A STUDY ON HEPATIC DYSFUNCTION IN DENGUE FEVER

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ABSTRACT

BACKGROUND

Dengue fever is a public health problem in India like many other countries. It causes epidemics almost each year in different parts of India causing a burden to our healthcare system. Apart from the classical manifestations, dengue fever causes involvement of different systems especially liver function. This fact is usually overlooked especially in peripheral centers.

The aim of the study is to estimate the proportion of patients who develop liver function abnormalities in dengue fever to understand whether liver function abnormalities have any association with the prognosis in these patients.

MATERIALS AND METHODS

150 patients admitted with confirmed dengue fever were studied. Clinical features and liver function alterations were checked during admission on 3-week follow up and again on 6-week follow up. The data was analysed with the software, SPSS version 21.

RESULTS

100% of the patients had fever, headache and myalgia. Almost, all patients showed elevation of transaminase levels. SGOT level >2x upper limit of normal was observed in 86.7% patients. SGPT level >2x upper limit of normal was noticed in 54%. Serum bilirubin ≥1.3 was noted in 15.3%. INR value >1.3 was present in 8%. On 3 weeks and 6 weeks follow up, only a limited percentage of patients showed persistence of mild elevation of transaminase level and bilirubin level. In those who showed elevated SGOT, SGPT, bilirubin and INR values, the hospital stay was found prolonged. The death rate was 1.3% (2 patients).

CONCLUSION

Hepatic dysfunction is common in dengue fever. The severity of hepatic dysfunction showed a statistically significant association with mortality, duration of hospital stay and persistent hyperbilirubinaemia.

KEYWORDS

Hepatic Dysfunction, SGOT Level, SGPT Level, Duration of Hospital Stay.

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BACKGROUND

Dengue Fever (DF) is causing epidemics in Kerala for the last one and a half decades. Annually, about 50 million cases and 0.5 million cases of Dengue Haemorrhagic Fever (DHF). DF epidemics were unknown to Kerala still 1990s. Analysis of DF patients have revealed that in addition to classic features of DF- fever, headache, myalgia, arthralgia, retro-orbital pain, vomiting, skin rash, thrombocytopenia and bleeding tendencies. There are other features such as liver dysfunction including a rise in serum transaminase levels, hepatomegaly, ascites, pleural effusion and leukopaenia.[1] Studies have been conducted on the liver involvement in DF, one such study conducted in North India in Era's Lucknow Medical College, UP, during 2010 showed an elevation of SGOT >2x upper limit of normal in 91% patients and SGPT >2x upper limit of normal in 48% of patients, ascites in 60% patients, hepatomegaly in 50%, splenomegaly in 21%, pleural effusion in 15% and leucopenia in 10%.[1]

Kerala is facing cyclic epidemics of DF since 2001 during and soon after monsoon periods. The first DF epidemic in Kerala was brought on record from Kottayam District in 1997 with 14 cases and 4 deaths.[2] Involvement of liver is not uncommon as reported in the literature since 1970.[3] In the Liver Function Test (LFT), most common abnormalities seen are elevated transaminases, which are involved in amino acid metabolism. In approximately, 90% of patients with DF Aspartate Aminotransferase (AST) is higher than Alanine Aminotransferase (ALT).[4,5] DF initiates the inflammatory responses leading to liver parenchymal damage and causing release of transaminases in circulation.[6] Deranged liver functions are common in patients of dengue infection lead to direct attack on liver cells or unregulated post immune response against the virus.[7] Hence, measurement of ALT and AST are mandatory to see the liver involvement.[8]

Although, DHF can cause mild-to-moderate liver dysfunction in most cases, only some patients suffer from acute liver failure leading to encephalopathy and death.[9]

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Liver injury from dengue virus is mediated by its direct infection of hepatocytes and Kupffer cells.[10] When hepatic dysfunction was associated with encephalopathy, the mortality is seem to be extremely high.[11,12,13] In this background, this study aims to estimate the liver function abnormalities and evaluate the utility of liver function tests especially transaminase levels in patients with DF. The study also analyses whether there is any association between liver function abnormalities and the prognosis in these patients.

MATERIALS AND METHODS

The study was conducted during the period March-September, 2015, among 150 patients (94 males and 56 females) with DF admitted in medicine wards in Government Medical College, Kottayam. DF patients were identified as per clinical criteria of WHO Guidelines and NS-1 antigen positivity or IgM dengue antibody positivity. Patients with chronic liver disease, chronic alcoholics, chronic hepatitis B or HCV infection, on statin therapy or on oral contraceptive pills were excluded from the study.

After obtaining permission from IRB, patients were selected after explaining the purpose of the study and procedure in detail and after getting their informed consent in written format. After discharge, the patients were followed up at 3 weeks and 6 weeks with repeat liver function test results. The data was statistically analysed using the software SPSS version 21.

OBSERVATIONS

Signs		Frequency	Percentage
Hepatomegaly	Yes	43	28.7
	No	107	71.3
Splenomegaly	Yes	27	18
	No	123	82
Jaundice	Yes	6	4
	No	144	96
Hypotension	Yes	11	7.3
	No	139	92.7

Table 1. Distribution of Study Subjects According to Signs (N=150)

(SGOT Level)	Number	Percentage
No (up to 80)	20	13.3
Yes (>80)	130	86.7
Total	**150**	**100**

Table 2. Hepatic Involvement in Terms of Level of SGOT at Admission

SGOT Level	Number	Percentage
No (up to 80)	69	46
Yes (>80)	81	5
Total	**150**	**100**

Table 3. Hepatic Involvement in Terms of Level of SGPT at Admission

Total Bilirubin	Number	Percentage
No (up to 1.299)	126	84
Yes (>/=1.3)	24	16
Total	**150**	**100**

Table 4. Hepatic Involvement in Terms of Level of Total Bilirubin Level at Admission

Alb. Level	Number	Percentage
No (>/=3.5)	111	74
Yes (<3.5)	39	26
Total	**150**	**100**

Table 5. Hepatic Involvement in Terms of Level of Serum Albumin Level at Admission

INR Level	Number	Percentage
No (up to 1.3)	137	91.3
Yes (>1.3)	12	8.0
Not done	1	0.7
Total	**150**	**100**

Table 6. Hepatic Involvement in Terms of Level of INR at Admission

	Outcome	N	Mean	Std. Deviation	T value	Significance (p value)
Max SGOT at IP	Died	2	1607.500	24.7487	24.599	0.001
	Alive	148	158.277	83.0159		

Table 7. Independent Sample t-Test Showing the Association between Level of SGOT at Admission and Outcome (Death) Among Study Subjects

	Outcome	N	Mean	Std. Deviation	t value	Significance (p value)
Max SGPT at IP	Died	2	1560.000	155.5635	34.84	0.001
	Alive	148	107.108	57.3625		

Table 8. Independent Sample t-Test Showing the Association between Level of SGPT at Admission and Outcome (Death) Among Study Subjects

	Outcome	N	Mean	Std. Deviation	T value	Significance (p value)
TB at IP	Died	2	3.2	0.01	11.74	0.001
	Alive	148	1.065	0.2563		

Table 9. Independent Sample t-Test Showing the Association between Level of Total Bilirubin at Admission and Outcome (Death) Among Study Subjects

	Outcome	N	Mean	Std. Deviation	T value	Significance (p value)
TB at IP	Died	2	6.3	0.4243	1.003	0.31
	Alive	148	6.552	0.3523		

Table 10. Independent Sample t-Test Showing the Association between Level of Total Protein at Admission and Outcome (Death) Among Study Subjects

	Outcome	N	Mean	Std. Deviation	T Value	Significance (P Value)
Serum albumin at IP	Died	2	3.6	0.28	0.028	0.978
	Alive	148	3.5924	0.37		

Table 11. Independent Sample t-Test Showing the Association between Level of Serum Albumin at Admission and Outcome-Death-among Study Subjects

SGOT Level		N	Mean	Std. Deviation	T Value	Significance
IP days	SGOT up to 80	20	4.000	1.0260		
	SGOT >80	130	4.577	1.04822	2.29	0.02

Table 12. Independent Sample t-Test Showing the Association between Mean IP Days and Hepatic Dysfunction at Admission Based on SGOT Level Among Study Subjects

RESULTS AND DISCUSSION

The study showed 86.7% patients showed an elevation of SGOT >2 times ULN and 54% showed an elevation of SGPT >2 times ULN. 4% patients developed jaundice, prolongation of INR values >1.3 was noted in 8%.

All patients (100%) had fever, headache and myalgia as presenting complaints. Retro-orbital pain was a complaint in 16 patients (10.7%). 97.3% had vomiting on sometime during the course of illness especially in the initial 2 days. 4% had jaundice during IP days. 73% patients developed hypotension at least once during the IP days. 28.7% had hepatomegaly and 18% had splenomegaly. The minimum platelet count during IP treatment noted was 3000 and the minimum average platelet count was 41612. Leucopenia (<4000) was noted in 47.3% and average minimum WBC count during IP was 4132. Mean Total Bilirubin (TB) was 1.093 during IP and mean Direct Bilirubin (DB) was 0.353. Mean Total Protein (TP) was 6.549 and mean albumin was 3.5925. Maximum SGOT was 177.6 and SGPT was 126.48. TB during hospital stay, 1.3 or above were observed in 16% (24 patients). TP less than 6.0 g/dL was seen in 4.7% (7 patients). SGOT more than 2x ULN was noticed in 86.7% (130 patients). SGPT more than 2x ULN was noticed in 54% (81 patients). An elevation of INR more than 1.3 was noticed in 8% (12 patients). Of the selected patients, 82 were IgM dengue Ab positive and 68 were NS1 antigen positive.

The results of this study show certain features of dengue fever, which are sometimes overlooked. There was almost a universal involvement of liver in the study subjects as evidenced by elevated SGOT levels. Involvement of liver in dengue fever can be described as an elevation of transaminases.[14] Involvement of liver in dengue has also been reported in children.[15,16] Liver involvement in adult population were observed in various studies conducted in India, Thailand, Brazil, Nepal, etc. and the rate of involvement were 30-90%.

This study showed a higher SGOT levels in comparison to SGPT. This type of transaminase elevation is also seen in alcoholic liver disease. The study conducted in Era's Lucknow Medical College up in 2010 also showed a preferential elevation of SGOT levels. But, there is one study conducted by Srivenu Itha, Rajesh Kashyap et al (2005) showed no such preferential elevation of SGOT.[17]

Apart from the fact that the SGOT levels were raised in almost all patients, 86.7% of the patients showed an elevation of SGOT>twice the upper limit of the normal and 54% of the patients showed an increase in SGPT more than twice the ULN. Majority of the patients presented about 3-4 days after the illness after being treated initially in peripheral hospitals. But, increase in transaminase was also noted in patients who presented on the 2nd and 3rd day itself. The presence of vomiting in early stages of the disease may indicate a hepatic dysfunction.

The relationship of SGOT elevation with duration of hospital stay was found to be significant (p value 0.02 by unpaired t-test).

The association of elevated SGPT also correlates with prolonged hospital stay (p value 0.01).

Association of TB level during IP treatment and duration of hospital stay was also significant (p value - 0.001).

Persistent hyperbilirubinaemia (more than or equal to 1.3) at 6 weeks was seen in 5 patients out of 148 patients. Persistent SGOT elevation at 6 weeks (>40) was noted in 18 patients and these patients showed only mild elevation in the range 41-48. Persistent elevation of SGPT (>40) at 6 weeks was noted in 4 patients.

CONCLUSION

Hepatic involvement is common in dengue fever. It may be in the form of elevation of transaminase levels, elevation of bilirubin levels, elevation of PT and INR or hepatomegaly. The most common abnormality revealed in this study was an elevation of transaminase levels. On follow up, vast majority of these patients showed a normal transaminase levels. This is also true with bilirubin levels.

In this study in those who had an elevated transaminase levels and bilirubin levels, the hospital stay was found to be prolonged (statistically significant).

RECOMMENDATIONS

A limited percentage of patients showed persistently increased bilirubin levels and transaminase levels.

Long-term follow up studies are required to assess the future complications of these findings.

LIMITATIONS

- This study was conducted in a tertiary care center where referral bias cannot be avoided.
- The death rate in this study maybe an underestimation because patients admitted in a critical stage with a short febrile illness and unexplained hypotension and who succumb to the illness maybe actually having a severe dengue (DHF/DSS). Though a provisional diagnosis of severe dengue was made in such patients, they could not be included in the study because they could not satisfy the inclusion criteria of IgM dengue/NSI positivity.

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