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ORIGINAL ARTICLE

THE SIGNIFICANCE OF ELEVATED ASPARTATE AMINOTRANSFERASE-ALANINE AMINOTRANSFERASE (AST-ALT) RATIO TO PROGNOSTICATE THE OUTCOME IN PEDIATRIC PATIENTS WHO WERE ADMITTED FOR DENGUE SHOCK SYNDROME (DSS) IN A TERTIARY HOSPITAL

ABSTRACT

Objectives: AST and ALT often rise in dengue patients up to five-fold; they usually peak in the second week of illness. This study aims to determine the significance of elevated AST, ALT; AST:ALT ratio among pediatric patients with Dengue Shock Syndrome(DSS).

Methods: From October 2008 to October 2009, 57 pediatric patients, who met the criteria for DSS, were admitted in the ICU. AST, ALT and AST:ALT determinations were done upon admission.

Results: The differences in the elevation of AST, ALT and AST:ALT in relation to age and sex of patients were not statistically significant (p-value= >0.05). A significance was noted in the ALT elevation when correlated to BMI (p-value 0.04) as opposed to only a marginal significance with AST. The more obese the patient, the higher the increase in the level of serum transaminases. There was only marginally significant difference in the elevation AST:ALT ratio according to BMI (p-values 0.06 and 0.09 respectively). A 4-fold increase in both AST and ALT were not significantly associated with the presence or absence of hepatomegaly (p-value = >0.05). However, there was a significant difference noted in the AST:ALT ratio according to outcome -- those who died had an elevated mean ratio than those who survived (p value = 0.01). On the other hand, there was a marginally significant difference in the AST elevation according to outcome (p value = 0.08). A four-fold increase in both AST and ALT were significantly associated with mortality (p-values 0.004 and 0.03 respectively).

Conclusion: AST and ALT elevation of >4-fold may prognosticate the outcome of patients with DSS. Further investigation is required.

KEYWORDS:

dengue shock syndrome, severe dengue, dengue hemorrhagic fever

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INTRODUCTION

In the Philippines, 21,690 cases of dengue has been reported from January to May 2014[1]. Fortunately this is 50% lower than the cases reported for the same time period in 2013. The deaths record in the same time period in 2014 was 91, which was only one half that reported in 2013 at 185 deaths.

One of the causes of mortality among pediatric patients with dengue shock syndrome is hepatic encephalopathy and acute liver failure. Therefore, there is a need to further understand the correlation of elevated AST, ALT and AST:ALT ratio among these patients so as to anticipate subsequent complication and to give prompt management.

This is a cross-sectional analytic study that aims to determine the significance of elevated AST, ALT; AST-ALT ratio among pediatric patients with dengue shock syndrome.

METHODS

This study was conducted at the Hospital of the Infant Jesus in Manila, Philippines from October 2008 to October 2009.

All pediatric patients aged 0-20 years who met the criteria of dengue shock syndrome were included in the study. Dengue patients with hepatomegaly and hepatic encephalopathy were also included. Determination of AST, ALTS levels, AST-ALT ratio was done upon admission regardless of the day of illness. All patients were promptly managed according to the hospital protocol on management of dengue shock syndrome. This included purely supportive treatment of dehydration, shock, and hemorrhagic manifestations; control of temperature, oxygenation, good nursing care, monitoring and treatment of complications.

Analysis of Data

Data were encoded and tallied in SPSS version 10 for windows. Descriptive statistics were generated for all variables. For nominal data, frequencies and percentages were computed. For numerical data, mean ± SD were generated. Comparison of the different variables under study was done using the following test statistics: *T test* was used to compare two groups with numerical data (compares means). ***Mann Whitney U test*** and ***ANOVA Fisher Exact test*** is were also used where is was appropriate.

RESULTS

In our hospital, during the one-year period of study, there were 160 pediatric patients admitted due to dengue shock syndrome. From this population, only 57 participated in the study. Fifty-three (93%) survived while four (7%) out of 57 (100%) patients died. Among those who died, one (1.75%) died due to dengue shock syndrome grade III with hepatic encephalopathy and septicemia; one (1.75%) due to dengue shock syndrome with ascites, pleural effusion, bilateral and carditis; and two (3.5%) due to dengue shock syndrome grade IV. The surviving patients made a complete recovery within a mean duration of 6 days of stay in the hospital.

Population Profile: The patients' age ranged from 2-20 years old. The most number of patients admitted for dengue shock syndrome belongs to the age bracket of six-to-ten years old. Thirty-one (54.3%) of the study population were females while 26 (45.6%) were males. Thirty-five (61.4%) had normal body mass indices, 18 (31.6%) are overweight/obese and four (7.0%) were underweight. Eighteen (31.6%) who had dengue shock syndrome were admitted on the fourth day of illness while 17 (29.8%) were admitted on the fifth day of illness. The mean duration of fever of patients who had dengue shock syndrome is seven days. Four out of 57 patients died due to dengue shock syndrome and its complications.

A summary of the means of hematologic parameters are seen in Table 2.

Elevated AST, ALT; AST-ALT Ratio In Relation To Different Patient Variables

Age

Having various age groups in our subjects, the results showed that there was no significant difference in the elevation of AST, ALT and AST-ALT ratio noted as proven by all p values >0.05.

Table 1. Demographic Profile of Children With Dengue Shock Syndrome

	Frequency (n= 57)	Percentage
Age (years)		
≤5	11	19.3
6 – 10	27	47.4
11 – 15	14	24.6
16 – 20	5	8.8
Mean age ± SD	9.76 ± 4.38	
Sex		
Female	31	54.4
Male	26	45.6
BMI		
Underweight	4	7.9
Normal	35	61.4
Overweight/Obese	18	31.6
Day of Illness on Admission		
1	3	5.3
2	1	1.8
3	5	8.8
4	18	31.6
5	17	29.8
6	8	14.0
7	4	7.0
8	1	1.8
Mean day of illness ± SD	4.58 ± 1.45	
Duration of Fever (no. of days)		
3	6	10.5
4	12	21.1
5	13	22.8
6	9	15.8
7	17	29.8
Mean duration of fever ± SD	5.33 ± 1.38	

There was no significant difference in the elevation of AST, ALT, AST:ALT ratio in relation to being a male or a female as proven by all p values of > 0.05.

Among our subjects, four were underweight, 35 were well nourished, eight were overweight and ten were obese. The results showed that there was a significant difference noted in the ALT elevation according to BMI as proven by the p-value of 0.04. The median ALT of overweight/obese subjects was significantly higher than those of the underweight or normal BMI. On the other hand, there was a marginally significant difference in the elevation of AST and AST:ALT ratio according to BMI as shown by the p values 0.06 and 0.09 respectively. (see Table 4)

Table 2. Mean and Standard Deviation of the Blood Parameters of the Subjects

Variable	Mean ± SD
Hb	13.5 ± 1.71
Hct	41.4 ±7.57
WBC	5.16 ± 2.96
Platelet count	89,250 ± 58,368.8
Protime	14.78 ± 3.383
Partial thromboplastin time	66.46 ± 20.57
ALT	165.57 ± 168.739
AST	357.15 ±558.208
AST:ALT Ratio	2.10 ± 0.882

Table 3. Comparison of the Elevated AST, ALT and AST-ALT Ratio According to Age Groups

Age in Years	AST (Mean ± SD)	ALT (Mean ± SD)	AST:ALT Ratio (Mean ± SD)
≤5	299.72 ± 127.34	145.27 ±86.83	2.32 ± 0.58
6 – 10	298.00 ± 271.92	157.39 ± 142.16	1.97 ± 0.89
11 – 15	493.92 ± 1064.54	180.64 ± 272.53	2.26 ± 1.06
16 – 20	420.00 ± 234.64	212.20 ± 43.63	2.25 ± 0.89
P value	0.46	0.24	0.53

Table 4. Comparison of the Elevated AST, ALT and AST-ALT Ratio According to Body Mass Index (BMI)

BMI	AST (Mean ± SD)	ALT (Mean ± SD)	AST:ALT Ratio (Mean ± SD)
Underweight (n= 4)	106.25± 32.67	47.00 ± 11.97	2.23 ± 0.46
Normal (n=35)	444.11 ± 690.00	187.66 ± 201.31	2.28 ± 0.84
Overweight & Obese (n=18)	243.83 ± 173.35	148.98 ± 90.04	1.73 ± 0.94
P value	0.06	0.04	0.09

Table 5. Association of the Increase in AST and ALT with Hepatomegaly

	AST		ALT		AST:ALT	
	< 4-fold increase	> 4-fold increase	< 4-fold increase	> 4-fold increase	<2	>2
With hepatomegaly	22	5	25	2	10	17
Without hepatomegaly	28	2	27	3	15	15
P value	0.23		1.00		0.32	

Table 6 shows the comparison of the elevated AST, ALT and AST:ALT ratio according to outcome. The results showed that there was a significant difference noted in the AST:ALT ratio according to outcome as proven by the p-value of 0.01. The mean AST:ALT ratio of those who died was significantly lower than those who were alive. On the other hand, there was a marginally significant difference in the AST elevation according to outcome as shown by the p-values 0.08.

Table 7 shows the association of elevated AST:ALT ratio with age, sex, BMI, and outcome. There is no significant difference in the AST:ALT ratio in relation to age, sex. BMI, and outcome of dengue shock syndrome.

Table 6. Comparison of the AST, ALT and AST-ALT Ratio According to Outcome

Outcome	AST (Mean ± SD)	ALT (Mean ± SD)	AST:ALT Ratio (Mean ± SD)
Dead (n=4)	105.50 ± 23.91	172.00 ± 126.64	1.05 ± 1.02
Alive (n=53)	376.15 ± 574.71	165.08 ± 172.44	1.05 ± 1.02
P value	0.08	0.94	0.01

Table 7. Association of the Different Variables with AST:ALT Ratio

	AST:ALT >/=2.0 (n= 32)	AST:ALT <2.0 (n= 25)	P value
Age (years)			
≤5	8	3	
6 – 10	12	15	0.27
11 – 15	8	6	
16 – 20	4	1	
Sex			
Female	15	16	0.19
Male	17	9	
BMI			
Underweight (n=4)	3	1	
Normal (n=35)	21	14	0.40
Overweight (n=18)	8	10	
Outcome			
Dead (n=4)	1	3	0.31
Alive (n=53)	31	22	

In our study, a fifteen year old, well nourished, and apparently well female adolescent obtained the highest value of AST and ALT which was 1,070 U/L and 4,140 U/L respectively. This particular subject was among the four subjects who succumbed to death. Table 8 shows the association of elevated AST and ALT with mortality. The results showed that a more than four-fold increase in both AST and ALT were significantly associated with mortality as proven by the p-values 0.004 and 0.03, respectively. Significantly more proportion of subjects who died have > 4-fold increase in AST and ALT.

Table 8. Association of the Increase in AST and ALT with Mortality

	AST N (%)		ALT N (%)		AST:ALT N (%)	
	≤ 4x Inc	> 4x inc	≤ 4x inc	> 4x inc	≤2	>2
Alive	49 (92.5)	4 (7.5)	50 (94.3)	3 (5.7)	22	31
Died	1 (25.0)	3 (75)	2 (50)	2 (50)	3	1
P value	0.004		0.03		0.31	

DISCUSSION

It was the aim of this study to determine whether function tests—AST, ALT, AST: ALT ratio would be useful to prognosticate the outcome of dengue shock syndrome patients.

Hepatic AST and ALT often rise in dengue patients and may be elevated up to five-fold. They usually peak in the second week of illness, with gradual normalization by the third to fourth week of illness[2]. In India, a total of 45 patients with dengue fever were studied, the AST and ALT activities were elevated in 43 patients (96%) each. Five-fold elevated levels were more frequent in severe disease[3]. In another study conducted in Thailand, DHF patients had AST levels significantly higher than ALT levels. They also tried to compare the mortality rate among those with DHF with acute liver failure and those who had acute liver failure due to other causes. The mortality rate was lower in the former group[4]. In one of the studies in Brazil, it was concluded that dengue virus may provoke varying degrees of damage to the hepatic parenchyma and therefore, the use of liver function tests to evaluate the degree of liver damage is of great importance, and markers such as AST and ALT may be used as parameters to evaluate severity[5].

In our study, we tried to establish if there were any other confounding patient variables that can cause elevated serum transaminases. The results showed us that the age and sex of the patients were non-contributory to the elevation of AST, ALT and AST:ALT ratio in our subjects. On the other hand, there was a significant elevation of ALT particularly among the overweight/obese subjects. This can further be explained by the association of obesity with fatty liver. Aside from detecting the effect of dengue virus on liver cells, a study confirmed the usefulness of the serum ALT test for screening fatty liver, and showed that a longer duration of obesity is generally associated with the occurrence of fatty liver in a pediatric obese population[6]. One should note that in our study population we only have ten subjects who were overweight/obese.

We have seen cases where hepatic encephalopathy complicates dengue shock syndrome and posed great risks. The serum determination of AST, ALT and serum ammonia aided us in focusing therapy on the prevention and management of acute liver failure. Thus, complications of acute liver failure were prevented. In a study by Petdachai, it was concluded that hepatic dysfunction is common in dengue infection and that the incidence increases with DSS. Aminotransferase levels are useful in predicting the occurrence of hepatic dysfunction and spontaneous bleeding[7]. The brief report in India suggested that there is a transient derangement of liver functions in childhood dengue infection, more so in DHF and DSS, with or without hepatomegaly[8].

In our study we noted that those with extremely or markedly elevated AST and ALT were the ones with poor prognosis in spite of aggressive management.

CONCLUSION

In summary, AST, ALT elevation of > 4-fold can prognosticate the outcome of patients with dengue shock syndrome. There must be early recognition of the anticipated complications of dengue shock syndrome such as hepatic and CNS complications (eg. hepatic encephalopathy) so as to apply prompt management.

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