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Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
<https://www.wjgnet.com>

PEER-REVIEW REPORT

Name of journal: *World Journal of Virology*

Manuscript NO: 91457

Title: Dengue induced acute liver failure: A meta summary of case reports

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00182114

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor, Surgeon

Reviewer's Country/Territory: Japan

Author's Country/Territory: India

Manuscript submission date: 2023-12-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-12-29 07:41

Reviewer performed review: 2023-12-29 09:01

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



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Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

NAC has been the drug of choice for the treatment of acetaminophen related liver failure since the 1970s. NAC helps neutralize free oxygen radicals and replenishes cytoplasmic and mitochondrial glutathione stores by acting as a glutathione substitute and directly combining with reactive metabolisms. It serves as a source of sulfate , thus enhancing non-toxic sulfate conjugation and preventing hepatic damage. I ask some questions to author. 1.Please let me know from what day and for how many days NAC should be administered after liver failure occurs. 2.What is the PT value to start NAC after acute liver failure? 3.Please tell me the etiology of liver failure due to dengue fever.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 07706979

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Brazil

Author's Country/Territory: India

Manuscript submission date: 2023-12-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-12-28 19:56

Reviewer performed review: 2024-01-05 15:17

Review time: 7 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The article entitled "Dengue duced acute hepatic failure: A meta summary of case reports" has an interesting approach to this complication of infection caused by dengue. It is a well-written work, with clarity in its general objective. In fact, I was unable to do so and have never seen any work that compiled case reports, clinical approaches and prognoses of patients with this complication. Understanding that this work can be important for updating and alerting health professionals who work in emergencies and intensive care units to think about the profile of the patient suffering from this complication. As there are 19 cases included in the study, I suggest that the authors include a table with the 19 studies, describing the author, publication data, title, which diagnostic method was used and how many patients were included in each study. It is important for the reader to have an overview of the work carried out. Regarding figure 2, I suggest using authorial figures, the DENV figure can be better represented in an illustrative way, the liver and hypoxia/ischemia as well. Redraw figure 2 and center the sentences.



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Peer-review model: Single blind

Reviewer's code: 00038995

Position: Editorial Board

Academic degree: FAASLD, MD, PhD

Professional title: Adjunct Professor, Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: India

Manuscript submission date: 2023-12-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-12-29 23:26

Reviewer performed review: 2024-01-06 18:52

Review time: 7 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors provide a "meta summary" of liver failure induced by Dengue. Although a very common disease in certain parts of the world, and further spread anticipated, there is a lack of information re liver failure and particularly well documented cases. The authors were able to identify some 19 cases from the world literature. They rightly conclude that frequent severe damage is extremely rare. Estimated of nominators/denominators are hard to identify. They discuss various aspects of pathophysiology and speculate about multiple factors that could contribute. Not a single evidence based recommendation can be provided. Although this author has very limited expertise with Dengue (mostly practicing in non-endemic areas, a few years Africa), he has considerable experience with liver transplant and liver failure,. My reflections and questions: 1. When discussing liver failure, too often not too stringent criteria are in use What were the criteria the authors applied or were able to extract from their search? I would suggest a more critically review and or delineation of the evidence of acute liver failure as an entity with multi-organ failure # liver failure (often more functional than anatomical) vs a disease affecting multiple organs and causing damage. Acute liver



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failure is associated with multi-organ failure but it tends to have often a particular pattern. I refer the authors to the landmark article by O'Grady et al (Lancet 1981) re hyperacute, acute and subacute liver failure. In the limited documented series they are able to report, the onset of symptoms was so early (4.5 days median) with relatively low bilirubin values and INRs. (Or do we speculate a longer prodromal phase?) The question comes up: Is the encephalopathy here portosystemic # liver failure or are we for dealing with acute brain damage # dengue encephalitis. This postulate could have major impact on diagnosis and treatment (transplant even less likely to help). There may indeed be acute cytopathic damage to various organs (as also suggested in some case of acute hepatitis A as well) and explaining early damage and response. Is there a role for acute anti-inflammatory agents like steroids? Will we ever be able to tests if so rare? 2. This brings me to another point that may deserve further highlighting, namely the recognition of liver failure vs significantly abnormal liver tests in the context of various infectious diseases not being viral hepatitis Leptospirosis is an interesting example with high bilirubins with lower transaminases and usually not very prolonged INR etc. So the recognition of acute liver failure with laboratory data consistent with that is relevant (INR runs off, creatinine increases etc.). As another example: Acetaminophen toxicity and acute ischemic damage (shock liver) can be accompanied by high transaminases (5-10.000 or higher) but the pattern and evolution and association with INR and creatinine matter for disease outcome etc.) The Dengue pattern would be consistent with acute ischemic damage and/or viral cytopathic damage. 3. Unfortunately, the extreme rarity, the limited numbers prevent any firm recommendations and liver failure as such is an extremely unusual event that speculation that liver transplant may help has -based on the current data - no merits 4. This brings me to the question as to for whom or with what purpose the article is written. Should it be more: Recognition of the rare occurrence of serious Dengue associated liver failure: common sense should guide us by lack of any



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evidence based data?