelet count are the most consistent laboratory findings in patients of Dengue fever.[18] This observation leads to the idea that raised Aminotransferases levels and thrombocytopenia may serve as early predictors of severity in the patients of dengue fever. The objective of this study was to evaluate Aminotransferases levels and platelet counts of the patients admitted with dengue fever as early predictors of dengue fever severity.

Materials and Methods

It was a cross sectional observational study conducted at Department of Medicine, District Head Quarter Hospital Rawalpindi, from 1st August 2014 to 31st December 2014. All diagnosed cases of Dengue fever, both males and females, from all age groups admitted in Dengue ward were included by convenient sampling. Patients with any of the following conditions were excluded: positive HBsAg or Anti-HCV antibodies, history of acute viral hepatitis in previous 3 months, history of idiopathic thrombocytopenia, those who had taken hepatotoxic drugs for any other illness in previous three months and DHF or DSS at the time of presentation. The diagnosis was suspected on the basis of two or more of the following symptoms: fever, headache, retro-orbital pain, myalgias, arthralgias, skin rash, nausea, vomiting, prostration and hemorrhagic manifestations, and confirmed by positive non-structural protein 1 (NS1) ELISA based antigen test as NS1 assay holds promise in early diagnosis of dengue infection.[19]

Patients were included consecutively, before enrollment; informed consent was taken from each patient. Ethical approval was obtained from Departmental Ethical Committee in this regard. Development of severe dengue (DHF, DSS) or discharge from the hospital without complications was the end point of the study.

Data was collected on a specially designed form. Platelet count and ALT levels were performed for all the patients on admission and were noted. Patients were classified into three groups on the basis of ALT level. Patients with normal ALT levels (6-39 IU/L) were included in Group-1, patients with level of ALT up to three times the normal value (40-127 IU/L) in Group-2 and those having ALT level above three times of normal (>127 IU/L) were classified as Group-3.On the basis of platelet count, patients were divided into four groups; those with platelet count more than 100,000/mm3 were classified as Group-A, count between 50,000 to 100,000/mm3 in Group-B, count between 20,000 to 50,000/mm3 in Group-C and count less than 20,000/mm3 were included in Group-D.

During hospital stay patients were monitored for the development of severe dengue. Severity was defined as presence of complications of dengue fever in the form of Dengue Hemorrhagic Fever or Dengue Shock Syndrome; both also known as Severe Dengue[11] Patients were later divided into three groups on the basis of disease severity and outcome observed; having dengue without complications; dengue hemorrhagic fever; and dengue shock syndrome. The relationship of ALT levels and platelet count were studied with the disease severity, development of complications and duration of hospital stay.

The statistical analysis of data was done in SPSS for Windows, version 20. Means and standard deviations were calculated for age, duration of fever at the time of presentation and duration of hospital stay. Frequency was used to calculate percentage for qualitative data like gender. Chi square test was used to compare categorical variables and to determine the relationship of ALT levels and platelet count with outcome of dengue fever. P values less than 0.05 were considered as significant.

Results

Total 124 confirmed dengue fever cases were

included in our study. Out of these 66.9% (n=83) were males and 33.1% (n=41) were females with mean age of 30.79 + 13.78 years (range 10 – 76 years). Fever was common presenting symptom in all the patients with mean duration of 5.59 + 1.32 days (range 2 – 11 days). The mean duration of hospital stay was 3.74 + 1.04 days (range 2 – 7 days).

Out of 124 patients only 20.2% (n=25) developed dengue hemorrhagic fever and 11.3%(n=14) developed dengue shock syndrome, with no significant correlation of severity of Dengue fever with Alanine Aminotransferase levels and Platelet count, shown in table I and II.

Table I: Correlation of ALT Levels with Severity of Dengue Fever

	ALT level (IU/L)			(p-value)
	7-39	40-127	>127	
Without complications	10	46	29	.733
Dengue Hemorrhagic Fever	3	14	8	
Dengue Shock Syndrome	0	8	6	
Total	13	68	43	

Table II: Correlation of Platelet Count with Severity of Dengue Fever

	Platelet count (cells/mm^3)				(p-value)
	> 100,000	50,000 – 100,000	20,000 – 50,000	<20,000	
Without complications	14	38	28	5	.513
Dengue Hemorrhagic Fever	2	10	10	3	
Dengue Shock Syndrome	1	4	8	1	
Total	17	52	46	9	

Discussion

Thrombocytopenia and raised ALT were two consistent findings in our study. But we did not find any significant relation between ALT levels at admission and development of DHF or DSS during hospital stay or with the duration of hospital stay. Also no such relation was found with platelet count.

Dengue is a common mosquito born infectious disease in many countries. In Asian countries dengue is more prevalent among males, many studies from Asian countries show male predominance.[20] Our results are in accordance with previous studies. Local studies also have almost same results.[17] But these results are in contrast with the studies from South America where male and females were equally affected.[20] This difference may be due to exposure difference among male and females in Pakistan and other Asian countries. Yew et al suggested that this may be due to difference in use of health facilities among two genders.[21]

Elevation of Aminotransferases and reactive hepatitis is a common complication of dengue infection[22], we found same. Our results are consistent with previous study by Kittitrakul et al who found raised AST and ALT levels in 88.2% and 69.3% of the patients, respectively.[23] Another study conducted in Vietnam showed raised ALT level in 97% patients also comparable with our results.[18] Though ALT levels were higher in majority of the cases in our study but raised ALT level was not found as an independent predictor of severity in our study. Same was concluded earlier by Villar-Centeno et al and Chhina et al.[24,25] Some other studies done by Khan et al and Ahmad A et al had different results. They showed that AST and ALT were statistically higher in patients with worse outcome thus can lead to early recognition of high risk cases.[8,26]

Thrombocytopenia is usually observed by 3rd or 4th day of the illness in dengue fever but is a constant feature and one of the diagnostic criteria of dengue hemorrhagic fever.[27]Thrombocytopenia was found in different national and international studies supporting our findings. Khan DM et al found thrombocytopenia in 71% patients in a study conducted in India.[28] The thrombocytopenia in Dengue may be due to decreased production of platelets due to bone marrow suppression.[27]

No significant correlation was found between degree of thrombocytopenia and severity of illness in our study. These results are contrary to the observation by Jayashree K, et al who stated that thrombocytopenia and platelet count is predictive as well as a recovery parameter of DF/DHF/DSS.[29] But another study conducted in Malaysia showed no relation between platelet count and hemorrhagic manifestations in dengue fever supporting our findings.[30]

The mean hospital stay reported in our study was 3.74 days. Various studies done at national and international level reported a mean stay of 3.4-6.2

days which are comparable to our results.[31] The duration of hospital stay had no significant correlation with severity of liver involvement or degree of thrombocytopenia in our study. Ahmad A et al had different results; they showed in their study that ALT level was significantly related with duration of hospital stay.[8]

Our study is subject to some limitations. First, our study included patients only at one hospital in Rawalpindi. Additionally, we enrolled patients with variable duration of fever at the time of presentation which may affect the laboratory investigations, however all the patients were enrolled before the development of complications. Furthermore, ALT level and platelet counts were not performed serially for every patient. Further studies should be conducted in other dengue endemic regions to establish the early predictors of dengue fever severity.

Conclusion

Neither Alanine Aminotransferase, nor low platelet count can predict the severity of Dengue fever. However more large scale multi-centre studies are required to confirm our findings.

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