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Letter to the Editor

Impact of the COVID-19 pandemic on asthma exacerbations in children: A multi-center survey using an administrative database in Japan

Dear Editor,

Since the first patient was reported,¹ the COVID-19 pandemic has caused dramatic changes in daily life. In Japan, a state of emergency was declared on February 27, 2020,² and all schools closed nationwide on February 27, 2020; however, preschools were excluded. Most schools re-opened by the first week of June 2020.² Our daily life behavior has changed, including staying at home, social distancing, regular handwashing, and facial mask-wearing. These changes had a suppressive effect on other respiratory viral infections such as flu.³ Asthma is one of the most common diseases in children. Acute exacerbation is one of the key features of asthma, which sometimes requires an emergency room visit and hospital admission. Inhaled allergens, irritant exposures, and respiratory tract infections are well known triggers of asthma exacerbations. SARS-CoV-2 infection is associated with a poorer outcome in patients with asthma.⁴ Patients with asthma are encouraged to keep regular controller medications to minimize the risk of asthma exacerbation. To evaluate the effect of the COVID-19 pandemic on asthma, we conducted a retrospective observational study using the Diagnosis Procedure Combination (DPC) database from the Quality Indicator/Improvement Project (QIP).⁵ We investigated the incidence of asthma-related hospitalization before and during the COVID-19 pandemic. We also investigated the prescription of inhaled medications during hospitalization to assess the trends during the pandemic. This was because the Japanese Society of Pediatric Allergy and Clinical Immunology recommended the prescription of pressurized metered-dose inhalers (pMDI) rather than an inhaler solution when possible to avoid aerosol generation which could enhance virus transmission. This study was performed with the approval of the Ethics Committee, Kyoto University Graduate School and Faculty of Medicine (approval number: R0135). Using the DPC database, we identified inpatients with discharge dates from July 1, 2018 to September 30, 2020. We selected hospitals with ≥ 9 months of data for both the first and second year of the dates from July 1, 2018 to September 30, 2020. We included patients aged ≤ 15 years and who had been diagnosed with asthma exacerbation according to the ICD-10 codes (J45.x, J46). An interrupted time-series analysis (ITS), including segmented regressions, was performed to evaluate the effect of the COVID-19 pandemic on population-level admissions. We statistically tested the admission volume changes based on the discharge date after adjusting for seasonality through a Fourier term.⁶ The start date of the COVID-19 pandemic was selected to be

March 2020, corresponding to 'a state of emergency' including self-quarantine, social distancing, and school closure. All analyses were computed using R statistical software (version 4.0.2).

We identified 10,226 in-patient cases in 83 hospitals who were diagnosed with asthma exacerbations. The median age was 2 (IQR 1, 5 years) years old, and 6152 patients were boys. The median value of the length of stay for each month was 4.96 days (IQR 3.96, 6.27). Unplanned admission (ICU admission) between October 2018 to September 2019 and October 2019 to September 2020 were 6988 (71) and 5373 (69) cases, respectively. Figure 1a shows the number of inpatients between October 2018 and September 2020. There was a seasonal increase for March to June 2019. However, the number of inpatients for March to June 2020 decreased. Figure 1b shows the results of the ITS analysis. The results showed a marked reduction in the number of inpatients during the pandemic; the reduction in the number of patients during this period was estimated to be 292 ($P < 0.001$). This trend was the same for all age classes, with statistically significant differences for ages < 3 years and 3–5 years (Fig. 1 c–e).

Prescriptions of both pMDI and inhaler solutions for inpatients decreased during the COVID-19 pandemic (Fig. 2a, b). The prescription per patient of inhaler solutions tended to decrease in contrast to an increase in pMDI (Fig. 2c).

Our study had two major findings. First, pediatric patients with moderate to severe asthma who needed hospitalization dramatically decreased during the COVID-19 pandemic. There were several reasons for this situation. One possible factor was the inhibition of other viral infections during the pandemic. In particular, respiratory tract infections are a major precipitating factor of asthma exacerbations in children. In Japan, epidemiological data from the National Institute of Infectious Diseases showed a decreased incidence of infectious diseases including influenza, RSV infection, and mycoplasma pneumonia. This trend was shown worldwide.⁷ Public health education and a change in daily life behavior would have contributed significantly.⁸ One other possible factor is environmental. An improvement in air pollution and decrease of PM2.5 levels during lockdown were reported⁹ in China and India, although the effect might have been lessened in Japan. The strength of the association between these factors was not assessed.

Second, our data demonstrated a significant decrease in the prescription of inhaler solutions during hospitalization, and conversely, the prescription of pMDI doubled during the pandemic. This trend would reflect the practical change of physicians following the expert recommendations, even though most of the

Peer review under responsibility of Japanese Society of Allergy.

<https://doi.org/10.1016/j.alit.2021.06.001>

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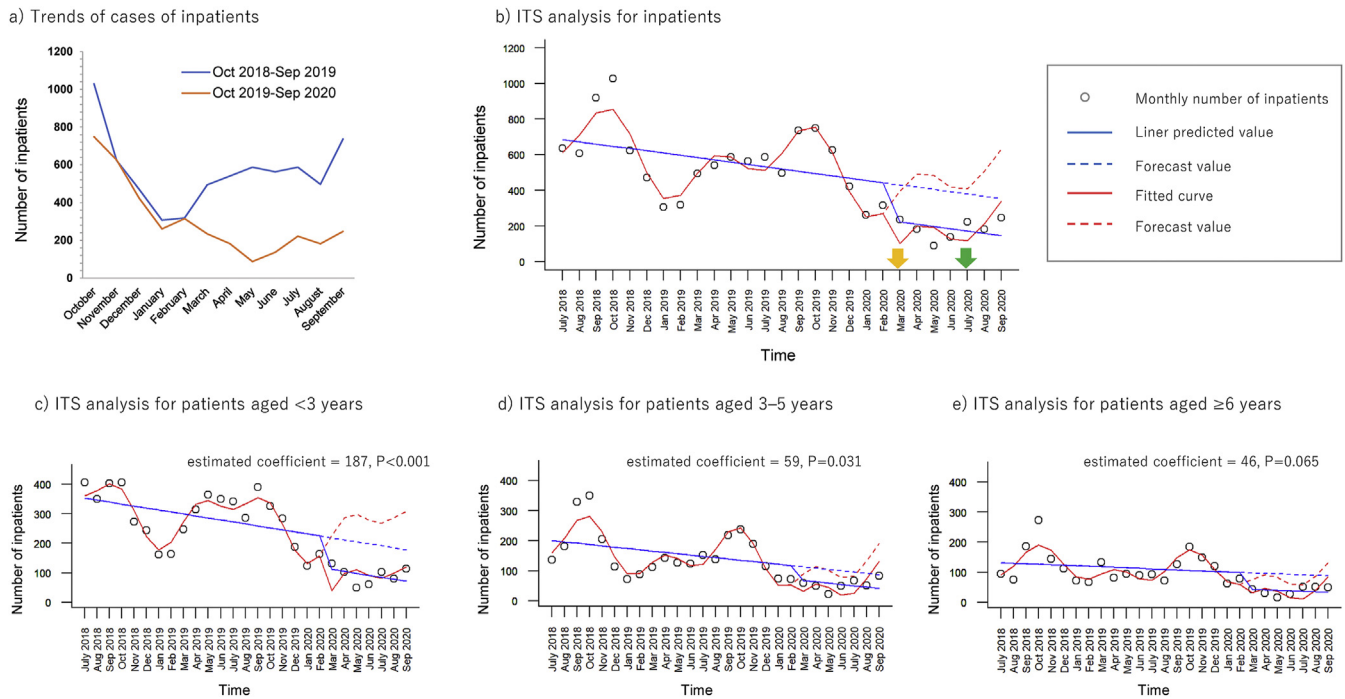


Fig. 1. Asthma patients during the COVID-19 pandemic. **a)** Trends of cases of inpatients between October 2018 to September 2019 and October 2019 to September 2020. **b)** An interrupted time-series (ITS) analysis for inpatients. The reduction in the number of patients during this period was estimated to be 292 ($P = 0.001$). A yellow arrow indicates the time of school closure, and a green arrow indicates the time of school re-opening. **c) – e)** Asthma inpatients during the COVID-19 pandemic for each age category. **c)** ITS analysis for patients aged <3 years. The reduction in the number of patients during this period was estimated to be 187 ($P < 0.001$). **d)** ITS analysis for patients aged 3–5 years. The reduction in the number of patients during this period was estimated to be 59 ($P = 0.031$). **e)** ITS analysis for patients aged ≥6 years. The reduction in the number of patients during this period was estimated to be 46 ($P = 0.065$).

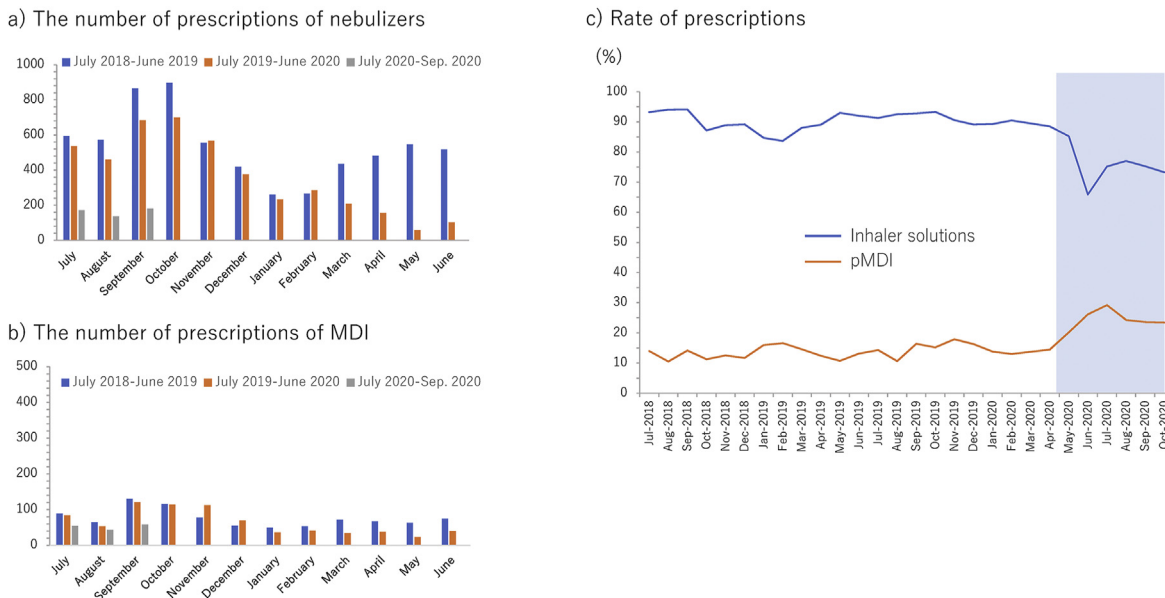


Fig. 2. Trends for the prescription of inhalers. **a)** The number of prescriptions of inhaler solutions **b)** The number of prescriptions of pMDI **c)** Rate of prescriptions.

study patients were thought to be non-COVID-19. Many clinical trials and meta-analyses indicate that the administration of bronchodilators via pMDI with a spacer is as effective as, and possibly superior to, inhaler solutions in infants and children.¹⁰ This practical change would be further enhanced in the pandemic era.

Our study had some limitations. The individual background data and clinical information associated with the hospital admissions were lacking in the DPC data, and therefore, the cause-

and-effect relationship could not be assessed. For example, possible triggers of asthma exacerbation that lead to hospital admission were not assessed in this study. Also, we could not know whether the severity of the asthma exacerbations affected the physicians' choice of inhaler medications. Nonetheless, we believe that the dramatic changes demonstrated in our study have significant implications for how changes in lifestyle can affect health outcomes.

In summary, our data demonstrated 1) a dramatic decrease in pediatric patients with asthma exacerbations who required hospital admission, and 2) a decrease in the prescription of inhaler solutions during hospitalization during the COVID-19 pandemic. We need to continue research into the trends of pediatric asthma patients following the COVID-19 pandemic in Japan.

Acknowledgments

This study was supported by JSPS KAKENHI Grant Number JP19H01075 from the Japan Society for the Promotion of Science, Health and Labour Sciences Research Grant from the Ministry of Health, Labour and Welfare, Japan [20HA2003 and 21IA1005] and by the GAP Fund Program of Kyoto University type B to Yuichi Imanaka. The funders played no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

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Received 10 February 2021
Received in revised form 28 May 2021
Accepted 1 June 2021
Available online 16 July 2021