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Preliminary results of real-world whole-blood hydroxychloroquine level monitoring in systemic lupus erythematosus: low target attainment and key pharmacokinetic determinants

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Introduction: Hydroxychloroquine (HCQ) is a cornerstone therapy in systemic lupus erythematosus (SLE), yet treatment benefit depends on adequate and sustained drug exposure. Whole-blood HCQ level measurement may provide an objective approach to detect subtherapeutic exposure and could potentially support individualised clinical decision-making.

The study aims to determine the proportion of SLE patients reaching a literature-defined therapeutic HCQ range and to identify independent pharmacokinetic determinants of measured HCQ concentrations in routine care.

Material and methods: In a cross-sectional observational study, consecutive adult SLE outpatients were recruited at Semmelweis University between November 1 and December 17, 2025. Whole-blood HCQ levels were quantified using a validated liquid chromatography coupled to tandem mass spectrometry (LC–MS/MS) method. Of 35 enrolled patients, 32 were included in the final analysis. Target attainment was defined as 750–1,200 ng/ml. A one-sided exact binomial test evaluated whether ≥ 50% of patients were within range. Multivariable linear regression modelled HCQ levels using weight-adjusted daily dose, estimated glomerular filtration rate (eGFR), and time from last intake to blood draw.

Results: Only 6/32 patients (18.8%) achieved the 750–1,200 ng/ml therapeutic range; this proportion was significantly below 50% ($p = 0.00027$; exact 95% CI: 0.000–0.337). In the regression model ($F = 8.98$, $p = 0.001$; adjusted $R^2 = 0.51$), higher eGFR was independently associated with lower HCQ levels (β = –13.49; 95% CI: from –23.58 to –3.40; $p = 0.011$), and longer time since last intake was also associated with lower levels (β = –14.79 per hour; 95% CI: from –26.80 to –2.78; $p = 0.018$). Weight-adjusted dose showed a positive but non-significant association (β = 64.64; $p = 0.237$).

Discussion: These preliminary findings suggest that subtherapeutic HCQ exposure is common in routine care despite ongoing treatment. The results highlight the limitations of dose-based prescribing, while emphasising the clinical relevance of pharmacokinetic factors such as renal function.

Conclusion: In this preliminary real-world cohort, most SLE patients did not achieve the predefined therapeutic HCQ exposure range despite ongoing treatment. These findings suggest that dose-based prescribing alone may be insufficient to ensure adequate drug exposure. Whole-blood HCQ monitoring could help identify patients with subtherapeutic levels and potentially support a more individualised therapeutic approach by distinguishing nonadherence from pharmacokinetic variability.