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Clinical Profile of Hepatic Dysfunction in Dengue

KEYWORDS: DENGUE, LIVER DYSFUNCTION, GB WALL OEDEMA, MACROPHAGE ACTIVATION SYNDROME

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ABSTRACT *•Background: An analysis of 60 patients suffering from dengue showed liver dysfunction was present in all patients. Hepatosplenomegaly and ascitis were also present in significant number of patients. SGOT levels were higher than SGPT levels. 7 patients presented with macrophage activation syndrome (MAS). Ultrasonography revealed gall bladder wall edema, altered liver texture, ascitis, perinehpric fluid collection. Clinicians should take a note of these clinical finding while dealing with dengue fever patients.*

•Results: Out of 60 patients 54%had hepatomegaly,78%SGOT increased, 45% had increased SGPT, 12% had X-Ray evidence of pleural effusion, 7 patients had macrophage activation syndrome, most common symptom being fever.

•Conclusion: In a tropical country like India there are various viral, bacterial infections, including dengue,malaria, leptospirosis, most of which have got multiorgan dysfunction. A high index of suspicion is required for diagnosing Macrophage Activation Syndrome in which there is cytokine storm which needs immunosupressive therapy in the form of corticosteroids or combination of corticosteroids and immunosuppressive agents both.

INTRODUCTION

Dengue is acute mosquito born viral disease prevalent in tropical and subtropical countries which occurs as epidemic and endemic form dengue is global health burden due to various causes like geographic expansion climate change globalisation travel and trade more than 125 countries all over the world are under threat of dengue disease it will become great social economic and health burden in near future according to WHO data 50 – 200 million /year persons suffer from dengue.1

50% world population lives in area where they are at risk of disease and approximately 50% live in dengue endemic countries .

Dengue is caused by arbovirus. It's a complex disease with wide clinical spectrum of presentation which ranges from self limiting benign acute febrile illness to life threatening manifestations like dengue haemorrhgic fever (DHF) dengue shock syndrome (DSS) multiorgan failure, macrophage activation syndrome, hepatitis , encephalitis e etc. There is no definitive treatment and vaccine available clinicians should be aware of spectrum of clinical presentation so that prompt diagnosis and treatment can be initiated.

Materials and Methods

A total of 60 patients were studied. These were patients who were admitted to Medicine wards at Smt Kashibai Navale Medical College Pune from June to November 2015 .Only those patients were included in the study who had classical features of dengue – fever with chills, body ache, headache, rash, bleeding manifestations and thrombocytopenia and had a positive ELISA test i.e. IgM antibodies against dengue virus. Patients who had malaria, enteric fever, alcoholic and drug induced hepatitis were excluded from the study. All patients were subjected to a detailed history and a thorough clinical examination. A complete blood count, liver function tests, renal function tests, serum Ferritin, serum fibrinogen, serum triglyceride levels, chest X-ray and USG abdomen USG thorax were also done.Macrophage activation syndrome was diagnosed based on Haemophagocytic lympho histiocytosis(HLH) -2009 guidelines.

Table 1
Clinical characteristics and lab parameters in the study subjects S. No. Parameter Value

1	Av. Platelet Count (per mm3)	32,000±17000
2	Av. Serum Bilirubin (mg%)	1.2±0.7
3	Av. SGPT(units/L)	143 ±204
4	Av. SGOT(units/L)	255 ±420
5	Av. Alkaline Phosphatase(units/L)	85±80
6	SGPT > 2xULN	34(48%)
7	SGOT > 2x ULN	64(91%)
8	Ascites	45(75%)
9	Hepatomegaly	32(54%)
10	Splenomegaly	07(11.66%)
11	Leucopenia	15(25%)
12	Gall Bladder Oedema	24(40%)
13	Perinephric Fluid Collection	06(10%)
14	Pleural Effusion	07(11.66%)
15	Ferritin level (>500mcg/L)	07 (11.66%)
16	Serum triglyceride> 265 mg/dL	07 (11.66%)
17	Serum Fibrinogen < 150 mg/dL	07 (11.66%)

(Values showing Mean +/- Std. Deviation or n (%)

Results

- Of the 60 patients studied, 42 were males and 18 females.
- The age range of patients was 14-58 years and the mean age was 28 years.

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- All patients had fever as presenting complaint.
- 80 % patients had body ache while 70% had vomiting. 23% patients had
- Bleeding tendency with upper GI bleed being the commonest presentation.
- The average platelet count of our patients was 32,000.The
- Average serum bilirubin level was 1.2mg/dL.
- The average SGPT levels were 143 units/L while average SGOT levels were 255 units/L.
- The mean alkaline phosphates levels were 85units/L.100% patients had an elevated SGOT level while 84% patients had elevated SGPT level.
- There were 78% patients who had their SGOT level> 2 xULN, while 45% patients had SGPT levels>2 x ULN.
- In patients who had raised levels of both enzymes, the SGOT levels were 2-3 times higher than SGPT levels (Table 1 and 2).
- 54% patients had hepatomegaly or hepatosplenomegaly.
- 32 patients had hepatomegaly on ultrasonography and 22 of them had liver enlargement clinically as well.
- 15 patients had splenomegaly on USG of which only 3 had spleen enlargement clinically.
- 45 patients had evidence of ascitis on ultrasonography. Only 3patients out these 45 had clinically detectable ascitis.
- Ascitis in all patients was minimal to mild.
- 12% patients had evidence of pleural effusion on USG/X-ray. 25% patients had evidence of leucopenia.
- 7 patients presented with macrophage activation syndrome (MAS) with Sr. ferritin level ranging from minimum of 6500 to 40000 mcg/L. these patients also had hypertriglyceridemia and hypofibrinogenemia fulfilling criteria for MAS.

Discussion

- *Our study showed a higher SGOT levels in comparison to S*GPT. This reversal is known to occur in alcoholic liver disease 4. There is one study where this reversal was seen in malaria and enteric fever.2 Our findings are different from that of Srivenu Itha et al.3 who found no preferential elevation of enzymes. 4
- The Mechanism of liver involvement in dengue fever is not clear and may involve direct injury to liver cells or an immunological response. Histopathological study of dengue related hepatic dysfunction shows microvesicular steatosis with small foci of hepatocellular necrosis with councilman bodies and kuffer cell hyperplasia and mononuclear infiltrate with NS3 antibody on immunohistochemistry .5 None of our patients had dengue shock syndrome and therefore shock as a cause of liver injury is ruled out.
- 55% of our patients had hepatomegaly with or without splenomegaly. Studies of liver involvement in children report a higher percentage of patients presenting with hepatomegaly, as high as 80-100%.3 There are few reports of spleen enlargement in dengue infection.11 The mechanism of liver involvement in dengue infection is not clear and may involve a direct injury to liver cells or an immunological response.
- Ascitis was present in nearly 75% patients. Ascitis in our patients were mild and detected usually on ultrasonography. Ascitis in dengue has been attributed to plasma leakage. However there is one study which attributes portal hypertension in addition to plasma leakage for development of ascitis.6 Hepatic dysfunction in dengue involves hepatic sinusoidal obstruction due to kuffer cells and endothelial cell edema which causes increased portal vein pressure leading to ascitis.
- Apart from ascitis altered echogenecity of liver, gall bladder wall edema, perinephric collection are common findings on ultrasonography examination7
- 15% of our patients had leucopenia. Leucopenia has been reported in dengue12 and has been attributed to transient marrow suppression by the virus and macrophage activation syndrome Serum Ferritin can be used as a marker to discriminate between dengue and other febrile illness. The occurrence of hyperferritinaemia in dengue virus infected patients is indicative for highly active disease resulting in immune activation and coagulation disturbance. Therefore we recommend that patients with hyperferritinaemia be monitored carefully. In our study all 7 patients having macrophage activation syndrome (MAS) received IV Dexamethasone and showed clinical improvement.9
- Indiscriminate use of paracetamol/ acetaminofine should be restricted to less than 4 gm/day due to its hepatic toxicity. In somecase series N acetyl cystein has shown some benefit in hepatic dysfunction.10
- Silra EM et al study showed that C1q is an interacting partner between NS1 protein and liver cell protein which causes hepatic dysfunction.11
- It is important to keep these features in mind particularly considering the fact that diagnosis of dengue may be difficult in some cases and ELISA for dengue may not be positive in first few days of infection.14 We need a prospective study to see for liver enzymes within 24-48 hours of onset of fever and also to see whether SGOT levels are higher than SGPT levels. The results of the present study show certain unusual manifestations of dengue.
- Haemophagocytosis in dengue- 6 patients had MODS (multiorgan dysfunction syndrome)
- *0f these 6 patients only 3 patients had HLH (*haemophagocytosis *lymphohistocytosis) who improved with dexamethasone 10mg/m^2*
- Ref –http:dx.doi.org/10.1016/j.jcv2012.06.605

Conclusion

- The present study shows that dengue fever has varied presentation of liver dysfunction it ranges from raised levels of Serum transaminases (SGOT and SGPT) which may or may not be preferential. The presence of raised liver enzymes in all patients, ascitis, hepatosplenomegaly, elevation of SGOT more than SGPT, sonographic findings of gall bladder edema, Perinephric collection of fluid, and pleural effusion should be kept in mind when evaluating patients with suspected dengue.
- In our study some patients presented with macrophage activation syndrome (MAS) which warrants special mention and needs appropriate therapeutic intervention. . A high index of suspicion is required for diagnosing Macrophage Activation Syndrome in which there is cytokine storm which needs immunosupressive therapy in the form of corticosteroids or combination of corticosteroids and immunosuppressive agents.
- DHF (dengue hemorrhagic syndrome) must be differentiated from viral hepatits with fulminant hepatic failure, malaria, leptospirosis, viral hepatitis, and drug induced hepatitis.

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Conclusion:

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