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Review Article

A REVIEW ON LIVER FUNCTION MARKERS AND DENGUE INFECTION

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Abstract:
The dengue viruses transmitted by mosquito vectors largely infect many cell types and cause diverse pathological and clinical effects in infected individuals. There are plenty of clinical and research reports available which strongly suggest that liver involvement take place during dengue infections. This review is aimed to describe the level of liver marker enzymes in dengue infected patents based on clinical observations

Keywords: Hepatic involvement, Dengue, ALT, AST.

Introduction

Dengue is caused by flaviviridae family alboviruses and these RNA viruses are transmitted by *Aedes aegypti* mosquitoes [1]. Dengue viruses are classified into four serotypes: DENV-1, DENV-2, DENV-3 and DENV-4 [2]. Occurrence of these serotypes varied from continents to continents. Most of the dengue patients exhibit atypical clinical manifestations which are assessed through clinical observations. Alteration in the liver parameters is one of the dengue associated clinical complications [3]. The vascular, muscular and haematological systems are majorly affected by Dengue virus. This mini-review summarizes the clinical observations of liver involvement during dengue infections: Dengue Hemorrhagic fever (DHF), Dengue shock syndrome (DSS) and Dengue fever (DF) [4].

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Marker Enzymes of Liver Dysfunction

Alanine and aspartate aminotransferases (ALT and AST), alkaline phosphatase (ALP) and gamma-glutumayltransferase (GGT) are the battery of liver. The upper limit of normal (ULN) implies that 2.5% of the liver tests from these healthy individuals exceed the ULN. The aminotransferases catalyze the reversible transformation of α-ketoacids into amino acids. Their serum levels represent the amount of

hepatocellular injury and cell death. Aminotransferases not only originate in hepatocytes but also in other tissues such as heart and skeletal muscles, kidney, brain, pancreas, lung, and red blood cells [5].

The liver contains 400 U ALT/g of cytoplasmic proteins and 500 U AST/g proteins (> 80 % contained in mitochondria and endoplasmic reticulum). Damage occurring in liver tissue ends up in a significant increase in the serum ALT and AST activity. Liver cell necrosis and destruction of mitochondria and endoplasmic reticulum also manifest the abnormal liver marker enzymes. Alkaline phosphatase is found in the biliary pole of the hepatocytes, the bile duct epithelia, osteoblasts, kidney, lung, intestine and placenta [6]. In cholestatic liver disease also, the elevated bile acids fuel ALP synthesis. Hepatic and non-hepatic causes of ALP elevation can be differentiated by measuring ALP isoenzymes in liver [6].

Dengue Associated Hepatic Diseases

High fever, arthralgias, myalgias, cephalea and gastrointestinal disorders are the principal manifestations in classic dengue patients. Paranechymatous lesions cause the release of AST and ALT into blood circulation [7]. ALT is found in lower concentration in muscle when compared to liver. Elevated level of AST and ALT as well are observed in infections, pancreatitis, cirrhosis, bilary obstruction, and hepato cellular carcinoma and dengue. In Brazil, Luiz Jose carried out 169 serological investigations among in which 85 cases were found to have elevated AST and ALT level. This significant increase in the liver marker enzymes was associated with severe liver damage [8].

In children admitted in Kolkata hospital (India), abnormal liver functions, hepatomegaly, hepatic encephalopathy and splenomegaly were frequently observed to occur. Splenomegaly among these manifestations is associated with severe dengue fever [9]. Therefore hepatic diagnosis has to be carried out in dengue infected patients. In adults, dengue infection elevates liver marker enzymes such as Alanine transaminase, and serum bilirubin. Prothrombin time also is increased. These people can survive only with effective therapy [10]. In Malaysia, 50 serologically confirmed dengue cases were adopted for a study in which 25 were infected with DF and the rest with DHF. Hepatomegaly was seen in 60% of the DHF individuals. Further liver marker enzymes also were elevated in DHF. The analysis showed that degree of liver dysfunction is associated with severity of the DHF. Billirubin, serum ALT, ALP levels were also found to have elevated in DHF. Increased level of liver marker enzymes were seen in bleeding cases than those without bleeding. Reduction in the number of immune cells was also another manifestation seen in DHF [11,12].

Mahmuduzzaman investigated the change of AST and ALT in severely infected 240 dengue patients among whom 125 were male cases. 157 were affected by classical dengue fever and 88 were having dengue hemorrhagic fever. AST and ALT levels were significantly elevated in DHF cases. However AST was observed to have risen equally in DF and DHF when compared to ALT. This observation was directly related to severity of the dengue infection [13].

Colpitts and his coworkers focused to find the molecular pathogenesis in dengue infection. He identified DENV capsid proteins present in the four histone proteins such as H2A, H2B, H3 and H4 in human liver cells. Viral capsid proteins possess ability to act as histone mimics [14]. Pires included 84 dengue patients from Brazil in his study. All of them were having dengue infection alone with fever, abdominal pain and vomiting. AST level was increased up to 143+ 1.28 mg/dL. Liver involvement and gastrointestinal disturbances were also observed [15].

In another study among children from India, Roy *et al* (2013) investigated the hepatic involvement in classic dengue fever in India. 80% of children had hepatomegaly and 46% hepatic tenderness. Jaundice also was seen in 60% of the patients. Other clinical findings such as increased AST/ALT levels, reduction in the prothrombin time (41.7%) and reduced serum albumin [10]. Ahmad *et al* (2013) selected 120 adults in Uttarkhand state for his study in dengue infection. Severe liver dysfunction and

lowered platelets level were significant manifestations in his observation [16].

Kularatne studied in a post mortem report of dengue patient from Sri Lanka. He found massive necrosis in the liver along with macro and micro vesicular steatosis. Inflammatory infilterate was also associated with the case [17]. Pegliaric analyzed 14 specimens of liver from dengue patients (DHF) for lesions. Increased vascular permeability and edema were noticed in the liver specimen of DHF patients. Plasma leakage was also observed. It showed that hepatic injury was involved with acute inflammatory response. Destruction of liver was found in both DF and DHF [18]. Santhosh conducted a retrospective study of diagnosis in 96 sero-positive dengue cases from India. 17 among them had been affected by hepatomegaly and liver complications including other features such as pleural effusion, splenomegaly and thickness of gallbladder wall [189. Rowe investigated liver dysfunction in 6989 cases of which 295 were elders and the rest were young patients. Most of the elders who were affected with serious dengue hemarrhogic fever were observed to have significant hepatomegaly. In case of young individuals, bleeding was noticed in the mucosal part. Elderly patients had higher rate of DHF, SD and liver damage [20].

Conclusion

Dengue is normally associated with liver damage and moderate increase in aminotransferases. Dengue was found to be self limiting and no cases of liver failure was found in the clinical observations. Viruses causing dengue diseases provoke varied degrees of damage to the hepatic parenchyma which range from mild increases in aminotransferases to increases of up to 30 times the standard range. Therefore, liver investigations are of great importance so as to evaluate the severity of liver damage and parameters such as AST and ALT.

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