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Original article

Hepatic and Pancreatic dysfunction in dengue in a tertiary care hospital of Kolkata

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Abstract:-

Introduction: Dengue fever is an important arboviral disease with significant impact of the disease burden specially in tropical countries. The virus seems to have some hepatotoxic and other gastrointestinal effects. Although asymptomatic in most cases, clinical manifestations like jaundice, and acute liver failure (ALF), acute pancreatitis may occasionally complicate the clinical scenario. Our present study focuses on the hepatic and pancreatic manifestations in dengue**.**

Materials and methods:- About hundred patients with acute febrile illness diagnosed to have dengue fever as per WHO criteria were included in our study.

Observation: - About 54 patients were males and 46 were females. Their age varied from 13 to 70 years with maximum incidence occurred in 21-30 years age range. Most of the cases presented with various gastro hepatic manifestations. The commonest gastrointestinal manifestation was transaminitis (96%) (Both symptomatic and asymptomatic) followed by hypoprotinaemia, elevated PT (INR),and acute pancreatitis (18%). Pain abdomen(33%) and vomiting(31%) were the common clinical presentations followed by jaundice, pallor, hepatosplenomegaly, GI bleeding, altered sensorium etc,. About 18% of patients presented with acute pancreatitis as per Revised Atlanta classification criteria.

Conclusion: Liver and pancreatic injury is very common in patients with Dengue fever. Severity of hepatic and pancreatic involvement can be a major contributing factor in morbidity and mortality in patients with Dengue . These various atypical manifestations should prompt us to investigate for dengue so that expanded dengue syndrome can be diagnosed and treated early.

Keywords: Dengue; acute pancreatitis; Acute liver failure; Transaminitis; expanded dengue syndrome.

Introduction:

Dengue is an acute febrile illness caused by infection with one of four dengue viruses (DENV) which is transmitted by Aedes aegypti or Aedes albopictus mosquitoes. All of the four dengue serotypes (DENV1-DENV4) circulate in tropical countries including India with frequent outbreaks during and after rainy season. Infection may be completely asymptomatic or it may present with varied clinical manifestations including a mild febrile illness to a life-threatening Dengue shock syndrome. The term Expanded Dengue syndrome is used for various unusual or atypical manifestations in dengue due to involvement of other organ systems like liver, kidney, nervous system etc. [(1)] These atypical manifestations may be potentially life threatening. Therefore, clinicians must be aware of these

atypical manifestations.

There are few studies related to liver involvement in dengue infection. Liver involvement in dengue infection can range from mild to moderate elevation of serum transaminases to fulminant hepatic failure. Various mechanisms are postulated to explain the hepatic dysfunction seen in dengue illness including direct viral damage, immunological injury and hypoxic injury due to reduced hepatic perfusion during shock . [2,3,4] Pathogenesis of pancreatic involvement in dengue is still not known. But it can be due to direct invasion of pancreas by the virus itself leading to inflammation and consequent destruction of pancreatic acinar cells; pancreatic damage due to dengue shock syndrome; or acute viral infection causing an autoimmune response to pancreatic islet cells and development of edema of the ampulla of Vater with obstruction to the outflow of pancreatic fluid. ([5,6] In our study we tried to identify the various patterns of liver and pancreatic dysfunction that occurs in dengue infection in eastern part of India.

Materials and methods:

This is a cross sectional study done in the Department of Medicine, Medical College, Kolkata. We selected the cases from patients admitted in medicine indoor and outdoor, between January 2017 to July 2018 at our hospital.

Total 100 cases , serologically diagnosed as Dengue fever as per the WHO criteria, were included in the study.

We have taken prior permission from ethical committee**.** All patients with primary hepatic or renal disease, or any other systemic disease causing liver or pancreatic dysfunction were excluded from the study. Proper clinical history and physical examinations were done in all cases. Investigations like liver function tests (LFT), serum amylase, lipase, hemogram, renal function tests (RFT), urinalysis and chest roentgenogram, ultrasound abdomen, prothrombin time (PT), INR and activated partial thromboplastin time (aPTT) were done in selected patients. CT scan of abdomen was done in only those who had pain abdomen and /or elevation of serum amylase , lipase levels.

Data were analyzed by standard statistical protocol using SPSS VERSION 21.0. The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test. The continuous data was expressed as mean ± standard deviation (SD) and comparison was done using independent sample t test. A probability value (p value) of less than or equal to 0.05 was considered as statistically significant.

Result and analysis:

Total 100 selected patients were taken for their data analysis. Different age groups of patients were suffered from the dengue infection. Age of the patients ranges from 13 to 70 years. Maximum incidence of dengue fever occurred in the age group of 21-30 years followed by 13-20 year. Out of 100 cases 54% patients were male and 46% patients were female.

Symptoms and signs related to gastrointestinal and hepatic systems are shown in **Table 1**. Majority of our patients had one or the other over lapping symptoms (vomiting, pain abdomen, bleeding manifestation, altered sensorium, shortness of breath, decreased urine output). Individually assessing these symptoms, pain abdomen was most common and seen in 33 patients (33%) followed by vomiting in 31 patients (31%). Decreased urine output(<500cc/day) and GI bleeding were seen in 9(9%) and 8(8%) patients respectively followed by other symptoms like altered sensorium and shortness of breath.

Blood pressure and pulse rate are important signs related to hepatic and pancreatic dysfunction as they can present with shock and cardiovascular compromise.in our study the mean systolic blood pressure (SBP) was 122 mm of Hg with SD of 17 mm of Hg. Where the mean and SD of diastolic blood pressure (DBP) and pulse rate were 72 mm of Hg, 9 mm of Hg and 92/min and 13/min respectively. None of our patients developed dengue shock syndrome.

Biochemical profile of hepatic function is shown in **Table 2**. The mean ± SD values of total bilirubin (T.B), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein (T.P), albumin, international normalized ratio of prothrombin time (INR) are 2.07±1.21 mg/dl, 111±63 U/L, 97±51 U/L, 113±33 U/L, 5.9± 0.6 g/dl, 3.3± 0.8 g/dl, 1.42± 0.24 respectively.

Total bilirubin level was found to be higher in 23% of the patients, SGOT level was found to be higher in 85% of the patients ,SGPT level was found to be higher in 96% of the patients with ALP level was found to be higher in 36% of the patients out of total 100 patients. Thus many of our patients had asymptomatic transaminitis.

Hypoproteinemia was found to be present in 72% of the patients ,

INR >1.5 was found in 39% of the cases with mean ±SD – 1.69± 0.11 and INR<1.5 was found in 61% of the cases with mean ±SD – 1.25± 0.13. None of them developed fulminant hepatic failure.

Pancreatitis in dengue is also a known but relatively rare complication. In our study serum amylase and lipase value were measured. Distribution of pancreatic enzymes among patients is shown in Table 3. Abnormal Serum amylase level was found in 20% of the cases with mean 285.5U/L. whereas lipase was found >200 U/L in only 4% of the cases with mean ± SD 250.75 ± 37.32U/L.

There was considerable overlap in patients with high amylase, lipase levels. Fourteen (14) patients had features of acute pancreatitis on CT scan/USG (diffuse enlargement of pancreas, heterogeneous attenuation of the gland with ill-definition of the border or reticular stranding of the surrounding fat, focal pancreatitis etc).

Overall eighteen patients had developed acute pancreatitis according to Revised Atlanta classification criteria.

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Symptoms/Signs	**Percentage**
Vomiting	31%
Pain Abdomen	**33%**
GI bleeding	**8%**
Altered sensorium	**7%**
Decreased urine output	**9%**
Pallor	**26%**
Jaundice	**29%**
Oedema	**6%**
Hepatomegaly	**27%**
Spenomegaly	**15%**
Ascites	**5%**

Table 1:-Distribution of symptoms and signs related to hepatic and pancreatic dysfunction

PARAMETERS	MEAN	SD
TOTAL BILIRUBIN(MG/DL) (NORMAL<1MG/DL)	**2.07**	**1.21**
DIRECT BILIRUBIN(MG/DL) (NORMAL<0.2MG/DL)	**1.15**	**2.03**
SGOT(U/L)(N<45U/L)	**111.9**	**63.13**
SGPT(U/L)(N<35U/L)	**97.3**	**51.29**
ALP(U/L)(N 98-279U/L)	**113.12**	**33.09**
TOTAL PROTEIN GM/DL)	**5.91**	**0.61**
ALBUMIN(GM/DL)	**3.34**	**0.89**
INR	**1.42**	**0.24**

Table 2:- Distribution of Biochemical parameters of hepatic dysfunction

		No of patients(Percentage)	Mean	SD
Amylase(u/l) (N<90U/L)	**Normal**	**80(80%)**	**63.53**	**17.84**
	Abnormal	**20(20%)**	**285.5**	**21.34**
Lipase(u/l) (N<200U/L)	**Normal**	**96(96%)**	**36.39**	**7.68**
	Abnormal	**4(4%)**	**250.75**	**37.32**

Table 3:- Distribution of biochemical parameters of Pancreatic dysfunction.

Discussion:

In this study we noted that the incidence of dengue fever varied from age of 18 years to a maximum age of 70 years with majority of patients were in the 3rd decade (37%). Similar result was found by Nishat Hussain et al in their study[7] (Table-1). Male patients (54%) outnumbered the female patients(46%).

In our study symptoms and signs related to hepatic and pancreatic dysfunction were studied. Among them jaundice, pallor and hepatomegaly were most common- 29%, 26% and 27% respectively followed by splenomegaly, edema and ascites which were15%, 6% and 5% respectively. Similar results were found in a study done by Amrita Roy, Debalina Sarkar et al [8] where jaundice and hepatomegaly were found to be the most common presentation of hepatic involvement in dengue.

Out of 100 patients, almost majority of our patients had involvement of liver as evidenced by elevated levels of SGPT(96%),SGOT(85%) levels. Involvement of liver in dengue has been described in textbooks as an elevation of transaminases. There are few studies in adults which showed elevated enzyme levels, ascites and hepatomegaly.[9-11]

Our study showed a slightly higher mean SGOT levels in comparison to SGPT which is not statistically significant. This corroborates with the study by Srivenu Itha et al, who found no preferential elevation of enzymes. [12]

Hypoproteinemia was found to be present in 72% of the patients with mean ± SD- 5.6±0.4 g/dl. Normal level of protein was found in 28% of the patients. Similar results were found in a study done by Wong M et al where elevated ALP was found in 76% of cases. [13]

Hypoalbuminemia was found to be in 64% of the patients with normal level of albumin in 36% of the patients. Similar results were found in a study done by Jagadish Kumar et al where hypoproteinemia was found in 66% of cases. [14]

INR >1.5 was found in 39% of the cases with mean ±SD – 1.69± 0.11 and INR<1.5 was found in 61% of the cases with mean ±SD – 1.25± 0.13. In a study done by Ashis Kumar Saha, Somnath Maitra & Subhas Ch Hazra [15], INR>1.5 was found in 11% of the cases which was lower than the prevalence observed in our study.

Pancreatitis in dengue is also a known but relatively rare complication. In our study serum amylase and lipase values were measured. Where amylase is relatively non-specific marker of pancreatic involvement, serum lipase is more specific marker of acute pancreatitis. In our study amylase level >250U/L was found in 20% of the cases with whereas lipase was found >200 U/L in only 4% of the cases. Prevalence of cases with normal serum amylase and lipase are 80% and 96% respectively. 14 patients had evidence of enlarged, diffuse edematous pancreas on imaging. Thus in our study acute pancreatitis was diagnosed in 18 patients who fulfilled Revised Atlanta Classification criteria [16] for acute pancreatitis of which only one patient had severe necrotizing pancreatitis. CT scan was normal in two of twenty patients with high amylase and pain abdomen suggesting possible mild pancreatitis. In all cases CT scan was performed after 72 hours of symptom onset ie onset of pain abdomen and or vomiting in the setting of dengue.Fifteen of 33 patients with pain abdomen had no evidence of pancreatic involvement ,suggesting other causes of abdominal pain like acute gastritis, acalculous cholecystitis ,hepatitis etc.

Till date, there have been only a few studies on acute pancreatitis complicating Dengue fever from across the world. Enlarged pancreas and hyperamylasemia have been known to occur in Dengue ; but acute pancreatitis is an atypical and rare presentation. [17,18,19] . Like septic shock, acute pancreatitis can be fatal .Therefore, acute pancreatitis as a complication of DHF is dangerous, and clinicians must know when to suspect pancreatitis in patients with Dengue Fever. It can go undiagnosed due to lack of awareness. Hence, clinicians might not request serum amylase or lipase investigation, despite abdominal pain and vomiting.

Conclusion:

In our study it is seen that there are some certain features of dengue which are not known to be usually associated with it. Presence of elevated liver enzymes in most of our patients, along with hepatosplenomegaly, jaundice, ascites, elevation of SGOT levels more compared to SGPT (just like alcoholic liver disease), acute pancreatitis, must be kept in mind by the clinicians while evaluating patients with suspected dengue. Because acute pancreatitis can prove to be a life threatening complication of Dengue, timely identification and understanding of pathogenesis can help clinicians to deal with complex systemic manifestations and thus guide proper management.

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