Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Conflicting evidence on the efficacy of hydroxychloroquine and azithromycin as the early treatment of COVID-19. Comment on "Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France"

In their open-label retrospective study of 1061 COVID-19 patients, Million et al. found that hydroxychloroquine/Azithromycin is an effective treatment in the early stage of the disease [1]. We are concerned this paper has several major limitations which we believe invalidate the conclusions of this study.

The inclusion criteria were rather unusual recruiting patients who were **asymptomatic**, much younger and less sick. In the New York study [2] 39.7% were women (thought to have a better prognosis), as compared to 54% in this study. One of the key risk factors for a poor prognosis is advancing age. The fatality is much higher in patients >70 years and highest in people aged 90 or older [2,3]. It is therefore not surprising that generally patients had a better outcome since the mean age was lower: 43.6 years in this study, compared to 63 in the New York and Lombardy cohort [2,3]. Chinese aged 60 years and older, had a 95% chance of survival following SARS-CoV-2 infection in the absence of comorbid conditions [4]. Thus, With 91,7% good outcomes in pauci-symptomatic young people, it is difficult to extrapolate that in symptomatic inpatients the drugs would had done better.

In addition, as many trials with unblinded treatment allocation and unblinded outcome assessment, interpretation of findings, such as viral clearance, may be problematic. The best primary endpoint is the clinical recovery from infection rather than swabbing again.

Another concern is the rather large cohort of 350 excluded patients. Of the 33 cases with cardiac contraindications, only prolonged QTc (10 patients) and Brugada syndrome (3 patients) wherein our opinion clear contraindications [5,6]. Left ventricular hypertrophy, bundle branch blocks, supraventricular tachycardia, and unspecified arrhythmia in 5 patients as well as unspecified ECG pattern in 66 patients are not clear-cut exclusion criteria. The exhaustive reasons that led to exclude these 350 patients do not apply in the daily practice worldwide where many countries and physicians manage COVID-19 patients with this protocol as the authors reminded. This lack of a full management work-up is more challenging in the low and middle-income countries where access to ECG is very limited [7].

Additional concern is that 7 out of 28 (25%) of references on which Million et al. relied to justify their results are preprint data (bioRvix and medRvix only). Indeed, preprint reports are not peer-reviewed, not finalized by authors, thus might contain errors *and report information that has not yet been accepted or endorsed in any way by the scientific or medical community*. The fact that the authors based their supportive arguments on unrecommended data seems rather not ethical for a pandemic which causes hundreds of thousands of deaths and paralyses the world economy. It is important that even in a pandemic, good quality data is used to guide clinical practice, as failure to do so risks clinical harm.

In conclusion, we feel that the findings of this study are contrary to current literature. As COVID-19 is self-limiting in the majority of asymptomatic or mild-symptomatic young patients, the findings of this study should be interpreted with extreme caution.

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