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Letter

High frequency of severe liver dysfunction in critically ill Dengue patients in the French West Indies



Dear Editor,

Dengue is a worldwide zoonosis, transmitted by mosquitoes and highly prevalent in tropical and subtropical areas. In recent years, its incidence has increased with a massive healthcare burden worldwide^[1] and recent climatic changes have expanded the geographic range of the insect vector with described outbreaks in Europe.^[2] Most patients present pauci-symptomatic infections, but some patients could present severe manifestations with high reported mortality^[3–5] and no specific therapeutic. Major bleeding, hemodynamic failure and various organ damage (cardiac, renal, neurological, and hepatic) are described in severe dengue (SD) patients.^[5] In the future, intensivists worldwide will be increasingly treating SD and the spectrum of severe organ impairment should be well known.

Between December 2019 and October 30 2023, 36 SD patients have been hospitalized in the Intensive care unit (ICU) of the University Hospital of Guadeloupe (UHG) with two large epidemic outbreaks (2020 and 2023). We retrospectively analyzed the characteristics and outcome of the 36 consecutive patients with dengue infection confirmed by PCR and/or NS1 positive antigen and criteria for SD according to WHO classification^[1].

Briefly, in our center, ICU patients had severe plasma leakage with shock ($n=17$, 47.2%), severe bleeding ($n=20$, 55.6%) and severe organ impairment ($n=20$, 55.6%). The striking pattern was the high frequency of acute liver failure (ALF) ($n=10$, 27.8%), defined as an international normalized ratio (INR) ≥ 1.5 , and any degree of mental alteration (encephalopathy) in a patient without preexisting cirrhosis. In all ALF patients except one, cardiac function was preserved, and all received N-acetyl cysteine therapy. At ICU admission, bacterial co-infection was present in 11.1% of the cases ($n=4$). Most of the SD patients ($n=22$, 61.1%) and all ALF patients ($n=10$, 27.8%) were dengue virus (DENV)-2 infected. Overall, 30-day mortality was 22.2%, and all deceased patients had DENV-2 ($n=8$). In univariate analysis, when comparing 30-day survivors vs. non-survivors, severe organ involvement, such as shock (33.4% vs. 100%), ALF (14.5% vs. 75.0%), neurological involvement (19.2% vs. 100%) at ICU admission were statistically associated with death. The mortality rate for SD in our ICU (22.2%) was consistent with previous reports.^[3,5,6] The burden of hemodynamic renal failure in critically ill SD was previously described.^[3–5] The low reported

incidence of dengue-related ALF in other ICU series^[3–6] starkly contrasts with our results (27.8%). Few previous reports of liver involvement report a poor prognosis.^[7] In the univariate analysis, we confirm that ALF is highly related to death. We should emphasize that ALF occurred during the 2023 outbreak and we hypothesize that it could be due to either a different genotype of DENV-2 or a specificity related to the Afro-Caribbean population. The therapeutic of SD is primarily supportive care, and there is no specific therapeutic for life-threatening organ involvement related to dengue infection (*i.e.* Myocarditis, ALF, encephalitis). Paracetamol should be avoided when hepatitis occurs and N-acetyl cysteine should probably be administered in the case of ALF. Other therapeutics, such as liver transplantation, seem precarious during the acute viral infection phase.^[8]

Nevertheless, we advise intensivists to monitor liver function in SD patients cautiously and call for studies to propose specific therapeutics for severe organ involvement related to Dengue infection.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRedit authorship contribution statement

Laurent Camous: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft. **Samuel Markowicz:** Methodology, Supervision, Validation, Visualization, Writing – original draft. **Cecile Loraux:** Data curation, Validation, Visualization. **Julien Jabot:** Validation, Visualization, Writing – original draft. **Jean David Pommier:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft.

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