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Transmission dynamics of SARS-CoV-2 Omicron variant infections in Hangzhou, Zhejiang, China, January-February 2022

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ABSTRACT

Objectives: We aimed to explore the transmission dynamics of the Omicron BA.1.1 variant in an outbreak in China.

Methods: We constructed 113 transmission pairs based on the time of exposure and symptom onset for identified infectors and infectees, using the epidemiological data collected during an outbreak in Hangzhou, Zhejiang province, China, between January and February 2022. The key epidemiological parameters were estimated.

Results: The mean estimates of the incubation period and latent period distributions were 3.8 days (95% credible interval: 3.5, 4.1) and 3.1 days (2.8, 3.5), respectively. The overall transmission risk peaked at symptom onset, and we estimated that 33.6% (24.8, 42.5) of transmission occurred before symptom onset. The forward generation time decreased from 5.2 days (4.7, 5.7) at the start of the outbreak to 2.2 days (2.0, 2.5) by the end. Allowing this variation over time in the generation time distribution, we estimated that the reproduction number dropped rapidly from 9.5 (3.5, 18.4) to 0.8 (0.3, 1.5) over the outbreak.

Conclusion: Shorter incubation period and latent period were estimated for the Omicron BA.1.1 variant. Stringent public health measures prevented a large epidemic by reducing transmission, as indicated by the shortened generation time.

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Introduction

From the end of 2020, multiple variants of concern have emerged during the COVID-19 pandemic. Most recently, the Omicron variant has become dominant worldwide over other strains, with the potential for the emergence of other new variants or subvariants in the future. The Omicron variants have demonstrated increased transmissibility and therefore are more challenging to control (Kraemer et al., 2021; World Health Organization, 2022).

In general, increased transmissibility for a variant indicates an increased transmission strength, a higher transmission speed, or both. The transmission strength refers to the intrinsic transmission ability of a variant, potentially measured by the reproduction number, whereas the transmission speed can be measured by the exponential growth rate (Hart et al., 2022). Time-delay parameters, i.e., generation time and serial interval, can determine the relationship between a variant’s strength and speed of transmission (Hart et al., 2022). Accurate estimation of disease parameters, i.e., incubation period, latent period, infectiousness profile, generation time, and serial interval, allow us to assess the role and effectiveness of control measures, such as mass testing, isolation, and contact tracing on transmission (Kraemer et al., 2021; Park et al., 2021). Some studies of the Omicron variant suggested that it has a shorter incubation period, generation time, and serial interval than previous variants (Bac2er et al., 2022; MeFin et al., 2022).

Between January 19, 2022 and February 4, 2022, a COVID-19 outbreak occurred in Hangzhou, Zhejiang province, China. The epidemiological investigation showed that all cases identified in this outbreak could be traced back to an index case, and the gene se-

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quency analysis revealed that all patients were infected with the Omicron variant sublineage of BA.1.1 (or Nextstrain clade 21K). Active case-finding strategies such as daily district-range mass polymerase chain reaction (PCR) and routine PCR testing among close contacts were implemented to identify all cases in this outbreak. The cases found were isolated, and detailed epidemiological information was collected, including infection source, exposure time, dates, and results of each time PCR test, etc. In this study, we investigated the transmission dynamics of the Omicron outbreak.

Methods

Data collection

We retrospectively collected information on all reverse transcriptase-PCR-confirmed COVID-19 cases infected with the Omicron variant (BA.1.1) from the outbreak between January 23, 2022 and February 4, 2022 in Hangzhou, Zhejiang province, China. Demographic information, including sex, age, and occupation, was collected. Other data such as underlying conditions, severity status, and vaccination status, were also collected. Patients’ severity status was categorized as asymptomatic, mild, moderate, severe, and critical (Supplementary materials). Vaccination status, including vaccine brand and type, the dose of vaccination, and date of the last dose, was collected for each case. Cases were defined as receiving incomplete vaccination series, complete primary vaccination series, or booster vaccination series if they received one, two, or three doses of an inactivated vaccine (BBP COVID-19, Sinopharm, Beijing, China, or CoronaVac; Sinovac Biotech Ltd, Beijing, China) 14 days or longer before the first day of exposure to an infector, respectively.

To estimate the incubation period distribution (time duration between infection and presenting symptoms), we collected information for each infectee on the first date of exposure (lower bound of infection date) and the last date of exposure (upper bound of infection date) to an infector along with the date of symptoms onset. The latent period describes the interval from infection to becoming infectious and was measured as the interval between exposure to an infector and the first positive PCR test in this study. The dates of the last negative PCR test (lower bound of the possible start of viral shedding) and the first positive PCR test (upper bound of the possible start of viral shedding) were used to inform the start time of viral shedding.

We constructed transmission pairs based on infectors and infectees identified from contact tracing, with an available infection time window and symptom onset dates. The generation time distribution (interval of infections between two successive cases in a transmission chain), serial interval distribution (interval of symptoms onset between two successive cases in a transmission chain), and infectiousness profile (transmission risk during the infectious period relative to the symptoms onset of infectors) were estimated based on these transmission pairs (Supplementary materials).

Statistical analysis

We estimated the incubation period and latent period distribution in a Bayesian framework. Gamma, lognormal, and Weibull distributions were fitted separately, and non-negative flat prior probability distributions were specified for the studied parameters for the three assumed distributions. The distribution with the lowest leave-one-out information criterion was selected as the final model. Interval censoring of the infection window and viral shedding window were accounted for in the estimation of the incubation period and the latent period.

We obtained the infection time for each infectee, including some infectors who were also identified as an infectee in the transmission chain, based on the estimated incubation period and latent period in every iteration in the model (Supplementary materials). The generation time distribution was then estimated by calculating the time interval between the infection time of infectors and infectees using all iterations in the model. The serial interval distribution was estimated using the time of symptoms onset of infectors and infectees. Because the distribution of generation time and serial interval could change over time during an outbreak, we estimated the time-varying forward distributions of the generation time and serial interval using a series of running time windows with a fixed time window of 4 days (Supplementary materials). Using the time-varying mean and standard deviation of the forward generation time and the daily incident case information, we estimated the daily instantaneous reproduction number ($R_t$) by applying the statistical methods used in the EpiEstim package (Cori et al., 2013) (Supplementary materials).

We estimated the infectiousness profile for Omicron infections in this outbreak based on individual time intervals between the infection time of the infectee and the symptom onset of the infector from all transmission pairs. The daily cumulative proportions of transmission were estimated in relation to the date of symptom onset of the infector, including the proportion of presymptomatic transmission.

Parameters and their uncertainties were estimated from posterior distributions using the rstan package in R software (R Foundation for Statistical Computing, Vienna, Austria).

Results

The outbreak

As of February 4, 2022, a total of 114 cases infected with the Omicron variant (BA.1.1) were reported in the outbreak in Hangzhou (Figure 1a), with cases numbers increasing from January 19, 2020, peaking on January 31, 2022, and declining rapidly thereafter. Half (45.6%) of the cases were male. The median age was 33.0 years (interquartile range: 25.3, 48.8), with 91 (79.8%) cases aged between 15 and 64 years. A total of 17 (14.9%) cases had underlying conditions before infection with COVID-19. The majority of the cases showed mild symptoms (107, 93.9%), and the remaining were moderate infections (7, 6.1%). There were 4 (3.5%), 70 (61.4%), and 22 (19.3%) cases with incomplete vaccination series, complete primary vaccination series, and booster vaccination series, respectively. Among the 92 cases with complete primary or booster vaccination series, 27 (29.3%) had their first exposure to a confirmed case within 90 days after the last vaccination dose and 65 (70.7%) beyond 90 days.

Parameter estimation

Information on infection, symptoms onset, and laboratory testing were available for all 114 cases for estimation of the incubation period and the latent period. Using the gamma distribution, we estimated the mean incubation period was 3.8 days (95% credible interval [CrI]: 3.5, 4.1), with 95% of the cases developing symptoms within 6.2 days (5.7, 6.9) after exposure (Figure 1a, Table S1). Cumulative frequency distribution showed that 98.0% (95.5, 99.3) of cases had symptom onset within 7 days and 100.0% (99.8, 100.0) within 10 days after exposure (Table S2). The mean latent period was estimated to be 3.1 days (2.8, 3.5), with the 95th percentile of 5.9 days (5.3, 6.8) (Figure S1b, Table S1). A total of 98.2% (95.7, 99.4) and 99.9% (99.6, 100.0) of the cases started shedding the virus within 7 days and 10 days, respectively (Table S2).

We constructed 113 transmission pairs with infection and symptoms onset information for both infectors and infectees (Figure S2), with 46 (40.7%), 47 (41.6%), and 20 (17.7%) pairs identifi-
fied in households, workplaces, and public areas, respectively. The mean estimates of the time-varying forward generation time were gradually dropped from 5.2 days (4.7, 5.7) to 2.2 days (2.0, 2.5) over the study period (Figure 1b). The time-varying mean serial intervals decreased from 6.0 days (5.5, 6.5) between January 19, 2022 and January 22, 2022 to 1.7 days (1.3, 2.0) between January 28, 2022 and January 31, 2022 (Figure 1b). The estimated $R_t$ declined rapidly from 9.5 (3.5, 18.4) on January 22, 2022 to 0.8 (0.3, 1.5) on February 4, 2022 (Figure 1c). We estimated that 4.4% (0.9, 8.0) of the transmissions occurred ≥4 days before symptom onset of ancestors, 33.6% (24.8, 42.5) of the transmission occurred before symptom onset, with the transmission risk peaking at onset, and all the observed transmission events occurring within 5 days after the infected’s symptoms onset (Figure 1d).

Discussion

In this study, we retrospectively collected detailed information on laboratory-confirmed COVID-19 cases infected with the Omicron variant with the lineage of BA.1.1. The characterized transmission pairs allowed us to estimate the transmission parameters of this variant. We showed that compared with the Delta variant of SARS-CoV-2, the Omicron variant had a shorter incubation period and latent period.

We estimated that the mean incubation period for the Omicron variant was 3.8 days (95% CrI: 3.5, 4.1), similar to the previously reported 3.5 days in Italy (Manica et al., 2022), but was almost 2 days shorter than the Delta variant (Kang et al., 2022). Along with the infectiousness peak at the day of symptom onset, a quicker coverage of outbreak control measures needs to be facilitated to suppress transmission. In the outbreak we studied, interventions, including district-range lockdown and daily screening using PCR testing, were implemented immediately after identifying the index case; all the cases found were treated and isolated in the designated hospital, and close contacts were quarantined in hotels. The measures implemented were proven effective, with the $R_t$ decreasing rapidly from 9.5 to 0.8 within 14 days.

Previous studies suggested that the faster epidemic growth identified for the Omicron variant was attributed to three epidemiological factors: immune evasion, higher intrinsic transmission potential (measured by reproduction number), and a shorter serial interval or generation time (Backer et al., 2022; Mefsin et al., 2022). Our analysis of a small outbreak in Hangzhou showed that the instantaneous reproduction number for the Omicron outbreak was 9.5 in the early stage of the outbreak and dropped to 0.8 at the end of the outbreak; no obvious increase was identified compared with the values in a Delta variant outbreak (Kang et al., 2022). Although the sample size was limited in our study, we could still conclude that higher intrinsic transmissibility of the Omicron variant may not be the only driver of the fast spread of Omicron.

We found the proportion of presymptomatic transmission was 33.6%, lower than the proportions identified for the ancestral strain.
(Ren et al., 2021). As shown in our study, the time difference between the mean estimate of the latent period (3.1 days) and incubation period (3.8 days) was only 0.7 days, significantly shorter than the time difference among wild-type SARS-CoV-2 (14 days) (Xin et al., 2022) and the Delta variant (19 days) (Kang et al., 2022). Therefore, a short infectious period before symptom onset might exist for the Omicron infections, limiting the potential for presymptomatic transmission compared with earlier strains with longer incubation periods.

The decreasing trend of time-varying generation time and the serial interval identified in this study was likely caused by earlier isolation of cases as the epidemic progressed, which reduced the later effective infectious period of SARS-CoV-2-infected individuals by preventing contacts with susceptible individuals later in the infectious period. An overall shorter generation time than the serial interval identified in this study indicated that the incubation period was shorter among infected than infectees in the transmission pairs. When estimating the time-varying forward generation time and serial interval (as in our study), the forward-looking incubation period of infectees should remain constant throughout an epidemic; however, the backward-looking incubation period of infectors tends to be shorter in the increasing phase of an outbreak and longer in the decreasing phase of an epidemic (Park et al., 2021). This is because the difference between forward generation time and the serial interval is the difference between the incubation period of infectors and infectees (Park et al., 2021), which leads to a shorter and longer generation time than the serial interval in the increasing phase of the epidemic and decreasing phase of the epidemic, respectively. This explains the difference between time-varying generation time and serial interval shown in Figure 1b. The generation time was shorter than the serial interval in the first nine running time windows, then reversed in the last one running time window. The more extended period of the increasing epidemic phase than the decreasing phase identified in the epidemic curve leads to an overall shorter generation time than the serial interval.

Some limitations exist in this study. First, the sample size was relatively small, decreasing the precision of the estimated parameters. Second, we used the time interval between infection and the first time of the positive PCR test (cycle threshold ≤ 40) as a proxy for the estimation of the latent period. However, there is a possibility that transmission will not occur until the viral load of the case reaches a certain level. Thus, our approach might underestimate the latent period. Third, we did not consider the impact of vaccination on the transmission dynamics of the Omicron variant outbreak. Future studies are needed to explore the relationship between vaccination and the risk of transmission. In addition, all individuals used to estimate the generation time and serial interval were symptomatic, which might result in an underestimation of the parameters because symptomatic cases tend to be isolated or self-isolated quicker than asymptomatic cases. Finally, the use of household transmission pairs might underestimate the generation time and serial interval given the possibility of multi-introduction of infection into the household.

In conclusion, our study revealed a shorter incubation period and latent period time for Omicron BA.1.1 infections than earlier variants of concern. Enhanced capacity in rapid testing, contact tracing, isolation of cases, and quarantine of close contacts is needed to interrupt the chains of transmission.

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Ethical approval

This study was approved by the institutional ethics committee of the Hangzhou Center for Disease Control and Prevention.

Author contributions

QK and BC conceived the study. Data collection and cleaning were conducted by ZW, SF, ZS, and LY. Data analyses were done by HX, ZW, and PW. HX wrote the first draft of the manuscript. All authors critically reviewed and revised the manuscript and approved the final version.

Declaration of competing interest

BJC consults for AstraZeneca, Fosun Pharma, GSK, Moderna, Pfizer, Roche, and Sanofi Pasteur. The others authors have no competing interests to declare.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.10.033.

References

Backer JA, Egunk A, Andeweg SP, Veldhuijzen JK, van Maarseveen N, Vermaas K, et al. Shorter serial intervals in SARS-CoV-2 cases with Omicron BA.1 variant compared with Delta variant, the Netherlands, 13 to 25 December 2021. Euro Surveill 2022;27.

Cori A, Ferguson NM, Fraser C, Cauchemez S. A new framework and software to estimate time-varying reproduction numbers during epidemics. Ann J Epidemiol 2012;175:1505–12.

Hart WS, Miller E, Andrews NJ, Wright P, Maini PK, Funk S, et al. Generation time of the alpha and delta SARS-CoV-2 variants: an epidemiological analysis. Lancet Infect Dis 2022;22:603–10.

Kang M, Xin H, Yuan J, ST Ali, Liang Z, Zhang J, et al. Transmission dynamics and epidemiological characteristics of SARS-CoV-2 Delta variant infections in Guangdong, China, May to June 2021. Euro Surveill 2022;27.

Kraemer MUG, Pybus OG, Fraser C, Cauchemez S, Rambaut A, Cowling BJ. Monitoring key epidemiological parameters of SARS-CoV-2 transmission. Nat Med 2021;27:1854–5.

Manica M, De Bellis A, Guzzetta G, Mancuso P, Venturini M, Ventreille F, et al. Intrinsically generation time of the SARS-CoV-2 Omicron variant: an observational study of household transmission. Lancet Reg Health Eur 2022;19.

Mefsun Y, Chen D, Bond HS, Lin Y, Cheung JK, Wong JY, et al. Epidemiology of infections with SARS-CoV-2 Omicron BA.2 variant in Hong Kong, January–March 2022. Emerg Infect Dis 2022;28:1856–8.

Park SW, Sun K, Champredon D, Li M, Bolker BM, Earn DJD, et al. Forward-looking serial intervals correctly link epidemic growth to reproduction numbers. Proc Natl Acad Sci U S A 2021;118.

Ren X, Li Y, Yang X, Li Z, Cui J, Zhu A, et al. Evidence for pre-symptomatic transmission of coronavirus disease 2019 (COVID-19) in China. Influenza Other Respir Viruses 2021;15:19–26.

World Health Organization. Enhancing response to Omicron SARS-CoV-2 variant. https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states, 2022 (accessed 17 April 2022).

Xin H, Li Y, Wu P, Li Z, Lau EHY, Qin Y, et al. Estimating the latent period of coronavirus disease 2019 (COVID-19). Clin Infect Dis 2022;74:1678–81.