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Short Communication

Transmissibility of asymptomatic COVID-19: Data from Japanese clusters

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ABSTRACT

Background: The epidemiological importance of asymptomatic individuals who would never develop illness, compared to those who eventually develop symptoms, has yet to be fully clarified.

Methods: The very first cluster data in Tokyo and Kanagawa (n = 36) were analyzed. Movement of all close contact was restricted for 14 days and they underwent laboratory testing with polymerase chain reaction. The reproduction numbers of symptomatic and asymptomatic cases were estimated.

Results: The reproduction number for symptomatic cases was estimated to be 1.2 (95% confidence interval (CI): 0.5–2.9). The relative infectiousness of asymptotically infected cases was estimated to be 0.27 (95% CI: 0.03–0.81) of symptomatic cases.

Conclusion: The relative transmissibility of asymptomatic cases is limited. Observing clusters starting with symptomatic transmission might be sufficient for the control.

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Introduction

The early estimate of asymptomatic ratio has been reported as ranging from 8 to 54% (Nishiura et al., 2020). Besides, more than half of secondary transmissions with coronavirus disease 2019 (COVID-19) are considered to occur from asymptotically infected people (Johansson et al., 2021). The estimate reflects the substantial number of secondary transmissions from pre-symptomatic individuals who eventually develop illness.

However, the epidemiological importance of asymptomatic individuals who would never develop illness, compared to those who eventually develop symptoms, has yet to be fully clarified. Sayampanathan et al. (2020) have excellently shown that the relative transmissibility of asymptomatic individuals is approximately 0.14–0.49 times of that among symptomatic cases, while He et al. (2020) indicated that the interpretation of relative transmissibility requires a cautious interpretation. Japan adopted the cluster-based approach to COVID-19 (Oshitani and Expert Members of The National COVID-19 Cluster Taskforce at The Ministry of Health, Labour and Welfare, Japan, 2020), focusing on contact tracing in high-risk setting that satisfies three C's condition (i.e., close contact in confined and crowded space), and we are

granted an opportunity to analyze the well-observed cluster data. Here we aimed to estimate the transmissibility of asymptomatic COVID-19 from the cluster data in Japan.

Methods

Cluster-based approach in Japan identified indoor environment as the focal area of transmission and retrospectively traced the contact, bringing all identified close contact of confirmed cases under observation and laboratory testing (Furuse et al., 2020). Accordingly, clusters that were observed from January to March 2020 were extremely well traced, and importantly, the incidence did not exceed the tracing capacity during the early period. All close contacts were followed up daily by healthcare workers and requested to check temperature twice a day. Regardless of symptoms, they undertook RT-PCR testing. Of the clusters that are reported, early identified clusters in 2020 thus contained the tracing results of asymptomatic individuals, and specifically the present study focused on the very first identified series of infection in Tokyo and Kanagawa.

A negative binomial distribution was employed to jointly estimate the reproduction number and dispersion parameter, because the close contact in indoor environment frequently results in clustering. To grasp the relative transmissibility, the reproduction numbers of both symptomatic and asymptomatic individuals were estimated along with the evaluation of dispersion. In this

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instance, the reproduction number of symptomatic/asymptomatic cases is defined as the average number of secondary cases produced by a single symptomatic/asymptomatic primary case throughout the course of infection. The reproduction number of asymptomatic individuals was assumed to be proportional to that of symptomatic cases, and the estimate acted as the relative infectiousness of asymptomatic individuals.

Results

Figure 1 shows chains of transmission in the earliest observed cluster in Tokyo and Kanagawa, involving a total of 36 confirmed cases. Online Supplementary data shows the epidemic curve by reporting date. The transmission event started with a night party on January 18, 2020 in Tokyo that stemmed from an exposure to tourist from Wuhan. Except for household transmission events, the majority of cases from this cluster did not contribute to secondary transmission. One of the tertiary cases contributed to subsequent chains of clusters in healthcare and welfare facilities and a household in remote area in a neighboring prefecture Kanagawa, including the first fatal case in Japan. The second case in Kanagawa was unlinked to clusters of cases in Tokyo, but there were no other cases observed in the relatively remote area in Kanagawa and it was highly probable that the case was a part of the very first cluster in Japan. There were 12 asymptomatic and 24 symptomatic confirmed cases. The average age of confirmed cases was 60.3 years (see Online Supporting material).

The reproduction number and the dispersion parameter for symptomatic cases were estimated to be 1.2 (95% confidence

interval (CI): 0.5–2.9) and 0.23 (95% CI: 0.09–0.62), respectively. Relative infectiousness of asymptomatically infected cases was estimated to be 0.27 (95% CI: 0.03–0.81) of symptomatic cases. Namely, symptomatic cases appeared to be 3.7 times more infectious than asymptomatic COVID-19. A geometric distribution analysis yielded similar estimate, i.e., 0.27 (95% CI: 0.06–0.68).

Discussion

While pre-symptomatic transmission plays a key role, the reproduction number of 0.27 among asymptomatic cases who remain asymptomatic for the entire course of infection indicates that their infectiousness is limited. This would assure the validity of cluster-based approach, and observing clusters starting with symptomatic transmission might be sufficient for the control.

An important limitation of the present study is that the sample size was limited, and thus, the uncertainty bound (i.e., 95% CI) was broad. Another issue to be acknowledged is the missing link of second Kanagawa case, which might even be pre-symptomatic or asymptomatic transmission. Thus, the tracing results did not perfectly capture all chains of transmission. A modelling study needs to be conducted to explore the impact of undetected cases on epidemiological parameter estimates such as ours. It should be noted that symptomatic cases might be more likely to cause symptomatic secondary cases (He et al., 2020), and future studies with greater sample size could help explore this matter.

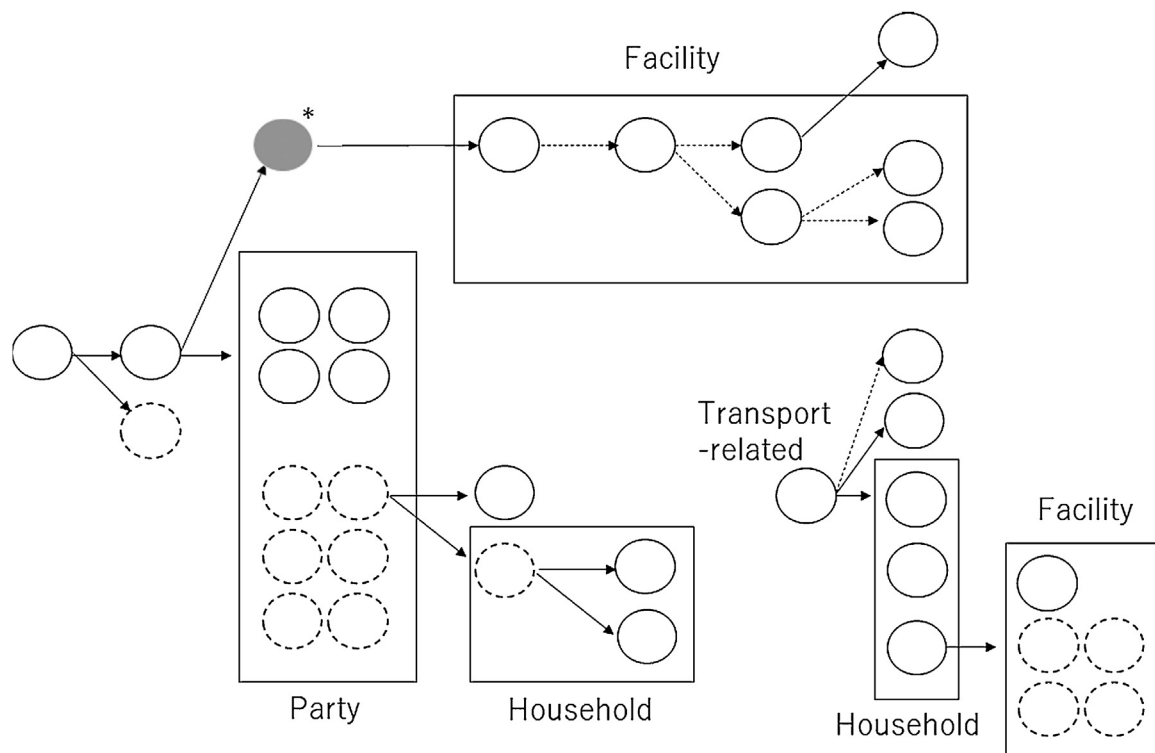


Figure 1. Transmission network of coronavirus disease 2019 (COVID-19) with cluster information in Tokyo and Kanagawa, Japan. Solid and dotted circles indicate symptomatic and asymptomatic cases, respectively. A large frame indicates common indoor environment/facility of transmission. Arrows indicate established link and dotted arrows represent the most plausible link, both based on contact tracing. A grey circle with asterisk-mark (*) indicates a case with unknown symptomatic status, and the transmission event from this case was thus omitted from our analysis. The chains of transmission on the lower right part of figure start with an unlinked case associated with transportation company, and the case was considered to have been associated with undiagnosed case associated with this cluster.

Besides, the finding encourages contact tracing and self-isolation, especially in resource-limited setting (Sayampanathan et al., 2020). Systematically collecting well-observed cluster datasets should be globally promoted, as it helps to quantify key indicators of transmission dynamics, like the relative transmissibility.

Ethical considerations

The present study used publicly available data, and thus, did not require ethical approval.

Conflict of interest

We declare that we have no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ijid.2021.02.065>.

References

- Furuse Y, Sando E, Tsuchiya N, Miyahara R, Yasuda I, Ko YK, et al. Clusters of coronavirus disease in communities, Japan, January–April 2020. *Emerg Infect Dis* 2020;26(9):2176–9, doi:<http://dx.doi.org/10.3201/eid2609.202272>.
- He D, Zhao S, Lin Q, Zhuang Z, Cao P, Wang MH, et al. The relative transmissibility of asymptomatic COVID-19 infections among close contacts. *Int J Infect Dis* 2020;94:145–7.
- Johansson MA, Quandelacy TM, Kada S, Prasad PV, Steele M, Brooks JT, et al. SARS-CoV-2 transmission from people without COVID-19 symptoms. *JAMA Netw Open* 2021;4:e2035057, doi:<http://dx.doi.org/10.1001/jama-networkopen.2020.35057>.
- Nishiura H, Kobayashi T, Miyama T, Suzuki A, Jung SM, Hayashi K, et al. Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). *Int J Infect Dis* 2020;94:154–5.
- Oshitani H, Expert Members of The National COVID-19 Cluster Taskforce at The Ministry of Health, Labour and Welfare, Japan. Cluster-based approach to coronavirus disease 2019 (COVID-19) response in Japan, from February to April 2020. *Jpn J Infect Dis* 2020;73(6):491–3, doi:<http://dx.doi.org/10.7883/yoken.JJID.2020.363.4>.
- Sayampanathan AA, Heng CS, Pin PH, Pang J, Leong TY, Lee VJ. Infectivity of asymptomatic versus symptomatic COVID-19. *Lancet* 2020;397(December) 93–4, doi:[http://dx.doi.org/10.1016/S0140-6736\(20\)32651-9](http://dx.doi.org/10.1016/S0140-6736(20)32651-9) S0140-6736(20)32651-9.