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The role of seasonal grass pollen on childhood asthma emergency department presentations

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Summary

Background Few studies have focused on the role of grass pollen on asthma emergency department (ED) presentations among children. None have examined whether a dose-response effect exists between grass pollen levels and these asthma exacerbations.

Objectives To examine the association between increasing ambient levels of grass pollen and asthma ED presentations in children. To determine whether these associations are seen only after a thunderstorm, or whether grass pollen levels have a consistent influence on childhood asthma ED visits during the season.

Methods A short time series ecological study was conducted for asthma presentations to ED among children in Melbourne, Victoria, and grass pollen, meteorological and air quality measurements recorded during the selected 2003 period. A semi-parametric Poisson regression model was used to examine dose-response associations between daily grass pollen levels and mean daily ED attendance for asthma.

Results A smoothed plot suggested a dose-response association. As ambient grass pollen increased to about 19 grains/m³, the same day risk of childhood ED presentations also increased linearly ($P < 0.001$). Grass pollen levels were also associated with an increased risk in asthma ED presentations on the following day (lag 1, $P < 0.001$).

Conclusion This is the first study to establish a clear relationship between increased risk of childhood asthma ED attendance and levels of ambient grass pollen below 20 grains/m³, independent of any impact of thunderstorm-associated asthma. These findings have important implications for patient care, such as asthma management programs that notify the general public regarding periods of high grass pollen exposure, as well as defining the timing of initiation of pollen immunotherapy.

Keywords asthma, environmental asthma, grass pollen

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Introduction

Childhood asthma is a global health problem and a national health priority in most western countries including Australia [1]. A sudden-onset severe asthma attack often requires attendance at an emergency department (ED) and/or hospital admission. This impairs the quality of life of affected individuals and places a growing financial burden on families, the community and the health care system. Sudden-onset asthma

attacks in children requiring ED attendance can be triggered by environmental factors such as viral infections [2], aero-allergen exposure [3], air pollution [4] and abrupt changes in weather, such as thunderstorm-associated asthma [5].

Aero-allergens including pollen and fungal spores can trigger allergic rhinitis in susceptible individuals. The various types of airborne pollen, particularly grass pollen, are important due to the distinct seasonality of their effects on human health. Pollen seasons occur

when plants flower, although the concentration of pollen in the atmosphere during the season will vary considerably from day-to-day and from year-to-year in response to a range of climatic factors and the duration and intensity of flowering. In addition, air pollution can exacerbate the impact of pollen on a susceptible individual [6]. As a consequence of these complexities, there are still many gaps in the evidence-base needed to develop clinical guidelines, including an understanding of the relationships between levels of particular types of airborne pollen that can trigger asthma and the incidence of sudden-onset asthma attacks.

In Melbourne, Australia, ambient concentrations of grass pollen exceeding 50 grains/m³ (measured by pollen monitoring stations) are considered to represent "high pollen days", and provide a trigger to initiate warnings for asthma patients about the importance of preventive medication on these high pollen count days. Such warnings assume that there is a threshold level in pollen counts that trigger hayfever and asthma and that other days during the pollen season may not be important. Using statistical techniques to account for non-linearity in the relationship between grass pollen counts and asthma hospital admissions by adults, we were the first to find this association was linear at first and reached a plateau at about 30 grains/m³ [7]. Our findings were replicated in a study of a group of adult asthmatics by Galan and colleagues [8]. However, the relationship between grass pollen counts and asthma exacerbations in children has not been as rigorously investigated.

In this study, we sought to determine the dose-response effect of grass pollen on ED presentations for childhood asthma during the 2003 grass pollen season in Melbourne, Australia. One notable event during this season was a severe thunderstorm that occurred in November, followed by several consecutive days of high grass pollen counts (i.e. daily counts > 50 grains/m³). The substantial rise in asthma ED presentations by children following this event provided an opportunity to tease out the associations due to the thunderstorm event from the influence of the grass pollen season on childhood asthma ED visits.

Methods

Study design

A time series ecological study was conducted using data from Victorian ED presentations for asthma in children, and pollen, meteorological and air quality measurements recorded during the selected 2003 period. We obtained ethics approval for the study from the human research ethics committees of La Trobe University and the Victorian State Government Department of Human Services.

Data

Airborne grass pollen levels over the University of Melbourne were recorded daily from 1st September to 31st December 2003. We used the method of Lejoly-Gabriel and Leuschner [9] to define the beginning and end of the season. Previous studies have suggested that all sensitive individuals will experience allergic symptoms on days when the grass pollen count is 50 grains per m³ or above (high pollen count day) [10–12]. We also use this classification system to define low grass pollen days as < 20 grains/m³, moderate grass pollen days as 20–49 grains/m³, high grass pollen days as 50–99 grains/m³ and extreme grass pollen days as > 100 grains/m³.

Daily ED attendances corresponding to this period were obtained from the Victorian Emergency Minimum Dataset which is maintained by the Department of Health. The ED attendance data were from patients under 15 years of age with a diagnosis related to childhood asthma [ICD10-AM, J45 and J46].

Air pollutant data were obtained from the Alphington air quality monitoring station (about 7 km North East of Melbourne CBD) and the meteorological data from Melbourne Airport (37.67°S, 144.83°E). The air pollutant data used were the 24-h average daily concentrations of the Airborne Particle Index (API) and maximum daily 4-h average concentrations of nitrogen dioxide (NO₂) and ozone (O₃). A single missing value was replaced with the average of the readings before and after the missing value. Daily maximum temperature, rainfall and average daily relative humidity were obtained from the Bureau of Meteorology for the same period.

Statistical methods

We defined the outcome variable as daily ED presentations for asthma among children less than 15 years of age. Primary exposure was daily ambient levels of grass pollen. Pollen was analysed as a continuous variable after a natural log transformation due to the extreme positive skew of the grass pollen distribution. We removed daily levels of pollen greater than 150 grains/m³ as these were considered as extreme observations. A cross-correlation function was used to examine any lag effects between the daily levels of grass pollen and ED presentations for asthma.

Daily relative humidity, maximum temperature and rainfall were considered as potential confounders. Due to the short time period involved, API (airborne particle index), NO₂ and O₃ concentrations were included separately in each model. A semi-parametric Poisson regression model [13] was used to examine the associations between the daily grass pollen levels and mean ED attendance for asthma among children.

Initially, we fitted a non-linear smoothing term for grass pollen exposure. However, due to the extreme observations and the positive skew of grass pollen it was difficult to decipher a meaningful pattern. We therefore took the natural log of grass pollen (+1) and used this transformed variable in the models. A base model was then developed with a time trend, day of the week effects (with Monday defined as the reference category), maximum temperature, a variable for rainfall, and various measures of humidity, including the relative humidity and the percentage change in average humidity, defined as $(\text{average} - \text{maximum})/\text{average} \times 100$. Non-linear associations were fitted using a generalized additive models (GAMs) approach [14]. Penalized regression splines were used to estimate smooth terms (automatic selection) in the models using the *gam* function in the *MGCV* package of R (version 2.10.0). The degree of smoothing was represented by the degrees of freedom. The air pollutants and weather data were kept in the model if they had a P value < 0.1 or if they changed the estimated effect of grass pollen by 10% or more. The diagnostic plots were checked for model fit and distribution of residuals. All statistical tests were two-sided with a 5% significance level.

Results

Figure 1 shows daily grass pollen levels and ED presentations for asthma in children over the study period. During this period, a total of 2,559 children attended an emergency department due to asthma (daily mean [SD] = 21 [8.1] and median = 20). One notable spike of grass pollen occurred on 15, 18 and 19 November, which were extreme grass pollen days when the daily count exceeded 100 grains/m³. This pollen spike was followed by a large spike in asthma emergency attendances on 20 November 2003.

In central Melbourne, severe thunderstorms occurred on 19 and 20 November, 2003. In addition, the wind speed was greater than 90 km/h on 15 and 17. During this period of severe thunderstorm activity, the daily ED attendance peaked at 70 visits per day, consistent with thunderstorm-associated asthma related to the preceding extreme grass pollen days and strong winds.

Table 1 shows summary measures of daily grass pollen levels, pollutant levels and weather variables during the 2003 pollen season. Using the classification system described in Sch  ppi et al. [12] there were 48 low grass pollen days (< 20 grains/m³), 19 moderate grass pollen days (20–49 grains/m³), 11 high grass pollen days (50–99 grains/m³) and 13 extreme grass pollen days (> 100 grains/m³). These ranges have previously been related to pollen allergy symptom scores.

To assess the relationship (including lags) between daily grass pollen counts and daily asthma ED presentations,

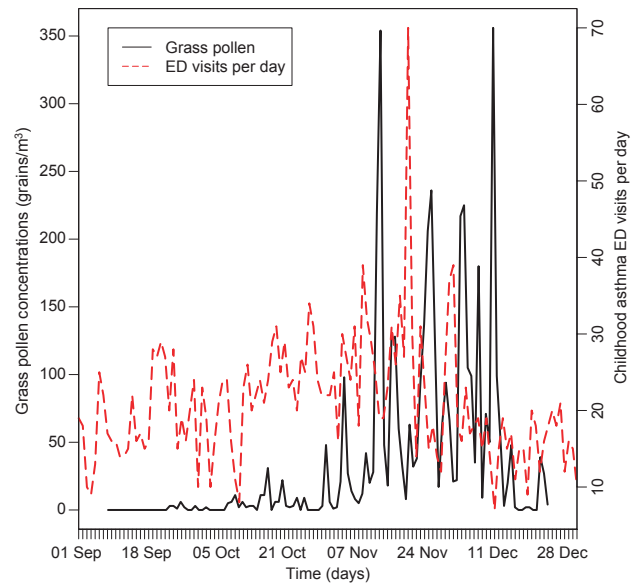


Fig. 1. Daily levels of grass pollen and asthma emergency department presentations among children less than 15 years of age in Victoria between January and December 2003. Dotted line represents emergency department presentations and solid line represents grass pollen during the 2003 grass pollen season.

cross-correlation function (CCF) plots were produced. These plots suggested both a same day and a 1 day lag effect. Both series were transformed to remove any confounding effects due to seasonality and day of the week effects (data not shown) before examining any lagged associations.

In the Generalized Additive Model (GAM), we included terms for day of the week effects, time trend, temperature and relative humidity (fitted as non-linear and linear terms, depending on which was statistically significant). In each model we included API, NO₂ and O₃ separately with grass pollen. As linear terms all three pollutants were not significant. However, when we separately entered each of them as smooth terms API was significant ($P = 0.02$). We fitted models with and without the spike in asthma ED presentations on the 20th November, to examine changes in the estimated effect size of grass pollen. However, there was no real change in the estimated effects so we only present the findings with the spike.

Figure 2 shows the non-parametric spline fit for grass pollen (with 95% CI) on ED presentations for childhood asthma, with the observed daily levels of grass pollen plotted on the X-axis, and the Y-axis representing the estimated smooth fit of daily levels of grass pollen on asthma ED presentations in children which represents change in risk. The smoothed plot shows that as ambient grass pollen increased to about 19 grains/m³ same day risk of childhood ED presentations also increased linearly (from about 6 grains/m³), then declined before further increasing as grass pollen levels reached about

Table 1. Summary measures of daily levels of pollen (total and grass), weather data and air pollutants during the 2003 pollen season in Victoria

	Mean	SD	Min.	Percentiles							
				5th	10th	25th	50th	75th	90th	95th	Max.
Total pollen/m ³	306.83	358.99	9	27.15	44	89.25	208	392	653.7	818.4	2647
Grass pollen/m ³	35.73	67.18	0	0	0	0	6	37.25	104.4	204.7	356
API	0.773	0.40	0.32	0.4	0.411	0.52	0.64	0.9	1.25	1.508	2.99
NO ₂ p.p.b.	21.22	6.92	5	12	12.1	16	21.5	25	29	31	51
O ₃ p.p.b.	29.01	9.49	9	18.05	19.1	23	27	31	45	49.9	59
Maximum temperature °C	20.87	6.82	12	13	14	16	19	25	31	33	40
Relative humidity	65.55	13.07	25.9	38.7	47.25	60.6	66	73.8	79.28	85.78	93.4

53 grains/m³ ($P < 0.001$ from the non-linear term for grass pollen).

Grass pollen was also associated with an increased risk in asthma ED presentations the following day (lag 1, $P < 0.001$). Two days after exposure to grass pollen was no longer significantly associated with asthma ED presentations in children.

Discussion

Our findings show that as ambient grass pollen levels increase to about 19 grains/m³ there is a corresponding increase in the same day risk of childhood asthma ED presentations and then the relationship flattens off. This is the first study to provide evidence of a strong effect of ambient concentrations of grass pollen on ED

presentations in children, independent of any impact of thunderstorm-associated asthma. It has also identified that grass pollen counts that trigger asthma attacks leading to ED presentations among children are much lower than the current definition of a high pollen day.

We use 50 grains/m³ to define a high grass pollen day which is based on earlier studies in Melbourne [11] using ranges as specified by the London study by Davies and Smith [10]. Our study shows that the risk of ED presentations among children with asthma is increased even at lower levels of grass pollen below the current defined cut-off. In addition, a recent cohort study has shown that exposure to grass pollen more than 2 grains/m³ was associated with wheeze and persistent cough among children aged between 4 and 12 years of age [15]. Based on these findings, it would be appropriate to review public health asthma programs and clinical guidelines in relation to advice regarding levels of pollen exposure that can precipitate an asthma exacerbation.

The effect of grass pollen was independent of the effects of API, NO₂ and O₃. Although, a non-linear effect of API was observed on ED presentations neither NO₂ nor O₃ were significantly associated with ED visits during the study period. We tested for an interaction between grass pollen and API, grass pollen and NO₂. None of these interaction terms were statistically significant.

Our findings of a continued increase in risk of an ED presentation for childhood asthma with concurrent increase in the outdoor levels of grass pollen increase suggest that rather than focusing on daily levels of pollen and informing the public accordingly, the pollen season should be considered as a 'whole' entity. The entire duration of grass pollination may be an important marker of adverse pollen exposure in triggering asthma. These findings have major implications for the day-to-day self management of asthma in individuals and families and also to clinical care, for example, when determining the most appropriate time to begin immunotherapy among patients with grass pollen allergy.

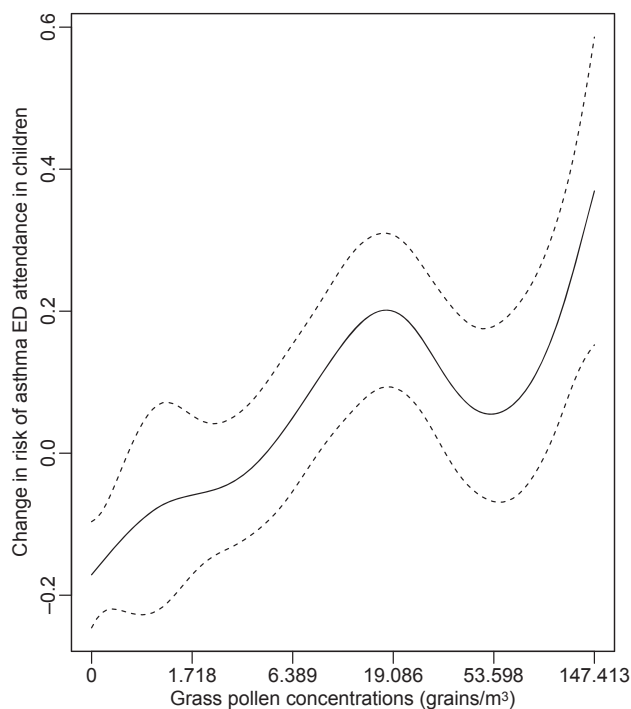


Fig. 2. Non-parametric smooth fit of asthma emergency department presentations in children and ambient levels of grass pollen.

Although our finding of a dose-response association is new, it is in agreement with other studies reporting the effects of high grass pollen counts on asthma ED presentations in children [16–18]. Lierl and Hornung [16] reported strong associations between the same day grass pollen counts and paediatric asthma ED visits in Cincinnati, USA. They initially found associations with the same day log pollen level (transformed because of the distribution), which became less significant after including up to 3 day lags of the log pollen level in the models. Asthma ED presentations by children were studied in relation to fine particles, ozone and pollen concentrations in ambient air by Babin et al. [17]. Grass pollen was not significantly associated with asthma presentations on the same day, but an increasing association was found for lags of 1–3 days. A large study of asthma ED presentations in children less than 9 years of age also found grass pollen to be significantly associated with asthma presentations only 3 days after exposure [18]. The difference in detected lagged effects is possibly due to the statistical methods used as all three studies used linear regression models and did not investigate non-linear effect as we did. Moreover, we did not investigate associations beyond lag 2, as we were limited by the short time series of grass pollen.

To the best of our knowledge, this is the first study to report a dose-response effect of grass pollen on asthma ED presentations in children. The only studies that have examined these effects in relation to pollen and emergency department presentations looked at mixed age groups of adults and children [8, 19]. Tobias et al. [19] found non-linear effects for a variety of pollens on asthma ED presentations, including pollen of *Olea*, *Plantago*, *Poaceae* and *Urticaceae* all of which are important components of the airborne pollen in Madrid. Likewise, in another case-control study in Madrid, with a sample of 241 patients, Galan et al. [8] examined various pollens and emergency health care within a hospital setting. Less than half of the cases (40.7%) were children aged between 4 and 14 years. They used logistic regression models and reported OR of 9.9 (95% CI 1.5–16.4) for grass exposure on 'epidemic' days defined as ambient grass pollen concentrations greater than 30 grains/m³. This observed risk remained significant after adjustment for house dust mites and fungal spores. Our results were not directly comparable, as they did not take account of ambient levels of grass pollen below 30 grains/m³.

However, our findings are not in agreement with Wang and Yousef [20], who found no relationship between grass pollen and asthma-related ED visits to a children's hospital in Delaware, USA. They classified days as low-visit days (no ED visits for asthma) and high-visit days (more than seven ED visits for asthma), then defined these as overall monthly averages and

examined associations with monthly levels of grass pollen. Given that the grass pollen season was of a short duration, it is possible that the use of monthly data limited the chance of identifying and detecting any real effect. Furthermore, no statistical modelling was carried out, as the authors only used *t*-tests to investigate the relationships. This too would have compromised the results.

We found strong independent effects of daily levels of ambient grass pollen on asthma ED presentations, following adjustment for the "thunderstorm associated" episodes. It is possible that grass pollen is not the only contributor to thunderstorm-associated asthma peaks and other environmental factors combined contribute such as fungal spores, air pollution and change in weather patterns during this period of thunderstorm activity. A recent study showed that sensitization to the fungus *Alternaria alternata* was a major predictor of the asthma epidemic after a severe thunderstorm in England in 2002 [21]. Using a case-control design, a study of cases who presented to ED after the July 2002 thunderstorm found an increased odds of 9.31 (95% CI 2.31–37.6) with a positive skin prick test to *Alternaria*. Other studies also suggest that the thunderstorm-associated increases in asthma are associated with increases in fungal spore counts [22, 23]. However earlier studies, such as that of Lewis et al. [24], suggest stronger effects of grass pollen than of thunderstorm activity per se. We do not have data on outdoor fungal spores and it is possible that fungal spores could be a potential confounder when examining these associations. *Cladosporium* and *Alternaria* peak during December and June with also high levels of *Alternaria* in November thereby overlapping with the grass pollen season [25].

A major strength of our study was the use of a comprehensive data linkage database from the Department of Human Services in Victoria. This database linked all emergency department presentations from all major public hospitals and some private hospitals across Victoria. There were unlikely to be much data missing, as the main public children's hospitals serviced the vast majority of Victorian children. However, limitations of the study should also be considered when interpreting the results. The time series under investigation was short (one grass pollen season), which may reduce the power to examine longer exposure lags. We did not conduct a stratified analysis by age due to the short time series. An Australian study of time trends for ED presentations for asthma in children suggest that younger children aged between 1–4 years are more likely to present to ED presentations compared with older age groups over time with peaks occurring during February and the winter months [26]. Effect modification by age may not be as important during the grass pollen season.

Another potential limitation was the misclassification of pollen exposure. As all of the pollen measurements were from one outdoor site, it was possible that the counts did not reflect the airborne grass pollen concentrations across the city. However, our earlier study showed that the pollen counts from three different sites across Melbourne were highly correlated [7]. Many researchers have detected fine (submicronic) pollen allergens in the atmosphere, but reliable quantitative measures remain elusive due to current technological limitations of collecting, extracting and quantifying highly diluted proteins. Thus, pollen counts are currently the only reliable exposure metric available.

Australia is known to have a high prevalence of sensitisation to grass within its population. Therefore, the 'at risk' subgroup is relatively large. The proportion of children sensitized to pollen is approximately 40% in a clinical cohort of children admitted to hospital with a principal discharge diagnosis of asthma (unpublished data). We did not have individual data on patients' sensitization status –and other risk factors for exacerbations, such as presence of respiratory viral infections, parental smoking and indoor exposures, which are possible confounders or effect modifiers of the association between pollen exposure and hospital admissions. However, these factors are unlikely to vary much over a

short time period, and therefore any such confounding effect would have a minimal impact on these associations. Notwithstanding these limitations, the findings from this study demonstrate consistent associations, even after an adequate adjustment for major confounders such as time trends, particulate matter and weather data.

In summary, we have found that lower levels of pollen can contribute to asthma symptoms, levels that are much lower than the current level of 50 grains/m³ which is used as the trigger point for warning asthma patients to avoid non-essential outdoor activities and/or take additional asthma medication. In the light of our findings, these limits need to be reviewed, and taken into account when planning the timing of initiation of immunotherapy. Larger epidemiological studies are required to enable fuller understanding of the influence of outdoor aeroallergens, combined with individual data on sensitisation, presence of respiratory virus, family history and the management of asthma and other allergies.

Conflict of interest

The authors have no conflict of interest to declare.

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