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ORIGINAL ARTICLE

Cross-sectional Survey of Allergic Diseases in Staff and Their Families at Designated Allergic Disease Medical Hospitals in Japan: Calculation of Age-adjusted Prevalence

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ABSTRACT

BACKGROUND

Continuous epidemiological surveys using consistent methodologies are essential for assessing the prevalence of allergic diseases. In 2021, a cross-sectional survey on allergic diseases was conducted, targeting staff and their families at Designated Allergic Disease Medical Hospitals across 41 prefectures in Japan. By 2022, these hospitals had been established in all 47 prefectures of Japan.

METHODS

A prevalence survey of allergic diseases was conducted in 2022 using the same questionnaire as that used in 2021, encompassing hospitals across all 47 prefectures. Age-adjusted prevalence rates were calculated using the 2015 population model for comparison with the 2021 survey data.

RESULTS

The 2022 survey included 76 hospitals and 24,444 participants (males, 10,668; women, 13,776; median age, 35 years; interquartile range, 18–50 years). The overall prevalence of allergic diseases was 63.0% (95% confidence interval:62.3–63.6). Age-adjusted prevalence of a history per 100,000 people for each allergic disease was as follows (; 95% confidence interval): bronchial asthma (13,279; 12,776–13,782), atopic dermatitis (12,786; 12,379–13,193), food allergies (13,143; 12,689–13,596), perennial allergic rhinitis (28,132; 27,673–28,982), pollinosis (38,959; 38,216–39,703), allergic conjunctivitis (19,751; 19,188–20,313), metal allergies (2,111; 1,898–2,325), drug allergies (4,478; 4,149–4,806), and anaphylaxis (1,602; 1,417–1,787). The prevalence of perennial allergic rhinitis, pollinosis, and allergic conjunctivitis was higher than that in 2021.

CONCLUSIONS

This survey is the first in Japan to calculate the age-adjusted prevalence of allergic diseases. Moreover, pollinosis is the most common allergic disease in Japan.

KEY WORDS

age-adjusted prevalence, allergy, cross-sectional study, designated allergic disease medical hospital

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INTRODUCTION

The development of allergic diseases is influenced by both genetic predisposition and environmental factors, with a significant shift in prevalence often observed with environmental changes. Susceptibility to environmental influences also varies with age and sex. In recent years, new preventive and therapeutic measures including allergen immunotherapies and biologics have been developed, which have substantially impacted disease outcomes[1]. Therefore, surveys using consistent methodologies are necessary to evaluate trends in the prevalence of allergic diseases. Although continuous surveys of the prevalence of childhood allergic disease have been reported in Japan[2], no comprehensive reports of allergic disease prevalence across all age groups are available.

In Japan, under the Basic Act on Allergic Disease Measures, each prefecture designates hospitals as Designated Allergic Disease Medical Hospitals (DADMHs) which serve as centers for allergy-related health services[3,4]. These hospitals were also tasked with contributing to this research. In 2021, a prevalence survey was conducted targeting 58 DADMHs and their staff and families across 41 prefectures[5]. To our knowledge, this is the first comprehensive assessment of the prevalence of allergic diseases across all age groups in Japan.

A 2021 survey revealed that approximately two-thirds of the participants reported having allergic diseases[5]. However, the survey population was predominantly female with an age distribution that differed from that of the general Japanese population. Additionally, no age-adjusted prevalence was observed.

By 2022, DADMHs were established in all 47 prefectures, with a total of 78 hospitals. Therefore, a similar survey was conducted in 2022 across all DADMHs. Age-adjusted prevalence was calculated using the 2015 Japanese population model to account for sex and age distribution biases, and the results were compared with those of the 2021 survey.

METHODS

STUDY DESIGN

The 2022 survey employed methodologies identical to those utilized in the 2021 survey[5]. An online questionnaire targeting DADMHs of staff and their families was used in this cross-sectional study. The targeted staff included physicians, nurses, administrative personnel, laboratory technicians, pharmacists, and full-time employees. The survey was distributed via leaflets or emails between January 2023 and February 2023. The survey period coincided with that of the 2021 survey, which accounted for seasonal allergic conditions. Participants voluntarily completed the online questionnaire.

ETHICAL CONSIDERATIONS

This study adhered to the principles outlined in the Declaration of Helsinki and the ethical guidelines for medical and health research involving human participants, as defined by Japan's Ministry of Health, Labour, and Welfare. This study was approved by the Toyama University Ethics Committee (ID: R2002145). Informed consent was obtained from all the participants.

QUESTIONNAIRE AND DEFINITIONS

The 2022 survey employed the same questionnaire as the 2021 survey but included an additional section focusing on anaphylaxis. The WEBCAS system (WOW WORLD Inc.) was used to administer the questionnaire in Japanese, which covered personal and familial histories of allergic diseases. Questions addressed demographic information including age, sex, occupation, place of employment, history of allergic disease, and current allergic symptoms. Diseases surveyed included bronchial asthma (BA), atopic dermatitis (AD), food allergies (FA), pollinosis (PO) (seasonal allergic rhinitis), perennial allergic rhinitis (pAR) (all-season allergic rhinitis), allergic conjunctivitis (AC), metal allergies (MA), drug allergies (DA), and anaphylaxis.

DETERMINING THE PREVALENCE OF A HISTORY OF ALLERGIC DISEASES

Respondents who answered "Yes" to the question "Have you (or your family members) ever been diagnosed by a physician with BA, AD, FAs, pAR, PO, or AC?" were categorized as "diagnosed". Those who answered "No, but I probably have the disease" were classified as "self-diagnosed". The prevalence of these allergic diseases was calculated based on both diagnosed and self-diagnosed cases. Regarding MAs, DAs, and anaphylaxis, participants were asked the following binary question: "Have you (or your family members) ever been diagnosed by a physician?" Those responding "Yes" were categorized as "diagnosed".

DETERMINING THE PREVALENCE OF CURRENT SYMPTOMS

Respondents with a history of BA, AD, AR, or AC were asked whether they or their family members had experienced symptoms of the disease or received treatment for it within the past 12 months. Furthermore, AR

was diagnosed if the respondent reported pAR or PO. Those answering "Yes" to either question was considered to have "current symptoms".

CALCULATION OF AGE-ADJUSTED PREVALENCE OF ALLERGIC DISEASES

Age-adjusted prevalence was assessed for both the prevalence of history and current symptoms of allergic diseases. Additionally, the age-adjusted prevalence was determined using a direct standardization method based on the 2015 standard population of Japan[6,7] (**Supplementary Table 1**). The data from the 2021 survey were similarly calculated and compared to the data in the 2022 survey. However, in the 2021 survey, responses regarding the current symptoms in the past 12 months for AR and AC were collected using the options "Throughout the year", "Specific months from January to December", or "Indefinite". In contrast, in 2022, responses were solicited as either "Yes" or "No", resulting in different response options. Therefore, the age-adjusted prevalence rates of current AR and AC symptoms in 2021 were not compared.

RESPONSE ANALYSIS AND STATISTICAL ANALYSIS

Age groups were divided into 14 categories: 12 categories spanning every 5 years from 0 to 59 years, one category for respondents aged 60–69, and one for those aged ≥70 years. A 95% confidence interval (CI) was calculated for symptoms and treatment of each disease. Data extraction and cleaning were conducted at Nagano Children's Hospital, Toyama University, and Sagamihara Hospital, whereas analysis and statistical processing were performed at Jichi Medical University, Yamaguchi University, and Tokyo Metropolitan Children's Medical Center. STATA-17 (StataCorp, Lakeway, TX, USA) software was used for statistical analyses.

RESULTS

OVERVIEW OF THE RESPONDENTS AND ANALYSIS PARTICIPANTS

Table 1 provides an overview of the surveys conducted in 2022. In the 2022 survey, 77 of 78 DADMHs (across 47 prefectures) participated. Approximately 9,412 respondents were included, of whom 74 did not provide consent and 53 were excluded due to input errors or duplication. Consequently, 9,285 valid respondents were included in the analysis. The total number of participants, including the family members, was 24,444. The gender ratio was 10,668 males to 13,776 females, with a higher number of females than males. The median age was 35 years (interquartile range 18–50). Overall, the proportion of participants reporting any allergic diseases was 63.0% (95% CI:62.3–63.6) (**Table 2**).

COMPARING THE PREVALENCE OF A HISTORY OF ALLERGIC DISEASES

The overall and sex-specific prevalence of allergic diseases is demonstrated in **Table 3**. The prevalence of allergic diseases in each age category in the 2022 survey is presented in **Supplementary Table 2**. The highest prevalence of a history of allergic diseases was observed in both males and females. The prevalence of a history of PO, AC, FAs, MAs, or DAs was higher in females than in males. The age-adjusted prevalence histories for the 2021 and 2022 surveys are presented in **Table 4**. The prevalence of PO was the highest overall, with 36,281 individuals per 100,000 (95% CI: 35,471–37,091) in the 2021 survey, and 38,959 individuals per 100,000 (95% CI: 38,216–39,703) in the 2022 survey. Following this, pAR and AC were the most prevalent, whereas BA, AD, and FAs affected approximately 13,000 individuals per 100,000. No significant differences in sex were observed for BA, AD, pAR, PO, or anaphylaxis; however, an increased prevalence of FAs, AC, MAs, and DAs was observed among females. Although no significant differences were observed between the 2021 and 2022 surveys for BA, AD, FAs, MAs, and Das. The prevalence of a history of pAR, PO, and AC was high in the 2022 survey after adjusting for age.

Table 1 Overview of the 2022 surveys

		2022 survey
Number of hospitals		77
Number of respondents		9285
Occupation	Nurses	3428 (36.9%)
	Physicians	1769 (19.1%)
	Clerks	1886 (20.3%)
	Medical technologists	384 (4.1%)
	Pharmacists	369 (4.0%)
	Others	1449 (15.6%)
Number of subjects (including family)		24,444
Male/Female		10,668/13,776
Median age (Interquartile range, min–max)		35 (18–50, 0–111)

Table 2 Comparison of prevalence of allergic diseases by age category

Age (years)	Number Male/Female	Any allergic diseases(%)[a] (95%CI)
0–4	1,533 798/735	35.8 (33.4–38.2)
5–9	1,875 931/944	53.1 (50.8–55.3)
10–14	1,664 850/814	64.6 (62.3–66.8)
15–19	1,298 695/603	64.5 (61.8–67.00
20–24	1,325 436/889	69.5 (67.0–71.9)
25–29	1,932 636/1,296	69.2 (67.1–71.2)
30–34	2,011 806/1,205	71.2 (69.1–73.1)
35–39	2,004 881/1,123	72.5 (70.5–74.4)
40–44	2,168 900/1,268	71.7 (69.8–73.6)
45–49	2,195 961/1,234	70.2 (68.3–72.1)
50–54	2,084 875/1,209	65.8 (63.7–67.8)
55–59	1,681 705/976	63.9 (61.6–66.2)
60–69	1,457 741/716	56.9 (54.3–59.4)
70+	1,217 453/764	35.1 (32.5–37.9)
Total	24,444 10,668/13,776	63.0 (62.3–63.6)

[a] "Any allergic diseases" is the percentage of subjects who have been diagnosed with bronchial asthma, atopic dermatitis, food allergies, allergic rhinitis, allergic conjunctivitis, metal allergies, drug allergies and anaphylaxis by a physician or self-diagnosed.
95%CI: 95% confidence interval

COMPARING THE PREVALENCE OF CURRENT ALLERGIC DISEASE SYMPTOMS

The prevalence of current symptoms of BA, AD, AC, and AR in each age category in the 2022 survey is demonstrated in **Supplementary Table 3**. The overall prevalence of current symptoms was 5.9% for BA (95% CI: 5.6–6.2), 9.7% for AD (95% CI: 9.3–10.1), 38.1% for AR (95% CI: 37.5–38.7), and 15.3% for AC (95% CI: 14.8–15.7).

The age-adjusted prevalence of current symptoms is displayed in **Table 5**. In the 2022 survey, AR affected 34,957 per 100,000 participants and AC affected 13,757. A comparison of BA and AD between the 2021 and 2022 surveys revealed no statistically significant differences within 95% of CIs.

DISCUSSION

Although this survey has inherent biases, as the population comprises healthcare workers and their families, allowing for continuous and longitudinal investigation using the same methods and participants in accordance with the Basic Act on Allergic Disease Measures is beneficial. Moreover, the procedure facilitates the study of the prevalence of various allergic diseases across all age groups and can be conducted with limited research funding.

A 30% increase in participants was observed in the 2022 survey, rising from 18,706 in 2021 to 24,444 in 2022 attributed to an increase in the number of DADMHs from 58 in 2021 to 77 in 2022.

In the 2022 survey, 63% of the respondents reported having some form of allergic condition. The results are almost identical to those of the 2021 survey[5]. This survey revealed a tendency toward a skewed distribution of respondents, with a high proportion of female respondents, likely due to the high representation of nurses. Responses were predominantly from individuals in their 20s and 50s, reflecting the age distribution of the workforce. The advantage of this survey, which targeted all age groups, was that age adjustments could be made to correct this above-mentioned bias.

This survey was a cross-sectional epidemiological investigation based on self-reporting. Allergic disease prevalence was determined by respondents reporting the presence or absence of a diagnosis by a physician, categorizing respondents as either "diagnosed" or "self-diagnosed".

The self-reported prevalence of allergic diseases often exceeds the figures derived from a physician's diagnosis. A systematic review reported that the lifetime prevalence of food allergies ranged from 9.5% to 35% in self-reported surveys, whereas the prevalence was only 4.7% in surveys based on physician diagnosis[8].

Allergic diseases are common, and in mild cases, individuals may not have been diagnosed by a physician. Therefore, differences in questionnaire content can lead to a varying prevalence of allergic diseases. Healthcare conditions vary by country. Conducting prevalence surveys using physician diagnoses of allergic diseases,

Table 3 Prevalence of a history of allergic diseases in overall

Diseases	Male	Female	Total
Bronchial asthma	15.0 (14.4–15.8)	14.3 (13.8–15.0)	14.7 (14.2–15.1)
Atopic dermatitis	16.1 (15.4–16.8)	16.5 (15.8–17.1)	16.3 (15.8–16.8)
Prenatal allergic rhinitis	31.3 (30.4–32.2)	31.0 (30.2–31.8)	31.1 (30.5–31.7)
Pollinosis	40.3 (39.4–41.2)	42.2 (41.4–43.0)	41.4 (40.8–42.0)
Allergic conjunctivitis	18.2 (17.5–19.0)	25.3 (24.6–26.1)	22.2 (21.7–22.8)
Food allergies	14.2 (13.5–14.9)	17.0 (16.4–17.6)	15.8 (15.3–16.2)
Metal allergies	0.6 (0.5–0.7)	3.5 (3.2–3.8)	2.2 (2.0–2.4)
Drug allergies	2.3 (2.0–2.6)	6.0 (5.6–6.5)	4.4 (4.2–4.7)
Anaphylaxis	1.6 (1.4–1.9)	1.9 (1.7–2.1)	1.8 (1.6–1.9)

Prevalence of a history represents the total proportion within the population of "Diagnosed" and "Self-diagnosed"
"Diagnosed" is is the number of subjects who diagnosed by a physician.
"Self-diagnosed" is the number of subjects who not diagnosed by a physician, but probably have the disease.
Data are presented as percentage and 95% confidence interval.

Table 4 A comparison of the age-adjusted prevalence of a history of each allergic disease with the 2021 survey

Diseases	years	Age-adjusted prevalence (per 100,000 persons)		
		Male	Female	Total
Bronchial asthma	2021	13,046 (12,231–13,860)	13,132 (12,356–13,907)	13,103 (12,544–13,662)
	2022	13,157 (12,416–13,897)	13,205 (12,516–13,894)	13,279 (12,776–13,782)
Atopic dermatitis	2021	12,124 (11,409–12,839)	12,124 (11,528–12,719)	12,154 (11,700–12,608)
	2022	12,571 (11,956–13,186)	12,880 (12,325–13,434)	12,786 (12,379–13,193)
Prenatal allergic rhinitis	2021	25,193 (24,101–26,284)	23,756 (22,834–24,679)	24,414 (23,718–25,109)
	2022	28,990 (27,994–30,037)	27,620 (26,726–28,513)	28,132 (27,673–28,982)
Pollinosis	2021	35,893 (34,660–37,126)	36,559 (35,466–37,652)	36,281 (35,471–37,091)
	2022	38,464 (37,329–39,599)	39,184 (38,178–40,191)	38,959 (38,216–39,703)
Allergic conjunctivitis	2021	13,781 (13,023–14,539)	18,708 (17,894–19,522)	16,644 (16,080–17,208)
	2022	16,292 (15,498–17,086)	22,304 (21,499–23,110)	19,751 (19,188–20,313)
Food allergies	2021	10,982 (10,271–11,693)	14,152 (13,403–14,902)	12,791 (12,273–13,309)
	2022	11,259 (10,638–11,880)	14,379 (13,730–15,028)	13,143 (12,689–13,596)
Metal allergies	2021	452 (293–611)	2,885 (2,511–3,260)	1,830 (1,610–2.051)
	2022	579 (413–744)	3,260 (2,899–3,621)	2,111 (1,898–2,325)
Drug allergies	2021	2,723 (2,289–3,157)	6,406 (5,801–7,011)	4,829 (4,437–5.221)
	2022	2,385 (2,019–2,750)	5,994 (5,482–6,505)	4,478 (4,149–4,806)
Anaphylaxis	2021	Nd	Nd	Nd
	2022	1,506 (1,218–1,793)	1,632 (1,391–1,872)	1,602 (1,417–1,787)

Data are presented as number of age-adjusted prevalence (per 100,000 persons) and 95% confidence interval.
Age-adjusted prevalence was calculated using the 2015 standard population of Japan.
Nd: No data

Table 5 A comparison of the age-adjusted prevalence of current symptoms of each allergic disease with the 2021 survey

Diseases	years	Age-adjusted prevalence (per 100,000 persons)		
		Male	Female	Total
Bronchial asthma	2021	4,680 (4,120–5,240)	5,892 (5,305–6,477)	5,403 (4,995–5,812)
	2022	4,667 (4,181–5,154)	6,195 (5,692–6,699)	5,572 (5,218–5,926)
Atopic dermatitis	2021	7,718 (7,135–8,301)	6,918 (6,459–7,377)	7,268 (6,910–7,626)
	2022	8,093 (7,586–8,600)	7,015 (6,601–7,430)	7,482 (7,166–7,799)
Allergic rhinitis	2021	Nd	Nd	Nd
	2022	35,954 (34,847–37,060)	34,119 (33,205–35,032)	34,957 (34,260–35,654)
Allergic conjunctivitis	2021	Nd	Nd	Nd
	2022	11,955 (11,261–12,649)	15,076 (14,401–15,752)	13,757 (13,274–14,241)

Data are presented as number of age-adjusted prevalence (per 100,000 persons) and 95% confidence interval.
Age-adjusted prevalence was calculated using the 2015 standard population of Japan.
"Current symptoms" is subjects who reported having symptoms or treatments within 12 months.
Nd: No data

including mild symptoms, presents challenges. In this survey, a high prevalence of a history of AR was observed, with a significant proportion of participants reporting symptoms without a formal diagnosis by a physician. In the 2022 survey, 29.4% of participants were diagnosed with PO by a physician, whereas 12.0% experienced symptoms through self-diagnosis (**Supplementary Table 2**).

However, Matsubara et al.'s 2019 study investigated the prevalence of allergic rhinitis among otolaryngologists and their families and reported a prevalence of 49.2%[9]. This survey has a high level of diagnostic accuracy because the otolaryngologists diagnosed their family members. The prevalence closely approximated the combined prevalence of diagnosed and self-diagnosed cases in this survey. Given that the prevalence of allergic diseases is greatly influenced by questionnaires and the population surveyed, evaluating temporal changes by surveying the same population using identical questionnaires is crucial.

The prevalence of PO, pAR, and AC was higher in the 2022 survey than in the 2021 survey, even after adjusting for age. Both surveys were conducted during the same season before the peak Japanese cedar pollen dispersal period. The symptoms of PO may have been influenced by the differences in the amount of pollen dispersed each year. According to a survey conducted by the Tokyo Metropolitan Government, the dispersal of Japanese cedar and cypress pollen increased in 2022 compared with that in 2021[10]. However, the increase in pAR could be attributed to the possibility that many respondents had both PO and pAR and may not have been able to distinguish between the two.

This study had some limitations. The respondents included healthcare workers and their families. Healthcare workers may also experience drug allergies as an occupation-related allergy[11]. The 2021 survey did not reveal any significant differences in allergic disease prevalence based on respondents' occupations[5]. However, further investigation is necessary, including comparisons with surveys using the same questionnaire in non-medical populations.

Additionally, since participation was voluntary, some concerns were present about response bias. The total number of staff members across all hospitals was estimated to be approximately 100,000. Requests for participation were made via paper pamphlets or PDF files, according to each facility's preference; however, it could not be confirmed whether all staff members were notified. Therefore, although the exact response rate could not be calculated, the rate was estimated to be approximately 10%.

Additionally, changes in lifestyle and infection control measures owing to the coronavirus 2019 (COVID-19) pandemic, which began in 2019, may have affected the onset of allergic diseases[12]. However, as this survey was conducted after the pandemic, the effects of the COVID-19 outbreak could not be evaluated. The 2015 standard population model was used to reflect the pre-pandemic population. Thus, when the Ministry of

Health, Labor, and Welfare revised the standard population model, adjustments were made to the survey accordingly.

In conclusion, this survey using DADMHs demonstrated a bias in the sex and age distributions of the respondents. By calculating the age-adjusted prevalence, evaluating trends in the prevalence of allergic diseases through future longitudinal surveys will be possible.

CONFLICTS OF INTEREST STATEMENT

The authors declare they have no conflicts of interest associated with this manuscript.

AUTHOR'S CONTRIBUTIONS

YI wrote the manuscript. YI, TK, and KT collected data, and NK, YM, and MT performed statistical analyses and interpreted results. All authors designed the study and read and approved the final manuscript.

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