INTRODUCTION

For the past 20–30 years, there has been a steady and rapid increase in the number of patients with allergic diseases worldwide. Identification of potential allergens is important not only for diagnosis but also for the treatment of patients, which can help avoid causative allergens and initiate early immunotherapy. Multiple allergosorbent simultaneous test chemiluminescent assay (MAST-CLA) can detect specific IgE antibodies against various allergens. It was introduced in Korea in the early 1990s and is most commonly used up to date.

Patients with allergies often have allergies to ≥2 antigens. Patients are often confirmed to have positive reactions to multiple fungal allergens and positive reactions to the allergens of the MAST-CLA were investigated.

Background: Exposure and sensitization to fungal allergens can evoke the development and worsen allergic diseases. Many patients with allergies show multiple positive reactions to different allergens.

Objective: The purpose of this study was to analyze the relationship between fungal allergens that are mostly found in South Korea and other positive reactions to the allergens of the multiple allergosorbent simultaneous test chemiluminescent assay (MAST-CLA).

Methods: We enrolled 1,040 (588 men, 452 women) patients who showed positive reactions to three fungi, namely, *Alternaria alternata*, *Aspergillus fumigatus*, and *Cladosporium herbarum*, using MAST-CLA at Daegu Catholic University Medical Center from January 2010 to July 2017. The epidemiology and relationship between positive reactions to multiple fungal allergens and positive reactions to the allergens of the MAST-CLA were investigated.

Results: *A. alternata* was the most common fungal species, followed by *C. herbarum* and *A. fumigatus* (78.8% vs. 52.1% vs. 20.1%). Patients who showed positive reactions to all fungal allergens had 4.97 other antigens on average. Statistically significant results were obtained when comparing positive reactions to all fungal allergens to other allergens (Spearman correlation coefficient = 0.129, \( p < 0.05 \)).

Conclusion: Patients should be educated on allergic diseases caused by other antigens if they are sensitized to fungal antigens.

Key Words: Allergen, *Alternaria alternata*, *Aspergillus fumigatus*, Chemiluminescent assay, Fungi
studies have focused on the link between fungal antigens and other antigens\(^2\). Several fungal species are known to cause severe respiratory and cutaneous allergic diseases\(^3\), but only a few epidemiological studies have shown the prevalence of allergic reactivity to fungi using skin tests or IgE detection\(^4-7\). Therefore, this study aimed to analyze the epidemiology and the relationship between fungal allergens and other allergens.

**MATERIALS AND METHODS**

1. **Data**

This study was a retrospective analysis of the electronic and written charts of patients with a positive reaction to, at least, one of the following three different fungi confirmed by MAST-CLA, which was performed at the dermatology department of Daegu Catholic University Medical Center (DCUMC) from January 2010 to July 2017. These fungal species were *Alternaria alternata*, *Aspergillus fumigatus*, and *Cladosporium herbarum*. Medical records were documented at DCUMC. Patient demographic data, namely, age, sex, department, season, and diagnosis, were analyzed. This study was conducted in accordance with the principles of the Declaration of Helsinki.

2. **MAST-CLA**

The MAST-CLA Allergy test (Hitachi Chemical Diagnostics, Inc., CA, USA) was used. The two types of MASTpettes\(^6\) were food panel and inhalant panel (Table 1). In the MASTpette\(^6\) chamber, 64 cellulose chambers are arranged in a ladder shape. The chambers consist of a positive control on the first line, negative control on the second line, anti-IgE on the third line, and 61 allergens from the 4th line to the 64th line. The test was performed according to the kit instructions. Patient’s serum was added to the chamber, sensitized at room temperature for 18 h, and then washed three times with washing buffer. The enzyme-labeled anti-IgE antibody solution was added to the chamber, sensitized at room temperature for 4 h and washed three times, and the reaction solution was sensitized at room temperature for 30 min. The results were sorted into six classes, 0, 1/0, 1, 2, 3, and 4, using a MAST-CLA-1 luminometer. In this study, class 2 and above were classified as positive.

3. **Statistical analysis**

All gathered data were coded as numerical values. Descrip-

| Allergen | No. (%) |
|----------|---------|
| *Dermatophagoides* pteronyssinus mite | 404 (38.8) |
| *D. farinae* mite | 344 (33.1) |
| Storage mite | 9 (0.9) |
| Cat | 115 (11.1) |
| Dog | 99 (9.5) |
| Egg white | 30 (2.9) |
| Milk | 61 (5.9) |
| Maize | 0 |
| Sesame | 0 |
| Soybean | 16 (1.5) |
| Crab | 52 (5.0) |
| Shrimp | 31 (3.0) |
| Potato | 10 (1.0) |
| Apple | 3 (0.3) |
| Cacao | 0 |
| Peach | 24 (2.3) |
| Mackerel | 17 (1.6) |
| CCD (bromelain) | 0 |
| Rye pollens | 137 (13.1) |
| House dust | 182 (17.5) |
| Cockroach | 77 (7.4) |
| *Cladosporium herbarum* | 541 (52.1) |
| *Aspergillus fumigatus* | 209 (20.1) |
| *Alternaria alternata* | 818 (78.8) |
| Alder | 92 (8.8) |
| Birch | 0 |
| Oak white | 28 (2.7) |
| Ragweed | 38 (3.7) |
| Mugwort | 96 (9.2) |
| Japanese hop | 0 |
| Food panel | |
| Pork | 20 (7.0) |
| Beef | 10 (3.5) |
Table 1. Positive rate of each allergen-specific IgE detected by MAST-CLA (Continued)

| Allergen                  | Food panel | Inhalant panel |
|---------------------------|------------|----------------|
| Cheddar cheese            | 6 (2.1)    | Hamster        |
| Chicken                   | 12 (4.2)   | Hazel          |
| Pupa, silk cocoon         | 0          | Sweet vernal grass 83 (11.0) |
| Tomato                    | 30 (10.6)  | Bermuda grass 8 (1.1) |
| Kiwi                      | 0          | Orchard grass 92 (12.2) |
| Mango                     | 0          | Timothy grass 9 (1.2) |
| Banana                    | 0          | Reed 71 (9.4) |
| Citrus mix                | 28 (9.9)   | Redtop, bent grass 0 |
| Peanut                    | 50 (17.6)  | Honey bee 0 |
| Walnut                    | 42 (14.8)  | Yellow jacket 0 |
| Chestnut                  | 0          | Latex 0 |
| Wheat flour               | 24 (8.5)   | Penicillium notatum 148 (19.6) |
| Barley meal               | 10 (3.5)   | Sycamore mix 74 (9.8) |
| Rice                      | 34 (12.0)  | Sallow mix 0 |
| Buck wheat                | 30 (10.6)  | Poplar mix 38 (5.0) |
| Garlic                    | 10 (3.5)   | Ash mix 29 (3.8) |
| Onion                     | 20 (7.0)   | Pine 44 (5.8) |
| Celery                    | 0          | Japanese cedar 107 (14.2) |
| Cucumber                  | 0          | Acacia 0 |
| Codfish                   | 10 (3.5)   | Hinoki cypress 0 |
| Mussel                    | 0          | Oxeye daisy 74 (9.8) |
| Tuna                      | 18 (6.3)   | Dandelion 72 (9.5) |
| Salmon                    | 10 (3.5)   | English plantain 0 |
| Clam                      | 0          | Russian thistle 0 |
| Squid                     | 0          | Goldenrod 0 |
| Anchovy                   | 0          | Pigweed 0 |
| Yeast, bakers             | 0          |                  |
| Mushroom                  | 0          |                  |
| *Candida albicans*        | 54 (19.0)  |                  |
| *Acarus siro*             | 122 (16.1) |                  |

Inhalant panel values are expressed in percentage. The analysis was performed using SPSS 19.0 version (SPSS, Inc., Chicago, USA). Spearman's correlation coefficient was used to investigate the relationship between the number of positive fungal allergens and other sensitized allergens.
RESULTS

1. Demographic analysis of all patients

A total of 1,040 patients had positive reactions to at least one fungal allergen using the MAST-CLA (Table 1). During the same time, we performed 3,450 MAST-CLA tests, and only 1,040 patients (30.14%) showed a positive reaction to the fungal allergens. Among the fungal species, patients mostly showed sensitivity to A. alternata, followed by C. herbarum and A. fumigatus (78.8% vs. 52.1% vs. 20.1%). Patients’ sex, age, season, department, and diagnosis were analyzed. Male predilection was observed with 588 (56.3%) patients (Table 2). Patient age ranged from 1 to 96 years, and the mean value was 33.1 (Table 3). Patients in their 20s had the largest proportion (24.8%). In the seasonal evaluation, the proportion of patients who reported the occurrence of allergies was the largest during summer (30.0%) (Table 4). Most patients visited the otorhinolaryngology department, followed by dermatology and internal medicine (Table 5). Patient diagnosis varied from mostly allergic diseases to other systemic diseases. The most common diagnosis was allergic rhinitis, followed by urticaria, atopic dermatitis, allergic contact dermatitis, asthma, drug eruption, and hypereosinophilic syndrome (Table 6). Others include various skin diseases, such as irritant contact dermatitis, Stevens-Johnson syndrome, prurigo, or suspected allergies.

Table 2. Sex distribution of patients with positive reaction to fungal allergens

| Variable | Male: Number (%) | Female: Number (%) | Total: Number (%) |
|----------|------------------|--------------------|-------------------|
| Sex      |                  |                    |                   |
| Male     | 81 (56.3)        | 63 (43.7)          | 588 (56.3)        |
| Female   | 27 (55.1)        | 22 (44.9)          | 452 (43.7)        |

Table 3. Age distribution of patients with positive reaction to fungal allergens

| Variable | 0–9: Number (%) | 10–19: Number (%) | 20–29: Number (%) | 30: Number (%) | 40: Number (%) | 50: Number (%) | 60: Number (%) | 70: Number (%) | 80: Number (%) | 90: Number (%) | Total: Number (%) |
|----------|-----------------|-------------------|-------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|-------------------|
| Age      |                |                   |                   |               |               |               |               |               |               |               |                   |
| 0–9      | 9 (6.3)         | 8 (16.3)          | 110 (25.3)        | 1 (3.7)       | 2 (14.3)      | 22 (8.7)      | 16 (13.4)     | 168 (16.2)    |               |               |                   |
| 10–19    | 26 (18.1)       | 3 (6.1)           | 150 (34.5)        | 6 (22.2)      | 3 (21.4)      | 49 (19.4)     | 21 (17.6)     | 258 (24.8)    |               |               |                   |
| 20–29    | 19 (13.2)       | 3 (6.1)           | 90 (20.7)         | 5 (18.5)      | 1 (7.1)       | 37 (14.7)     | 11 (9.2)      | 166 (16)      |               |               |                   |
| 30       | 15 (10.4)       | 6 (12.2)          | 23 (5.3)          | 5 (18.5)      | 0             | 21 (8.3)      | 11 (9.2)      | 81 (7.8)      |               |               |                   |
| 40       | 9 (6.3)         | 6 (12.2)          | 14 (3.2)          | 3 (11.1)      | 3 (21.4)      | 21 (8.3)      | 16 (13.4)     | 72 (6.9)      |               |               |                   |
| 50       | 26 (18.1)       | 7 (14.3)          | 14 (3.2)          | 3 (11.1)      | 2 (14.3)      | 35 (13.9)     | 12 (10)       | 99 (9.5)      |               |               |                   |
| 60       | 20 (13.9)       | 9 (18.4)          | 12 (2.8)          | 2 (7.4)       | 2 (14.3)      | 20 (7.9)      | 16 (13.4)     | 81 (7.8)      |               |               |                   |
| 70       | 13 (9)          | 6 (12.2)          | 18 (4.1)          | 2 (7.4)       | 0             | 42 (16.7)     | 14 (11.8)     | 95 (9.1)      |               |               |                   |
| 80       | 7 (4.9)         | 1 (2)             | 3 (0.7)           | 0             | 1 (7.1)       | 2 (0.8)       | 2 (1.7)       | 16 (1.5)      |               |               |                   |
| 90       | 0               | 0                 | 1 (0.2)           | 0             | 0             | 3 (1.2)       | 0             | 4 (0.4)       |               |               |                   |
| Total    | 144 (13.8)      | 49 (4.7)          | 435 (41.8)        | 27 (2.6)      | 14 (1.3)      | 252 (24.2)    | 119 (11.4)    | 1,040 (100)   |               |               |                   |
2. Demographic analysis of patients with positivity for fungal allergen and concurrent fungal allergens

Of the patients, 628 showed a positive reaction to only one fungal allergen: 144 (13.8%) patients to *Cladosporium herbarum*, 49 (4.7%) patients to *Aspergillus fumigatus*, and 435 (41.8%) patients to *Alternaria alternata*. In addition, 293 patients had a positive reaction to two fungal allergens: 27 (2.6%) patients had positive reaction to *C. herbarum* and *A. fumigatus*, 14 (1.3%) to *A. fumigatus* and *A. alternata*, and 252 (24.2%) to *C. herbarum* and *A. alternata*. Moreover, 119 (11.4%) patients had a positive reaction to all three fungal allergens in the MAST-CLA.

For the demographic study, more male patients had a positive reaction to only one fungal allergen (61.6%), but more female patients had a positive reaction to multiple fungal allergens (51.2%).

Only a small number of younger patients showed a positive reaction to *A. alternata*. Patients showing a positive reaction to only *C. herbarum* or *A. fumigatus* were evenly distributed regardless of age. Patients showing multiple positive reactions to allergens were also evenly distributed. No significant difference was noted in other groups, except that *A. alternata* allergies occurred most frequently in the summer, indicating a seasonal distribution. Among the patients who visited the otorhinolaryngology department, most had positive reactions to *A. alternata* and *A. fumigatus*. For patients who visited the dermatology department, most visits were due to a positive reaction to *C. herbarum*. The highest frequency of positive reactions to multiple allergens was observed in patients who visited the dermatology department. Among all groups, allergic rhinitis was the most common diagnosis in patients with a positive reaction to *A. alternata*.

Table 4. Seasonal distribution of patients with positive reactions to fungal allergens

| Season | Positive fungal allergen | Total |
|--------|--------------------------|-------|
|        | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 |
| Spring | 34 (23.6) | 22 (44.9) | 87 (20) | 10 (37) | 4 (28.5) | 44 (17.5) | 28 (23.5) | 229 (22) |
| Summer | 51 (35.4) | 12 (24.5) | 142 (32.6) | 8 (29.6) | 4 (28.5) | 65 (25.8) | 29 (24.4) | 311 (30) |
| Autumn | 28 (19.4) | 6 (12.2) | 96 (22.1) | 5 (18.5) | 2 (14.3) | 67 (26.6) | 29 (24.4) | 233 (22.4) |
| Winter | 31 (21.5) | 9 (18.4) | 110 (25.3) | 4 (14.8) | 4 (28.5) | 76 (30.1) | 33 (27.7) | 267 (25.7) |
| Total  | 144 (13.8) | 49 (4.7) | 435 (41.8) | 27 (2.6) | 14 (1.3) | 252 (24.2) | 119 (11.4) | 1,040 (100) |

Table 5. Department distribution of patients with positive reactions to fungal allergens

| Department | Positive fungal allergen | Total |
|------------|--------------------------|-------|
|            | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 |
| DT         | 58 (40.3) | 18 (36.7) | 144 (33.1) | 11 (40.7) | 6 (42.9) | 94 (37.3) | 43 (36.1) | 374 (36) |
| IM         | 34 (23.6) | 7 (14.3) | 52 (12) | 2 (7.4) | 2 (14.3) | 75 (29.8) | 37 (31.1) | 209 (20.1) |
| ENT        | 49 (34) | 21 (42.9) | 218 (50.1) | 13 (48.1) | 6 (42.9) | 79 (31.3) | 37 (31.1) | 423 (40.7) |
| PD         | 0 | 0 | 17 (3.9) | 0 | 0 | 2 (0.8) | 1 (0.8) | 20 (1.9) |
| Others     | 3 (2.1) | 3 (6.1) | 4 (0.9) | 1 (3.7) | 0 | 2 (0.8) | 1 (0.8) | 14 (1.4) |
| Total      | 144 (13.8) | 49 (4.7) | 435 (41.8) | 27 (2.6) | 14 (1.3) | 252 (24.2) | 119 (11.4) | 1,040 (100) |

DT, dermatology; IM, internal medicine; ENT, otorhinolaryngology; PD, pediatric
3. Positive reactions to multiple allergens

Mites and house dust are associated with fungal allergens. Among the mite species, *Dermatophagoides pteronyssinus* take up the largest proportion followed by *D. farinae* and house dust. When excluding mites and house dust, the most common concurrent allergens to *C. herbarum* are *Penicillium* and *Acarus siro* (flour mite). *A. fumigatus* showed the highest simultaneous positive reaction rate with rye and orch. *A. alternata* showed the highest simultaneous positive reaction rate with cats and dogs. Mites were the most common simultaneous positive allergens for patients with all three fungal allergens, followed by cedar, *Penicillium*, and house dust (Table 7).

We examined the number of allergens showing simultaneously positive reactions to only one fungal allergen, two fungal allergens, and all three fungal allergens. When the reaction to only one fungal allergen was positive, the number of simultaneously positive allergens was 2.82 on average. When the reaction to two fungal allergens was positive, the number of simultaneously positive allergens was 3.41 on average. When the reaction to all three fungal allergens was positive, the number of other simultaneously positive allergens was 4.97 on average. Nonparametric method correlation analysis was performed, and Spearman's correlation coefficient showed a positive value of 0.129 ($p < 0.05$) (Fig. 1).

**DISCUSSION**

People are exposed to allergens in various settings, both indoors and outdoors. Fungi are ubiquitous airborne allergens and are important causes of various human diseases. Several epidemiological and diagnostic studies reported the prevalence of fungal allergies using skin tests or IgE detection. However, epidemiological investigation of fungal allergens has not been made yet. This is because identifying the role of specific fungi, which can cause allergy, is difficult.

In this study, male patients were more likely to have a positive reaction to fungal allergens than female patients were. However, no significant difference was found between both

| Diagnosis                  | Positive fungal allergen | Total |
|----------------------------|-------------------------|-------|
| AD                         | 1 only                  | 133   |
|                            | 2 only                  | (12.8)|
|                            | 3 only                  | (12.8)|
|                            | 1+2                     | (19.3)|
|                            | 2+3                     | (10.8)|
|                            | 1+3                     | (7.4)|
|                            | 1+2+3                   | (7.4)|
| Urticaria                  | 1 only                  | 176   |
|                            | 2 only                  | (16.9)|
|                            | 3 only                  | (16.9)|
|                            | 1+2                     | (16.9)|
|                            | 2+3                     | (16.9)|
|                            | 1+3                     | (16.9)|
|                            | 1+2+3                   | (16.9)|
| ACD                        | 1 only                  | 50    |
|                            | 2 only                  | (4.8)|
|                            | 3 only                  | (4.8)|
|                            | 1+2                     | (4.8)|
|                            | 2+3                     | (4.8)|
|                            | 1+3                     | (4.8)|
|                            | 1+2+3                   | (4.8)|
| AR                         | 1 only                  | 436   |
|                            | 2 only                  | (41.9)|
|                            | 3 only                  | (41.9)|
|                            | 1+2                     | (41.9)|
|                            | 2+3                     | (41.9)|
|                            | 1+3                     | (41.9)|
|                            | 1+2+3                   | (41.9)|
| Hypereosinophilic syndrome | 1 only                  | 6     |
|                            | 2 only                  | (0.6)|
|                            | 3 only                  | (0.6)|
|                            | 1+2                     | (0.6)|
|                            | 2+3                     | (0.6)|
|                            | 1+3                     | (0.6)|
|                            | 1+2+3                   | (0.6)|
| Asthma                     | 1 only                  | 36    |
|                            | 2 only                  | (3.5)|
|                            | 3 only                  | (3.5)|
|                            | 1+2                     | (3.5)|
|                            | 2+3                     | (3.5)|
|                            | 1+3                     | (3.5)|
|                            | 1+2+3                   | (3.5)|
| Drug eruption              | 1 only                  | 15    |
|                            | 2 only                  | (1.4)|
|                            | 3 only                  | (1.4)|
|                            | 1+2                     | (1.4)|
|                            | 2+3                     | (1.4)|
|                            | 1+3                     | (1.4)|
|                            | 1+2+3                   | (1.4)|
| Others                     | 1 only                  | 188   |
|                            | 2 only                  | (18.1)|
|                            | 3 only                  | (18.1)|
|                            | 1+2                     | (18.1)|
|                            | 2+3                     | (18.1)|
|                            | 1+3                     | (18.1)|
|                            | 1+2+3                   | (18.1)|

**Table 6. Diagnostic distribution of patients with positive reactions to fungal allergens**

| Variable | Number (%) |
|----------|------------|
| Variable | Number (%) |
| Diagnosis | Positive fungal allergen |
|          | (1 = *Cladosporium herbarum*, 2 = *Aspergillus fumigatus*, 3 = *Alternaria alternata*) |
| AD       | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |
| Urticaria | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |
| ACD      | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |
| AR       | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |
| Hypereosinophilic syndrome | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |
| Asthma   | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |
| Drug eruption | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |
| Others   | 1 only | 2 only | 3 only | 1+2 | 2+3 | 1+3 | 1+2+3 | Total |

AD, atopic dermatitis; ACD, allergic contact dermatitis; AR, allergic rhinitis
sexes. In previous reports, the proportion of male patients who had atopic dermatitis, asthma, and hay fever were higher than female patients were, although these differences became narrower over time\(^9\)\(^{19}\). The incidence of allergic respiratory disease is higher in children than in adults. Longitudinal studies suggest that children with mild disease are likely to become asymptomatic as teenagers, whereas those with more severe disease will have symptoms that persist throughout their lifetime\(^17\). In one MAST-CLA study, the overall prevalence of positive allergens was the highest among teenagers. In that study, the 10–15 years age group showed the highest total IgE level, but the overall positive reaction rate and the number of positive allergens decreased with age. In the present study, teenagers had the largest proportion among all age groups. However, the prevalence of a positive reaction to multiple fungal allergens was distributed evenly in all age groups. This suggests that patients who are sensitized to multiple allergens may continue to be sensitized to multiple allergens over time.

C. herbarum and A. alternata allergies occur throughout the year, but they are highly observed in the late summer and autumn when plants grow\(^20\)\(^{21}\). The seasonal pattern of fungal spores has been reported to have little regional difference in the temperate zone, and domestic reports showed similar results\(^5\). In Korea, the growth of both types of fungi increased rapidly from mid-June and decreased at the end of October, and there was a slight increase in winter\(^22\). Meanwhile, A. fumigatus is usually considered an indoor fungus,

| Table 7. Simultaneous positive reactions to other allergens and each fungal allergen |
|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Rank | Variable | Number (%) | Variable | Number (%) | Variable | Number (%) | Variable | Number (%) |
| 1st  | Cladosporium herbarum | 29.2 | Aspergillus fumigatus | 42.3 | Dermatophagoides pteronyssinus mite | 36.7 | Dermatophagoides pteronyssinus mite | 49.6 |
| 2nd  | Dermatophagoides farinae mite | 27.1 | Dermatophagoides farinae mite | 40.8 | Dermatophagoides farinae mite | 33.1 | Dermatophagoides farinae mite | 41.2 |
| 3rd  | House dust | 13.2 | Rye | 34.7 | House dust | 14.3 | Cedar | 33.6 |
| 4th  | Penicillium | 12.5 | House dust | 28.6 | Cat | 13.1 | Penicillium | 32.8 |
| 5th  | Acarus siro | 9.7 | Orch | 28.6 | Dog | 10.1 | House dust | 27.7 |
| 6th  | Cat | 8.3 | Sweet vernal grass | 26.5 | Alder | 8.0 | Acarus siro | 21.0 |
| 7th  | Rye | 7.6 | Dandelion | 24.5 | Rye | 7.6 | Rye | 16.8 |
| 8th  | Dog | 6.3 | Reed | 24.5 | Acarus siro | 7.4 | Candida | 16.8 |

![Fig. 1. Proportion of simultaneous positive reactions to other allergens according to the number of fungal allergens](image-url)
rarely found in outdoor air, and can be found throughout the year. Similar to previous studies, in this study, sensitization to fungus commonly occurs in summer. However, the proportion of patients who were sensitized in the winter was lower compared to that during summer. In particular, no particular seasonal difference was found for positive reactions to multiple fungal allergens. Therefore, seasonal deviations suggest that the frequency of patients having positive reactions to multiple fungal allergens is not significantly different by season.

Many studies have reported that exposure to fungus can cause an allergic reaction. Respiratory symptoms have been mostly reported, which is thought to be an allergic reaction caused by fungal spores floating in the air. There are also reports of allergic reactions due to skin contact with spores. Allergies to fungi are often expressed as type I immediate, IgE-mediated hypersensitivity. Atopic sensitization can manifest as asthma, rhinitis or conjunctivitis, urticaria, or atopic dermatitis. Sometimes, an allergic reaction can be expressed as a type II hypersensitivity reaction. An example of type III hypersensitivity is allergic alveolitis and bronchopulmonary aspergillosis (ABPA). ABPA is a pulmonary disease caused by hypersensitive Th2 response to A. fumigatus, which can worsen asthma and the condition of patients with cystic fibrosis. Allergy to A. fumigatus is common in atopic asthma as well as in patients with cystic fibrosis. Bronchopulmonary aspergillosis is characterized by wheezing and pulmonary infiltrates, which can lead to pulmonary fibrosis or bronchitis. However, it is difficult to judge whether allergic diseases are clearly caused by fungi. This is because of the difficulty in finding the cause of allergic diseases, and patient distribution in each institution varies. In this study, patients are mostly diagnosed with allergic rhinitis, followed by dermatologic diseases. Thus, to determine the frequency of allergic diseases caused by fungi, clearly identifying allergens through multicenter studies is necessary.

Patients with allergies often have allergies to multiple allergens. Patients with positive reactions to multiple allergens are often identified through the MAST-CLA test. Several studies reported on the positive reaction to each allergen in the MAST-CLA test, but information on the positive reaction to a combination of allergens and fungal allergens in the MAST-CLA panel is still unclear. In many reports, D. farinae mite and D. pteronyssinus mite were the most commonly found co-existing allergens in the MAST-CLA test, and in this study, the positive reaction rate to D. farinae mite and D. pteronyssinus mite was the highest for both groups of patients who had a positive reaction to single and multiple fungal allergens. In addition, we investigated allergens that showed the highest co-positive allergenic rate excluding mites and house dusts, which are well-known co-positive allergens. Regarding C. herbarum, A. siro was the most commonly observed co-positive allergen followed by the cat, rye, and dog. Regarding A. fumigatus, rye was the most commonly observed co-positive allergen followed by orch, sweet vernal grass, dandelion, and reed. Regarding A. alternata, the cat was a most commonly observed co-positive allergen followed by the dog, alder, rye, and A. siro. For allergens showing simultaneously positive reactions to all three fungal allergens, cedar rye was the most commonly observed co-positive allergen, followed by A. siro and rye.

In one study, the MAST-CLA panel allergens were divided into eight allergens with high simultaneous allergenicity, which were compared based on the similarity in the molecular structure. D. pteronyssinus mite, D. farinae mite, A. siro, house dust, dog, and cat were on cluster 5. Cross-reactivity among D. pteronyssinus mite, D. farinae mite, and A. siro are well established by Spitzauer et al., in which albumin was identified to demonstrate cross-reactivity to the aforementioned allergens. House dust sensitization could be a result of co-sensitization to cat and dog, as they are all indoor allergens.

In this study, we aimed to investigate the correlation between the number of positive reactions to fungal allergens and the number of positive reactions to other sensitized allergens. The correlation analysis showed a positive correlation. This suggests that the number of positive reactions to fungal allergens has a positive correlation with the number of positive reactions to sensitized allergens. The most common allergens that showed multiple positive reactions with fungi were pollens, cat, and dog.

Despite our findings, it is difficult to conclude whether the multiple positive reactions are co-sensitizations caused by exposure to each allergen and whether the multiple positive reactions are cross-reactivities caused by one allergen, in which the patient had previous exposure, and other allergens that show similar structure, but the patient had no previous exposure.

The robustness of the allergen test has not yet been confirmed because the substances used in the allergen test are not quantified. Until now, only the molecular structures of the substances are identified, but their characteristics are unknown. Amino acid sequence, three-dimensional structure, and gene structure of allergic reactions were elucidated only recently. The development of allergen diagnostic reagents made of recombinant antigens will enable cross-reactivity and simultaneous sensitization and will be useful for the diagnosis and differential diagnosis of allergic disease and immunotherapy.

Fungal allergens are still the major causes of numerous allergic diseases. The demographic results of this study are not
much different from those in previous studies, but the present results are meaningful as they help determine the occurrence of fungal allergens in southeastern Korea. This study provides useful information on the positive reactions to multiple allergens associated with fungal allergens. Therefore, the results can be used in choosing allergens when applying avoidance therapy.

Nevertheless, this study had some limitations. This study was conducted in one center in Korea; hence, it does not fully reflect regional and ethnic differences. Further multicenter studies and studies involving patients in other regions are needed. Moreover, data on the relationship between the clinical signs and positivity of fungal allergens will be more meaningful information to clinicians. Despite these limitations, this study can be a good reference for clinicians when educating patients with allergic diseases.

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CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

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