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EFFECT OF DENGUE INFECTION ON LIVER FUNCTION

Rajeswari S[1], Tasneem Banu[2] and Swaminathan S*[3]

[1]Department of Biochemistry, [2]Department of Microbiology, [3]Department of Biochemistry,
Apollo Specialty Hospitals, Ayanambakkam, Chennai 600095, Tamilnadu, India.

ABSTRACT

In recent years Dengue infection related metabolic disturbances particularly in liver is on the increase. Data available from research on Dengue related diseases mainly point out alterations in liver enzymes, notably transaminases. This research article is an attempt to find out the association between liver function tests in dengue infected patients in comparison with controls. Among the liver function tests significant associations were found between patients and controls for Bilirubin fractions, ALT and GGTP but not for AST as ALT is more liver specific than AST.

Key words: Dengue, Dengue Infection, ALT, AST.

INTRODUCTION

Liver damage is a common complication in all dengue related cases and alterations in liver enzymes compared to normal controls will predict the degree of liver damage. Any infections will alter liver enzymes but to varying levels according to the microorganisms involved. Dengue related diseases are grouped as endemic and epidemic in nature and laboratory diagnosis is an important tool to assess the degree of Dengue infection. This study is to confirm if there are any alterations in liver function tests, in patients with Dengue and Dengue fever.

REVIEW OF LITERATURE

Globally, the number of adults hospitalized with dengue has increased markedly in recent years. It has been suggested that hepatic dysfunction is more significant in this group than among children. Transaminase levels increased in virtually all dengue patients and correlated with other markers of disease severity. However, peak enzyme values usually occurred later than other complications. Clinically severe liver involvement was infrequent and idiosyncratic, but usually resulted in severe bleeding. Chronic co-infection with hepatitis B was associated with modestly but significantly increased levels of Alanine Transaminase (ALT) but did not otherwise impact the clinical picture [1].

Liver damage is a common complication of dengue infection and transaminase levels are a valuable marker for monitoring these cases [2]. Dengue fever may cause hepatic injury and transaminase elevation similar to that in patients with conventional viral hepatitis. In epidemic or endemic areas, dengue fever infection should be considered in the differential diagnosis of hepatitis [3]. Abnormal levels of Aspartate Transaminase (AST) and ALT were observed in 97.7 and 37.3% of Dengue patients but a significantly higher elevation of AST and ALT was observed in Dengue Hemorrhagic Fever (DHF) patients with gastrointestinal haemorrhage [4]. Atypical manifestations of dengue infection with liver involvement have frequently been reported, ranging from mild elevations of transaminase levels to fulminant hepatitis. Liver damage with alteration of transaminase is a common complication of dengue infection (DI) and valuable marker for monitoring these patients [5].

Dengue is an arboviral disease endemic in many parts of the world. Although it is known to cause hepatic involvement commonly, it only occasionally results in acute hepatic failure [6]. Data are scarce on liver involvement in adult patients with DI. Liver injury is common in adult patients with DI and more studies are needed to determine the mechanism of liver injury in this disease [7]. All the cases with DHF and Dengue Shock Syndrome (DSS) had raised AST, ALT and Alkaline Phosphatase (ALP) levels and the mean levels of these enzymes were significantly higher as compared to Dengue

Corresponding Author :- **S. Swaminathan** Email:- glorynathan@gmail.com

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Fever (DF) suggesting a transient derangement of liver functions in DSS and DHF, with or without hepatomegaly [8]. A virus belonging to the Flaviviridae group causes DHF. Dengue presenting as acute liver failure is rare. Dengue is endemic in India. The last epidemic of dengue occurred in Delhi in 2003 with 2185 confirmed cases. Dengue virus serotypes 2 and 3 were responsible for this epidemic [9]. Hepatic dysfunction was observed more in DHF and DSS group compared to DF group. About 17.27% of children had >10 fold increase in the liver enzymes. There was no correlation between the degree of hepatic enlargement or hepatic tenderness with the abnormalities of liver functions. Any child with fever, jaundice and tender hepatomegaly in geographical areas where dengue is endemic, the diagnosis of DI should be strongly considered [10].

DI is caused by a single-stranded RNA virus, which has four serotypes (DEN 1-4); mosquitoes of the genus Aedes serve as vectors of transmission. Risk factors for DI are related to both the host and virus. Age, gender, immune status, and genetic background of the host all contribute to the severity of DI. Recently, international travel to endemic areas has also been identified as a major risk factor for both primary and secondary DI. Dengue remains a diagnostic challenge, given its protean nature, ranging from mild febrile illness to profound shock. The most severe manifestation of DI is DSS, which has an estimated mortality rate close to 50%. While hepatocellular damage has been reported previously in DI, acute liver failure and hepatic encephalopathy was observed after recent travel to an endemic area [11]. Liver injury due to dengue viral infection is not uncommon. Acute liver injury is a severe complicating factor in dengue, predisposing to hemorrhage, Disseminated Intravascular Coagulation (DIC) and encephalopathy [12]. Severe haemorrhagic necrosis of the liver was the cause of death in these patients probably due to direct viral infection. Predilection for severe liver disease remains unknown. Therefore, it is prudent to think beyond plasma leak as the main pathology of DI and attempts should be made to develop other treatment modalities to prevent and manage unforeseen fatal complications of DI [13].

Along with Fever, jaundice, hepatomegaly and altered liver function tests, the diagnosis of DI should be strongly considered in areas where DI is endemic [14]. DF and DHF are important arthropod-borne viral diseases. Each year, there are ~50 million DI and ~500,000 individuals are hospitalized with DHF, mainly in Southeast Asia, the Pacific and the USA. Illness is produced by any of the four dengue virus serotypes. A global strategy aimed at increasing the capacity for surveillance and outbreak response, changing behaviours and reducing the disease burden using integrated vector management in conjunction with early and accurate diagnosis has been advocated. Antiviral drugs and vaccines that are currently under development could also make an important contribution to dengue control in the future [15]. The frequency of dual dengue and malaria infection was 23.21%. The serology of the dengue and malaria showed negative results in 30.35%. The diagnosis of dual infections could be made on the basis of history, clinical examination supported by hematological results. It is recommended that all the patients suspected for dual infections should be treated concomitantly for dengue and malaria in malaria endemic areas [16].

Among the liver enzymes the greatest alterations was observed in AST and ALT among females, cases of DHF and cases with sequential infections. Liver damage with elevation of transaminases and reactive hepatitis was a common complication of dengue virus infection in these patients [17]. It is important to analyse the characteristics of abdominal pain (right upper quadrant) presence of Murphy's sign, ultrasound and liver enzymes levels for appropriate diagnosis and clinical management [18].

MATERIAL & METHODS

This study involves 50 patients who were confirmed to have Dengue fever by serological tests in the age group of 1-74 years and an equal number of controls who showed negative results for Dengue.

CS 400 analyser and Dialab reagents were used to measure all the analytes. The accuracy of all LFT were validated by the use of Bio-Rad accuracy controls at two levels. For Statistical analysis of data, a software download from the website http:// www.graphpad.com was used to calculate correlation coefficient (r), Student 't' distribution (t) and probability (p) between Dengue infected patients and controls.

RESULTS

Table 1 shows the mean & SD obtained for all the patients and controls studied. A visual inspection of this Table reveals that all LFT results shows higher levels for patients compared to controls.

Table 2 presents the statistical parameter viz r, t, and p between patients and control groups for each analyte. A higher significant association was observed between patients and control groups for Total and direct bilirubin as well as ALT and GGTP, the two liver specific enzymes.

Table 3 gives statistical parameters for males and females. While male patients results for ALT were significantly different from controls, such significant was observed for GGTP in the case of female patients.

It is concluded that the statistical results presented in Tables 2 and 3 confirms that ALT and GGTP, the two key liver enzymes are elevated in all dengue infected patients.

DISCUSSION

Many previous studies have confirmed that increase in liver enzymes occurs in all Dengue infected patients and Transaminases elevation is the key observation in such cases.[2,3,8,17]As this study was carried out in all generalised Dengue positive cases, we did

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not group patients according to DHF or DSS and hence ALP did not show any association between patients and controls. However our study had shown significant association between Dengue infected patients and normal controls for Bilirubin fractions, ALT and GGTP and but not for AST since ALT is more liver specific than AST.

Table 1. Mean + 2 SD values for Dengue Negative & Positive patients

		n		TBILI	DBILI	TP	ALB	SGPT	GGTP	ALP
Dengue Negative	**All patients**	50	Mean	0.56	0.19	6.76	3.91	37.1	38.36	90.84
			SD	0.12	0.07	0.83	0.49	26.16	45.89	53.36
	Male	25	Mean	0.8	0.21	6.71	3.88	39.53	58.37	109.44
			SD	0.15	0.08	0.99	0.55	30.21	68.46	64.73
	Female	25	Mean	0.56	0.18	6.76	3.96	35.5	23.38	84.08
			SD	0.09	0.07	0.77	0.52	25.28	13.11	46.57
Dengue Positive	**All Patients**	50	Mean	0.98	0.50	6.73	3.87	120.05	129.95	113.79
			SD	0.83	0.61	0.67	0.43	110.69	151.75	98.42
	Male	25	Mean	0.72	0.33	6.59	3.88	89.67	87.20	101.80
			SD	0.59	0.42	0.72	0.42	102.25	114.74	75.82
	Female	25	Mean	0.53	0.20	6.47	3.86	66.46	57.32	94.92
			SD	0.13	0.11	0.77	0.42	93.25	65.67	54.61

Table 2. Statistical parameters r, t & p (All Patients n=50)

Analytes compared	r	t	p
P.TBILI VS N.TBILI	-0.0895	3.5416	0.0006
P.DBILI VS N.DBILI	-0.2429	3.5701	0.0006
P.ALT VS N.ALT	-0.0718	5.1569	0.0001
P.GGTP VSN.GGTP	0.0677	4.0851	0.0001

Table 3. Statistical parameters r, t & p (Male & Female Patients)

	Analytes Compared	r	t	p
Male (n=25)	P.ALT VS N.ALT	0.0532	2.3514	0.0229
Female (n=25)	P.GGTP VSN.GGTP	0.0968	2.5341	0.0146

CONCLUSION

Good Associations exists for LFT between Dengue infected patients and normal controls. Except AST, other liver specific enzymes such as ALT & GGTP were found to be elevated in Dengue infected patients. This study confirms that in all Dengue infected patient LFT test results may reveal the degree of infection based on the elevation of LFT, particularly liver specific enzymes. Further studies are to be done to find out the associations in different groups of DF, DHF and DSS patients.

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