Dengue Fever Induced Fulminant Hepatic Failure
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Dengue fever is considered as one of the major health issues in Pakistan.1,2 It is an acute febrile illness caused by Aedes Aegypticus mosquito borne flavivirus which has four serotypes i.e. DEN I to DEN IV.3 The clinical manifestations of dengue infection range from asymptomatic stage through mild flu like symptoms to its serious clinical spectrum known as dengue hemorrhagic fever and dengue shock syndrome.4,6 Globally, each year around 400 million cases are being reported with 0.5 million cases of DHF and mortality of less than 1% if treated.7 Dengue viral infection is endemic in around 125 countries of world. It is more prevalent in tropical and subtropical regions.8,9 It causes mild to moderate elevation in levels of transaminases but severe liver impairment is rare.10 Dengue related liver failure is rare and has high fatality rate due to its complications like severe coagulopathy and bleeding manifestations, hepatic encephalopathy, metabolic acidosis and renal failure.11,12 Dengue with high level of viremia causes multiple organ impairment including liver. 13 Virus can have direct effect on hepatocytes or through immune mechanism dysregulation.14 Pathogenesis of liver dysfunction includes hepatic steatosis, necrosis and destruction of kupffer cells.15,16

Case Summary
A 35 years old woman presented to Department of Infectious Diseases Holy Family Hospital Rawalpindi with 8 days history of fever, headache, myalgias, arthralgias and backache. She had symptoms of jaundice, deepening of colour of urine and altered mentation for 2 days. She was married and had 2 children. As she had menorrhagia and fibroid uterus she underwent hysterectomy 3 weeks ago and was given antibiotics for surgical complications. Examination revealed a middle age lady who was confused, irritable, jaundiced and had petechial rash over body. Pulse was 120 beats per minute, BP 130/60 mm Hg, respiratory rate 34/minute, temperature 102°F, Chest and abdominal examinations were unremarkable, CNS examination showed confusion irritability, pupils were equal and reactive bilaterally, plantars were bilaterally down going. Initial diagnosis of acute hepatic failure, cerebral malaria, septicemia, DIC and multi organ failure was made. Initial investigations showed Hemoglobin14.5 g/dL, total leukocyte count (TLC)12.7x10⁹/L, Platelets 32 x 10⁹/L , hematocrit 42.3 %, serum bilirubin3.6 g/dL, serum alanine transaminase (ALT) 1913 IU/L, serum alkaline phosphatase ( ALP) 1112 IU/L, Prothrombin time (PT) 9 seconds increased and activated partial thromboplastin time(aPTT)32 Seconds prolonged. Fibrinogen was 137 mg/dL (180-450 mg/dL)and FDPs >1600 (<200). Renal function tests were normal. Considering the symptoms, signs and endemicity of dengue infection in the region it was also considered in differential diagnosis and serology was sent. Her ultrasonography abdomen revealed normal study. She was started on intravenous imipenem, vancomycin, omeprazole, intravenous artesunate, IV fluids, oral N-acetylcysteine and intravenous vitamin K. Next day her condition continuously worsened and had multiple episodes of hematemesis, melena, epistaxis and gum bleeding which was managed with blood and fresh frozen plasma transfusions. She developed type 1 respiratory failure,for which ventilatory support was given. Dengue markers turned out to be positive. All the other serological and immunological markers were negative. Serum ammonia levels were 347 µg/dL (31-123µg/dL). Diagnosis of dengue induced fulminant hepatic failure and dengue expanded syndrome was coined. Ultrasound abdomen was repeated which revealed fatty hepatomegaly, increased echogenicity of liver and gall bladder wall thickness. Chest radiograph and ultrasound chest showed right sided moderate pleural effusion. On day 3 of admission bleeding from gums continued despite supportive therapy whereas upper gastrointestinal bleeding settled as conscious level of patient. Liver function tests and coagulation profile also improved. Over the period of her hospital stay of 9 days she developed ventilator associated pneumonia, sepsis, pneumothorax, disseminated intravascular coagulation and multi organ failure. Despite treatment by multidisciplinary team she could not be revived.

Discussion
The spectrum of dengue hepatitis usually ranges from asymptomatic stage to its severe form as acute fulminant hepatic failure. Clinical manifestations of
disease include abdominal pain, nausea, anorexia and vomiting, hepatomegaly and abdominal tenderness.17-19 These clinical manifestations are more often seen in dengue fever (DF) than in dengue hemorrhagic fever (DHF). Clinical deep jaundice has rarely been reported.20 Dengue hepatitis usually occurs during first or second week of illness but has rarely been reported during the recovery phase of infection.21 In clinical practice viral hepatitis and drugs are the major cause of acute fulminant hepatic failure. Dengue viral hepatitis and fulminant hepatic failure is one of the rare causes and has rarely been related in adults. Most of the cases that are reported occur in children.3, 21-24 The biochemical manifestations of dengue hepatitis include raised transaminases where aspartate transaminase (AST) is raised more as compared to alanine transaminase (ALT), likely due to release earlier from myocytes.25 These biochemical markers tend to reduce in three weeks. Management of dengue induced fulminant hepatic failure is usually supportive.26 N-Acetylcysteine and MARS therapy had been instituted in literature with good clinical outcome of patients.15, 26-28.

Our patient presented with symptoms of fever, myalgias, arthralgias, jaundice and confused status of 1 week duration. As patient had history of hysterectomy and had leukocytosis initially diagnosis of sepsis and multi organ failure was made. Keeping in consideration patient’s deranged LFTs and coagulopathy with raised ammonia; acute liver failure was diagnosed due to dengue infection as dengue markers were positive. Dengue viral hepatitis was diagnosed as AST was deranged more as compared to other transaminases contrary to that seen in other viral causes of hepatic failure.26 She was treated with N-Acetylcysteine for hepatic failure as it proved to have good clinical outcome of patients with fulminant hepatic failure.26-28
despite all the specific and supportive measures patient developed ventilator associated complications, sepsis, multiorgan failure and unfortunately she died. The management in such cases is usually supportive along with prophylactic antibiotics to prevent bacterial infection, N-Acetylcysteine, careful IV fluids administration. Most of the patients with dengue related fulminant hepatic failure recover with supportive therapy.

References