2307. Risk factors for Cytomegalovirus (CMV) reactivation and Association with Clinical Outcomes in Critically Ill Adults with Sepsis: A Pooled Analysis of Prospective Studies

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Background. CMV reactivation in seropositive, non-immunosuppressed adults with sepsis has been associated with worse clinical outcomes. To inform rational design of interventional trials determining whether CMV prevention improves outcomes, it is critical to identify the independence and strength of the association of CMV reactivation measures with clinically-relevant endpoints. Identification of patient factors associated with CMV reactivation would allow for optimization of the study population.

Methods. We performed a secondary pooled analysis of two prospective cohorts with sepsis: an observational cohort of ICU patients ($n = 40$) and the placebo cohort from a randomized, double-blind trial of ganciclovir to prevent CMV reactivation in acute critical illness ($n = 66$). Personnel blinded to the PCR results assessed clinical variables; CMV DNAemia was measured by quantitative plasma PCR twice weekly. Multivariable modeling using logistic and linear methods was used to examine the associations of CMV with clinical outcomes and between baseline patient factors and measures of CMV reactivation (adjusted for age, race, gender, transfusion status, study cohort, and APACHE score).

Results. CMV reactivation occurred at any level in 38/106 (36%), at >100 IU/mL in 25/106 (24%), and at >1,000 IU/mL in 14/106 (13%). In a multivariate model, CMV reactivation at any level, >100 IU/mL, or >1,000 IU/mL was associated with fewer days alive and not requiring ventilation: mean difference of −3.5 days ([95% CI −7.0, 0], $P = 0.057$), −5.1 days ([−8.9, −1.2], $P = 0.012$), and −6.1 days ([−10.9, −1.2], $P = 0.016$), respectively. Multiple measures of CMV reactivation were associated with other clinically-relevant outcomes, even after adjustment for baseline factors (Table 1). The association of APACHE score with CMV reactivation measures was inconsistent and with small effect size. We did not identify other patient variables associated with subsequent CMV reactivation.

Conclusion. CMV reactivation in seropositive adults with sepsis is independently and quantitatively associated with clinically-important outcomes, including death or continued hospitalization by day 28, ventilator-, ICU-, and hospital-free days. These effect sizes provide key data to inform design parameters of future interventional trials.

Table 1. Clinical outcomes within 28 days after enrollment[a]

	Hospitalized or died by day 28[b]	Ventilator-free days[c]	ICU-free days[c]	Hospital-free days[c]
CMV reactivation any level	2.9 (1.1, 8.1) p=0.038	-3.5 (-7.0, 0) p=0.057	-4.1 (-7.5, -0.7) p=0.020	-4.9 (-8.1, -1.7) p=0.004
CMV reactivation >100 IU/mL	5.6 (1.9, 17.8) p=0.003	-5.1 (-8.9, -1.2) p=0.012	-5.8 (-9.6, -2.1) p=0.003	-6.2 (-9.7, -2.7) p=0.001
CMV reactivation >1000 IU/mL	5.6 (1.5, 24.0) p=0.003	-6.1 (-10.9, -1.2) p=0.016	-7.4 (-12.0, -2.7) p=0.003	-6.4 (-10.9, -2.0) p=0.006
Average AUC CMV viral load (log IU/mL)	1.9 (1.0, 4.0) p=0.057	-1.6 (-4.1, 0.8) p=0.190	-2.5 (-4.8, -0.2) p=0.039	-2.9 (-5.1, -0.6) p=0.013
Peak CMV viral load (log IU/mL)	1.6 (1.1, 2.4) p=0.009	-1.5 (-2.8, -0.3) p=0.020	-1.9 (-3.1, -0.6) p=0.004	-2.1 (-3.2, -0.9) p=0.001

CMV, cytomegalovirus; AUC, area under the curve; ICU, Intensive Care Unit
[a]After adjustment for age, race, gender, baseline transfusion status, study cohort, and a standardized score created from APACHE II and APACHE III scores used in the individual studies.
[b]Estimates represent odds ratios and associated 95% CIs
[c]Estimates represent the difference in mean days and associated 95% CIs

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2308. Comparison of Clinical Characteristics Between Laboratory-Confirmed Positive and Negative Patients with Severe Fever with Thrombocytopenia Syndrome

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Background. Severe fever with thrombocytopenia syndrome (SFTS) is a tick-borne emerging infectious disease caused by SFTS virus (SFTSV). Mortality of SFTS estimated to be 21.8% in South Korea, and this disease is difficult differential diagnosis. Here, we analyzed clinical characteristics between SFTS positive group (SPG) and negative group (SNG) in a primary clinical setting.

Methods. In this prospective observational study, data were collected on patients with SFTS test performed at the single teaching hospital, in South Korea, between April 2013 and December 2018. The association between each demographic, climatic, clinical, and laboratory variable was assessed. All SFTS was confirmed by the KCDC by detecting the M segment gene of SFTSV RNA using reverse transcription-polymerase chain reaction (RT–PCR), and were confirmed at our laboratory by S segment gene of SFTSV RNA using RT–PCR about patient's family member and those with close contact.

Results. Of the 199 patients in the study periods, 61 (31%) were SPG and 138 (69%) were SNG. Mean age was 55.1 ± 20.3 years, and 103 (52%) patients were male. In SPG, the comorbidity score and history of tick bite were significantly higher compared with SNG. SPG and SNG were prevalent in summer and autumn, respectively (60.7% vs. 45.7%, $P < 0.05$). SPG was associated with mean outdoor temperature, humidity and rainfall compared with SNG (22.9°Cvs. 18.9 ℃; 78.8% vs. 70.6%; 12.6 mm vs. 8.5 mm, all $P < 0.01$). Dizziness, poor oral intake, nausea, and diarrhea were common in SPG. In laboratory findings, white blood cell counts, absolute neutrophil count, and C-reactive protein were significantly lower in SPG. Lymphocyte fraction, activated partial thromboplastin time, and creatinine phosphokinase were significantly higher in SPG. Case fatality of the SPG and SNG were 9.8% and 1.0%, respectively. In multivariate analysis, mean outdoor temperature, humidity, dizziness, and low CRP were predictive factors in SPG.

Conclusion. Early prediction of SFTS diagnosis is important because this emerging zoonotic disease was a high fatality in endemic areas. When a physician wants to do SFTS test, they would consider according to this predictive variable for differentiating SFTS in primary care settings.

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2309. Could Mean Platelet Volume Predict Platelet Count Recovery in Dengue Virus Infection?

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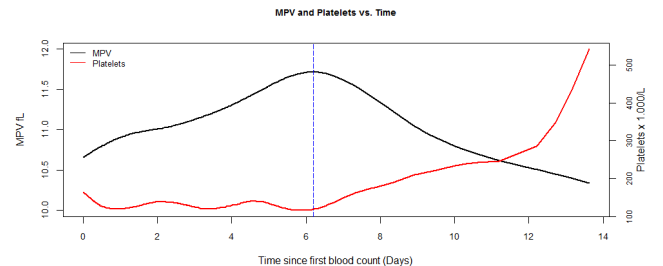
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Background. Dengue fever, a major public health problem throughout tropical and subtropical regions, has often unpredictable clinical evolution and outcomes. Thrombocytopenia is a common laboratory finding in dengue fever and severe dengue during the dengue critical phase. To the best of our knowledge, there is no clinical data about patient and disease factors that could predict in a short time the platelet recovery. Mean platelet volume (MPV), a measurement of platelet size, has a strong inverse correlation with platelet count and could indirectly reflect bone marrow activity. The aim of this study was to describe the behavior of MPV during the platelet count nadir and recovery.

Methods. An observational prospective study was conducted. We included patients with confirmed dengue virus infection with SD BIOLINE Dengue Duo kit (Abbott, Santa Clara, USA; former Alere Inc., Waltham, USA) attended at Fundación Valle del Lili, Cali - Colombia. Blood count was analyzed by xn-3000 system impedance method (Sysmex, Kobe, Japan). Laboratory and clinical data were recollected from clinical charts and clinical laboratory database. Platelet count (PC) and MPV were measured repeatedly during clinical management. Time was measured from the first blood count. A non-parametric analysis with a cubic smoothing spline was performed for platelet count and MPV.

Results. A total of 54 patients were analyzed from April 2016 to January 2016. 50% of patients had at least three blood counts. The median of the lowest PC was 112,500/L (IQR = 67,000–148,500), and the median of the highest MPV was 11. 25 fL (IQR = 10. 42–12. 15). MPV increased from the first blood count until day six, while platelets presented slight fluctuations. On the sixth day after first blood count, MPV presented a high peak that suggests an inverse relationship with a platelets decrease (Figure 1).

Conclusion. MPV increased with thrombocytopenia during the critical period and its decline precedes platelet count recovery. MPV could be useful to predict the platelet count recovery.

MPV and Platelets vs. Time

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