

## The Relationship Between Psychosocial Stress and Allergic Disease Among Children and Adolescents in Gwangyang Bay, Korea

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**Objectives:** Stress is considered a causal factor in many diseases, allergic disease being one of them. The prevalence of allergic disease is increasing in Korea, but the relationship between allergic symptoms and stress is not empirically well known. We aimed to evaluate the relationship between allergy-related symptoms and stress in children and adolescents.

**Methods:** We investigated 698 children and adolescents living in Gwangyang Bay, Korea, using a multi-stage cluster sampling method. Using the International Study of Asthma and Allergies in Childhood and the Psychosocial Well-being Index, these subjects were surveyed on allergy-related symptoms and psychosocial stressors in their lives, respectively. We used a multivariate logistic analysis for odds ratios for the complaint rate of allergic symptoms, after adjusting for age, gender, household income, body mass index, and residence.

**Results:** After adjustments, lifetime rhinitis (odds ratio [OR], 1.024), rhinoconjunctivitis (OR, 1.090), diagnosis of itchy eczema (OR, 1.040), treatment of itchy eczema (OR, 1.049), 12-month allergic conjunctivitis (OR, 1.026), diagnosis of allergic conjunctivitis (OR, 1.031), and treatment of allergic conjunctivitis (OR, 1.034) were found to be significantly associated with stress.

**Conclusions:** Our results support the notion that there is a relationship between stress and allergic symptoms in children and adolescents. Further research into any causal relationship between stress and allergies, as well as preventative public health plans for decreasing stress in children and adolescents are needed.

**Key words:** Psychological stress, Asthma, Rhinitis, Atopic dermatitis, Allergic conjunctivitis

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### INTRODUCTION

Allergic diseases are among the major health problems in children and adolescents [1]. Multiple studies have attempted to estimate the prevalence of allergic diseases in these age groups. The International Study of Asthma and Allergies in Childhood (ISAAC) was first conducted in 1996 [2]. Following this initial phase, the ISAAC study has repeated every five years [3]. The Republic of Korea, as part of collaborative international studies to investigate prevalence of allergic diseases in chil-

dren and adolescents, conducted nationwide questionnaire surveys in 1995, 2000, and 2010. Epidemiologically, between 1995 and 2010 the prevalence of allergic rhino-conjunctivitis and eczema increased but the prevalence of asthma changed very little [4]. The significant overall increase in the prevalence of allergic diseases in Korean children and adolescent is what is most important.

Studies have shown that children who experience psychosocial stress are significantly more likely to be sick and to have had medical treatment [5]. Chronic stress is linked to a number of serious diseases, such as cardiovascular disease, depression, endocrine diseases like diabetes, and cancers. In addition, stressful experiences may provoke asthma attacks in asthmatic children [6]. Physiologically, chronic stress triggers the central nervous system and the immune system, which may provoke a hypersensitive reaction and result in allergic disease [7].

Recent epidemiological studies have assessed the effects of mental health on the expression of allergic disease in children. However, most of these studies focused primarily on parenting stress in early childhood and, if they focused on the personal characteristics of children at all, the study population were small [8]. Also, Korean children and adolescents, especially vulnerable groups, were not heavily represented in these studies. We conducted the present study to explore the relationship between psychosocial stress and allergic disease in Korean children and adolescents, basing our study in the Gwangyang Bay area of the Korea.

## METHODS

### Study Population

We used a cluster sampling method to obtain our data population. We selected two cities in Gwangyang Bay: Yeosu-si and Namhae-gun. We selected dong in Yeosu-si and Namhae-gun, which were Yeocheon-dong, Hwayang-myeon, Gohyeon-myeon, Seo-myeon, and Idong-myeon. We obtained a list of 23 schools located in these areas. We randomly selected two elementary schools, four middle schools, and four high schools from this sample. Informed consent was obtained by the legal guardians of those under the age of 16 years. This study was conducted from the May 17 to June 23, 2010. The sample consisted of 704 children and adolescents. Six subjects with incomplete stress and allergy questionnaires were excluded from the study. In total, the final analysis included 698 subjects. Ethical approval was granted by the Soonchunhyang

University Cheonan Hospital institutional review board (2007-15-02).

### Questionnaires and Physical Examination

Trained interviewers surveyed the subjects to for self-reported information about age, gender, average household income, religion, stress and allergic symptoms. We measured the height and weight of each subject.

To assess children and adolescent's exposure to stressful experiences, we administered the Psychosocial Well-being Index (PWI) short form. This interview, which consists of 18 questions, is a modified, Korean-translated version of Goldberg's General Health Questionnaire-60. Each question had a 4-point Likert scale, ranging from 0 to 3. Total PWI score ranged from 0 to 54 [9]. PWI scores were divided into 2 levels: upper 25 percentile (45 to 54 scores) and lower 75 percentiles (0 to 44 scores) [10].

We also used a modified, Korean-translated version of ISAAC questionnaire to obtain information on allergic symptoms. The questionnaire interrogates subject history and symptoms in four main areas of allergic disease: asthma, allergic rhinitis, itchy eczema, and allergic conjunctivitis. A response of 'yes' to at least one of the allergic symptoms listed in the questionnaire was recorded as 'allergic diseases overall'.

### Statistical Analysis

We used the chi-square test for categorical variables to summarize the characteristics of the study population. To evaluate the association stress with allergic symptoms, two models were constructed. Model 1 used univariate logistic regression and model 2 used multivariate logistic regression after adjustment for five covariates (age, gender, household income, body mass index, and residence). We selected these covariates from a relevant literature review [11-13]. The data were put into Excel (MS Office 2007; Microsoft, Seattle, WA, USA) and statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was accepted for  $p < 0.05$ .

## RESULTS

In our sample the mean age of the 698 children and adolescents was 15.59 years; 59.2% were male, 40.8% were female. The general demographic characteristics of the study participants were shown in Table 1. As seen in Table 2, significant differences were observed between the upper 25 percentile (45

**Table 1.** General characteristics of subjects (n=698)

| Characteristics                      | Male       | Female     | Total      | p-value <sup>1</sup> |
|--------------------------------------|------------|------------|------------|----------------------|
| Age                                  |            |            |            |                      |
| < 15                                 | 132 (32.0) | 114 (40.0) | 246 (35.2) | 0.03                 |
| ≥ 15                                 | 281 (68.0) | 171 (60.0) | 452 (64.8) |                      |
| Household income (won/mo)            |            |            |            |                      |
| < 500 000                            | 372 (90.1) | 252 (88.4) | 624 (89.4) | 0.49                 |
| ≥ 500 000                            | 41 (9.9)   | 33 (11.6)  | 74 (10.6)  |                      |
| Body mass index (kg/m <sup>2</sup> ) |            |            |            |                      |
| < 25                                 | 361 (87.4) | 256 (89.8) | 617 (88.4) | 0.33                 |
| ≥ 25                                 | 52 (12.6)  | 29 (10.2)  | 81 (11.6)  |                      |
| Residence                            |            |            |            |                      |
| Yeosu-si                             | 310 (75.1) | 169 (59.3) | 479 (68.6) | < 0.001              |
| Namhae-gun                           | 103 (24.9) | 116 (40.7) | 219 (31.4) |                      |

Values are presented as frequency (%).

<sup>1</sup>p-value of chi-squared test.

to 54) and the lower 75 percentile (0 to 44) of PWI, with regard to baseline characteristics. Generally, people with high PWI scores were older in age and had a lower household income level than those with low PWI score ( $p < 0.05$ ).

Those with high PWI scores had a significantly higher proportion of short-term (12-months) and life-long symptoms and/or diagnosis of rhinitis, eczema, and allergic conjunctivitis as compared to those with low PWI scores (Table 3). Table 4 shows the results from the logistical regression of allergic symptoms and PWI scores after controlling for other mediating variables. The PWI score was found to be significantly associated in a univariate analysis (model 1). After adjusting for five covariates, the PWI score was found to be significantly associated with allergic symptoms: rhinitis (odds ratio [OR], 1.024; 95% confidence interval [CI], 1.005 to 1.043); 12-month rhino-conjunctivitis (OR, 1.090; 95% CI, 1.008 to 1.178); lifetime diagnosis of itchy eczema (OR, 1.040; 95% CI, 1.013 to 1.068); 12-month treatment of itchy eczema (OR, 1.049; 95% CI, 1.013 to 1.086); 12-month allergic conjunctivitis (OR, 1.026; 95% CI, 1.001 to 1.052); lifetime diagnosis of conjunctivitis (OR, 1.031; 95% CI, 1.007 to 1.055); the 12-month treatment of conjunctivitis (OR, 1.034; 95% CI, 1.003 to 1.065); overall allergic rhinitis (OR, 1.019; 95% CI, 1.001 to 1.038); and overall itchy eczema (OR, 1.028; 95% CI, 1.004 to 1.052) (model 2).

## DISCUSSION

In this cross-sectional study, we examined the prevalence of allergic symptoms and their association with stress in children

**Table 2.** Distribution of stress according to baseline characteristics of the study subjects (n=698)

| Variables                            | Psychosocial Well-being Index |               | p-value <sup>1</sup> |
|--------------------------------------|-------------------------------|---------------|----------------------|
|                                      | 0-44 (n=509)                  | 45-54 (n=189) |                      |
| Age                                  |                               |               |                      |
| < 15                                 | 197 (38.7)                    | 49 (25.9)     | 0.002                |
| ≥ 15                                 | 312 (61.3)                    | 140 (74.1)    |                      |
| Gender                               |                               |               |                      |
| Male                                 | 309 (60.7)                    | 104 (55)      | 0.18                 |
| Female                               | 200 (39.3)                    | 85 (45)       |                      |
| Household income (won/mo)            |                               |               |                      |
| < 500 000                            | 445 (87.4)                    | 179 (94.7)    | 0.005                |
| ≥ 500 000                            | 64 (12.6)                     | 10 (5.3)      |                      |
| Body mass index (kg/m <sup>2</sup> ) |                               |               |                      |
| < 25                                 | 453 (89.0)                    | 164 (86.8)    | 0.42                 |
| ≥ 25                                 | 56 (11.0)                     | 25 (13.2)     |                      |
| Residence                            |                               |               |                      |
| Yeosu-si                             | 347 (68.2)                    | 132 (69.8)    | 0.67                 |
| Namhae-gun                           | 162 (31.8)                    | 57 (30.2)     |                      |

Values are presented as frequency (%).

<sup>1</sup>p-value of chi-squared test.

and adolescents in the Gwangyang Bay region of Korea. The nationwide prevalence of 12-month asthma symptoms in children and adolescents was 10.3% in 6- to 7-year-olds and 8.3% in 13- to 14-year-olds. The prevalence of 12-month eczema symptoms was 17.9% in 6- to 7-year-olds and 11.2% in 13- to 14-year-olds [4]. From the 2009 Korean National Health and Nutrition Examination Surveys (KNHANES), the nationwide prevalence of 12-month asthma symptoms was 8.8% for 1- to 11-year-olds and 3.7% for 12 to 18-year-olds. Also, the nationwide prevalence of lifetime diagnosis of eczema was 16.3% for 1- to 11-year-olds and 9.2% for 12- to 18-year-olds [14].

Compared to the results from these nationwide studies, the prevalence of 12-month asthma symptoms in children and adolescents aged 10 to 18 years in Gwangyang Bay was relatively low: 6.2%. The prevalence of 12-month eczema symptoms in this cohort was 7% and the prevalence of a lifetime diagnosis of eczema was 14.9%. This is similar to the prevalence reported in other studies.

In 2009 researchers examined the prevalence of allergy symptoms in children and adolescents in Gwangyang Bay, specifically Gwangyang-si, Yeosu-si, and Hadong-gun [15]. The prevalence of allergic symptoms in our survey was similar to or slightly lower than the results of that study.

We also used a multivariate logistic regression analysis. After

**Table 3.** Distribution of stress according to allergic symptoms of the study subjects (n=698)

| Variables                                    | Psychosocial Well-being Index |               | p-value <sup>1</sup> |
|--|-------------------------------|---------------|----------------------|
|  | 0-44 (n=509)                  | 45-54 (n=189) |                      |
| Wheeze                                       | 58 (11.4)                     | 27 (14.3)     | 0.30                 |
| Wheeze (last 1 year)                         | 26 (5.1)                      | 17 (9.0)      | 0.06                 |
| Sleep disturbed by wheezing (last 1 year)    | 8 (1.6)                       | 4 (2.1)       | 0.74                 |
| School absence due to wheezing (last 1 year) | 4 (0.8)                       | 4 (2.1)       | 0.22                 |
| Diagnosis of asthma                          | 27 (5.3)                      | 7 (3.7)       | 0.38                 |
| Treatment of asthma (last 1 year)            | 12 (2.4)                      | 2 (1.1)       | 0.37                 |
| Rhinitis                                     | 158 (31)                      | 87 (46)       | <0.001               |
| Rhinitis (last 1 year)                       | 111 (21.8)                    | 60 (31.7)     | 0.007                |
| Rhinoconjunctivitis (last 1 year)            | 6 (1.2)                       | 6 (3.2)       | 0.10                 |
| Diagnosis of allergic rhinitis               | 84 (16.5)                     | 37 (19.6)     | 0.34                 |
| Treatment of allergic rhinitis (last 1 year) | 63 (12.4)                     | 25 (13.2)     | 0.76                 |
| Itchy eczema                                 | 46 (9.0)                      | 22 (11.6)     | 0.30                 |
| Itchy eczema (last 1 year)                   | 31 (6.1)                      | 18 (9.5)      | 0.12                 |
| Sleep disturbed by itchy rash (last 1 year)  | 15 (2.9)                      | 7 (3.7)       | 0.61                 |
| Diagnosis of itchy eczema                    | 66 (13.0)                     | 38 (20.1)     | 0.02                 |
| Treatment of itchy eczema (last 1 year)      | 32 (6.3)                      | 24 (12.7)     | 0.01                 |
| Allergic conjunctivitis                      | 99 (19.4)                     | 55 (29.1)     | 0.01                 |
| Allergic conjunctivitis (last 1 year)        | 69 (13.6)                     | 42 (22.2)     | 0.005                |
| Diagnosis of conjunctivitis                  | 82 (16.1)                     | 48 (25.4)     | 0.005                |
| Treatment of conjunctivitis (last 1 year)    | 47 (9.2)                      | 25 (13.2)     | 0.12                 |
| Asthma <sup>2</sup>                          | 75 (14.7)                     | 31 (16.4)     | 0.59                 |
| Allergic rhinitis <sup>2</sup>               | 183 (36.0)                    | 100 (52.9)    | <0.001               |
| Itchy eczema <sup>2</sup>                    | 84 (16.5)                     | 42 (22.2)     | 0.08                 |
| Allergic conjunctivitis <sup>2</sup>         | 151 (29.7)                    | 77 (40.7)     | 0.01                 |

Values are presented as frequency (%).

<sup>1</sup>p-value of chi-squared test.

<sup>2</sup>Allergic disease overall: subject answered 'yes' to at least one of the questions in the allergy symptoms questionnaire.

multivariate adjustment, we found allergic rhinitis, itchy eczema, and allergic conjunctivitis to each have a significant association with PWI. This is consistent with the results of previous studies, which also describe allergic symptoms to be associated with stress in children and adolescents. Asthma symptoms in the present study, on the other hand, had no significant association with PWI. Perhaps this is because the prevalence of asthma symptoms overall in Gwangyang Bay was relatively lower than the nationwide average.

Previous studies focused on two types of psychosocial stress,

**Table 4.** OR (95% CI) of allergic symptoms according to Psychosocial Well-being Index in a logistic regression model (n=698)

| Outcome variables                            | Crude OR (95% CI)    | Adjusted OR (95% CI) <sup>1</sup> |
|--|----------------------|-----------------------------------|
| Wheeze                                       | 1.006 (0.980, 1.033) | 1.004 (0.978, 1.031)              |
| Wheeze (last 1 year)                         | 1.023 (0.986, 1.060) | 1.021 (0.984, 1.059)              |
| Sleep disturbed by wheezing (last 1 year)    | 1.007 (0.943, 1.075) | 1.009 (0.943, 1.080)              |
| School absence due to wheezing (last 1 year) | 1.040 (0.956, 1.131) | 1.050 (0.959, 1.149)              |
| Diagnosis of asthma                          | 0.975 (0.938, 1.014) | 0.975 (0.937, 1.014)              |
| Treatment of asthma (last 1 year)            | 0.997 (0.939, 1.059) | 1.018 (0.955, 1.086)              |
| Rhinitis                                     | 1.026 (1.007, 1.044) | 1.024 (1.005, 1.043)              |
| Rhinitis (last 1 year)                       | 1.015 (0.995, 1.036) | 1.013 (0.993, 1.034)              |
| Rhinoconjunctivitis (last 1 year)            | 1.083 (1.005, 1.168) | 1.090 (1.008, 1.178)              |
| Diagnosis of allergic rhinitis               | 0.990 (0.968, 1.012) | 0.990 (0.968, 1.013)              |
| Treatment of allergic rhinitis (last 1 year) | 0.994 (0.969, 1.019) | 0.993 (0.967, 1.019)              |
| Itchy eczema                                 | 1.014 (0.985, 1.044) | 1.015 (0.985, 1.046)              |
| Itchy eczema (last 1 year)                   | 1.007 (0.974, 1.041) | 1.010 (0.976, 1.046)              |
| Sleep disturbed by itchy rash (last 1 year)  | 1.000 (0.953, 1.049) | 0.996 (0.948, 1.047)              |
| Diagnosis of itchy eczema                    | 1.032 (1.007, 1.058) | 1.040 (1.013, 1.068)              |
| Treatment of itchy eczema (last 1 year)      | 1.040 (1.007, 1.075) | 1.049 (1.013, 1.086)              |
| Allergic conjunctivitis                      | 1.027 (1.006, 1.049) | 1.020 (0.998, 1.042)              |
| Allergic conjunctivitis (last 1 year)        | 1.034 (1.009, 1.059) | 1.026 (1.001, 1.052)              |
| Diagnosis of conjunctivitis                  | 1.036 (1.013, 1.060) | 1.031 (1.007, 1.055)              |
| Treatment of conjunctivitis (last 1 year)    | 1.036 (1.006, 1.066) | 1.034 (1.003, 1.065)              |
| Asthma <sup>2</sup>                          | 1.135 (0.719, 1.792) | 0.992 (0.968, 1.016)              |
| Allergic rhinitis <sup>2</sup>               | 2.002 (1.427, 2.807) | 1.019 (1.001, 1.038)              |
| Itchy eczema <sup>2</sup>                    | 1.446 (0.954, 2.190) | 1.028 (1.004, 1.052)              |
| Allergic conjunctivitis <sup>2</sup>         | 1.630 (1.152, 2.306) | 1.019 (1.000, 1.039)              |

OR, odds ratio; CI, confidence interval.

<sup>1</sup>Adjusted for age (years), gender (male and female), household income (<500 000, ≥500 000 won/mo), body mass index (kg/m<sup>2</sup>) and residence (Yeosu-si and Namhae-gun).

<sup>2</sup>Allergic disease overall: subject answered 'yes' to at least one of the questions in the allergy symptoms questionnaire.

exposure to stressors and mental health problems. Sandberg et al. [5] surveyed 90 children with asthma living in Scotland between 6 and 13 years old. The researchers reported that acute negative life events that triggered high chronic stress significantly increased the risk of new asthma attacks within two weeks of the event. Acute negative life events that occurred without high chronic stress also significantly increased the

complaint rate of asthma symptoms and the risk of asthma exacerbations within two weeks of the event. Marin et al. [16] conducted a study in 71 asthmatic children and 76 healthy children aged 13 years. Children who had high levels of both chronic stress and acute stress were shown to have more asthma symptoms, as they had significantly higher IL-4, IL-5, and IFN- $\gamma$ .

Regarding mental health, many studies examined behavior problems and internalizing symptoms. Weil et al. [17] surveyed 1260 children with asthma between 4 to 9 years of age using a child behavior checklist. Children who had behavior problems had significantly more days of wheezing and lower general functional status as a result of asthma symptoms. Stevenson and ETAC Study Group [18] reported that behavior problems preceded the onset of asthma by surveying 265 children with atopic dermatitis. Calam et al. [19] showed behavior problems predated the development of wheezing. On the other hand, many studies have reported that internalizing symptoms were not associated with asthma [20,21].

Some research has focused on allergic rhinoconjunctivitis or allergic dermatitis. Kilpeläinen et al. [22] surveyed 10 667 people and found that stressful life events, such as severe disease, the death of a loved one, or inter-personal conflicts, increased the risk of allergic rhinoconjunctivitis and atopic dermatitis. Oh et al. [23] examined atopic dermatitis patients and concluded that anxiety was associated with the induction of pruritus in atopic dermatitis. Recent studies suggest that emotional stress is an important factor in the development of atopic dermatitis [24].

The exact biological mechanisms that link psychosocial stress with allergies are not understood, but continue to be investigated. Potential mechanisms may be the autonomic nervous system (ANS) and hypothalamic-pituitary-adrenal (HPA) axis. The ANS consists of two systems: the sympathetic and the parasympathetic system, the latter of which includes the non-adrenergic system in the gastrointestinal tract.

Stress may activate the hypothalamic paraventricular nucleus, which secretes a corticotropin-releasing hormone (CRH). CRH stimulates the anterior hypophysis lobe and locus coeruleus. The anterior hypophysis secretes adrenocorticotrophic hormone to stimulate the adrenal cortex and the adrenal medulla (HPA axis). The adrenal cortex secretes corticoids, which, in turn, produces IL-4, IL-10, and IL-13. Production of these interleukins increases T-helper (Th) 2 cell. The adrenal medulla secretes adrenalin and noradrenalin. The locus coeruleus is

stimulated by CRH and secretes noradrenalin that results in activating the brain stem, spinal cord, and sympathetic nervous system. Noradrenalin, which is produced by the sympathetic nervous system and the corticoids, adrenalin and noradrenalin, which are produced by the adrenal gland, suppress IL-12. As a result, IL-12 suppresses the production of Th1. This Th1/Th2 imbalance, in which Th2 cytokines predominate, favors a Th2-mediated allergic reaction [25,26].

There were several limitations to this study that should be considered when interpreting its findings. First, given its cross-sectional design, we were unable to demonstrate a one-way causal relationship between stress and allergic symptoms. Because reverse causality could not be excluded. Thus, a prospective study will be required to investigate any causal relationships between stress and allergy. Second, because this study was based on the self-report of allergic symptoms by subjects with varying levels of health-awareness and body-consciousness, we could not fully control for information bias. Third, this study was not conducted on a nationwide scale, so our findings may not be easily generalized. Nonetheless, after adjusting for confounding factors, there does exist a relationship between stress and allergic disease in children and adolescents living in Gwangyang Bay.

In addition, most of nationwide surveys in Korea, such as the KNHANES, measured stress in children and adolescents by asking only one question: "Do you feel stress in your daily life?" However, in this cross-sectional study, we measured the incidence of allergic disease and psychosocial stress of Korean children and adolescents in the Gwangyang Bay area using ISAAC and PWI, thus allowing for more nuanced and interpretable findings. These findings could be used as a basis for planning preventive intervention among high risk groups: patients suffering chronic allergies and children suffering from chronic stress.

In conclusion, we observed a possible relationship between psychosocial stress and the complaint rate of allergic symptoms in Korean children and adolescents. These results are consistent with the literature on stress and disease, particularly allergic disease, among youth. Future research on this subject should address the challenge of determining correlation and eliminating rival explanations.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest with the material presented in this paper.

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