



Correspondence

Prophylactic use of hydroxychloroquine among healthcare workers in a case-control study

Sir,

It is with great interest that we read the article by Chatterjee *et al*¹ and appreciate the work done by the authors in the trying times of COVID-19. The attempt to bring out both risk and protective factors for the disease, including hydroxychloroquine (HCQ), among healthcare workers (HCWs), is indeed pertinent in the times of the ongoing discussion on the subject in scientific community. The study has also brought forth certain other issues which deter evidence generation from the national-level data. The case-control design to identify new risk factors if any, was most suitable to carry out the study in the shortest possible time based on the real data. The information being from across the country and the range of HCWs also added to the strength of the study. The positivity of confirmed SARS-CoV-2 of five per cent among the symptomatic HCWs was certainly reassuring. Further, it proves beyond doubt that personal protective equipment (PPE) is protective and the results substantiate the guideline insistence on appropriate PPE for all HCWs.

The study provided the first published literature on the benefits of HCQ prophylaxis and could generate evidence that intake of four or more maintenance doses of HCQ was protective against COVID-19 infection¹. *In vitro* studies on HCQ have already found it to have antiviral properties as well as immunomodulatory effects². The fact that the number of HCWs in the study who experienced side effects was low, further strengthens the case for using HCQ chemoprophylaxis. The evidence regarding usefulness of HCQ in COVID-19 so far had been derived only from anecdotal reports and studies without a control group³. Hence, the present study does put forth some

evidence of its usefulness, and with the postulated mechanism of action at a molecular level, it may have some role in the prevention of COVID-19 in the early stage of the disease. However, in spite of existing guidelines from the government, it is not a happy situation to note that barely, 50 per cent of HCWs seemed to be taking HCQ as evident from the available data¹.

In the study, regardless of having records of nearly 23,000 symptomatic HCWs with more than 1000 positive patients, the estimated sample size for cases and controls could not be met which does not augur well for our data quality. A high proportion of non-response in both cases and controls also indicates towards a low motivation among HCWs to participate in the research studies, which may generate important data for the benefit of others. The study could have been more robust if the minimum required sample size could have been achieved and non-response minimized. The initial increased odds observed in cases with lesser number of doses of HCQ taken by the HCWs also posed some questions which could not be explained fully. Notwithstanding the same and some other minor analytical issues, we are of the opinion that it may be a case for starting the HCQ prophylaxis early, *i.e.* 2-4 wk before being put on duty in the COVID facilities, keeping in mind the fewer side effects in these data. We also feel that it would be of interest to compare the severity of symptoms among the positive patients between those with and without HCQ.

Although the use of various non-pharmacological measures, such as hygiene measures, social distancing, and PPE, is being actively promulgated as the preventive measure against COVID-19, these have not

proved to be sufficient for protecting the HCWs, and therefore, some form of pharmacological intervention is essentially required. The present study¹ generated some evidence of HCQ effectiveness. However, the convincing evidence of HCQ utility in prophylaxis against COVID-19 will still require some well-planned large-scale clinical trial. At present, a large number of clinical trials (some of which are multicentric) have been registered with ClinicalTrials.gov that focus on prophylaxis effect of HCQ⁴, and it is hoped that, in the near future, these will be able to generate definitive evidence of HCQ utility in the containment of COVID-19 pandemic.

Conflicts of Interest: None.

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