



STUDY OF HEPATIC DYSFUNCTION IN PATIENTS INFECTED WITH DENGUE VIRUS

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ABSTRACT

Dengue fever is a fatal infection affecting the lives of the patients and this study was designed to further explore its pathological effects. A total of 200 consecutive of dengue viral infection were included in this prospective descriptive study conducted at the Department of Pathology, University of Veterinary and Animal Sciences, Lahore from October, 2009 to September, 2010. A special proforma was designed to collect all the relevant clinical information from each patient. All the strip positive cases of dengue virus were further confirmed by performing IgM capture ELISA and then analyzed for hepatic impairment through liver function tests including serum bilirubin, serum alkaline phosphatase, serum ALT and AST. The results were then gathered and analyzed. The already existing liver diseases like hepatitis A, B, C, E and inherited liver disorders were not included in the study. Total number of patients included in study with Dengue IgM +ve were 200. Out of 200 cases 130 were male and 70 were females. The patients were categorized into two classes according to severity of sign symptoms like puerperal rash on the body. The classes are dengue fever (DF) and dengue hemorrhagic fever (DHF). The total number of DF cases was 28.50% (57/200) and number of DHF cases was 71.50% (143/200). The patients of DHF group were found to have more liver derangement that is 90.20% (128/200) while the patients belonging to DF group were at a less risk for impairment of liver function that is 9.80% (15/200). The patients with dengue hemorrhagic fever are more prone to have liver enzyme derangement and it has a direct relation with the titer IgM in the body of patients infected with dengue virus. The liver enzyme which are found to be more raised are serum ALT and AST while serum alkaline phosphatase and serum bilirubin are not markedly raised.

Keywords: Dengue fever, Blood, Serum, ALT, AST, ELISA.

Contribution/ Originality

This study contributes to the existing literature by exploring pathological effects of dengue fever in humans and relation with biochemical parameters. The logical analysis has primary contribution in its finding that dengue fever is more prevalent in males and serum liver enzyme level rises as IgM level raises.

1. INTRODUCTION

Dengue is most important and wide spread arthropod-borne viral illness of public health importance now a day compared to nine reporting countries in 1950's. The geographic distribution includes more than hundred countries worldwide, many of these had not reported dengue for twenty years or more and several have no known history of disease [1].

The 2.5 billion peoples are at risk of dengue infection and most may have this disease with no symptoms. In the second half of the previous century, dengue spread throughout the tropics threatening the health of a third of world population.

Although dengue fever is an emergent and epidemic disease in parts of the Americas, little is known about its clinical presentations in our region [2].

In the perspective of age relation of dengue fever, it is also known as a disease of childhood and a cause of pediatric hospitalization in South East Asia but the increased incidence of Dengue fever (DHF) is among older age groups. Increased incidence of disease is in those people who live near markets, open sewers. A cost analysis of epidemic of Dengue fever (DF) and DHF in Puerto Rico using upper and lower limits of incidence including medical care, an epidemic control measures range between 2.4 and 4.7 million USD, respectively [3]. The first reported epidemic occurred in the French West Indies in the 17th century, but it was the Southeast Asia pandemic created by the ecological disruption that followed World War II which is credited for its worldwide spread. Over the past several decades, the gradually increasing incidence has been attributed to multiple factors, including global demographic changes with associated uncontrolled urbanization and population growth as well as overcrowding with inappropriate sanitation.

Dengue virus causes acute febrile disease every year including more than five lac cases of severe form of disease that is dengue hemorrhagic fever and dengue shock syndrome [4]. The highest incidence of dengue fever is seen in Southeast Asia particularly Vietnam and Thailand which together account for more than two third of the overall reported cases of the Asia (Pan American Health Organization, 1977-1980).

The clinical signs and symptoms include; erythematous rash in adults but infants and young children usually present with nonspecific symptoms such as fever, runny nose, rash and diarrhea. Older children and adults have the classic "break bone fever", as described previously. Dengue fever can have hemorrhagic manifestations without including the entire constellation of DHF. The hemorrhagic manifestations associated with dengue fever include a positive tourniquet test, petechiae/purpura, mucosal and gastrointestinal bleeding. The child in the first case had petechiae

and a positive tourniquet test. The initial picture of classical dengue fever is followed by painful conditions [5].

In Latin America, the superimposed geographical areas for malaria, viral hepatitis and yellow fever represent a challenge for identifying the etiology of acute febrile syndrome complicated by hepatitis liver enlargement, vomiting, hematemesis, epistaxis and diarrhea [6]. It may be asymptomatic or may give rise to undifferentiated fever, dengue fever, dengue hemorrhagic fever (DHF), or dengue shock syndrome. Annually, 100 million cases of dengue fever and half a million cases of DHF occur worldwide. Ninety percent of DHF subjects are children less than 15 years of age. At present, dengue is endemic in 112 countries in the world. No vaccine is available for preventing this disease. Early recognition and prompt initiation of appropriate treatment are vital if disease associated morbidity and mortality are to be limited [7].

A lot of work has been done on dengue virus pathogenesis but the current study is aimed at determining the extent of hepatic dysfunction in dengue virus infected patients on the basis of liver enzyme assays [8].

2. METHODOLOGY

A total of 200 patients were included in the study. The experimental design of the study included the random selection of places for collection of samples, setting inclusion criteria, categorization of patients and screening of IgM positive patients with rapid strip testing method, confirmation of positive cases by capture Enzyme Linked immunosorbent assay (ELISA).

The samples of the patients were taken from Outpatient Departments (OPDs) of different Govt. Hospitals including Mayo, Services, Ganga Ram Hospital and Social Security Hospitals (Shahdara and Multan Road) of the Lahore city, Punjab. The age of the patients belonging to either sex varied from 1-70 years. Those patients were included in the studies who were suffering from high grade fever for the last 6-7 days, the time when dengue IgM starts rising its level in the blood of the patient. For the random screening of the patients they were screened by dengue IgM strip testing method. Patients already having any preexisting liver disease like Hepatic Cirrhosis, Hepatitis B and C or having any congenital biliary disease were not included in the study.

A 5ml blood volume from each patient was sampled out from the cephalic vein in disposable syringe and poured into a vacutainer without EDTA. The blood sample was centrifuged at 5000Rpm to separate the serum. Patients were categorized into DF group and DHF group according a WHO criterion according to which the patients having high grade fever with thrombocytopenia <100,000 platelet count, blood haemo-concentration and hemorrhagic manifestation were belonging to DHF category. Clinical signs and symptoms of each individual case were recorded on specially designed pforma. The patients were further divided into various age groups to minimize the physiological bias in the study. The groups included; 1-10 yrs., 11-20 yrs., 21-30 yrs., 31-40 yrs., 41-50 yrs., 51-60 yrs. and 61-70 yrs..

All the dengue positive patients were evaluated for liver function tests including; Alanine Aminotransferase (ALT or SGPT) Estimation, Aspartate Aminotransferase (AST or SGOT) Estimation and Alkaline Phosphatase Estimation. Tests, especially liver enzymes like SGPT, SGOT and Alkaline phosphates. About 80% of patients scanned raised enzyme levels. This study establishes the fact that LFT's can be used as a diagnostic tool for diagnosis of dengue fever in the patients with history of pyrexia of unknown origin. It will also be very important to say that the recovery of patients will be accomplished by the reversal of the liver enzyme level back to normal level. The recovery of hepatic dysfunction indicates good prognosis of patients.

The fact that dengue viral infection causes hepatic impairment was confirmed by the study of [Thepparit and Duncan \[9\]](#). They stated that dengue virus is the causative agent of dengue fever, dengue shock syndrome, and dengue hemorrhagic fever, infects susceptible cells by initially binding to a receptor(s) located on the host cell surface. Evidence to date suggests that receptor usage may be cell and serotype specific, and this study sought to identify dengue virus serotype 1 binding proteins on the surface of liver cells, a known target organ.

This study showed that dengue virus type-I binds to the protein on the surface of liver cells thus absorbed into the cells starting damaging structure and functions which is indirectly indicated by the raised level of serum enzymes that has been established by the current study.

Our study also correlate to the study by KUO, 2001 in Taiwan who reported similar results with elevations of AST and ALT in 93.30 % and 82.20% of the patients, respectively. He noticed that AST began to rise from the third day of illness and returned to normal after three weeks. These results are comparable with the present study which showed that 90% of the patients with AST high and 76% of the patients with high ALT high levels.

3. RESULTS

Total number of patients included in study with Dengue IgM +ve were 200. Out of 200 cases 130 were male and 70 were females. The patients were categorized into two classes according to severity of sign symptoms like puerperal rash on the body. The classes are dengue fever (DF) and dengue hemorrhagic fever (DHF). The total number of DF cases were 28.50% (57/200) and number of DHF cases was 71.50% (143/200). The patients of DHF group were found to have more liver derangement that is 90.20% (128/200) while the patients belonging to DF group were at a less risk for impairment of liver function that is 9.80% (15/200).

After statistical analysis it was found that mean levels of Dengue IgM is statistically different in male and female. It shows that DF and DHF are more common in males than females the reason being unknown. One possibility may be that males are more exposed to the external environment.

It has also been observed that mean levels of Dengue IgM is statistically significant in different age groups. In other words dengue IgM is statistically different in various age groups.

Above table shows that DF and DHF are more prevalent in patients belonging to the age group of 21-30 years.

We conclude that S.ALP, SGPT and SGOT are correlated with Dengue IgM, so there is a strong positive correlation between Dengue IgM & SGPT, SGOT, but weak positive relationship with S.ALP.

4. DISCUSSION

This study is aimed to establish the fact that dengue fever infection is damaging the liver parenchyma and increases liver enzymes level in blood the assumption was made and establish by including 200 dengue positive patients in study and doing their liver function. Measuring aminotransferase in blood sample from patients serologically diagnose according to MAC ELISA protocols. The results were summarized by categorizing the cases of liver dysfunction into four grades. Grade A was patient having normal liver function test. Grade B was the patients having at least one of the enzymes raised. Grade C was the group having at least having one of the enzymes raised at level higher than three times the upper reference value. Grade D was the patients having acute hepatitis with enzyme level at least 10 times upper than reference value. While comparing the studies it is found that the raised enzyme levels in the acute phase of dengue viral infection is due to live damage, Liver damage is a common complication of dengue infection and aminotransferase levels are a valuable marker for monitoring these cases [10]. This study highlighted the fact that enzyme level was ten times upper than the reference value in those patients who were categorized into the dengue hemorrhagic fever group while this change was not very well appreciated in the other group that is dengue fever group.

5. CONCLUSION

The results obtained from study went in favor of assumption made before starting the study. The analysis established that DF is more common in 21-30 years of age group, more prevalent in males and the level of serum liver enzyme rises as the serum level of dengue IgM raises that is with the increase of severity of infection of dengue virus.

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