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Seasonal and monthly variation in peak expiratory flow rate in children with asthma

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ABSTRACT

Background: Although understanding the seasonal patterns of asthma deterioration is important to prevent asthma exacerbation, previous approaches have limitations in evaluating the actual trend of asthma exacerbation.
Objective: This study aimed to evaluate the seasonal and monthly variations in the peak expiratory flow rate (PEFR) among children with asthma.
Methods: A total of 89 patients with asthma were enrolled between December 2012 and March 2015. The PEFR in the morning and evening was recorded daily, and the percentage change in PEFR from baseline was calculated. Generalized estimating equation models were constructed after adjusting for age, sex, body mass index, and sensitization to house dust mites or pollen.
Results: The PEFR records of 11,222 person-days showed a significant decrease in the morning and evening in autumn than in winter by −1.9% (95% confidence interval [CI], −3.73 to −0.15) and −2.1% (95% CI, −3.80 to −0.37), respectively. The morning PEFR was significantly lower in April, August, October, and December than in January with changes of −4.2% (95% CI, −7.08 to −1.23) in April, −3.1% (95% CI, −5.79 to −0.47) in August, −3.7% (95% CI, −6.09 to −1.21) in October, and −1.9% (95% CI, −3.62 to −0.12) in December. The percentage change of evening PEFR significantly decreased by −3.3% (95% CI, −6.38 to −0.25) in April and by −3.3% (95% CI, −5.56 to −1.07) in October.
Conclusion: The PEFR in children with asthma was lower in autumn than in winter. In terms of monthly patterns, the PEFR was significantly reduced in April and October than in January. These results can serve as a basis for preventing asthma exacerbations by developing seasonal or monthly management strategies for children with asthma.

Keywords: Asthma; Seasonal variation; Month; Peak expiratory flow rate; Child

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Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Jihyun Kim. Formal analysis: Young-Min Kim, Soohyun Ahn, Sun-Young Baek. Investigation: Jihyun Kim, Hyunmi Kim, Kangmo Ahn. Methodology: Minji Kim, Young-Min Kim. Project administration: Jihyun Kim, Kangmo Ahn. Writing - original draft: Minji Kim, Hea-kyoung Yang. Writing - review & editing: Jihyun Kim, Kangmo Ahn.

INTRODUCTION

Asthma is a common chronic disease characterized by persistent inflammation of the airways and hyperresponsiveness to physiologic or triggering factors. According to the International Study of Asthma and Allergies in Childhood, the 12-month prevalence of asthma symptoms in Korean elementary schoolchildren increased from 4.9% in 2000 to 10.3% in 2010 [1]. A recent study conducted in the United States reported that 50% of children with asthma had experienced at least one asthma attack in the past year [2]. Patients with asthma missed an average of 3.2 school days, and 5.5% of patients experienced limitations in their daily activities due to the occurrence of asthma symptoms [2]. Moreover, asthma is associated with unhealthy lifestyle habits, such as obesity and sedentary behaviors, which lead to decreased physical and psychological wellness. Therefore, asthma is recognized as a major global health issue [3].

Although asthma exacerbations can occur at any time throughout the year, several studies have reported seasonal patterns of asthma attacks, demonstrating that asthma exacerbations occur most commonly in the fall and least commonly during summer [4, 5]. Most previous studies analyzed the number of prescription drugs or the frequency of healthcare visits to assess the level of asthma severity [4, 6-8]. However, those assessments are influenced by the availability of medical care or the behavior of individual patients in terms of coping with an asthma attack. Now, many patients with asthma use symptom relievers, and not all patients visit the emergency department when they experience asthma exacerbations. Therefore, the previous studies had limitations in evaluating the actual trend of asthma symptom prevalence because the indicators could not reflect the individual-level estimates of daily asthma symptom.

The peak expiratory flow rate (PEFR) is the maximum expiratory flow rate after a hard inspiration and is correlated with forced expiratory volume in 1 second (FEV_1) [9]. As the PEFR values objectively indicate airway obstruction, its measurement can help monitor the individual-level fluctuations in the lung functions of patients with asthma; PEFR measurement is easy to perform, less time consuming, and low cost [9-11]. The PEFR is a valuable tool for assessing asthma status, even in patients with low perception of respiratory symptoms, and for evaluating the influence of environmental triggers. A recent study has demonstrated that low PEFR variability could be a useful indicator of good asthma control [12].

South Korea could experience intense dust storms during spring when the peak level of particulate matter (PM) concentration is affected by dusts originating from China and Mongolia [13]. Yellow dust or Asian dust generally occurs from March to May [14]. The seasonal average levels of PM with a diameter <10 μm (PM_{10}) and total suspended particles in Korea are the highest during spring [15, 16]. We hypothesized that environmental changes may influence the asthma control status in Korean children according to the season or month, and it must be assessed in an objective manner, different from that in the previous studies. Therefore, this prospective study aimed to evaluate the seasonal and monthly patterns of the lung function by daily monitoring of the PEFR in children with asthma.

MATERIALS AND METHODS

Study population and study design

We enrolled 89 children aged below 18 years with asthma between December 2012 and March 2015 and followed them for at least 1 year. Asthma was diagnosed by a pediatrician on the basis of clinical symptoms and positive airway hyperresponsiveness [17]. Spirometry was performed at baseline in all patients following the American Thoracic Society guidelines [18]. Airway hyperresponsiveness was confirmed by assessing the provocation concentration of methacholine causing a 20% decrease in FEV_1 (PC_{20}) (<16 mg/mL). Patients treated with corticosteroids 2 months prior to the clinical evaluation and with severe comorbidities, including congenital heart disease, bronchiolitis obliterans, and malignant disease were excluded. This study was approved by the Institutional Review Board of Samsung Medical Center, Seoul, Korea (IRB No. 2016-02-090-003). The requirement to obtain an informed consent was waived.

The skin prick test (SPT) was performed on the backs of children using a standard method [19]. Commercial extracts of the following common allergens were used (Allergopharma, Reinbek, Germany): house dust mites (HDMs, *Dermatophagoides pteronyssinus*, and *D. farinae*), molds (*Alternaria*, *Aspergillus*, *Cladosporium*, and *Penicillium*), pollen (timothy, bermuda, meadow grass, alder, birch, elder, oak, Japanese cedar, ragweed, mugwort, short ragweed, Japanese hops, pine, and fat hen), animal dander (dogs and cats), and cockroach. Histamine and isotonic saline were used as positive and negative controls, respectively. A mean wheal diameter of ≥3 mm indicated a positive SPT.

For the PEFR measurement, patients inhaled until they reached their total lung capacity and then rapidly exhaled as forcefully as possible through the PEFR meter (Mini-Wright peak flow meter, Clement Clarke International, Harlow, UK) before receiving their daily dose of bronchodilator in the morning and evening. Patients were educated on how to use the PEFR meter by a trained researcher and a pharmacist. The highest measurement achieved after 3 attempts at each time point was recorded in a diary or mobile application and used to calculate the percentage change of PEFR. Data from the first 3 months were excluded from the analysis as they may not have reflected the patterns of seasonality during the initial period of treatment.

Statistical analysis

Data were expressed as mean ± standard deviation and analyzed using the SAS ver. 9.1 software (SAS Institute, Cary, NC, USA). Percentage change in the PEFR from baseline in each patient was expressed as PEFR change from 80% of the personal best PEFR: percentage change in the PEFR = [(daily PEFR–80% of personal best PEFR)/80% of personal best PEFR] × 100. The average values of percentage change in the PEFR in each season or month were calculated, and a generalized estimating equation (GEE) method was applied for repeated measures to compare the change in the PEFR by season or month. To adjust for the intra-individual correlation, a working correlation structure was selected using quasi-likelihood under the independence model information criterion. Seasons were defined according to the meteorological definitions: winter as December–February, spring as March–May, summer as June–August, and autumn as September–November.

The GEE models were constructed to explore the influence of season and month on PEFR differences after adjusting for age, sex, body mass index (BMI), and sensitization to HDMs or pollen. The BMI was calculated as weight in kilograms divided by height in meters squared. In addition, a subgroup analysis was performed based on the HDM sensitization status and estimated the effect of sensitization to each pollen, such as tree, grass, or weeds. A *p* value of <0.05 was considered significant.

RESULTS

Overall, 89 patients (62 boys and 27 girls) were enrolled. The patients' mean age was 8.9 ± 2.9 years (range, 4.3–17.9 years) (**Table 1**). The methacholine PC_{20} of all patients was <16 mg/mL (geometric mean, 1.79 mg/mL; range, 0.09–13.62 mg/mL). Of the PEFR records of 11,222 person-days, 2,619 (23.3%) were collected in spring, 2,347 (20.9%) in summer, 2,958 (26.4%) in autumn, and 3,298 (29.4%) in winter. Each patient filled out a symptom diary for 197.6 ± 145.8 days.

In the adjusted GEE model, the morning PEFR was significantly lower in autumn than in winter (–1.9%; 95% confidence interval [CI], −3.73 to −0.15) (**Fig. 1**). However, no significant decrease was found in spring (–1.8%; 95% CI, −3.63 to 0.10) and summer (–1.1%; 95% CI, −3.13 to 0.97). Meanwhile, the evening PEFR was significantly lower in autumn than in winter (−2.1%; 95% CI, −3.80 to −0.37) (**Fig. 1**). Likewise, there was no statistical difference in the evening PEFR in spring (–1.3%; 95% CI, −3.36 to 0.67) and summer –1.1% (95% CI, −3.31 to 1.01).

The monthly pattern was analyzed with January as the reference month. The morning PEFR was significantly lower in April, August, October, and December than in January in the adjusted GEE model: −0.6% (95% CI, −2.09 to 0.91) in February, –1.3% (95% CI, −3.63 to 0.95) in March, −4.2% (95% (CI, –7.08 to –1.23) in April, −2.6% (95% CI, −5.45 to 0.30) in May, −0.2% (95% CI, −2.69 to 2.35) in June, −2.1% (95% CI, −4.78 to 0.58) in July, −3.1% (95% CI, −5.79 to −0.47) in August, −2.3% (95% CI, −5.12 to 0.54) in September, −3.7% (95% CI, −6.09 to –1.21) in October, −2.1% (95% CI, −4.37 to 0.11) in November, and –1.9 (95% CI, −3.62 to −0.12) in December (**Fig. 2**). The evening PEFR was significantly lower in April and October than in January, with percentage changes in PEFR of 0.1% (95% CI, –1.46 to 1.61) in February, −0.3% (95% CI, −2.62 to 2.07) in March, −3.3% (95% CI, −6.38 to −0.25) in April,

Table 1. Characteristics of the study subjects at enrollment (n = 89)

Characteristic	Value
Male sex	62 (69.7)
Age (yr)	8.9 ± 2.9
Body mass index (kg/m^2)	17.7 ± 2.8
PC_{20} (mg/mL)	2.9 ± 2.7
FEV_1 (L)	1.86 ± 0.73
FEV_1 (% predicted value)	85.7 ± 12.9
Sensitization	
House dust mite	70 (78.6)
Tree pollen	38 (42.7)
Weed pollen	32 (36.0)
Grass pollen	21 (23.6)
Dog	25 (28.1)
Cat	24 (27.0)
Mold	31 (34.8)
Cockroach	6 (6.7)

Values are presented as number (%) or mean ± standard deviation.
PC_{20}, provocative concentration of methacholine causing a 20% decrease in FEV_1; FEV_1, forced expiratory volume in 1 second.

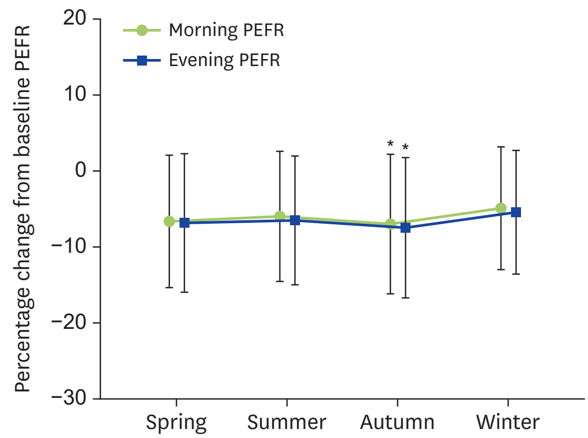

Fig. 1. Seasonal patterns of peak expiratory flow rate (PEFR) measured in the morning and in the evening. Seasonal variation was analyzed using a generalized estimating equation. The percentage change in morning and evening PEFR was significantly increased in autumn relative to the reference season of winter. *$p < 0.05$.

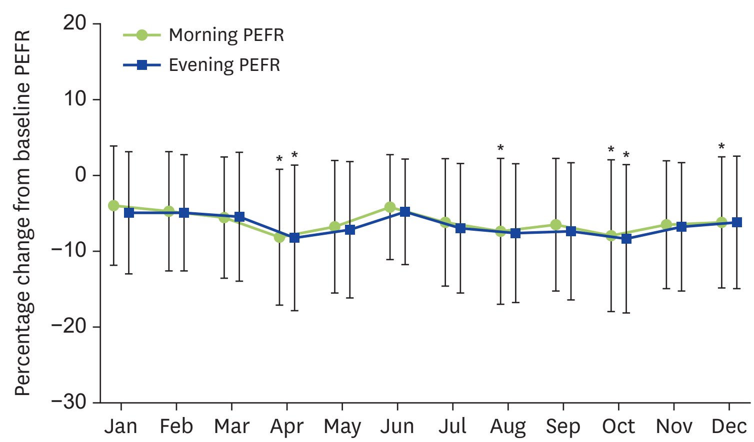

Fig. 2. Monthly patterns of peak expiratory flow rate (PEFR) measured in the morning and evening. Monthly variation was analyzed using a generalized estimating equation. The decrease in morning and evening PEFR was significant in April and October relative to the reference month of January. *$p < 0.05$.

−2.0% (95% CI, −5.07 to 1.04) in May, 0.3% (95% CI, −2.39 to 2.92) in June, −2.0% (95% CI, −4.75 to 0.80) in July, −2.6% (95% CI, −5.33 to 0.07) in August, −2.3% (95% CI, −5.13 to 0.45) in September, −3.3% (95% CI, −5.56 to −1.07) in October, −1.6% (95% CI, −3.73 to 0.47) in November, and −1.2% (95% CI, −2.88 to 0.46) in December (**Fig. 2**).

A subgroup analysis was performed after the patients were divided into 2 groups according to the HDM sensitization status. In patients who were sensitized to HDMs, the morning PEFR was significantly lower in April, July, August, and October than in January: −5.8% (95% CI, −7.90 to −1.02) in April, −4.4% (95% CI, −5.98 to −0.20) in July, −5.2% (95% CI, −6.52 to −1.17) in August, and −5.7% (95% CI, −6.97 to −1.80) in October (**Fig. 3**). The evening PEFR was significantly lower in April, August, September, and October than in January: −7.1% (95% CI, −7.8 to −0.49) in April, −6.3% (95% CI, −6.07 to −0.61) in August, −6.2% (95% CI, −6.17 to −0.18) in September, and −6.7% (95% CI, −6.02 to −1.48) in October (**Fig. 4**). In patients who were not sensitized to HDMs, no statistical significance was found in the monthly variations in PEFR measured in the morning or evening.

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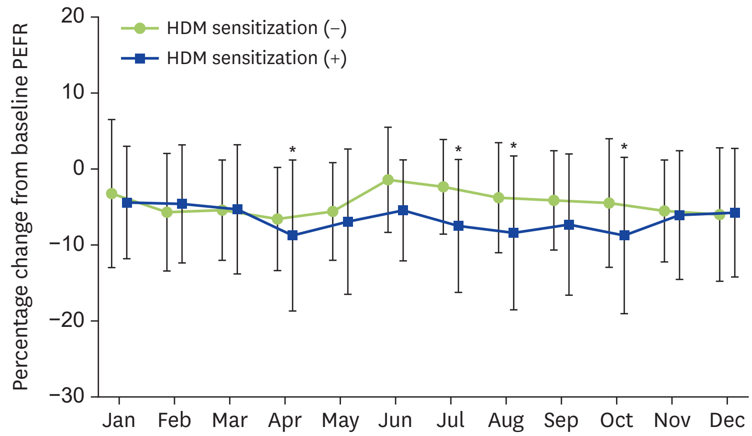

Fig. 3. Monthly pattern of morning peak expiratory flow rate (PEFR) in patients who were sensitized or not sensitized to house dust mites (HDMs). Monthly variation was analyzed using a generalized estimating equation. The decrease in morning PEFR was significant in April, July, August, and October relative to the reference month of January in patients who were sensitized to HDMs. *$p < 0.05$.

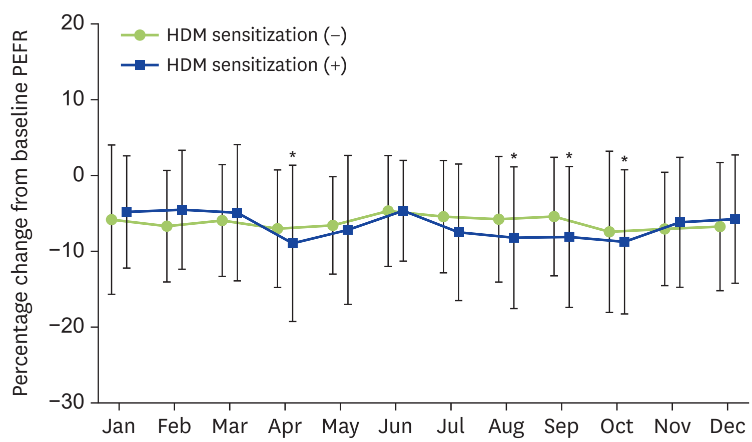

Fig. 4. Monthly pattern of evening peak expiratory flow rate (PEFR) in patients who were sensitized or not sensitized to house dust mites (HDMs). Monthly variation was analyzed using a generalized estimating equation. The decrease in evening PEFR was significant in April, August, September, and October relative to the reference month of January in patients who were sensitized to HDMs. *$p < 0.05$

We also analyzed the effect of sensitization to pollens after adjusting for age, sex, and BMI. We found a significant effect of the tree pollen sensitization to the morning PEFR (p = 0.007). In addition, the grass pollen sensitization had a significant influence on the evening PEFR (p = 0.036).

DISCUSSION

This panel study investigated the seasonal and monthly patterns of the lung function in children with asthma. This study was designed to continuously measure and monitor the PEFR in Korean children with asthma within 1 year. We obtained the PEFR change data and investigated the variability according to season or month after the first 3 months, because appropriate management of asthma might not have been performed yet during this period. Our results demonstrated that individual-level lung function was the worst in autumn, followed by spring, summer, and winter. The PEFR was significantly lower in April and

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October than in January. These results are consistent with a recent study, which reported that the monthly number of emergency department visits related to asthma peaked during fall [6].

There have been conflicting reports regarding seasonal variations in asthma symptoms. In a Taiwanese study using one-stage stratified cluster random sampling and a questionnaire, the frequency of asthma aggravation peaked in winter [7].

An Italian study that investigated the number of emergency calls for asthma exacerbations revealed that the prevalence of asthma symptoms peaked in autumn and spring [4]. Similarly, a recent large-scale population-based study in Israel showed that unscheduled visits to the primary care physician and drug prescriptions for asthma deterioration were most common in September [5]. These conflicting results could be due to the differences in study design, climate conditions, or the method of assessing asthma exacerbations. In particular, patient's behavioral patterns toward asthma exacerbation, such as the use of symptom reliever or visits to the hospital for emergency care vary in different countries. Therefore, the number of prescription drugs or the frequency of healthcare visits does not always reflect the symptom changes or physiologic status of individual patients with asthma. By contrast, we used daily measurements of PEFR in this prospective study in order to overcome the methodological limitations of previous studies. Finally, we verified the results of previous Korean studies; i.e., the prevalence of asthma exacerbation peaked in spring or autumn [6, 20].

The worsening of the lung function in autumn and spring relative to winter could be attributed to several environmental factors, including meteorological factors, viral infections, air pollution, and indoor or outdoor allergens. The largest diurnal temperature range (DTR) was observed in spring and autumn, which is associated with a higher frequency of emergency department visits or hospitalizations [21, 22]. Although the mechanism of asthma aggravation by DTR remains unclear, temperature changes within a short period of time can induce mild inflammation in the airway, which increases the risk of susceptibility to respiratory illness [21]. It is also presumed that patients with asthma avoid worsening of symptoms by staying indoors during the winter season [22]. In addition, respiratory virus infection was associated with 85% of the cases of asthma exacerbation, indicating their important role in asthma exacerbations in children [23, 24]. In particular, rhinovirus and influenza were more frequently detected in patients with asthma exacerbation than other respiratory viruses [25-27]. The Korean Centers for Disease Control reported that the incidence of rhinovirus and influenza infection was the highest in autumn and spring [28].

In Korea, the major source of PM in spring is the Asian dust from northern China and Mongolian desert with 40 $\mu m/m^3$ increase in PM_{10} within 3 days of dust outbreak [14]. PM causes direct inflammation in the airways, mucosal edema, and cytotoxicity [29]. A recent meta-analysis found that exposure to high levels of PM significantly increased the risks of emergency room visits and hospital admissions in patients with asthma [30]. In another Korean study, $PM_{2.5}$ and PM_{10} increased the hospital admission rate in spring and winter, respectively [31]. There was also an increase in the rate of Emergency Department visits due to asthma exacerbation after Asian dust days in Nagasaki, the western part of the Japanese island [32]. A recent Chinese study demonstrated a significant association between PM and poor respiratory outcomes, such as hospitalization and mortality in the winter season [33]. Subgroup analysis in the present study revealed that sensitization to HDMs had interaction effects on the monthly patterns of PEFR, especially in April, July, August, September, and October. A previous Korean study reported that the concentration of HDMs was the highest

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in August, September, and October, which coincides with the months with higher number of individuals who had worse lung function reported in our previous study [34]. Our analysis also showed that the low PEFR in April, July, and August was associated with sensitization to tree or grass pollens. These results highlight the importance of inhalant allergens as factors that aggravate asthma because the levels of tree and grass pollens are usually high in the months of March to May and May to September, respectively, in Korea [35].

This study has some limitations. We did not adjust for respiratory viral infection and the use of controllers, which are the most important factors for asthma exacerbation. Participants who developed symptoms of respiratory tract infections were not allowed to undergo tests for determination of viral etiologies. In addition, the number of patients who used asthma controllers was higher in spring and autumn than in summer and winter without statistical significance (data not shown); this finding indicates that there is no need to adjust for the statistical analysis. Although the exact causes were not completely identified, our results are still considered significant because asthma is a complex disease aggravated by various risk factors, such as infection, allergens, climate, and air pollution. Indeed, seasonal variations in asthma exacerbation are the consequences of multiple environmental triggers. Second, sensitization to HDM was observed in 78.6% of the study patients. This finding implies that our study has a selection bias, which partly contributed to the reduction in the lung function in autumn. Lastly, we had difficulty maintaining the compliance of the patients with regard to recording their daily PEFR measurements all year round. It led to the wide variation in the number of records among the study participants. Nevertheless, our study provides useful information on the seasonal and monthly patterns of asthma status that can be used to develop individualized management plans depending on the season or month.

In conclusion, the lung function in Korean children with asthma is lower in autumn than in winter. In terms of monthly patterns, the PEFR is significantly lower in April and October than in January. These results can be used to prevent asthma exacerbations by developing seasonal or monthly management strategies for children with asthma.

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REFERENCES

1. Ahn K, Kim J, Kwon HJ, Chae Y, Hahm MI, Lee KJ, Park YM, Lee SY, Han M, Kim WK. The prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in Korean children: Nationwide cross-sectional survey using complex sampling design. J Korean Med Assoc 2011;54:769-78.
CROSSREF
2. Akinbami LJ, Moorman JE, Liu X. Asthma prevalence, health care use, and mortality: United States, 2005-2009. Natl Health Stat Report 2011;(32):1-14.
PUBMED
3. Roncada C, de Oliveira SG, Cidade SF, Sarria EE, Mattiello R, Ojeda BS, Dos Santos BR, Gustavo Ada S, Pinto LA, Jones MH, Stein RT, Pitrez PM. Burden of asthma among inner-city children from Southern Brazil. J Asthma 2016;53:498-504.
PUBMED | CROSSREF

4. Tosca MA, Ruffoni S, Canonica GW, Ciprandi G. Asthma exacerbation in children: relationship among pollens, weather, and air pollution. Allergol Immunopathol (Madr) 2014;42:362-8.
PUBMED | CROSSREF

5. Cohen HA, Blau H, Hoshen M, Batat E, Balicer RD. Seasonality of asthma: a retrospective population study. Pediatrics 2014;133:e923-32.
PUBMED | CROSSREF

6. Won YK, Hwang TH, Roh EJ, Chung EH. Seasonal patterns of asthma in children and adolescents presenting at Emergency Departments in Korea. Allergy Asthma Immunol Res 2016;8:223-9.
PUBMED | CROSSREF

7. Kao CC, Huang JL, Ou LS, See LC. The prevalence, severity and seasonal variations of asthma, rhinitis and eczema in Taiwanese schoolchildren. Pediatr Allergy Immunol 2005;16:408-15.
PUBMED | CROSSREF

8. Pothirat C, Tosukhowong A, Chaiwong W, Liwsrisakun C, Inchai J. Effects of seasonal smog on asthma and COPD exacerbations requiring emergency visits in Chiang Mai, Thailand. Asian Pac J Allergy Immunol 2016;34:284-9.
PUBMED

9. Bheekie A, Syce JA, Weinberg EG. Peak expiratory flow rate and symptom self-monitoring of asthma initiated from community pharmacies. J Clin Pharm Ther 2001;26:287-96.
PUBMED | CROSSREF

10. Yoos HL, Kitzman H, McMullen A, Henderson C, Sidora K. Symptom monitoring in childhood asthma: a randomized clinical trial comparing peak expiratory flow rate with symptom monitoring. Ann Allergy Asthma Immunol 2002;88:283-91.
PUBMED | CROSSREF

11. Dobra R, Equi A. How to use peak expiratory flow rate. Arch Dis Child Educ Pract Ed 2018;103:158-62.
PUBMED | CROSSREF

12. Tsurikisawa N, Oshikata C, Sato T, Kimura G, Mizuki M, Tsuburai T, Shoji S, Saito H, Shimoda T. Low Variability in peak expiratory flow predicts successful inhaled corticosteroid step-down in adults with asthma. J Allergy Clin Immunol Pract 2018;6:972-9.
PUBMED | CROSSREF

13. Ahmed E, Kim KH, Shon ZH, Song SK. Long-term trend of airborne particulate matter in Seoul, Korea from 2004 to 2013. Atmos Environ 2015;101:125-33.
CROSSREF

14. Altindag DT, Baek D, Mocan N. Chinese Yellow Dust and Korean infant health. Soc Sci Med 2017;186:78-86.
PUBMED | CROSSREF

15. Kim J, Kim H, Kweon J. Hourly differences in air pollution on the risk of asthma exacerbation. Environ Pollut 2015;203:15-21.
PUBMED | CROSSREF

16. Kim SE, Honda Y, Hashizume M, Kan H, Lim YH, Lee H, Kim CT, Yi SM, Kim H. Seasonal analysis of the short-term effects of air pollution on daily mortality in Northeast Asia. Sci Total Environ 2017;576:850-7.
PUBMED | CROSSREF

17. Crapo RO, Casaburi R, Coates AL, Enright PL, Hankinson JL, Irvin CG, MacIntyre NR, McKay RT, Wanger JS, Anderson SD, Cockcroft DW, Fish JE, Sterk PJ. Guidelines for methacholine and exercise challenge testing-1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. Am J Respir Crit Care Med 2000;161:309-29.
PUBMED

18. American Thoracic Society. Standardization of spirometry, 1994 update. Am J Respir Crit Care Med 1995;152:1107-36.
PUBMED

19. Heinzerling L, Mari A, Bergmann KC, Bresciani M, Burbach G, Darsow U, Durham S, Fokkens W, Gjomarkaj M, Haahtela T, Bom AT, Wöhrl S, Maibach H, Lockey R. The skin prick test - European standards. Clin Transl Allergy 2013;3:3.
PUBMED | CROSSREF

20. Lee SW, Lee S, Sheen YH, Ha EK, Choi SH, Yang MS, Hwang S, Kim SS, Choi JH, Han MY. Seasonal cycle and relationship of seasonal rhino- and influenza virus epidemics with episodes of asthma exacerbation in different age groups. Allergy Asthma Immunol Res 2017;9:517-25.
PUBMED | CROSSREF

21. Qiu H, Yu IT, Tse LA, Chan EY, Wong TW, Tian L. Greater temperature variation within a day associated with increased emergency hospital admissions for asthma. Sci Total Environ 2015;505:508-13.
PUBMED | CROSSREF

22. Kwon JM, Shim JW, Kim DS, Jung HL, Park MS, Shim JY. Prevalence of respiratory viral infection in children hospitalized for acute lower respiratory tract diseases, and association of rhinovirus and influenza virus with asthma exacerbations. Korean J Pediatr 2014;57:29-34.
PUBMED | CROSSREF

23. Eggo RM, Scott JG, Galvani AP, Meyers LA. Respiratory virus transmission dynamics determine timing of asthma exacerbation peaks: Evidence from a population-level model. Proc Natl Acad Sci U S A 2016;113:2194-9.
PUBMED | CROSSREF

24. Thomas AO, Lemanske RF Jr, Jackson DJ. Infections and their role in childhood asthma inception. Pediatr Allergy Immunol 2014;25:122-8.
PUBMED | CROSSREF

25. Jamieson KC, Warner SM, Leigh R, Proud D. Rhinovirus in the pathogenesis and clinical course of asthma. Chest 2015;148:1508-16.
PUBMED | CROSSREF

26. Proud D. Role of rhinovirus infections in asthma. Asian Pac J Allergy Immunol 2011;29:201-8.
PUBMED

27. Lambert KA, Prendergast LA, Dharmage SC, Tang M, O'Sullivan M, Tran T, Druce J, Bardin P, Abramson MJ, Erbas B. The role of human rhinovirus (HRV) species on asthma exacerbation severity in children and adolescents. J Asthma 2018;55:596-602.
PUBMED | CROSSREF

28. Acute respiratory infectious diseases surveillance weekly report [Internet]. Cheongju (Korea): Korea Centers for Disease Control and Prevention; [cited 2020 Mar 14]. Available from: http://www.cdc.go.kr/npt/biz/npp/iss/ariStatisticsMain.do

29. Zosky GR, Iosifidis T, Perks K, Ditcham WG, Devadason SG, Siah WS, Devine B, Maley F, Cook A. The concentration of iron in real-world geogenic PM_{10} is associated with increased inflammation and deficits in lung function in mice. PLoS One 2014;9:e90609.
PUBMED | CROSSREF

30. Zheng XY, Ding H, Jiang LN, Chen SW, Zheng JP, Qiu M, Zhou YX, Chen Q, Guan WJ. Association between air pollutants and asthma emergency room visits and hospital admissions in time series studies: a systematic review and meta-analysis. PLoS One 2015;10:e0138146.
PUBMED | CROSSREF

31. Kim H, Kim H, Park YH, Lee JT. Assessment of temporal variation for the risk of particulate matters on asthma hospitalization. Environ Res 2017;156:542-50.
PUBMED | CROSSREF

32. Nakamura T, Hashizume M, Ueda K, Shimizu A, Takeuchi A, Kubo T, Hashimoto K, Moriuchi H, Odajima H, Kitajima T, Tashiro K, Tomimasu K, Nishiwaki Y. Asian dust and pediatric Emergency Department visits due to bronchial asthma and respiratory diseases in Nagasaki, Japan. J Epidemiol 2016;26:593-601.
PUBMED | CROSSREF

33. Li P, Xin J, Wang Y, Li G, Pan X, Wang S, Cheng M, Wen T, Wang G, Liu Z. Association between particulate matter and its chemical constituents of urban air pollution and daily mortality or morbidity in Beijing City. Environ Sci Pollut Res Int 2015;22:358-68.
PUBMED | CROSSREF

34. Jeong KY, Park JW, Hong CS. House dust mite allergy in Korea: the most important inhalant allergen in current and future. Allergy Asthma Immunol Res 2012;4:313-25.
PUBMED | CROSSREF

35. Oh JW, Lee HB, Kang IJ, Kim SW, Park KS, Kook MH, Kim BS, Baek HS, Kim JH, Kim JK, Lee DJ, Kim KR, Choi YJ. The revised edition of Korean calendar for allergenic pollens. Allergy Asthma Immunol Res 2012;4:5-11.
PUBMED | CROSSREF