**Acute Liver Failure in a young patient with Dengue Shock Syndrome: A Case Report**

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Author’s contribution:

1. Lukash Adhikari: Design of study, involved in patient management, data collection, manuscript writing and revision
2. Eliz Achhami: Design of study, data collection, evidence collection, manuscript writing and revision.
3. Shumneva Shrestha: Data collection, manuscript writing and revision.

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Abstract:

Dengue fever is caused by the *Aedes* species, which has four different serotypes. This virus is endemic to Southeast countries, including Nepal. The clinical presentation can range from asymptomatic to life-threatening acute liver failure. Prompt diagnosis and management are necessary in order to prevent complications.

Keywords: Dengue Fever, Dengue Shock Syndrome, Acute Liver Failure, South Asia.

Introduction:

Dengue fever is an arboviral infection of a significant burden in tropical countries. *Aedes aegypti* and *Aedes albopictus* transmit it.(1). The dengue virus has four distinct serotypes, namely DEN 1 to DEN (2). Dengue fever is endemic in Southeast Asia, including Nepal. [2]. The previous infection protects against reinfection with the same serotype, but reinfection with different serotypes results in a worse clinical prognosis (3). Clinically, dengue fever is diagnosed by the presence of fever with at least two additional symptoms like ocular pain, headache, muscle/joint pain, rash, or leukopenia (4). The incubation period of this illness is 3-7 days, and it is divided into 3 phases; a febrile phase (2–7 days), a critical phase (day 3–7 of illness, with vascular leakage), followed by a convalescent-phase (2). Liver is one of the major organ that is damage due to dengue virus through multiple mechanisms. The virus directly affects the Kupffer cells and hepatocytes. There is immunological hyperactivity that leads to T cell-mediated cytokine storm and circulatory failure, leading to decreased hepatic perfusion(5). Effects on the liver range from asymptomatic transaminitis to acute liver failure (ALF).We present a case of a young female with dengue fever complication leading to acute liver failure and about her management.

Clinical presentation:

A 26 years non-alcoholic female presented to the Emergency Department with a history of 4 days fever which was intermittent; the maximum temperature recorded was 102 F, associated with headache, retroorbital pain, and myalgia but without chills and rigor. There was no history of mucocutaneous bleeding or bruises. There was a history of multiple episodes of nausea and vomiting along with diffuse abdominal pain and distension, which was progressive, loss of appetite, and the generalized weakness associated with acute shortness of breath. There was no history of chest pain, palpitation, orthopnea, dizziness, loss of consciousness and abnormal body movements, or altered sensorium. There was no similar history in the past.

On examination, her Blood pressure was 100/60 without a significant postural drop, pulse 106 beats per minute, oxygen saturation at room temperature was 98%, respiratory rate was 20/minutes, and the temperature was 101.4 F. She was well oriented to time, place, and person. On abdominal examination, it was grossly distended with dull percussion with decreased bowel sound. There was the presence of crackles over the lower surface of both lung fields. Her heart sound was normal. A necessary initial investigation showed (**Table 1)** were sent.

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| --- | --- | --- |
| Investigation done in the day of admission | | |
| Investigations | Results | Reference range |
| Total leukocyte count | 11950 Cells/Cumm | 4000-11000 |
| Differential count | Neutrophils(N)60.90% , Lymphocytes(L) 34.30% | N(40-70), L(20-45) |
| Hemoglobin(Hb) | 12.4 gms% | 11.9-14.6 |
| Packed Cell Volume(PCV) | 35.20% | 40-50 |
| Platelets | 78000 Cells/Cumm | 150000-450000 |
| ALT: Alanine transaminase | 2202 U/L | 9.0-52 |
| AST: Aspartate transaminase | 74160 U/L | 14-36 |
| Total bilirubin | 4.70 mg/dl | 0.2-1.3 |
| Conjugated bilirubin | 1.40 mg/dl | 0-0.3 |
| Unconjugated bilirubin | 1.20 mg/dl | 0.0.1 |
| Alkaline phosphatase | 311 U/L | 30-126 |
| Prothrombin time | 19.50 sec | 11.0-16 |
| Control | 14 sec |  |
| Random blood glucose | 60 mg/dl | 80-140 |
| C-Reactive Protein(CRP) | 87 mg/L | 0-10 |
| Creatinine | 0.60 mg/dl | 0.52-1.04 |
| Urea | 19 mg/dl | 15-45 |
| Total Protein, Serum | 5.30 g/dL | 6.3-8.2 |
| Albumin, Serum | 2.20 g/dL | 3.5-5.0 |
| Serum Lactate | 5.1 mmol/L | 0.7-2.0 |

**Table 1**: Investigations done on the day of Admission.

The malarial parasite was not visualized in peripheral blood smear - scrub typhus rapid antigen(Immunochromatography)was negative- Hepatitis A IgM was negative, anti-hepatitis E IgM was negative- Hepatitis B surface antigen was negative - Hepatitis C IgM was negative-Leptospira IgM was negative; Dengue fever antibodies IgM; subtype NS1 was positive and IgG was negative.

(NS1: non-structural protein 1, IgM: immunoglobulin M, IgG: immunoglobulin G.)

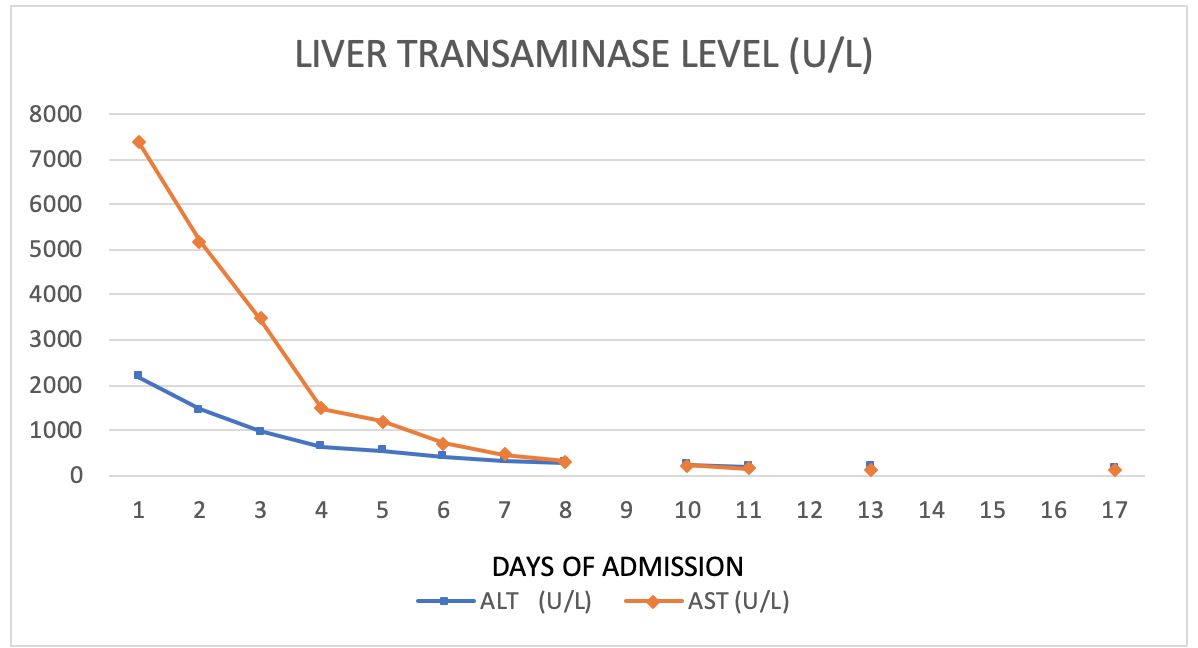
The ultrasound of the abdomen and pelvic done on the day of admission showed moderate ascites with bilateral pleural effusion. Within the day of admission, she had 4-5 episodes of nausea and vomiting, for which she was kept NPO. She was started on IV fluids and antiemetics due to worsening lactate levels and persistent tachycardia; later that day, she complained of severe abdominal pain and respiratory difficulty, for which she was shifted to the Intensive care unit(ICU). During 3rd day her abdominal distension progressively increased, and she became tachypneic, confused, drowsy, and restlessness. Working diagnosis of Dengue shock syndrome with acute liver failure grade III Hepatic Encephalopathy was made. She was started on antibiotics, enema, diuretics, proton pump inhibitors, methylprednisolone, lactulose, 20% albumin infusion, N-acetylcysteine (NAC), and Total Parenteral Nutrition(TPN). Hepatotoxic medications were avoided.

Computed Topography(CT)scan of whole abdomen was done(**Figure A**). Therapeutic tapping of ascitic fluid was done which provided her sense of relief. Therapeutic tapping was transudative and fluid cytology was negative for malignancy.

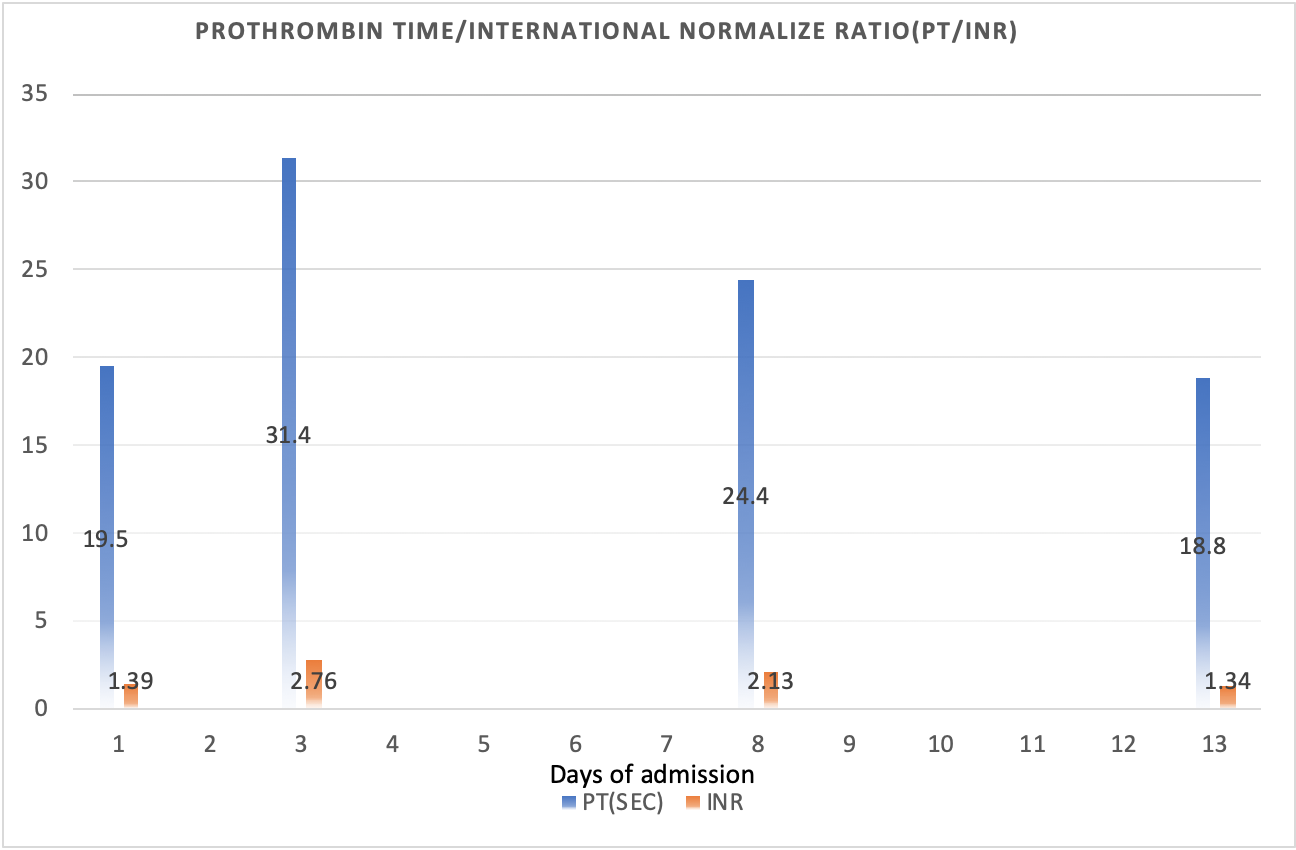


**Figure A:** Computed Topography(CT)scan of whole abdomen: **Gross ascites with large amount of bilateral pleural effusion with bilateral lower lobe atelectasis.**

Over time her deranged transaminases(**Table 2**) level also decreased. Her Coagulopathy which was deranged(**Table 3**), was appropriately managed with fresh frozen plasma and Vitamin K.



**Table 2**: Liver transaminases level; AST: Aspartate transaminase; ALT: Alanine transaminase.



**Table 3** : Change in PT/INR levels

Slowly her clinical status, as well as biochemical profiles, were improved. She was completely weaned off the ventilator on the fifth day of intubation. After 20 days, she was discharged from the hospital. Later during follow up visit her transaminase levels were within normal range.

Discussion:

The spectrum of dengue fever caused by different serotypes of dengue virus dengue fever clinical spectrum extends from asymptomatic to dengue fever, dengue hemorrhagic fever, and the most lethal dengue shock syndrome with ultimate acute liver failure (1,4). Dengue hemorrhagic fever (DHF) is diagnosed by the presence of fever with signs of hemorrhages, thrombocytopenia, and plasma leakage (4). Dengue shock syndrome (DSS) is the most severe form of dengue, which can affect several organs, including the liver, brain, and kidney, and result in fatal outcomes (1,4).

Liver involvement in dengue is a crucial feature, and the effect ranges from an asymptomatic rise in liver enzymes to the development of acute liver failure (4).Dengue patients who presented with abdominal pain, nausea, vomiting, and anorexia should be evaluated for liver involvement (6). The exact pathophysiology behind liver failure in dengue is not clear. The possible hypothesis includes T cell-mediated host immunity and the underlying cytokine storm, which is also known as cytokine “Tsunami” (4,7,8). Interleukin-22 (IL-22) and interleukin-17 (IL-17) are particularly responsible for liver injury (9).

Acute liver failure often results in multiorgan dysfunction including hemodynamic instability, renal failure, cerebral edema, and even death because of shock (4,7).

Souza et al. found that 74.2% of patients with serologically confirmed dengue had significantly elevated transaminase (9). Later Kuo et al. and Nguyen et al. found that the level of aspartate aminotransferase (AST) was higher than that of alanine aminotransferase (ALT) (10,11). The liver enzymes usually come back to normal limits within three weeks (10). Damaged striated muscle, cardiac muscle, and erythrocytes release the AST, which could be the reason for the high level of AST as compared to ALT (12,13).

Treatment principles include administration of N-Acetyl Cysteine(NAC), which has a crucial role in preventing free radicals mediated hepatocyte damage and prevention of hypoperfusion, dengue shock syndrome, or dengue hemorrhagic fever. Although this plays a specific role in mitigating the process, none is proven beneficial in all cases. Only a few therapeutic options are available in the current era for severe liver disease. The last resort is a Liver transplant in the case of ALF; however, it is not that feasible due to a limited number of donors. Therefore, new methods should be developed to prevent as dengue virus spread and new drugs should be discovered to prevent hepatotoxic injury (14,15).

Conclusion:

Dengue fever has been a significant burden in countries with poor resources. Prompt diagnosis and management are necessary to prevent the life-threatening complications of acute liver failure. People infected more than one time with different serotypes increase the risk of severe complications and mortality. Since there are no proper antiviral treatment, prompt diagnosis and adequate hydration is the mainstay of treatment. However, despite proper diagnosis and management, there are increasing cases of dengue complications. Therefore, proper medications and vaccines targeting the virus development would help to bend the curve of dengue virus incidence and complications.

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