Correspondence

A critical appraisal of a case-control study on healthcare workers

Sir,

We read the article with interest by Chatterjee et al., published recently and want to congratulate the authors for conducting this study in such a short span of time during this pandemic. We would like to contribute a few points.

In this study, controls are taken in less number than cases. During a case-control study, the desired ratio between cases and controls should be at least 1:1 and preferably may be 1:2 or even 1:3\(^2\). This study was most appropriate to have 1:2 or 1:3 ratio as only a small proportion of healthcare workers (HCWs) were affected. Matching is usually done for age and sex between cases and controls\(^3\). Only symptomatic persons were considered in this study for cases and controls. Asymptomatic cases were not considered which constitute 40-45 per cent of the infective cases\(^3\). Hence, selection bias must have been introduced vitiating results. The proportion of non-responders is extremely high ranging from 32 to 40 per cent. The number of participants who completed interview was far less than the minimum required number. It is likely that the history of consuming hydroxychloroquine (HCQ) may be different among them. It is usual experience that non-respondents are either from uppermost or lowermost quartile\(^4\). High non-response rate certainly vitiates the results. The time period of enrolment and data collection constitutes approximately seven weeks. Chatterjee et al.\(^1\) have not given precise information about details of consumption of HCQ. Initial guidelines were to take HCQ for seven weeks. There may be some HCWs who consumed HCQ for more than six weeks but stopped after that. The effect will be washed off. It was also not clear if the consumption history was at the time of telephonic interview or at the time of collection of sample. It could have been mentioned clearly. When adjusted odds ratio was calculated, there was no need to give crude odds ratio in the first few Tables. Further, the risk-benefit ratio of HCQ administration needs to be closely examined and this could have been easily done. It has major side effects such as retinal disorders, prolongation of QT interval and haemolytic anaemia\(^5\).

These are the few observations and comments from my side.

Conflicts of Interest: None.

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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. Celentano DD, Szklo M. Observational Studies. *Gordis epidemiology*. 6th ed. Philadelphia: Elsevier; 2018. p. 167-9.
3. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: A narrative review. *Ann Intern Med* 2020; M20-3012.
4. National Research Council. Nonresponse bias. In: Tourangeau R, Plewis TJ, editors. *Nonresponse in social science surveys: A research agenda*. Washington, DC: The National Academies Press; 2013. p. 40-50.
5. D’Cruz M. The ICMR Bulletin on targeted hydroxychloroquine prophylaxis for COVID-19: Need to interpret with caution. *Indian J Med Ethics* 2020; 5 : 100-2.
We thank the authors for a close reading of our article. Given the known biases in recruiting study participants for a case-control study, we decided to choose symptomatic HCWs who were tested for SARS-CoV-2 infection to maintain evenness in the way cases and controls were selected. We would like to posit that the reasons for which asymptomatic HCWs got tested were likely to be different from those of symptomatic HCWs. Hence, to maintain comparability between the cases and controls, we decided to include only symptomatic HCWs. We tried to adhere to the basic tenets of case-control investigations - the cases and controls should be comparable, except in that the case group experienced the outcome of interest. In addition, we would like to add that an analysis of one million tests conducted in India between January and April 2020 has shown that about 28 per cent of SARS-CoV-2-positive patients are asymptomatic.

The standard practice in developing logistic regression models begins with the selection of independent variables using multiple strategies - known or established theories, existing evidence, exploratory analyses or a combination of these and other strategies. The purpose of the univariate analysis was to identify the variables that were more likely to be statistically and biologically associated with the outcome of interest. To construct a parsimonious model, we chose to include biologically plausible variables which met a cut-off value ($P<0.1$). This is clarified in the subsection titled ‘multivariate analysis’. Further, we would like to emphasize that it is important to limit the number of independent variables to avoid a mathematically unstable model with limited generalizability beyond the current data. In order for readers to appreciate the process, and to declare the associations observed through the univariate analyses, we chose to present both analyses.

While we acknowledge the lower response rate, this is a known shortcoming of telephone-based surveys. While in-person interviewing remains the method providing the highest yield in terms of response efficiency and representativeness, it was an untenable strategy given the realities of the ongoing pandemic and restrictions imposed on the movement of people by the nationwide lockdown. Also noteworthy is that, compared to online, mail, or self-reported data collection, telephone-based surveys provide better representativeness, more complete data and higher data yield. To improve the response rate, we employed different strategies such as training of interviewers and multiple call attempts at different times of the day. Further, our study received higher response rates than similar methodologies employed to cover HCWs in India (paediatricians: 57%) and abroad (Germany: physicians, 56%; France: physicians, 59% and USA: internists, 64%).

The study participants were asked to declare the side effects experienced by them in our investigation. As noted in the ‘Results’ section, a very small proportion of the participants self-reported adverse effects linked to HCQ intake, and the frequency of occurrence of side effects was not significantly different across the case and control groups.

Pranab Chatterjee, Tanu Anand, Kh. Jitenkumar Singh, Reeta Rasaily, Ravinder Singh, Santasabuj Das, Harpreet Singh, Ira Praharaj, Raman R. Gangakhedkar, Balram Bhargava & Samiran Panda

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. ICMR COVID Study Group, COVID Epidemiology & Data Management Team, COVID Laboratory Team, VRDLN Team. Laboratory surveillance for SARS-CoV-2 in India: Performance of testing & descriptive epidemiology of detected COVID-19, January 22 - April 30, 2020. *Indian J Med Res* 2020; 151: 424-37.

3. Stoltzfus JC. Logistic regression: A brief primer. *Acad Emerg Med* 2011; 18: 1099-104.

4. Hosmer DW, Lemeshow S. Logistic regression for matched case-control studies. In: Shewhart WA, Wilks SS, editors. *Applied logistic regression*. Hoboken (NJ): John Wiley & Sons, Inc.; 2005. p. 223-59.

5. Szolnoki G, Hoffmann D. Online, face-to-face and telephone surveys - Comparing different sampling methods in wine consumer research. *Wine Econ Policy* 2013; 2: 57-66.

6. Patnaik S, Brunskill E, Thies W. Evaluating the accuracy of data collection on mobile phones: A study of forms, SMS, and voice. International Conference on Information and Communication Technologies and Development (ICTD2009); 2009 Apr 17-19; Doha, Qatar. p. 74-84.

7. Zhang RL, Thacker N, Choudhury P, Pazol K, Orenstein WA, Omer SB, *et al.* Comparison of two survey methods based on response distribution of pediatricians regarding immunization for children in India: Mail versus telephone. *Int J Trop Dis Health* 2016; 16: 1-10.

8. Gahr M, Eller J, Connenmann BJ, Schönfeldt-Lecuona C. Subjective reasons for non-reporting of adverse drug reactions in a sample of physicians in outpatient care. *Pharmacopsychiatry* 2016; 49: 57-61.

9. Peretti-Watel P, Bendiane MK, Pegliasco H, Lapiana JM, Favre R, Galinier A, *et al.* Doctors’ opinions on euthanasia, end of life care, and doctor-patient communication: Telephone survey in France. *BMJ* 2003; 327: 595-6.

10. DuVal G, Clarridge B, Gensler G, Danis M. A national survey of U.S. internists’ experiences with ethical dilemmas and ethics consultation. *J Gen Intern Med* 2004; 19: 251-8.