Correspondence

Observations on healthcare workers & SARS-CoV-2 infection

Sir,

In an interesting case-control study by Chatterjee et al, the authors suggested the role of hydroxychloroquine (HCQ) in the prevention of SARS-CoV-2 infection among healthcare workers. Here are some of our observations that we would like to highlight.

In this case-control study, symptomatic healthcare workers (HCWs) testing positive on reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 were defined as cases, whereas controls were symptomatic HCWs who tested negative on RT-PCR for SARS-CoV-2 under similar considerations. Given the fact that up to 5-80 per cent patients with COVID-19 infection remain asymptomatic, the major population that may qualify for cases were left from the study.

As the ICMR’s advisory for the use of HCQ prophylaxis was released on March 22, 2020, assuming that the high-risk workers started prophylaxis from the next day, it was unlikely that the patient pool in this study received six or more doses of HCQ prophylaxis, assuming even distribution of patients being tested between the first week of April and the end of the first week of May 2020. The findings of 56 participants from control group taking six or more doses of HCQ remained unexplained. It was also worthwhile to note whether the question about number of HCQ doses consumed was asked till the diagnosis of COVID-19 or till the time of data collection?

Cases and controls seemed to be not matched in this study. Cases had inadequate infection control practices and were more exposed to aerosol-generating procedures like endotracheal intubation, and a greater percentage of cases were in intensive care unit (ICU) having patients on ventilators. In addition, stratification of HCWs was also not mentioned. Probably, HCWs from primary or secondary level healthcare centres were more exposed due to inadequate personal protective equipment or lack of infection prevention control (IPC) training. At the same time, the sample size of this study was inadequate for subgroup analysis leading to unexplained apparently erroneous conclusions such as increased risk of infection in up to three doses of HCQ. We consider that increased risk at lesser number of doses and protection at a greater number of doses do not indicate a dose-response relationship as claimed by the authors, but it rather indicates contradictory and inconclusive finding.

The authors also mentioned that the role of HCQ in severe COVID-19 patients was obscure contradictory to the role of HCQ in prophylaxis as concluded by them due to biological possibility of starting the medication before the onset of infection. However, the management guidelines released on March 31, 2020 have suggested that HCQ along with azithromycin may be considered in patients with severe disease and requiring ICU management. Now, the guidelines released on June 13, 2020 recommended HCQ for mild and moderate COVID-19 cases. The recent guidelines recommended to avoid it in severe disease. Similarly, one more contradictory finding was HCQ alone and with vitamins and non-allopathic drugs decreasing risk but not with azithromycin combination. There was a possibility that HCWs started taking combination of HCQ and azithromycin based on the results of a study by Gautret et al which was available online on March 20, 2020, rather than the recommendations given by the ICMR in its advisory released on March 22,
All that one can conclude from this study is that overall HCQ group is showing a trend towards protection which is not significant ($P=0.087$).

An elucidation from the authors about the results and interpretations taking into account the above observations will benefit the scientific community.

**Conflicts of Interest:** None.

**Prajak Barde**, **Pankaj Sarkate** & **Nitin Gaikwad**

1Clinical Research & Development, Rhizen Pharmaceuticals S.A., CH-2300 La Chaux-de-Fonds, Switzerland, 2Pharmacovigilance Division, Symogenesis, New Delhi 110 085 & 3Department of Pharmacology, All India Institute of Medical Sciences, Raipur 492 099, Chhattisgarh, India

*For correspondence:
nitingaikwad2707@aiimsraipur.edu.in*

Received July 6, 2020

**References**

1. Chatterjee P, Anand T, Singh KJ, Rasaily R, Singh R, Das S, *et al*. Healthcare workers & SARS-CoV-2 infection in India: A case-control investigation in the time of COVID-19. *Indian J Med Res* 2020; 151: 459-67.

2. Zhou X, Li Y, Li T, Zhang W. Follow-up of asymptomatic patients with SARS-CoV-2 infection. *Clin Microbiol Infect* 2020; 26: 957-9.

3. World Health Organization. Q&A: Influenza and COVID-19 - similarities and differences. Available from: https://www.who.int/news-room/q-a-detail/q-a-similarities-and-differences-covid-19-and-influenza, accessed on June 10, 2020.

4. National Task Force for COVID-19. Recommendation for empiric use of hydroxy-chloroquine for prophylaxis of SARS-CoV-2 infection; March 22, 2020. Available from: https://www.mohfw.gov.in/pdf/AdvisoryontheuseofHydroxychloroquinasprophylaxisforSARSCoV2infection.pdf, accessed on June 13, 2020.

5. Directorate General of Health Services (EMR Division), Ministry of Health & Family Welfare. *Revised Guidelines on Clinical Management of COVID - 19*. New Delhi: MoHFW, Government of India; 2020.

6. Directorate General of Health Services (EMR Division), Ministry of Health & Family Welfare. *Clinical Management Protocol: COVID-19*. New Delhi: MoHFW, Government of India; 2020.

7. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, *et al*. Hydroxychloroquine and azithromycin as a treatment of COVID-19: Results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents* 2020; 105949.