

Letter to Editor

Asian Pacific Journal of Tropical Medicine

apjtm.org

doi: 10.4103/apjtm.apjtm_186_26

Serotype-dependent cytopathic effects and replication dynamics of dengue virus serotypes 1 and 2 in Chang liver cells

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Dengue virus (DENV) infection remains an important public health concern, particularly in endemic regions such as Malaysia. Although all four DENV serotypes can cause dengue, differences in viral behaviour and their association with liver pathology remain incompletely understood[1-3].

In this light, we investigated the cytopathic effects (CPE) and replication dynamics of DENV-1 and DENV-2 in Chang liver cells. DENV-1 and DENV-2 are frequently associated with major dengue outbreaks worldwide; therefore, studying these serotypes provides critical insights into viral interactions, pathogenesis, and disease severity[1,3]. DENV-1 induced earlier and more pronounced cellular damage, including vacuolization, cell rounding, detachment and clumping, than DENV-2 (Figure 1A and B). This was supported by the progressive decline in cell viability following DENV-1 infection throughout the infection period (Figure 1C). In contrast, DENV-2 demonstrated a slower progression of CPE, with a delayed cell death compared with DENV-1 (Figure 1D). These findings suggest that dengue serotypes may interact distinctively with hepatic cells, hence the varied cytopathogenicity[4,5].

The distinguishable cytopathic progression was further supported by the viral *CprM* gene amplification, which is widely used for dengue virus serotyping and molecular epidemiological studies due to its serotype-specific sequence variability[6]. DENV-1 exhibited earlier and sustained detection of the *CprM* gene, whereas DENV-2 was only detectable at later stages of infection (Figure 1D), highlighting distinct replication patterns that may differentially affect host cell responses and clinical outcomes[7]. The more pronounced cellular damage induced by specific serotypes may reflect a greater pathogenic potential and contribute to increased disease severity[8].

In a nutshell, a deeper understanding of serotype-dependent viral replication patterns and CPE, and host cellular responses is essential for precisely delineating dengue pathogenesis and the heterogeneity of clinical manifestations. These perspectives can support the development of targeted antiviral and host-directed therapeutic strategies. Future studies incorporating advanced hepatic models, transcriptomic profiling, and mechanistic analyses are warranted to further define the involvement of serotype-specific liver injury in dengue disease outcomes.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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How to cite this article: Rosmen SAS, Yaakob AI, Apandi NAHM, Yap WB. Serotype-dependent cytopathic effects and replication dynamics of dengue virus serotypes 1 and 2 in Chang liver cells. Asian Pac J Trop Med 2026; 19(8): 374-376.

Article history: Received 17 April 2026 Revision 16 June 2026
Accepted 21 July 2026 Available online 29 July 2026

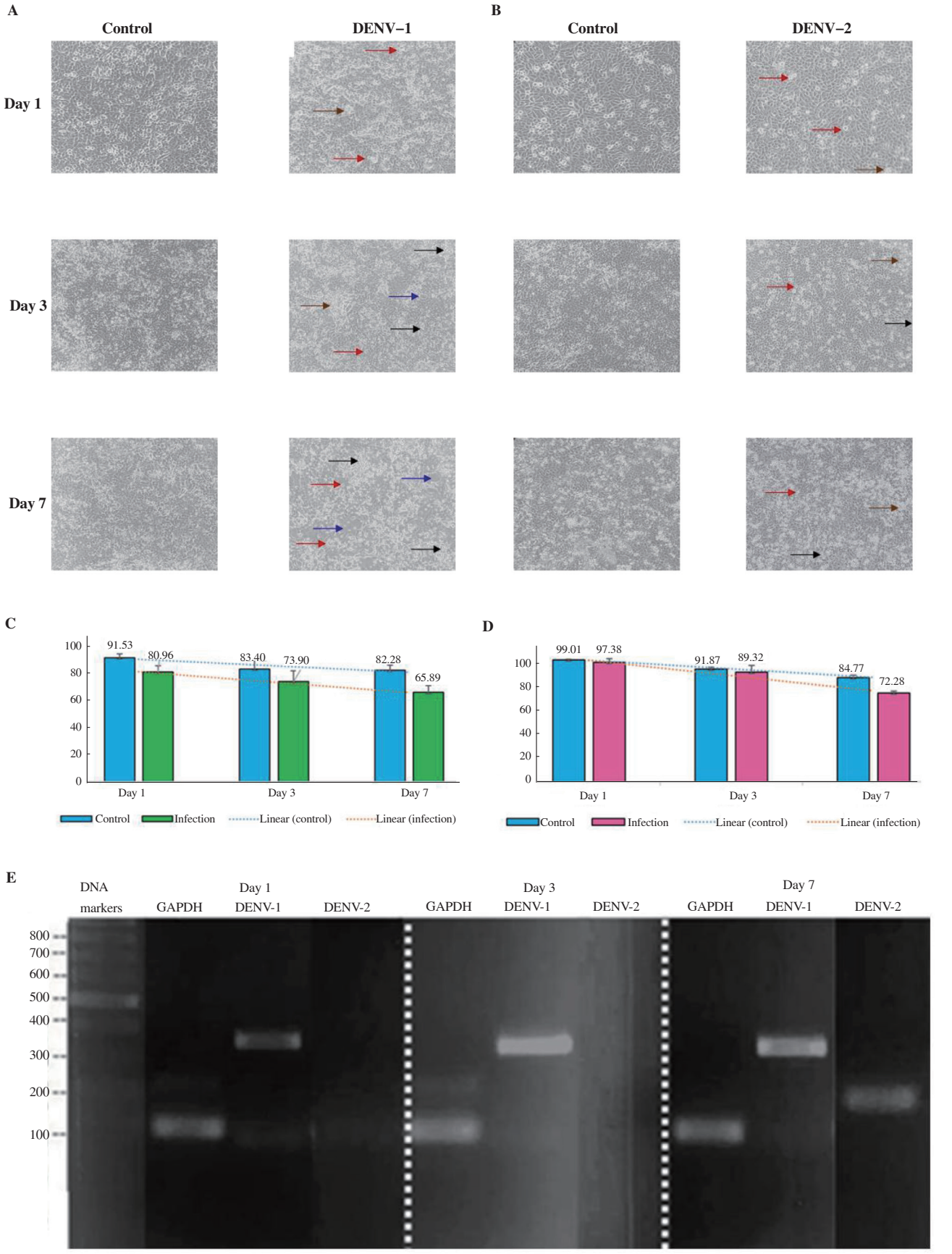

Figure 1. Comparison of cytopathic effects in DENV-1 (A) and DENV-2-infected (B) Chang liver cells, and the cell viability following DENV-1 (C) and DENV-2 (D) infections. Amplification of DENV-1 (343 bp) and DENV-2 (251 bp) *CprM* genes from infected Chang liver cells (E). *GAPDH* gene served as the reference gene. DENV-1 induced earlier and more pronounced cellular damage, including vacuolization (red arrows), cell rounding (red arrows), detachment (blue arrows) and clumping (brown arrows)

Funding

This work was funded by the FUNDAMENTAL RESEARCH GRANT SCHEME, Malaysia Ministry of Higher Education (MoHE), grant number: FRGS/1/2021/STG03/UKM/02/2.

Authors' contributions

SASR, AIY, NAHMA and WBY jointly developed the study concepts and design, performed literature search, SASR, AIY and NAHMA completed experimental studies and data analysis, and SASR, AIY and NAHMA prepared the manuscript. RSAS carried out manuscript review; AIY undertook manuscript editing; WBY defined intellectual content, revised the manuscript and acted as the guarantor. All authors read and approved the final version of the manuscript.

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Edited by Pan Y, Lei Y, Zhang Q