



## **Answering reviewers**

**Reviewer 1:** This is a clinically relevant article highlighting dengue as a differential diagnosis for hepatomegaly and acute liver failure in a paediatric population. There are however multiple grammatical errors in the article which need addressing which i have highlighted as track changes. Lab results in the case report part are better outlined in a table than a paragraph. The discussion requires more in depth details regarding clinical symptoms / clinical manifestations and further detail on hepatology and laboratory abnormalities.

**Reply:** Our apologies for the grammatical errors. We have corrected the mistakes to best of our abilities.. Lab results are added as a table. Discussion on clinical manifestation has been elaborated.

**Reviewer 2:** This is a case report on a 3-month-old male infant with severe dengue who died of fulminant hepatic failure and showed pan lobular necrosis on post mortem liver biopsy. The case is being presented to highlight life threatening complication of dengue in young children, and dengue viral infection as a cause of acute liver failure in endemic areas. Thus dengue fever should also be considered as one of the differential diagnosis in children presenting with fever and fulminant hepatic failure in endemic regions. This case report has some scientific and clinic significances, which is helpful for us to further understand the pathogenesis and diagnose of severe dengue fever in children. It is suggested that the author should clearly describe the diagnostic criteria of acute liver failure, and provide other clinical parameters such as anti-HEV, prothrombin time, INR, etc. This case report is recommended to be published in the journal after minor revision.

**Reply :** Diagnostic criteria of ALF defined. Clinical parameters like anti HEV, PT highlighted in tabular form.

**Reviewer 3:** Manuscript is well written but has several grammatical and typographical errors. I would suggest adding a table on the lab parameters of the patient. I would like to know why post-mortem biopsy was performed in this patient? Is it a general practice in your hospital?

**Reply:** We are sorry for the errors. We have tried to correct the mistakes to best of our ability. Table on lab parameter added. Child had a very short stay in our hospital, to have a definitive diagnosis,



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post mortem biopsy was done after discussing with parents. It is not a usual policy. But where we don't have a definitive diagnosis, we encourage such practice if parents are willing.

**Reviewer 4:** The authors present an interesting case of Dengue causing acute liver failure. This is rapidly becoming a major health problem in certain parts of the world. However, there are major limitations as pointed out below. Introduction please change "one of the most important cause" to "causes" as suggested by Word. Please give reference for this statement "Liver is the most common organ affected but is generally asymptomatic." Please give reference for these statements "Liver involvement ranges from derangement of liver enzymes, increased bilirubin to clinical jaundice and acute liver failure rarely. DENV is known to cause severe manifestation in infants." Case report Please try and make this more succinct. We don't need to know irrelevant details like "presented to the pediatric department", "treated as bronchiolitis". The word child is a common noun. It doesn't need to start as upper case. We do not need to know the differential diagnosis. Just be very specific to the case. It is convincing enough that this infant had Dengue. Again, exact lab values may not be necessary. Negative labs may not be necessary. What is "per standard protocol for ALF management"? Also, please define ALF before using abbreviated version. Discussion Hepatitis B is never a major cause of ALF in any part of the world. It usually causes chronic or acute-on-chronic liver disease. Please cite other examples of similar cases and case series and discuss your case in comparison with those cases. For example see PMID: 18376367. Dengue ALF has been reported in the past. However, the interesting factor about your case is the age. Please discuss Dengue infection in infants. Also, do you think that the source of the infection was transmission via breast milk? What is the effect of maternally transmitted anti-Dengue antibody on infection? Table 1 is irrelevant to the case. Such knowledge can be obtained from textbooks. Also, some of the statements in the table may not be completely accurate. In summary, the case is interesting. There is convincing evidence that this is Dengue ALF. Authors have discussed the liver pathology in an appropriate manner. However, the clinical discussion may be a bit lacking. As mentioned above, the age of the child and dynamics of dengue infection at this age needs elaboration. Table 1 may be replaced by a comparison of clinical/lab factors in your case with cases previously reported. Please do address the language and spelling errors. There are multiple such errors.

**Reply :** We thank the reviewer for his valuable opinion. We have tried to incorporate changes as much as possible. Discussion has been elaborated. Table 1 is important for overall understanding of the manuscript. Hepatitis B does cause acute liver failure (see PMID 19125959). Comparison with previously published cases will be difficult due to lack of similar reports in this age group. References are added later in the text as suggested.

We understand the reviewer's concern about transmission of dengue through breast milk but there was no history of dengue infection in the mother. Presence of maternal antibody can be both protective and detrimental depending on host factors. Some infants may show antibody-dependent cytotoxicity in presence of maternal antibody and may have more serious manifestation.

