



Pollen of *Broussonetia papyrifera*: An emerging aeroallergen associated with allergic illness in Taiwan

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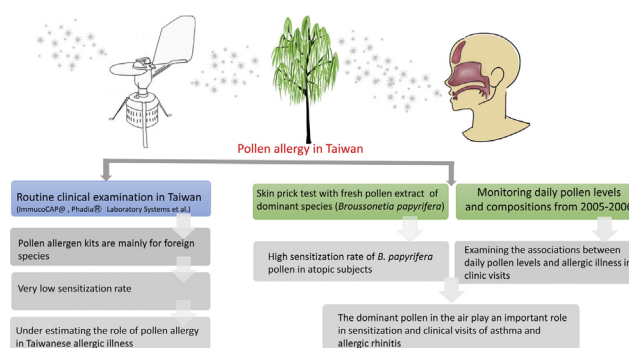
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HIGHLIGHTS

- The role of pollen allergy has long been underestimated in Taiwan.
- Daily pollen counts and skin prick test of fresh pollen extracts were used.
- *Broussonetia papyrifera* pollen is an important allergen in Taiwan.
- The observed association between dominant pollens and clinical admissions for asthma and allergy show that adequate aeroallergens monitoring is needed.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:

Received 19 July 2018

Received in revised form 18 November 2018

Accepted 21 November 2018

Available online 22 November 2018

Editor: Wei Huang

Keywords:

Aeroallergen

Asthma

Broussonetia papyrifera

Pollen

Skin prick test

ABSTRACT

Pollen has long been recognized as a major allergen, having diverse patterns of allergenicity caused by differences in climate, geography, and vegetation. Our research aimed to explore the role of a regionally dominant pollen in Taiwan, *Broussonetia papyrifera*, on clinical sensitization and daily 5 collected and extracted for a skin prick test on 30 volunteers recruited from a medical college. Daily atmospheric pollen levels were measured using a Burkard 7-day volumetric trap. The association between daily atmospheric pollen levels and clinic visits for allergic illness was examined using a generalized additive model with a normal assumption. After excluding four participants with a positive response to a negative control, 10 participants (38.4%) were determined to be sensitive to *B. papyrifera* pollen extract. The three-day lagged concentration of *B. papyrifera* pollen exhibited the highest risk of daily asthma visits (relative risk [RR] = 1.166, 95% confidence interval [CI]: 1.014–1.341) and allergic rhinitis visits (RR = 1.119, 95% CI: 0.916–1.367) when the pollen increased equally in magnitude to its mean. Our study is the first to provide evidence indicating that the most dominant airborne pollen in Taiwan, *B. papyrifera*, plays a major role in sensitization and clinic visits for asthma and allergic rhinitis, thus highlighting the need to integrate aeroallergen monitoring with clinical diagnosis.

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1. Introduction

Pollen has long been recognized as a major allergen that triggers allergic rhinitis and other allergic syndromes. Dominant pollen taxa vary throughout the world because of differences in climate, geography, and

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vegetation. Considerable evidence of pollen allergy has been collected in European and North American countries with a long history of aeroallergen monitoring for clinical diagnosis and treatment (D'Amato et al., 2007; Taylor et al., 2007). However, only limited information is available concerning tropical and subtropical regions where a routine monitoring system for consistently collecting data for further study is often lacking (Johnston et al., 2009; Tiwari et al., 2009). Unlike the many studies from European and North American countries that have documented a generally high prevalence of pollen allergy in patients with childhood- and adult-onset asthma, far less information concerning sensitization in tropical countries has been documented (D'Amato et al., 2007; Walker et al., 2001).

Taiwan has a marine tropical climate with a high diversity of vegetation across the island. One study reported that the pollen sensitization rate for rice—the most dominant crop in Taiwan—in patients with asthma was nearly 9% (Huang et al., 1998). Another study that examined sensitization to pollen allergy in patients with clinically diagnosed allergic rhinitis indicated that pollens were a less common allergen among Taiwanese individuals with allergies (Liang et al., 2010). However, the pollen allergens used in clinical examination were mostly taxa that were not common in Taiwan's ambient air or found among its natural vegetation (Huang, 1998; Huang et al., 1998). Without frequent exposure to such pollen taxa, the discovery of a low sensitization rate upon clinical examination was to be expected. Public awareness and understanding concerning pollen allergy in this region could be misled by these results because the allergenic properties of the pollens dominant in Taiwan's ambient air are far less well understood.

In historical aeroallergen monitoring data collected from 1994 to 1995 in six Taiwanese cities, *B. papyrifera* was the most common pollen, accounting for 79.39% of total pollen in Taipei, 66.82% in Taichung, 39.08% in Tainan, 15.30% in Pingtung, and 51.31% in Hualien, and has a long flowering period that extends from March to October (Huang et al., 1998). However, the study in question only collected data for one year and did not consider its health implications. We therefore established a long-term aeroallergen monitoring station to collect atmospheric pollen samples in Tainan to further analyze the effect of *B. papyrifera* on respiratory allergies in Taiwan. The pollen was identified by referencing pollen flora morphology in Taiwan (Huang, 1972; Huang et al., 1998). Fresh extract of *B. papyrifera* was also used to test preliminary allergy patterns in volunteers recruited from a medical college. The association between daily atmospheric pollen levels and clinic visits for allergic illness was examined using data from January 2005 to December 2006.

2. Materials and methods

2.1. Sensitization to *B. papyrifera*

Volunteers were recruited from among students at the medical college at National Cheng Kung University to undergo the skin prick test (SPT) and blood collection. A questionnaire was used to assess their history of clinically diagnosed allergic diseases and allergic symptoms during the previous 12 months. Blood samples were collected, and serum samples were used for an inhalant atopy screening test (using 23 common inhalant allergens) using ImmunoCAP Phadiatop® (Immuno CAP, Phadia, Taiwan) and total IgE levels.

Fresh pollen of *B. papyrifera* was collected on the campus near the medical college from March to May. Proteins were extracted according to the procedure described by Hurkman and Tanaka (1986). The total extracted protein content was measured using the Bio-Rad protein assay dye reagent at 595-nm absorbance with reference to the bovine serum albumin standard curve. The pollen extracts were diluted using normal saline to 0.1, 1.0, and 10.0 µg/mL before being used for the SPT. All patients underwent SPT should also have a

positive histamine control (1.0 mg/mL) and negative diluent (saline) control. The SPT was performed using these pollen extracts and evaluated after 15–20 min of exposure; positive results were identified by a wheal of ≥3-mm diameter appearing in response to three different concentrations. The negative control was used to exclude the presence of dermographism. The Institutional Review Board of the Medical Center at National Cheng Kung University approved this study (HR-95-124).

2.2. Atmospheric pollen and other parameters

A Burkard 7-day volumetric spore trap (Burkard Mfg. Co., Rickmansworth, UK) was used to collect atmospheric pollen in Tainan at a flow rate of 10 L/min. The sampling equipment was placed approximately 15 m above ground level on the flat roof of a large research building (N 23°00'12", E 120°12'45") at the medical college of National Cheng Kung University and routinely operated year round. Pollen and spores were trapped onto silicone-coated adhesive tape attached to a drum that rotated at 2 mm/h and completed a single cycle every seven days. After each seven-day cycle, the tape was measured and cut into seven segments proportionate to the exact length of the sampling time. Each segment was then placed onto a glass slide with 10% Gevatol. Glycerin jelly with phenosafranin was used to mount and stain the collected samples. In most cases, each segment represented a 24-h collection period. A light microscope operated at 400× was used to identify pollen numbers and taxa. All these procedures followed the standard guidelines of the American Academy of Allergy and Immunology. Pollen taxa were identified according to the atlas of pollen in Formosa (Huang, 1972). In this study, samples collected from January 2005 to December 2006 were selected for priority analysis. The Markov Chain Monte Carlo method was used for multiple imputation of missing data.

Meteorological data from the Taiwan Central Weather Bureau's station in the center of Tainan (N 23°02'22", E 120°13'43") were used. Daily air pollutant data, including daily average particulate matter (PM₁₀), ozone (O₃), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and carbon monoxide (CO), were measured at the outdoor air pollution monitoring station (N 23°2'58", E 120°12'33") nearest to our aeroallergen sampling location and obtained from Taiwan's Environmental Protection Administration.

2.3. Clinic visits

Daily hospital admission data that employed the codes in the 9th revision of the International Classification of Diseases (ICD-9) were obtained from a computerized database at National Cheng Kung University Hospital in Tainan where the aeroallergen station was located. Our study included all patients presenting to clinics and receiving a principal diagnosis of allergic rhinitis (ICD-9: 477) and asthma (ICD-9: 493) in 2005 and 2006.

2.4. Statistical analysis

In this study, daily clinic visits were the dependent variable and daily accumulated pollen was the major independent variable. Multiple-lag effects were analyzed for one to four days. A generalized additive model (GAM) with a normal assumption was used to assess multiple-lag effects of pollen concentrations and air pollutants on asthma and allergic rhinitis clinic visits. The statistical procedure was performed using SAS version 9.4. The GAM's purpose was to maximize the quality of prediction of a dependent variable Y in various distributions through the estimation of nonspecific (nonparametric) functions of predictor variables linked to the dependent variable with a specified degree of freedom. We modelled the variables both parametrically and semi-parametrically relative to the natural cubic spline. Moreover, all models

were adjusted for the multiple-lag effects of daily air pollution, temperature, and long-term pattern, as follows:

$$\ln[E(Y_t)] = \text{Intercept} + \beta x_{t-l} + ns(T_{t-l}, df_T) + ns(RH_{t-l}, df_{RH}) + ns(AP_{t-l}, df_{AP}) + ns(\text{Month}, df_M) + \alpha \text{Dow}^t$$

where Y_t : allergic rhinitis and asthma clinic visits in Tainan on day t ; β : coefficient relating pollen concentrations to clinical visits; x_{t-l} : pollen level (increments of 10 grains/m³) on day t of lag days l ; $ns(T_{t-l}, df_T)$: natural spline of temperature or air pollutants on day t of lag days l with df_T (three) degrees of freedom; $ns(RH_{t-l}, df_{RH})$: natural spline of temperature on day t of lag days l with df_{RH} (three) degrees of freedom; $ns(AP_{t-l}, df_{AP})$: natural spline of air pollutants on day t of lag days l with df_{AP} (three) degrees of freedom; $ns(\text{Month}, df_M)$: natural spline of month with df_M (11) degrees of freedom; α : regression coefficient relating the day of the week to clinic visits; and Dow^t : day of the week on day t .

The selection criterion for goodness-of-fit was based on minimizing the Akaike Information Criteria (AIC). Only those independent variables with statistical significance ($p < 0.05$) were considered in the final model.

3. Results

A total of 30 volunteers, consisting of 12 male and 18 female students between 23 and 38 years old, were recruited for this study. Three of them had clinically diagnosed allergic rhinitis with concurrent symptoms in the atopy screening test and SPT. A total of 22 participants (73.3%) reported sneezing or a runny or stuffy nose without cold or flu during the previous 12 months, and 20 participants (66.67%) were identified as sensitive to inhalable allergens to varying degrees according to the Phadiatop® test (Table 1). Total IgE levels ranged from 5.88 to 780 kU/L and were higher than 100 kU/L in 11 participants (36.7%). Four participants were excluded after the SPT because of a positive response to a negative diluent (saline) control. Among the 26 remaining

Table 1
Demographic, serological, and clinical characterization of participants.

Variables	n (%)
Sex	
Male	12 (40.0%)
Female	18 (60.0%)
Clinical diagnosis of allergic rhinitis	3 (10%)
Reported symptom in the past 12 months	
Dry cough more than two weeks without having a cold or the flu	1 (3.3%)
Sneezing or a runny or stuffy nose without having a cold or flu	22 (73.3%)
Sneezing, runny or stuffy nose, or itchy and watery eyes after contact with furred animals	4 (13.3%)
Sneezing, runny or stuffy nose, or itchy and watery eyes after contact with pollen, tree, or grass	2 (6.7%)
Itchy rash (eczema) in the past six months	2 (6.7%)
Phadiatop® inhalable allergen	
0	10 (33.3%)
1	1 (3.3%)
2	7 (23.3%)
3	7 (23.3%)
4	3 (10.0%)
5	2 (6.7%)
Total IgE > 100 kU/L	11 (36.7%)
SPT positive (n = 26) ^a	10 (38.4%)

Phadiatop®. SPT positive: Wheal size ≥ 3 mm for each of three concentrations.

^a Four participants were excluded after the SPT because of a positive response to a negative diluent (saline) control.

participants, 10 (38.4%) were sensitive to *B. papyrifera* pollen extract. Of the 20 participants with a positive response in the Phadiatop® inhalable allergen test, 50% were sensitive to *B. papyrifera* pollen extract. Seven participants (77.78%) with total IgE levels higher than 100 kU/L were sensitive to *B. papyrifera* pollen extract in the SPT. As expected, total IgE levels were significantly higher in participants sensitive to pollen extract in the SPT; these participants had a median IgE level of 119.00 kU/L compared with a median level of 40.60 kU/L in participants with a negative SPT (Fig. 1). Optical density values of specific IgE levels in response to fresh *B. papyrifera* pollen extract were also significantly higher in participants with a positive SPT response. These results indicated a potentially high sensitization to *B. papyrifera* pollen in atopic participants classified through a common clinical examination. A certain percentage of the general population might thus also be sensitive to *B. papyrifera* pollen, which cannot currently be identified using commercially available diagnostic kits commonly used for clinical tests.

The temporal patterns of daily levels of total and *B. papyrifera* pollen matched quite well from 2005 to 2006. One pollen peak occurred in 2005 (March 23) and two peaks occurred in 2006 (March 30 and April 30). *B. papyrifera* pollen comprised approximately 30% of the total pollen present in the air throughout the year (Fig. 2). The highest total pollen level was 1634.21 grains/m³ and the highest *B. papyrifera* pollen level was 406.4 grains/m³, both of which occurred on the same day (March 23, 2005).

Descriptive statistics for metrological variables, number of clinic visits for asthma and allergic rhinitis, and levels of airborne pollens and selected air pollutants from 2005 to 2006 are listed in Table 2. A total of 13,369 clinic visits for asthma and 15,238 for allergic rhinitis were registered during the study period, yielding a daily mean of 18.31 and 20.87 visits, respectively, to the study hospital. The lowest number of clinical visits for asthma was in summer (July to September) and the highest in winter, thereby demonstrating a clear seasonal difference; the number of visits was also associated with the day of the week. The core GAM model included indicator variables for day of the week and a temporal trend adjustment using a natural spline smoothing function and was used to examine associations between total and *B. papyrifera* pollen exposures and the number of clinic visits. Of all the weather variables, daily average temperature on the visit date was the best predictor for accounting for day-to-day variations in the number of clinic visits, according to the AIC inclusion criteria used in the stepwise regression analysis. Therefore, only day of the week, as a categorical variable, and natural spline smoothing for daily average temperature were included in subsequent core GAM analysis. To determine the lag effects of pollen exposure on clinic visits for asthma and allergic rhinitis, we compared the relative risk (RR) of various lag models, with a maximum lag of four days. The three-day lagged concentration of *B. papyrifera* pollen was associated with the highest risk of daily asthma (RR = 1.166, 95% confidence interval [CI]: 1.014–1.341) and allergic rhinitis visits (RR = 1.119, 95% CI: 0.916–1.367) when the pollen increase equaled 10 grains/m³. As expected, total pollen levels exhibited similar patterns to *B. papyrifera* pollen for 3-day lagged concentration was associated with the highest risk of daily asthma (RR = 1.046, 95% CI: 0.991–1.104) and allergic rhinitis visits (RR = 1.052, 95% CI: 0.974–1.136; Fig. 3a, b). We also compared the RR when adjusting for PM₁₀, which was associated with various air pollutants in this study. A significant increase in the RR of asthma visits occurred in association with an increase of *B. papyrifera* pollen levels when adjusting for a three-day lag of PM₁₀ in the model (RR = 1.180, 95% CI: 1.020–1.364; Fig. 3c). The RR of asthma visits tended to remain significant regardless of PM₁₀ levels, thus indicating an independent effect of *B. papyrifera* pollen on asthma.

4. Discussion

The paper mulberry (*B. papyrifera*, syn. *Morus papyrifera* L.) is a common East Asian tree in the family Moraceae and a major indicator

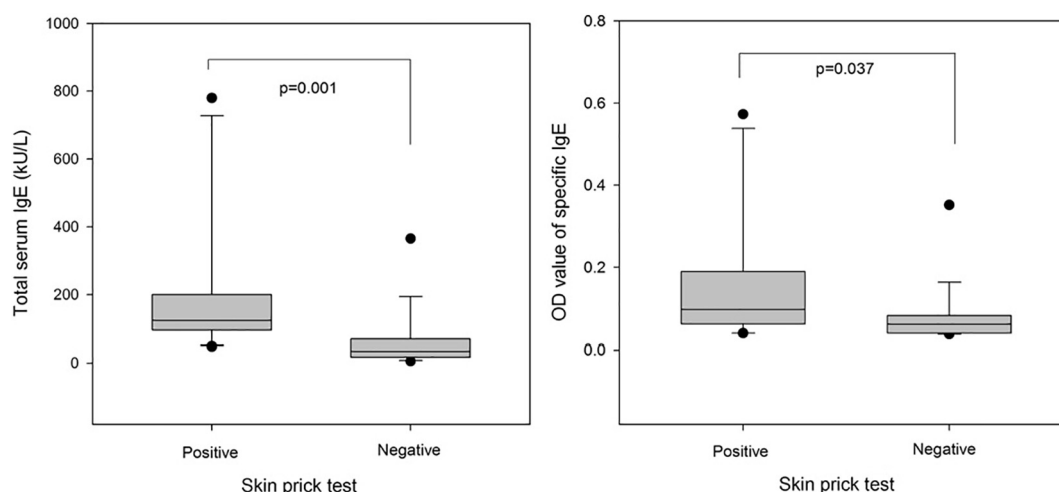


Fig. 1. Response of total and specific IgE levels to fresh *B. papyrifera* pollen extract in participants with various skin prick test responses.

species for historical human movements in the Pacific region (Chang et al., 2015). It is considered a highly invasive species that displays characteristic rapid growth when introduced to nonnative areas and can quickly disrupt native habitat. Parts of Latin America, the United States, and South Asia have been invaded by this species, which has quickly replaced the native flora in many cities (Barnes et al., 2014). Similar to trees of the genus *Betula* (e.g., birch), the catkins of *B. papyrifera* contain about 200 flowers each and produce an enormous amount of pollen during the season.

As an invasive species in the United States, *B. papyrifera* has been reported to be a cause of hay fever and asthma since the 1930s (Balyeat and Rinkel, 1931). Mulberry tree pollen has long been recognized as a major aeroallergen in many cities of the United States, Spain, and India (Hernandez Prieto et al., 1998; Singh and Kumar, 2003; Sneller et al., 1993; White and Bernstein, 2003). Exposure to white mulberry (*Morus alba*) pollen has been associated with hypersensitivity in clinical diagnostic rhinitis and asthma throughout the world. At an aeroallergen monitoring station in Islamabad, Pakistan (one of only a few such stations in subtropical and tropical Asia), *B. papyrifera* was recorded as producing the highest spring pollen count, accounting for 73%–75% of total

pollen and attaining a maximum daily level of approximately 1400 grains/m³, which is 3.5 times greater than the highest level observed in Tainan. *B. papyrifera* pollen first came to attention when it was recognized as an allergenic threat to human health in Islamabad. The same study also demonstrated that of 702 individuals selected irrespective of age or sex, 338 (48%) had positive SPT results in response to *B. papyrifera* pollen extract (Abbas, 2009). The SPT was performed on over 1000 patients at the Pakistan Allergy, Asthma, and Clinical Immunology Centre in Islamabad, and 41.9% of patients responded positively to *B. papyrifera* pollen (Abbas et al., 2012). In addition to these studies documenting how *B. papyrifera* is a high pollen producer and cause of seasonal allergic diseases in Pakistan, a case report from Italy determined that allergic rhinitis was caused by *B. papyrifera* pollen after using the SPT with fresh pollen (Zanforlin and Incorvaia, 2004).

B. papyrifera is widely distributed in the Yellow, Changjiang, and Pearl River basins and has been cultivated for animal feed, fibers, and traditional herbal medicine. Studies have also demonstrated this plant possesses positive properties that act against toxic air pollutants such as sulfate dioxide and chlorine, suggesting that it could be a suitable species for wide cultivation in China, especially in areas with serious

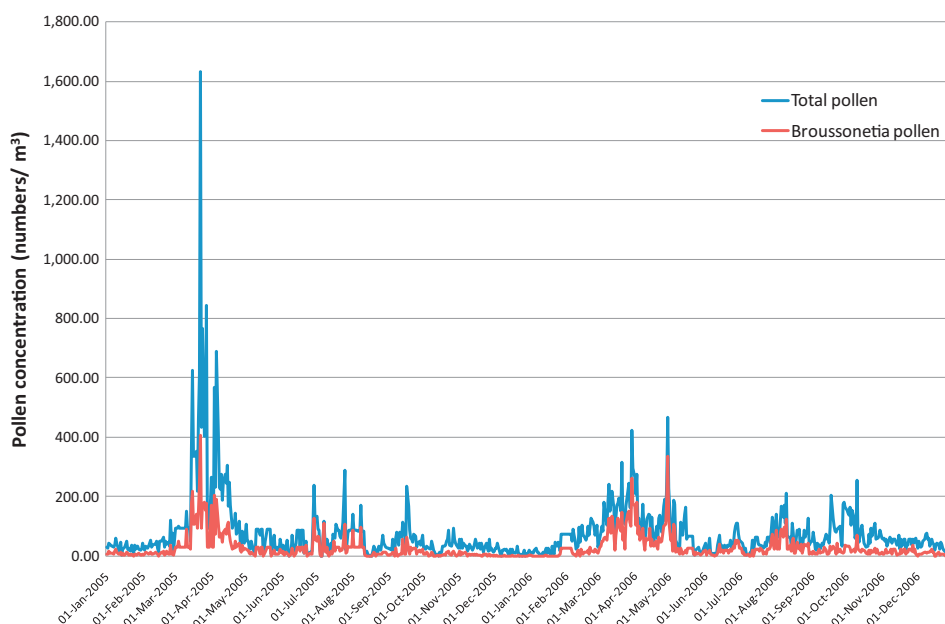


Fig. 2. Pollen calendar from 2005 to 2006.

Table 2

Descriptive statistics for daily asthma clinic visits, pollen concentrations, and weather parameters from January 2005 to December 2006.

	Mean	Min.	25th	50th	75th	Max.
Daily visits						
Daily asthma visits	18.31	0.00	3.00	19.00	29.00	65.00
Daily allergic rhinitis visits	20.87	0.00	2.00	17.00	33.00	99.00
Pollen (grains/m ³)						
Total pollen	75.64	0.00	26.22	50.25	88.48	1634.21
<i>B. papyrifera</i> pollen	26.36	0.00	4.37	10.92	28.52	406.37
Meteorological						
Average temperature, °C	24.80	9.30	20.90	26.40	28.80	31.50
Maximum temperature, °C	29.14	11.40	26.40	30.50	32.80	36.60
Minimum temperature, °C	21.77	7.80	17.30	23.60	25.90	29.40
Relative humidity	77.83	49.00	73.00	77.00	83.00	100.00
Air pollutants (µg/m ³)						
CO	62.08	10.50	46.14	61.57	75.58	165.96
CH ₄	119.34	92.27	114.28	119.56	124.99	141.68
NO	0.66	0.06	0.35	0.55	0.84	2.88
NO ₂	3.50	0.26	2.37	3.45	4.45	8.56
NO _x	4.17	0.57	2.93	3.96	5.10	11.16
O ₃	6.18	1.12	4.21	5.72	7.68	16.59
PM ₁₀	75.56	16.67	44.79	69.56	100.00	198.92
SO ₂	1.56	0.15	1.02	1.39	2.00	4.42

air pollution problems (Yang et al., 2002). In studies monitoring pollen in the ambient air in various Chinese cities, *B. papyrifera* was determined to be the dominant pollen present from April to May in Shanghai and Nanjing (Xu and Zhang, 2011; Zhang and Jiang, 1992) and was also reported to be the dominant species during spring in eastern China (Yang et al., 2015). One study conducted in Shanghai attempted to identify and purify major allergens from *B. papyrifera* pollen using serum antibodies from sensitized patients. Two proteins, 72 kDa and 15 kDa, were identified as allergens, thus demonstrating the potential allergenicity of *B. papyrifera* pollen in an Asian population (Chen et al., 2013). However, only quite limited information concerning pollination, monitored levels of airborne pollen, and sensitization in the allergic and general

populations is available. The antigens in commercial kits such as ImmunoCAP® and Phadia® Laboratory Systems used for clinical examinations are mostly from species not commonly found in Taiwan's natural vegetation or its atmospheric environment. This suggests an underestimation of the pollen sensitization rate in Taiwan and other countries that lack routine aeroallergen monitoring stations collecting background information for clinical diagnostic development. Our pilot study tested a limited sample size using the SPT and documented a 38% positive allergy rate among young college students living near a monitoring station. Among these students, >50% of the allergic participants were sensitive to fresh *B. papyrifera* pollen extract, suggesting that *B. papyrifera* pollen is a major aeroallergen in Taiwan and Asia in general and one that must have its bioactive components identified for clinical diagnosis and other purposes.

Epidemiological evidence has established the role of pollen sensitization in asthma development. Routine aeroallergen monitoring is conducted in many parts of the world to identify and quantify changes in atmospheric levels of *B. papyrifera* pollen and explore its potential effect on the clinical burden of allergic illness. Ecological time series analysis indicated an association between daily *B. papyrifera* pollen levels and clinic visits for asthma in Tainan. A three-day lag between exposure and clinic visits was observed in models measuring pollen as both a categorical and continuous variable, and a significantly higher RR was apparent after adjusting for weather and day of the week. These findings concerning *B. papyrifera* pollen were consistent with other evidence that tree, grass, and weed pollen exposure is associated with short-term increases in hospitalization for allergic illness and asthma (Dales

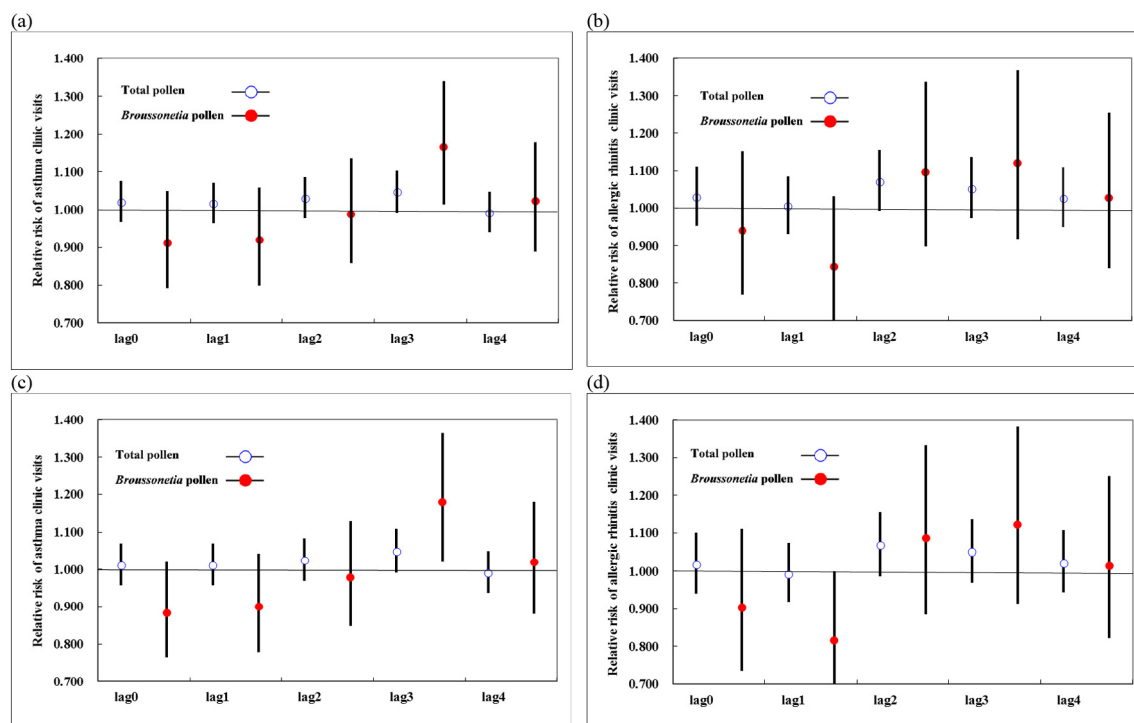


Fig. 3. The relative risk (95% CI) of asthma (a, c) and allergic rhinitis clinic visits (b, d) associated with total and *B. papyrifera* pollen increased in proportion to its mean for various lag models, with a maximum lag of four days; (a) and (b) adjusted for month, day of week, relative humidity, and temperature; (c) and (d) adjusted for month, day of week, relative humidity, temperature, and PM₁₀.

et al., 2008; Jariwala et al., 2011; Lovasi et al., 2013; Osborne et al., 2017; Sun et al., 2016). In this study, significant associations between *B. papyrifera* pollen and clinic visits for asthma and allergic rhinitis were found, with the strongest association at a three-day lag. This lag effect was consistent with other studies reporting increased hospital admissions and allergy medication sales within two to five days of pollen exposure (Darrow et al., 2012; Osborne et al., 2017; Sheffield et al., 2016). When PM₁₀ exposure was factored into the model, an independent effect of pollen on asthma was evident. Various mechanisms whereby air pollution increases the likelihood of allergen sensitization have been proposed. Air pollutants may act as carriers for allergens to the lower respiratory tract and lungs, increasing the permeability of epithelium cells and enhancing the response of immunological cells to allergens and also possibly interacting with antigenic protein to increase its allergenic potency (Olaniyan et al., 2016). Moreover, limited evidence has been found in both animal and epidemiological studies for biological mechanisms of allergies and asthma from the combined exposure to biological agents (e.g., pollen and house dust mites) and air pollutants. One study examined the effect of diesel exhaust particles (DEP) on house dust mite (HDM)-specific memory responses using an asthma model and demonstrated that mice that were co-exposed to HDM and DEP exhibited a significantly exacerbated airway hyperresponsiveness and significantly increased lung cell numbers compared with mice exposed to either DEP or HDM alone. These findings suggested that DEP exposure results in the accumulation of allergen-specific TH2/TH17 cells in the lungs, potentiating secondary allergen recall responses and promoting the development of allergic asthma (Brandt et al., 2015). An ecological study indicated that the RR of asthma visits from an interquartile increase in tree pollen was greater on days with higher PM_{2.5} values, namely 1.179 compared with 1.124 (Cakmak et al., 2012). By using a population-based epidemiological design, our study identified an association between regional pollen and asthma visits, an association which was slightly increased by higher PM₁₀ exposure, thus indicating a possible synergistic effect between pollen allergens and air pollutants. Compared with studies conducted in North America using multiyear datasets, this study had a relatively limited set of data. Although we acknowledge that using multiyear data to analyze the aforementioned associations has the advantage of accounting for long-term changes in selected variables, our study represented the first direct and reliable research on the disease burden attributable to pollens in this part of the world, regardless of this minor limitation.

5. Conclusions

This study used the SPT and clinical tests and was the first to demonstrate that *B. papyrifera* pollen could be a major aeroallergen for the allergic population in Taiwan. On the basis of daily pollen counts and corresponding hospital admissions in the neighboring region, we also demonstrated a consistently positive association between *B. papyrifera* pollen exposure and increased clinic visits for asthma. Pollen exposure appeared to have a three-day lag effect on the number of clinic visits for asthma and a potentially synergistic effect on the elevated risk of such visits resulting from concurrent exposure to ambient pollen and particulate matter pollution. This study highlighted the necessity of characterizing the bioactive components of *B. papyrifera* pollen for clinical diagnosis and other purposes. Regular aeroallergen monitoring and allergic plant identification in urban green spaces in many Asian cities should also be priority undertakings.

Acknowledgments

The authors are in great debt to many temporary assistants who have helped over the time for samples collection year-round. The study was in part supported by the grant from the Taiwan National Science Council (NSC99-2621-M-309-001). The authors do not have a

commercial and other association that might pose a conflict of interest. This manuscript has not been submitted or accepted elsewhere and all authors have seen and approved the content and contributed significantly to the work. This manuscript was edited by Wallace Academic Editing.

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