

# Assessing the prevalence of pediatric allergy in Phitsanulok, Thailand

## ORIGINAL ARTICLE BY

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## ABSTRACT

### OBJECTIVE

To evaluate the prevalence of asthma, allergic rhinitis and eczema among children in Phitsanulok, Thailand

### METHODS

A cross-sectional survey was conducted between January and February 2007 in two age groups (6–7 and 13–14 years old) living in Phitsanulok, Thailand. Data were collected by using standardized Thai version of The International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire for both age groups and a video questionnaire for the older children.

### RESULTS

In this study, a total of 2,369 students aged 6–7 years and 3,173 students aged 13–14 years were included. For the younger age group, it showed that the recent (12-month period) prevalence of asthma was 8.71% (95% confidence interval (CI); 7.53 to 9.88), that of rhinitis was 28.93% (95% CI; 27.04 to 30.83), and that of eczema was 14.53% (95% CI; 13.06 to 16.00). For the older age group, we found that the recent prevalence of asthma was 12.26% (95% CI; 11.10 to 13.43), that of rhinitis was 36.59% (95% CI; 34.89 to 38.29), and that of eczema was 8.04% (95% CI; 7.07 to 9.00). In terms of life time (ever) prevalence of the three allergic conditions, in the younger age group, it showed that the life time prevalence of asthma was 14.32% (95% CI; 12.86 to 15.78), that of rhinitis was 34.11% (95% CI; 32.14 to 36.08), and that of eczema was 15.57% (95% CI; 14.06 to 17.08). For the older age group, we found that the life time prevalence of asthma was 19.16% (95% CI; 17.77 to 20.56), that of rhinitis was 44.88% (95% CI; 43.13 to 46.62), and that of eczema was 10.66% (95% CI; 9.57 to 11.76).

### CONCLUSION

Pediatric asthma, rhinitis and eczema were less prevalent in Phitsanulok than in Bangkok. However, in comparison to Chiang Mai, children in Phitsanulok had a higher prevalence of asthma but a lower prevalence of eczema.

## INTRODUCTION

Allergic conditions, encompassing asthma, allergic rhinitis, and atopic dermatitis, profoundly impact individuals' daily lives and overall well-being on a global scale.<sup>1-3</sup> The prevalence of these conditions displays significant regional variations, particularly among 6-7 year old and 13-14 year old children, as documented in The International Study of Asthma and Allergies in Childhood (ISAAC). This study involved Phase I surveys across 56 countries between 1996 and 1997 and Phase III surveys covering 1,200,000 children from 2001 to 2003.<sup>4-6</sup> These surveys consistently reveal that global allergy prevalence, as observed in Phase III, tends to remain relatively stable compared to Phase I.<sup>4-6</sup>

However, a specific study in Bangkok, Thailand, using the ISAAC Phase I questionnaire from 1995 and the ISAAC Phase III questionnaire from 2001, indicated an upward trend in asthma (12.3% to 14.5%), current rhinitis (38% to 50.3%), rhinoconjunctivitis (12.7% to 18.7%), and flexural eczema (9.7% to 11.9%) among children aged 6-7 and 13-14 years.<sup>7,8</sup> Yet, it is noteworthy that 14 years later, the Global Asthma Network (GAN) Phase I survey in 2015, which included Bangkok data and employed a core questionnaire based on ISAAC, found no significant change in allergic disease prevalence between 2001 and 2017.<sup>9</sup>

The prevalence of allergic diseases among children in Phitsanulok, a province in Thailand's lower northern region, remains unreported. Notably, ISAAC Phase I in 1995 and Phase III in 2001 studies conducted in Chiang Mai, a northern Thai province with similar age groups, revealed an increasing trend in the prevalence of rhinitis, rhinoconjunctivitis, and atopic dermatitis.<sup>7</sup> The results from these Chiang Mai studies indicated variations in asthma (9.1% vs. 8.3%), current rhinitis (28.4% vs. 35.1%), rhinoconjunctivitis (10.2% vs. 11.7%), and flexural eczema/atopic dermatitis (10.5% vs. 12.5%) between the two

phases.<sup>7</sup> These variations may be influenced by geographic differences within northern Thailand, with Chiang Mai characterized by more mountainous terrain and a colder climate. This possibly contributes to higher atopic dermatitis rates in Chiang Mai, as seen in both ISAAC Phase I and III studies compared to Bangkok.<sup>7-10</sup>

Moreover, it's important to consider the impact of air pollution levels in Bangkok and Chiang Mai, which have been historically higher compared to Phitsanulok.<sup>11</sup> These elevated pollution levels likely worsen respiratory allergies like asthma and allergic rhinitis.<sup>12-14</sup> Therefore, it is plausible that the prevalence and severity of allergic diseases in Phitsanulok might be lower due to differences in climate and reduced air pollution levels.<sup>7-10</sup> Therefore, the primary objective of this study is to investigate the prevalence and severity of the three most common allergic diseases specifically asthma, allergic rhinitis, and atopic dermatitis in children aged 6-7 and 13-14 years residing in Phitsanulok. This research aims to shed light on the allergic disease landscape in this region and contribute valuable insights into the potential influence of geographic and environmental factors on the prevalence of these conditions.

## METHODS

### STUDY DESIGN AND ETHICAL APPROVAL

The current investigation adopted a cross-sectional research design. Prior to commencement, this study received ethical approval from the Human Research Ethics Committee at Naresuan University, Thailand.

### STUDY POPULATION

As per the recommendations of the ISAAC Steering Committee, a sample size of 3,000 was deemed necessary to ensure the reliability of prevalence estimates for wheezing, rhinitis, eczema, and

**Table 1. Positive responses to the questions**

Positive response to	6–7 years	% (95% confidence interval)	13–14 years	% (95% confidence interval)
Asthma-related symptoms				
Wheeze ever*	317/2213	14.32 (12.86–15.78)	586/3058	19.16 (17.77–20.56)
Asthma ever	217/2142	10.13 (8.85–11.41)	355/3037	11.69 (10.55–12.83)
Symptoms in the past 12 months				
Wheeze†	193/2217	8.71 (7.53–9.88)	373/3042	12.26 (11.10–13.43)
Wheezing attacks ≥ 4 times	59/2228	2.65 (1.98–3.31)	92/2883	3.19 (2.55–3.83)
Night waking	106/2151	4.93 (4.01–5.84)	158/2877	5.49 (4.66–6.32)
Severe wheeze	34/2190	1.55 (1.03–2.07)	91/2881	3.16 (2.52–3.80)
Exercise-induced wheeze	91/2254	4.04 (3.22–4.85)	405/2920	13.87 (12.62–15.12)
Night cough	385/2275	16.92 (15.38–18.46)	655/2931	22.35 (20.84–23.86)
Rhinitis-related symptoms				
Nose symptoms ever*	760/2228	34.11 (32.14–36.08)	1397/3113	44.88 (43.13–46.62)
Hay fever ever	460/2047	22.47 (20.68–24.34)	627/2851	21.99 (20.47–23.51)
Symptoms in the past 12 months				
Nose†	638/2205	28.93 (27.04–30.83)	1130 /3088	36.59 (34.89–38.29)
Eyes	179/2147	8.34 (7.17–9.51)	418/2906	14.38 (13.11–15.66)
Activity limited	748/2226	33.60 (31.64–35.57)	996/2891	34.45 (32.72–36.18)
Eczema-related symptoms				
Rash ever*	344/2209	15.57 (14.06–17.08)	326/3057	10.66 (9.57–11.76)
Eczema ever	321/2032	15.80 (14.21–17.38)	298/2890	10.31 (9.20–11.42)
Flexural area	268/2204	12.16 (10.80–13.52)	167/2998	5.57 (4.75–6.39)
Symptoms in the past 12 months				
Rash†	321/2209	14.53 (13.06–16.00)	245/3049	8.04 (7.07–9.00)
Clearance of rash	295/2034	14.50 (12.97–16.03)	199/2994	6.65 (5.75–7.54)
Sleep disturbance from rash	252/2148	11.73 (10.37–13.09)	90/2995	3.01 (2.42–3.68)

\*Questions to determine the life time (ever) prevalence of the three allergic conditions

† Questions to determine the recent (12-month period) prevalence of the three allergic conditions

**Table 2. Positive responses to video-based questionnaires**

Positive response to	13–14 years	% (95% confidence interval)
Wheeze at rest	107/3173	3.37 (2.47–4.00)
Exercise-induced wheeze	174/3173	5.48 (4.69–6.28)
Night wheeze	36/3173	1.13 (0.77–1.50)
Night cough	355/3173	11.19 (10.09–12.28)
Severe wheeze	43/3173	1.36 (0.95–1.76)

severe asthma, maintaining a significance level of 1% and a study power of 95% to detect disparities among centers.<sup>15</sup> Centers with smaller populations were advised to provide a sample size of no fewer than 1,000 per age group.

In this study, a purposive sampling method was employed, enrolling a total of 5,542 students from primary and secondary schools in Phitsanulok. The criteria of selection were large public provincial schools in order to recruit all students in grade 1 (6–7 years of age) and/or grade 7–8 (13–14 years of age), of which most students were from many districts surrounding the city. This sample was divided into two age groups: 2,369 students aged 6–7 years and 3,173 students aged 13–14 years. Data collection took place between January and February of 2007, with impressively high participation rates in both age groups, reaching 96% for the younger age group and 95% for the older age group.

### QUESTIONNAIRE

The survey encompassed both written and video components. The written survey employed a validated Thai version of the ISAAC standardized questionnaire, which had been used in previous studies, including the 1995 ISAAC Phase I, ISAAC Phase III, and an adult 2003 survey in Phitsanulok.<sup>8,10,16,17</sup> This self-administered written questionnaire contained inquiries aimed at

assessing the prevalence of wheezing, rhinitis, eczema, and the severity of related symptoms.

Additionally, the video questionnaire, comprising five video sequences depicting wheezing occurrences at rest, during exertion, at night, night cough, and severe wheeze, was utilized. This video questionnaire corresponded to the international version of ISAAC questionnaires employed in Phase I and Phase III studies.<sup>7,8</sup> and was administered exclusively to older children. Specifically, children aged 13–14 years were selected for this component since they could independently complete both the written and video questionnaires. Importantly, this video questionnaire had been validated against nonspecific bronchial hyperresponsiveness.<sup>18</sup>

The rationale behind employing a video questionnaire was to eliminate potential language-related misunderstandings, particularly concerning the term "wheezing" in the Thai language used in the written questionnaire. By viewing the audio-visual questionnaire illustrating the symptom of "wheezing," any ambiguity was minimized.<sup>18</sup>

For 6–7 year old students, parents completed the written questionnaires on their behalf. In contrast, 13–14 year old students self-administered the written questionnaires before proceeding to the video questionnaire on asthma. Moreover, in the validated Thai version of the ISAAC standardized questionnaire,<sup>7,8</sup> the term "allergy to

Table 3. Percentage of positive responses to questions regarding sex

Positive response to	6-7 years (n=2,369)			13-14 years (n=3,173)		
	Male	Female	P Value	Male	Female	P Value
	(%)			(%)		
Current wheeze	10.8	7.1	0.002	12.8	11.7	0.35
Asthma ever	13.9	7.0	<0.001	14.0	9.3	<0.001

the air" was employed as a translation for "hay fever", a commonly used term in the Thai language to describe this condition.

### STATISTICAL ANALYSIS

The data analysis was conducted utilizing STATA software, focusing on determining the prevalence of the three allergic diseases within the two distinct age groups. To explore the relationship between age, gender, and allergic disorders, a 2x2 contingency table was employed, with Chi-square analysis and Yates' correction applied to assess correlations. The prevalence estimates of current asthma or wheezing, rhinitis, and eczema were calculated based on questionnaire responses confirming the presence of symptoms within the preceding 12 months, in accordance with the criteria established by the ISAAC Steering Committee.<sup>19</sup> The prevalences were presented in terms of percentage (%) together with 95% confidence interval (CI).

## RESULTS

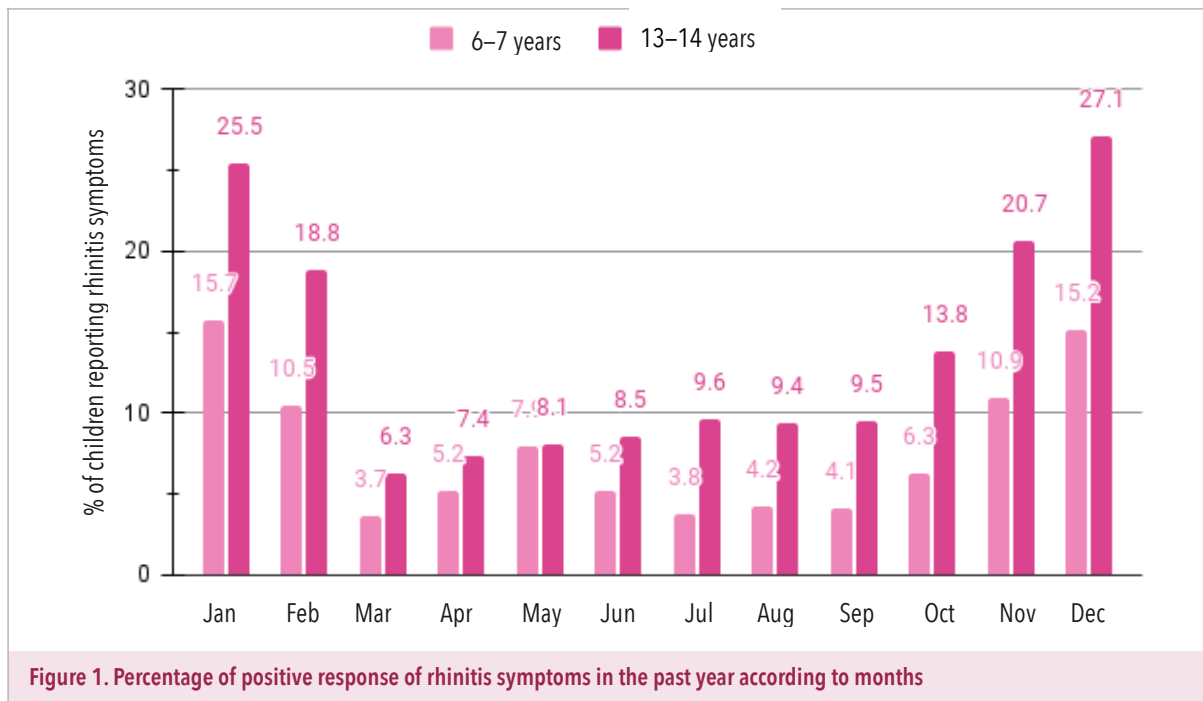
In this study, a total of 2,369 students aged 6-7 years and 3,173 students aged 13-14 years were included. The distribution of gender in 6-7 year and 13-14 year age groups displayed females vs. males were 54.8% vs 45.2% and 48.5% vs 51.5% respectively. For the younger age group, it showed that the recent (12-month period) prevalence of

asthma was 8.71% (95% CI; 7.53 to 9.88), that of rhinitis was 28.93% (95% CI; 27.04 to 30.83), and that of eczema was 14.53% (95% CI; 13.06 to 16.00). For the older age group, we found that the recent prevalence of asthma was 12.26% (95% CI; 11.10 to 13.43), that of rhinitis was 36.59% (95% CI; 34.89 to 38.29), and that of eczema was 8.04% (95% CI; 7.07 to 9.00).

In terms of life time (ever) prevalence of the three allergic conditions, in the younger age group, it showed that the life time prevalence of asthma was 14.32% (95% CI; 12.86 to 15.78), that of rhinitis was 34.11% (95% CI; 32.14 to 36.08), and that of eczema was 15.57% (95% CI; 14.06 to 17.08). For the older age group, we found that the life time prevalence of asthma was 19.16% (95% CI; 17.77 to 20.56), that of rhinitis was 44.88% (95% CI; 43.13 to 46.62), and that of eczema was 10.66% (95% CI; 9.57 to 11.76).

The results derived from the video-based questionnaires shown in Table 2. Revealed that among children aged 13-14 years, there was a lower positive response rate for wheezing at rest, exercise-induced wheezing, night wheezing, night cough, and severe wheezing within the past 12 months when compared to the responses obtained from the written questionnaires (3.4%, 5.5%, 1.1%, 11.2%, 1.4%, respectively)

Positive responses to questions regarding sex shown in Table 3. Among children aged 6-7 years, an analysis of the association between



gender and asthma-related symptoms revealed that males exhibited a significantly higher prevalence of wheezing within the preceding 12 months and a significantly greater prevalence of asthma-ever, in comparison to females (10.8% vs. 7.1%,  $P=0.002$ ; 13.9% vs. 7.0%,  $P<0.001$ ). For the 13-14 year old respondents, males displayed a significantly higher prevalence of asthma-ever than females (14.0% vs. 9.3%,  $P<0.001$ ). However, no statistically significant difference was observed between genders concerning wheezing within the past 12 months (12.8% vs. 11.7%,  $P=0.35$ ).

Moreover, children in the 6-7-year and 13-14-year age groups, who were diagnosed with rhinoconjunctivitis, had a significantly higher prevalence of current wheezing than children without rhinoconjunctivitis within the same age range (37.9% vs. 6.5%,  $P<0.001$ ; and 30.1% vs. 9.5%,  $P<0.001$ ; respectively).

In the Figure 1 illustrates that both age groups exhibited a higher incidence of rhinitis symptoms during the rainy and winter seasons.

Notably, in January, 15.7% of the younger age group reported experiencing these symptoms significantly, while in December, 27.1% of the older age group reported the same.

## DISCUSSION

This research represents the initial epidemiological investigation of allergic diseases among children in Phitsanulok, a region situated in the lower northern area of Thailand. The survey was conducted six years subsequent to the ISAAC phase III study, which encompassed the global pediatric population, including Bangkok and Chiang Mai in Thailand, in 2001. Scientists from the International Study of Asthma and Allergies in Childhood (ISAAC) 1991-2012 and the International Union Against Tuberculosis and Lung Disease (The Union) later established the Global Asthma Network (GAN) in 2012. GAN phase I builds on the ISAAC findings by collecting further information.<sup>9</sup> Following ISAAC phase III, a GAN phase I survey of the prevalence



and severity of allergic diseases was conducted in Bangkok in 2017.<sup>9</sup> Our study revealed that the prevalence of current wheeze among children in Phitsanulok was lower than that observed in Bangkok, but higher than the prevalence reported in Chiang Mai during ISAAC phase III.<sup>7</sup> The current wheezing in this study in both age categories was still lower than those in the GAN phase I trial in Bangkok ten years later.

The discrepancies in the prevalence of wheezing derived from both the written and video questionnaires in our study can be attributed to the different perceptions and linguistic differences across different centers and regions. As a study on agreement between written and video questionnaire from 40 countries for comparing asthma symptoms in ISAAC phase I demonstrated a wide variation for agreement within regions, in which centers in Southeast Asia showed the most variation.<sup>20</sup>

The higher prevalence of rhinitis during the rainy and winter seasons in our study may be related to the elevated humidity during rainy season and the increased incidence of viral respiratory tract infection in both seasons in Thailand. In our pediatric population, the occurrence of allergies was primarily attributed to house dust mites, which thrive in highly humid environments. In addition, viral respiratory tract infection may worsen allergic rhinitis symptoms during colder seasons. The prevalence of current rhinitis and rhinoconjunctivitis in Phitsanulok among children of all age groups was found to be lower than that observed in Bangkok, as evidenced by the results of both ISAAC phase III and GAN phase I surveys. In Phitsanulok, children aged 6–7 had a higher prevalence of current rhinitis and rhinoconjunctivitis, whereas children aged 13–14 years old exhibit fewer nasal and eye symptoms in comparison to their peers of the same age in Chiang Mai. Variation in genetic predisposition to atopy and environmental factors, particularly being

in the agricultural sector and air pollution, may account for the varying prevalence.

There were many studies demonstrating that traditional farming characteristics associated with a higher microbial load leading to a lower prevalence of allergic diseases,<sup>21</sup> supporting the hygiene hypothesis and later the microbiota hypothesis.<sup>21</sup> Phitsanulok and Chiang Mai are semi-agricultural cities where there are more rural and agricultural areas than Bangkok, a capital city of commercial significance. Another possible explanation is air pollutants that are known to impact on respiratory health, including nitric oxide, nitrogen oxide, carbon monoxide, carbon dioxide, sulfur dioxide, formaldehyde, biological, and particulate matter.<sup>1</sup> These pollutants are generated through industrial activities, vehicular transportation, and combustion processes.

Research has indicated that the risk of asthma is higher in individuals who are exposed to outdoor pollutants, particularly those residing in close proximity to major roads.<sup>13,14</sup> Furthermore, it has been estimated that up to four million new cases of pediatric asthma may be attributed to exposure to traffic-related air pollution.<sup>12</sup> Prenatal NO<sub>2</sub>, SO<sub>2</sub>, and PM<sub>10</sub> exposures are associated with an increased risk of asthma in childhood.<sup>22</sup> Bangkok is a commercially significant capital city which is more heavily polluted than Phitsanulok. These factors may account for higher prevalence of allergic diseases in Bangkok; but they do not explain why Phitsanulok had a higher prevalence of current wheezing than Chiang Mai. For many years Chiang Mai has been listed as one of the most polluted cities in the world due to its extremely high PM 2.5 levels.<sup>11</sup> Children aged 13 to 14 years in Chiang Mai may have a higher prevalence of rhinitis and rhinoconjunctivitis than those in Phitsanulok due to the city's expanding air pollution.

The ISAAC Committee has demonstrated that nasal symptoms accompanied by ocular

allergic symptoms have a higher predictive value for detecting atopy than nasal symptoms alone.<sup>23</sup> Since most childhood asthma is predominantly associated with atopy, this may explain why our children with rhinoconjunctivitis had 3.2–5.8 fold increase in asthma compared to children without rhinoconjunctivitis. This result is also consistent with other studies which confirms the concept of “the united airway” that asthma and allergic rhinitis frequently coexist.<sup>24,25</sup>

In relation to eczema, our findings indicate that younger children exhibited a greater prevalence of eczema symptoms than older children, which was consistent with the results of the Bangkok and Chiang Mai studies. This result is not surprising since atopic dermatitis usually occurs in younger children than older children. On the other hand, flexural rash, which is a typical symptom of atopic dermatitis, had a lower prevalence among children in Phitsanulok than in Bangkok and Chiang Mai. The higher prevalence of eczema in Chiang Mai compared to Phitsanulok may be attributed to the colder climate, which has been found to exacerbate atopic eczema by inducing dryness of the skin. The key strengths of our study included utilizing standardized written core questionnaires of ISAAC questionnaires with well-established standardized ISAAC protocol, and high response rate. This basic epidemiological data can be comparable internationally to other ISAAC surveys involving over millions of children and more than 50 countries worldwide. Furthermore, this knowledge can still serve as a valuable reference for future research and contribute to the

improvement of medical care. On the other hand, the limitation of our study could be selection bias in that sampling school children were mostly living in the city and information bias such as recall bias due to measuring through questionnaires relying on memory. Moreover, this survey was conducted over 10 years ago. Nonetheless, the trend of allergic diseases prevalence in Bangkok over the last 16 years has not changed as evidenced by the ISAAC phase III in 2001 and GAN phase I in 2018.<sup>8,9</sup>

In summary, the prevalence of asthma, allergic rhinitis and atopic dermatitis among children in both age groups living in Phitsanulok was lower than that in Bangkok. When compared to Chiang Mai, which is located in northern Thailand, children in Phitsanulok had a higher prevalence of asthma but a lower prevalence of eczema. The proliferation of house dust mites in environments with elevated humidity, combined with the potential worsening of allergic rhinitis symptoms during colder seasons as a result of viral respiratory tract infections, may contribute to the increased prevalence of rhinitis symptoms among children during rainy and winter seasons.

The incidence of rhinitis and rhinoconjunctivitis was higher among younger children in Phitsanulok than in Chiang Mai, while older children in Phitsanulok had a lower percentage. The difference in the prevalence of these allergic diseases among different regions in Thailand may be attributed to genetic predisposition, environmental factors, especially air pollution, and the microbiota hypothesis.

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