Correspondence on 'Clinical course of coronavirus disease 2019 (COVID-19) in a series of 17 patients with systemic lupus under long-term treatment with hydroxychloroquine'

We thank Mathian *et al* for reporting the outcomes of COVID-19 disease in a series of 17 patients with systemic lupus erythematosus (SLE) from several hospitals across France.[1] In a context where there is substantial interest in the role of hydroxychloroquine (HCQ) as a potential preventive or therapeutic agent for severe acute respiratory syndrome–coronavirus-2 (SARS-CoV-2), these cases are noteworthy.

While the authors have correctly acknowledged the limitations of this case series report, we wish to emphasise several important points that impact the interpretation of the findings. The denominator of all patients with lupus on hydroxychloroquine who are 'at risk' of COVID-19 in this setting is unknown and may indeed be impossible to even estimate as it would need to be adjusted for risk of exposure to SARS-CoV-2. Notwithstanding occupation and travel, presently, the risk of exposure to the virus differs from one geographical location to another, even within each country.[2] For example, having 17 infections among several thousand individuals at risk may indeed be consistent with some protective effect of hydroxychloroquine. Moreover, as hydroxychloroquine is a staple maintenance treatment in the majority of patients with SLE, it may not be possible to source valid comparator groups who are not on hydroxychloroquine, and matching for other pertinent risk factors may not be possible across disease groups, such as rheumatoid arthritis and ankylosing spondylitis, as the demography of these diseases and their intrinsic impact on the immune system are distinctly different from those of SLE.

Second, we note the high burden of comorbidity and immunosuppressive medications among these patients with SLE, with 59% being obese, 47% having chronic kidney disease and 41% being treated with immunosuppressant drugs. Other comorbidities in this series of patients included cerebrovascular and cardiovascular disease, hypertension, malignancy and chronic lung disease. It is indeed possible that such high burden of comorbidities and concomitant immunosuppressive treatment may have overcome any protective effect of hydroxychloroquine. For example, while there are no head-to-head comparisons of antiviral response, immune-compromised patients with influenza have higher viral loads, higher frequency of viral mutation, prolonged viral shedding, and hence poorer treatment response and outcomes than immunocompetent hosts.[3] During the H1N1 influenza pandemic in 2009, despite treatment with oseltamivir, poor outcomes were reported in an immune-suppressed cancer population.[4]

In conclusion, we advise caution in relation to making any inferences regarding the preventive or therapeutic efficacy of HCQ for SARS-CoV-2 based on this case series alone. There may still be a place for HCQ in the prevention of SARC-CoV-2 in at-risk individuals without comorbid conditions who are not immune suppressed. Only well-designed randomised placebo-controlled trials will be able to shed light on this matter.

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