Article

Impact of Preventive Measures on Subjective Symptoms and Antigen Sensitization against Japanese Cedar, Cypress Pollen and House Dust Mites in Patients with Allergic Rhinitis: A Retrospective Analysis in the COVID-19 Era

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Abstract: For >2 years, Japan’s government has been urging the populace to take countermeasures to prevent COVID-19, including mask wearing. We examined whether these preventive behaviors have affected the rate and degree of sensitization against pollen and house dust antigens in patients with allergic rhinitis. We retrospectively surveyed 2565 patients who had undergone allergy blood testing during the period 2015–2021. We subdivided this period into eras based on the COVID-19 pandemic: the pre-COVID (2015–2019, n = 1879) and COVID (2020–2021, n = 686) eras. The positive rates for Japanese cedar and cypress in the 40–59-year-olds and those for house dust in the 20–39-year-olds were significantly reduced in the COVID era versus those in the pre-COVID era. Each group’s mean antigen-specific CAP scores decreased significantly from the 1st to 2nd era: from 1.98 to 1.57 for cedar (p < 0.01), 1.42 to 0.95 for cypress (p < 0.05), and 2.86 to 2.07 for house dust (p < 0.01). Our survey of the patients’ clinical records indicates that 47.5% of the pollinosis patients reported improvement in nasal symptoms after the three seasons of pollen dispersion in the COVID era. Japan’s quarantine policies designed to combat the spread of COVID-19 thus coincide with pivotal measures to alleviate allergic reactions.

Keywords: allergic rhinitis; face mask; COVID-19; house dust mite; Japanese cedar pollen; Japanese cypress pollen; preventive behavior; subjective symptoms

1. Introduction

Coronavirus disease 2019 (COVID-19) is an ongoing pandemic infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. For over 2 years, Japan’s government has urged the populace to take countermeasures to prevent COVID-19, with guidance such as “wear a mask”, “wash your hands frequently”, and “stay home and avoid the 3Cs outside (crowded places, close contact settings, and closed spaces)” [2]. These measures have helped suppress respiratory viral infections and the risk of asthma exacerbations [3]. We hypothesized that these preventive behaviors may also have affected the severity of nasal symptoms and the rate and degree of sensitization against common...
Antigens among patients with allergic rhinitis (AR) in Japan. We conducted a retrospective survey of the data of 2565 patients who showed allergic symptoms and had undergone allergy blood testing during the period from 2015 to 2021. We subdivided the period into two eras based on the outbreak of the COVID-19 pandemic in Japan: the pre-COVID-19 era (2015–2019) and the COVID-19 era (2020–2021). The patients’ data in the two eras were compared based on four age groups: 0–19, 20–39, 40–59, and ≥60 years old. We also conducted a survey to investigate changes in the patients’ social behaviors and subjective nasal symptoms after the start of the COVID-19 pandemic.

Allergic rhinitis (AR) can be classified into seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR). Japanese cedar/cypress and house dust mites are major causative antigens for SAR and PAR, respectively [4], and the numbers of individuals in Japan with SAR or PAR both increased markedly in the pre-COVID-19 era. The results of a nationwide epidemiological survey conducted in 2019 revealed the presence of cedar pollinosis in 38.8% of the respondents compared with 16.2% in 1998 and 26.5% in 2008 [5]. The presence of PAR has also shown gradual increases from 18.7% in 1998 to 23.4% in 2008 and 24.5% in 2019 [4].

The elimination and avoidance of antigens are pivotal measures to alleviate allergic reactions, and these measures coincide with quarantine policies designed to combat the spread of COVID-19 [4,6,7]. We have found no prior study that specifically assessed the impact of anti-COVID-19 measures on AR patients in Japan based on both objective and subjective parameters.

2. Materials and Methods

2.1. Patient Enrollment and Pollen Counts

We retrospectively analyzed the data of 2565 patients who showed allergic symptoms and had allergy blood tests against common antigens at Hiroshima University Hospital during the years 2015–2021. The antigens included Japanese cedar pollens (Cryptomeria japonica), Japanese cypress pollens (Chamaecyparis obtusa), and house dust mites (Dermatophagoides pteronyssinus). The patients’ antigen-specific IgE levels were determined by the ImmunoCAP™ Specific IgE system (ThermoFisher Scientific, Waltham, MA, USA). The blood tests are sandwich tests in which the solid phase of specific antigens ensures binding of all relevant antibodies, providing a uniquely high binding capacity. The CAP score system is graded as follows: 0, ≤0.34 UA/mL; 1, 0.35–0.69 UA/mL; 2, 0.70–3.49 UA/mL; 3, 3.50–17.4 UA/mL; 4, 17.5–49.9 UA/mL; 5, 50.0–99.9 UA/mL; 6, ≥100 UA/mL. The CAP-RAST scores ≥2 are regarded as positive, 1 as borderline, and 0 as negative, respectively. The diagnosis of AR was based on the combination of the CAP score ≥2 and the presence of nasal symptoms such as sneezing, nasal discharge, and nasal congestion [4].

We divided the study period 2015–2021 into two eras based on the outbreak of the COVID-19 pandemic in Japan: the pre-COVID (2015–2019) and COVID (2020–2021) eras. We compared patients in the two eras classified into four age groups: 0–19, 20–39, 40–59, and ≥60 years old. The proportion and distribution of patients with positive ImmunoCAP scores were determined for each age group, and we compared the differences in these scores between the two eras.

In addition, to assess the possible changes in the patients’ social behaviors and subjective allergic symptoms after the start of the COVID-19 pandemic, we analyzed the clinical records of pollinosis patients who visited the above-mentioned hospital or related ENT clinics (led by KK, YN and KM) in Hiroshima City after the onset of the COVID-19 pandemic. The records included whether the patient (1) had engaged in limited outdoor behaviors in accord with social regulations, i.e., wearing a mask, and (2) reported improvement in his or her nasal and ocular symptoms in the pollinosis seasons after the change in social behaviors.

The degree of pollen dispersion was monitored annually by a gravitational pollen sampler on the roof of the Hiroshima University Hospital. The cypress and cedar pollen
counts were determined daily by staining with Calberla solution from 15 January to 31 May each year.

This study was performed in accordance with the Declaration of Helsinki, with approval from the Hiroshima University School of Medicine Institutional Review Board (approval no. E-1738; approval date: 4 September 2019).

2.2. Statistical Analyses

The Kruskal–Wallis and Mann–Whitney U test were used for between-group comparisons. Fisher’s exact test was used to compare qualitative data. *p*-values < 0.05 were considered significant. JMP Pro ver. 14 (SAS, Cary, NC, USA) was used for the analyses.

3. Results
3.1. Changes in the Proportions of SAR and PAR Patients

A total of 1879 patients in the pre-COVID era and 686 patients in the COVID era were enrolled (Table 1). There were no significant differences in the age or gender distributions between the two eras. The pollen counts and dispersion periods of cedar and cypress fluctuated annually, due mainly to weather conditions in the previous summer. The amounts of mean season cedar pollens and the mean dispersion periods of cypress pollens tended to increase during the COVID era, but no significant between-era differences in these values were observed (Mann–Whitney U test, *p* = 0.6985 for cedar pollen counts and *p* = 0.0506 for cypress dispersion periods) (Table 2). We also collected information on the air pollutant levels in Hiroshima City that exert adverse effects on allergic symptoms [8] (Table 2). The mean levels of particulate matter (PM) 2.5 and related gaseous materials (SO2 and NOx) tended to improve in the COVID era, but a significant between-era difference was not observed (Mann–Whitney U test).

Table 1. Demographics of the study population, air pollutants, and pollen dispersion in Hiroshima City.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>0–19</td>
<td>522 (316/206)</td>
<td>200 (124/76)</td>
<td></td>
</tr>
<tr>
<td>20–39</td>
<td>268 (137/131)</td>
<td>95 (48/47)</td>
<td></td>
</tr>
<tr>
<td>40–59</td>
<td>421 (223/198)</td>
<td>164 (79/85)</td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>668 (347/321)</td>
<td>227 (130/97)</td>
<td></td>
</tr>
<tr>
<td>Antigen-positive, n Cedar/cypress</td>
<td>999 (523/476)</td>
<td>361 (181/180)</td>
<td></td>
</tr>
<tr>
<td>House dust</td>
<td>667 (389/278)</td>
<td>195 (108/87)</td>
<td></td>
</tr>
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Table 2. Comparison of pollen dispersion counts and periods, and air pollutants in Hiroshima City.

<table>
<thead>
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<tbody>
<tr>
<td>Mean season pollen counts, /cm²</td>
<td>Cedar</td>
</tr>
<tr>
<td></td>
<td>Cypress</td>
</tr>
<tr>
<td>Mean pollen dispersion period, days</td>
<td>Cedar</td>
</tr>
<tr>
<td></td>
<td>Cypress</td>
</tr>
<tr>
<td>Mean air pollutant level, PM2.5, µg/m³</td>
<td>12.56 (11.1–13.7)</td>
</tr>
<tr>
<td>SO₂ and NOₓ, ppm</td>
<td>0.0136 (0.012–0.015)</td>
</tr>
</tbody>
</table>

Figure 1 illustrates the time-course changes in the proportion of patients with positive ImmunoCAP scores (≥2) from 2015 to 2021. In the SAR patients, the positive rates for both cedar and cypress in the 40–59-year-olds were significantly reduced in the COVID era.
era compared with those in the pre-COVID era (Figure 1a,b). In this age group, the mean positive rates decreased significantly from 63.2% to 51.4% for cedar \( (p < 0.05) \) and from 53.7% to 31.0% for cypress \( (p < 0.01) \). The positivity tended to be lower for both antigens in 2021 compared with 2020. No similar significant between-era differences existed in the other age groups. In the PAR patients, the positive rates for house dust in the 20–39-year-olds were significantly reduced in the COVID era compared with those in the pre-COVID era (Figure 1c). In this age group, the mean positive rates decreased significantly from 70.5% to 47.8% \( (p < 0.01) \). We further compared positive antigen rates of the patients between the two eras stratified by 10-year-olds generation, gender and CAP scores for each antigen (Table 3). The positive rates in the pre-COVID era for the antigens in each generation were compatible with those by previously published data in 2006 and 2016 [9]. A significant decrease in the positive rates for both SAR and PAR was observed in the generations of COVID-19 era that corresponded to the results shown in Figure 1. No significant differences were detected in the gender proportions between the two eras.

![Figure 1](image1.png)  
**Figure 1.** Changes in the positive antigen rate against (a) cedar, (b) cypress, and (c) house dust mites for each age group before and after the COVID-19 outbreak. * \( p < 0.05 \), ** \( p < 0.01 \), Fisher’s exact test.

### 3.2. Changes in the CAP Scores for Pollens and House Dust

We also examined the CAP score for the responsible antigens in each age group between the pre-COVID and COVID eras. The results are consistent with those of the antigen proportion rates. Seasonal AR patients in the 40–59-year-old group showed a
significant reduction in CAP scores in the COVID era compared with those in the pre-COVID era (Figure 2). The mean CAP scores decreased from 1.98 to 1.57 for cedar \( (p < 0.01) \) and from 1.42 to 0.95 for cypress \( (p < 0.05) \). No similar significant differences were identified in the other age groups. In the PAR patients, the 20–39-year-old group showed a significant reduction in CAP scores in the COVID era versus those in the pre-COVID era (Figure 3). The mean CAP scores for house dust decreased from 2.86 to 2.07 \( (p < 0.01) \).

Table 3. Comparison of positive antigen rates of the patients between the two eras stratified by 10-year-old generation and CAP scores for each antigen.

<table>
<thead>
<tr>
<th>Patient, %</th>
<th>Cedar</th>
<th>Cypress</th>
<th>House Dust</th>
</tr>
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<tbody>
<tr>
<td>CAP Score</td>
<td>Total (Male/Female)</td>
<td>2–3</td>
<td>≥4 Total (Male/Female)</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–9</td>
<td>18.5</td>
<td>31.5</td>
<td>50.1 (51.9/44.5)</td>
</tr>
<tr>
<td>10–19</td>
<td>23</td>
<td>39.5</td>
<td>62.6 (62.7/62.5)</td>
</tr>
<tr>
<td>20–29</td>
<td>29.6</td>
<td>36.3</td>
<td>65.9 (71/60)</td>
</tr>
<tr>
<td>30–39</td>
<td>35.6</td>
<td>30.3</td>
<td>65.9 (70/62.5)</td>
</tr>
<tr>
<td>40–49</td>
<td>41.7</td>
<td>21.1</td>
<td>62.7 (62.7/62.7)</td>
</tr>
<tr>
<td>50–59</td>
<td>45.4</td>
<td>18.2</td>
<td>63.6 (60.4/66.1)</td>
</tr>
<tr>
<td>60–69</td>
<td>34.9</td>
<td>12.6</td>
<td>47.5 (47.5/47.5)</td>
</tr>
<tr>
<td>70–79</td>
<td>28.6</td>
<td>10.7</td>
<td>39.3 (38.7/40)</td>
</tr>
<tr>
<td>80–</td>
<td>21.6</td>
<td>4.5</td>
<td>26.1 (31.7/21.3)</td>
</tr>
</tbody>
</table>

\( \dagger p = 0.125, \ast p < 0.05, \ast\ast p < 0.01 \) versus the corresponding groups of the pre-COVID era.

3.3. Changes in Subjective Nasal Symptoms after the Start of the COVID-19 Pandemic

Figure 4 illustrates the changes in the patients’ social behaviors and reported subjective allergic symptoms after the start of the COVID-19 pandemic, based on our survey of their clinical records. We collected records from 122 patients with cedar/cypress pollinosis based on a positive CAP score. Their mean age was 42.3 years, with 49 males and 73 females. Regarding outdoor behaviors compared with before the COVID-19 pandemic, almost 90% of patients (111/122) reported that they always wore masks when out in public, in accordance with the Government’s request. The proportions of patients who reported improvement in nasal symptoms and ocular symptoms after the start of the COVID era were 47.5% (58/122) and 30.3% (37/122), respectively; the nasal symptom improvement rate is significantly higher than that of ocular symptoms \( (p < 0.01) \).
Figure 2. Comparison of CAP scores for cedar and cypress in each age group between the pre-COVID-19 (2015–2019) and COVID-19 (2020–2021) eras. (a) 0–19, (b) 20–39, (c) 40–59, (d) ≥60 years old groups. The data are mean ± SD (error bars). * p < 0.05, ** p < 0.01.

Figure 3. Comparison of CAP scores for house dust in each age group between the pre-COVID-19 (2015–2019) and COVID-19 (2020–2021) eras. (a) 0–19, (b) 20–39, (c) 40–59, (d) ≥60 years old groups. The data are mean ± SD (error bars). ** p < 0.01.
were 47.5% (58/122) and 30.3% (37/122), respectively; the nasal symptom improvement rate is significantly higher than that of ocular symptoms ($p < 0.01$).

**Figure 4.** Changes in the social behaviors and the severity of subjective allergic symptoms after the start of the COVID-19 pandemic. Clinical records were surveyed from 122 cedar/cypress pollinosis patients who visited the hospital/clinics from April to May in 2022. **$p < 0.01$, Fisher’s exact test.**

4. Discussion

Environmental variations induced by industrialization and climate change partially explain the increases in the prevalence and severity of allergic disease. The prevalence of cedar/cypress pollinosis and that of house dust mite-induced PAR continue to show increasing trends in Japan, accompanied by environmental and circumstantial increases in antigen exposure [4,8]. During the post-World War II period 1946–1980, approx. 20% of Hiroshima prefecture’s land area (1660 km$^2$) was planted with cedar or cypress forests in compliance with a massive national afforestation policy designed to secure timber and maintain land preservation. The resulting increased exposure to pollens among younger individuals has been reported to have led to early sensitization to pollen antigens [10].

Each year during the Japanese cedar pollen-dispersion season (February to April), followed by that of Japanese cypress (April to May), a large number of pollinosis patients experience severe nasal and ocular symptoms. Because Japanese cypress pollens contain several components that cross-react with cedar pollens, about 70% of pollinosis patients suffer the symptom burdens from both types of trees. A severe affliction due to cedar and cypress pollens is also attributable to the nature of the pollens’ dispersion, i.e., their large quantities and long (nearly 100-km) airborne distances [11].

As a quantitative test, CAP scoring enables monitoring of the development and severity of allergic diseases [12]. In sensitized pollinosis patients, antigen-specific IgE levels are strongly affected by the amount and periods of cedar or cypress pollen exposure [8,13]. These patients’ CAP scores rise after they experience larger amounts and/or longer periods of pollen exposure, and their scores remain high through to the next season. We recently reported the trends in pollen dispersion and their possible relationship with the degree of antigen sensitization against cedar and cypress pollens from 2001 to 2018 in the same single-
Our present analyses revealed that the proportion of patients with positive CAP scores for both cedar and cypress increased continually over the past 18 years, with the increase rate of the cypress CAP scores more prominent at 25%. These results indicate that the levels of pollen dispersion have provided sufficient exposure to maintain antigen sensitization during daily activities before the COVID-19 outbreak in Japan. In contrast, the preventive measures during the COVID-19 pandemic appear to have attenuated the potential pollen sensitization. Inhaled airborne allergens such as pollen (10–100 µm) and house-dust mite feces (10–40 µm) play a significant role in triggering IgE-mediated immunologic responses in typical allergic rhinitis symptoms [4].

Our present findings indicate that both the positive rates and the mean CAP scores for both cedar and cypress in the 40–59-year-old group of SAR patients decreased significantly in the COVID era, i.e., 2020 and 2021. The improvement of these objective parameters could be attributable to the potential contribution of wearing non-woven surgical masks that can filter particles > 3 µm [15]. The scrupulous nature of Japanese citizens, who have agreed to change their outdoor behaviors as requested by the Government, is likely to have reinforced the protective effects. Our analyses considered environment factors such as air pollutants, which have adverse effects on allergic symptoms; the analyses revealed no significant difference in the mean annual levels of PM$_{2.5}$ and related gaseous materials (SO$_2$ and NOx) between the pre-COVID and COVID eras.

The present findings are in line with the recent reports in other countries describing a reduction in the subjective burden of screened nasal symptoms that are due to seasonal or perennial allergic rhinitis after the adoption of anti-COVID-19 measures [6,7,16]. Mengi et al. evaluated the use of face masks on AR symptoms in 50 pollen allergy patients who were compulsorily using face masks due to the COVID-19 pandemic in Turkey [6]. They found that the rate of participants with severe-moderate nasal symptoms decreased significantly during the pandemic with the use of face masks, from 92% (46/50) to 56% (28/50), and the corresponding rate of ocular symptoms decreased significantly from 60% (30 patients) to 32% (16 patients). An investigation conducted in Northern Italy examined the effects of quarantine and face-masking policies on nasal and ocular symptoms in a pool of 124 patients suffering from ragweed allergy [16], and the results demonstrated that the overall burden of oculorhinitis decreased significantly during the 2020 ragweed season. Reductions in the use of the common anti-allergic medications, such as oral antihistamines and nasal steroids, were also observed. To assess the impact of face masks on subjective AR symptoms, Dror et al. analyzed the data of a multicenter questionnaire distributed in 2020 for 2 weeks to hospital nurses in Israel, and they reported reductions in AR symptoms [7]. Our present findings also showed that 70% of the SAR patients described an improvement in nasal symptoms after the three seasons of pollen dispersion in the COVID era. Together the above-cited results highlight the potential benefit of face masks for AR patients.

Several reasons have been proposed in relation to the worldwide increase in PAR caused by house dust mites. The exacerbation factors include global warming as well as the increased time spent indoors with air conditioning inside higher and more airtight residences [17,18]. In the present study’s PAR patients, a significant decrease occurred in the positive rates and the mean CAP scores for house dust in the 20–39-year-olds after the outbreak of COVID. In this sense, the elimination and avoidance of mite antigens are pivotal measures to alleviate allergic reaction. They coincide with official quarantine policies designed to combat the spread of COVID-19, i.e., mask-wearing and improved or frequent ventilation of indoor spaces [2].

Our patients in the 40- to 59-year-old age group of SAR patients and those in the 20- to 39-year-old PAR group showed significant reductions in positive rates and CAP scores in the COVID-19 era. There are possible explanations for the differences between the age groups. The prevalence of Japanese cedar pollinosis is most common among middle-aged individuals, especially 40–49-year-olds, whose morbidity rate is up to 40%. In contrast, house dust mite allergy is prevalent mainly among younger individuals, i.e., 20–39-year-olds [4,5]. Yonekura et al. reported that SAR induced by cedar pollen took chronic courses.
in the majority of middle-aged patients [19]. The prevalence of cedar pollenosis in Chiba, Japan increased over 10 years from 1995 to 2005 probably due to a high level of pollen exposure. It is thus likely that preventive behaviors would manifest their inhibitory effects in these corresponding age groups.

Another possibility is that the individuals in these generations tend to be more amenable to social infection-avoidance behaviors such as remote indoor working and restrictions on outdoor activities as well as mask-wearing and hand-washing [20]. In any case, the importance of determining the reason(s) for the age-group differences should be acknowledged, as the possible relationship between lifestyle habits and associated exposure routes might have non-negligible effects on the present outcomes worldwide.

This study has several limitations. It was cross-sectional and based on a regional sample collection. A causal relationship between the two eras cannot be directly determined. We did not include information on the severity of nasal and ocular symptoms of the subjects that correspond directly to CAP scores. A direct relationship between the subjects' lifestyle and associated exposure routes was not clarified. Possible important factors that determine the age-group differences should be further assessed, including lifestyle habits and associated exposure frequencies. Further studies on a larger scale and with control groups are also necessary to elucidate the effects of personal protective equipment.

At the time of writing the manuscript (18 June 2022), Japan’s government still enforces mask-wearing to the citizens and applies other virus-related preventive rules. However, acknowledgement of increased vaccination certificates and changes in genome shifts to omicron variants with mild virulent forms might lift regulation guidelines on how to prevent the spread of the coronavirus. In this sense, our data presented herein would be of value as the reference.

In conclusion, the COVID-19 pandemic has provided an opportunity to assess the effects against allergen exposure to pollens and other air pollutants. Our findings suggest that appropriate COVID-preventive actions are important and effective measures as reflected by the decreased allergic parameters (both objective and subjective) in the Japanese population investigated herein.


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Institutional Review Board Statement: This study was performed in accordance with the Declaration of Helsinki, with approval from the Institutional Review Board at the Hiroshima University School of Medicine (approval no. E-1738; approval date: 4 September 2019).

Informed Consent Statement: Informed consent was obtained from all participants involved in the study.

Data Availability Statement: The data presented in this study are available on reasonable request from the corresponding author.

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Conflicts of Interest: The authors declared no potential conflict of interest with respect to the research, authorship, and/or publication of this article.
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