



Commentary

Do asymptomatic carriers of SARS-COV-2 transmit the virus?

Claude P. Muller

Department of Infection and Immunity, Luxembourg Institute of Health, 29, rue Henri Koch, L-4354 Esch-sur-Alzette, Luxembourg

ARTICLE INFO

Article History:

Received 2 March 2021

Accepted 4 March 2021

Available online 20 March 2021

Wilmes et al. recently reported in The Lancet Regional Health – Europe that asymptomatic index cases (AIC) play an important role in the transmission and spread of SARS-CoV2 infections [1]. Secondary attack rates of 283 AIC were significant (0.02) but lower than those of the 567 symptomatic index cases (SIC; 0.04). AIC infected on average 0.6 contacts, only slightly less than SIC (0.7 contacts). Higher values but similar differences were found within households.

These results are in line with 13 other studies including 111 AIC, reviewed in a recent meta-analysis [2]. Transmission rates of AIC ranged from 0–2.2% compared to 0.8–15.4% for SIC [2]. Another meta-analysis found that household transmission from AIC was 0–4.9% compared to 18.0%; for SIC [3]. In another household study, AIC were four times less likely to pass the virus to a household contact, but ultimately caused one fifth of household infections [4]. All of these studies agree that AIC transmit SARS-COV2 to contacts, although to a somewhat lesser extent than SIC.

However, a large study from post-lockdown Wuhan came to a very different conclusion [5]. After 11 weeks, the total lockdown was lifted by April 8th, 2020. Between April 8th and May 10th only 6 new COVID19 cases were confirmed. Four days later (May 14th), the city embarked on a comprehensive 19-days screening effort including 92% of its residents irrespective of their COVID19-status. Among 34,424 recovered COVID19 patients, 107 tested positive, corresponding to 310 per 100,000 patients. Among those without COVID19 history, there were no new symptomatic cases detected, but 300 asymptomatic PCR-positive cases (3 per 100,000). The 1,174 close contacts of these AIC were all PCR-negative and none became positive during isolation. The authors concluded that asymptomatic PCR-positive individuals do not transmit the virus to others [5].

How can this apparent disparity be reconciled? Several lines of evidence suggest that the epidemiological context in Wuhan was very different from the one in Luxembourg and most other studies.

E-mail address: claudio.muller@lih.lu

- (i) In the Luxembourg study 66% of index cases were symptomatic while only 33% were asymptomatic [1]. In the above meta-analysis overall 83% of cases were symptomatic [2]. Thus, in all studies the vast majority of PCR-positives were symptomatic, while in Wuhan there were none at the time of the study.
- (ii) Two thirds of the asymptomatic cases in the Wuhan study had already anti-viral IgG [5], suggesting that they became infected weeks or more before.
- (iii) Most studies on asymptomatic cases were conducted during ongoing incidence waves of COVID19, suggesting that most AIC were in early stages of their infection [1,2,3,4]. In contrast, the Wuhan study was initiated only when there were essentially no cases in the city for at least 5 weeks since the roll-back of the lockdown, and a dwindling number of cases during the last weeks of the lockdown, further suggesting that the asymptomatic infections happened weeks or months earlier.

Thus, while in the other studies most AIC were in early stages of their infection, the above arguments coalesce to suggest that those in Wuhan were in late stages of their infection with long-term persistence of virus yet to be cleared - so to speak long-term carriers of virus. Indeed, a number of other studies detected virus persisting for weeks and even up to several months after infection [6,7,8]. In 43 studies RNA was detected on average for 17 days, but durations of up to 83 days were reported. The latter meta-analysis included “only” a total of 3,229 subjects [8]. In contrast, the massive screening in Wuhan was essentially a follow-up study of 10 million participants, including 50,000 confirmed cases and almost 10 times as many antibody-positives (with past inapparent infections). Among these, 300 individuals continued to harbor detectable virus RNA weeks and months later corresponding to roughly 60 per 100,000 infected. This is fully consistent with the rare long-term virus persistence as described before [8].

What would be the difference between early and late-stage asymptomatic cases? The above review compared their virus dynamics [8]: Although, RNA detection was shorter after oligo/asymptomatic disease in 5 of 11 studies, there was no such difference in the other studies. Also, viral loads were similar (four studies) or lower (two studies) in asymptomatic compared to symptomatic cases, both peaking within days after infection. Thus, similar virus dynamics suggest that there may not be much difference in levels of viable virus between symptomatic and asymptomatic individuals, within the

early days after infection, when most AIC transmission studies were done. Thus, it is not surprising that AIC were found to be infectious, even if to a somewhat lower degree than SIC.

During later stages of the disease, symptomatic patients recover and clear the virus, but a very small number continue to produce virus for several months: In Wuhan 310 per 100.000 recovered patients did not clear the virus even after several months. As reviewed above, AIC clear the virus faster. In Wuhan only 3 AIC per 100.000 (i.e. 100 times less) continued to harbor virus and, as the study showed, at this later stage of the infection none of these long-term carriers were still infectious.

Thus, we suggest that asymptomatic individuals are infectious during the early stage of infection, but some rare cases (3/100.000) become long-term virus carriers which are no longer infectious. This would reconcile the Wuhan post-lockdown study with the other studies including the one from Luxembourg. This conveys several important messages for science and public health: (i) During the acute phase of a COVID19 wave, asymptomatic individuals should definitively be included in the testing strategy and their contacts traced, because they can drive the inapparent spread the virus similar to symptomatic cases. (ii) Among AIC there is a category of rare long-term SARS-CoV-2 carriers (3/100.000), with minimal risk for virus transmission, despite detectable viral RNA. (iii) Despite low absolute numbers, the *proportion* of this category of asymptomatic carriers will increase as the virus retreats. (iv) Finally, it cannot be excluded that rare long-term carriers may become virus reservoirs, with the potential to cause recurrent outbreaks. This has important implications for future SARS-CoV-2 public health and surveillance, and our understanding of yet another pitfall of this cunning virus.

Authors contribution

The author is solely responsible for all aspect of this article including the research, the interpretation and the writing of it.

Declaration of Competing Interest

The author declares no competing interests.

Acknowledgements

None

Funding

None

References

- [1] Wilmes P, Zimmer J, Schulz J, et al. SARS-CoV-2 transmission risk from asymptomatic carriers: results from a mass screening programme in Luxembourg. *Lancet Regl Health Eur* 2021 in press.
- [2] Byambasuren O, Cardona M, Bell K, et al. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. *J Assoc Med Microbiol Infect Disease Canada (JAMMI)* 2020;4:223–34.
- [3] Madewell ZJ, Yang Y, Longini IM, et al. Household Transmission of SARS-CoV-2. A systematic review and meta-analysis. *JAMA Netw Open* 2020;3(12):e2031756. doi: [10.1001/jamanetworkopen.2020.31756](https://doi.org/10.1001/jamanetworkopen.2020.31756). 12.18.20.
- [4] Qifang B, Lessler J, Eckerle I, et al. Household transmission of SARS-CoV-2: insights from a population-based serological survey. *medRxiv*. doi: [10.1101/2020.11.04.20225573](https://doi.org/10.1101/2020.11.04.20225573).
- [5] Cao S, Gan Y, Wang C, et al. Post-lockdown SARS-CoV-2 nucleic acid screening in nearly ten million residents of Wuhan, China. *Nat Commun* 2020;11:5917. doi: [10.1038/s41467-020-19802-w](https://doi.org/10.1038/s41467-020-19802-w).
- [6] Bongiovanni M, Bini F, Guiliani G, et al. Insight into the reason of prolonged viral RNA shedding in patients with COVID-19 infection. *J Infect* 2021 Jan 3 0163–4453 (21)00002–5. doi: [10.1016/j.jinf.2020.12.030](https://doi.org/10.1016/j.jinf.2020.12.030).
- [7] Liu Y, Li M, Liu D, et al. Developing a multivariable risk prediction model to predict prolonged viral clearance in patients with COVID-19. *J Infect* 2020 Dec 31 0163–4453(20)30787–8. doi: [10.1016/j.jinf.2020.12.026](https://doi.org/10.1016/j.jinf.2020.12.026).
- [8] Cevik M, Tate M, Lloyd O, et al. SARS-CoV-2, SARS-CoV-1 and MERS-CoV viral load dynamics, duration of viral shedding and infectiousness – a living systematic review and meta-analysis. *Lancet Microbe* 2021;2:e13–22.