



Invasive Pneumococcal Disease diminish during the onset of COVID-19 in Japan between 2019 and 2022

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ABSTRACT

Invasive pneumococcal disease (IPD) is a severe infection caused by *Streptococcus pneumoniae*. This study explores the influence of COVID-19 on IPD occurrence in Japan by using the time trend analysis. We found that the IPD trend changed dramatically after the emergence of COVID-19; first, the number of IPD cases decreased. Second, the seasonality of IPD disappeared after the COVID-19 pandemic. Interestingly, the number of IPD cases increased between the waves of COVID-19.

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Streptococcus pneumoniae can cause invasive pneumococcal disease (IPD) at a patient's sterile site, including the cerebrospinal fluid and blood, and commonly presents with septicemia, meningitis, and pneumonia (Dowell *et al.*, 2003). In Japan, both children and older individuals receive public support for pneumococcal vaccination. Pneumococcal vaccine coverage has been increased since the launch of the vaccine program (Naito *et al.*, 2020).

COVID-19 is a critical health issue globally (Chiu *et al.*, 2020). This infection can be spread in various ways, including inhalation of droplets or contact with mucous membranes with contaminated hands (Bulfone *et al.*, 2021). Nonpharmaceutical interventions (NPIs), for example, hand hygiene, wearing a mask, social distancing, and school and border closures, have been vigorously promoted to contain COVID-19 globally. It was reported that these NPIs also helped to reduce other respiratory infections (Chiu *et al.*, 2020). There are also reports of a decrease in the number of influenza cases during the COVID-19 pandemic, including in Japan (Itaya *et al.*, 2020). We therefore conducted our analysis to understand the pattern of pneumococcal infection changes under unusual circumstances for future IPD control at the national level. We obtained the number of IPD cases in the Infectious Diseases Weekly Report issued by the National Institute of Infectious Diseases from 2014 to 2022. The aggregated COVID-19 data were collected from the official COVID-19 resource in Japan

(<https://covid19.mhlw.go.jp/en/>). All data were combined and analyzed using STATA version 17.

Time trend analysis was used to track IPD cases before and after the occurrence of COVID-19 to assess its effect. The data from 2014 to 2019 were set as before the COVID-19 pandemic, and the information from 2020 to 2022 was designated as during COVID-19. An analysis using time trend analysis is shown in Figure 1. The cumulative number of IPD cases increased every year before COVID-19. However, the number of IPD cases decreased, and the slope of the time trend declined after COVID-19. Furthermore, the mean IPD cases per year fell from 41.90 to 19.59 cases in 2019 and 2020, respectively (Supplement S1). Our findings are consistent with previous studies in Hong Kong, Taiwan, and Singapore (Lim *et al.*, 2020; Juan *et al.*, 2021; Teng *et al.*, 2022). The IPD cases and six waves of COVID-19 pandemic in Japan are overlaid in Figure 2. It shows that IPD cases have remained low since the emergence of COVID-19. The number of COVID-19 cases and the period for each wave are shown in Supplement S2. Before the COVID-19 pandemic between 2014 and 2019, the IPD cases showed remarkable seasonal trends; the minimum trend was observed in September, and the cases increased during winter from October to March (Supplement S3). The seasonality of IPD in Japan showed a similar pattern in the US (Dowell *et al.*, 2003); however, it was not clearly observed after the COVID-19 pandemic (Supplement S4).

Surprisingly, we found that some notable trends of IPD cases increased between the peaks of each COVID-19 wave. Decreasing the number of COVID-19 cases might have increased the number of IPD reports owing to improved accessibility of patients to the

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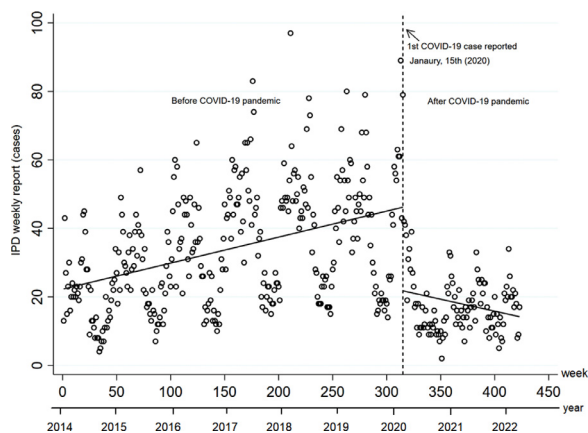


Figure 1. Interrupted time series analysis on weekly IPD counts before and after COVID-19 in Japan. Each plot represents the weekly cases. (IPD: invasive pneumococcal disease)

hospitals, or improved reporting capacity of health facilities. Alternatively, the subsidence of COVID-19 transmission might have mitigated the commitment to NPI in the community. Nevertheless, we still lack certainty in identifying the cause of this finding.

To elucidate what and why specific infectious diseases decrease in frequency during COVID-19 epidemics, we evaluated additional time trend analysis for gastroenteritis, group A Streptococcal infection, respiratory syncytial virus infection, tuberculosis, and influenza in comparison to invasive pneumococcal disease (Supplement S5-S9). Based on the results, we found that NPIs against COVID-19 were able to reduce the number of not only IPD and influenza infections but also Group A streptococcal infections in Japan.

This study has four significant limitations that need to be addressed in future investigations. First, it did not consider the impact of vaccination programs for both IPD and COVID-19. Second, we did not consider that there were different intensities of COVID-19 pandemic for each wave. Third, there might be an interfering effect of parallel infection of SARS-CoV-2 and *S. pneumoniae* (Amin-Chowdhury et al., 2021). Finally, the ever-changing infection control policy may have affected the capacity of health administrations.

In conclusion, the COVID-19 pandemic led to a marked decrease in the number of reported cases of IPD in Japan. Public health

strategies and NPIs, namely, wearing a mask, hand hygiene, and avoiding the 3 Cs, implemented to control COVID-19 inevitably worked to reduce the incidence of infections such as influenza, Group A streptococcal infections, and IPD, where droplet and contact transmission is the main route of infection. School and border closures temporarily suppressed gastroenteritis and RSV infections, but the effect was limited. Further research is expected to improve infection control measures in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of interests

The authors have no competing interests to declare.

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Ethical approval

Ethical approval for this study was not required. Data were extracted from public sources. The authors conducted the research under the Ethical Guidelines for Medical and Health Research Involving Human Subjects, Japan.

Consent for publication

Both authors signed the consent to publish this article.

Availability of data and materials

These data are available on public websites. We collected and transformed the data.

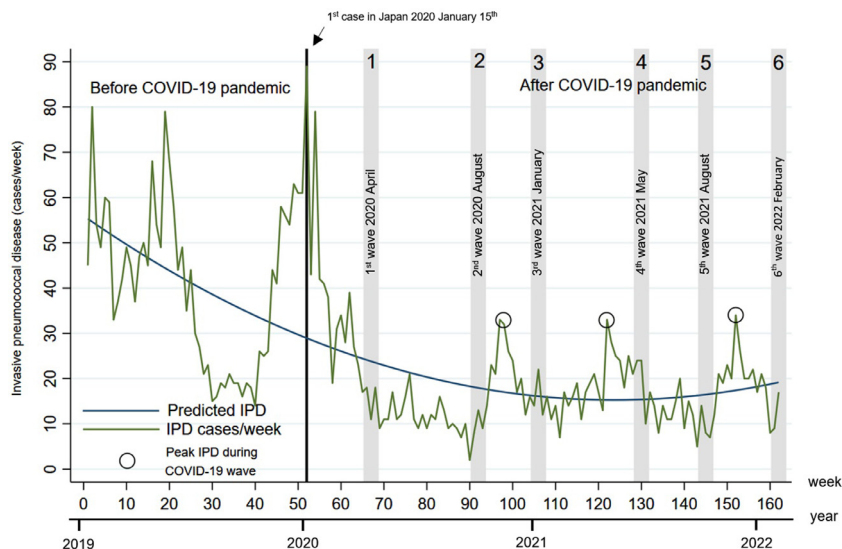


Figure 2. The trend of weekly IPD incidence and the waves of COVID-19 in Japan from 2019 to 2022. (IPD: invasive pneumococcal disease)

Author contributions

Thanawat Khongyot is the main person who developed the conceptual idea, collected and interpreted the data, and wrote the manuscript. Taeko Moriyasu supervised the research and checked and wrote the manuscript. Both authors have reviewed and approved the final manuscript.

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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.2022.05.064](https://doi.org/10.1016/j.ijid.2022.05.064).

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