

Transmission dynamics of the delta variant of SARS-CoV-2 infections in Daejeon, South Korea

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Research Article

Keywords: COVID-19, delta variant, transmissibility, superspreading, Korea

Posted Date: September 30th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-934350/v1>

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Version of Record: A version of this preprint was published at The Journal of Infectious Diseases on December 2nd, 2021. See the published version at <https://doi.org/10.1093/infdis/jiab586>.

Abstract

Background

The delta variant of SARS-CoV-2 is now the predominant variant worldwide. However, its transmission dynamics remain unclear.

Methods

We analyzed all case patients in local clusters and temporal patterns of viral shedding using contact tracing data from 405 cases associated with the delta variant of SARS-CoV-2 between 22 June and 31 July 2021 in Daejeon, South Korea.

Results

Overall, half of the cases were aged under 19 years, and 20% were asymptomatic at the time of epidemiological investigation. We estimated the mean serial interval as 3.26 days (95% credible interval 2.92, 3.60), and 12% of the transmission occurred before symptom onset of the infector. We identified six clustered outbreaks, and all were associated with indoor facilities. In 23 household contacts, the secondary attack rate was 63% (52/82). We estimated that 15% (95% confidence interval, 13–18%) of cases seeded 80% of all local transmission. Analysis of the nasopharyngeal swab samples identified virus shedding from asymptomatic patients, and the highest viral load was observed two days after symptom onset. The temporal pattern of viral shedding did not differ between children and adults ($P=0.48$).

Conclusions

Our findings suggest that the delta variant is highly transmissible in indoor settings and households. Rapid contact tracing, isolation of the asymptomatic contacts, and strict adherence to public health measures are needed to mitigate the community transmission of the delta variant.

Introduction

On 27 April 2021, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lineage B.1.617.2 (delta variant) was first identified in an international traveler at the South Korean port of entry [1], and on 18 May 2021, the delta variant was first identified in the local community in South Korea [1]. As of early September 2021, which seems to be the middle phase of a fourth community coronavirus 2019 (COVID-19) epidemic, the delta variant is now predominant in South Korea [2].

The delta variant has a mutated spike protein, which increases its affinity to the ACE2 receptor resulting in its higher replication efficiency in the human airway epithelial system [3]. Furthermore, the delta variant is reported to be less sensitive to vaccine-elicited antibodies than the wild type of SARS-CoV-2 [3]. Therefore, it is likely to contribute to the increased transmissibility of infection in the community. Recent epidemiological studies in China also demonstrated that the transmissibility of the delta variant could be higher than that of the wild type of SARS-CoV-2 [4, 5]. However, the epidemiology of the delta variant and the transmission dynamics, including its superspreading potential, remain unclear.

On 27 June 2021, the first local outbreak associated with the delta variant of SARS-CoV-2 was identified in Daejeon metropolitan city, located in the central region of South Korea with a population of 1.5 million [6]. For controlling the outbreak, active case finding under the strict test-trace-isolation strategy was implemented by the public health authority [7, 8]. In this study, we analyzed patient data associated with the delta variant outbreak and explored the epidemiological characteristics, transmission dynamics, and temporal pattern of viral shedding.

Methods

Epidemiological investigation

An epidemiological investigation was conducted on all the cases of SARS-CoV-2 infection in Daejeon metropolitan city, South Korea between 22 June 2021 and 31 July 2021. The demographic information and the presentation of symptoms were screened at the time of epidemiological investigation if the individuals had any history of contact with the primary case patient.

During the investigation of the outbreak, human specimens were collected from the suspected carriers of SARS-CoV-2 via a nasopharyngeal swab. All specimens were tested using a commercial kit (PowerChek™, Kogen-eBiotech, Seoul), which is approved by the Korea Centers for Disease Control and Prevention Agency. This kit targets N and RdRP genes for screening SARS-CoV-2 infection and targets L452R, E484Q, and P681R for the delta variant [9]. We defined positive cases when the cycle threshold (C_t) value for the N-gene was ≤ 40 and that for L452R, E484Q, and P681R was ≤ 35 at the first test during the epidemiological investigation [9].

To evaluate the household secondary attack rate, we sought information on the number of households quarantined, household contact, and individuals with confirmed diagnosis during their quarantine from available resources in the clusters of a sports academy (number of households = 23), reading room (n = 6), and other settings (n = 3). Mandatory testing for all household contact was conducted using reverse transcription-polymerase chain reaction (RT-PCR) on the day when symptoms developed and the first and the last days during the 14-day home quarantine.

Cluster analysis

Using the obtained case line lists including contact tracing data, we characterized the clusters of SARS-CoV-2 infection and established a transmission network. We defined local clusters as two or more confirmed SARS-CoV-2 infections with contact with the index case patient [10]. Cases that were not linked to any cluster were defined as sporadic local cases. Subsequent transmission was traced back to the primary case based on the epidemiological investigation report.

Serial interval and offspring distribution

Serial interval is an important parameter for estimating the reproduction number (R), the mean number of infectees resulting from an infector. To identify the serial interval of the delta variant, we excluded individuals who had received any dose of coronavirus 2019 (COVID-19) vaccination. Then, we examined a subset of cases with symptom onset dates and reconstructed the transmission pairs by identifying the infector–infectee pair from the epidemiological investigation report. We estimated the serial interval distribution, which was fitted to a normal distribution [11].

We also generated the observed offspring distribution by calculating the number of secondary cases. We fitted the offspring distribution to a negative binomial distribution and presented the parameters including R and dispersion (k), which indicate the individual level of heterogeneity in the transmission [12]. We also identified superspreading events (SSE) with the superspreading threshold, defined as 8–12 secondary cases corresponding to the 99 percentile of the Poisson distribution, given that the delta variant has R_0 in the range of 3–6 [13]. Following a previous study [14], we estimated the proportion of cases that are responsible for 80% of secondary cases. Using the *rstan* package in R software, we estimated the parameters through Markov chain Monte Carlo simulation. For four chains, 15,000 samples of posterior distribution were stored after 5,000 burn-in samples.

Temporal pattern of viral shedding

To identify the temporal patterns of viral shedding of the delta variant, we assessed the temporal trend of C_t values for the N-gene in samples from all patients with the delta variant excluding patients who had received any dose of COVID-19 vaccination. The lower the C_t value, which needs fewer RT-PCR cycles to be positive, the greater is the quantity of viral nucleic acid (viral load) in the tested specimen [15]. Although the C_t value does not provide a direct measurement of viral load, it provides a useful proxy measure of the viral load of the patient [16]. The generalized additive model (GAM) was fitted to the C_t values with the function of the symptom onset date to visualize the temporal trends. Predicted C_t values from the GAM were plotted with boxplots. We analyzed the statistical differences in the C_t values in different age groups and sex by using Welch's t-test or Mann-Whitney test, as appropriate. All statistical analyses were performed in R version 4.0.1 (R Foundation for Statistical Computing).

Results

Of the total 405 cases of local infections, 222 (54.8%) were male patients, and the overall median age of the patients was 19 years (1–71 years) (Supplementary Table 1). There were 12 (3%) and 6 (1%) patients

who had received one and two doses of COVID-19 vaccination (AstraZeneca or Pfizer-BioNTech) \geq 14 days before a positive test result, respectively. All the individuals who received the COVID-19 vaccination were household contacts of the index case patient. There were 325 (80.2%) symptomatic cases. In the welfare facility for the disabled, the proportion of asymptomatic cases was the largest (41%, 11 cases out of 27 cases), and reporting delay was the longest (median 2.7 days, interquartile range [IQR], 1–3.3 days) (Supplementary Table 1).

We identified six clustered outbreaks including a sports academy ($n = 249$, 61.5% of total clusters), karaoke center ($n = 47$, 11.6%), physical education high school ($n = 41$, 10.1%), welfare facility for the disabled ($n = 27$, 6.7%), and other settings (Fig. 1 and Supplementary Table 1).

The outbreak related to a sports academy, the largest clustered outbreak, constituted two SSE (SSE #1 and SSE #2, Fig. 2A). The second-largest cluster was related to a karaoke center and accounted for one SSE (SSE #3, Fig. 2B). The third-largest cluster was from a high school with one SSE (SSE # 4, Fig. 2C). All remaining clusters are shown in Fig. 2D.

For the household secondary attack rate, we obtained available data of 32 households, and 63.4% (52 cases out of 82 cases) household contacts tested PCR positive during their quarantine.

We identified 258 infector–infectee transmission pairs. The median serial interval was 3 days (IQR, 2–4 days). The mean serial interval fitted to a normal distribution was 3.26 days (95% CrI 2.92–3.60) (Fig. 3A). We estimated that 12.12% (95% confidence interval [CI], 9.23%, 15.54%) of the transmission occurred before symptom onset of the infector by using the area under the fitted curve.

The overall R , estimated from the observed offspring distribution and negative binomial distribution, was 0.99 (95% CI, 0.79–1.25), and K was 0.23 (95% CI, 0.18–0.30) (Fig. 3B and Supplementary Fig. 1). From the estimated R and K , we estimated that 15% (95% CI, 13–18%) of cases were responsible for 80% of all local transmission in Daejeon, South Korea.

We identified 80.2% (325/405) symptomatic cases in which the virus started shedding within 14 days, and in 19.8% ($n = 80$) cases, the virus started shedding before symptom onset (Supplementary Tables 1 and 2). However, the lowest number of C_t value (median, 16.19; IQR, 13.49–18.90) was identified on the second day after symptom onset and then gradually increased (Fig. 4A and Supplementary Table 2). A similar pattern was observed among different groups based on age and sex (Fig. 4B and Fig. 4C). The viral load did not significantly differ by sex ($P = 0.90$) or age ($P = 0.48$) (Supplementary Tables 3 and 4, and Supplementary Fig. 2).

Discussion

In many countries where enhanced public health measures against COVID-19 have been implemented, a surge of COVID-19 cases associated with the delta variant was reported in early August 2021 [17]. Our study provides evidence of this surge by demonstrating the transmission dynamics of the delta variant in

South Korea, where strict social distancing measures and active case finding for eliminating COVID-19 have been implemented [18].

In our study, all clustered outbreaks were associated with indoor facilities, where activities in close proximity had taken place. Our result is consistent with the finding of other studies suggesting that the delta variant is highly transmissible in indoor facilities [19, 20]. Our mean estimate of the serial interval of the delta variant of 3.3 days was shorter than that in the mean serial interval of the wild type from a previous Korean study (4.0 days) [21, 22]. A Chinese study also reported a shorter serial interval of the delta variant than that of the wild type [23]. We also identified that 12% of the transmission occurred during the asymptomatic period of the infector, which warrants the current Korean strategy of test-trace-isolation of asymptomatic contacts with the patient.

The overall estimated R_0 of 0.99 in the study was larger than that in a previous Korean study (R_0 of 0.7–0.8) during the COVID-19 pandemic in 2020 [14]. Previous studies demonstrated that a larger R_0 , which indicates higher transmissibility, results from higher viral replication [3] and a longer duration of viral shedding in the human respiratory tract [24]. We also identified that the expected proportion of cases responsible for 80% of secondary transmission in our study (15%) was smaller than that reported in a previous study in which 26% of the cases were of the wild type infection, which suggests the increased transmission potential of the delta variant [14].

The household secondary attacks rate (63%) in our study was larger than that in previous studies conducted in Korea in 2020 (19%) [8] and pooled estimates of 17% for the wild type infection [25]. However, our finding is similar to the finding (53%) from a study of the delta variant in the United States [19]. As the household transmission of SARS-CoV-2 is one of the main drivers of the pandemic, a high household secondary attack rate is likely to contribute to the rapid surge in cases during the fourth community epidemic wave in South Korea.

Previous studies demonstrated a positive correlation between lower C_t value (higher nucleic acid level) and greater ability to culture SARS-CoV-2, which in turn, correlated with higher infectivity [26, 27]. Based on the viral shedding pattern, we identified that the delta variant has transmission potential before symptom onset, similar to the finding of a previous study of the wild type infection [28].

We observed no significant difference in the viral load across the different groups based on sex and age, similar to previous studies of the wild type infection [28, 29]. In our study, about half of the patients were under 19 years old. An increased proportion of COVID-19 cases among children was also observed in the United States [30]. This change in age distribution is likely due to the increased immunity among older age groups and increased social interactions as a result of reopening of schools.

Because the risk-benefit ratio for children remains unclear, unimmunized children are likely to be a potential transmission driver of SARS-CoV-2 in the community. Therefore, strict adherence to public health measures and personal preventive measures including universal use of masks in schools by children is needed to reduce the SARS-CoV-2 transmission risk in the population [30].

Our study has some limitations. First, the presence of some individuals with SARS-CoV-2 immunity in the community may bias our results of the superspreading potential. Overall, as of early August 2021, 17% of the South Korean population (52 million) had received two doses of the vaccination [31]; however, the vaccination program has not yet been extended to the public below 55 years of age [32], which comprised 98% of patient population in the present study. Second, some cases may have been incorrectly attributed to the clusters while the true source of infection was elsewhere. Third, in our study, the mean reporting delay of 1.7 days, the period between symptom onset and case confirmation, was shorter than the previous estimate (mean of 3.3 days) [33]. The reduced reporting delay with rapid case isolation could shorten the serial interval by truncating the infectious period of an infector [34]. Fourth, we did not account for potential confounding factors such as comorbidities of the patients, which could modify the viral shedding dynamics [35]. Lastly, we were unable to examine the potential deterministic factor for the household secondary attack rate including the characteristics of the index case, households, and household contacts.

In conclusion, the asymptomatic transmission and superspreading potential and the higher transmissibility of the delta variant likely contribute to shorter serial interval and increased secondary attack rate. Strict adherence to personal preventive measures during indoor activity and rapid case finding under the test-trace-isolation strategy remain essential to reduce the spread of the delta variant in the community.

Declarations

Acknowledgments

We thank the COVID-19 case and contact investigation team at Daejeon metropolitan government, South Korea.

Funding

This work was supported by the Basic Science Research Program through the National Research Foundation of Korea by the Ministry of Education (grant number NRF-2020R1I1A3066471).

Potential conflict of interest

The authors report no potential conflict of interest.

The need for ethical approval for this study was not necessary because the study was conducted as a public health response and assessment. Therefore, the IRB was waived from the Korean National Institute for Bioethics Policy.

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Figures

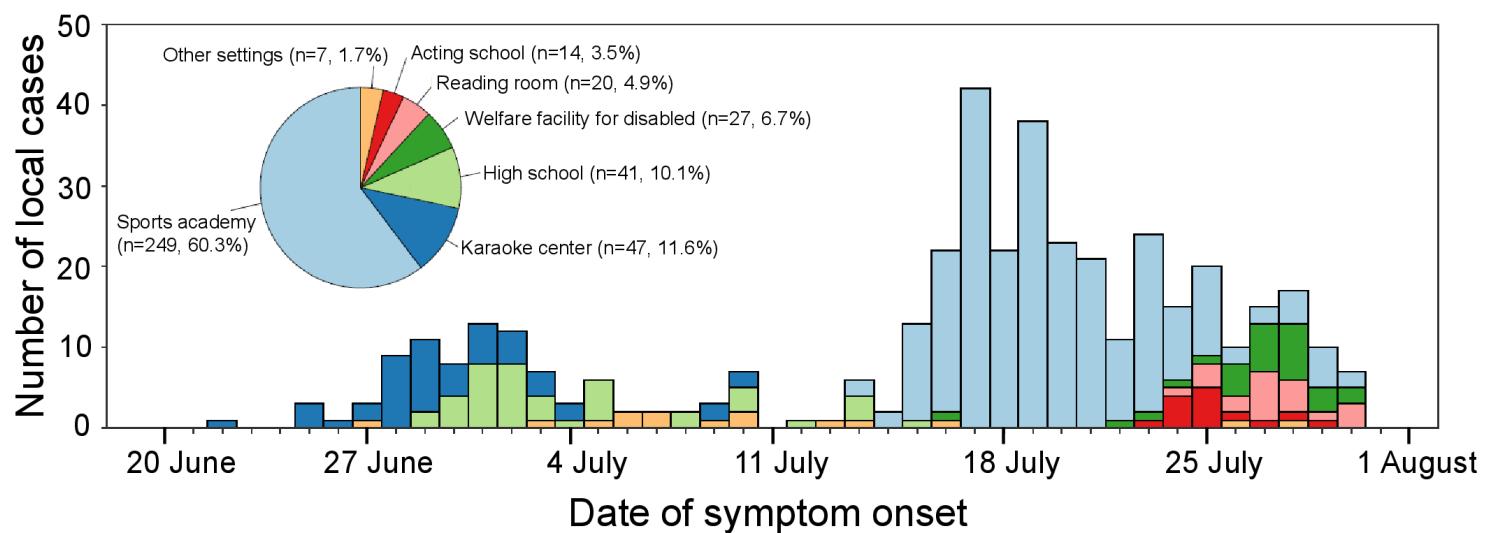


Figure 1

Epidemic curve associated with the delta variant of SARS-CoV-2 in Daejeon, South Korea. The epidemic curve of daily cases based on symptom onset and colored by the cluster category (n=405). Asymptomatic cases (n=20) are included by the date of laboratory confirmation.

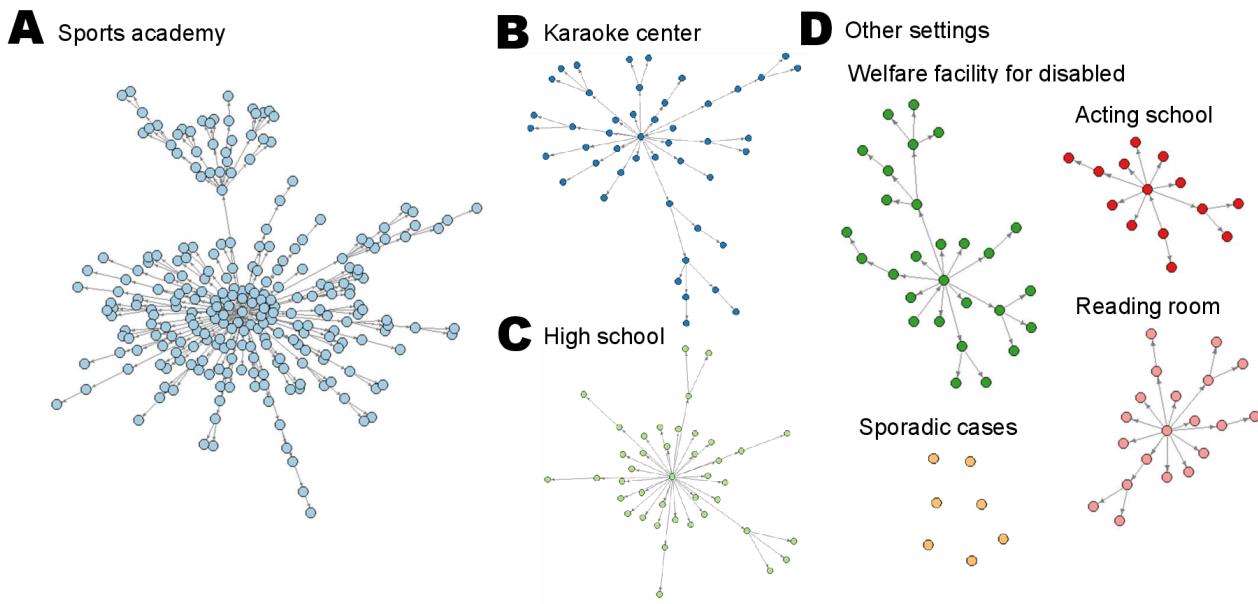


Figure 2

Transmission network associated with the delta variant of SARS-CoV-2 in Daejeon, South Korea. (A) Transmission network associated with the sports academy ($n=249$). (B) Transmission network associated with the karaoke center ($n=47$). (C) Transmission network associated with the high school ($n=41$). (D) Transmission network associated with welfare facility for the disabled ($n=27$), reading room ($n=20$), acting school ($n=14$), and sporadic patients ($n=7$).

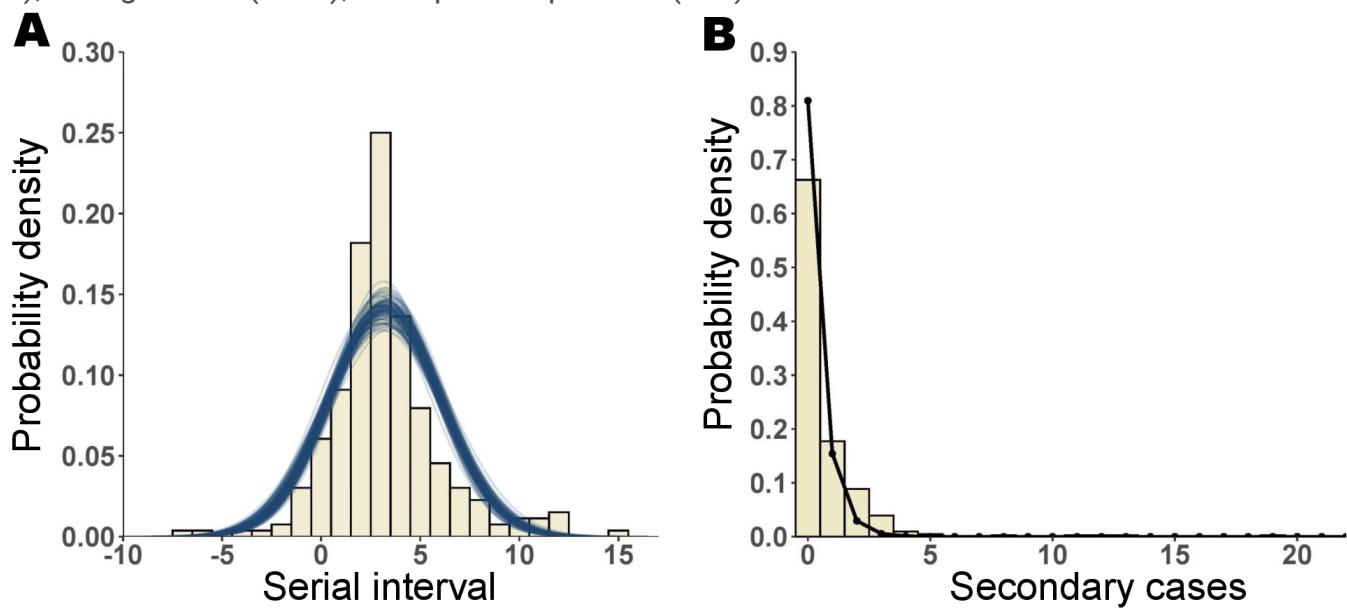


Figure 3

Estimated serial interval distribution and observed offspring distribution of the cases associated with the delta variant. (A) Distribution of serial interval among 258 infector-infectee pairs and fitted to a normal distribution. The gray vertical bar indicates the frequency of the serial interval, and the blue lines indicate

the estimated distribution. (B) Distribution of the offspring of the cases and fitted to a negative binomial distribution with R=0.99 and K=0.23.

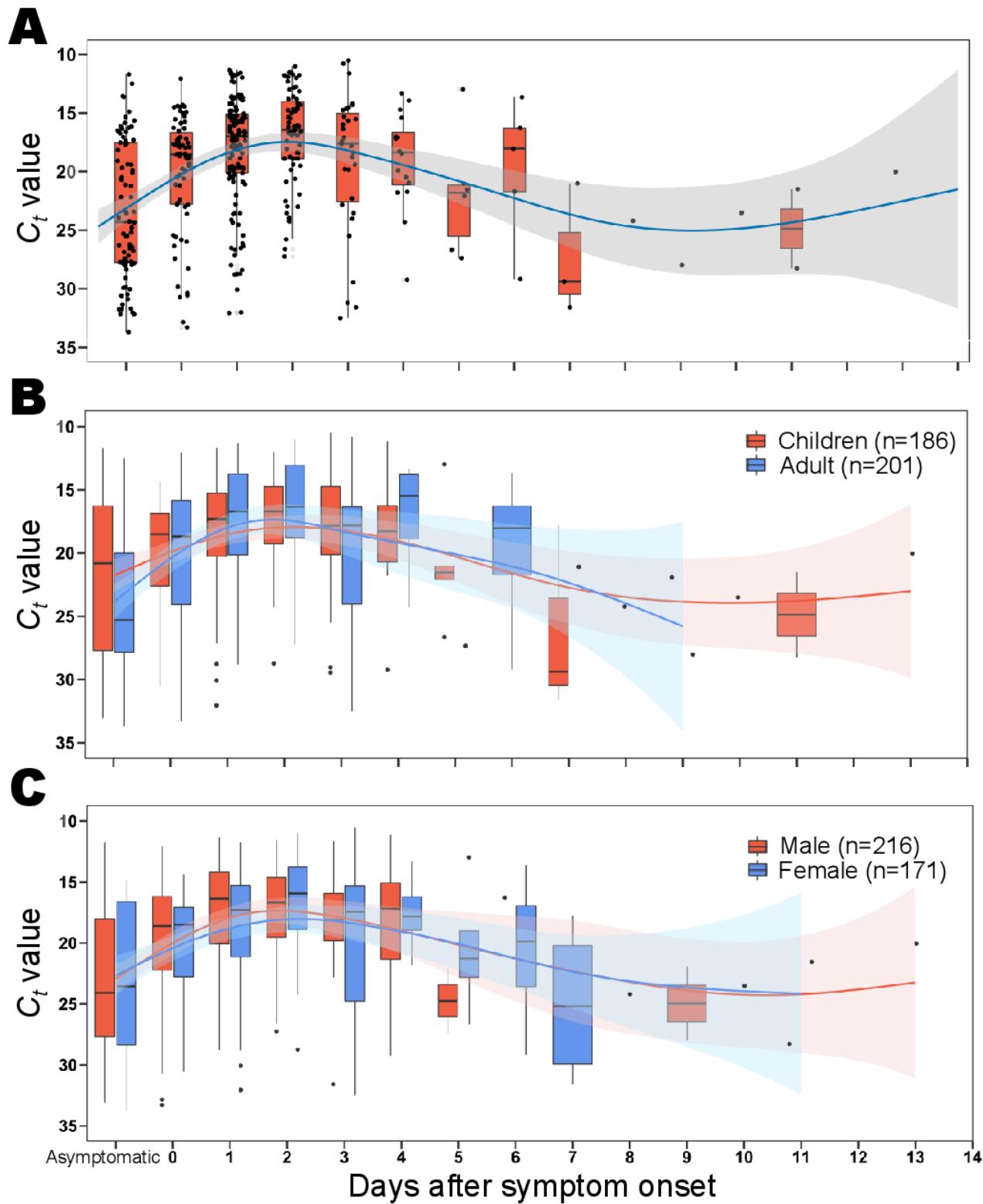


Figure 4

Temporal patterns of viral shedding for the delta variant of SARS-CoV-2. Cyclic threshold (C_t) values of the first RT-PCR in nasopharyngeal swabs for the delta variant infections, (A) overall, and stratified by (B) age, and (C) sex. Dots represent C_t values for the RT-PCR analysis of the N gene. Box plots indicate the

median and interquartile range. The thick curve indicates the trend in viral load using smoothing splines with 95% confidence interval (shaded area).

Supplementary Files

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